GRIGORE T. POPA UNIVERSITY OF
MEDICINE AND PHARMACY IASI

- THE VOICE OF HEARING -

- HABILITATION THESIS -

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Abreviations

AHL - asymmetrical hearing loss
AIQ - anterior and inferior quadrant
AN - acoustic neuroma
ASQ - anterior and superior quadrant
ATLS - Advanced Trauma Life Support
CCA - common carotid artery
CI - confidence interval
CR - chance report
CSF - cerebrospinal fluid
CT - computed tomography
ECA - external carotid artery,
ENT - Ear, Nose and Throat
FESS - functional endoscopic sinus surgery
FFE - fast field echo
ICA - internal carotid artery
MRI - magnetic resonance imaging
NF2 - as neurofibromatosis 2
NLAO - angle of the mouth
NLIO - infraorbital region
NLJ - jugal region
NLLS - the upper lip
OME- otitis media with effusion
PR - relative risk
PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSQ - posterior and superior quadrant
PTA - pure-tone audiometric
RR - risk ratio
SAT - subannular insertion of the ventilation tubes
SD - standard deviation
T1W - axial, T1-weighted
T1W–FFE axial with contrast agent.
T2W - T2-weighted
TSE - turbo spin echo
VS- as vestibular schwannoma
VT - ventilation tube

Abstract of the thesis

Any academic career most brings together the profession of scholar mentor, researcher and medical practitioner. It is situated on the top of the educational system and its success is based on perseverance and self-indulgence, responsiveness and openness to new ideas and concepts. Characteristics such as flexibility, dynamism and critical reflection are also required. Entire assessment and implementation of professional goals and standards in academic careers is essential and mandatory in order to ensure the continuous increase in quality of the educational process and of the scientific and surgical results.

Nowadays, state of the art academic careers meet standards and highlights awareness of the need for continued training, the integration of modern methods into teaching and surgical practice. Heretofore these criteria are met, they lead to an increase of the educational process quality and its outcomes, the improvement of scientific performance and the success in the surgical career.

The academic instructor career has and must have a significant impact upon the entire academic community. It has to harmoniously combine a series of skills and qualities, such as: solid and constantly updated scientific acquaintance, availability and pleasure to communicate and teamwork, along with the desire to be part of a team. Sum of these adds the ability to create and coordinate functional structures, based on the ability to identify and motivate human resources through their own standard.

This thesis of habilitation in conducting PhD studies summarizes my entire professional, academic and scientific activity after the completion of doctoral research. It is structured according to the criteria recommended and approved by CNATDCU, in three major sections.

Thus, the present paper highlights both the overall picture and the detailed overview of the main concerns and objectives of my academic career so far. Considering on personal experience in areas of interest, I will detail the management of the ongoing research projects, along with the studies and implementation opportunities that they open.

Among the cardinal concerns I have since the beginning of my academic career is to address new areas of research with direct implications in surgical practice and, particularly, for the benefit of patients. It is now unfolded in a series of future projects which are describe in the corresponding section of the thesis. Also it accommodates detailed descriptions of the future research projects that I want to follow in the coming years.

Within this manuscript I summarize my research, didactic and medical work carried out since 2004, year which corresponds to the finalization and presentation of my PhD thesis.

The structure of the paper is divided into three main sections: SECTION A detailing my academic, surgical and research work, SECTION B, which maps on the main results of my research activity, materialized by publication of ISI rated articles with impact factor as a point of continuation of the research started and SECTION C which contains future research projects.

SECTION B presents the results of my professional, scientific and academic work in four chapters and summarizes the main personal contributions in the field of ENT surgery and especially the oncologic one. These are the two major areas of ENT surgery to which I have devoted almost my entire career.

Exposing personal motivation in choosing research topics and the way ahead and implementing them reveals both the capacity to initiate and develop personal research projects, as well as my team working abilities. The ultimate goal of the efforts and work carried out by me and the teams I co-ordinate is the patient's benefit in everything that means comfort, social reinsertion, distinguished postoperative aesthetic results and long survival.

The performance achieved in the surgical career is based on the opportunities opened by the continuous medical training courses that I have followed in the country and abroad.

The scientific research I have had so far has materialized in book publications, articles, and communications at congresses. All this hides behind the hard work teamwork and passion for what we do. The dissemination of the results of the scientific research would not have been possible without the help of the medical school trainers who coordinated my medical and academic career and from whom I learned this specialty in the field of general surgery. I am convinced that the academic level I have achieved ensures a great international visibility and, directly, the prestige of the university I represent.

The theme chosen for the doctoral study - "Optimizing methods of diagnosis and treatment of malignant rhinosinusal tumors" - and its manners and opportunities for continuity have opened the way to research in the field of Head and neck surgical oncology. In the doctoral study I learned and perfected my research skills so necessary for my future career. I have been familiar with the early, clinical and radiological diagnostic techniques of these pathologies.

My research in this direction focused on highlighting the modern means of diagnosis and treatment in rhino-sinus tumours. The development of study models of the etiopathogenesis and evolutionary patterns of these pathologies, management and research in training operative teams, phenomenographic approach of surgical patient are current and some of the main areas of interest in my career.

The mathematical and physical formulas that characterize the theory related to the management of the outpatient in the day surgery reveal new perspectives in this field of perioperative assessment of the surgical patients in both elective and emergency interventions.

In the second part - SECTION C - I grouped my scientific and professional achievements in order to certificate my future research projects which are detailed in this section.

The perioperative assessment of the surgical patients in both elective and emergency interventions, research in training operative teams, one day surgery and phenomenographic approach of surgical patient are motivated by the passion we have always had for surgery, and especially then gastrointestinal one. In order to be able to perform in any field, it is necessary to put some feeling into what you do and to constantly update your knowledge in the field.

These branches and directions of general surgery have also benefited from the current advances in related fields: radiology, computing, oncology and bioengineering.

Modern trends are centered on minimal invasive skull base surgery, adequate training on the necessary equipment, minimizing the operation time and a vast experience in the field. The results of current surgical practice are mirrored in materials published in ISI-rated journals with impact factor.

I emphasize this section's material proves my interest in researching new methods of early diagnosis and staging of these conditions. The results of my personal research on the patient management specificities from the main interest domains are also represented. Finally, this section puts into perspective my personal achievements in the niche areas represented by the applicability of the outcomes from the management research, mathematical and physical theories and formulas which fit my areas of interest.

The final chapter of the thesis - entitled References - represents the scientific support of my research activity up to date and the basis for my future research plans and projects. This section contains all the bibliographic references that I have built up my current knowledge in the fields of interest and the support of their permanent updating.

Rezumatul tezei

Orice carieră academică reunește cel mai mult profesia de mentor savant, cercetător și medic. Este situat în vârful sistemului educațional, iar succesul său se bazează pe perseverență și auto-indulgență, receptivitate și deschidere către idei și concepte noi. De asemenea, sunt necesare caracteristici precum flexibilitatea, dinamismul și reflexia critică. Evaluarea și implementarea integrală a obiectivelor și standardelor profesionale în carierele academice este esențială și obligatorie pentru a asigura creșterea continuă a calității procesului de învățământ și a rezultatelor științifice și chirurgicale.

În zilele noastre, carierele academice de ultimă generație îndeplinesc standardele și evidențiază conștientizarea necesității de formare continuă, integrarea metodelor moderne în predare și practica chirurgicală. Până acum aceste criterii sunt îndeplinite, duc la creșterea calității procesului educațional și a rezultatelor acestuia, la îmbunătățirea performanței științifice și la succesul în cariera chirurgicală.

Cariera de instructor academic are și trebuie să aibă un impact semnificativ asupra întregii comunități academice. Trebuie să îmbine armonios o serie de abilități și calități, precum: cunoștințe științifice solide și actualizate constant, disponibilitate și plăcere de a comunica și lucru în echipă, alături de dorința de a face parte dintr-o echipă. La suma acestora se adaugă capacitatea de a crea și coordona structuri funcționale, bazate pe capacitatea de a identifica și motiva resursele umane prin propriul standard.

Această teză de abilitare în efectuarea studiilor de doctorat rezumă întreaga mea activitate profesională, academică și științifică după finalizarea cercetării doctorale. Este structurat după criteriile recomandate și aprobate de CNATDCU, în trei mari secțiuni.

Astfel, prezenta lucrare evidențiază atât imaginea de ansamblu, cât și imaginea de ansamblu detaliată a principalelor preocupări și obiective ale carierei mele academice de până acum. Având în vedere experiența personală în domenii de interes, voi detalia managementul proiectelor de cercetare în derulare, împreună cu studiile și oportunitățile de implementare pe care acestea le deschid.

Printre preocupările cardinale pe care le am încă de la începutul carierei mele academice este să abordez noi domenii de cercetare cu implicații directe în practica chirurgicală și, în special, în beneficiul pacienților. Acesta este acum desfășurat într-o serie de proiecte viitoare care sunt descrise în secțiunea corespunzătoare a tezei. De asemenea, găzduiește descrieri detaliate ale viitoarelor proiecte de cercetare pe care vreau să le urmăresc în următorii ani.

În cadrul acestui manuscris rezumă munca mea de cercetare, didactică și medicală desfășurată începând cu anul 2004, an care corespunde finalizării și prezentării tezei mele de doctorat.

Structura lucrării este împărțită în trei secțiuni principale: SECȚIUNEA A care detaliază activitatea mea academică, chirurgicală și de cercetare, SECȚIUNEA B, care prezintă principalele rezultate ale activității mele de cercetare, concretizate prin publicarea unor articole cotate ISI cu factor de impact ca punct de continuare a cercetării începute și SECȚIUNEA C care conține planurile pentru proiecte viitoare.

SECȚIUNEA B prezintă rezultatele muncii mele profesionale, științifice și academice în patru capitole și rezumă principalele contribuții personale în domeniul chirurgiei ORL și în special al celui oncologic. Acestea sunt cele două domenii majore ale chirurgiei ORL cărora le-am dedicat aproape întreaga mea carieră. Expunerea motivației personale în alegerea temelor de cercetare și a modului de urmat și implementarea acestora dezvăluie atât capacitatea de a inița și dezvolta

proiecte personale de cercetare, cât și abilitățile mele de lucru în echipă. Scopul final al eforturilor și muncii depuse de mine și echipele pe care le coordonez este beneficiul pacientului în tot ceea ce înseamnă confort, reinserție socială, rezultate estetice postoperatorii distinse și supraviețuire îndelungată. Performanța realizată în cariera chirurgicală se bazează pe oportunitățile deschise de cursurile de pregătire medicală continuă pe care le-am urmat în țară și în străinătate.

Cercetările științifice pe care le-am avut până acum s-au concretizat în publicații de carte, articole și comunicări la congrese. Toate acestea se ascund în spatele muncii asidue, a muncii în echipă și a pasiunii pentru ceea ce facem. Diseminarea rezultatelor cercetării științifice nu ar fi fost posibilă fără ajutorul formatorilor școlii de medicină care mi-au coordonat cariera medicală și academică și de la care am învățat această specialitate în domeniul chirurgiei generale. Sunt convins că nivelul academic pe care l-am atins asigură o mare vizibilitate internațională și, direct, prestigiul universității pe care o reprezint.

Tema aleasă pentru studiul de doctorat – „Optimizarea metodelor de diagnostic și tratament al tumorilor maligne rinosinusale" – și manierele și oportunitățile sale de continuitate au deschis calea cercetării în domeniul oncologiei chirurgicale capului și gâtului. În cadrul studiului de doctorat mi-am învățat și perfecționat abilitățile de cercetare atât de necesare carierei mele viitoare. Am fost familiarizat cu tehnicile de diagnostic precoce, clinice și radiologice ale acestor patologii.

Cercetarea mea în această direcție s-a concentrat pe evidențierea mijloacelor moderne de diagnostic și tratament în tumorile rino-sinusale. Dezvoltarea modelelor de studiu a etiopatogeniei și modelelor evolutive ale acestor patologii, managementul și cercetarea în formarea echipelor operative, abordarea fenomenografică a pacientului chirurgical sunt actuale și unele dintre principalele domenii de interes în cariera mea. Formulele matematice și fizice care caracterizează teoria legată de managementul ambulatoriului în chirurgia de zi dezvăluie noi perspective în acest domeniu al evaluării perioperatorii a pacienților operați atât în intervenții elective, cât și de urgență.

În partea a doua - SECȚIUNEA C - am grupat realizările mele științifice și profesionale pentru a-mi certifica viitoarele proiecte de cercetare care sunt detaliate în această secțiune.

Evaluarea perioperatorie a pacienților operați atât în intervenții elective, cât și în cele de urgență, cercetarea în formarea echipelor operative, intervenția chirurgicală de o zi și abordarea fenomenografică a pacientului chirurgical sunt motivate de pasiunea pe care am avut-o întotdeauna pentru operație, și mai ales pentru cea gastrointestinală. Pentru a putea performa în orice domeniu, este necesar să pui ceva sentiment în ceea ce faci și să-ți actualizezi constant cunoștințele în domeniu.

Aceste ramuri și direcții de chirurgie generală au beneficiat și de progresele actuale în domenii conexe: radiologie, informatică, oncologie și bioinginerie. Tendințele moderne sunt centrate pe operația minim invazivă a bazei craniului, pregătirea adecvată cu echipamentul necesar, minimizarea timpului de operație și o vastă experiență în domeniu. Rezultatele practicii chirurgicale curente sunt reflectate în materiale publicate în reviste clasificate ISI cu factor de impact. Subliniez că materialul acestei secțiuni dovedește interesul meu pentru cercetarea unor noi metode de diagnosticare precoce și stadializare a acestor afecțiuni. Sunt reprezentate și rezultatele cercetării mele personale privind specificul managementului pacienților din principalele domenii de interes. În final, această secțiune pune în perspectivă realizările mele personale în domeniile de nișă reprezentate de aplicabilitatea rezultatelor cercetării în management, teorii și formule matematice și fizice care se potrivesc domeniilor mele de interes.

Capitolul final al tezei - intitulat Bibliografie - reprezintă suportul științific al activității mele de cercetare la zi și baza planurilor și proiectelor mele de cercetare viitoare. Această secțiune conține toate referințele bibliografice pe care le-am acumulat cunoștințele actuale în domeniile de interes și sprijinul actualizării permanente a acestora.

SECTION A - OVERVIEW OF THE ACADEMIC, SCIENTIFIC AND PROFESSIONAL ACHIEVEMENTS

Since the evolution of my university career, both a professional side and a didactic and research side are present, being the comprehensive and extensive result of personal life experiences. This makes it possible for efforts made to achieve top academic and medical performance and recognition to be enhanced by results in surgical practice.

Of my entire surgical experience of over 19 years, 18 have been complementary to my academic career. Thus, I can state that the results obtained throughout my academic career are related and consistent with the complexity of the requirements and demands of the medical activity and, not least, of the research activity. During this whole period I gained a rich experience in the management of the student series, the activity with the residents but also regarding my main goal - surgery of rhino-sinus tumors.

The research perspective of this field stimulated me throughout my academic career and focused on medical and surgical activity with the aim of ensuring the highest possible quality of the surgical intervention time. This theme has a major socio-economic impact. The research directions that we have carried out up to this moment are mostly aimed at reducing operative time, the incidence of immediate and remote post-interventional complications, as well as obtaining the best possible aesthetic result.

In this sense, I performed surgical interventions, as an operator or assistant, both in the scope of the main field of interest and on the other levels of ENT surgery, both in elective and emergency interventions. The accumulated experience in the field of oncological ENT surgery led me to research this field in detail, through the lens of the preoperative assessment of patients as well as their management in the immediate and distant post-interventional period.

The main future goals of my professional career are related to the continuation of research in that great direction mentioned; in the short and medium term, I consider it a priority to establish new research opportunities and topics, such as minimally invasive skull base surgery and the training of operative teams, one-day surgery.

At the same time, the marked efforts made by me and the medical team I coordinate are focused on the complex study of rhino-sinus, laryngeal and pharyngeal tumor pathology, through the lens of modern early diagnosis techniques, such as endoscopic ultrasound. We anticipate that the results of this study will materialize through reference publications and would be an extremely valuable working tool in assessing the socio-economic, demographic impact and in creating a management protocol, so necessary for these patients.

In parallel and in close connection with rhino-sinus oncology surgery, I developed my interest and expertise in the subfield of minimally invasive surgery. I intend that all these approaches and efforts have the expected impact and manage to co-interest as many colleagues as possible, with the aim of coagulation of elite, multidisciplinary medical centers and teams that will also be medical school trainers in this direction, both in the realization of the medical act as well

as in research. Without such collaborations and the related human resource, our research in the mentioned areas would not be possible.

Hard work and passion for what I do have been and are the foundation of my academic career, along with the awareness of the imperative need for research and the opportunities offered by training internships carried out in the country and abroad. This first step towards exchanges of experience and research with prestigious centers outside, in the co-domains of interest is essential to keep us in touch with current trends and the latest discoveries.

I consider it a great opportunity given to me by the possibility that I have to correlate the three big sides of my career - teaching, surgery and research - around the main theme of interest - gastrointestinal surgery - which unites all the others.

√ **Professional progress**

I started my university career in 2002 as an associate assistant at the "Grigore T. Popa" University in Iasi, Faculty of Medicine and Pharmacy. My work as a primary surgeon in the ENT Surgery Clinic of the "Sf. Spiridon" from Iasi represents a significant part of my activity to date. Medical practice for over 19 years, together with an academic experience of over 18 years, gives me the experience that I have mirrored in the activity of guiding future doctors, residents as well as in the scientific research side. I had the opportunity to train academically and, implicitly professionally, under the coordination of elite personalities and in nationally and internationally recognized centers.

To all this must be added the participation in postgraduate training courses in the co-domains of interest, materialized by obtaining professional certificates that allow me to practice maneuvers and techniques that are so necessary and useful in my current practical and research activity:

- Competence in rhinosinusal endoscopy
- Competence in Laser ENT

After 19 years of medical practice and the academical experience, I can say that the results of my career are integrated into the complexity of the requirements and demands of the medical field.

The activity with the residents has materialized in guiding and encouraging them in the practice of surgical techniques and in conducting scientific works for publishing / presenting at conferences and encouraging them by co-opting in the team of authors.

During my medical activity I was member in specialty exam comities, I developed colaborations on both medical and scientifical fields with other romanian ENT centers: Bucuresti, Cluj, Timișoara and Craiova.

√ **Academic activity and career overview**

My academic activity has materialized during these years in the possibility of qualitative and quantitative appreciation of the importance of the role of the teaching staff, as an agent of change, who promotes understanding and tolerance. That is why the responsibility placed on the shoulders of teachers is enormous, because they are among those who participate in the formation of the characters of the new generation and are models for students. Collaboration with students, concretized by case presentations, co-opting students in medical practice. I teached student from General Medicine Faculty, but aso from faculty of general medical assistants. I held optional courses with the students and I guided the students in their undergraduate theses. The main themes

of my career research have also been found in this activity, guiding and encouraging young colleagues to deepen them.

In the current conditions, in which the contemporary world evolves at such an alert pace, the need to update and permanently improve the level of knowledge, as well as the teaching techniques used, is obvious. Equally, however, the society based on knowledge implies the generation of knowledge, especially through scientific research, their transmission through education and professional training, their dissemination using the means of information and communication technology, the valorization of knowledge through technological innovation.

Also, the milestones identified as a result of needs analysis and student opinion barometers showed the need to focus university activities mainly on the student through the use of active-participative strategies, the application of academic group management and the diversification of evaluation techniques with a focus on student performance and on the skills formed. This approach assumes a well-established route, characterized by defining some objectives of the didactic activity and finding ways to achieve them through various activities, which means, in short, student-centered education.

These things made me pursue the consolidation of the education process and continuous qualitative improvement in accordance with the requirements of the national education system, but also international requirements.

√ **Research projects and scientific activities**

Through the research activity that I have carried out throughout my career, I have followed the continuation and completion of research projects undertaken in groups and individually and the involvement in new ones.

A very important aspect is the valorization of research results through the publication of studies and articles in ISI-quoted journals with an important impact factor. In order to achieve this objective, it is necessary to develop research through interdisciplinary initiatives and expand collaboration in order to develop research projects.

I have always considered it essential to attract an increasing number of students, master's students and even resident doctors and young specialists in scientific research activity.
The final goal of the entire research activity is to increase visibility on a national and international level.

Starting from the premise that academic cooperation is an essential component of the research strategy, the development and diversification of collaborations with teaching staff/researchers from other university centers in the country and abroad were and are a continuous concern of mine. Constant involvement in research and didactic activity, through scientific projects, student and resident guidance activities, constitutes a long-term guarantee of academic and surgical skills and professionalism.

The fact that I coordinated several medical teams during the years of experience in surgery and collaborated with other reference centers in the field in the country and abroad made my training as a researcher possible and provided me with a vast experience in the field.

The novelty with which my research activity comes to the fore is given by its direct and implicit clinical applicability and the adaptability that I and my team have shown in approaching

new surgical techniques and principles. We have thus managed to orient and restructure each study that we have carried out according to the feedback received in real time from the subjects, information that we have interpreted and analysed.

The careful monitoring of patients, both during the hospitalization period and at a distance, made it possible to obtain a valuable database, with a strong potential for research in future studies. Personally, I consider winning and implementing Grant-type study projects, national and international, to be a mandatory and inherent added value of my research activity.

Until now, we have carried out retrospective and prospective clinical studies, on statistically significant groups of patients, in the field of gastrointestinal, elective and emergency surgery.
The results of these studies were disseminated through the publication of articles in ISI rated journals, with an impact factor and communications within congresses and conferences. The main beneficiaries of my research activity and the projects carried out in this regard are and must be the patients.

Considering my personal, surgical and scientific experience, I intend to approach research areas related to my previous work. Thus, I consider it a great opportunity to study the modern management and control techniques of the ENT surgical patient, at a distance from the operative moment. Within these fields, I conducted cohort and multicenter studies on large groups of patients, considerations due to which I divided my work into four main fields: firstly, the field of oncological orl surgery, focused on rhino-sinus and laryngeal cancer surgery, one of the second field, that of the surgical risk of the patient with various comorbidities, the third field referring to the multifactorial context of the oncological patient and the fourth field related to the theme of diseases of the stomatognathic system with implications in the surgical prognosis.

The desire to deepen research in the field of minimally invasive skull base surgery and day surgery will be put into practice by applying for Grant-type research projects on this topic. I wish to obtain funding in these directions through national and international projects.

√ **Synthesis of the PhD thesis**

Achieving these results signifies the recognition of my experience and the team I lead in this field. My research activity started with my PhD thesis. The doctoral study that I completed was titled " Optimizarea metodelor de diagnostic si tratament tumorile maligne rinosinusale" under the coordination of Prof. Dr. Dinu Cezar. The anticipated impact of implementing new research directions on academic careers and personal international visibility is extremely important. It offers the possibility to obtain funding for its proposed objectives and opens significant opportunities to future projects, as well as the dissemination of the obtained results.

The immediate expected impact of this future research is primarily a human one, to reduce mortality and the rate of post-interventional complications following elective or emergency surgery. At the same time, the results obtained from the proposed studies are directly applicable in my academic activity, to stimulate medical students who want to pursue a career in the field of endocrine surgery.

In order to achieve the expected results, it is necessary to follow the subjects in the study groups for a period of at least 1 year and to adjust their management protocol.

SECTION B - SCIENTIFIC ACHIEVEMENTS FROM THE POSTDOCTORAL PERIOD

Chapter 1:PERSONALIZED ENT - NEW SURGICAL AND MORFOFUNCTIONAL APROACHES OF PARANASAL SINUSES

1.1. State of the arts

Entire history of medicine is the history of man himself. Since prehistoric man was prone to regard disease as an evil spirit or the work of such a spirit. It is not possible to know how the man of the Neolithic period (10,000 to 4000 BC) faced different diseases. Thus, by studying discovered bones, it was found that he knew how to immobilize fractured bones.

In any primitive societies priest, magician, and physician were one and the same, and the medicine was practiced in a way we call today folk medicine.' Scientific medicine developed from this folk and magic medicine (Renfrew 1973).

The early days of medicine as a scientific system started as a Mediterranean phenomenon, whereas the development of a rational, scientific concept of disease not as a demon or something inside the body, but as altered physiology, is essentially modern. This turn of mind is believed to date from the middle of the 16th century with Claude Bernard.

ENT followed closely the path of medicine. The oldest traces of information regarding ear, nose, and throat diseases are to be found in folk medicine, which is probably the oldest form of medical practice and was perpetuated by speech rather than by writing. The history of ENT can be classified into the following periods: the time of legends and folk medicine; the prehistoric age (before 4000 BC); the Egyptian, Minoan, and Chinese periods; the Greek and Hindu periods; the Roman, Byzantine, and Arabic periods; the Middle Ages and the Renaissance periods; and the modern period (19th and 20th centuries) (Stevenson et al., 1949).

A great number of fascinating references with regard to ear, nose, and throat diseases are found among different people. Folklore remedies which have been used since ancient times are in use even today. A huge ammount of vegetables, fruits, juices of plants and snails, and the urine of bulls and humans have been used for treating numerous disorders of the head and neck area. In northern Greece in remote villages, acute otitis media is still treated by dropping human urine into the ear canal, and in western Bohemia nasal catarrh is treated by having the patient inhale a child's warm urine.

The treatment of the diseases of the throat, folklore remedies include the use of the juice of crabs, the ashes of a burnt swallow, cabbage, nettles, garlic, sorrel, and injection of butter boiled with honey. In Morocco on the 25th of March rain water is collected to be used for curing diseases of the ear and nose. For treating epistaxis several remedies have been also used among different people, including cold water and vinegar or salt applied to the forehead of hands and feet (Lupton TA 1601), various prayers, the use of the patient's own blood to write the words "consummatum

est" on his forehead,3 frying one's own blood and applying it a snuff (Moncrief J. 1716), and various plant and animal products.

The perception of the ear as an organ of reproduction is found in Indian, Mongolian, and Persian legends and also in the writings of Rabelais and Moliere.' The size and shape of the ear was supposed to determine the character of the individuals Small ears denoted high mental ability and large ears indicated dullness. Also, large noses were connected with the sexual organs and there was thought to be a relationship between the size of the nose and the size of the penis (Weir N. 1990).

In Eb (854~) it is written that the deaf man cannot open his mouth, and in Eb (418) nasal cattarh is mentioned. For its treatment, the milk of a woman who has a male child is mixed with an odiferous glue and this mixture is then inserted into the nose for the treatment of rhinorrhea. Surgery of the ears is also discussed and several recipes are described many times in other undeciphered languages.

Another text comes from the Ebers papyrus, with extensive sections on the ear, (Trump I-ID. 1960; Garrison HF 1921) was obtained by George Ebers at Thebes in 1872, and is dated to about 1550 BC.

One of the most valuable medical papyruses is that acquired by Edwin Smith (1722-1906) at Thebes in 1862. In Edwin Smith's papyrus (1600 BC) are written 48 cases of clinical surgery covering, among others, injuries to the head, nose, and temporal bone. For example, deafness is mentioned as related to fracture of the temporal bone. In crushing injuries of the neck, deafness and the loss of speech is mentioned. Hyperacusis also is described, which accompanies fractures of the temporal bone. In Smith's papyrus fracture of the nasal septum is presented as the cause of disfigurement and epistaxis, which is prevented by nasal packing. Besides trauma, infections are also discussed along with their treatment.

Scientists described two tablets dating from the beginning of the dynastic period, one belonging to Aha and the other to Djer.' They show a person sitting and directing a sharp instrument towards the neck of a kneeling person. Also their is a believe that this was a magical ceremony tracheotomy meant to insufflate life into the aged king (Vikentieff W. 1949-1950). The egyptian medicine also developed fields of specialization. Herodotus, in regard to the practice of medicine in Egypt, writes, "Each physician is a (specialist) in one illness and in no more . . . some are set as Ophthalmologists other as (physicians) of the middle body cavities, and other of Internal illnesses."

They seemed to understand well the anatomy of the nose and its relationship to the bases of the skull and brain. The same Herodotus describes in detail the technique for mummification practiced by the Egyptians: "As much as possible of the brain is extracted through the nostrils with an iron hook, and what the hook cannot reach is rinsed out with drugs. The drawback lays in the fact, that the nasal septum, was destroyed which resulted in a slight flattening of the nose (Sudhoff 1912).

Than, the Ptolemies supported medicine and helped its further progress. Meanwhile, the most famous Alexandrian physicians were Herophilus and Erasistratus (300 BC) who described the salivary gland and he called the hyoid bone the "parastate, " because it was situated near the nostrils. Erasistratus is believed to have combine the words "trachea" and "arteria" to distinguish

the windpipe from the arteries. It is a disaster that all the writings of those two great men and possibly of many others were lost when the library of Alexandria was burned.

On the other side, Hindu medicine showed great progress. Maybe the most famous Hindu surgeon was Susruta around the fifth century BC. It is considered that Hindu medicine was influenced by Hippocratic medicine, and even that the name "Susruta" may be a Hindu corruption of Hippocrates. Within the classic Sanskrit Atharva-veda documents of the ancient civilization of Hindus (700 BC) there is much medical information on diseases of the ear, nose, and throat.

One of the greatest achievement of Hindu otorhinolaryngologic surgery was the reconstruction of new noses by the use of flaps obtained from the cheek or the forehead. One of the best known ancient physicians was Aretaeus from Cappadocia, who lived about ALI 80 to 160. He is perhaps the one who made the earliest allusion to tracheotomy.

Almost all of the next thousand years in medicine were dominated by Galen who was born at Pergamos in Asia Minor (ca AD 131-201). He lived most of his professional life in Rome and he was the chief physician of the Emperor Marcus Aurelius who had said, "we have but one physician, Galen."

Galen noted that the auditory nerve connected the ear with the brain, that the outer ear collected the sound, and he was the first to apply the term "labyrinth" to the inner ear. Galen was perhaps one of the first to perform mastoid surgery. His surgical advise is astonishing when he states that carious bone should be removed after making an incision behind the ear. He treated deafness by diet and purgatives, an uncanny resemblance to the diuretics used today in cochlear hydrops, and for tinnitus he recommended opium of mandragora.

He described the cartilages of the larynx and the anatomy of the trachea, and he divided diseases of the nose into polypi and ozaena and classified inflammations of the throat into five groups (Wunderlich GH. 1975).

In the early years after the fall of the Roman Empire in AD 476, medical knowledge was kept alive by a group of men: the Byzantine Compilers, such as Paul of Aegina (Paulus Aegineta) who was the last of the Byzantine Compilers. Paulus Aegineta practiced at Alexandria, and died there about AD 690 (Aegineta et al., 1847). We are indebted to him for our knowledge of Antyllus, another Byzantine Compiler who recognized the value of laryngotomy in cases of airway obstruction. Paul of Aegine described the removal of tonsils by hook and scalpel, different ways to treat ear discharge, earache, and tinnitus, and he noted that congenital deafness is incurable.

Until the Renaissance little progress in medical knowledge was made, and it is fortunate that medical learning was kept alive by the Christian church and Arabic physicians. The study of human anatomy was discouraged by both the above. However there were some great Arabic physicians, such as Rhazes, Avicenna, Abulcasis, and Maimonide, who had a profound effect upon later European medicine. They embraced Greek and Roman medical science and made their own contributions. The caliph al-Mamun encouraged Syrian scholars and physicians to collect the Greek manuscripts, translate them, study them and make them known to the Caliph and his circle. x In addition, Galen's texts became available to all those Arabians who could not read Greek. Far behind Galen in popularity were the texts of the Hippocratic Corpus. Albucasis (AD 936-1013) practiced in Cordova and in his work called the Collection of Tasrif the use of tonsil guillotine is

described." Whereas Hippocratic and Galenian medical knowledge was kept alive in Byzantium and the Islamic world, the knowledge of medicine drastically declined in the medieval Western Europe (Vryonis S. 1991). Those centuries were rather sterile for otolaryngology.

In Salerno was the first organized medical school in Europe and flourished during the era of the Crusades (1096-1270). By the 13th century new schools emerged, the most famous being the school of Naples and the Universities of Montpellier and Bologna, at which human cadaver dissection was extensively practiced.

Guy de Chauliac (1300-1367), one of the well-known anatomists and surgeons of this period was the French surgeon who believed that the basis of surgery was anatomy. He was perhaps the first to use an ear speculum, to facilitate the entrance of sunlight into the external auditory meatus in an attempt to remove foreign bodies, and to treat quinsy by incision.

Mediterranean medicine originated in Egypt and Crete, it was developed in Greece and Rome, and was transmitted by the Arabians to western Europe in the Middle Ages. The Renaissance began about the end of the 14th century and reached its zenith 200 years later. Great progress was made in this period in almost all aspects of human cultural and scientific activities. Enlightened artists did not hesitate to exchange brush for scalpel to better understand the human body and to be able to better express themselves.

Leonardo da Vinci (1452-1519) was the greatest among all artists in this period whose genius made great contributions in aviation, warfare, art, and anatomy. In the ear, nose, and throat area he is noted for his description of maxillary and frontal sinuses.30 Following da Vinci came Andreas Vesalius (1514-1564). He was the first to give an accurate description of the malleus and the incus and also described the oval and round windows, the tensor tympani muscle, the auditory nerve, and the maxillary frontal and sphenoid sinuses (Cotterell A. 1979).

Another great anatomist of this period, Giovanni Philippi Ingrassia (1510-1580) described the stapes and observed that teeth could conduct sound.

The great discoveries in the anatomy of the ear continued with Bartolomeus Eustachius (1520-1574) who held the chair of anatomy at Rome (Sakelarakis J. 1965). He described the eustachian tube and he noted that the chorda tympani was a nerve.

Another name also very familiar to otolaryn-gologists is that of Gabriel Fallopius (1523-1562) who succeeded Vesalius at Padua. He names the cochlea, labyrinth, velum palati, and tympanum. He described and named the trigeminal nerve, the chorda tympani, the auditory nerve, and the fallopian aqueduct. He was also a surgeon and he is known for his method of removing nasal polyps with a wire snare. He treated aural polyps with sulphuric acid poured down a lead tube which protected the external auditory cana1 (Doro L. 1926).

During the 16th century is also the period where tracheotomy became a standard procedure. Fabricius considered tracheotomy a lifesaving procedure, although he never performed it. Antonio Musa Brasavola (1490- 1554) was actually the first to perform a laryngotomy in 1546. Others known to have performed this procedure were Sanctorius (1561-1636) and Nicolas Habitat (1550-1624), who had four successful cases. The word "tracheotomy" appeared for the first time in the Libri Chirurgiales XII by Thomas Fienus (1567-1631). Most of the practitioners of the 16th century

were adept in procedures such as uvulotomy, tonsillotomy, and the removal of nasal polyps (Hollander 1915).

Between them, one of the great physicians of the time was Thomas Willis (1621-1675), who in his book De Anima Brutorum described the wellknown symptom the "parakusis of Willis" (hearing better in a noisy environment) found in patients suffering from conductive hearing loss. He was followed by Antonio Valsalva (1665-1723) who succeeded Malpighi in the chair of anatomy at Bologna in 1697. Valsalva divided the ear into the outer, middle, and inner ear, and he applied the term "labyrinth" to the entire inner ear. He introduced the terms Scala vestibuli and Scala tympani. Also, he gave a detailed account of the muscles of the pharynx and uvula, and, 100 years before Politzer, during the course of a dissection, he found a case of ankylosis of the stapes. The maneuver named after him was used by him to expel pus from the ear in cases of otitis or to replenish air in the middle ear cavity when the eustachian tube was blocked. It was also Valsalva who applied the name "eustachian" to the pharyngotympanic tube in honor of Eustachius.

Another anatomists were Morgagni (1682- 1771, Cotugno (1736-1822), and Antonio Scarpa (1747-1832). The first one who was professor anatomy at Padua, described in detail the ventricles of the larynx, and he was the first to prove that brain abscesses might occur as a complication of otitis. Cotugno, professor in anatomy and surgery in Naples (1760), was the first to show that the labyrinth was entirely filled with fluid. Antonio Scarpa demonstrated that the configuration of the membranous labyrinth is similar to that of the bony labyrinth.

The invention of the eustachian catheter was fascinating form the point of view that, like the laryngoscope which was invented a century later, both were developed by nonmedical persons in Paris. Edme-Gilles Guyot, a postmaster at Versailles in 1724, succeeded in treating his own deafness by passing a curved tube into the mouth behind the soft palate and into the pharyngeal opening of the eustachian tube.

Arround 1649 Johannes Riolanus The Younger (1577-1657) suggested trephining the mastoid for treating tinnitus. It was not until the 18th century, however, that Jean Louis Petit (1674-1750) of Paris performed the first successful operation of the mastoid in a case of mastoid abscess. The operation fell into disrepute, however, because it was used indiscriminately with very bad results. Such an example was the Danish court physician, Baron Jahann von Berger, who died in 1791 of meningitis following a mastoid operation (Kasas 1978).

Quelmaltz was the first to discuss deformities of the nasal septum, in 1750. His believe was that the cause of obstruction was pressure put upon the nose during difficult labor, falls in infancy, continually pushing the finger into the nose in childhood, and inflammatory conditions.

Prosper M&i&e (1799-1862) reported the famous case history of a girl suffering from vertigo which led to the recognition of the disease bearing his name. Sir Charles Wheatstone (1802-1875) used the tuning fork, which was invented by John Shore in the 17th century, a sergeant trumpeter to James II, to test the hearing. Ernst Heinrich Weber (1795-1878), professor of anatomy and physiology in Leipzig, Germany, described the tuning fork test which bears his name.

Adolf Rinne (1819-1868) of Gottingen (Germany), Dagoberg Schwabach (1846-1920) of Berlin (Germany), and Bing (1891) also described tuning fork tests which now bear their names. Thomas Buchanan (1782-1853) of Hull (England) was one of the first to advise the use of artificial

light as a means of inspecting the tympanic membrane; he called the instrument used by him "Inspector Auris."

Joseph Toynbee (1815-1866) in 1860 published the textbook Diseases of the Ear which was the most advanced and detailed work of its kind. Toynbee described ankylosis of the stapes, cholosteatoma, and he practiced myringotomy and mastoid surgery. The maneuver of opening the eustachian tube while the patient swallows holding his nose is associated with Toynbee. He died at the age of 51 after trying to inhale the vapors of hydrocyanit acid and chloroform while doing the Valsalva insufflation in an effort to relieve his tinnitus.

Sir William Robert Wills Wilde (1815-1876) father of Oscar Wilde, practiced in Dublin, Ireland, and was recognized as a great otologist. He designed an aural snare and he is known for the Wilde's incision used in mastoiditis. Hermann Schwartze (1837-1900) improved the technique of mastoid surgery, and later he extended simple mastoidectomy to include removal of the posterior meatal wall and middle ear contents.

Adam Politzer (1835-1920), known as the father of modern otology, taught otology in Vienna to a score of students from Europe and all over the world. His teachers were Claude Bernard, Prosper Mbniere, Joseph Toynbee, Helmoltz, and other great names of his time.
He is best known for his contributions to the knowledge of ear anatomy, otitis media with fluid, cholosteatoma, labyrinthitis, otosclerosis, and more. He is also well known for his technique of inflation of the eustachian tube, the politzerization.

Robert Barany (1876-1936), the most eminent of Politzer's students, received the Nobel Prize for his work on the physiology and pathology of the vestibular organ. In 1915 he described the Barany noise box, the Barany rotating chair, and the caloric test of vestibular function.

Manuel Patricia Rodriquez Garcia (1805- 1906) was a professor of singing at the Paris Conservatory and later at the Royal Academy of Music in London who succeeded in observing his larynx with a dentist's mirror, where before him many others with more medical and scientific training had failed.30 Than, Theodor Billroth (1829-1892) from Vienna, performed in 1873 the first total laryngectomy for cancer, whereas the first laryngectomy in the United States was performed by Solis Cohen in 1884. One of the great laryngologists of the time was Morel Mackenzie (1837-1892) from London who is known as the father of British laryngology. He was involved in the medical management of Crown Prince Frederick who suffered from laryngeal cancer. The Crown Prince succeeded Emperor Frederick III of Germany but only reigned for 99 days before dying of cancer (Spink and Lewis 1973).

An important step in cancer surgery was the radical neck dissection. The method was first described by Crile in 1906, it was later improved by Hayes Martin in 1941, and in 1967 Bocca described the modified neck dissection.

The practice of otolaryngology in the future will be and must be different. Much emphasis will be given to the prevention and primary care, and the number of sick people going to specialists and hospitals will probably decline. A number of interventions will be done through blood vessels, where implants will administer drugs for destroying tumors. Other implanted devices will restore the function of different organs. At the same time imaging in the form of "virtual reality" will allow

the surgeon to better perform different procedures, and the same method will be also used for training and rehearsal surgery.

In laser surgery the introduction of new laser systems will allow for more precise surgery, dry and free of complications. Robotic surgery will have also its place when the surgeon wants to perform minute procedures. Genetic screening will allow improved genetic counciling and may eventually lead to gene or gene expression product replacement therapy for some inherited diseases. Molecular biology will continue playing a major role in understanding diseases and boosting progress in diagnosis and treatment.

ENT practitioners of today and tomorrow have an obligation to know the past in order to be able to appreciate the significance of the efforts of their predecessors who helped to give the specialty its present status.

This research direction has been materialized by publishing the following articles:

1. Cobzeanu BM, Baldea V, Costan VV, Cobzeanu MD, **Palade DO**, Gheorghe L, Radulescu L, Severin F, Lupascu Ursulescu C, Bandol G, Martu C, Rosu AM, Cobzeanu ML. Anatomical Variants of Internal Carotid Artery—Results from a Retrospective Study. *Medicina* 2023, 59, 1057.
2. Hînganu MV, Hînganu D, **Palade DO**, Eva I, Volovăţ SR, Cucu RP, Costan VV. Clinical and morphofunctional identity of the nasal SMAS. *Rom J Morphol Embryol* 2023, 64(2):199–206.
3. **Palade DO**, Hainarosie R, Pertea M, Anghelina F, Zaharia P, Pietroșanu C, Calu V, Ardeleanu V, Manole F. Reconstructive challenges of sinonasal tumors: A case report. *Experimental And Therapeutic Medicine* 2022, 23: 419.
4. Hainarosie R, Domuta EM, Tusaliu M, Dabija MG, Anghelina F, Radeanu D, **Palade DO**. Influence of Environmental Factors on Rhinosinusal Tumours. *REV CHIM (Bucharest)* 2019, 70(5): 1818-1821.
5. **Palade DO**, Cobzeanu BM, Zaharia P, Dabija M. 3D Reconstruction Role in Surgical Treatment of Sinonasal Tumours. *REV CHIM (Bucharest)* 2018, 69(6): 1455-1457.
6. **Palade DO**, Cobzeanu BM, Zaharia P, Dabija M. Combined Approach of the Anterior Skull Base in Sinonasal Tumours. *REV CHIM (Bucharest)* 2018, 69(5): 1191-1193.

1.2. Human anatomy variations – implications in ENT

1.2.1. Introduction

One of the most commonly variable anatomical structures in the human anatomy is that of the nasal cavities and paranasal sinuses. Recognizing these anatomical elements is crucial for a sinus surgeon due to their intricate three-dimensional architecture and wide range of anatomical variances. One of the key strategies for treating chronic rhinosinusitis and a variety of other sinus illnesses is functional endoscopic sinus surgery (FESS) (Mokhasanavisu et al., 2019). Prior to any surgical procedure, a complete evaluation needs to be conducted using computed tomography (CT) of the paranasal sinuses, which gives the anatomical "road map" to detect the existence of important structural anomalies with higher degree of clarity and precision (Al-Abri et al., 2014).

The most common indications for FESS include chronic rhinosinusitis, acute rhinosinusitis (<4 weeks), and subacute rhinosinusitis (between 4 and 12 weeks) (Homsi et al., 2020, 4. Thejas et al., 2023). The contraindications of this procedure are represented by patients who have general contraindications for general or local anesthesia; lesions or disorders extending into the palate, skin or soft tissues, or laterally into or above the orbit; lateral recesses of the frontal sinus; or advanced intracranial involvement (Homsi et al., 2020).

One of the most serious and dreaded side effects of endonasal transsphenoidal surgery is injury to the internal carotid artery (ICA), which has an estimated incidence of 0.1–0.3%, and may reach 5–9% in cases of prolonged endonasal approaches. The incidence of this complication is much lower with improved surgical experience, CT scan quality, and higher resolution endoscopy (Keast et al., 2008, Lien et al., 2010).

The internal carotid artery possesses distinct anatomical characteristics in terms of its course and plays a vital role in providing blood supply to the brain. It exhibits variable curvatures along different segments of its pathway, underscoring its unique nature. Occasionally, the ICA may feature one or two flexures near the base of the skull. Furthermore, as it traverses the carotid canal and extends along the lateral aspect of the sphenoid bone, it assumes a serpentine or 'S'-shaped configuration, resembling the shape of a cobra hood . This intricate course highlights the complexity and significance of the ICA in cerebral circulation. Determining the relationships between the intra-cavernous and supra-cavernous ICA is crucial for the neurosurgeon when considering an endoscopic endonasal transsphenoidal approach (Haussen et al., 2016).

In relation to the lateral wall of the sphenoid sinus, the internal carotid arteries can be situated at a distance from the sinus, within the sinus without indentation, or with varying degrees of procidentia, ranging from discrete forms to almost complete protrusion. The bony lamella covering the carotid artery within the sphenoid sinus is an important element of interest in CT examination and can exhibit dehiscence (Kang et al., 2022).

There may be varying degrees of pneumatization in the sphenoid sinus and surrounding bony structures. Sphenoid sinuses are closely associated to several variants, including cavernous sinus, internal carotid artery, optic and vidian canals (Badran et al., 2022).

Multiple studies have demonstrated that the configuration of the internal carotid artery (ICA) and optic nerve can be influenced by the pneumatization of the sphenoid sinus, resulting in noticeable bulging on the sinus sidewall (Kang et al., 2022, Famurewa et al., 2018). Furthermore, the sinus wall may exhibit regions where the artery and nerve are exposed without a protective bony covering. The involvement of the sphenoid sinus has been observed in approximately 65.2% of patients diagnosed with chronic sinusitis. Additionally, the sphenoid sinus serves as a favorable pathway for accessing the anterior and middle cranial fossa during various surgical procedures, such as pituitary gland surgery (Sumaily et al., 2020).

The Onodi cell, also known as the sphenoethmoidal air cell, represents a distinct anatomical variation of the posterior ethmoid cell. This cell is characterized by its superior and lateral pneumatization towards the sphenoid sinus and its proximity to the optic nerve. A recent study by Jaworek-Troć et al. performed a retrospective analysis of 296 CT scans for the evaluation of the prevalence of the Onodi cell in the Polish population (Jaworek-Troć et al., 2023). The authors reported a relatively frequent occurrence of the Onodi cell, which was observed in 31 patients, with a higher prevalence in males (20 patients) than females (11 patients). No lateral preference was observed for this anatomical pattern among the female cohort; on the other hand, the prevalence of the Onodi cell was observed to be higher on the left side in the male group. A bilateral presence of Onodi cells was observed in only one case.

In addition, a dehiscence in the bone that protects the internal carotid artery may cause the artery to come into touch with the sinus mucosa directly, which might result in an infection of the cavernous sinuses. On the other hand, carotid artery damage might cause blindness or a fatal hemorrhage if the surgeon was not aware of this variance prior to surgery (Dal Secchi et al., 2018).

During surgical procedures involving the carotid artery or optic nerve, surgeons must exercise utmost caution when encountering regions where these structures lack a protective bony covering. This is crucial to minimize the risk of inadvertent damage and ensure their preservation throughout the operation. According to the literature, complications of sinus surgery, such as orbital lesion, dural or intracranial injury, and damage to the internal carotid artery, range from 1.3 to 9.3% (Lum et al., 2019). Intraoperative injury to the ICA during FESS is a rare but potentially life-threatening complication.

The occurrence of such complications is infrequently reported in the literature, with only a limited number of documented case. In cases of traumatic injury to the ICA during exploration of the sphenoid sinus, significant hemorrhage occurs, accompanied by severe limitations in accessing the sinus and impaired vision. Managing the profuse bleeding in such situations poses significant challenges, and, unfortunately, it can quickly become a life-threatening situation for patients, leading to fatal outcomes within minutes (Badran et al., 2022).

Limited data from clinical studies on various populations are available in the literature regarding the implications of anatomical variants of the ICA for FESS procedures.

The aim of this study was to describe the anatomical variations of the internal carotid artery in relationship with sphenoidal sinuses using CT scans.

1.2.2. Materials and Methods

We performed an anatomic-radiological retrospective study that evaluated the variations of the ICA in relationship with sphenoidal sinuses in a cohort of 600 patients who were assessed between January 2020 and December 2022 in 'Saint Spiridon' Emergency Hospital from Iasi, Romania. Ethical approval for this study was obtained from the Institutional Ethics Committee of 'Saint Spiridon' Emergency Hospital (No. 44/02.05.2023).

Patients with various disorders (ophthalmological, neurological, dental, ear–nose–throat pathologies, or trauma) needing CT examinations were included in the study. The exclusion criteria comprised patients with age less than 18 years (such patients have incomplete anatomical structures), important artifacts on CT examinations revision surgery cases, or incomplete medical records.

The imaging protocol was performed using a Phillips AURA CT device and helicoidal technique on axial, coronal, and sagittal planes, with reconstruction of 1.0/1.0 mm to 1.0/1.0 mm slices (slice thickness/increment). Paranasal sinus CT images were obtained in axial projections. Coronal and sagittal images were reconstructed using the same (non-enhanced) bone shadow settings.

Based on the images acquired by the tomography scans, the following variables were assessed: the type of pneumatization of the sphenoidal sinus, the anatomic variations of the ICA, the presence of septations, and the position of the sphenoidal septum.

Medical records were also reviewed and demographic characteristics were retrieved: age, gender, medium of living. Descriptive statistics and univariate analysis of the variables were performed using chi-squared test and SPSS software version 25.0 (SPSS Inc., Chicago, IL, USA). A p values less than 0.05 was considered statistically significant.

1.2.3. Results

A total of 600 patients were included in this retrospective study. The first anatomical variant studied was ICAs at distance from sphenoidal sinus. In total, 150 cases were evaluated for the presence of this variant, and their description is presented in table 1.1. The global prevalence of this anatomical variant in our cohort of patients was 54% (n = 81 patients). The majority of ICAs at distance from sphenoidal sinus (SS) were unilateral (55.5%, n = 45 patients), and in the left side (66.6%, n = 30 patients). We could not find any statistically significant difference between groups regarding their demographic characteristics.

Selected CT scans of the ICA at distance from SS sinus are presented in Figure 1.1.a–c.

The second anatomical variant studied was the procident ICA in 150 cases, presented in table 1.2. The global prevalence of this anatomical variant in our cohort of patients was 58% (n = 87 patients). The majority of procident ICAs were bilateral (55.1%, n = 48 patients). We could not find any statistically significant difference between groups regarding their demographic characteristics, excepting the medium distribution of left and right procident ICAs (p = 0.016). A selected CT scan of the procident ICA is presented in figure 1.2.

Table 1.1. Internal carotid artery at distance from sphenoidal sinus—case descriptions.

Demographic Characteristics	ICA at Distance from SS								
	Yes (*n* = 81)	**No (*n* = 69)**	***p*Value**	**Bilateral (*n* = 36)**	**Unilateral (*n* = 45)**	***p*Value**	**Left (*n* = 30)**	**Right (*n* = 15)**	***p*Value**
Age, years (mean and standard deviation)	53.75 ± 18.87	53.20 ± 14.93	0.84	52.11 ± 18.79	55.07 ± 19.05	0.73	60.27 ± 15.87	64.67 ± 21.71	0.31
Gender (*n*/%)	Male = 34 (42%) Female = 47 (58%)	Male = 34 (49.3%) Female = 35 (50.7%)	0.37	Male = 16 (44.4%) Female = 20 (55.6%)	Male = 18 (40.0%) Female = 27 (60%)	0.61	Male = 13 (43.3%) Female = 17 (56.7%)	Male = 5 (33.3%) Female = 10 (66.7%)	0.56
Medium (*n*/%)	Urban = 36 (44.4%) Rural = 45 (55.6%)	Urban = 32 (46.4%) Rural = 37 (53.6%)	0.81	Urban = 17 (47.2%) Rural = 19 (52.8%)	Urban = 19 (42.2%) Rural = 26 (57.8%)	0.87	Urban = 10 (33.3%) Rural = 20 (66.7%)	Urban = 9 (60%) Rural = 6 (40%)	0.21

ICA—internal carotid artery; SS—sphenoidal sinus.

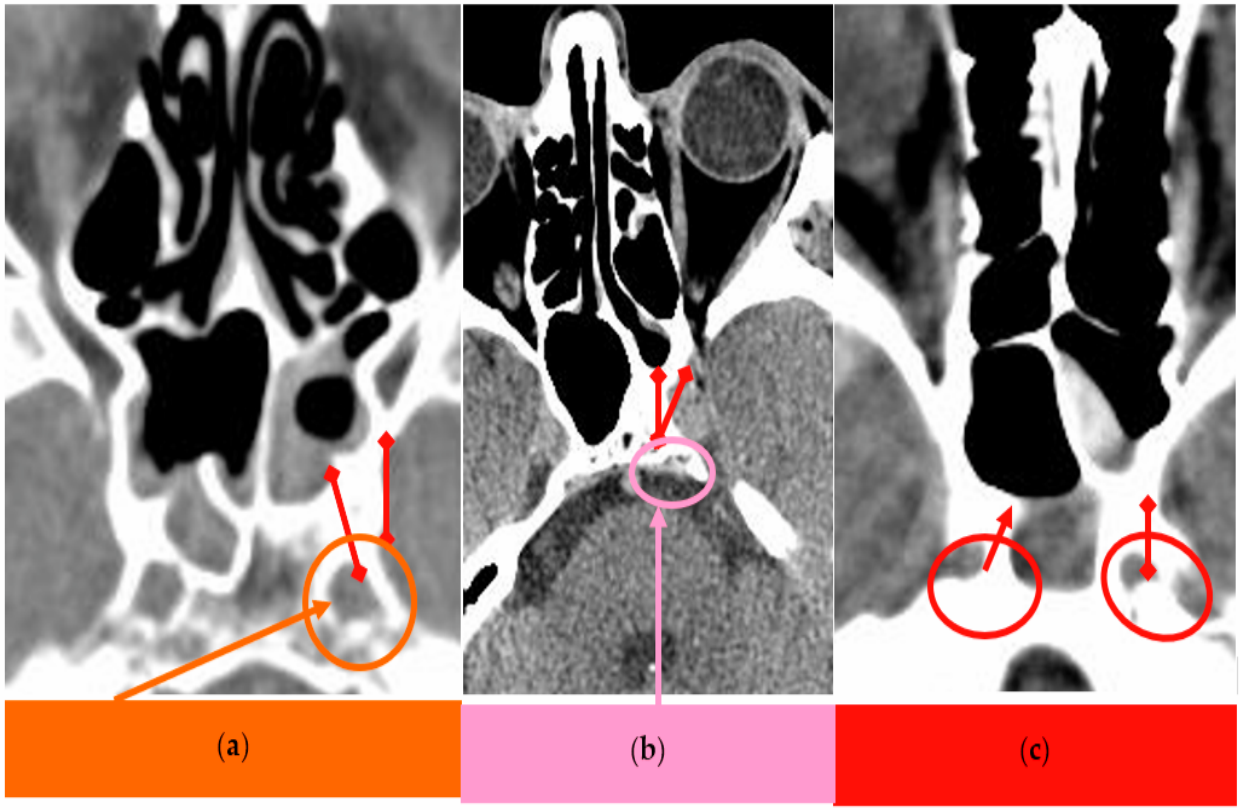


Figure 1.1. (**a**) Left ICA at distance from presellar SS. (**b**) Left ICA at distance from left conchal sinus. (**c**) ICAs at distance from sphenoidal sinuses.

Table 1.2. Procident internal carotid artery—case descriptions.

Demographic Characteristics	Procident ICA								
	Yes (*n* = 87)	**No (*n* = 63)**	***p*Value**	**Bilateral (*n* = 48)**	**Unilateral (*n* = 42)**	***p*Value**	**Left (*n* = 21)**	**Right (*n* = 21)**	***p*Value**
Age, years (mean and standard deviation)	60.90 ± 15.85	56.25 ± 17.43	0.10	62.46 ± 15.46	59.57 ± 16.08	0.13	60.27 ± 15.87	64.67 ± 21.71	0.31
Gender (*n*/%)	Male = 36 (41.4%) Female = 51 (58.6%)	Male = 30 (47.6%) Female = 33 (52.4%)	0.44	Male = 18 (37.5%) Female = 30 (62.5%)	Male = 20 (47.6%) Female = 22 (52.4%)	0.54	Male = 9 (42.9%) Female = 12 (57.1%)	Male = 11 (52.4%) Female = 10 (47.6%)	0.70
Medium (*n*/%)	Urban = 36 (41.4%) Rural = 51 (58.6%)	Urban = 28 (44.4%) Rural = 35 (55.6%)	0.70	Urban = 14 (29.2%) Rural = 34 (70.8%)	Urban = 23 (54.8%) Rural = 19 (45.2%)	0.05	Urban = 15 (71.4%) Rural = 6 (28.6%)	Urban = 8 (38.1%) Rural = 13 (61.9%)	0.016

ICA—internal carotid artery.

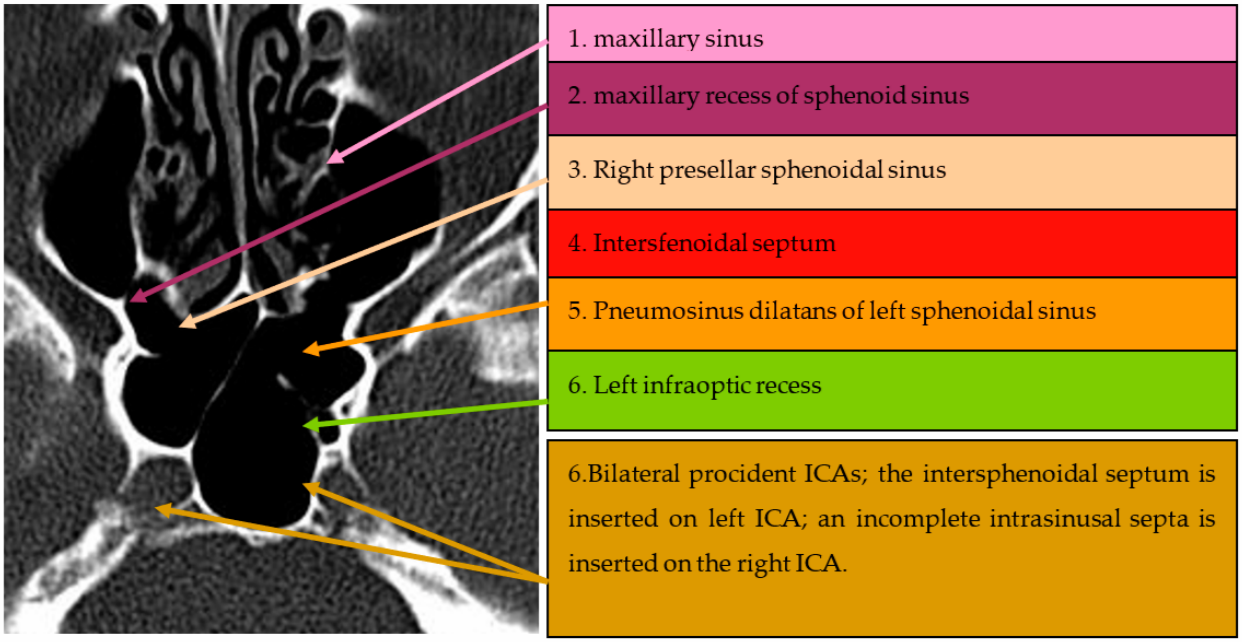


Figure 1.2. Axial CT section of paranasal sinuses with procidence of both ICAs, on which are inserted two septa.

The third anatomical variant studied was the dehiscent ICA in 150 cases presented in Table 1.3. The global prevalence of this anatomical variant in our cohort of patients was 52% (n = 78 patients). The majority of dehiscent ICAs were unilateral (69.2%, n = 54 patients). We could not find any statistically significant difference between groups regarding their demographic characteristics. Selected CT scans of dehiscent ICAs are presented in Figure 1.3.

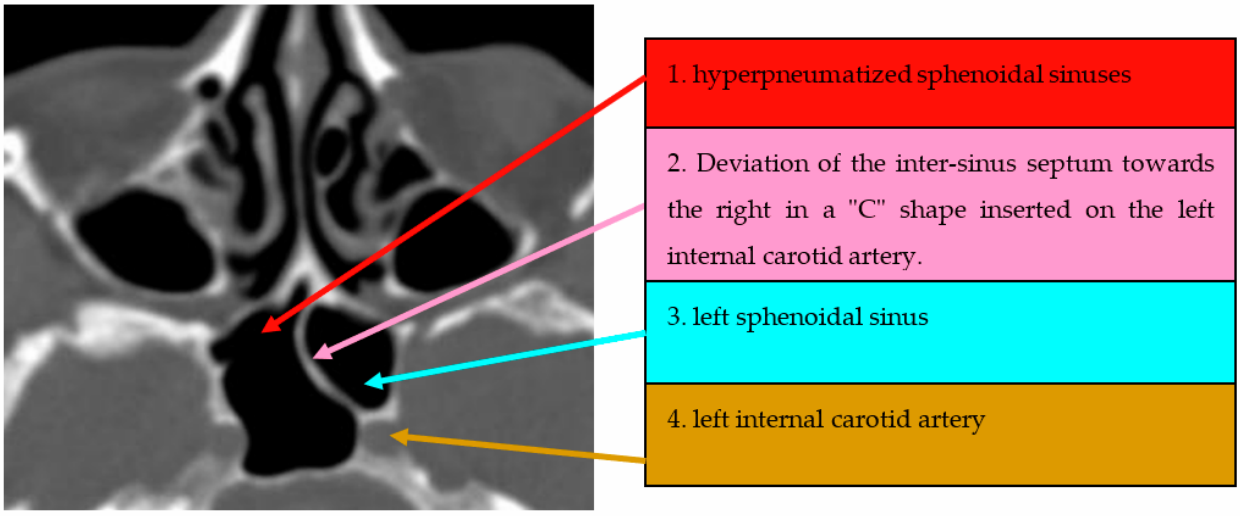


Figure 1.3. Axial CT section of paranasal sinuses with deviated intersphenoidal septum towards right, in a "C" shape, inserted on the internal carotid artery.

Table 1.3. Dehiscent internal carotid artery—case descriptions.

Demographic Characteristics	**Dehiscent ICA**								
	Yes (*n* = 78)	**No (*n* = 72)**	***p*Value**	**Bilateral (*n* = 24)**	**Unilateral (*n* = 54)**	***p*Value**	**Left (*n* = 27)**	**Right (*n* = 27)**	***p*Value**
Age, years (mean and standard deviation)	54.83 ± 16.50	54.97 ± 14.77	0.95	50.79 ± 18.80	56.63 ± 15.22	0.31	53.11 ± 15.54	60.15 ± 14.31	0.15
Gender (*n*/%)	Male = 29 (37.2%) Female = 49 (62.8%)	Male = 28 (38.9%) Female = 44 (61.1%)	0.82	Male = 8 (33.3%) Female = 16 (66.7%)	Male = 21 (38.9%) Female = 33 (61.1%)	0.87	Male = 10 (37%) Female = 17 (63%)	Male = 11 (40.7%) Female = 16 (59.3%)	0.94
Medium (*n*/%)	Urban = 40 (51.3%) Rural = 38 (48.7%)	Urban = 33 (45.8%) Rural = 39 (54.2%)	0.50	Urban = 13 (54.2%) Rural = 11 (45.8%)	Urban = 27 (50%) Rural = 27 (50%)	0.75	Urban = 14 (51.9%) Rural = 13 (48.1%)	Urban = 13 (48.1%) Rural = 14 (51.9%)	0.93

ICA—internal carotid artery.

The fourth anatomical variant studied was intrasinusal septa with posterior insertion on the ICA in 150 cases presented in table 1.4. The global prevalence of this anatomical variant in our cohort of patients was 58.6% (n = 88 patients). The majority of intrasinusal septa were unilateral (75%, n = 66 patients), and on the left side (63.6%, n = 42 patients). We could not find any statistically significant difference between groups regarding their demographic characteristics. Selected CT scans of this anatomic variant are presented in figure 1.4 and figure 1.5.

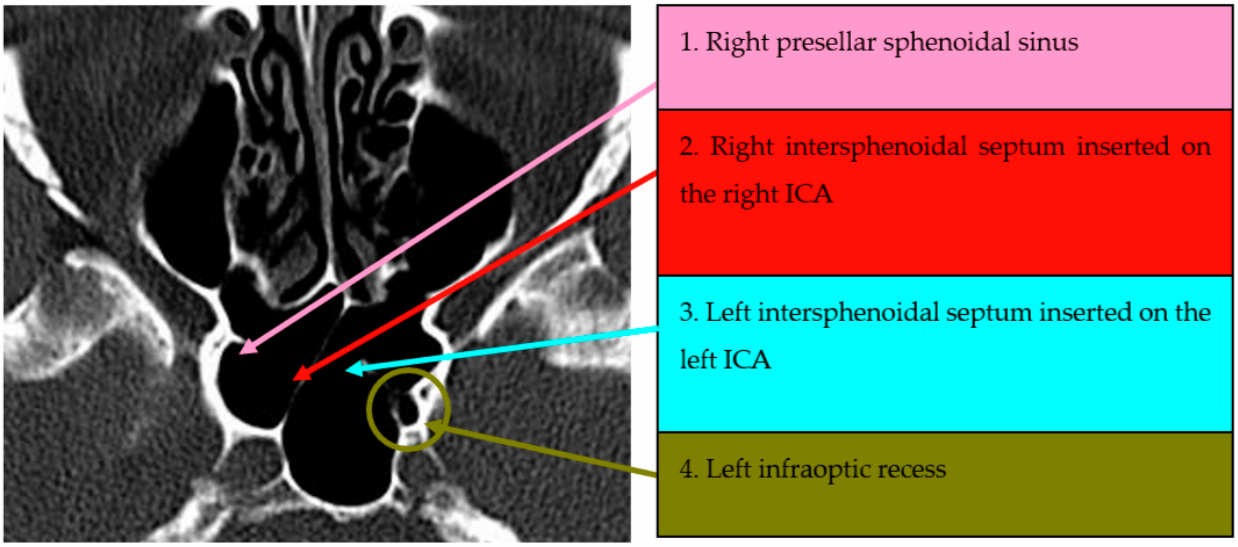


Figure 1.4. Axial CT section of paranasal sinuses. Right intersphenoidal septum. Incomplete left intrasphenoidal septum, posteriorly inserted on the ICA.

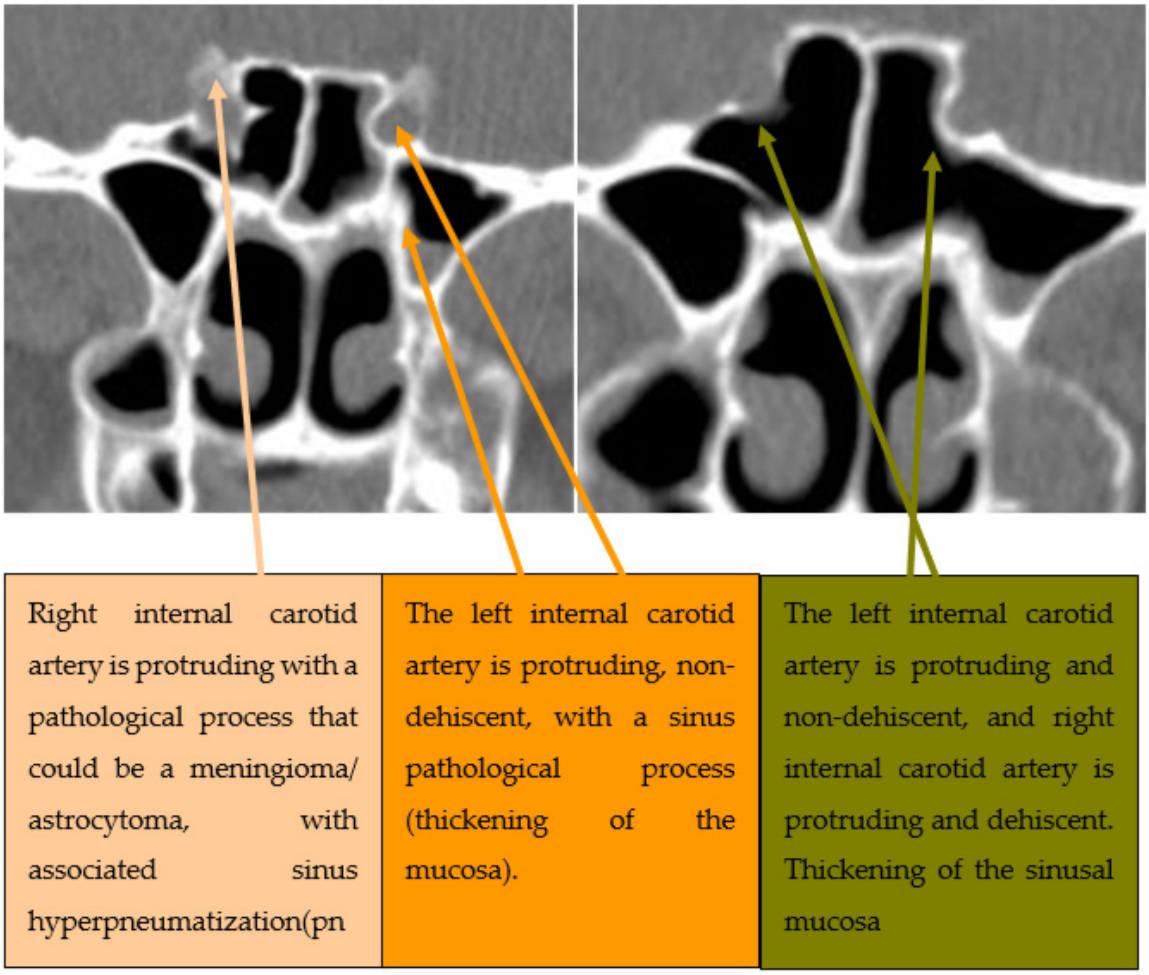


Figure 1.5. Coronal CT section of paranasal sinuses. Various degrees of protrusion of the internal carotid arteries.

Table 1.4. Intrasinusal septa with posterior insertion on internal carotid artery—case descriptions.

Demographic Characteristics	Intrasinusal Septa with Posterior Insertion on Internal Carotid Artery								
	Yes (*n* = 88)	**No (*n* = 62)**	***p*Value**	**Bilateral (*n* = 27)**	**Unilateral (*n* = 66)**	***p*Value**	**Left (*n* = 42)**	**Right (*n* = 24)**	***p*Value**
Age, years (mean and standard deviation)	57.09 ± 14.53	55.84 ± 15.33	0.12	55.85 ± 13.32	56.92 ± 14.98	0.08	53.11 ± 15.54	57.64 ± 14.23	0.19
Gender (*n*/%)	Male = 23 (26.1%) Female = 65 (73.89%)	Male = 19 (30.6%) Female = 43 (69.4%)	0.54	Male = 7 (25.9%) Female = 20 (74.1%)	Male = 18 (27.3%) Female = 48 (72.7%)	0.91	Male = 12 (28.6%) Female = 30 (71.4%)	Male = 6 (25%) Female = 18 (75%)	0.93
Medium (*n*/%)	Urban = 53 (60.2%) Rural = 35 (39.8%)	Urban = 34 (54.8%) Rural = 28 (45.2%)	0.51	Urban = 20 (74.1%) Rural = 7 (25.9%)	Urban = 38 (57.6%) Rural = 28 (42.4%)	0.13	Urban = 23 (54.8%) Rural = 19 (45.2%)	Urban = 15 (62.5%) Rural = 9 (37.5%)	0.82

1.2.4. Discussion

Endoscopic sinus surgery has emerged as the established and widely accepted approach for the treatment of chronic sinusitis. Acquiring a better understanding of the diverse regional anatomy of the sphenoid sinus plays a crucial role in reducing surgical complications associated with trans-sphenoidal and functional endoscopic sinus surgery. Previous studies have emphasized that the sphenoid sinus is recognized as the most variable cavity within the human body, posing challenges in terms of surgical access and intervention. By familiarizing themselves with the intricate anatomy of the sphenoid sinus, surgeons can enhance their surgical techniques, optimize patient outcomes, and minimize the risk of complications during these procedures.

This retrospective study provided an overview of the main anatomical variants of ICAs in relationship with the sphenoidal sinus. By definition, the internal carotid arteries, in their intracavernous course, exhibit a protrusion within the sphenoid sinus, similar to the optic nerve (Aibar-Durán et al., 2021). This results in a certain degree of indentation within the sinus. When this degree of indentation becomes abnormal, it manifests as the anatomical variation known as procidentia. This condition can be expressed in varying degrees, ranging from discrete forms to almost complete protrusion into the sinus, with or without dehiscence.

The most prevalent anatomical variant was represented by intrasinusal septa with posterior insertion on the ICA (58.6%), followed by procident ICA (58%) and dehiscent ICA (52%). We could not find any statistical significance regarding demographic characteristics among groups, and our results are in line with previously published literature (Dziedzic et al., 2020, Ngubane et al., 2018).

Wide openings of the sphenoid sinus are often necessary for extended endoscopic endonasal approaches in order to enable simple access to the operated area and allow for adequate visualization of the posterior wall of the sinus. The septa from the sphenoid sinus must often be removed for this stage. A specific focus on the ICA anatomical course should be given during the opening of the sphenoid sinus. Internal carotid artery dehiscence and protrusion have a broad range of prevalence, ranging from 2% to 23% and 5.2% to 67%, respectively (Refaat et al., 2020).

Rereddy et al. discovered a statistically significant correlation between dehiscent or protruding internal carotid artery and dehiscent or protruding optic nerve (Rereddy et al., 2014).

The optic nerve is located in the superolateral part of the sphenoid sinus and, similar to the internal carotid artery, its canal can exhibit dehiscence. Dehiscence of the optic nerve canal can also occur when it reaches the sphenoid or ethmoid sinus and leaves an osseous imprint on the lateral walls (Refaat et al., 2020). This serves as a significant surgical landmark when the optic nerve has an intrasinusal course. During endoscopic sinus surgery, an unintended fracture of the intersphenoidal septum that is connected to the bony wall of the ICA or optic nerve canal can lead to injury of these structures. This can result in significant intraoperative bleeding or even blindness. Therefore, utmost care must be taken to prevent such fractures and minimize the risk of complications during the surgical procedure.

The number of septa and the pattern of septation inside the sphenoid sinus seem to be unaffected by gender or ethnicity (Abdullah et al., 2001). In total, 4.7% of cases have been documented to include carotid canal insertion of an intersphenoid sinus septum. The sphenomaxillary plate is another anatomical variation in which the sphenoid sinus and the maxillary sinus are connected by a bony septum at the back. To prevent ocular damage during surgery, this structure has to be identified on the CT scans (Lantos et al., 2016).

Examining the anatomical variations of the internal carotid artery (ICA) enables radiologists to provide more precise descriptions of patients who necessitate endoscopic endonasal approaches (EEA) to the skull base (Nitinavakarn et al., 2005). This comprehensive evaluation emphasizes key anatomical characteristics, including the classification and extensions of SS pneumatization, irregularities in the walls of the parasellar and paraclival segments of the ICA, the relative position of the septum with respect to the ICA, and the presence of septations within the SS.

Therefore, Fernandez-Miranda et al. (2009) evaluated the anatomical relation between intrasphenoid septations and ICAs using 27 CT angiographic scans on live patients and 27 CT scans of fresh-frozen cadaveric heads. The authors reported 85% and 41% of the scans from the first group had at least one or two septa, respectively, touching one of the ICAs. When evaluating the second group, the authors concluded that 89% had at least one septation inserted in the ICAs.

The presence of sphenoidal septa that attach to the ICA has been identified as a potential risk factor for ICA injury during surgical procedures. Previous studies have established a correlation between septations within the sphenoid sinus and the ICA, with many intrasphenoidal septa inserting near the parasellar or paraclival carotid prominences (Dziedzic et al., 2020, Gibelli et al., 2020). Manipulation or dissection of these septa during surgery can result in damage to the ICA, as they are physically attached to the vessel wall and located in close proximity to these structures.

We only included adult patients, although patients older than 12 years old, when the sphenoid sinus achieves its full size and ultimate anatomical structure, may also have comparable findings. Pneumatization, which typically begins 12 months after birth, comes to a halt at this time (Reittner et al., 2001). During trans-sphenoidal pituitary surgery, postsellar pneumatization from

the sphenoid sinus, especially pneumatization of the dorsum sella, may cause penetration of the posterior wall of the sphenoid and a cerebrospinal fluid (CSF) leak (Mehendale et al., 2002).

For the purposes of our study, we used CT axial scans, which were completely repetitive when compared to coronal scans and found to be superior in most studies for identifying septa in preoperative imaging, although one publication found that coronal scans were superior to axial scans for assessing septa (Abdullah et al., 2001, Unal et al., 2006).

A recent study by Dal Secchi et al., on 90 patients' CT scans, revealed a prevalence of 26% for the protrusion of the parasellar ICA, and of 35% for the paraclival ICA. The same study indicated a prevalence of only 3.6% for the paraclival ICA (Dal Secchi et al., 2018). Moreover, another study by Sasagawa et al., suggested that carotid artery protrusion and dehiscence occur more frequently among acromegalic patients (Sasagawa et al., 2016). It was also demonstrated that between 5 and 28% of patients with rhinosinusitis or facial trauma have internal carotid artery protrusion into the sphenoid sinus (Tomovic et al., 2013, Raseman et al., 2020).

Both ICA procidence and dehiscence were included in the CT checklist before sellar and parasellar surgery, along with the presence of sphenoid sinus pneumatization or intersphenoid septa (Raseman et al., 2020). Unspecific symptoms may result from a dehiscent ICA canal, which is characterized by a thinning of the bony plate separating the ICA from the middle ear (Schutt et al., 2013). Prior to beginning surgical procedures, it is crucial to undergo the proper imaging to rule out potentially fatal complications as this illness sometimes resembles other middle-ear abnormalities (Moeller and Welch 2010).

The dehiscence of the osseous wall protecting the carotid canal is estimated at 6% in many studies (Fadda et al., 2022). This anatomical variation increases the risk of posttraumatic rupture or intraoperative injury during sphenoidectomy, leading to intrasinus hemorrhage through the branches of arteries that traverse the clivus. In some cases, pseudoaneurysm of the intracavernous internal carotid artery or dural fistula may develop (Gardner et al., 2019). Dehiscence, along with procidentia, further increases the risk of catastrophic hemorrhage, especially when combined with lateralization of the intersphenoidal septum or an intrasphenoidal septum attached to the vessel.

In addition, it is crucial to be well-prepared for other potential complications that may arise during FESS, including cerebrospinal fluid leak, retrobulbar hematoma, and bleeding from the internal carotid artery (ICA). Familiarity with the appropriate treatment modalities for each complication is essential. A laceration to the ICA during FESS procedure should be managed immediately with bilateral common carotid artery compression in the neck region; prompt compression of both common carotid arteries can significantly reduce bleeding (although it may not completely stop it due to collateral blood flow from the vertebral artery system), gauze packing, and even ligation of the artery. Each surgeon performing FESS should be aware of the local anatomy and variants of important neurovascular structures, and must be able to promptly recognize intraoperative complications and their management (Weidenbecher et al., 2005, Gardner et al., 2019).

This study has some limitations due to its retrospective, descriptive design on Caucasian patients. One strong point of this study is represented by a relatively large cohort of patients, with variate addressability to the imaging department in a 3-year time-frame. More powerful imaging

techniques based on artificial intelligence could potentially determine with more accuracy the anatomical variants of ICA at the level of sphenoidal sinuses, and could offer surgeons a comprehensive anatomical picture before proceeding to FESS.

1.2.5. Conclusions

The preparedness of surgeons prior to conducting endoscopic skull base surgery through computed tomography scanning plays a crucial role in facilitating a favorable outcome. Specifically, it equips them with essential tools to anticipate the intraoperative findings, thereby mitigating the risk of iatrogenic complications such as inadvertent damage to the internal carotid artery or other delicate anatomical structures. Consequently, the utilization of preoperative CT imaging enables surgeons to effectively strategize and plan the surgical approach. It is imperative that radiologists accurately document the anatomical variations and their interrelationships for comprehensive reporting.

Although FESS is generally considered a safe procedure, the occurrence of carotid artery injury is a catastrophic complication that necessitates careful consideration during surgical planning. To mitigate this risk, it is crucial to identify patients with significant risk factors and conduct preoperative imaging to assess the anatomical variations and potential proximity of the carotid artery. Implementing a multidisciplinary approach and adhering to established management protocols are essential for minimizing morbidity and mortality associated with such complications.

1.3. Facing the future – multidisciplinary approach

1.3.1. Introduction

Superficial musculo-aponeurotic system (SMAS) is an anatomical and surgical concept (Jost et al., 1984, Mitz and Peyronie 1976) that is not yet completely understood or accepted by researchers. Several authors have previously reported their evaluations of the morphofunctional features of the SMAS, particularly the parotid, masseteric, and labial regions (Hinganu et al., 2017, Hinganu et al., 2018).

Soft tissue of the face is topographically formed by the following layers: skin, subcutaneous adipose tissue, superficial fascia, facial muscles, parotidomasseteric fascia, and the parotid duct, facial nerve, and buccal fat tissue (Stuzin et al., 1992).

It has been demonstrated that the nasal SMAS unites similar structures of nearby regions (Dzubow 1986). In the nasal region, adipose trabeculae forms and provides antigravitational support of the superficial soft tissues. It provides fixation and elevation of the SMAS of the upper lip (Hinganu et al., 2018).

From an anatomical and surgical perspective, the nasal region comprises the following parts: (*i*) The nasal root, which is the upper part of the nose that joins with the forehead (Sperber 2006). It is located under the glabella, forming a prominence known as the nasion. (*ii*) The nasal

dorsum, which is the boundary between the root and the tip of the nose; this has a different appearance in different profiles (Meskell 2010). (*iii*) The *ala nasi*, which is the inferior lateral surface of the outer nose, is mostly made up of cartilage. (*iv*) The nasolabial groove. The SMAS layer is the central part of the nose, which is accompanied by a superficial adipose layer. The main function of this layer is to allow the movement of the superficial layers of the nasal region, to form laminae carrying vessels and nerves, to maintain the thickness of the skin, and to transmit the contractile force of the nasal muscles to the skin (Kim and Jeong 2019). The SMAS layer mainly consists of procerus, anomalous nasi and the transverse nasal crease (Neves et al., 2021).

The superficial, conventional limits of this region are: (*i*) superior – the horizontal plane through the infraglabellar notch, corresponding to the frontonasal suture and the cephalometric landmark called the nasion; (*ii*) inferior – the transversal plane between the posterior part of the nasal septum and nasolabial groove; and (*iii*) lateral – the two planes that unite the nasolabial groove with the nasogenian groove on each side (Field et al., 2012, Maur et al., 2014).

The nasal region can be subdivided into the proper nasal region (*regio nasalis* – RN) and the nasal wing (*ala nasi* – AN). There are major differences between these two regions from morphological and visual points of view. The nasolabial groove (*sulcus nasolabialis* – SNL) connects the AN, the infraorbital and oral regions, through the SMAS. The superficial fascia of the nose inserts to the periosteum, because of skin attachment of the *levator anguli oris* muscles, *zygomaticus*, and *levator labii superioris* (Hagan and Walker 1988, Mendelson 1992, Rubin et al., 1989, Yousif et al., 1994, Ozturk et al., 2013, Schenck et al., 2018).

Multiple anatomical relationships between the facial muscles and the surrounding bones, structures, and skin can be visualized on magnetic resonance imaging (MRI). In this study, we only used MRI because it does not produce Roentgen radiation and provides the same results as computed tomography (CT) (Hutto and Vattoth 2015, Marinkovic et al., 2000).

The nasal muscles (*procerus*, and the *compressor naris major* and *minor*) are considered part of the SMAS in this region. The SMAS in the nasal region communicates with surrounding SMAS through the *levator labii alaeque nasi* and the *dilator nasi* muscles (Saban et al., 2008). The transverse segment of the nasalis muscle is of major importance for the surgical SMAS flap which attaches to the maxilla and ascends to the dorsum of the nose (Kim et al., 2016).

We aimed to investigate and describe the settlement of the SMAS in various parts of the nasal region: the radix, the nasal dorsum, nasolabial fold, and *ala nasi*. We also evaluated the morphological and topographical features of the nasal subregional area and attempted to configure the functional anatomy of this structure and the related implications for nasal surgery (Seagal 2017). However, the distribution, morphology, and functionality of the SMAS at the nasal level have yet to be determined by the literature. Our study presents new and relevant data about the nasal SMAS cytoarchitecture and its extensions and places the functionality of this anatomical structure in the context of the entire facies. We make this statement because the present study is an integral part of our research team's project on the morphofunctional and clinical characteristics of SMAS at the level of the entire face, which began in 2004 and is still ongoing.

1.3.2. Materials and Methods

1.3.2.1.Anatomical study

The anatomical study was performed on 24 cadaveric specimens from Ion Iancu Institute of Anatomy, Grigore T. Popa University of Medicine and Pharmacy, Iaşi, Romania. Through dissection, we identified the overlapping layers: the dermoepidermal layer, the adipose subcutaneous layer, the superficial fascia layer, the superficial muscular layer, and the deep fascia, perichondrium, and periosteum, which were dissected in the coronal plane, from the superficial to the third plane, as demonstrated by the schematic illustration in Figure 1.6 Of the donors, three were male and nine were female (age range: 63–90 years).

An incision was made by following the medial edge of the nasolabial groove over its entire length, up to the periosteum. Then, we removed the superficial layers from the entire surface of the heminose from root to tip. We continued the dissection to the lateral part by separating the SMAS from the deep periosteum.

The macroscopic study was performed using the SOM 62 Kaps microscope made by Karl Kaps Germany (zoom adjustment: 5×–8×–12.8×; objective lens: f=250), from the Laboratory of Quantitative Microanatomy of the Ion Iancu Institute of Anatomy, Grigore T. Popa University of Medicine and Pharmacy, Iaşi.

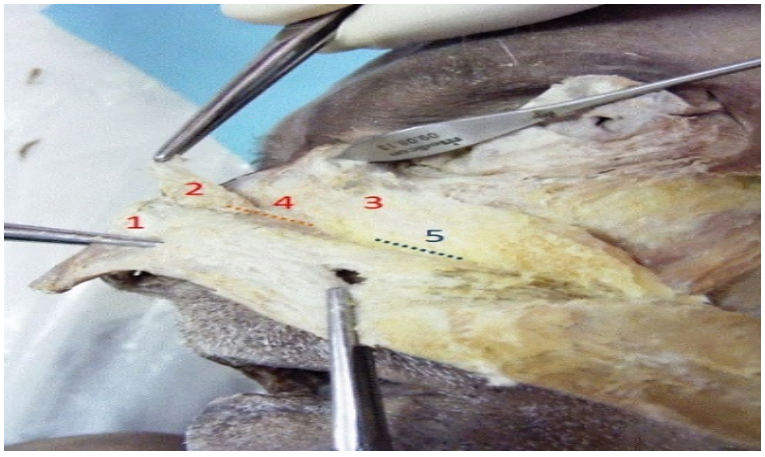


Figure 1.6. Spatial disposition in the anterior regions of the face. 1: The skin layer, epidermis, and dermis, with the denser deep part, serving as the insertion for the muscles of facial expressions; 2: The subcutaneous fat layer; 3: The superficial plane of the facial muscles, which differs according to the studied region; 4: The plane of the branches of the facial nerve – dissection plane medial to the nasolabial groove; 5: The deep plane of the facial muscles, which differs from one region to another – dissection plane lateral to nasolabial groove

1.3.2.2. Histological study

For the histological study, we collected tissue fragments from the skin to the deep layers, from 4% formalin-embalmed cadaver specimen, which can be used reliably for histo-pathological investigation if cellular morphology is the major criteria for diagnosis. These layers were processed using a paraffin technique and stained using special Verhoeff's and Szekely techniques (Stopak

and Harris 1982, Thaller et al., 1990, Wassef 1987, Drenckhahn and Benninghoff 2003) to highlight collagen, elastin, and muscle fibers. These fragments were collected from the lateral side of the nasolabial groove at the junction with the infraorbital region (NLIO), the jugal region (NLJ), the angle of the mouth (NLAO), and the upper lip (NLLS).

Quantitative measurements were performed on microscopical pictures using an image acquisition system, after which the Prodit 5.2 professional software (BMA, Amsterdam, The Netherlands) was used. The results were processed. Stereology used the standard grid with Weibel parallels to quantify the percentage volumes of the main parietal structures of the blood vessels. This procedure allows estimation of the percentage volumes of the tumor's component structures (tumor cells, stroma, and blood vessels). The digital overlay of the standard grid over the acquired video image from the histology slide is used. The grid corresponded to the parameters of the structures to be studied to meet the optimal quantification conditions.

1.3.2.3. Quantitative study

We used stereology to evaluate the percentage volumes of the studied structures. The main stages of the measurement are: (*i*) determining the reference structures: collagen fibers, elastic fibers, muscle fibers, interstitium; (*ii*) defining the Weibel geometric grid superimposed on the microscopic image; (*iii*) determining the total number of points to be counted and counting them by pressing the keys corresponding to the intersections with the reference structures; (*iv*) automatic calculation of the stereological ratio; (*v*) statistical evaluation of the calculated parameters; (*vi*) graphic representation of the observed changes; (*vii*) formulating conclusions.

In each case, a test surface corresponding to 540 points on the test grid with Weibel parallels, with a distance between two points of d=15.07 μm, was studied with the 40× objective. The orientation of the test lines was changed during quantifications to ensure random intersection of all structures.

The statistical report assessed the percentage volumes of the reference structures in each case, then on the topography of the veins. The results of the quantifications were then represented graphically.

1.3.2.4.Radiological study

The radiological study was conducted on a group of 11 people (eight males and three females) using MRI at the Arcadia Medical Imaging Center, Iaşi. All subjects were adults aged between 27 and 51 years, and MRI investigations and 3D reconstructions had been performed previously for reasons related to oromaxillofacial or plastic surgery pathology. We highlighted the continuity of the SMAS in the nasal region on the acquired images.

The group of patients investigated using the MRI technique were subjected to this examination due to their basic pathology: facial aesthetics issues (wrinkles, facial prolapse) as well as parotid and submandibular tumors. They were meticulously selected so that the underlying disease would not affect the quality of the acquired images, nor their interpretation. The following

MRI sequences were used: T2-weighted (T2W)–turbo spin echo (TSE) axial, T1-weighted (T1W)–fast field echo (FFE) axial native, and T1W–FFE axial with contrast agent.

Ethical considerations

This study followed the principles outlined in the Declaration of Helsinki. The Ethics Committee Approval of Grigore T. Popa University of Medicine and Pharmacy, Iaşi (Approval No. 195/June 3, 2022) and the Ethics Committee Approval of St. Spiridon Emergency County Clinical Hospital, Iaşi (Approval No. 13/February 25, 2022) are attached to this manuscript.

1.3.3. Results

Our study demonstrated the continuity of the SMAS in the nasal region. The SMAS had a different morphofunctional structure in the nasal wings compared to the nasolabial groove. We also demonstrated the continuity of the nasal SMAS with the surrounding regions.

√ **Anatomical study**

We identified the buccinator muscle in the deep plane of the nasolabial groove. Laterally (nasal wing), this plane was no longer found, and the superficial layer between the skin and nose muscles showed a thin layer of adipose tissue (Figures 1.7. and 1.8.; Figure 1.9., a and b).

The existence of a deep adipose layer of SMAS at this level allowed a block dissection of the superficial layers in the axial plane between a line that followed the medial edge of the nasolabial groove and the *dorsum nasi*. The same resectable area extended craniocaudally between the skin insertion of the *procerus* muscle and the parallel plane to the anterior edge of the homolateral nostril, about 3 mm above it.

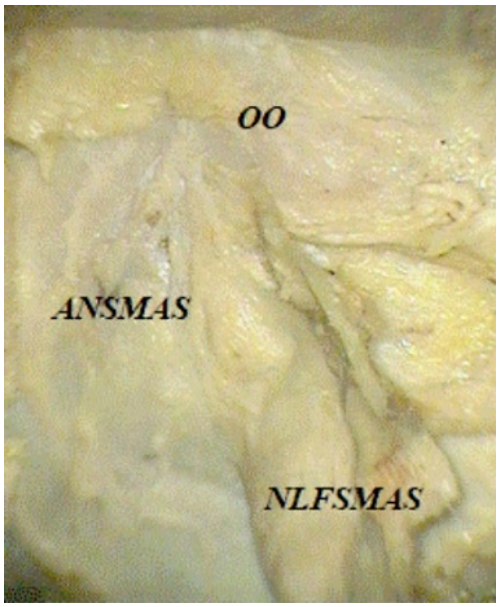


Figure 1.7. Perioral muscles and nasal region. The levator anguli oris alae nasi (LAON) muscle, SMAS at the ala nasi (ANSMAS), orbicularis oris (OO) muscle, and SMAS in the nasolabial fold (NLFSMAS). Dissection specimen (SOM 62 Kaps microscope, ×20 oculars), 10/1 scale. SMAS: Superficial musculo-aponeurotic system.

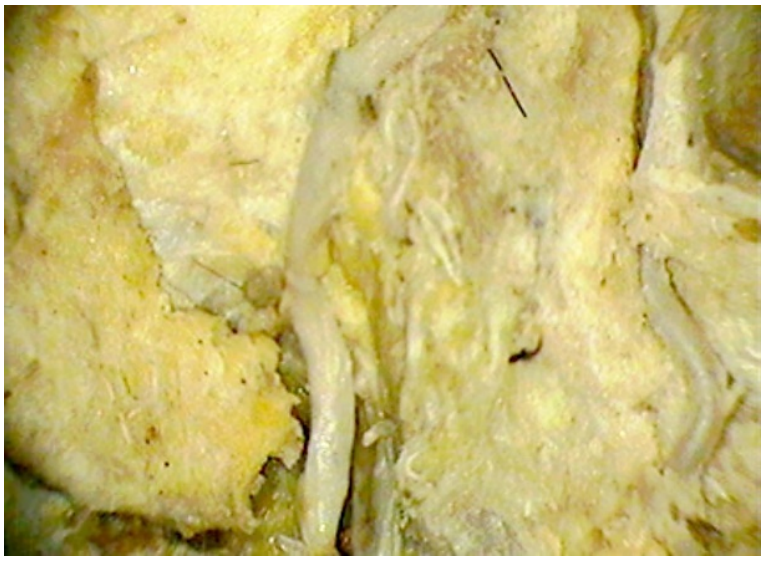


Figure 1.8. Inferior part of the nasolabial groove with the terminal part of the facial artery. Dissection specimen (SOM 62 Kaps microscope, ×20 oculars), 10/1 scale.

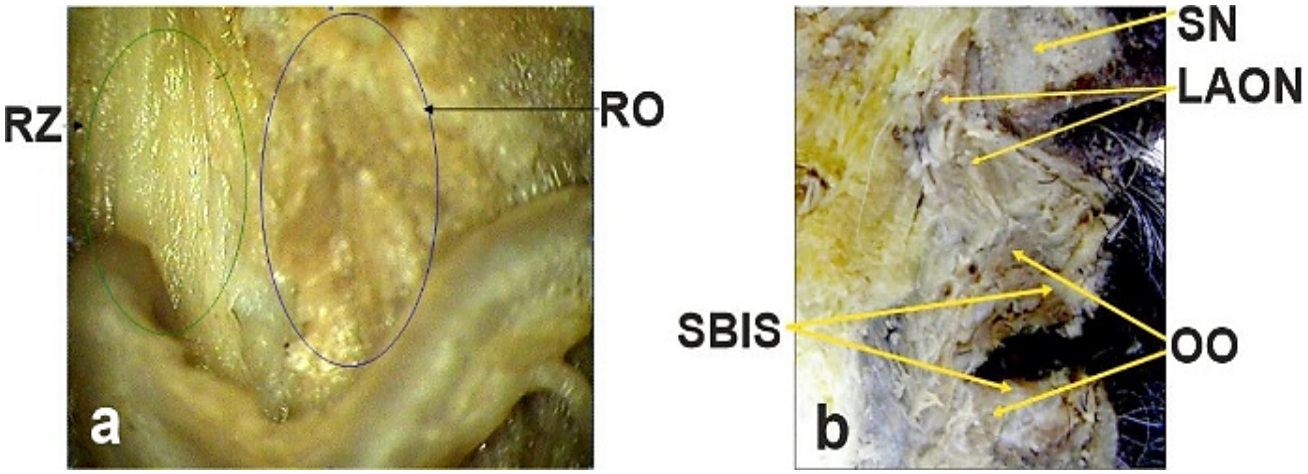


Figure 1.9. (a) Skin insertion of the zygomaticus, levator labii superioris, and levator anguli oris muscles – the border area between the zygomatic region (RZ) and cheek (RO); image taken with the operating microscope; (b) Perioral muscles and nasal region; the levator anguli oris alae nasi (LAON) muscle, SMAS at the level of the wing of nose (SN), orbicularis oris (OO) muscle, SMAS at the level of the lower and upper lips (SBIS).

The medial to the nasolabial groove, the *levator anguli oris*, *levator labii superioris*, and *zygomaticus* muscles showed skin insertion. At the same time, the *orbicularis oris muscle adhered tightly to the deep surface of the skin (Figure 1.9, a and b; Figure 1.10, a and b). These insertions made dissection at this level difficult (Figure 1.11, a and b).*

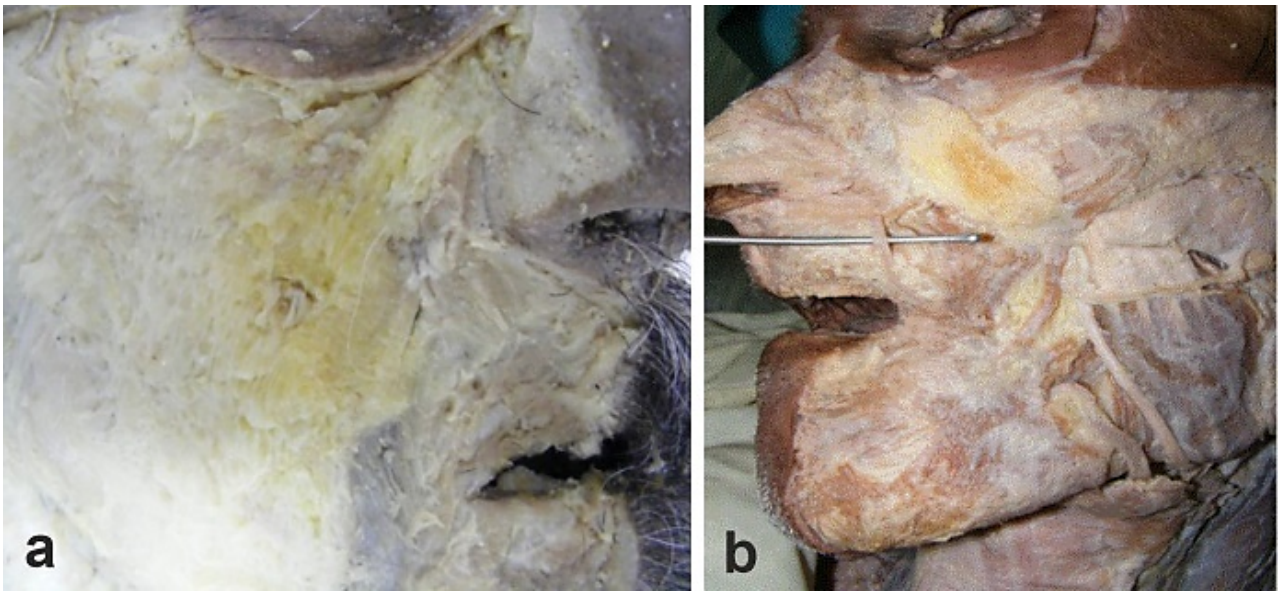


Figure 1.10. (a) Dissection area lateral and medial to the nasolabial fold; (b) Facial vessels, connective tissue, fat, and fibers of the muscles of the nose. Dissection specimen.

Figure 1.11. Adhesions and perioral muscles of the nasal region: (a) Ligamentary adhesions that secure the SMAS to the deep fascia; dissection specimen (SOM 62 Kaps microscope, ×20 oculars), 10/1 scale; (b) Conjunctival adipose tissue in the cheek, prebuccinator, and perioral region; dissection specimen.

√ **Histological study**

The deep adipose layer was thin, crossed by collagen septa, and the superficial fibroadipose layer was very well represented. The histological study identified the SMAS on the nasolabial groove in the form of a thick concentration of medium-sized collagen fibers. For the lateral to the nasolabial groove, there were numerous elastic fibers of various sizes (Figure 1.12, a–d). The

fragments from the lateral side of the groove were collected from the boundary with the adjacent regions: infraorbital, cheek, mouth angle, and upper lip.

The SMAS structure in this region also contained isolated muscle fibers or small fascicles, most of which came from the cutaneous muscles that passed through the superficial area to the deep face of the skin (Figure 1.13, a and b).

Quantitative study

To determine the proportions of the SMAS, we considered the proximity of the nasolabial groove. Thus, we determined the percentage of fibrous connective tissue in relation to the elastic and muscular tissue at the level of the nasolabial groove, and we also determined the morphological and functional aspects that continued into the neighboring regions.

Connective tissue had the highest percentage volume in the nasolabial groove, then in the infraorbital region and the cheek region and the lowest percentage volume in the upper lip. Muscular fibers had the higher percentage volume in the upper lip, then in the cheek and at the infraorbital level, and the lowest percentage volume in the parotid region.

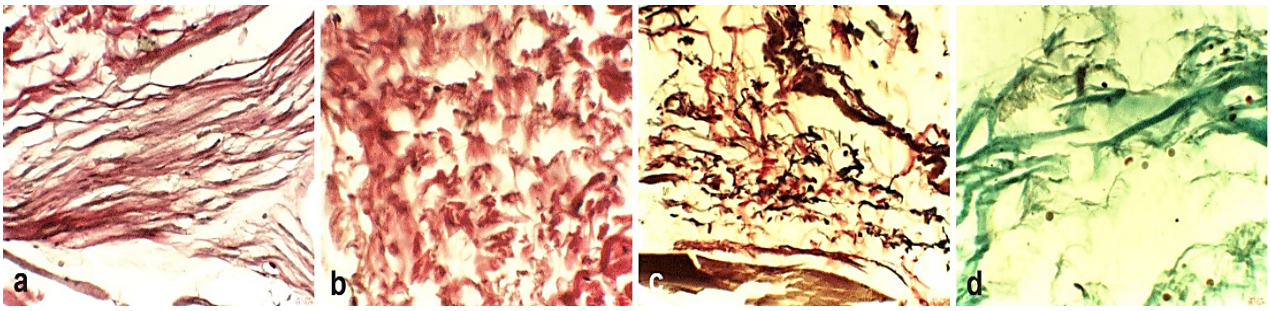


Figure 1.12. Fibers of the SMAS: (a) SMAS medial to the nasolabial groove, with longitudinal collagen fibers; (b) Thinner collagen fibers and numerous elastic fibers, along with muscle fibers longitudinally arranged in the superior lip of the SMAS; (c) SMAS structure in the angle of the mouth, with numerous interlaced collagen fibers with elastic fibers almost absent; (d) Fibrous attachments that cross the infraSMAS adipose layer in the infraorbital region. Verhoeff's staining: (a and b) ×400; (c) ×600. Szekely staining: (d) ×400.

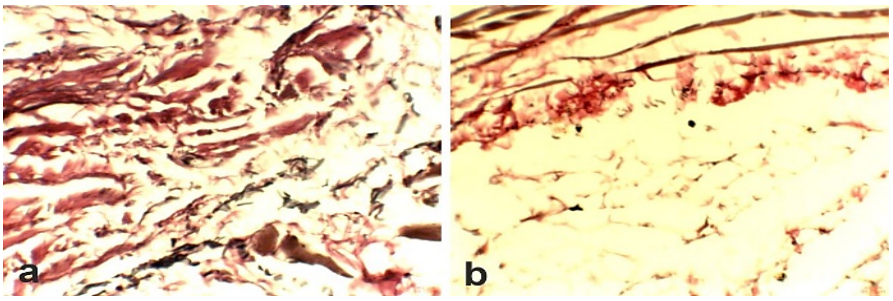


Figure 1.13. Various fibers of the SMAS: (a) Elastic fibers of various sizes in the SMAS structure, more numerous on the side of the nasal region; (b) Isolated muscle fibers or small bundles, most of which come from cutaneous muscles that pass through the superficial fascia, medial to the nasolabial groove. Verhoeff's staining: (a and b) ×400.

The SMAS from the NLJ region showed the following quantified percentage volumes: connective tissue – 59.07%, muscular fibers – 27.22%, and interstitium – 13.70%. The

stereological quantification from the SMAS in the NLIO showed the following percentage volumes: connective tissue – 67.59%, muscular fibers – 16.11%, and interstitium – 16.30%. The SMAS from the NLLS showed the following quantified percentage volumes: most of it was conjunctive tissue approx. 50%, muscular fibers approx. 40%, and interstitium approx. 20%. The SMAS from the NLAO showed the following percentage volumes: connective tissue – 79.07%, muscular fibers – 1.11%, and interstitium – 19.81%.

Figure 1.14 shows the significance of these findings, highlighting the regional variability of the SMAS at the facial level.

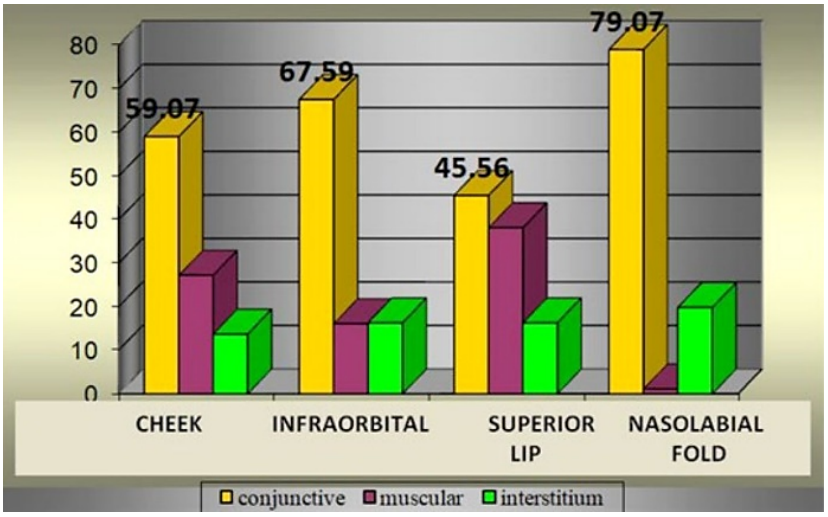


Figure 1.14. Graphical representation of quantified percentage volumes in the SMAS in the studied regions.

√ **Radiological study**

The results of the MRI study showed that the SMAS in the nasal region continued cranially with the procerus muscle fascia and then with the frontal fascia. The SMAS was laterally continuous with the SMAS from the jugal and infraorbital regions (Figure 1.15, a and b; Figure 1.16, a and b).

In MRI exploration, the SMAS behaved just as we had seen during dissections, facilitating the insertion of nasal mimic muscles into the deep surface of the skin (Figure 1.15, a and b; Figure 1.16, a and b). The MRI showed the same strong periosteal and perichondral insertions of the SMAS at the radix, *dorsum nasi*, and nasolabial groove. The area between these inserts mediated the transfascial attachments of the nasal and adjacent muscles into the deep surface of the skin.

The results of our histological, quantitative, and qualitative studies are correlated with our radiological study and demonstrated that our findings based on classical anatomical dissection are reliable and sustainable.

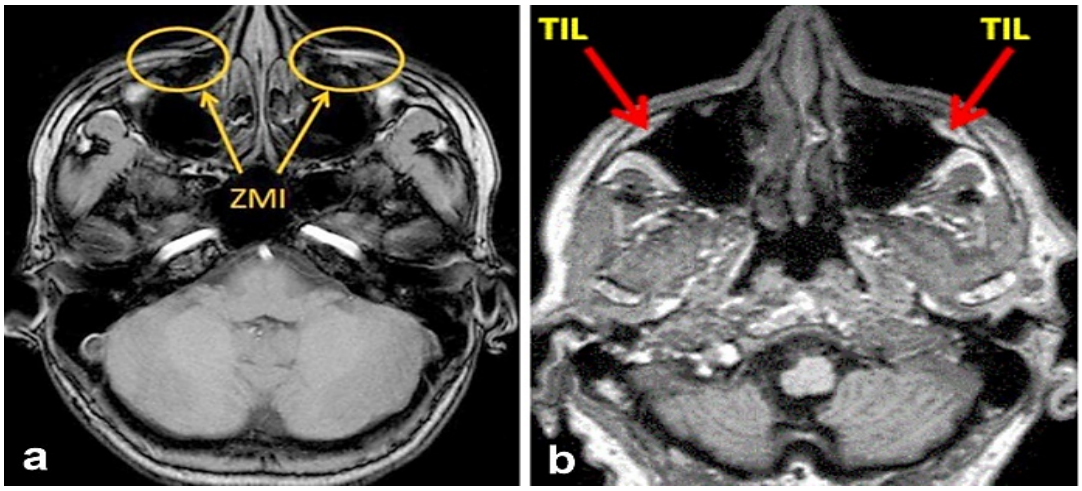


Figure 1.15. Axial MRI: (a) Infraorbital insertion and transSMAS of the major zygomatic muscle (ZMI); (b) TransSMAS insertion of the levator labii superioris muscle (TIL). MRI: Magnetic resonance imaging.

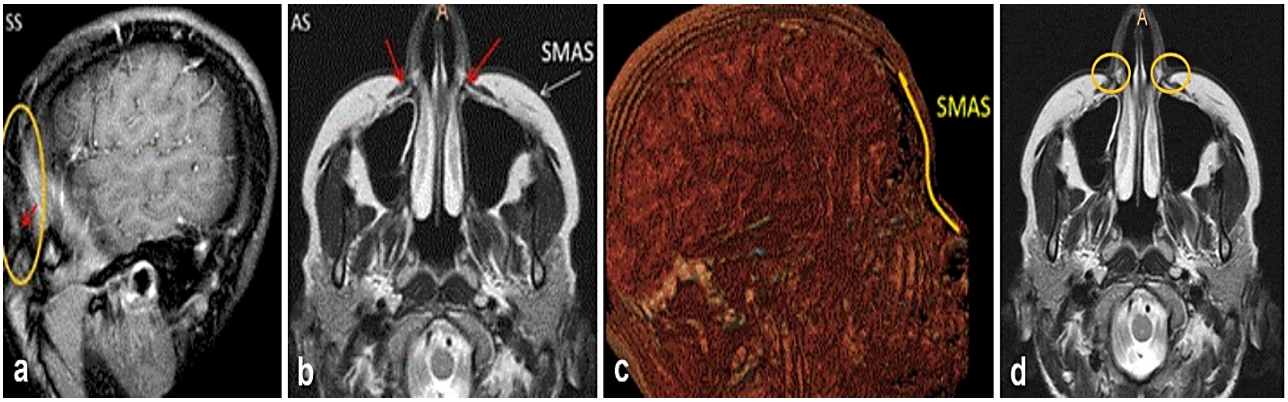


Figure 1.16. Specimen sections: (a and c) Sagittal section (SS) through the wing of the nose; SMAS continues to the frontal fascia; (b and d) Axial section (AS) highlighting the jugal SMAS and the insertions into the skin of the nasal muscles, marked with red arrows. A: Anterior insertion of the SMAS on the dorsum nasi.

1.3.4. Discussion

The nasal SMAS was identified as a superficial fascia and a subcutaneous adipose layer. The anatomical dissection study together with histological and radiological evaluations demonstrated the presence of SMAS in the nasal region. We identified peculiarities of nasal SMAS in two areas: in the *ala nasi* where it is thinner, and the deep part of the dermis does not adhere to the underlying structures and at the root and *dorsum nasi*, where the fatty plane is very thin. Through anatomical study, we confirmed the presence of a superficial musculoaponeurotic layer in the nasal region in all explored cadavers.

In the nasal region, we identified the following layers (from superficial to deep): (*i*) the skin, epidermis, and dermis, with a deep thinner part, which support mimic muscles; (*ii*) the subcutaneous fat layer; (*iii*) the superficial fascia; (*iv*) the superficial plane of the facial muscles.

The results of this study support the findings of other authors (Giacomini et al., 2020, Ozdilek et al., 2020) who reported five layers of the nasal region, which are: the subcutaneous fatty layer, the fibromuscular layer, the profound fatty layer, the fibrous longitudinal layer, and a layer that contains interdomal ligaments. We consider that, at this level, the SMAS is represented by a second layer: a fibromuscular one, which interconnects with the alar muscles and distributes power to the dermis.

The superficial fascia is gradually thinned to the *modiolus* but remains visible as a net layer both on the MRI and in the dissected specimens. In the upper part of the region, towards the radix base, the two fasciae (superficial and deep) join in a dense connective structure. This structure is the dermocartilaginous ligament (Letourneau et al., 1988, Pitanguy 1965, Pitanguy et al., 1995, Pitanguiy 2001). Medial to the nasolabial groove, the superficial fascia is more obvious and protects the upper branch of the angular artery, the homonymous vein, and the superficial branches from the facial nerve.

Through histological, quantitative, and qualitative studies, we have demonstrated that the nasal SMAS differs both macroscopically and microscopically in the AN compared to the *radix*, *dorsum*, or nasolabial groove. On one hand, at the AN level, the muscles at this level are inserted into the dermis transfascially, clearly delineating the SMAS line, while in the *nasal dorsum* the superficial fascia has no muscular fascicles.

The results of the stereological and histological study showed that the structure and architecture of the SMAS from the nasal region, especially from the nasolabial groove, allow the traction of conjunctive and fibroadipose structures underlying the skin. Together with the superficial muscles, it also allows them to return to a repose state.

Medial to the nasolabial groove, the SMAS shows a longitudinal disposition of the collagen fibers. A similar structure is found where it continues with the SMAS from the mouth angle and infraorbital region. In contrast with this structure, the nasal SMAS becomes more elastic at its continuity with the superior labial region of the SMAS (Pensler et al., 1985, Barton 1992, Surek 2019). At this level, collagen fibers become scarce and muscular fibers predominate. Collagen fibers are disposed on successive longitudinal and transverse planes and gradually, as we descend, they lose their proper structure, arranging themselves in different types of lamellae, especially at the level of the modiolus.

These findings can be applied to modern surgical practice, particularly in various facial rejuvenation techniques, such as injectable filler treatment (Sykes et al., 2015, Rohrich et al., 2009, Trussler et al., 2011, Calderon et al., 2044, El-Sabbagh 2017).

The buccinator muscle forms the profound muscular plane of the nasolabial groove, except for the *ala nasi*. Under the dermis, we found collagen fibers, fat cells, and muscle fibers mixed with nasal muscle fibers, which form a distinctive layer between the dermis and the nasal muscles. Quantitative CT measurements performed by Macchi et al. (2007), at the nasolabial fold, showed that the superficial fibroadipose layer was low represented and the profound adipose layer had an increased thickness. Meanwhile, where the SMAS continued to the facial expression muscles, this layer had an average thickness of 2.41±0.05 mm. Our previous studies showed that the SMAS structure at the level of the nasolabial groove was similar to that of the parotidomasseteric region

(Hinganu et al., 2018). Under the same structural shape, the SMAS continues to the infraorbital, jugal, and angle of the mouth areas.

Unlike classical anatomy, where it is considered that subcutaneous adipose tissue is missing from the superficial fascia where the skin adheres to the subjacent layers, our study demonstrated its continuity into the nasal region without subdivision, which is already deemed clinically relevant (Patron et al., 2019). This correlates with the results obtained by other researchers in the field and has implications for injectable filling procedures performed at this level. The filling will be gravitationally dispersed in the nasal regions compared to areas in which the fat layer is compartmentalized, which ensures the fluid remains in the desired position (Pessa 2016, Yoo et al., 2013).

Another important clinical application of the notion of the SMAS is facial rejuvenation surgery, especially rhytidectomy. In the nasal region, the SMAS is used as nasolabial flaps for deep plane rhytidectomy surgery (Oneal et al., 2010, Robotti et al., 2022). This is preferable to other interventional methods due to the special structure of the nasolabial SMAS collagen matrix, which delivers remarkable results at a distance. The nasal skin has lack of mobility; this is why the repair of nasal skin defect with a local flap is challenging to plastic surgeons (Doğan and Özyazgan 2014).

From a functional perspective, the manner of attachment of the SMAS to the viscerocranium is of utmost importance. This provides facial skin firmness and acts as a fixed point in facial muscle contraction.

Even though the superficial fascia gradually narrows to the *modiolus*, its thickness remains and appears as a net layer on MRI. This was also observed during the dissection of specimens. At the base of the nasal pyramid, it appears that the superficial and deep fascia are joined in a dense connective structure, most likely the dermocartilaginous ligament (Ercin et al., 2020). To the medial side of the nasolabial groove, the superficial fascia becomes more obvious and mediates the cutaneous insertion of the zygomatic muscles. The strong insertion of the SMAS into the periosteum of the nasolabial groove makes this region a hinge and suspension mechanism for the soft tissues of the upper lip, and for the perioral muscular apparatuses. At the same time, these insertions act as a barrier to possible infections at or from this level.

It is clearly important for cosmetic surgeons who perform rhytidectomy procedures to have a good understanding of the SMAS, given that the SMAS is dissected and mobilized during these procedures. Our findings have applications in many other medical fields. Firstly, knowing the anatomy of this region is crucial to understanding the evolutionary particularities of tumors that develop at this level, the principles of tumor excision, and for the selection of appropriate reconstructive techniques for soft tissue defects located in the nasal pyramid. In addition, palatine cleft surgery is based on studies of anatomy and embryology, which are absolutely indispensable for achieving the best aesthetic and functional results. Several previous articles have reported that preoperative MRI evaluation of facial anatomy is useful for surgical planning and postoperative follow-up in patients with a cleft palate (Honig 1997, Freilinger et al., 1987, Kleinheinz and Joos 2001). Tumor and traumatic lesions that affect the nasal region also require interventional techniques based on the concept of the unique cervicofacial layer (Fischbein et al., 2001, Sandulescu et al., 2018).

1.3.5. Conclusions

Our study presents the cytoarchitecture, morphology, and topography of the nasal SMAS from an integrative, functional, anatomical, and clinical perspective. During the study, we faced several limitations. Firstly, dissections were performed on hemifacial that had been fixed in formalin; had such dissections taken place on hemifacial that had not been fixed in formalin, the results may have been different. Secondly, a greater MRI magnetic field strength may have produced different results. Despite these limitations, we demonstrated that the SMAS is a continuous layer of the nasal region between two adipose layers. Understanding nasolabial groove anatomy and adjacent areas allows a surgeon to achieve much more accurate results. The results of our research define nasal SMAS as a unit of great value in facial surgeries, such as facial rejuvenation, the resolution of malformations, or tumor removal.

1.4. Changing the future – new ENT techniques

1.4.1. Introduction

Cancer of the nasal cavity and paranasal sinuses is quite rare. For example, in the UK the incidence is 8:1,000,000, while in the United States, where it represents 1% of all neoplasia, it has an incidence of 5:1,000,000. In both countries, the incidence rate for men:women is approximately equal, with the most common occurrence being in the second decade of life (Carrau and Myers 2014).

Although many studies give the maxillary sinus topography more frequent than the ethmoid sinus, it is hard to tell how such a conclusion has been reached as long as the clinical signs occurs only when the tumour reaches beyond the sinus. 80-100% of patients have radiologic signs of bone destruction.

The tumours of the nasal cavity are thus associated with the maxillary and ethmoidal sinuses. Those that start from the nasal vestibule and nasal septum raise particular problems and, although rare, form a particular group of cases among the rhinosinusal tumours.Cancers that invade only the inferior part of the jaw are better classified as cancers of the upper extension of buccal cavity (Maran 1990).

Given that rhinosinusal neoplasia is not very common, it is difficult to identify favoring or determining factors. For example, smoking, the first favorable cause of other cancers of the respiratory tract, is not associated with rhinosinusal neoplasia. Perhaps the best proven factor in the UK and France is working in the wood and coal industry. This was found by epidemiological studies with laboratory confirmation. People working in the wood industry have the same risk of developing an ethnoid adenocarcinoma as smokers to develop a broncho-pulmonary neoplasia. It seems to be a long latency associated with this factor (28-43 years) (Acheson et al., 1981, Andrew et al., 1995, Baxter et al., Cecchi et al., 1980, Manetje 1999).

Radiation exposure, viral infections and constitutional factors were associated with the occurrence of rhinosinusal neoplasia also, but the evidence is inconclusive and indicates that only a small proportion of all squamous carcinomas can be attributed (Roush 1996, Bimbi et al., 2004).

Nickel workers are at a risk of 870 times higher rhinosinusal tumours, most of them appearing after 10 years of exposure, but with improved working conditions, the incidence has fallen rapidly. The average latency period in these cases was 24 years. Patients who have worked in the chromium industry have a 21-fold higher risk of latency of 23 years (Barton 1977, Battista 1983).

Non-occupational agents such as thorium dioxide injected into the maxillary sinus, exposure to hydrocarbons and isopropyl alcohol also increase the risk of rhinosinusal tumours. All of these injuries appear to develop as a result of nasal fossil air currents that trap and deposit irritating particles either at the anterior portion of the nasal septum or at the middle cornet, resulting in squamous metaplasia and then carcinoma (Birt and Briant 1981).

The purpose of this study is the complex retrospective analysis of the cases of rhinosinusal malignancies diagnosed and treated in the Otolaryngology Clinic of the St. Spiridon Emergency Clinical Hospital in Iasi between 1990 and 2004. We evaluated the characteristics of the patient group using a statistically significant analysis of the age, gender, background, and factors of affiliation. Specific tests and indicators have been used.

1.4.2. Materials and methods

We used a study group of 143 patients diagnosed with rhinosinusal malignant tumours in the oto-rhyno- laryngology clinic of Sfantu Spiridon Hospital in Iasi. These patients were monitored clinically, radiologically, paraclinically and anamnestically, in the pre-surgical period.

As methods, we used statistical series of dynamic variation of periods and dynamic momentum variation. For the square test, the x1 test is a nonparametric test used for statistical deductions in the case of two or more samples randomly drawn from a population and having a different frequency distribution between them.

This test compares two or more frequency distributions for two batches from the same population, so with a similar frequency distribution, but with a different feature. Absolute figures are taken into account, thus making it more laborious to compute the average, the dispersion, the moments.

Also, this test applies only to those situations where the expected events exclude each other, in the sense that only one of them is possible.

For df = l (degree of freedom) and a 95% confidence we have Chi - square X2 = 3.84. If the calculated value is greater than this value means that there is association and the exposure has an influence on the studied disease.

Once the contingency table (or cross classification) is made, we calculated the odds ratio (CR) and the relative risk (RR) ratio.

1.4.3. Results

Chance report (CR) expresses the chances of those who are exposed to a certain feature are OR or higher than the odds of the unexplored ones.

The risk ratio (RR) expresses the risk of those exposed is RR or higher than those unexposed (Table 1.5, 1.6).

Table 1. 5. Patients distribution by gender

GENDER	NUMBER	PERCENT
Female	40	29,97%
Male	103	72,03%

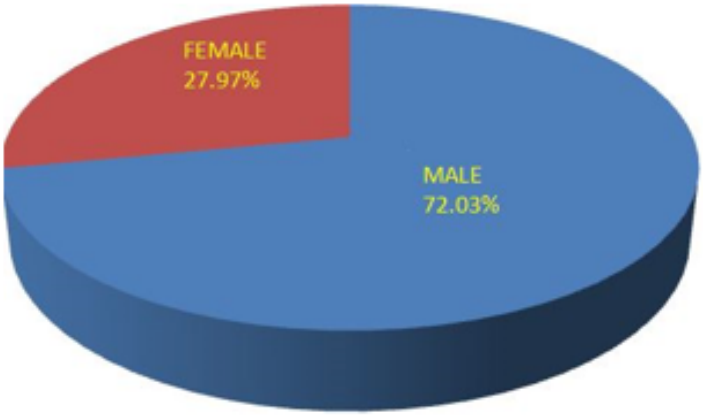


Figure 1.17. Cases distribution by gender

The incidence of females cases was 27.97%, small compared to the incidence of male cases.

Table 1.6. Patients distribution by demographic origin

DEMOGRAPHIC ORIGIN	NUMBER	PERCENT
Rural	97	67,83%
Urban	46	33,17%

Achieving the contingency table allowed the study of patient involvement in the presence of TMRS.

A control group of patients (60 cases) without TMRS, randomly selected from the ENT Clinic, was used (Table 1.6, 1.7, Fig 1.17)

The very high values of Chi-square (x2 = 20.45) and the Spearman Rank correlation coefficient (r = -0.74) lead to the conclusion that rhinosinus malignant tumors are significantly

present in rural areas (p-0.000003, 0.05), which also results from the analysis of the regression line (table 1.7., 1.8, fig. 1.18, 1.19).

The slope of the regression line indicates the significant correlation between the patient's background and the presence of TMRS.

Table 1.7. Patients distribution by demographic origin and TMRs

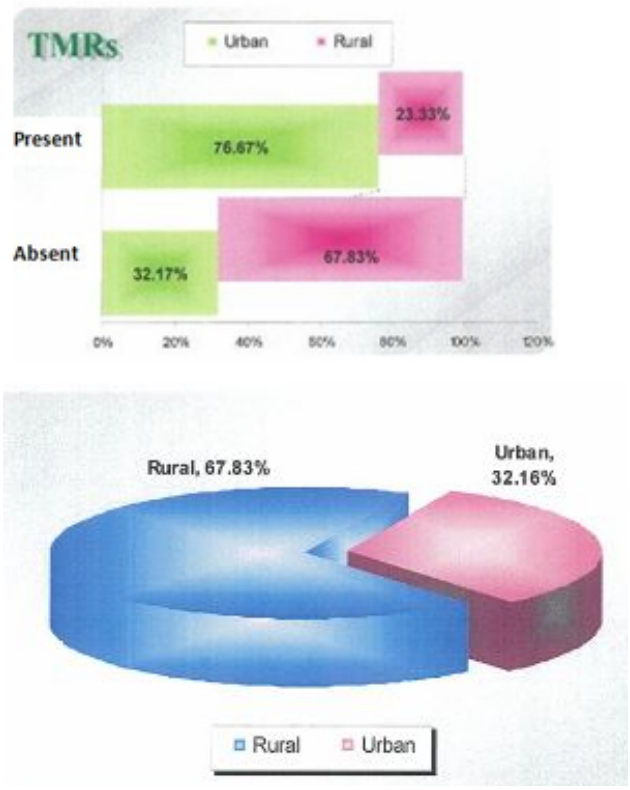


Figure 1.18. The incidence of cases by the origin of the patients and TMRs

Table 1.8. SQUARE-CHI TEST RESULTS

Demographic origin vs TMRs	Chi-Square test X^2	df	p
M-L-SQUARE-CHI Test	20.45789	1	0.00001
Contingency coefficient	-0.592772		
Spearman Rank correlation coefficient	-0.747748		0.000003

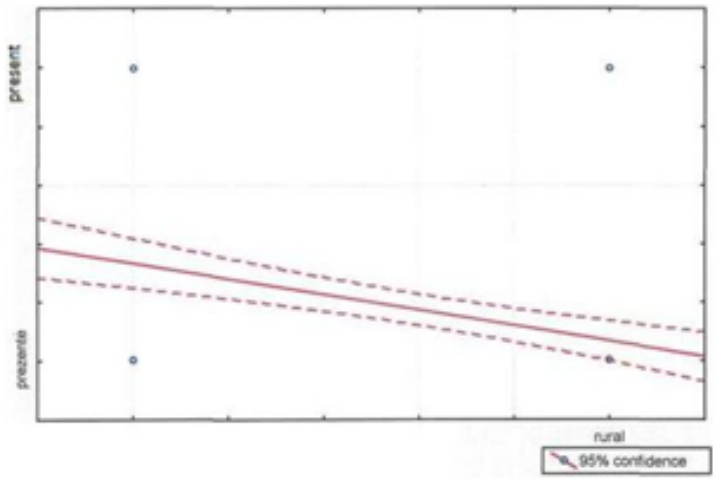


Figure 1.19. Correlation of the demographic origin and the presence of rhinosinusal malignancies

The histogram of the age of patients with rhinosinus malignancies reveals the normal distribution of cases by age (Gaussian distribution).

Table 1.9. Distribution of cases by age of patients

AGE	NO. OF CASES	%
≤10	3	2.1
10≤AGE≤20	6	4.2
20≤AGE≤30	12	8.39
30≤AGE≤40	18	12.59
40≤AGE≤50	26	18.18
50≤AGE≤60	30	20.98

Major incidences of cases with rhinosinusal malignancies occur in patients aged 50-70 years (20.98%) (table 1.9, fig. 1.20).

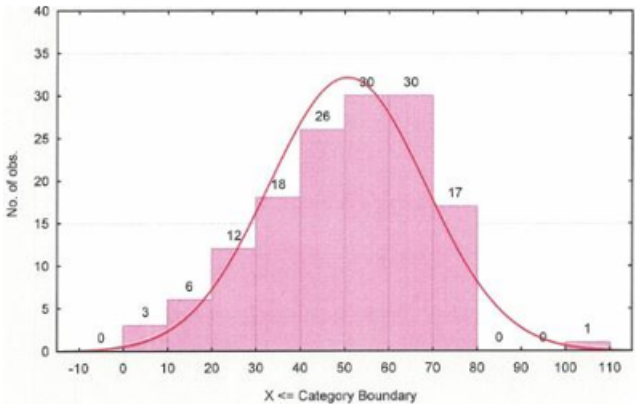


Figure 1.20. Distribution of cases by age of patients

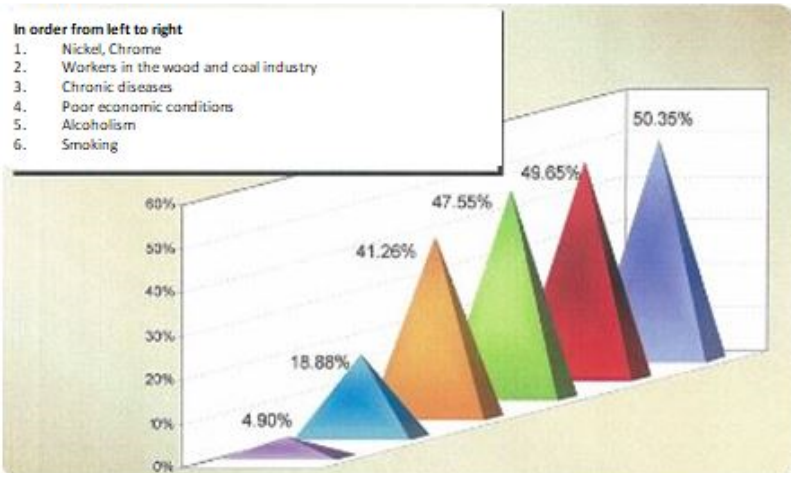


Figure 1.21. The incidence of risk factors in the the etiopathogenesis of malignant tumors of the hypophar ynx

Table 1.10. The involvement of risk factors in the presence of tumors

Predisposing factors involved in the etiopathogenesis of malignant rhinosinusal tumours	CR Chance report	RR Risk Report	X^2	p
Workers in the wood and coal industry	5.28	2.47	14.07	0.0001763
Nickel, Chrome	4.15	2.26	11.13	0.0008479
Chronic diseases (liver, diabetes, cardiovascular)	3.21	2.02	7.29	0.0069444
Alcohol consumption	2.71	1.86	5.28	0.0215787
Poor economic conditions	2.49	1.78	4.37	0.0366590
Smoking	2.37	1.68	4.12	0.0428729

By applying the specific Spjotvoll / Stoline test scores for the age of patients with rhinosinusal malignant tumour by gender, it was found that there was no statistically significant difference between these mean values. This is explained by the value of the significance level p = 0.0776 which is much higher than the reference value of 0.05 corresponding to a confidence interval of 95%.

1.4.4. Discussion

In the etiopathogenesis of rhinosinusal malignant tumors a number of external factors are involved. They were identified and analyzed in the patients of the study group as compared to their presence in the control group, thus demonstrating their involvement in the presence of rhinosinusal malignant tumors (table 1.10, fig. 1.21).

The retrospective analysis of the involvement of certain risk factors in the occurrence of rhinosinusal malignant tumours leads shows that in the studied group the risk of rinosinusal malignant tumors is 5.28 times higher in persons working in the wood industry, 4.15 times higher in those who work in other toxic environments (exposure to nickel, chromium). Also, chronic illnesses, alcohol consumption, smoking, poor economic conditions due to lack of hygiene, lack of

adequate nutrition, neglect of health, and the chance for these people to develop rhinosinusal malignancies are more than twice as high (Esping et al., 1980, Acheson et al., 1981, Andrew 1995).

1.4.5. Conclusions

We can not specify the existence of a determinant or favoring factor of the occurrence of rhinosinusal tumours but the statistical analysis noticed an ncreased risk for patients working in the wood industry(5.28), which are exposed to chromium, nickel (4.21) as well as to theassociated diseases (liver, cardiovascular, diabetes).It is not to be neglected the effects of the poor economic conditions andthe lack of education of the population, by postponing the moment of presentation tophysician, influencing the therapeutic decision, postoperative evolution. Thesepatients often present different degrees of malnutrition,immunodepression, etc. Statistical processing showed that thesepatients have a twofold risk of developing rhinosinusal tumours.

1.5. Implications of reconstruction

1.5.1. Conceptual background

Sinonasal tumors are a rare pathological entity, representing ~3% of upper respiratory tract tumors and being characterized by marked anatomopathological diversity (Banuchi et al., 2015). The affected areas include the nasal cavity and the paranasal sinuses and, in advanced cases, the tumors may extend to involve the surrounding anatomical structures, with no significant clinical symptoms until late in the course of the disease (Haerle et al., 2013, Kauke et al., 2018). Their proximity to vital structures, such as the optic nerves and brain, poses a challenge for surgeons when proceeding with reconstructive treatment. The common extension areas for this type of tumor are the cribriform plate, crista galli and the roof of the ethmoid, the orbit and, occasionally, the facial soft tissues (Suarez et al., 2008). Performing an extensive resection of the tumor with clear margins may result in sizeable cranial and facial skin defects, which must then be covered with the aid of a multidisciplinary team (Naara et al., 2020).

Tumours of the nasal cavity and paranasal sinuses represent a wide spectrum of histologies, tissues of origin, and anatomic primary sites. The distinctive difficulty in generalizing treatment approaches is obvious, given the numerous variables associated with the broadly-based term, paranasal sinus malignancy. Sinonasal and skull base neoplasms are rare tumors that constitute about 3% of tumours in the upper respiratory tract (Dhruba et al., 2017). Patients usually are refered late in the evolution to thhe ENT surgeon due to the non-specfic symptoms which may lead to a delayed diagnosis and treatment. The presence of regional or distant metastases is a poor prognostic sign.

Since the first reported maxillectomy by Syme in 1828 (Mc Guirt 1995) the maxillary reconstruction has been a controversial theme and in a constant debate mainly due to the complexity of the maxillary structure and its important diverse functions.

It is often difficult to identify the specific origin of these tumors due to the contiguity of the nasal cavities with the paranasal sinuses. They are often late diagnosed due to similar symptoms of sinusitis: nasal discharge, pressure sensation in the midface, nasal obstruction, difficulty breathing through nose and sometimes nosebleeds. Patients are usually alarmed when the tumors are in late stages determing specific symptoms for cancers (double or blurred vision, tearing, loss of vision, loosening and numbness of the upper teeth, eye bulging, bleeding, blocked nose, anosmia) or even extremely advanced stage lesions (the inability to open the mouth, hypoacusia, headaches, otalgia, mental status changes).

Frequent risk factors of the carcinogenesis of various types of sinonasal malignant tumors are: exposures to industrial smoke, wood dust, nickel refining, exposure to mineral oils, chromium, isopropyl oils etc (Binazzi et al., 2015). Even through recent studies demonstrated a higher incidence of nasal cancers in cigarettes smokers, tobacco is not considered yet to be a significant etiologic factor (Benninger 1999, Caplan et al., 2002). Neuroimagining evaluation, intensive perioperative care, advanced surgical techniques and adjuvant treatment are constantly improving the results of patient evolution (Caplan et al., 2002).

Because the tumours proximity to vital structures (brain, optic nerves, and internal carotid artery), they pose significant challenges for their treatment and may be the source of significant morbidity to the patients. Particulary challenging for the treatment of these tumour represents the assessment for the invasion of important anatomical structures such as the orbit and skull base, expanding the boundaries of the classic surgical techniques with improved strategies to deliver adjuvant radiation, which substantially improved the outcomes in patients with malignancies of the sinonasal tract and skull base (Banuchi et al., 2015).

The primary concern in choosing the surgical approach should consider the oncological principles: en bloc excision with safe margins of resection and secondary, a good visualization, the ability to achieve hemostasis, manage potential vascular complications and reconstruction surger y.

- **Cranio facial approach**

The primary concern is adherence to oncological principles: en bloc excision with adequate margins. Secondary concerns include visualization, the ability to achieve hemostasis and deal with vascular complications, and reconstruction. The primary concern is adherence to oncological principles: en bloc excision with adequate margins. Secondary concerns include visualization, the ability to achieve hemostasis and deal with vascular complications, and reconstruction. The primary concern is adherence to oncological principles: en bloc excision with adequate margins. Secondary concerns include visualization, the ability to achieve hemostasis and deal with vascular complications, and reconstruction. The gold standard approach for sinonasal tumours extended to the anterior skull base is the cranio facial resection with the dissection of the tumor by frontal craniotomy, making possible the en bloc removal of the tumour. This technique also allows direct access for reconstruction of the skull base defect with a pericranial flap. The transbrow approaches and subfrontal approaches have decreased brain retraction, facial scarring and minimized the morbidity percentage (Lee 2015).

The subcranial approach is an adjustment of traditional craniofacial resection that provides almost similar broad access to the anterior skull base, but with lower mortality and morbidity. It is a safer and more effective technique to successfully treat advanced sinonasal tumours with anterior skull base extension. Combination of transfacial and transcranial procedures in order to allow broad exposure of the anterior cranial fossa and subcranial compartment. This procedure still involves a high risk of postoperative complication. The main limitation of this approach is the need for frontal lobe retraction, which may lead to encephalomalacia, brain edema, the presence of the cosmetic inconvenience, and subdural bleeding, especially in elderly population.

The subcranial approach have multiple advantages: wide direct exposure of the anterior skull base from anterior to posterior, allows simultaneous intradural and extradural tumour removal, does not require facial incision, minimal frontal lobe manipulation but there is a high risk of bone osteonecrosis post radiotherapy (Figure 1.22.).

Figure 1.22. Different external approaches/incisions

Physicians encounter great challenges when dealing with malignancies of the paranasal sinuses. An ideal method for tumors that involve surrounding soft tissue, the palate or the orbit is a transfacial or craniofacial approach, that allows a wide resection, even en bloc. Some of the standard transcranial approaches include a frontotemporal craniotomy and a sub-basal variation of frontal craniotomy.

Although modern surgery techniques are continuously improving, traditional open surgical approaches still remain the golden standard in certain tumors. This is the reason why skull base surgeons need to permanently improve their technical skills in order for them to be able to manage situations in which endoscopic techniques are insufficient due to anatomical constrains.

- **Endoscopic approach**.

Endoscopic surgery has been used in rhinosinusitis surgery since the 1980s (Tichenor et al., 2008). As the knowledge and experience with endoscopic surgery has improved, and the image guidance systems and surgical instruments for endoscopic surgery have evolved, endoscopic surgery has been increasingly used for the treatment of benign tumors and as experience with benign tumor surgery evolved, endoscopic surgery was adapted for the treatment of malignant tumors (Snyderman and Carrau 2008).

This approach is classified into saggital (frontal sinus to C2) and coronal (midline of the roof of the orbit (anterior), the floor of the middle cranial fossa (middle) and the jugular foramen (posterior) offers direct access to the ventral skull base, while eliminating the need for the manipulation of neurovascular structures. This type of approach is indicated in the resection or debulking of neoplasms (benign and malignant), decompression of neural structures and reconstruction of skull base defects.

Complex skull-base pathology has benefited from a great evolution of minimally invasive endoscopic techniques which has facilitated a good management and surgical outcome (Kwon et al., 2010). By using the endoscopic approach, there are multiple advantages: no external incisions or scars, improved quality of life, significantly reduction of postoperative pain and discomfort, shorter operative times and fewer days of hospitalisation, superior magnification, distal illumination and visualization of the surgical target. Furthermore, there is a lower risk of neurovascular injury, incomplete removal of the tumor or inadequate reconstruction of a dural defect.

The endoscopic technique has proved that it certainly has an important role in the management of patients with sinonasal and anterior skull base malignancies and it is essential for contemporary skull base surgery (Lee 2015).

However, endoscopic surgery has its limits in the treatment of patients with sinonasal malignancies. Hemostasis is indispensable for endoscopic visualization of the anatomical structures. Improved visibility of the surgical field consist in controlled hypotension and reduction of intraoperative bleeding which must be considered during the treatment planning. Also, the preoperative preparations must include the optimization of comorbidities and cessation of anticoagulation therapy (Amorocho 2016). Moreover, the surgeon must have the proper training, expertise and experience and the ability to reconstruct the resulting defect.

Complete endoscopic surgical resection followed by radiation therapy have drastically minimized the local recurrence, morbidity and cosmetic deformity (Buchmann 2006). The microscopic view provided by endoscopy, with or without complementary approaches, allows the complete removal of the tumour.

- **Combined approach**

The goal of surgery is complete removal of all tumor with clear resection margins while maintaining the key oncological principles (Roxubury et al., 2016).

Overall, surgical planning using both open and endoscopic approach has better outcomes and surgical performances.

Currently, the improved craniofacial surgical techniques, the advanced technology and equipment, high-quality imaging and good interdisciplinary management may improve the appearance of the face after surgery (Eskander et al., 2017). The main purpose of an efficient obstructive prosthesis for a patient who has had the hard palate removed is to create a barrier between the nasal cavity and the mouth, main- taining good speaking and swallowing functions (Suarez et al., 2008, Mello et al., 2012). The defect can be repaired by using skin grafts, bone grafts, flaps and even facial prostheses, in order to achieve satisfac- tory functional and aesthetic results. The prostheses are designed and adjusted by a maxillofacial prosthodon- tist, who is trained to construct devices that replace the anatomical structures of the head and neck, including those in the oral cavity, adapted to the requirements of each patient (Paprocki 2013).

Nowadays, the three-dimensional printing is becoming increasingly important and useful in medicine and especially in the surgical field. The current clinical value of 3D printed surgical guides in resection and reconstruction after surgical treatment of sinonasal tumours is under constant development. The 3D printed surgical guides may significantly improve the postoperative functional and aesthetic results after resection and reconstruction of sinonasal tumours and can reduce the incidence of complications. Furthermore, the 3D printed cranial prosthesis are simple, feasible and represent an useful solution that may significantly improve the cosmetic outcomes. Moreover, it seems that it has the potential to decrease perioperative complications like infections and resorptions, and also, it lowers the morbidity rate.

Three-dimensional printing may allow otorhino- laryngologists to remove the maxillary anterior wall and provide the reconstruction using the 3D print custom cranioplastic prosthesis during the reminder of the intervention (Evins et al., 2017).

Furthermore, in office virtual surgical planning using 3D, for creating surgical models and guides seems to be an beneficial method and allows for a more cost-effective and less time consuming method. This also improves intraoperative efficiency, surgical precision. Overall, it lowers the cost for different types of craniofacial and reconstructive surgery (Mendez et al., 2015).

After extensive resection, a large defect results which must be covered. There are various methods available such as skin grafts, local or distant flaps or prosthesis. The primary reconstruction of soft tissue should reduce the operative morbidity, re-establish the integrity of the dura mater, and offer the patient an acceptable appearance. Facial reconstructive surgery must aim at a functionally and aesthetically rehabilitated patient. The performance of facial plastic surgery requires an understanding and the application of many important principles.

Usually, the difficulties in facial reconstruction come from the particular unique character of the face and the low availability of local matching tissues. The midface and orbitonasomaxillary complex is an intricate three- dimensional entity with important functional and aesthetic purpose. The principles of aesthetics and function are very important for successful facial cutaneous reconstructive surgery: local flaps must have an appropriate tissue donor sources, the mechanisms and dynamics should be well known, including the effects of tissue movement, and techniques for

scar camouflage. These principles may be difficult to apply to particular cases, determing the surgeon to look for new reconstructive options.

The use of different technological devices that allow the creation of three-dimensional models is in constant evolution, allowing a greater application of these technologies in different fields of health sciences and medical training.

The radical resection of the sinonasal tumours extensively invading the skull base appears justified and feasible under certain conditions. If there is the possibility for the patient to obtain a true benefit of this severe mutilation, he must have a reasonable chance of cure, otherwise the postoperative result should at least be compatible with reasonable quality of life. For this reason, immediate reconstruction of the cavity with soft tissue or prosthesis during the first stage of tumour resection is essential.

Reconstruction of the skull base is mandatory if the defect includes bones and dura mater because of the risk of cerebral fluid leakage. Various methods have been described for covering large sinonasal defects. Resurfacing of the wound with skin grafts is often unable to prevent infection.

3D printing represents an important part of the surgical practice and research area and has gained a lot of interest in the past few years. It has a wide variety of applications, from anatomical models, which can be used with success in surgical planning, to implants and other surgical features. Although 3D printing has numerous advantages, a cost- effectiveness analysis must be developed in order to establish a balance between the increased intervention costs and the benefits of the applications (Tack et al., 2016).

By depicting precise personalized anatomy, 3D printing brings important improvement in many fields of surgery, with a large variety of applications such as implants, prostheses and surgical planning. In addition, medical students and young doctors can use this technique for educational learning instead of using conventional cadaver. With numerous trials still ongoing, research is extended for multiple use, such as vascular grafts, ear reconstruction and developing in the area of skin, nerve and vascular graft preparation. However, 3D printing has its limitations consisting in high cost, long processing time and suboptimal accuracy 9Li et al., 2015).

In the field of otorhinolaryngology, 3D printing has been used for reconstruction procedures, prostheses, grafting and also educational training (provides an opportunity for young doctors to better visualize anomalies and to practice surgical techniques) (Crafts et al., 2017).

A challenge encountered by surgeons is endoscopic sinus surgery, due to complex and variable anatomy (Cobzeanu et al., 2014) and the risk of major complications. This is the reason why there is a need of creating and providing a 3D printed simulator of the nose and paranasal sinuses, in order for the young doctors to practice and assimilate better techniques (Alrasheed et al., 2017). The surgeon must be very careful to both function and anatomy when performing bony reconstruction of defects that were caused by resection of malignancy or trauma. Replacement of bone should be done in the functional anatomic position. Some of the principles of a successful facial cutaneous reconstructive surgery include: use of appropriate tissue donor sources, knowledge of the mechanisms and dynamics and the effects of tissue movement.

Moreover, surgery is a must, in the treatment of the majority of epithelial and salivary malignancies and recent studies have underlined the importance of postoperative oncologic applications. Also, non-epithelial malignancies, including the wide variety of sarcomas arising in this region, most commonly require multimodality treatment such as chemotherapy, radiation, surgery. In addition, due to surgical advances, complex tumour removal is now possible, along with an optimal reconstruction and cosmetic outcome. However, there is a need for additional clinical trials in order to properly evaluate the locoregional control and rate survival according to the currently available treatments (Day et al., 1995).

Among other available reconstructive options there is also the application of free-tissue transfer flaps, a safe and effective method for repairing large midfacial and cranio- orbito-facial defects[9], osteocutaneous free flaps are useful to restore contour and structural support for massive midfacial defects with insufficient bony support (Wells et al., 1995).

The aim of this paper is to prove that the 3D printing reconstruction of maxillectomy defects after resection of sinonasal tumour represents a good option with truly expectation of good functional and aesthetic results. Although, due to defect complexity and large number of reconstructive options, this is not yet the perfect solution. The individual assessment of the patient and the defect may provide the best method for the reconstructive planning.

1.5.2. Experimental parts

√ Combined approach

We reviewed the general principles in the surgical management of sinonasal malignancies, the technical aspects of open and endoscopic approach alone and highlighted the advantages of the combined approaches of the sinonasal tumors.

Furthermore, we selected one particular case of a 50 years old male patient diagnosed with inverted papilloma with frontal sinus invasion, who required combined surgical approach.

This patient was admitted to our clinic with complaints of nasal obstruction, fullness sensation and headache located to the frontal region. Past history revealed that the patient was treated twice before for similar complaints in other ENT Departments. No epistaxis, cervical lymphadenopathy or visual changes were declared by the patient. Clinical examination revealed a papillomatous mass to the left and right of the nasal septum with extension into the posterior and superior nasal cavity.

Additional investigations concluded a diagnosis of inverted papilloma with frontal sinus invasion (Fig. 1.23).

In this case a mixed approach is used as treatment for inverted papilloma with frontal sinus invasion, having better outcome than using the classical ones.

Because the invasion of the anterior wall of the frontal sinus the endoscopy alone doesn't give a good exposure and a complete resection. The external approach alone would allow complete resection but possible with some small parts (infracentimetric) left in place (Fig. 1.24, 1.24,1.26, 1.27). That's why, in our opinion, the combined procedure will give a complete exposure and a complete resection even of the hidden areas in the sphenoid and posterior ethmoid sinuses.

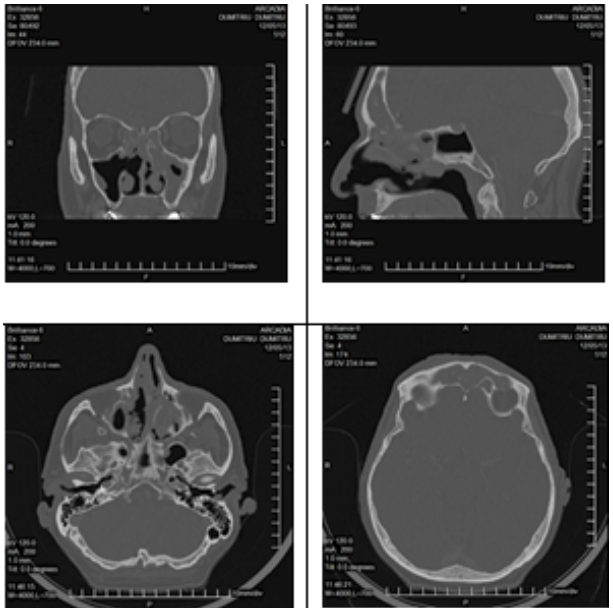


Figure 1.23. CT-scan

Combined approach was selected as the treatment of choice:

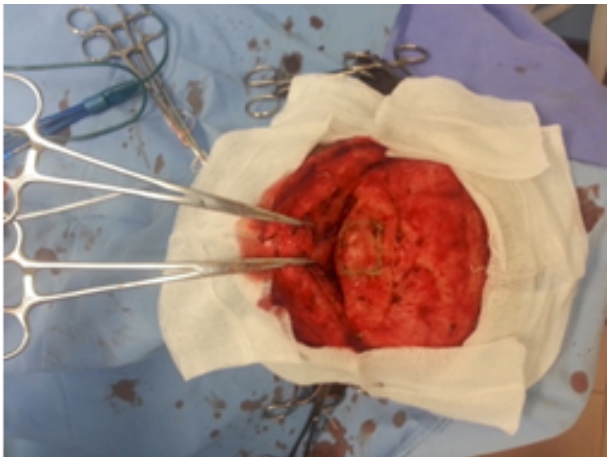


Figure 1.24. Marking the osteotomy area

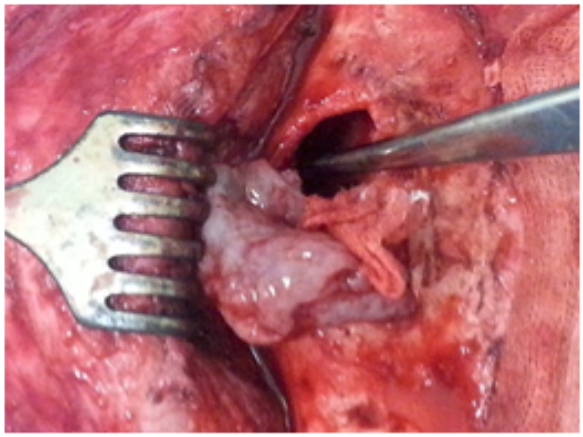


Figure 1.25. Revealing the tumour and showing the right frontal sinus

Figure 1.26. Cavity left after the complete excision

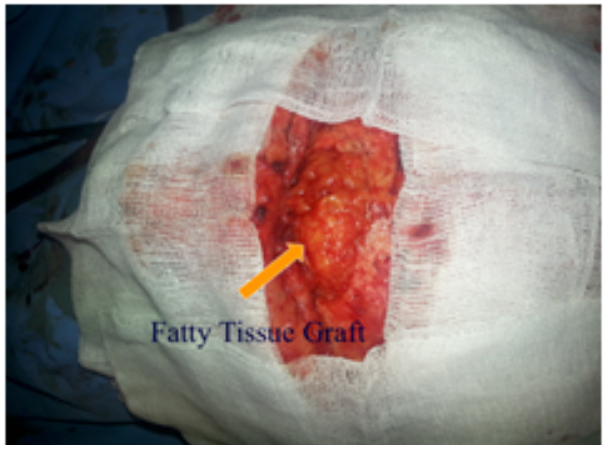


Figure 1.27.The exclusion of the frontal sinuses using a fatty tissue graft

- √ **3D Reconstruction**
  - o **First study**

We herein present the case of a 33-year-old male patient, with no significant comorbidities, who was diagnosed with sinonasal carcinoma treated with radical surgery in 2019 followed by radiotherapy treatment, who required a complex surgical approach and facial reconstruction.

This patient was admitted to the Department of Otorhinolaryngology and Head and Neck Surgery from 'Sf. Spiridon' Clinical Hospital in September 2019 with complains of left hemicrania, left nasal obstruction, left reflex otalgia, left clear rhinorrhea and recurrent left epistaxis. These symptoms had worsened during the last 5 months prior to hospitalization, with no improvement following medical treatment for maxillary sinusitis. Clinical examination at this stage revealed the following: Left exophthalmy, and a tumor of reddish color and soft consistency that occupied the entire left nasal cavity and was associated with an extensive swelling in the left maxilla.

Another CT scan was performed followed by cranial MRI examination that showed a large irregular tumor mass with heterogeneous density filling the left nasal cavity and involving the left

paranasal sinuses. An expansive osteolytic bone destruction pattern was observed in the ethmoid bone, medial and lateral walls of the left maxillary sinus and orbital floor. Left obstructive sinusitis and left exophthalmy were also present. The lesion was isointense on T1 weighted images and exhibited mild hypointensity on T2 weighted images (Figure 1.28). There was no evidence of metastasis on the total body scan.

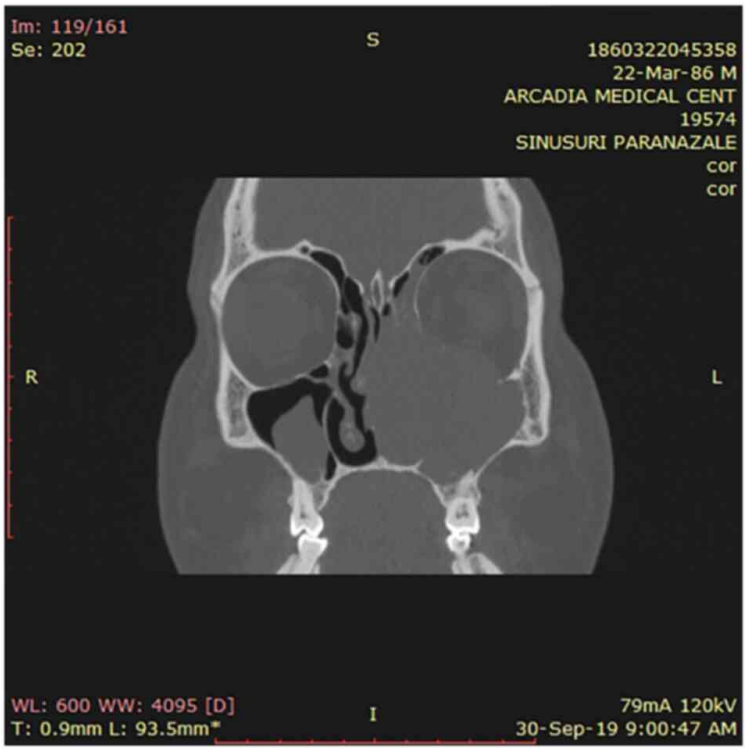


Figure 1.28. Paranasal CT prior to surgery revealed the presence of a mass in the left maxillary and ethmoidal sinuses, bone destruction of the orbital floor, nasal septum and the medial, anterior and inferior wall of the left maxillary sinus.

The clinical diagnosis was a malignant tumor of unknown type. A biopsy was performed, along with histopathological examination, which concluded that the tumor was a sarcoma composed of fusiform cells arranged in long intersected, irregular fascicles. Tumoral proliferation with moderate cellularity was observed, with non-homogeneous chromatin, elongated nuclei, some nucleoli, with a homogeneous, moderately pleomorphic cell population. Moderate mitotic activity was observed, with no tumor necrosis, and a Ki-67 index of 50%.

The final diagnosis of grade 2 fibrosarcoma (score 3 according to the Fédération Nationale des Centres de Lutte Contre Le Cancer 2022) was based on the clinical, radiographic and histopathological characteristics and immunohistochemistry examinations (smooth muscle actin was negative in the tumor cells and positive in the vascular walls; S100 was negative in the tumor cells and positive in the nerve fibers of the mucosal chorion; CD34 was negative in tumor cells and positive in the endothelial cells of intratumoral capillaries; CKAE1/3 was negative in the tumor cells and positive in the mucosa and glands of the chorion; and vimentin was positive in the tumor cells). The stage was T4N0M0 and the treatment of choice was extended surgical resection with facial reconstruction and radiotherapy.

The surgical strategy included radical maxillectomy of the left side with removal of the left inferior orbital wall and left nasal cavity, as well as left-side ethmoidectomy, in order to ensure clear tumor resection margins (Figure 1.29).

Figure 1.29. Intraoperative view of the exposed tumor.

The inferior orbital wall was replaced by a titanium mesh and a temporoparietal fascial flap was used to cover it, elevated and transposed to the orbit through a subcutaneous tunnel. An acrylic obturator prosthesis was especially designed and adapted to the patient's postoperative defect.

Resection of the cervical lymph nodes in this case was not deemed necessary.

Postoperatively, the patient underwent radiotherapy treatment with Cobalt-60 using a linear accelerator at a total dose of 50 Gy divided into 1.8-2 Gy per cycle of treatment over 5 weeks, with good preservation of the covering flap. The patient experienced no major side effects after the radiotherapy.

The patient was able to speak, eat and chew without any problems after 5 days. In addition, there were no difficulties with swallowing. The prosthesis allowed the patient to lead a normal life. He was satisfied with the postoperative cosmetic result and had no social problems or other complaints.

Control assessments were performed at 6 and 12 months postoperatively, showing no evidence of locoregional recurrence, systemic metastases or distant complications. The last check-up was in May 2021, revealing a good outcome for the patient.

This procedure achieved optimal reconstruction of the anterior wall of the left maxillary sinus and inferior orbital wall. Moreover, it has greatly improved the aesthetic postoperative outcomes (Fig. 1.30)

Figure 1.30. Postoperative clinical aspect.

- **Second study**

We discuss the case of a 48 years old male patient, with no important pathology associated, diagnosed with sinonasal cancer, which was treated with radical surgery in July 2017. This case required a multidisciplinary surgical team: ENT and Plastic Surgery.

The tumour was resected within oncologic limits and the anterior wall was replaced by a titanium prosthesis tailored and folded after the 3D printed mold (Figs. 1.31,1.32,1.33).

Figure 1.31. Exposing the tumour

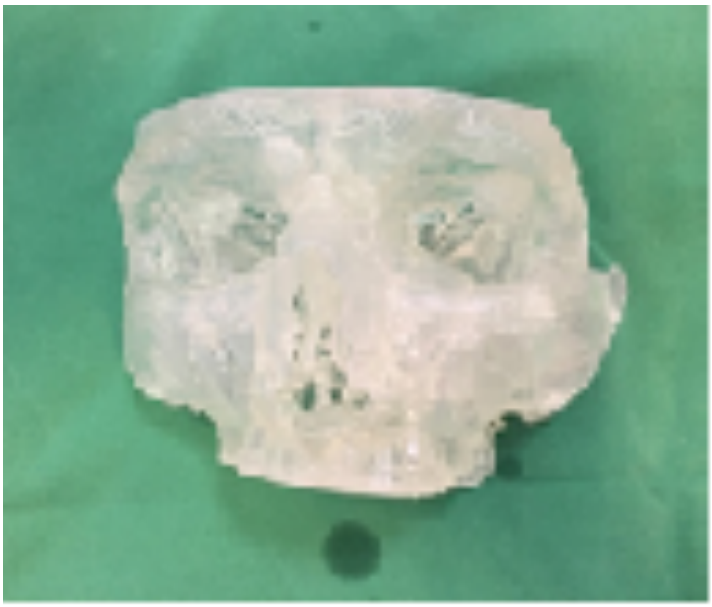


Figure 1.32. The 3D printed mold used for tailoring the titanium mesh

Figure 1.33. Intraoperative aspect

In our experience, this procedure was perfectly adapted to the reconstruction of the anterior wall of the left maxillary sinus and inferior orbital wall, providing easier reconstruction using titanium mesh which proved to be safe and effective (Figs 1.34, 1.35). This significantly reduced the operative time and improved the aesthetic outcomes of postsurgical reconstruction.

Figure 1.34.Placing the titanium mesh

Figure 1.35. Postoperative reconstruction aspect

That model was printed using the preoperative CT scan and reproducing the contralateral side. The wide, external approach allowed a large exposure of the tumour and a complete resection with clear margins. The titanium mesh that was used to replace the anterior wall of the maxillary

sinus, was previously folded over the 3D printed reconstructive model. Postoperative functional and aesthetic results were significantly positive. After the surgical treatment, the patient underwent radiotherapy with good preservation of the covering skin graft. There are no signs of recurrence or local and distant complications after 6 months.

1.5.3. Discussions

Sinonasal fibrosarcoma is a rare malignant tumor, with only 1% of fibrosarcomas occurring in the head and neck region, whereas the majority are found at the extremities (Patel et al., 2016). Final diagnosis and staging are based on histopathology, immunohistochemistry examination and on the imaging evaluation (Ekinci et al., 2018).

Sinonasal fibrosarcomas are associated with a high risk of local recurrence, but a low risk of distant metastasis (Plaza et al 2006). The indicated treatment with the best results is complete surgical resection of the tumor followed by reconstruction and combined with postoperative radiotherapy (Ekinci et al., 2018).

The biggest challenge of sinonasal reconstruction is to repair a complex three-dimensional structure, with the varying thickness of the tissue covering it, to restore its function and aesthetic appearance to the greatest possible extent (Gentile et al., 2009) and to achieve facial symmetry with a good aesthetic outcome (Summers and Siegle 1993). The prosthesis should provide a natural look adapted to the patient's physiognomy, with no visible defects or scars, and with minimal risk of complications. The local flap alone may not be able to fully reestablish all the essential functions (Little et al., 2009).

Particular cases, such as in the first study, highlight the dilemma when selecting the appropriate method of reconstruction for a young patient with a sizeable facial defect that may result after radical surgery, which must be resolved to the greatest possible extent. The combination of craniofacial prosthetic techniques with temporoparietal flaps has been proven to be a successful technique (Kim et al., 2010, Hu et al., 2017). However, this method may not be suitable for all patients undergoing sinonasal cancer surgery, as sometimes a simple flap alone may be a better option (for example, in elderly patients or those who cannot adapt or do not have the ability to remove the prosthesis) (Ali et al., 2018). Furthermore, certain activities, such as speaking and swallowing, may be more difficult with a flap than with an obturator prosthesis alone (Hoasejoe et al., 1994).

The reconstruction of the orbital floor is another complex issue after an extensive surgical resection. It is important to maintain the orbital contents in place, to prevent a later dystopia, diplopia or the risk of a non-functional eye (Santamaria and Cordeiro 2006). There must be enough soft tissue coverage of the bone or titanium mesh, complete isolation of sinonasal structures and an adequate orbital cavity depth in order to achieve a realistic appearance and facial symmetry (Gliklich 1998).

Another crucial factor that can change the reconstructive strategy is the patient's history. For those with a history of diabetes and tobacco use, there is a higher risk of skin necrosis, which may require adaptation of the approach. In addition, the patient's expectations and facial features

may change the surgeon's perspective. For example, older patients may not have the same appearance expectations and tissue availability as younger patients (Burget and Menick 1985). In order to achieve superior aesthetic and functional results, a local flap with appropriate tissue donor sources associated to an obturator prosthesis and a multilevel reconstructive method may be the most viable option. The location, size and depth of the surgical defect, and also adapting the technique to the patient's particularities and needs, represent important variables in this field (20). Moreover, it is mandatory to ensure good postoperative care and follow-up in order to optimize the final result. A compliant and well-informed patient regarding the importance of postoperative care may significantly improve the final cosmetic result (Gliklich 1998).

Due to the complexity of the facial structures and the surgical approach, the multidisciplinary team working on the case must be experienced enough to elaborate the entire treatment plan, to manage any potential intraoperative complications (for example, the craniofacial area is highly vascular and there is a high risk of hemorrhage, a large residual defect may be left after resection, nerve injury may occur, etc.), as well as postoperative complications. The nutritional status is crucial for the healing process, as the survival of the flap depends on both the vascular supply and the local defense mechanisms. In addition, all the steps involved in the management process must be thoroughly explained to the patients, including surgery and adjuvant therapy, to ensure proper compliance to treatment, which may result in an improved overall outcome (Burget and Menick 1985).

In the first study, the patient was young, with no remarkable medical history, and this allowed us to employ a multimodal reconstructive technique with better functional outcomes compared with either flap reconstruction or prosthesis alone. Good communication and patient compliance were established early during this process, which was also an important factor that allowed us to implement improved solutions.

Overall, the management of large craniofacial defects after advanced sinonasal cancer resection represents an important challenge for the majority of surgeons. In order to achieve satisfactory results, it is important to adapt the technique to each patient's particularities, cosmetic expectations, age and prognosis, while preserving vital functions. On the other hand, these challenges allow us to implement improved reconstructive techniques and methods, striving to preserve the patient's quality of life to the greatest extent possible.

1.5.4. Conclusions

Combined approach is superior to any of the simple approach alone. Endoscopic approach is useful to assess the limits of the excision and its minimal invasive natur results in fewer complications, faster recovery time and better cosmetic results. Unfortunately, not all lesions involving the sinonasal region and anterior skull base are accessible to sinonasal endoscopy. Therefore, it is mandatory for the surgeon to be able to convert every moment the endoscopy into an open approach.

Even though there are so many advantages of 3D printing, the additional expensive cost and the time needed to produce devices by current 3D technology still limit its widespread use in

hospitals. There is a need for a formal cost-effectiveness analysis. However, the development of guidelines to improve the reporting of experience with 3D printing in surgery is highly desirable

Chapter 2: The art of hearing – clinical and surgical approaching in middle ear pathology

2.1. State of the arts

Like other sensory organs that allow mankind to experience the environment, the ear has long held a special fascination for scientists. In mammals, the inner workings of the ear are encased in the hardest bone of the body. It contains the smallest bones, the smallest muscles, and the smallest, yet one of the most elegant organs of the body, the cochlea (part of the inner ear).

In 1740, Antonio Valsalva published his anatomical observations (Valsalva, 1740) on the human auditory system in which he pointed out the importance of the ossicular chain and the oval window for hearing and also observed that the innervation target for the auditory nerve was not the osseous spiral lamina as previously suggested by Professor Claude Perrault (Hawkins, 1988), but was instead the membranous portions of the cochlea and that these areas of sensory epithelium represented, in the opinion of Professor Valsalva, the true receptors of sound.

Progress in understanding the structure and function of this tiny, relatively inaccessible organ has been slow and the milestones broadly spaced. By the 15th century, the presence of the ear drum and two of the three bones of the middle ear had been noted. Almost 300 years would pass before Domenico Cotugno would find that, in contrast to the air filled middle ear, the inner ear is fluid-filled, in his report entitled “De aquaeductus auris humanae internae anatomica dissertatio”.

This liquid within the bony labyrinth that Professor Cotugno observed was termed “liquor Cotunni” to honor his discovery of this watery fluid and later became known as perilymph. Because Cotugno did not observe the inner membranous component of the cochlea, his observation of liquid within the inner ear only addressed perilymph located within the outer chambers of the cochlea, that is, scala tympani and scala vestibuli. It was Professor Cotugno's contention that there was a neural tissue partition suspended in the labyrinth's perilymph and that the acoustic nerves were like strings that oscillated within this perilymph and transmitted the sensation of hearing to the auditory centers of the brain.

The observation of a liquid present within the cochlea's inner membranous compartment, that is, scala media, would have to wait for the sharp observational skills of one of his anatomical colleagues, that is, Professor Antonio Scarpa. The name of Antonio Scarpa is most closely associated with Scarpa's Ganglion which is the peripheral ganglion of the vestibular sensory epithelial receptors and so named to honor the anatomical contributions of Professor Scarpa to inner ear anatomy. The name of this famous 18th century physician-anatomist has also been closely associated with the early descriptive anatomy of the bony and membranous labyrinths with the first

identification and detailed description of the human bony and membranous labyrinths published by Professor Scarpa in 1789.

His work entitled “Anatomicae disquisitions de auditu et olfactu” (Scarpa, 1789) was published while he was Professor and Chair of Anatomy at the University of Pavia. In this publication, Scarpa described in detail the anatomical features of dissected human membranous labyrinths aided by his dissection of the inner ears of animals and birds. Antonio Scarpa's descriptive anatomical work on the vestibular portion of the human inner ear with three curvilinear canals located in the bony portion of the vestibular labyrinth encasing three membranous semicircular canals with associated ampullae was presented in his original 1789 publication. He noted the attachment of these semicircular ducts to the mucosal lining cells that invest the walls of the bony canals and the association of these semicircular canals with a utricle (termed by Scarpa as a common cavity in relationship to the semicircular ducts) and the presence of a saccule (referred to by Scarpa as a small spherical vestibular pouch). Innervation of the three ampullae and the maculae of both the utricle and the saccule were described as occurring via fibers emanating from the acoustic nerve. He described the vestibular (Scarpa's) ganglion as a small, plump, reddish chamber enclosed within the middle of the acoustic nerve. Scarpa based on his anatomical observations of the innervation of the inner ear by what he understood to be various branches of the auditory nerve mistakenly attributed the sense of hearing to all the sensory receptor structures that he had observed to form the membranous labyrinth which included all the vestibular sensory receptors.

In Scarpa's anatomical studies of the cochlea, he describes in detail the osseous spiral lamina, the series of fine nerve fibers that emanate from the cochlear nerve, and the presence of the three scala, that is, media, vestibuli, and tympani, with a connection between the scalae tympani and vestibuli via a small apical turn area of communication termed the helicotrema. It was Antonio Scarpa who also noted the presence of a clear fluid within the semicircular ducts of the canals and also present within the cochlea's scala media which he called “Scarpa's fluid,” now known as endolymph. This represented a major advance that would at a later date aid in our understanding of cochlear function. Antonio Scarpa was a gifted anatomist and also a gifted artist with all his descriptive narrative of inner ear anatomy accompanied by his excellent drawings that depicted dissected specimens of cadaver temporal bones revealing the structure of both the bony and membranous labyrinths.

His very important contributions to the early understanding of the anatomical structure of the human inner ear and a description of his professional life can be found in a more recent publication by Canalis et al. (2001). Another important contribution to inner ear anatomy by Antonio Scarpa occurred when he was still at the University of Moderna, Italy and was performed prior to his descriptive work on the membranous labyrinth (Scarpa, 1772). This work involved the anatomical aspects of the human round window membrane and addressed the structure–function of this membrane with a translation of this work found in a paper by Sellers and Anson (1962). Professor Scarpa suggests in his book on “Anatomical Observations on the Round Window” that it was Professor Fallopia at the University of Padua who first described both the oval and the round windows and was responsible for the naming of both of these inner ear structures (Fallopia, 1562;

Sellers and Anson, 1962). Antonio Scarpa referred to the oval window as the secondary tympanum and in addition to a detailed description of its anatomy; he suggested that this membrane covering the round window opening acted along with the oval window as a transmitter of sound energy into the cochlea hence his reference to this structure as the secondary tympanum. Antonio Scarpa provided a detailed anatomical description of both the round window membrane and its attachments as well as a similar detailed description of the niche in which it is located. According to Scarpa, Valsalva was a strong proponent of only the oval window in cooperation with the tympanic membrane and the ossicular chain for the transmission of sound energy into the cochlea (Valsalva, 1740) while Scarpa developed a strong argument for an additional contribution from the round window via the sound waves created within the tympanic cavity (Scarpa, 1772). It has now been shown that indeed the path of sound transmission proposed by Valsalva was correct with ossicular coupling via the oval window providing the major conversion of sound wave energy into fluid wave energy within the cochlea.

Acoustic coupling that transmits sound energy to both the round and oval windows is now known to provide only a very small input from the sound energy within the middle ear cavity, therefore in a normal functioning middle and inner ear, the dominant transfer of sound energy occurs through the actions of the tympanic membrane/ossicular chain and oval window-stapedial footplate route (Rosowski and Merchant, 2005). It is important to note that all of Antonio Scarpa's descriptive anatomies of the bony and membranous labyrinths were accomplished without the aid of either advanced histological techniques or a compound microscope and that all the illustrations which accompanied his descriptive text were his own hand drawn illustrations.

A century later Ernst Reissner described the presence of two distinct fluid compartments in the cochlea. Improvements in microscopic methods during the 19th century led to Alfonso Corti's painstaking description of the cells comprising the sensory receptor organ of the inner ear (Depew 2008).

The World Health Organization (WHO) estimates that 466 million people or about 5.5% of the population suffers from some degree of hearing loss. While this number is estimated to rise due to increase in population and more exposure to loud noises, among other factors hearing loss is not a new issue for humans. One of the greatest factors is that in the past our life expectancy was much shorter. Only about 100 years ago our life expectancy was 60 years old and now it averages at 78. Many people don’t begin to experience issues with hearing until 65 which greatly increases the number of people dealing with hearing impairment these days. Even so, we have dealt with hearing loss since we have had the potential to hear. Let us explore early artifacts that inform us of how our ancestors lived and treated hearing issues throughout history to get us to this point in hearing technology (Lam 2004).

Hearing loss may be either partial or total. This may be a result of injury or damage, congenital disease, or physiological causes. When hearing loss is a result of injury or damage to the outer ear or middle ear, it is known as conductive hearing loss. When deafness is a result of injury or damage to the inner ear, vestibulochoclear nerve, or brain, it is known as sensorineural hearing loss.

Causes of conductive hearing loss include an ear canal blocked by ear wax, ossicles that are fixed together or absent, or holes in the eardrum. Conductive hearing loss may also result from middle ear inflammation causing fluid build-up in the normally air-filled space, such as by otitis media.

Today hearing loss in the US is estimated to affect as many as 48 million people and is expected to rise to 1 in 10 people in the next 30 years. While there is no cure for the most common forms of hearing loss, hearing aids are found to help combat the dangerous effects of hearing loss. These tiny digital devices have come a long way throughout history, helping to reduce strains on relationships, and prevent chronic depression, anxiety and cognitive decline associated with unaddressed hearing loss. To understand the amazing advancements, we've made in hearing care it's important to remember from where we've come.

The earliest instances of hearing loss were discovered in skeletal remains dating over 10,000 years ago in the *Shanidar Caves in Iraqi Kurdistan*. Archeologists found exostoses, which are bony growths in ear canal that can cause conductive hearing loss.

The earliest written document historians have uncovered which discusses hearing loss dates back to *ancient Egypt*, which spanned from 3100 BC to 320 BC. The document was recorded in an ancient medical journal called the Ebers Papyrus and discussed a remedy for the "Ear-that-hears-badly. The remedy described a concoction of olive oil, red lead, ant eggs, bat wings and goat urine which was to be inserted into the ears. The effects of the treatment may not have been successful, however olive oil is still used as a at home remedy for clearing a minor amount of earwax in the ear canal.

Ancient Egypt spanned 30 centuries from 3100 B.C. to its conquest by Alexander the Great in 332 B.C. The earliest known written record of hearing loss was noted in the Ebers Papyrus, a medical journal dating back to 1550 BC. The text describes a remedy for "Ear That Hears Badly" which includes injecting olive oil, red lead, ant eggs, bat wings and goat urine into the ears. While many of these ingredients may have been ineffective, olive oil in the ears is still sometimes used to loosen up blockages of earwax as a home remedy.

In the early 10th-century household names and philosophers, Plato and Aristotle both spoke of hearing loss. However, their comments within the context of what we understand about the hearing impaired and deaf community now sound uncaring and incorrect. They both observed that "ability to reason was intrinsically linked with the ability to speak." This suggests that they believed that a person's hearing ability was linked to a lack of intelligence. Fortunately, we now understand that while people with hearing loss don't always hear what you say it doesn't link to their intellect and these communication issues can be helped with the diligent use of hearing aids (Tsucalas et al., 2017).

Sign language is an amazing language for the deaf and hard of hearing that has its origins from the monks of ancient Burgundy in the 10th century. Monks who committed to a vow of silence created hand signals to communicate which eventually became known as Cluniac sign language (Feldman 2007). This nonverbal language spread across the monasteries of Europe with many noting that the language 'would have been sufficient if they lost the use of their tongues'. This was the inspiration for what eventually became modern sign language.

Early physician-anatomist Andreas Vesalius in his work entitled “De humani coporis fabrica” (Vesalius, 1543) and Bartolome Eustachi in his work entitled “Epistola de auditus organis” (Eustachi, 1564) provided early but incomplete descriptions of human inner ear anatomy and both of these physician-scientists' supported the theory postulated by Aristotle (Ross, 1906) and later by Galen (Galen, 1542) that the inner ear was filled with a type of purified air, that is, “aer ingenitus.” The earliest forms of hearing aids were ear trumpets made from animal horns and sheet iron, derived in the 17th century. By the 18th century they were mass-produced. It wasn’t till Alexander Graham Bell’s invention of the telephone in 1876 that inventors were able to incorporate this technology into the first amplified electronic hearing aids. In 1889 Miller Reese Hutchison introduced the first electronic hearing aids (Jagannathan et al., 2009).

The invention of the telephone created the opportunity to use this technology in the world’s first hearing aids. The first commercial electronically amplified hearing aids were produced in 1913 by the Siemens company, who still manufactures hearing aids today.

In 1956, one of the most thorough ultrastructural analyses of the anatomical differences in the two different types of vestibular sensory hair cells and their pattern of afferent and efferent innervation was provided by the elegant and thorough ultrastructural study of the cristae ampulares from the vestibular labyrinths' of guinea pigs (Wersäll 1956). This was the Docent thesis of Jan Wersäll as he studied in the famous Histology Department of the Karolinska Institute and this was accomplished in the same laboratory where Magnus Gustav Retzius performed his exceptional anatomical studies on the comparative anatomy of inner ear sensory receptors and reported on the anatomical structure of the human auditory receptor (Retzius 1884). Docent Wersäll summarized his characterization of the two different type of vestibular hair cell that he observed in the guinea pig crista in a simple but elegant schematic drawing found in Fig. 9 of his thesis that was published as Supplement #126 in Acta Oto-Laryngologica (Wersäll 1956).

As the 20th century continued innovations in hearing aid technology started to improve at a faster speed than the previous 100 years before that. This may have been in part due to the need for smaller, portable electronics to aid in World War II. This propelled the availability of hearing aids which were smaller, lighter and more durable using transistor technology developed by the invention of transistors in 1947. The transistors were smaller and used less battery power than the previous technology, which was vacuum tubes. However, when these were introduced in 1913, for the World Fair, these devices were large and cumbersome. By 1920 vacuum tube technology improved the portability and function of hearing aids and was the standard until the mid-1940 with the invention of transistor technology developed for WWII. With the invention of microprocessors in the mid-1970s and ’80s gave us faster lighter and more powerful hearing aids who used analog technology.

The 1990s welcomed the first digital technology which continued to shrink the size of hearing aids while adding power and reducing feedback. Digital hearing aids continue to improve the ability to address individual hearing loss more specifically (Sapci et al., 2007).

The next major development in hearing aids did not come about until the 1970s with the invention of the microprocessor. A microprocessor is described as a computer processor where the data processing logic and control is included on a single integrated circuit. This means that a much

smaller piece of technology can create much more power and precise amplification. By 1982 the City University of New York had developed the first hearing aid using microprocessor technology. It used FM technology to transmit the audio signal to the inner ear, controlled by a microprocessor. It wasn't until 1995 that the first all-digital hearing aid was developed by Oticon. Digital hearing aids convert sound waves into numerical codes similar to computer codes, then amplify them. Digital technology is still being developed and used in today's hearing aids; thought the newest features they offer may surprise you. Today's hearing aids offer multiple settings, noise suppression and even artificial intelligence. Just imagine what hearing aids will offer in 50 years as technology rapidly advances.

Today's digital technology can not only address specific hearing loss but suppress background noise, mask tinnitus, link wirelessly to telephones and media as well as use artificial intelligence to adapt to your surroundings.

This research direction has been materialized by publishing the following articles:

1. Pertea M, Ciobanu P, Poroch V, Velenciuc N, Lunca S, Anghelina F, **Palade DO**. Arterial only anastomosis associated with modified Baudet technique in ear replantation. Case reports and literature review. Medicine 2021;100:13(e25357).
2. Gheorghe L, Negru D, Cobzeanu MD, **Palade OD**, Botnariu EG, Cobzeanu BM, Cobzeanu ML. The Diagnostic Accuracy of Pure-Tone Audiometry Screening Protocols for Vestibular Schwannoma in Patients with Asymmetrical Hearing Loss—A Systematic Review and Meta-Analysis. Diagnostics 2022, 12, 2776. https://doi.org/10.3390/ diagnostics12112776.
3. Anghelina F, **Palade DO**, Bologa R, Camen A, Patru A, Anghelina L, Hainarosie R, Voiosu C, Osman A. Plastic ventilation tubes and their impact on middle ear pathology. Mater. Plast., 59 (1), 2022, 148-155.

2.2. New perspectives in replanting

2.2.1 Introduction

The description of a "perfect" human face takes into account the relationships between its elements: eyes, ears, nose, and mouth (Mizumoto et al., 2009).

The human ear confirms to the shape of the Fibonacci spiral/helix sequence (Ricketts 1982, Gupta et al., 1998, Marinković et al., 2012). The design channels the sound in a very directional and organized way. Thus, the ear is a structure with complex shape and function, playing an important role in facial esthetics (Marinković et al., 2012). Its absence has a major emotional impact on the patient, and the reconstruction of such a structure is a real challenge for any surgeon. Total, isolated, post-traumatic ear amputation is not a common injury (Senchenkov and Jacobson

2013). Often, such an injury is associated with other types of traumas to the cephalic extremity, which will be brought to the fore. Total auricular amputation can result from animal bites, traffic or workplace accidents (Gailey et al., 2020). Over time, the complexity of reconstruction has resulted in the description of many reconstructive techniques useful in cases of total or partial ear amputations. Nonvascularized reattachment of avulsed ears as a composite graft was reported as early as 1898 (Brown 1898, Purcell 1898). Unfortunately, the anatomical conditions, auricular vascularization, the size of the blood vessels at this level (0.3–0.7 mm) and the difficulty of identifying them and distinguishing arteries from veins, and last but not least the difficult access and the small size of the surgical field do not allow, in many of these cases, the performance of microanastomoses at the arterial, and especially venous level (Mutimer 1987, Turpin et al., 1988). That is why the described techniques aim at improving the vascularization in case of circulatory failure or insufficiency, and also at treating venous congestion due to the insufficiency of venorraphy or impossibility of performing it. The use of retroauricular and cervical flaps and of biochemical or medical leeches, respectively, proved beneficial in terms of the outcomes of ear replantation (Magritz and Siegert 2014, Watson and Hecht 2017, Hussey and Kelly 2010). At the end of 2017 at least 87 ear replantations were reported over 37 years, the first successful ear replantation being reported in the literature in 1980 by Pennington et al. (Dvořák and Stupka 2002). We reported the cases of 3 male patients aged 45 to 58 years old with total ear amputation (grade IV auricular injury according to Weerda classification) following workplace accidents. In all 3 cases only arteriorraphy was performed, and in the immediate postoperative period medicinal leeches were used to treat venous congestion. To improve vascularization, besides arterial reconstruction, incisions were made into the cartilage (Baudet technique) associated with skin excisions for increasing the cartilage-recipient site contact area. In all cases, the outcome was good, with the survival of the entire replanted auricle.

2.2.2. Material and methods

We reported the cases of 3 male patients, all of them were the victims of similar workplace accidents resulted in total ear amputations. All three previously mentioned patients gave their consent to participate in this study and authorized the photo- graphs for publishing. The approval of the Hospital Ethics Commission was obtained (for each of three cases), according to international regulations.

2.2.3. Results

2.2.3.1. Case 1

A 45-year-old male patient, smoker for over 20 years, who was admitted in the Emergency Room 3 h after a wood-saw accident. The diagnosis at admission was work trauma with complete left ear amputation (grade IV ear injury according to Weerda classification) and left-hand metacarpal II and III closed fractures. The amputated segment was transported in good condition. Patient was informed about surgery, the technique used and the possible complications and failure

of the surgery. The patient signed a written informed consent. Ear, Nose and Throat (ENT) examination did not identify associated injuries in the other ear segments. Emergency surgery was performed under general orothracheal anesthesia. For the microsurgical time, operating microscope, microsurgery instruments, and 10-0 nylon suture wires were used. For skin suture 5-0 nylon was used. Only one end-to-end arterial microanastomosis was performed. Venous anastomosis was not possible because the ends of the veins to be anastomosed could be identified concomitantly in the segment to be replanted and recipient area. Surgery began with the preparation of the amputated segment by debridement of the wound edges and identification of an arterial stump to perform anastomosis. The arterial stump at the level of the recipient site was identified and prepared, too. Next, we proceeded to the excision of an arc-shaped skin band in order to expose a larger cartilage surface. A similar skin excision (approximately 4 mm wide) was performed at the level of the remaining post- amputation defect. Thus, we obtained a wider contact surface of the cartilage with a larger well-vascularized bed and less tissue to be revascularized. Cartilage incisions were made at different depths and levels (as in the Baudet technique), some of them are transfixation incisions. End-to-end arterial microanastomosis was done with 10-0 nylon thread. A venous stump could not be identified in the replanting segment. Surgery was completed with 5-0 nylon skin suture with minimum stitches. Because of the poor blood flow to the ear, systemic anticoagulant treatment with weight-based heparin, dextran 40 and warm room was used. Venous congestion in the immediate postreplantation period, consequence of the absence of a draining vein, was treated with medicinal leeches. The application of medicinal leeches was initiated at 6 h postoperatively and was maintained for six days. The hirudotherapy was preceded by the psychological prepara- tion of the patients, ruling out blood diseases, infections, hepatorenal diseases or malignancies, as well as a history of chronic treatments with anticoagulants or immunosuppressants. Between medicinal leech therapy (MLT) sessions heparin was administered locally. Antibiotic therapy was administered for the prophylaxis of infections due to the most often intense contamination of lesions but also for the prophylaxis of possible *Aeromonas hydrophila* infections due to the use of medicinal leeches. Ciprofloxacin 500 mg/day was used. Systemic anti- coagulation treatment was also given in this case. The sutures were removed after 21 days. Hospitalization time was 10 days.

2.2.3.2. Case 2

A 50-year-old male patient, non-smoker, who was admitted in the Emergency room at 2 h after a work accident (fall of concrete slab). The diagnosis at admission was work accident with complete right ear amputation, cervical spine cord contusion. The amputated segment was transported in a dry recipient. Patient was informed about surgery, the technique used and the possible complications and failure of the surgery. The patient signed a written informed consent. Ear, Nose and Throat (ENT) examination did not identify associated injuries. Neurosurgical examination allowed the emergency surgery under general anesthesia, recommending the permanent wearing of a cervical collar for 3 weeks. Surgery was performed under general orothracheal anesthesia. For the microsurgical procedure, operating microscope, microsurgery instruments, and 11-0 nylon suture wires were used. For skin suture 5-0 nylon was used. Only one

end-to-end arterial microanastomosis was performed. Venous anastomosis was not possible because the stump of the vein to be anastomosed could be identified in the segment to be replanted. The wearing of the cervical collar throughout the microsurgical procedure brought additional discomfort to the surgical team, the patient position on the operating table and neck immobilization making the positioning of the operating microscope being extremely difficult (Fig. 2.1.)

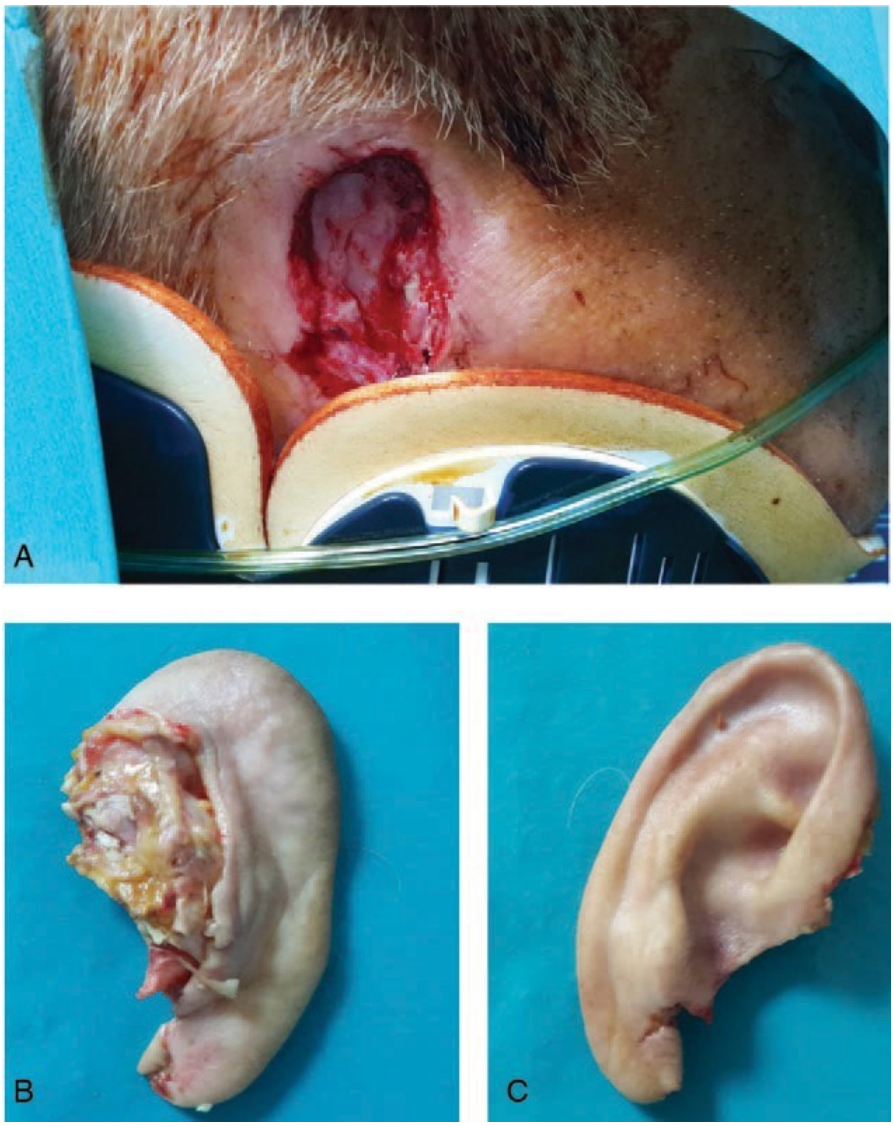


Figure 2.1. Total auricular amputation (A). Patient with total ear amputation and cervical spine contusion (with cervical collar) (B). Posterior aspect of the amputated stump (C). Anterior aspect of the amputated stump.

Surgery began, as in other cases, with the preparation of the amputated stump by debridement of the wound edges and identification and preparation of an arterial stumps to perform anastomosis. We proceeded to the excision of an arc-shaped skin band for exposing a larger cartilage surface. A similar skin excision was performed at the level of the recipient site. We obtained a larger contact surface of the cartilage with the recipient site. Cartilage incisions were made at different depths and levels (modified Baudet technique), some of them are transfixation

incisions. End-to-end arterial microanastomosis was done with 10-0 nylon thread (Figs. 2.2 and 2.3). Surgery was completed with 5-0 nylon skin suture. The surgery lasted 6 h. We also used systemic anticoagulant treatment with weight-based heparin, dextran 40. At 6 h postoperatively, the first signs of venous congestion was reported. Medicinal leech therapy was started at 10 h postoperatively, after the psychological prepara- tion of the patient and was continued for 5 days when there was no more venous congestion (Fig. 2.4). Hirudotherapy was supplemented by local administration of heparin.

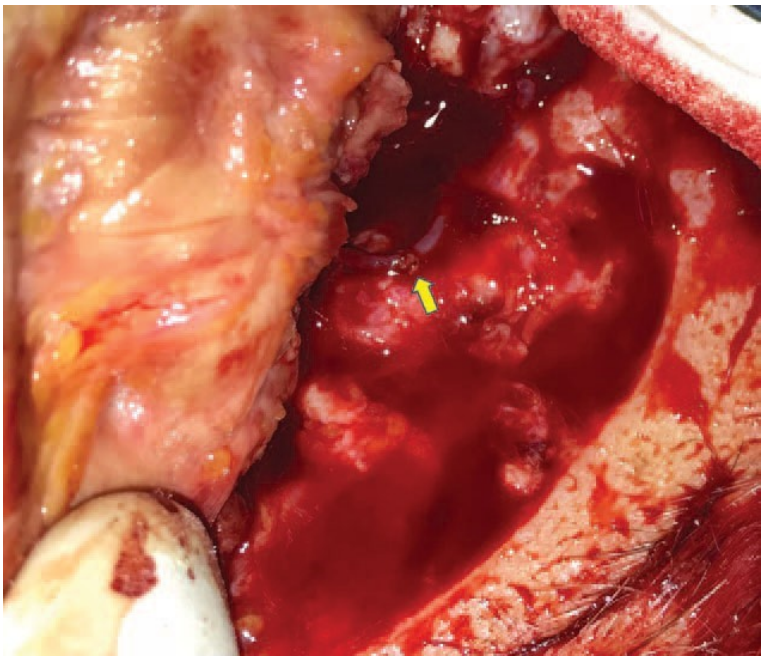


Figure 2.2. End-to-end arteriorraphy.

Figure 2.3. Surgical technique.

Systemic anticoagulation was also done. The sutures were removed after 14 days. Prolongation of operative time to 6 h was due to the technical difficulties related to patient and consequently of the position of the microscope, awkward posture of the surgeon, all related to the fact that patient had to wear the cervical collar. The patient remained hospitalized for a period of 12 days.

1.2.3.3. Case 3

A 58-year-old male patient, non-smoker, the victim of a work accident (falling from the same level and contact with a cutting object). He was admitted in the Emergency Room at 6 h after the accident. At the admission in the Plastic Surgery clinic the diagnosis was work accident with complete left ear amputation and sprained right ankle.

Figure 2.4. (A). Venous congestion of the replanted segment treated with medicinal leech therapy (hirudotherapy) (B). Appearance of the replanted ear after leeching on postoperative day 10 (C). Appearance of the replanted ear on postoperative day 21**.**

Table 2.1 - Results.

	Sex	Age (y)	Surgical technique	Leeches used	Moment of leeches application after surgery	Anti coagulant therapy	Time of surgery (h)	Ischemia/ necrosis	Blood transfusion	Infection	Viability of the replantated segment	Patient satisfaction
1	M	45	Only-artery anastomosis with cartilage incisions and skin excision	Yes	4 h	+	6	no	no	no	complete	Very satisfied
2	M	51		Yes	4,5 h	+	4	no	no	no	complete	Very satisfied
3	M	58		Yes	6 h	+	4,5	no	no	no	complete	Very satisfied

M = male, y = year, h = hours.

No other ENT lesions was identified. The consultation of an orthopaedic surgeon was necessary. He indicated and performed the immobilization of the sprained ankle. The operative steps were similar as in the other two cases, using the same tools and the same sutures. We performed only one arterial anastomosis with no vein anastomosis. We also performed an arc-shaped skin band excision at both stumps (approximately 4 mm wide) to increase the contact area of the denuded cartilage with the recipient site. The surgery lasted 6 h. Medicinal leech therapy was started 12 h postoperatively and was continued for 7 days, when the signs of venous congestion disappeared. We used systemic anticoagulant treatment with weight-based heparin, dextran 40. Antibiotic therapy was administered, as in all cases, for the prophylaxis of infections due to the contamination of lesions but also for the prophylaxis of possible *Aeromonas hydrophila* infections. We also used ciprofloxacin 500 mg/day. The patient was discharged on the 11- th postoperatively day. The sutures were removed after 14 days. In none of the study cases the great auricular nerve neuro-rrhaphy was performed.

Complete survival of the amputated segment was obtained in all cases, without areas of marginal necrosis or other compli- cations that would require reintervention or subsequent second-ary intervention for reconstruction. In none of the reported cases postoperative or leeching-related bleeding did not occur that required blood transfusions. No infections were recorded. During MLT, patients' complete blood count (Hb, Ht) was repeated and secretions were collected from both the suture path and from where the leeches were placed. All 3 patients were fully satisfied with the results, as they regained their bodily integrity and esthetic appearance of the face. At the last follow-up visit 12 months after replantation all 3 reported cases showed esthetic appearance of the ear comparable with the normal contralateral ear, and even without primary neurorraphy, are covered a protective sensitivity of the replanted auricle (Table 2.1).

2.2.4.Discussions

The first microsurgical ear replantation was performed by Pennington in 1980, after Buncke announced in 1966 the first experimental microsurgical ear replantation (Buncke and Schulz 1966). Over time, different classifications of ear trauma have been made. For clinical aspect Weerda proposed a classification into 4 grades (Punjabi et al., 1997). All cases included in the current report correspond to grade 4 in the Weerda classification (Weerda 2004). As to the non-microsurgical recon- struction of the ear, it has been done since 1898, when Brown, reattached the

amputated segment as a composite graft (Brown and Cannon 1946). The psychological impact on the patient with such a trauma was veryhigh and esthetics was the major concern. The importance of the ear as an essential element of facial esthetics, makes that in cases of total or partial ear amputation, the indication for replantation or reconstruction surgery to be an absolute one. That is why new reconstruction techniques have been reported over time, but microsurgical replantation remains the one with not only the best functional but also esthetic outcome (Adler et al., 2008, Ghassemi et al., 2013, Inbal et al., 2017). Although the techniques and used devices have evolved over time, microsurgi- cal ear replantation is still a real challenge for any microsurgeon or plastic surgeon. In 1966 Buncke and Shultz performed the first ear replantation in a rabbit, and in 1980 Pennington reported the first successful replantation in a patient with total ear amputation. In 2005, Steffen published a 25-year review (1980–2004) of ear trauma. 37 of the review cases were total ear amputations in which microsurgical repair was performed. Of these, in 14 cases venorraphy was not performed. Total recovery rate when venorraphy was not performed was 5 out of 8 cases, while when venorraphy was performed it was 13 out of 18 cases (Steffen and Frenzel 2015). Because this type of lesion is quite rare, a systematic review conducted by Momeni and published in 2015 showed that in the interval 1980–2013 in 40 articles 60 cases of ear replantation after total amputation were reported. Of these, in 19 cases (31.7%) only arteriography was performed (Momeni et al., 2016). Jung in 2013 also published a review of 52 replanted ears (Jung et al., 2013). At the end of 2017 Dvorak et al reported that at least 84 replantations had been described in the literature over a period of 37 years. In 2020 Gailey et al reported a review covering the interval 2017– 2020 of 132 cases of ear amputations. Most of these patients were aged 20–40 years (48%), followed by those aged 40–60 years (23%), the same age range as in our study patients. It is assumed that the rarity of this type of trauma is due to the fact that it is often included in polytrauma, in which there may be injuries of much higher severity.[14] In the current report, as in the other similar studies in the literature, this type of trauma is much more common among men. Good results have been also reported when replantation was performed 10 h after trauma (Liang et al., 2004). Microsurgical replantation in cases reported so far in the literature consisted of either restoring an artery and a vein, only an artery (as in our case reports), the use of a venous graft, arteriovenous shunt or arterialization of the venous system (Veseli et al., 2002, Momeni et al., 2014). A vein can be reconstructed by end to-end anastomosis, venous graft, or arteriovenous shunt. The success rate of a replantation when venorraphy is performed is 68%. Many authors choose to restore only one artery, and the treatment of postoperative venous congestion due to the impossibility of vein reconstruction or insufficiency or thrombosis of the reconstructed vein to be done by using biochemical or medicinal leeches (Bonastre-Juliá et al., 2017, Talbi et al., 2001, Weerda 2010, Baudet 1973). Venous congestion occurs in 75% of replantation cases. Venorraphy increases the operative time significantly but the chances of amputated stump survival are less. Classical replantation resulted in a replanted segment survival rate of 27% (Senchenkov and Jacobson 2013). The Baudet technique increased the chances of survival of the replanted auricle to 38% (Kraemer et al., 1998). Starting from the Baudet technique, using cartilage incisions, some of them transfixion incisions, we added to this procedure the increase in contact surface of the microsurgically transplanted cartilage with the well vascularized exposed (retroauricular) area

(also obtained by excision of a skin island), which can increase the chances of cartilage revascularization, adding imbibition as in the case of the composite graft. By increasing the exposed cartilage area by the excision of a 4–6 mm- wide skin island, the amount of tissue to be revascularized has also decreased. As in the cases described in the literature so far, therapy for venous congestion consisted of the use of medicinal leeches concomitantly with biochemical leech at the level of transfixion incisions made at the level of the replanted cartilage. In all our three cases, the resulting bleeding did not require blood transfusion, although in about 50% of the reported cases blood transfusion was required due to significant bleeding. According to reports, the duration of surgery for ear replantation varies between 4 and 6 h as in the present study. As in the cases described in the literature, we administered systemic anticoagulant therapy without the combined use of aspirin.[33] Prophylaxis by administering ciprofloxacin 500 mg/ day prevented a possible leech-related *Aeromonas hydrophila* infection. As in the cases reported in the literature, the patients who underwent ear replantation surgery were fully satisfied with the outcome. Also, as in the reported studies in the absence of great auricular nerve neurorraphy one-year restoration of sensitivity was quite satisfactory (Kraemer et al., 1998).

2.2.5.Conclusions

As with many other human body segments, the Fibonacci spiral/ helix sequence, with its complex, difficult to reproduce structure, underpins the shape of the external human ear. The ear is essential in the esthetic appearance of a person, its absence implicitly have a psychological impact. So far, none of the multiple reconstructive surgical techniques for the amputated auricle has been able to fully reproduce the shape of the ear. Therefore, microsurgical replantation is the gold standard of surgical treatment in cases of total ear amputation. Hirudother- apy is the treatment for venous congestion with very good results. We believe that cartilage incisions and the increased surface of contact between denuded cartilage and receptor site has an adjuvant role in ear revascularization. In all cases of total or partial ear amputation, efforts must be made so that the patients are satisfied with the appearance.

2.3. Cutout

2.3.1. Introduction

The chronic otitis media with effusion (OME) is defined by the persistence of the middle ear effusion for at least 3 months and consists of a challenge for ENT doctors to treat.

The first to introduce the use of plastic ventilation tubes for the treatment of chronic otitis media with effusion (OME) was Armstrong in 1954. The tube would ensure continuous ventilation of the middle ear, as well as proper drainage of the fluid located there (Armstrong, 1954). The tube was made out of fluoroplastic, a highly resistant fluoropolymer. A fluoropolymer is a fluorocarbon-

based polymer with multiple carbon–fluorine bonds. It is characterized by high resistance to solvents, acids and bases.

The great diversity of ventilation tubes regarding material, length, inside and outside diameter or means of placement has provided a background for extensive research. Ventilation tubes can be set in place for a short time, as the first treatment option with an extrusion rate of 6 to 18 months, whereas the long term ventilation tubes have an extrusion time greater than 2 years. The extended periods of ventilation associate an increasing rate of complications. Long term tympanostomy tubes are indicated in case of OME recurrence as a second option or in the case of ventilation problems of the middle ear, as in the case of persistent Eustachian tube dysfunction, this condition is especially relevant in young children (Lindstrom et al., 2004). The Armstrong Grommet, Paparella tube type I and the Shepard tube are ventilation tubes usually used for short periods. Representatives for long term usage are the Paparella tube type II, the Sheehy tube, the Reuter Bobbin tube and the Goode T tube. Some authors may consider the Shah tube useable for intermediate periods (Walker 1997).

After their insertion, the natural evolution of ventilation tube placement is considered to be that of lateral displacement towards the external auditory canal without any need for surgical management. However, when taking into consideration the particularities of each patient and their individual history, one cannot rule out the risk of tube retention or early extrusion, as well as other complications such as chronic otorrhea, tube obstruction, the accumulation of granulation tissue around the tympanostomy site or inside the ventilation tube itself, retraction pockets, perforations of the tympanic membrane or even iatrogenic cholesteatoma following removal (Sparks et al., 2020). A promising type of insertion that has been lately taken into consideration is the subannular insertion of the ventilation tubes (SAT). SAT represents a good option of placement when the tympanic membrane is too thin to support the grommet or in case of large perforations or retraction pockets, as well as in cases of adhesive otitis, chronic Eustachian tube disease when there is a need for long term aeration of the middle ear to obtain the resolution of the background disease (Saliba et al., 2011).

2.3.2. Materials and methods

In the current paper, we investigate the connection between ventilation tube usage, the materials out of which they are made, the techniques involved and how these factors may influence disease resolution rates.

2.3.2.1. Study inclusion criteria

We searched through the ScienceDirect database using key words such as “grommet cholesteatoma”, “tympanostomy tube cholesteatoma” and the PubMed database for “ventilation tube extrusion”, “ventilation tube quadrant”, “grommet extrusion rate”. Inclusion criteria were considered to be studies reporting data regarding ventilation tube (VT) type, time intervals between the insertion of the VTs and their absence from the tympanic membrane, whether by spontaneous extrusion or surgical removal, the presence of complications related to VTs such as recurrence of

otorrhea, VT related tympanic perforations, retraction pockets, tympanosclerosis and even cholesteatomas.

2.3.2.2. Exclusion criteria

The exclusion criteria we most often employed was the lack of access to full-text articles, also excluding the majority of abstracts that could not provide reliable data regarding the types of tubes used or the timespan of usage. We also excluded studies that included patients with craniofacial abnormalities. The search criteria were not limited to a certain time and we included all translatable languages. We used related articles found in Pubmed and ScienceDirect for their list of references to identify further relevant articles for the subject and this led to the extension of the search to Researchgate and DeepDyve for further full text articles.

2.3.3. Results and discussions

2.3.3.1. Ventilation tube placement

Previous recommendations regarding the placement of VTs avoided the PSQ (posterior and superior quadrant) because of its vicinity to the incudostapedial joint, the main placement of the tube in the AIQ (anterior and inferior quadrant) is regarded as first intention followed by placement in the ASQ (anterior and superior quadrant) for patients who need prolonged aeration of the middle ear. April et al conclude that the importance of prolonged ventilation should rely mainly on the design of the tube and not so much on its placement, as they encountered equal lifespans for VTs in a study conducted on 16 patients. An equally long time before extrusion was discovered for both types of placements (ASQ and AIQ) when type 1 Paparella tubes were used (Gibb and Mackenzie 1985, April et al., 1995). The Paparella tubes used were made out of silicone. Silicone is used in some ventilation tubes for its many useful characteristics that include low chemical reactivity, low toxicity, non-stick properties and its unfriendliness towards microbiological growth. Gibbs and MacKenzie presented no difference in the lifespan of tubes inserted in the anterior quadrants as opposed to those inserted in the PIQ as cited by literature, disregarding the ease for the anterior VT positioning (Gibb and Mackenzie 1985).

Tube placement in the ASQ can imply great effort depending on the external auditory canal configuration even though VT placed in this quadrant are theoretically expected to be retained for a longer time because of epithelial migration patterns, there is no significant difference between the lifespan of VTs in the superior versus the AIQ, with a mean time before extrusion of 12 months, respectively 12.8 months. Walker's conclusion on the matter pleaded towards greater importance given to the type of tube used, rather than the tympanic quadrant chosen for its placement when prolonged ventilation is necessary (Walker 1997). Silicone seems to be well tolerated in most patients and does not generate high extrusion rates. Assessing the lifespan and placement of 3 tube types, Shepard, Reuter Bobbin and Polyethylene-90, the Shepard tube showed a significant difference when placed in the ASQ and the AIQ, with better function in the ASQ of the intact tympanic membrane while the Reuter tube functioned best in the IQ (inferior quadrant), and in the AIQ in cases which had previous tubes inserted. In both normal or modified TM (tympanic membranes), the Reuter Bobbin tube lasted longer in place, with no important difference when

placed in patients with tympanosclerosis (Leopold and McCabe 1980). The Reuter Bobbin tube can be made out of titanium or fluoroplastic, with both materials being well tolerated by patients.

2.3.3.2. Subannular ventilation tube placement

For the patients with chronic middle ear disease that require constant ventilation, VTs can be inserted in more than one position, the most frequent first option being the placement through the tympanic membrane. Sometimes, the tympanic membrane can suffer extensive damage ranging from small perforations, to larger ones, or even atrophy and damage to such extent, that it disqualifies as a good recipient for further tympanotomies.

Taking into account the extended need for appropriate middle ear ventilation in patients with chronic ear disease, in some cases, the proper treatment after multiple trans-tympanic ventilation tube insertions is considered to be the use of subannular ventilation tubes. An important aspect of the subannular VTs usage is the position of insertion, as the choice is based on the present status of the tympanic membrane. Tubes can be inserted in the anterior and posterior quadrants, the posterior wall of the external auditory canal or the posterior and inferior annulus, or the anterior part of the annulus (Elluru et al., 2001). The anterior annulus seems to remain unaffected in patients with chronic ear disease and in those that underwent mastoid surgery (O'Hare and Goebel 1999), as some of the techniques require a canal wall down type.

The first to describe an alternative technique for VTs insertion through a tunnel between the annulus and the external auditory canal epithelium was Simonton in 1968 (Simonton 1968, Kristensen 1992). This VT placement can be kept in place longer and without being affected by the centrifugal healing pattern of the tympanic membrane.

We have identified a study assessing the subannular insertion of VTs in the posterior and inferior quadrant. The authors' choice was a long term usage tube - a Goode T tube (made out of silicone) - inserted in the external auditory canal where a tunnel was drilled beforehand. A tympanomeatal flap was also used in this technique (Yang et al., 2020). Most papers approaching the subannular insertion of ventilation tubes consider the use of Goode T tubes most appropriate, given the advantages of the silicone such as safety, little TM damage and low complications rate. The low complication rate seems to correlate directly to the tolerance towards silicone and its antimicrobial properties.

The age group between 5 and 9 years of age is considered most prone to infections and thus associating frequent Eustachian tube dysfunction and the need for proper middle ear ventilation (Cloutier et al., 2005). Children in this group also have the most SAT insertions as shown by Yang et all, Cloutier et al. (2005), while Saliba et al. (2011) present the average age for the SAT insertion to be 7,4 years old (Yang et al., 2020).

Cloutier et al. (2005) confirm that the long term usage of SATs, highlighting the lifespan difference between the fluoroplastic tubes and the Goode T tubes, (17,8 months compared to 23.8 months) correlates with the need for reintervention, as shown by studies. The lifespan for SATs has a variability between 13.4 months in the O'Hare's study and 41.3 months in Yang's paper, with a mean lifespan of 35 months presented by both studies conducted by Saliba and Cloutier. Silicone tubes seem to reside more in place than fluoroplastic ones.

The eardrum insertion of the SATs may differ, as Yang, Cloutier and Saliba used the posterior part of the annulus for insertion, whereas O'Hare and Elluru preferred the anterior annulus (Yang et al., 2020). Considering the average lifespan of the SATs, O'Hare highlighted the minimal time for SATs to reside in place was 13 months, most probably because of the short follow-up period. Considering the outcomes presented, 16 out of 19 patients presented a functional SAT and an aerated middle ear and no retraction of the tympanic membrane in O'Hare's paper while Elluru presented aeration of the middle ear in 84% of patients, patent T-tube in 89% of patients and complications in just 29%. The most frequent complications were posterior tympanic membrane retraction, thus highlighting the possibility of better anterior middle ear ventilation supported by the anterior placement of the SATs. As shown in the studies, the retraction was reversible in most cases, with the surgical removal of the VT (O'Hare et al., 1999, Elluru et al., 2001).

Comparing the use of the posterior quadrant for SAT placing and multiple anterior quadrant TTTs placements, most of the SATs followed previous attempts of TTTs placements, more than 60% of SAT patients receiving at least 2 TTTs before having the SAT inserted. When considering the lifespan of all the tubes, the average in-place duration of 35 months for SATs and 7 months for TTTs, the difference between the two is significant ($p<0.001$). The early extrusion of the trans-tympanic tubes highlights SATs as possible solutions to the need for long term ventilation and prevent unwanted events such as early extrusion and the need for early replacement. Due to their materials and the technique involved, SATs can be maintained in place for about 5 years or until the age of 12, when aeration is probably unnecessary. Because of their shape and resistance towards natural extrusion their removal is carried out by the ENT doctors in 11% of cases, in comparison to only 5% of cases for the TTTs (Saliba et al., 2011).

The most common complication associated with the Goode T tubes was otorrhea. Half of the suppurative complications of tube placement occurred earlier for the TTTs, 19 months after their placement compared to 72 months for the SATs group. Luminal blockage by discharge and granulation tissue also appeared earlier in the TTTs group (20.8% at 9 months versus 13.7% at 48 months, respectively and 75% at 15 months versus 25%). Discharge blockage is considered to be related to the recurrence of otorrhea. Other noteworthy complications are iatrogenic cholesteatomas following the insertion process for subannular grommets (Saliba et al., 2011).

2.3.3.3. Complications associated with ventilation tubes - tympanic membrane perforation

In the case of tympanic membrane perforation following tube extrusion, the closure is determined by the migration of the epithelial layer, followed closely by the fibrous and the mucosal layers to patch up the perforation (Kristensen 1992). Permanent tympanic membrane perforations can be directly associated with the time the ventilation tube was present, the perforation rate increasing from almost 10% at 6 months, to around 40% at 18 months (Abdel-Nabyawad 2016).

The majority of VTs are retained in place in the anterior and superior quadrant, associating a TM perforation chance of 1-15%. Long term placement tubes (Paparella type 2, Richards modified T tube, U tubes) are more likely to associate a persistent perforation, especially in patients older than 10 years according to Brown and Behar (2019). More than one previously inserted VT and tympanosclerosis doubles, respectively triples, the risk of persistent perforations [16]. It goes without saying that the bigger the perforation's diameter, the bigger its chances of persistency.

Brown also highlights that perforations post VTI larger than 10% of the entire diameter of the TM are more likely to lead to persistent perforations five times more often. The rate of persistent perforations associated with short term VT placement (Armstrong) is around 6.6%, considerably lower than the 20% rate associated with the long term ones (Brown and Behar 2019).

The perforation rate for short term placement tubes remains under 10%. The Shepard tube placed in the anterior and inferior quadrant yields a 5.5% perforation rate in Fior's study, perforation that healed during follow-up. The rate is much lower in Walker's study with only 1 tube out of 212 reported for TM perforation (Fior and Veljak 1984).

2.3.3.4. Complications associated with ventilation tubes - tympanic membrane retraction

An important entity that Buckingham and Ferrer also considered that may lead to cholesteatoma formation is represented by retraction pockets that require aeration of the affected middle ear (Buckingham and Ferrer 1966). Taking into account the usage of grommets to ensure proper middle ear aeration and thus preventing the negative middle ear pressure, tympanic retractions represent one complication that should be taken into account after the grommets' extrusion or removal, as an important aspect of the follow-up (Mawson 1974).

2.3.3.5. Complications associated with ventilation tubes - Cholesteatoma

There is great debate whether the presence of cholesteatoma in patients with ventilation tubes can be directly attributed to their use or not, as almost 8% of responses in Armstrong's study found a direct correlation between the two (Armstrong 19680). Buckingham supported the theory of grommets associated cholesteatoma formation based on finding the promontory covered in shredded epithelial layers (Buckingham 1968). Even though no cholesteatoma was found during the study conducted by Hughes, it highlights the presence of 3 attical cholesteatomas after VT insertion and extrusion (Hughes et al., 1974).

Considering a 10-year follow-up as a sufficient long period of time, Fior and Veljak reported no cholesteatomas associated to tympanostomy site in the use of the Shepard grommet in the anterior and inferior quadrant.

Cholesteatomas can develop secondary to a malpositioned VTs or it can develop more or less in parallel with a partially functioning grommet, such as the case highlighted by Kokko, associating 2 attical cholesteatomas non-related to VT placement, 2 situated postero-superiorly of pars tensa: one VT- related cholesteatoma and one non-VT related (Kokko and Palva 1976). It seems that placing the VT improperly along the TM margin increases the risk of perforation and cholesteatoma with no clear involvement related to the materials used (Kokko and Palva 1976).

2.3.3.6. Complications associated with ventilation tubes - extrusion time

Based on current literature, the extrusion time for VTs is difficult to correlate with risk factors. As ventilation tubes are usually inserted for improving the middle ear aeration and for the reduction in discharge, there is no apparent correlation between the presence and/or viscosity of the effusion and the time of VT extrusion (Degirmenc et al., 2020).

When assessing the extrusion time for ventilation tubes, the period was calculated as half the timespan between the last moment when the tube was in place and the first consult when the tube wasn't identified in the TM (Goldstein et al., 1996).

There is support towards the lack of significance of the insertion quadrant of the VT and its extrusion time, at least for the Paparella type I, and the Shah grommet type when assessing the ASQ and the AIQ insertions (Hern and Jonathan 1999).

The surgeon's experience might be a factor regarding the interval before extrusion, both Hussain and MacKenzie reported a longer period before VT extrusion when the Shah and Shepard tubes were inserted by senior staff members. An average of 11.72 months versus 9.34 months for the Shepard tube and 13.03 months versus 12.97 months for the Shah tube were compared for senior versus junior surgeons. In MacKenzie's report, at one-year evaluation, 11 out of 12 inserted tubes were present versus 1 tube out of 46 for junior staff members (Hussain 1992, Mackenzie 1984).

2.3.3.7. Spontaneous versus surgical extrusion of the ventilation tube

In Fior and Veljak's study, 92.3% of the Shepard tubes from the AIQ were reported to be spontaneously extruded after an average period of 9.8 months and only 8% of them required surgical removal by the specialist doctor. Comparing the Shepard tube and the Goode T- tube, the short term tube extrusion rate is much faster with an average lifespan of 160.5 days, in comparison to 274.1 days for the long term tubes (Jin et al., 2019).

Going further and comparing the average duration before extrusion for 3 tube types (Shepard, Shah, Sheehy tubes) positioned in the ASQ and AIQ, there was no statistical difference for both quadrants, the life span increased as expected to short, medium and long term tube usage. For these types of tubes, extrusion rates did not correlate with positioning, but rather with their materials. Fluoroplastic tubes seem to be well tolerated and retained despite their placement. Gibb and MacKenzie concluded on the Sheehy ventilation tube as being a favorite all-rounder because of its easy to insert design and also being a safe choice for up to 24 months.

2.3.3.8. Otitis media with effusion recurrence

The recurrence of chronic otitis media with effusion was reported to be higher when the Goode T-tube was removed earlier than 12 months. The recurrence rate was different, lowering over time. At 6 months, the recurrence rate was around 20%, at 12 months around 10%, and at 24 months, less than 5%.

Discharge has been presented as being a normal postoperative occurrence, with a 1.8% recurrence rate for Shepard's short-term placement tube, in comparison to 15.7% discharge recurrency rate during follow-up of up to 15 years. When compared with the use of the Goode T-silicone tube, the Shepard grommet associates a 63.6% rate of recurrence for post extrusion discharge, with no significant difference to the long term T tube (72.8% recurrence) (Jin et al., 2019). In contrast, Yaman et al conclude that a lower recurrency rate for OME is associated with a longer life span of the Shepard tube, showing a 36.54% recurrency after 6 months following tube extrusion. Considering a general rate of recurrence of 20.7% for OME, the primary school age group associated the highest rate, with no significant modifications of this rate after VT extrusion (Yaman et al., 2010).

2.3.3.9. Tympanic membrane Atrophy

The usage of the Shepard tube is associated with a 5.5% rate of tympanic membrane atrophy, which can be considered as a preliminary state for future tympanic retraction pockets or

even perforations. It is unclear if prolonged use of fluoroplastic materials is more likely to cause tympanic atrophy as opposed to silicone materials. Further studies are required in this direction, as few articles target this aspect.

2.3.3.10. Disease resolution

The timespan of the follow-up and the age of the patient are both very important, as the time needed for the middle ear mucosae to heal is considered different depending on the host's immunological status and its previous damage. A 2 to 3 year period is the timespan needed by the middle ear mucosal layer to recover after a chronic secretory active otitis media, as the poorest results were seen in patients during the first 2 to 3 years of follow up. Using the TTTs in patients under 7 years yielded resolution in 80% of the cases, most probably given the shorter period of mucosal aggression and the type of existing effusion. In children with chronic OME the outcome is poorer than in those with only Eustachian tube and middle ear ventilation dysfunction. 80% of patients with chronic OME, at some point, underwent bilateral TTTs insertions (Yaman et al., 2010).

Most patients with an average age of 3 that received short term AIQ VT insertions (for example Shepard's fluoroplastic tube) displayed a rate of resolution considered satisfactory in more than half of treated cases. Fior reports better resolution rates of 67.6% at 5 to 15 years post grommet extrusion when fluoroplastic materials are used.

2.3.4.Conclusions

Our extensive literature review concludes that silicone is still a good "all-rounder" material when it comes to its biological uses; the short-term placement VTs made out of it are well tolerated and their extrusion is not influenced by the material type or position of its trans-tympanic placement. However, should a longer ventilation time be necessary, a subannular VT insertion is to be looked into as long term silicone VTs may offer the best middle ear aeration in this case. Factors that influence the success rates of this tubes' usage also include the experience of the operating surgeon.

For the subannular placement, the anterior part of the annulus seems to offer a better choice of placement, and, disregarding the material used (silicone, titanium or fluoroplastic) this technique implies a certain rate of cholesteatoma formation.

Fluoroplastic materials hold their own right, being better tolerated than polyethylene tubes, and also presenting good success rates when placed under the tympanic annulus. The risk of tympanic membrane perforation doesn't seem to be linked to the type of material used but a history of previous ventilation tube placements, especially if trans-tympanic, heightens this risk. Fluoroplastic materials also seem to present the best OME resolution rates, but we consider more studies are needed to be able to link OME resolution rates to the material used in VTs.

2.4. The sound of displasia

2.4.1. Introduction

The Schwann cells of the vestibular (8th cranial) nerve give rise to the benign tumor known as vestibular schwannoma (VS)/acoustic neuroma (AN). Despite their benign character, these tumors have the ability to grow and can cause severe ontological symptoms, such as unilateral sensorineural hearing loss/asymmetrical hearing loss (AHL), vertigo, and tinnitus, due to impairment of the vestibulocochlear nerve function (Tveiten et al., 2015, Pinna et al., 2012). Gradual, high-tone hearing loss with higher asymmetry in the frequency range of 2–8 kHz is a typical characteristic of VS (Kotlarz et al., 1992). Headaches, visual changes, hypoesthesia, and palsies are just a few of the additional symptoms that could manifest as a result of a VS (Kellermeyer et al., 2021, Matsushima et al., 2022).

A VS typically grows between 0.99 and 1.11 mm every year, but certain characteristics of the tumor, including cystic and hemorrhagic appearances, as well as erythropoietin treatment, have been proven to indicate an accelerated growth (Paldor et al., 2016).

Regarding the epidemiological profile of VS, it was demonstrated that the radiologically confirmed vestibular schwannoma rates increased in recent years in the United States of America (2006–2017: annual percentage change—1.7%; 95% confidence interval, CI: 0.5–3.0%) (Withrow et al., 2021). A retrospective longitudinal study that evaluated the incidence of acoustic neuroma in Iceland for a time frame of 30 years indicated an incidence rate of 1.24/100,000, as well as an ascending trend in the diagnosis of this condition (Gudmundssonet al., 2013). At the same time, a recent systematic review that assessed the global incidence of sporadic vestibular schwannoma on four distinct populations from Denmark, the Netherlands, Taiwan, and the United States reported an incidence rate ranging from 3.0 to 5.2 per 100,000 person years, as well as an increased lifetime prevalence of sporadic vestibular schwannoma (>1 per 500 persons) (Marinelli et al., 2022). Moreover, it appears that the age of the patient at the time of diagnosis of VS has been slowly increasing from 49 years in 1976 to 58 years (Stangerup et al., 2012).

Although a consistent association between long-term mobile phone use and the risk of developing VS has not been documented, there is heterogeneity within investigations, and higher risks have been noted in several studies for use of more than 10 years (Röösl et al., 2019, Mornet et al., 2013, Hardell et al., 2013). Exposure to high doses of radiation and mutations of tumor suppressor genes, such as neurofibromatosis 2 (NF2) gene, were linked to the development of sporadic or genetic variants of the disease (Warren et al., 2003, Preston et al., 2002).

Magnetic resonance imaging (MRI) is the gold standard investigation for all patients who present with asymmetrical hearing loss (Halliday et al., 2018). The use of MRI in the diagnosis of VS was the subject of a systematic review and cost-effectiveness analysis by Fortnum et al (2009). Despite the fact that gadolinium-enhanced T1-weighted MRI is considered as the gold standard, there was little difference between it and non-contrast T2-weighted scans in terms of sensitivity

and specificity. Additionally, non-contrast T2-weighted scans were thought to be more affordable for use in clinical settings.

However, screening methods have been devised to save and maximize resources because the number of MRI exams required for this group of patients is very high, and the number of schwannomas discovered is relatively low. An objective approach is represented by audiometric protocols based on quantifying the pure-tone audiometric (PTA) threshold by the difference in "decibel" and "frequency regions" between two ears (Cheng et al., 2012). Currently, there are multiple PTA protocols described in the literature, reported to have variable sensitivities and specificities for the diagnosis of VS depending on their definition of interaural asymmetry.

The aim of this systematic review and meta-analysis was to evaluate the diagnostic accuracy of different PTA screening protocols for vestibular schwannoma in patients with asymmetrical hearing loss and to compare it with the gold standard represented by MRI.

2.4.2. Materials and Methods

We performed a systematical search of published studies that evaluated PTA protocols for the screening of VS, in comparison with MRI examination in MEDLINE, EMBASE and Cochrane Library using synonyms of 'magnetic resonance imaging', 'asymmetrical hearing loss', 'vestibular schwannoma', and Boolean operators AND/OR in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Supplementary Material S1–S3: Search strategy). This systematic review and meta-analysis is registered in the Open Science Framework Registry (DOI: 10.17605/OSF.IO/FRGTC (accessed on 9 October 2022)).

The time frame settled for this research was from the beginning of the databases up to the first of September 2022, and we applied English language restriction as a filter. Additional research consisted of manual screening of references cited in the evaluated papers in order to ensure that all relevant studies were included. Duplicates were removed using EndNote software version 20.4 (Clarivate, Philadelphia, PA, USA). The full-text papers were independently reviewed by two investigators (M.D.C and D.N.) to establish their eligibility for the review. Any differences between the two were remedied by a third reviewer (M.L.C.) if a consensus could not be reached.

The inclusion criteria were represented by observational studies, both prospective and retrospective, with a diagnostic study design that compared at least one PTA screening protocol to MRI findings in patients with AHL and comprised sufficient data for a 2 × 2 contingency table creation. We excluded opinion papers, animal studies, and case reports from the search.

Two investigators (B.M.C and M.L.C) retrieved data from the eligible studies separately using a standard process. Data concerning the first author, publication year, study design, characteristics of the population examined, number of cases and controls, cut-offs used, and the information needed to create a 2 × 2 table were obtained. Two independent reviewers (B.M.C and M.L.C) assessed the methodological quality of the included studies using the QUADAS-2 technique (Quality Assessment of Diagnostic Accuracy Studies-2) (Whiting et al., 2011). Any disagreements (Pinna et al., 2012) were resolved by discussion with a third reviewer (L.G.).

We summarized data from each study in 2 × 2 tables of true-positive, false-positive, true-negative and false-negative values, and we calculated sensitivity, specificity, and positive and negative likelihood ratios, as well as diagnostic odds ratio. For hierarchical modeling, a hierarchical summary receiver operating characteristic (HSROC) model will be utilized to generate equal summary estimates for sensitivity and specificity, taking into account variability both between and within studies (heterogeneity). In order to show variation and explore heterogeneity for sensitivity and specificity, we drew Forrest plots, likelihood ratios scattergrams, bivariate boxplots, and Fagan nomograms. I2 statistic was used to quantify the degree of heterogeneity. The statistical analyses were performed using STATA SE (version 14, 2015, StataCorp LLC, College Station, TX, USA).

2.4.3. Results

Our search yielded 400 unique records, out of which only 7 were included in the meta-analysis after abstract and full text screening (Fig. 2.5.). We did not retrieve additional items after screening references and related articles.

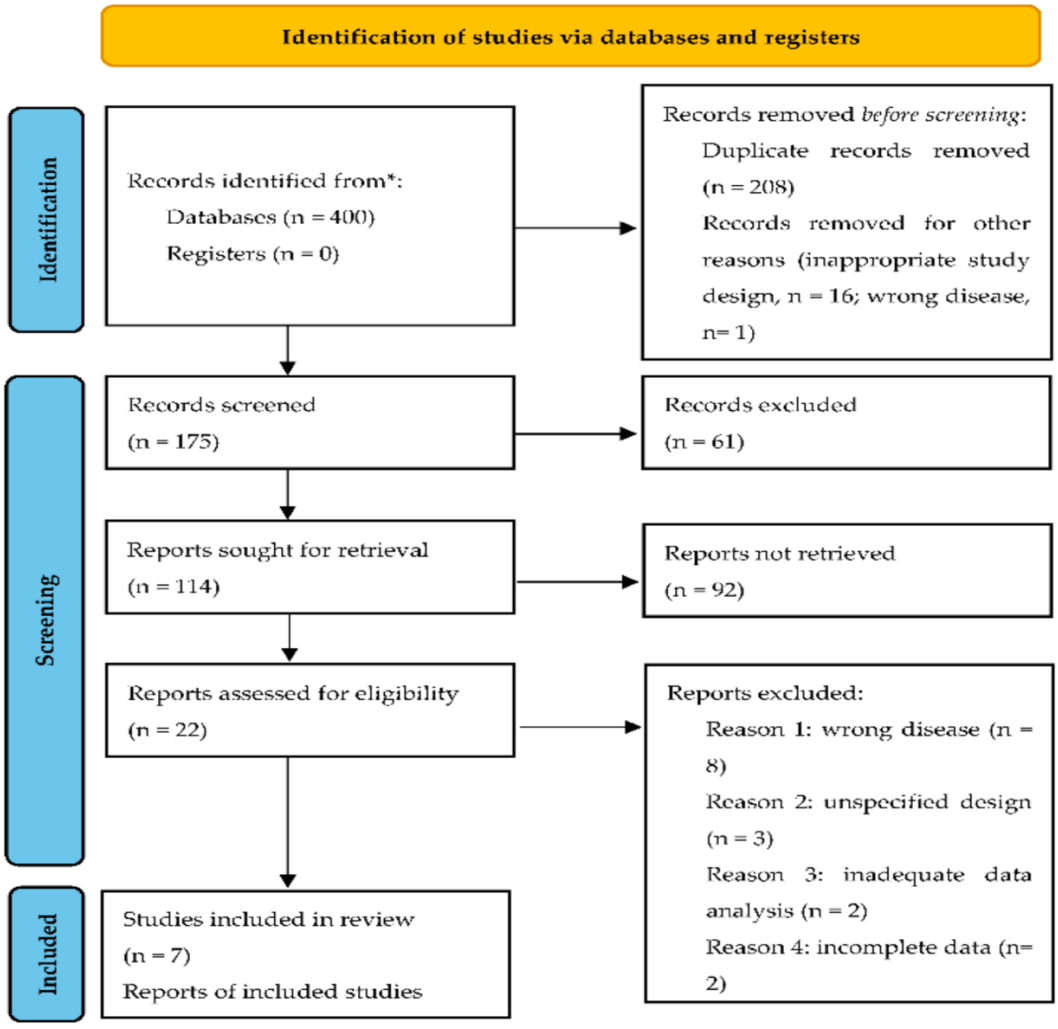


Figure 2.5. Flow diagram of search and selection of studies. * markup of data source.

The characteristics of the included studies are presented in Table 2.2.. A total of 4369 patients and 11 PTA protocols were included for further analysis. For the purpose of this meta-analysis, we evaluated the diagnostic accuracy of PTA protocols that were evaluated at least four times in the included studies mainly because the statistical analyses were not informative when using insufficient data. The included PTA protocols and their definition of asymmetrical hearing loss are presented as supplementary material (Table S1—Definitions of the included PTA protocols).

Table 2.2. Characteristics of the included studies.

Author	Year	Study Design	Number of Patients Included	Index Tests
Obholzer et al.	2004	Case-control	128	9 PTA protocols
Gimsing	2009	Case-control	424	PTA shapes 8 PTA protocols
Saliba et al.	2011	Cohort	212	8 PTA protocols
Cheng et al.	2015	Cohort	1751	15 PTA protocols
Bhargava et al.	2019	Cross-sectional	1059	14 PTA protocols
Vnencak et al.	2020	Case-control	688	14 PTA protocols
Celis-Aguilar et al.	2022	Cross-sectional	107	15 PTA protocols

Legend: PTA—pure tone audiometry.

Overall, the quality of included studies was low-to-moderate (Table 2.3). Two studies found a high risk of bias in one domain (patient selection) (Vnencak et al., 2021, Celis-Aguilar et al., 2022). For the rest of the domains, the risk of bias was assessed as low and unclear. For the domains, patient selection, index test, and reference standard, respectively, none of the included studies scored highly on concerns regarding applicability. For the majority of the articles, there was little concern that applicability of the articles did not fit the review question. No studies were excluded from the analysis based on the quality.

Table 2.3. Quality assessment of the included studies.

Study	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Gimsing (2009)	?	?	☺	?	☺	☺	?
Obholzer et al. (2004)	?	?	?	?	☺	☺	☺
Saliba et al. (2011)	☺	☺	☺	?	☺	☺	☺
Bhargava et al. (2019)	?	?	?	?	?	☺	☺
Vnencak et al. (2020)	☹	?	?	?	?	☺	☺
Cheng et al. (2012)	?	?	?	?	☺	?	☺
Celis-Aguilar et al. (2022)	☹	☺	?	?	?	☺	☺

Legend: ☺ Low Risk; ☹ High Risk; ? Unclear Risk.

The pooled estimates and confidence intervals of sensitivity, specificity, positive and negative likelihood ratios, and diagnostic odds ratio, corresponding to the evaluated PTA protocols are presented in Table 2.4.

Table 2.4. Pooled estimates of diagnostic accuracy parameters for the included PTA protocols.

PTA Protocol	Sensitivity (Pooled Estimate/95% CI)	Specificity (Pooled Estimate/95% CI)	Positive Likelihood Ratio (Pooled Estimate/95% CI)	Negative Likelihood Ratio (Pooled Estimate/95% CI)	Diagnostic Odds Ratio (Pooled Estimate/95% CI)
Mangham (1991)	0.93 (0.76–0.98)	0.40 (0.26–0.55)	1.5 (1.2–2.1)	0.17 (0.04–0.79)	9 (2–55)
Sunderland (Dawes and Jeannon 1998)	0.90 (0.80–0.95)	0.32 (0.17–0.52)	1.3 (1.1–1.6)	0.32 (0.22–0.46)	4 (3–7)
DOH (Neary et al., 1996)	0.89 (0.85–0.92)	0.45 (0.35–0.55)	1.6 (1.4–1.9)	0.25 (0.20–0.32)	6 (5–9)
Schlauch et al., 1995	0.73 (0.64–0.80)	0.55 (0.44–0.66)	1.6 (1.2–2.3)	0.49 (0.31–0.77)	3 (2–7)
Sheppard et al., 1996	0.77 (0.65–0.85)	0.52 (0.32–0.71)	1.6 (1.0–2.5)	0.45 (0.24–0.85)	4 (3–10)
Seattle (Hunter et al., 1991)	0.85 (0.80–0.89)	0.53 (0.42–0.64)	1.8 (1.4–2.4)	0.28 (0.18–0.45)	6 (3–13)
Oxford (Sheppard et al., 1996)	0.85 (0.79–0.90)	0.43 (0.34–0.53)	1.5 (1.3–1.8)	0.34 (0.23–0.52)	4 (3–8)
Obholzer et al., 2004	0.82 (0.77–0.86)	0.58 (0.38–0.75)	1.9 (1.3–3.0)	0.31 (0.23–0.42)	6 (3–13)
Amclass (Margolis et al., 2008)	0.93 (0.89–0.95)	0.34 (0.20–0.51)	1.4 (1.1–1.8)	0.21 (0.11–0.42)	7 (3–17)
AAO (Urben et al., 1999)	0.85 (0.77–0.90)	0.60 (0.49–0.70)	2.1 (1.6–2.9)	0.25 (0.15–0.43)	8 (4–18)
Nashville (Welling et al., 1990)	0.91 (0.86–0.94)	0.31 (0.21–0.42)	1.3 (1.1–1.6)	0.29 (0.14–0.61)	5 (4–11)

Legend: CI—confidence interval; PTA—pure tone audiometry; AAO—American Academy of Otolaryngology protocol; DOH—Department of Health.

The highest pooled sensitivity was achieved by the following protocols: Mangham 0.93 (95% CI: 0.76–0.98), Amclass 0.93 (95% CI: 0.89–0.95) (Cheng et al., 2012, Saliba et al., 2011, Bhargava et al., 2019, 25. Celis-Aguilar et al., 2022), and Nashville 0.91 (95% CI: 0.86–0.94), while the highest pooled specificity and pooled positive likelihood ratio was achieved by the American Academy of Otolaryngology protocol (AAO) at 0.60 (95% CI: 0.49–0.70) and 2.1 (95% CI: 1.6–2.9) (Cheng et al., 2012, Saliba et al., 2011, Bhargava et al., 2019, Celis-Aguilar et al., 2022).

The highest pooled negative likelihood ratio corresponded to the Sheppard protocol 0.45 (95% CI: 0.24–0.85) [18,21,23,25], and the highest pooled diagnostic odds ratio was attributed to the Mangham protocol 9 (95% CI: 2–55) (, Bhargava et al., 2019, Celis-Aguilar et al., 2022).

Figs 2.6.a–d is a graphical representation of the diagnostic accuracy of the Mangham protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 87.4%) and specificity (I2: 98.3%) of this protocol (Figure 2.6.a). The area under

the curve (AUC) for this protocol was 0.66 (95%CI: 0.61–0.70) (Figure 2.6.b). The likelihood ratio scattergram (Figure 2.6.c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram (Figure 2.6.d) revealed that, for a given pre-test probability of 20% of vestibular schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 28 and 4%, respectively.

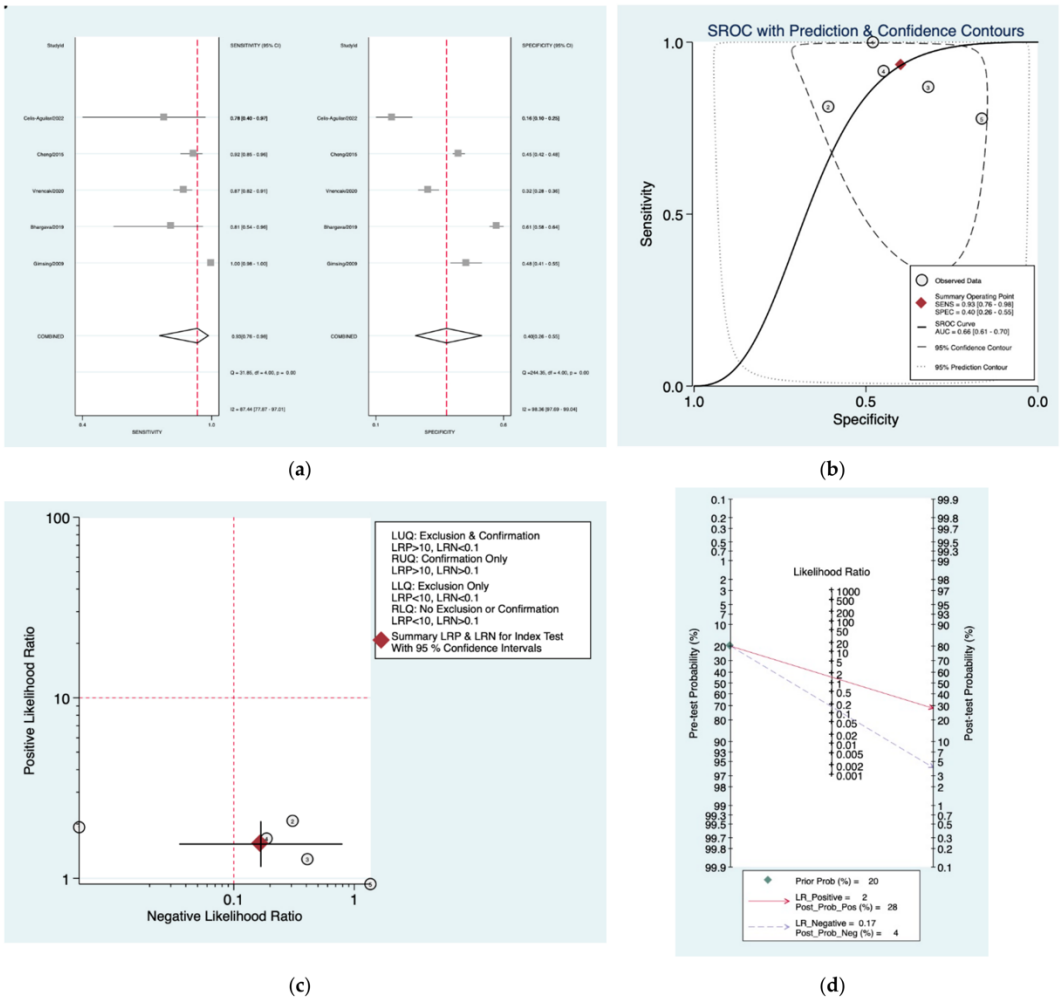


Figure 2.6. Meta-analysis of Mangham protocol. (a) Forrest plot of pooled sensitivity and specificity (Bhargava et al., 2019, Celis-Aguilar et al., 2022); (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

Figure 2.7.a–d is a graphical representation of the diagnostic accuracy of the Sunderland protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 84.9%) and specificity (I2: 98.3%) of this protocol (Figure 2.7.a). The area under the curve (AUC) for this protocol was 0.76 (95%CI: 0.72–0.80) (Figure 2.7.b). The likelihood ratio scattergram (Figure 2.7.c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram

(Figure 2.7.d) revealed that, for a given pre-test probability of 20% of vestibular schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 25 and 7%, respectively.

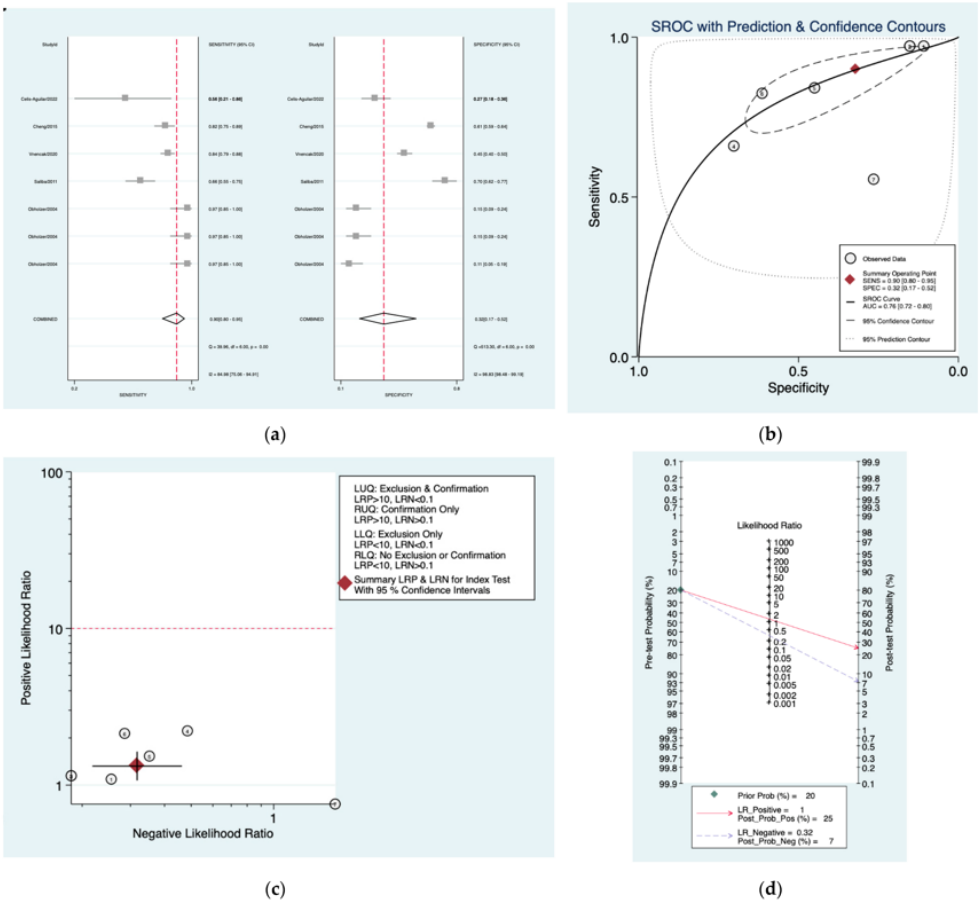


Figure 2.7. Meta-analysis of Sunderland protocol. (a) Forrest plot of pooled sensitivity and specificity (Cheng et al., 2012, Gimsing et al., 2010, Bhargava et al., 2019, Celis-Aguilar et al., 2022); (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

Figure 2.8 a–d is a graphical representation of the diagnostic accuracy of the Department of Health protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 60%) and specificity (I2: 97.2%) of this protocol (Figure 2.8.a). The area under the curve (AUC) for this protocol was 0.83 (95%CI: 0.80–0.86) (Figure 2.8.b). The likelihood ratio scattergram (Figure 2.8.c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram (Figure 2.8.d) revealed that, for a given pre-test probability of 20% of vestibular schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 29 and 6%, respectively.

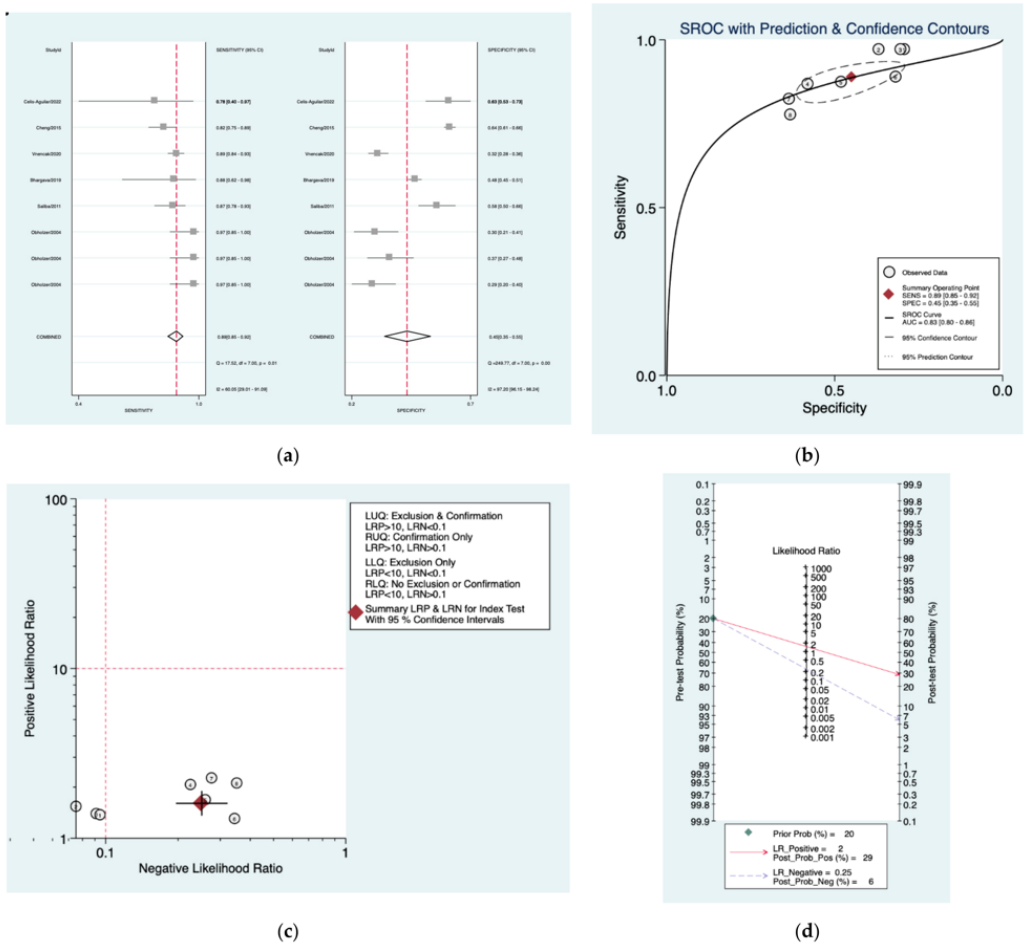


Figure 2.8. Meta-analysis of Department of Health protocol. (a) Forrest plot of pooled sensitivity and specificity (Saliba et al., 2011, Bhargava et al., 2019, Bhargava et al., 2019, Celis-Aguilar et al., 2022); (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

Figure 2.9.a–d is a graphical representation of the diagnostic accuracy of the Schlauch and Levine protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 69.9%) and specificity (I2: 96.9%) of this protocol (Figure 2.9.a). The area under the curve (AUC) for this protocol was 0.70 (95%CI: 0.66–0.74) (Figure 2.9.b). The likelihood ratio scattergram (Figure 2.9.c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram (Figure 2.9.d) revealed that, for a given pre-test probability of 20% of vestibular schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 29 and 11%, respectively.

Figure 2.10.a–d is a graphical representation of the diagnostic accuracy of the Sheppard protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 75.1%) and specificity (I2: 98.9%) of this protocol (Figure 2.10.a). The area under the curve (AUC) for this protocol was 0.74 (95%CI: 0.70–0.78) (Figure 2.10.b).

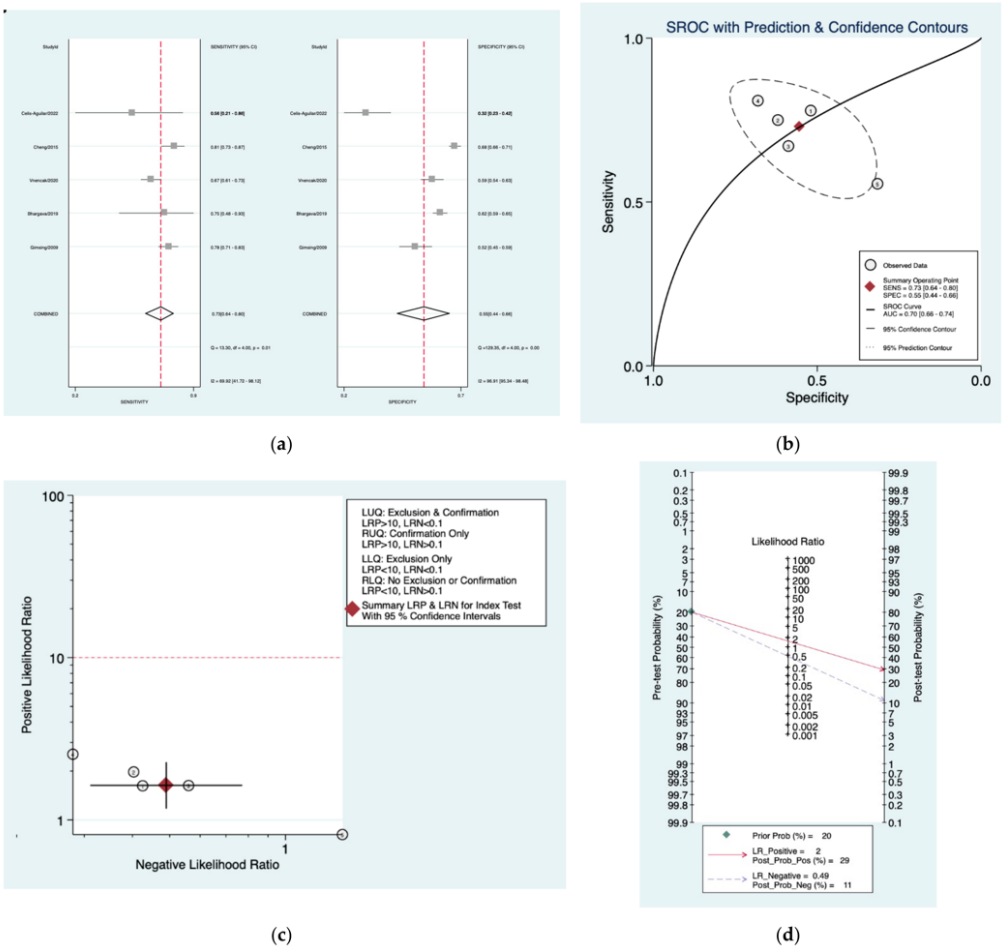


Figure 2.9. Meta-analysis of Schlauch and Levine protocol. (a) Forrest plot of pooled sensitivity and specificity (Saliba et al., 2011, Bhargava et al., 2019, Bhargava et al., 2019, Celis-Aguilar et al., 2022); (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

The likelihood ratio scattergram (Figure 2.10.c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram (Figure 2.10.d) revealed that, for a given pre-test probability of 20% of vestibular schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 28 and 10%, respectively.

Figure 2.11.a–d is a graphical representation of the diagnostic accuracy of the Seattle protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 42.4%) and specificity (I2: 94%) of this protocol (Figure 2.11.a). The area under the curve (AUC) for this protocol was 0.82 (95%CI: 0.79–0.85) (Figure 2.11.b). The likelihood ratio scattergram (Figure 2.11.c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram (Figure 2.11.d) revealed that, for a given pre-test probability of 20% of vestibular schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 31 and 7%, respectively.

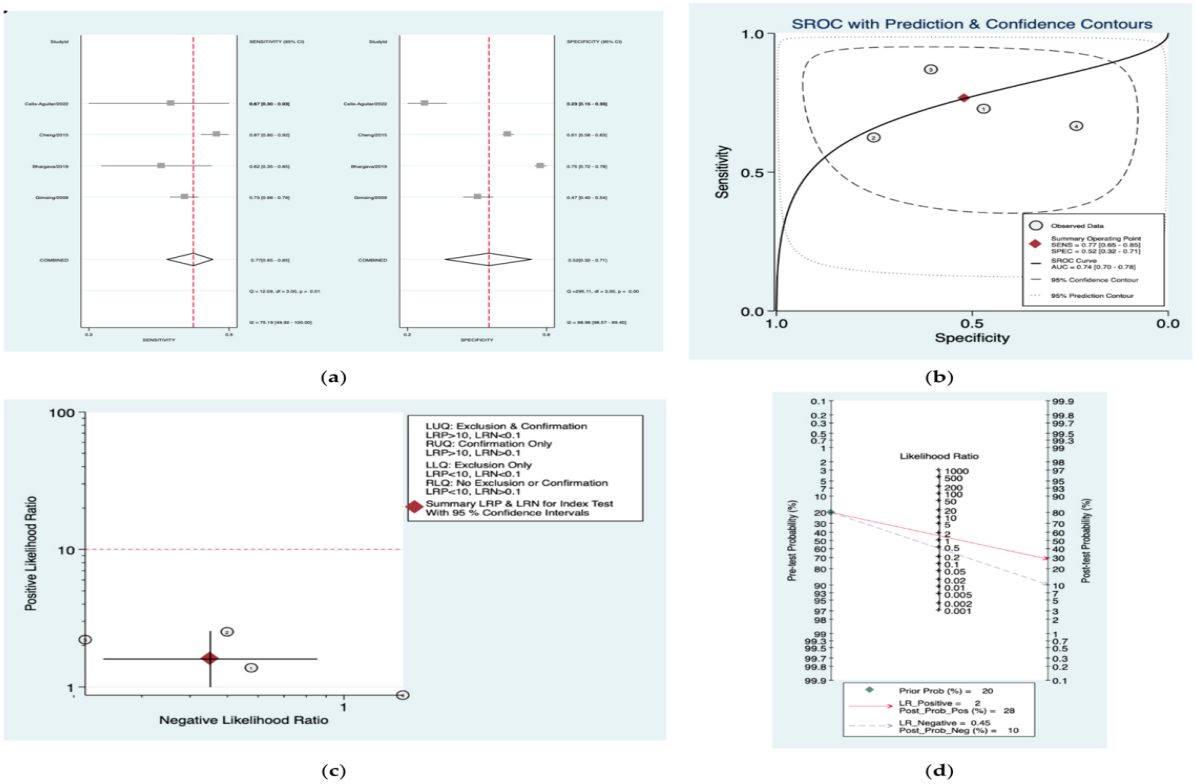


Figure 2.10. Meta-analysis of Sheppard protocol. (a) Forrest plot of pooled sensitivity and specificity (Saliba et al., 2011, Bhargava et al., 2019, Bhargava et al., 2019, Celis-Aguilar et al., 2022); (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

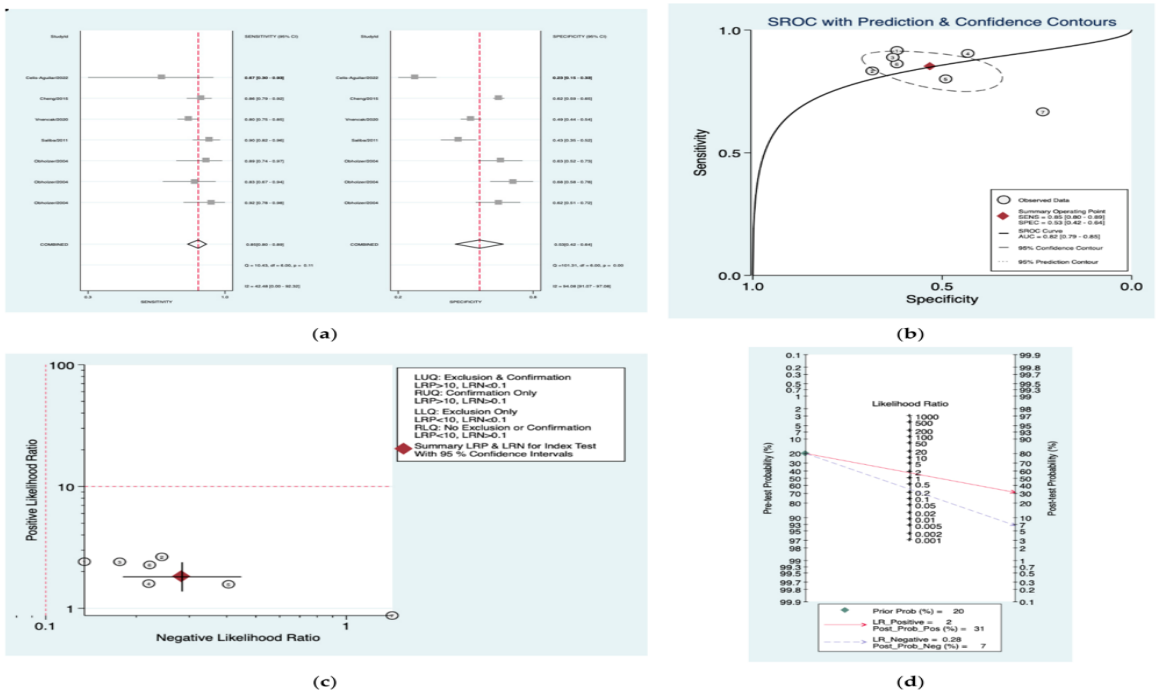
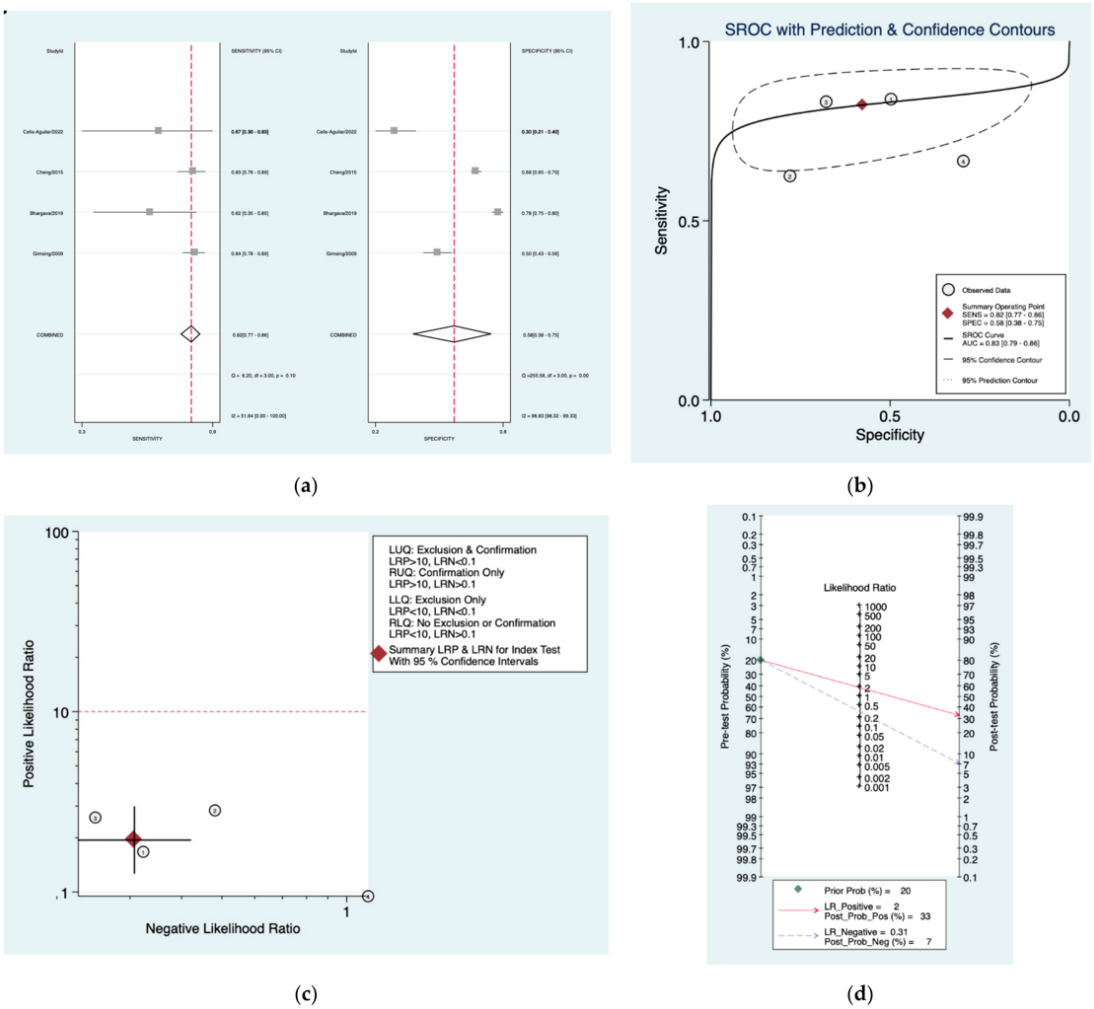


Figure 2.11. Meta-analysis of Seattle protocol. (a) Forrest plot of pooled sensitivity and specificity; (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

Figure 2.12.a–d is a graphical representation of the diagnostic accuracy of the Oxford protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 66.6%) and specificity (I2: 97.2%) of this protocol (Figure 2.12.a). The area under the curve (AUC) for this protocol was 0.77 (95%CI: 0.73–0.81) (Figure 2.12.b). The likelihood ratio scattergram (Figure 2.12.c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram (Figure 2.12.d) revealed that, for a given pre-test probability of 20% of vestibular schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 27 and 8%, respectively.



(a) (b) (c) (d)

Figure 2.12. Meta-analysis of Obholzer protocol. (a) Forrest plot of pooled sensitivity and specificity; (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

Figure 13a–d is a graphical representation of the diagnostic accuracy of the Amclass protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 43%) and specificity (I2: 99.2%) of this protocol (Figure 2.13.a). The area under the curve (AUC) for

this protocol was 0.92 (95%CI: 0.89–0.94) (Figure 2.13.b). The likelihood ratio scattergram (Figure 2.13.c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram (Figure 2.13.d) revealed that, for a given pre-test probability of 20% of vestibular schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 26 and 5%, respectively.

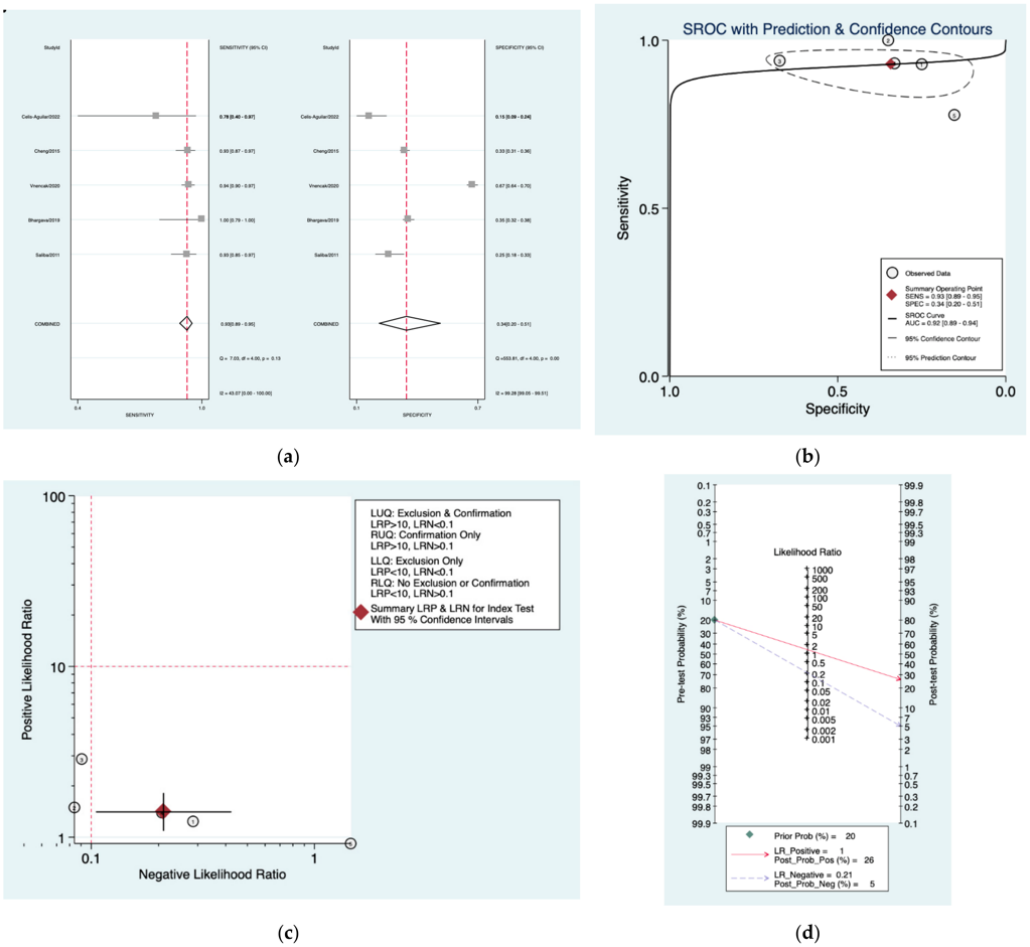


Figure 2.13. Meta-analysis of Amclass protocol. (a) Forrest plot of pooled sensitivity and specificity (Saliba et al., 2011, Bhargava et al., 2019, Bhargava et al., 2019, Celis-Aguilar et al., 2022); (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

Figure 2.14a–d is a graphical representation of the diagnostic accuracy of the AAO protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 76.6%) and specificity (I2: 94.4%) of this protocol (Figure 2.14a). The area under the curve (AUC) for this protocol was 0.81 (95%CI: 0.78–0.86) (Figure 2.14b). The likelihood ratio scattergram (Figure 2.14c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram (Figure 2.14.d) revealed that, for a given pre-test probability of 20% of vestibular

schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 35 and 6%, respectively.

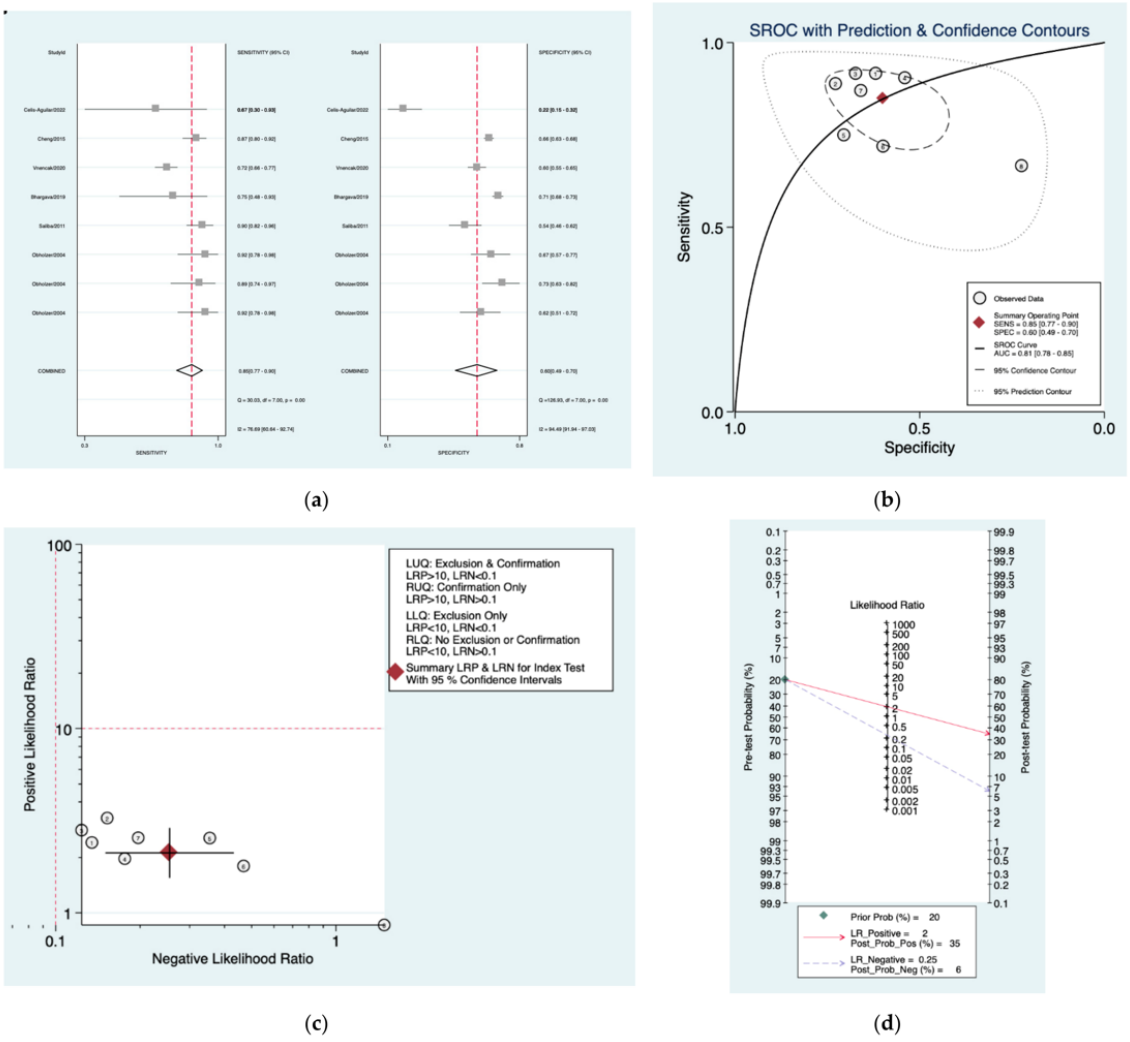
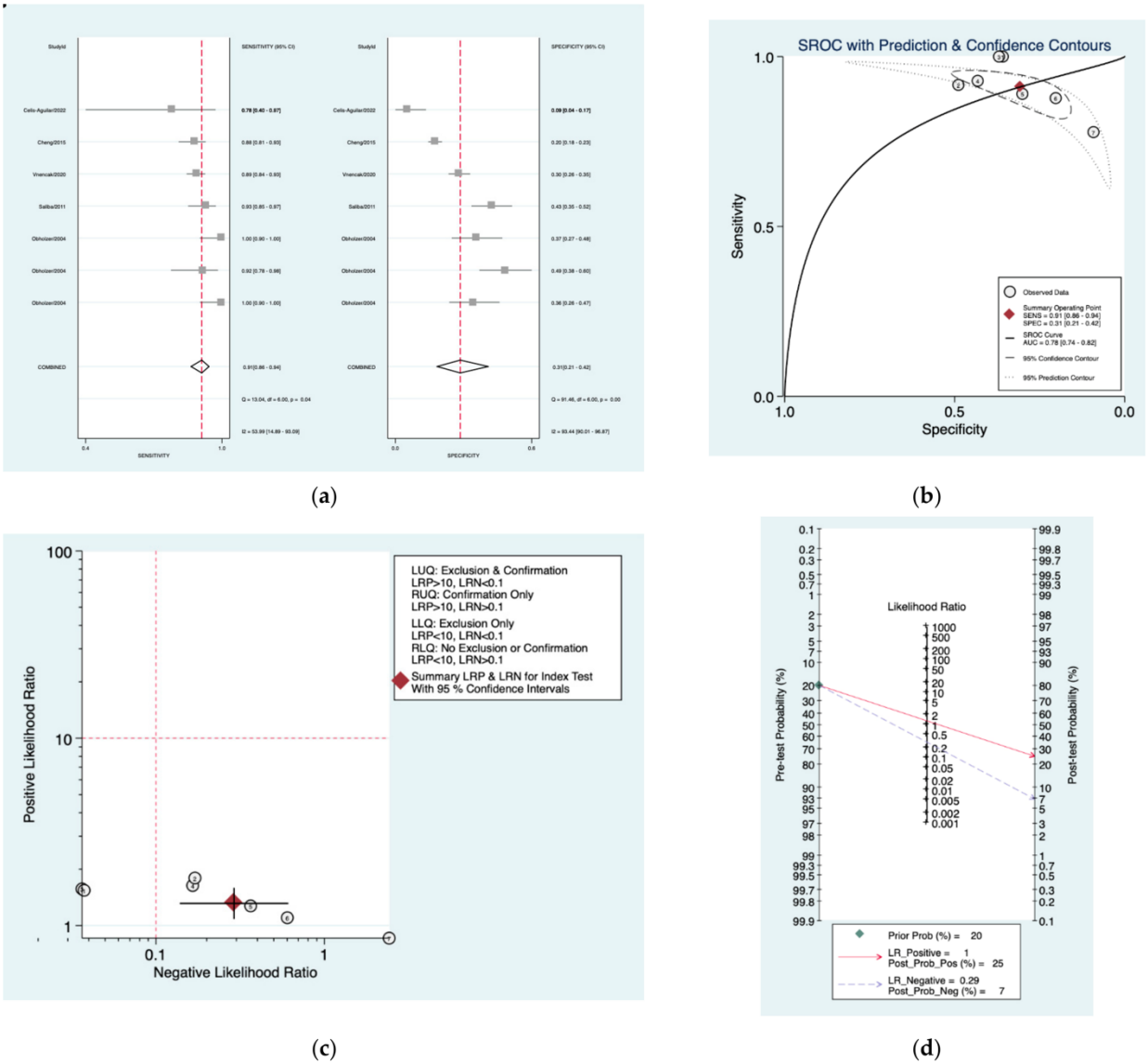


Figure 2.14. Meta-analysis of AAO protocol. (a) Forrest plot of pooled sensitivity and specificity (Saliba et al., 2011, Bhargava et al., 2019, Bhargava et al., 2019, Celis-Aguilar et al., 2022); (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

Figure 2.15.a–d is a graphical representation of the diagnostic accuracy of the Nashville protocol. We have identified a great heterogeneity among studies regarding the reporting of sensitivity (I2: 53.9%) and specificity (I2: 93.4%) of this protocol (Figure 2.15.a). The area under the curve (AUC) for this protocol was 0.78 (95%CI: 0.74–0.82) (Figure 2.15.b). The likelihood ratio scattergram (Figure 2.15.c) indicated that this protocol is comprised in the right lower quadrant and that it could not be used for exclusion or confirmation of the disease. Finally, the Fagan nomogram (Figure 2.15.d) revealed that, for a given pre-test probability of 20% of vestibular schwannoma, the post-test probability for positive and negative diagnosis of this protocol was 35 and 6%, respectively.



(**a**) (**b**)

(**c**) (**d**)

Figure 2.15. Meta-analysis of Nashville protocol. (a) Forrest plot of pooled sensitivity and specificity (Saliba et al., 2011, Bhargava et al., 2019, Bhargava et al., 2019, Celis-Aguilar et al., 2022); (b) Hierarchical summary receiver operating characteristic (HSROC) curve; (c) Likelihood ratio scattergram; (d) Fagan nomogram.

2.4.4.Discussion

This systematic review and meta-analysis evaluated the diagnostic accuracy of 11 pure-tone audiometry protocols, which were previously reported to the gold standard examination—MRI, for the diagnosis of vestibular schwannoma in patients with unilateral hearing loss. As the incidence rate of this condition is following an ascending trend (Marinelli et al., 2022), patient selection and their risk stratification becomes more important to clinicians.

Our results showed that the pooled sensitivity of these protocols was good, ranging between 0.73 and 0.93, with the highest values achieved by Mangham (0.93), Amclass (0.93), and Nashville

(0.91) protocols. On the other hand, the specificity of the evaluated protocols was heterogeneous and low, ranging from 0.31 (Nashville) to 0.60 (AAO).

Our study results revealed good values for the HSROC curve, ranging from 0.66 (Mangham) to 0.92 (Amclass). Nonetheless, all protocols were located in the right lower quadrant on the likelihood scattergram, which indicated that none of them could be used for exclusion or confirmation of the disease. Moreover, the post-test probabilities for positive and negative diagnosis of these protocols were extremely low.

These arguments support the hypothesis that the evaluated pure-tone audiometry protocols cannot be used for a proper screening or diagnosis of vestibular schwannoma despite of their good sensitivity. Thus, MRI investigation remains the gold standard for the evaluation of patients with unilateral hearing loss, even though its costs are high (Basu et al., 2019, Wilson et al., 2010, Pan et al., 2016).

Even though PTA protocols could be used in low-resource medical settings due to their high sensibility, simplicity, objectivity, easiness to apply, and low costs, clinicians must take into consideration their low specificity, which may give a high number of false positives when evaluating patients with unilateral hearing loss (Jayawardena et al., 2019). Moreover, the European Association of Neuro-Oncology (EANO) recommends annual follow-up with microbeam radiation therapy and audiometry in patients with conservatively treated, radiated, and incompletely resected VS (Goldbrunner et al., 2020).

In recent years, data collected from PTA along with the patient's clinical characteristics were incorporated into algorithms for the prediction of the need for active treatment with approximately 90% accuracy (Profant et al., 2021). This paves the way for a perspective surrounding the improvement of PTA protocols that would result in a higher specificity of the tests, and thus to a better patient selection.

Our results are comparable to those reported in a 2017 systematic review and meta-analysis that evaluated the diagnostic accuracy of different non-imaging screening protocols that can be used to select patients at high risk of VS (Hentschel et al., 2017). The authors indicated good sensitivity (88–91%) but low specificity (31–58%) for the analyzed protocols. Despite the heterogeneity of the reported data, its results constitute another argument that favors the use of MRI for the evaluation of patients with unilateral hearing loss.

The results from this meta-analysis should be evaluated considering some inherent limitations. First of all, we could not assess all the published PTA protocols because the limited information extracted from the included studies did not allow a coherent statistical analysis. Secondly, we could not include randomized controlled trials in this study, and the results are based on observational studies, such as cohort, cross-sectional, or case-control.

Thirdly, we did find a high degree of heterogeneity regarding the reporting of sensitivity and specificity data. All these limitations could derive from the disparity of data reported in the literature about the topic. Moreover, it is expected that PTA protocols will be updated based on the data emerging from the new integrative technologies that use artificial intelligence (Song et al., 2015, Rahne et al., 2016).

2.4.5. Conclusions

Further studies, on larger cohorts of patients, or several randomized controlled trials could represent scientific material of higher quality for the next meta-analysis. Meanwhile, we consider that our results support the use of pure-tone audiometry protocols in low resource settings, at least for the risk stratification of patients with asymmetric hearing loss and a high degree of suspicion for vestibular schwannoma. Newer technologies, such as those based on artificial intelligence and machine learning techniques, could help in the process of risk stratification of patients who have a high risk of developing vestibular schwannoma (Smole-Orehek et al., 2019, Carey et al., 2022, Dang et al., 2021).

Chapter 3: Breaking the wall of trauma - Multidisciplinary management of cervico-facial trauma

3.1. State of the arts

Mankind is essentially an aggressive species whatever spiritual and intellectual qualities he may also possess. Indeed, were it not for this aggressive characteristic, the human species would not have survived for a sufficient period to permit the development of its superior mental attributes. Hippocrates (460-370 B.C.) asserted that: ”War is the only proper school for a surgeon' and it must be admitted that much of our present knowledge of maxillo-facial injuries has been derived from the treatment of battlefield casualties.” (Adams 1849).

Nowadays, the student has at his disposal sophisticated audio-visual techniques but, in the final analysis, it is still the human computer which wields the knife at the operating table. Arround 5000 B.C. the Sumerians, who occupied the present-day country of Iraq, developed in the city of Babylon a well-organized civilization, and the clay bricks, from which the city was built, survive to this day. Hammurabi drew up a legal code on clay tablets which contains one of the first written references, in the Cuneiform script, to the treatment of fractures: ”If a physician set a broken bone for a man, or cure his diseased bowels, the patient shall give five shekels of silver to the physician.” (Lefevre 1834).

There was no Medical Protection organization existed in those remote times, but a more powerful incentive to exercise all due skill and care was ensured in another part of the Code, which stated: ”If a physician shall make a severe wound with a bronze operating knife and kill him . . . his hands shall be cut off.”

Professor Breasted translated the Edwin Smith papyrus, unearthed in Egypt about 1600 B.C., and appears to be the work of a military surgeon. There it is written that in the case of a dislocated mandible, the operator is advised to: ”Put thy thumbs upon the ends of the two rami of the mandible inside his mouth and thy two claws (groups of fingers) under his chin, and thou shouldst cause them to fall back so that they rest in their places.” (Breasted 1930).

Only the simple jaw fractures were treated by bandages, obtained from the embalmer, and soaked in honey and white of egg, while wounds were treated by the application of fresh meat on the first day, a method which may well have introduced tissue enzymes and thromboplastins without, one hopes, too many associated bacteria. In case of the compound fractures of the mandible were viewed in a different light: ”If thou examinest a man having a fracture in his mandible, thou shouldst place thy hand upon it. Should thou find that fracture crepitating under thy fingers, thou shouldst say concerning him: "One having a fracture in his mandible, over which a wound has been inflicted and he has fever from it." An ailment not to be treated.” (Baudens 1840). Meanwhile, in Ancient India, techniques were developed for the use of pedicle flaps from the forehead or cheek to repair defects of the nose or lips, often inflicted as a form of punishment. Harvey Graham, writing in his book Surgeons All, comments: ”Egypt and India must have ranked equal. The decline and fall of surgery followed almost exactly the same lines in the two countries. In each case an over-specialisation was the first step.”

Asklepios, or Aesculapius as he was known to the Romans, was a Chief of Thessaly who achieved fame from his treatment of battle wounds during the Trojan Wars of 1300 B.C. His symbol of the Caduceus-two snakes wound around a staff - has been adopted by the medical profession as its symbol since these early times. The nature of the casualties at the fighting around Troy has been immortalized in Homer's Iliad (Annandale 1875).

In the course of time, temples to Asklepios were set up and the secular assistants to the priests, known as Asklepiadae, assumed responsibility for the treatment of patients. To one of these assistants, in the year 460 B.C. on the island of Cos in the Aegean Sea, was born a son, Hippocrates. His treatment for dislocation of the mandible was essentially similar to that advocated by the Ancient Egyptians. However, he would appear to have been the first to advise, in the case of fractures of the mandible, that: ”If the teeth at the wound be distorted and loosened when the bone is adjusted, they should be connected together, not only two but more of them, with a gold thread if possible, but otherwise with a linen thread, until the bone be consolidated.” (Corron 1875).
The support for the fragments was provided by broad strips of Carthaginian leather, glued to the skin adjacent to the fracture site and the essentials of this method of bandaging persisted well into the present century. Hippocrates shrewdly commented that: ”It should be well known that, in fractures of the jaw, dressing with bandages if properly performed is of little advantage, but occasions great mischief if improperly done.” ”(Wiseman 1686).

During the early medieval period During the period of the Roman Empire little if any true advances were made in the treatment of maxillo-facial injuries, and reliance was placed upon the traditional Hippocratic methods. Antyllus, in his seven-volume work, Compendium Medicinae, written about A.D. 150 gives a precise description of the operative technique for tracheotomy, pointing out the dangers of injuring the carotid arteries and the recurrent laryngeal nerve, making a transverse incision in the neck and also through the space between the third and fourth tracheal rings. No tube was introduced, the patient having to keep the neck hyperextended in order to breathe. Guido Guidi, in his textbook of surgery published in Paris, in 1544, appears to have been the first to have advocated the introduction of a gold or silver tube, this method certainly being in

current practice about half a century later as evidenced from an illustration in the Tabulae Anatomicae of Julius Casserius originally published at Ferrara in A.D. 1600 (Pare 1634).

It was the first European Medical School to be established at Salerno in Italy, and Guglielmo Salicetti, or William of Saliceto, in 1275 gave, in his Praxeos Totius Medicinae, precise instructions upon the treatment of fractures of the mandible. These were essentially similar to those first defined by Hippocrates but, in a later edition of Salicetti's treatise which was printed at Lyons in A.D. 1492, the reader is advised, following completion of the traditional method of wiring the teeth of the lower jaw to one another, as follows: ”This done, tie the teeth of the uninjured jaw to the teeth of the injured jaw in this way.” (Reverdin 1869)

This seems to have been the first clear indication of using the teeth in the stable upper jaw for immobilization of the lower jaw. It is quite remarkable that this extremely valuable concept should have lapsed into oblivion until it was revived by Gilmer in 1886.

Ambroise Pare, one of the most famous surgeons of Mediaeval Europe, published the Cinq Livres de Chirurgie in Paris in 1572, the English translation by Thomas Johnston appearing in London in 1634 (Chopart and Desault, 1779). Pare, speaking of the "Fierie Engeines" of war, attributes the discovery to: ”A Germane of obscure birth and condition, who demonstrated the use of Gunpowder to the Venetians when they warred with the Genoveses about Fossa Claudia, in the year of our Lord 1380. 1 think that the deviser of this deadly Engeine hath this for recompense, as not meriting for this, his most pernicious invention, any mention from posterity.” (Heath 1868, Casserius 1600).

This technique was applied as recently as the 1914-18 war and illustrated in an article written in the British Dental Journal by the late W. Warwick James. Pare also was renowned for the introduction of artificial noses and eyes, and obturators for palatal defects. These were constructed of beaten silver and suitably painted.

In the same time, Tagliacozzi, professor at the University of Bologna, perfected a technique originally introduced by Branca in Sicily for reconstructing an amputated nose from a flap raised on the inner aspect of the upper arm and transferred, in stages, to the nasal stump.

By this they established the basis of the present surgical technique of the so-called ”Italian Rhinoplasty'. In his book De Curtorumn Chirurgia per Institionem, published in Venice in 1597, he clearly appreciated the psychological aspects of the injuries when he wrote: ”We restore, repair and make whole those parts of the face which Nature has given but which Fortune has taken away, not so much that they may delight the eye, but that they may buoy up the spirit and help the mind of the afflicted.” (Ringelmann 1824).

During the Civil War in England contains many interesting references to maxillo-facial injuries, the most notable being made by Richard Wiseman in his book Several Chirurgical Treatises and dedicated, as Sergeant-Surgeon, to His Most Excellent Majesty, King Charles II.

In the early 18th century many advances in anatomical and physiological knowledge had been made, and the era of Scientific Dentistry was ushered in by the publication of a book, in 1728, by Pierre Fauchard, entitled Traite de Chirurgie Dentaire. Although Fauchard did not make any special contribution to the treatment of jaw fractures, the impetus which he gave to the development of dental prostheses stimulated others to devise techniques for the dental control of the fragments

other than by the use of simple ligation of the teeth and support from a bandage. Also Chopart and Desault, in their Traite des Maladies Chirurgicales, published in Paris in 1779, described a splint which was essentially a shallow trough of iron which was inverted and placed on to the occlusal surfaces of the lower teeth on either side of the fracture line, being tightened into firm contact by screws acting upon rods connecting a sub-mental plate of sheet-iron to the intra-oral device (Fauchard 1728).

The movement of the fragments was thus prevented by compression between the occlusal surface of the teeth and the lower border of the mandible. Variations of this principle were employed for almost a hundred years, being introduced into Germany by Rutenick in 1799, who applied further stabilization by means of a head harness; England by Lonsdale in 1833, and into Holland by Hartig and Grebber in 1840 (Keen 1909).

Most likely the first apparatus for external cranio-maxillary suspension was devised by von Graefe who, in 1823, described its application in the case of a coachman who was kicked in the face by a horse. The first aid treatment in this case is also of great interest, being analogous to the modern naso-pharyngeal tube. The patient made an excellent recovery from his unfortunate experience (Heslop 1956).

During the development of the intra-oral/extra-oral splint, others were experimenting with the use of wire passed through or around the mandible either to fix the bone fragments or to hold in place some form of intra-oral apparatus. According to MacIntosh and Obwegeser (1967), Ringelmann in 1824 had reported that Laudet, in 1812, had passed a wire through the alveolar bone in the region of the canine fossa to aid in the retention of an upper denture. This is the counterpart of the present method of per-alveolar wiring to retain an acrylic splint in position in an upper edentulous jaw. Baudens, in 1840, reported to the Academy of Medicine in Paris a method for controlling an oblique fracture of the mandible by passing a wire, by means of a surgical needle, around the circumference of the bone and tying it over a molar tooth.

Deriving from this procedure was developed the modern method of circumferential wiring used to retain a splint in position in an edentulous mandible. The technique was later described by Gilmer (1881), who credited Black, of Jacksonville, Illinois, with the introduction of this technique into the United States (Macintosh and Obwegeser 1967).

Transosseous wiring of the bone ends, using malleable iron wire, was first performed by Buck (1847); and using silver wire by Kinloch (1858) in the United States.

Before the advent of plastic surgery, and even in some instances today, the only possibility of rehabilitating the unfortunate victims of a severe facial and jaw injury lay in the hands of the skilled craftsman in metal, a forerunner of the present maxillo-facial technologist. By the construction of an intra-oral and an extra-oral prosthesis, the patient could then mingle with his fellow-men and women to some extent rather than being confined to a military asylum, as in former times, or condemned to live the life of a recluse.

One of the best examples of the work of the prosthetist of this era is afforded by the singular story of the ”Gunner with the Silver Mask”, one Alphonse Louis, a private in the Artillery who, in the trenches before the siege of Antwerp in 1832, was struck by a shell fragment which carried

away a major portion of the mandible with the exception of the rami and the body of the lower jaw as far forward as the first molar tooth on the right side.

During the middle of the 19th century, many advances were made in plastic surgery, both in the use of rotation and pedicled flaps and free skin grafts. Reverdin (1869) published his results with small pinch grafts of full-thickness skin; Wolf, an oculist of Glasgow, reported in 1875 his use of the larger full-thickness skin graft from which the subcutaneous fat had been removed, and Thiersch (1874) described the split-skin graft, taken with a razor, of the type currently used to-day. It now became more fully appreciated that intermaxillary fixation, rather than fixation of the mandibular fragments alone, was desirable if the best results were to be achieved. Gilmer (1887) rediscovered the technique lost to maxillo-facial surgery for many centuries, of ligating individual teeth in the upper and lower jaws with soft annealed copper wire and joining the twisted ends of these wires together so as to immobilize the mandible. Oliver (1910) used a wire ligature with a loop, a technique later improved upon by Eby (1920) and Ivy (1922).

The First World War, because of the static nature of the trench warfare and the high velocity of the missiles used, produced a large number of severe maxillo-facial injuries (James and Fickling, 1940).

Roentgen discovered of X-rays in 1898 and enabled surgeons to assess with accuracy the results of their endeavours to align the bone fragments.

The technique of bone grafting, with tissue derived from the iliac crest, rib, or tibia reached a high level of efficiency which is remarkable considering the absence of any chemotherapy or antibiotics.

The development of skin grafting intra-orally and the discovery of the tube pedicle in 1917 by Gillies further facilitated the techniques of facial reconstruction. Splints for the jaws were, however, still made in one piece and the fragments fitted into the splint at the time of reduction.
At the commencement of the Second World War, it was immediately appreciated that, for the first time, maxillo-facial Units must be instituted both at home and in the Services and that the specialties of plastic surgery, anaesthesia, and dental surgery must work in close co operation with the neurosurgeon and the ophthalmic surgeon.

A major advance was made in 1942 with the introduction, by Adams, of the concept of internal skeletal fixation using subcutaneous suspension wires passed from holes drilled in the zygomatic process of the frontal bone, the inferior orbital rim, or the zygomatic bone, to support either the maxilla or mandible. Thoma (1943) advocated the use of wires passed through the rim of the pyriform aperture as a point of fixation.

Mclndoe (1941) at East Grinstead made major contributions both to the understanding of the treatment of fractures of the middle third of the facial skeleton, and to the care of the burned patient. Mowlem (1944) at St. Albans developed the use of the cancellous chip bone graft as a means of securing rapid union under adverse conditions, a major step forward in the concept of bone grafting (Fraser-Moodie 1969).

Right after the Second World War advances continue at an ever-increasing tempo, matching the intensity and velocity of modern transportation, by the introduction of a wide range of

antibiotics and the perfection of anaesthetic and radiographic methods greatly facilitate operative techniques and enlarge the scope of maxillo-facial surgery (Graham 1939).

Internal skeletal suspension methods gain in popularity and transosseous wiring, both at the upper or lower border of the mandible, is more extensively employed. Cubero (1948) and Lesney (1953) described the use of circum-zygomatic suspension wires, and Roberts (1964) and others have perfected the use of small bone plates for mandibular fractures. Better instruments, specially designed for the purpose, are available.

Than, the plaster headcap is tending to be replaced by the lightweight frame directly applied to the outer table of the skull by four specially shaped pins, a method first introduced by Crawford in 1943 but which is only now gaining favour.

Converse (1957) drew attention to the 'orbital blow-out' fracture, disintegration of the thin orbital floor without fracture of the orbital rim, which, if undiagnosed and untreated, results in enophthalmos and restriction of ocular movement. The development of the silicone rubbers, such as Silastic, has, in some cases, eliminated the need for bone grafts in such cases.

In order to maintain my perspective, it would be well to conclude with the words of Paracelsus from the Grosse Wundarznei, written in the 16th century: ”The balsam which naturally lies in the bone heals fractures, the balsam in the flesh heals flesh. . . . Every surgeon should know that it is not he that heals, but it is the balsam in the body which heals.”

This research direction has been materialized by publishing the following articles:

1. Severin F, Rosu AM, Tiglis M, Checherita LE, Stegaru G Cobzeanu MD, Hainarosie R, Cobzeanu BM, **Palade OD.** Multidisciplinary Therapeutic Management in Complex Cervical Trauma. Medicina 2023, *59*, 596.
2. Rosu, AM, Severin F, Rosu OC, Cobzeanu BM, Gherasimescu S, Sava FP, **Palade DO**, Drochioi CI, Costan VV, Cobzeanu MD Patterns and Characteristics of Midface Fractures in North-Eastern Romania. Medicina 2023, 59, 510.
3. Dabija MD, Nechifor S, Dabija VA, stefanescu CD, Hainarosie R, Pietrosanu C, Toader C, Rusescu A, Amza EO, **Palade OD**. Management of frontal sinus fractures – our experience. Rom J Leg Med 2020, 28: 294-298.

3.2. New horizons in cervical trauma

3.2.1. Introduction

The management of cervical trauma has been a topic of great interest and controversy over the years. The need for surgical exploration of all cervical wounds' dates back to the time of the Second World War (WWII). However, the evolution of the emergency medical system and paraclinical investigations has contributed to the improvement of global statistics regarding the mortality and morbidity of this pathology.

Currently, studies reported by various authors show similar mortality and morbidity regarding the approach of clinical surveillance and non-exploratory diagnosis in selected cases versus surgical management for all patients. The universal clinical indication for urgent surgical exploration of the patient with complex cervical trauma is the presence of the following symptoms: unstable vital signs, significant pulsatile bleeding, hematoma with a substantial increase in size, shock, airway obstruction, open airway wound, hematemesis or hemoptysis (Bent et al., 1993). Proponents of mandatory surgical management argue that any injury that penetrates the platysma should be explored in the operating room. In particular, zone II is mainly due to the rich content of critical neurovascular structures.

On the other hand, in the last five years, the current otolaryngology opinion issues the hypothesis, with already quite a few followers, in favor of selective surgical management. Paraclinical examinations are required, which include angiography, esophagography, panendoscopy, and computed tomography. Explorations are indicated only in hemodynamically and respiratory stable patients. This management strategy is preferably performed only in hospital facilities with appropriate logistics (Greaves 2010).

We present a retrospective and prospective study of complex cervical trauma pathology secondary to various accidents or aggressions, which required surgical interventions. Our main objectives were to analyze the management of complex cervical trauma in a reference university medical center, and the analysis of the patient's characteristics under different aspects (demographic, pathological aspects, therapeutic).

3.2.2. Materials and Methods

The study group was made up of 103 patients admitted to the Ear, Nose and Throat (E.N.T.) Clinic, "St. Spiridon", Iasi, between 2012–2016, with complex cervical trauma pathology produced by various mechanisms, such as car accidents, domestic accidents, assaults, ballistic trauma, self-inflicted attempts, hanging or strangulation. However, this study was partially limited by the fact that information on particular patients was incomplete, due to the retrospective nature of the research and the lack of uniformity regarding the description of the operative technique, along with the results of the paraclinical investigations performed, as there was no existing standardized protocol; a situation that could bring some damage to the data identified on this study. The study

was started in 2014 and it consisted of two parts. The patients included in the retrospective study were those admitted to the ENT clinic of "Saint Spiridon" Hospital, Iasi, in the period 2012–2014. Likewise, the patients included the prospective study were those patients admitted to the ENT Clinic in during 2014–2016. We defined the complex cervical trauma as the lesions that are penetrating platysma and involve at least the superior aero-digestive tract, vascular, neurologic, thyroidian or salivary gland structures.

The data were centralized in an SPSS 18.0 database and processed with the statistical functions to which they lend themselves at the significance threshold of 95%. Using specific statistical methods, it was possible to calculate the mean value and the standard deviation (SD); quantitative variables were compared using the Student's t-test, and the Chi-square test assessed quantitative parameters. The ANOVA test was used to evaluate descriptive statistical indicators: minimum, maximum, mean, median, standard deviation, standard error of the mean, and variance. The Skewness, Kurtosis ($-2 < p < 2$) method tests the normality of the series of values. In calculating the significant difference between the two means, the Student's t-test considers the measurement of variability and the weight of the observations. F-test (ANOVA) was used to compare values with normal distributions in three or more groups. The Pearson correlation coefficient was used to establish the existence of correlations, and their intensity between various numerical variables studied. The type of correlation was expressed by the sign of the Pearson correlation coefficient, and the power of the link between the variables was represented by its value. Statistical significance was set at the $p < 0.05$ threshold for a 95% confidence interval. Univariate and multivariate analysis by logistic regression was used to determine the variables correlated with the presence or absence of the studied events, identifying statistically significant independent parameters.

General inclusion criteria had in view the information selected from the observation sheets and fell into the following categories: demographics data, epidemiological characteristics, lesion appearance and mechanism, location cervical corresponding to the defined areas of the neck, the type and extent of the damaged tissues, paraclinical investigations carried out, associated pathologies or relapses, therapeutic approach, complications along with the data obtained from the periodic consultations performed upon discharge from the hospital.

General exclusion criteria were under 18 years of age, the patient's refusal to participate, the presence of previous cervical trauma, but without pathological lesions or only superficial lesions without being accompanied by the above-mentioned symptoms.

3.2.3. Results

The patients selected for this study presented with closed and open penetrating cervical traumatic injuries caused by self-inflicted, interpersonal aggression and accidental mechanism. The symptoms and clinical signs identified varied according to the location of the injury and the affected visceral or extra-visceral structure, and the concomitant existence of other traumas with other sites. Dysphonia, dyspnea, various degrees of acute respiratory failure, cervical subcutaneous emphysema, and a mid-cervical blowing wound are characteristic elements of the involvement of

the laryngotracheal axis. Pharyngoesophageal damage is characterized by dysphagia and subcutaneous emphysema. A descending injury from zone I is associated with acute respiratory distress, pneumothorax or hemothorax, signs of cardiac tamponade suggesting damage to the apex of the lung and the vessels at the base of the neck, nerve involvement of the cervical plexus or cranial nerves, which may decrease the sensitivity and motility of the superior limbs. In parallel with the clinical examination, respiratory and cardiac vital signs were monitored, blood samples were taken, and the indication was established regarding paraclinical investigations or the need for emergency surgical exploration depending on the stability of Surgical explorations.

In the study group, made up of 103 patients hospitalized in the ENT clinic, the age varied between 17 and 78 years, the average age was 43 years (standard deviation = 15.67), registering a slightly higher average value in the male sex (43.41 vs. 42.09 years; $p = 0.793$). patients come more frequently from rural areas (56.6%), they are predominantly male (89.6%), under the age of 45 (55.7%); the lesional determining mechanism is noted more frequently through aggression (39.6%), followed by the self-inflicted mechanism (39.6%) and the accidental mechanism (22.6%).

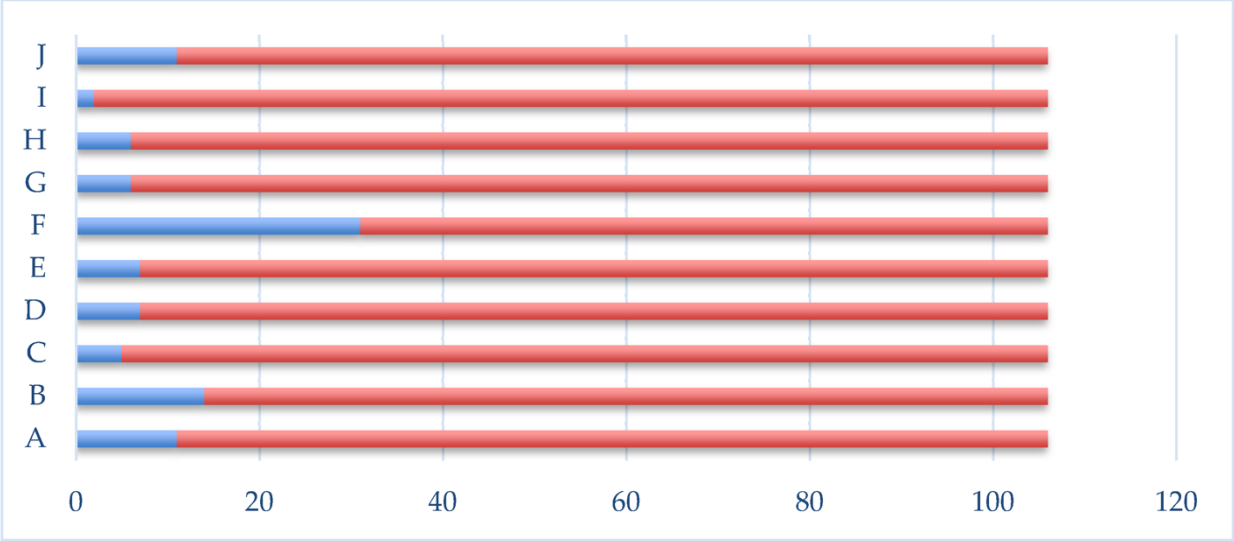


Figure 3.1. Distribution of complex aero-digestive cervical trauma cases and associated injuries. A—section of the thyrohyoid membrane with the interest of the hypopharynx. B—fracture of the laryngeal cartilages with laceration of the epiglottis, vocal cords, and pyriform sinuses. C—dilacerations with retrocricoid hematomas. D—sectioning of the cricothyroid membrane and partial or total involvement of the cricoid cartilage. E—sectioning of the crico-tracheal membrane and the tracheal rings. F—dissection of the superficial jugular veins. G—internal jugular vein involvement. H—thyroid gland interest and I—the interest of the submandibular gland. J—Polytraumatism.

In this study, the cases that required surgical intervention were characterized by complex aero-digestive, thyroid, vascular, and polytrauma injuries. Thus, the following were identified: section of the thyrohyoid membrane with involvement of the hypopharynx (11 cases), fracture of the laryngeal cartilages with dilaceration of the epiglottis, vocal cords and pyriform sinuses (14 cases), dilacerations with retrocricoid hematomas (5 cases), sectioning of the cricothyroid membrane and interest partial or total cricoid cartilage (7 cases), sectioning of the crico-tracheal

membrane and tracheal rings (7 cases), sectioning of the superficial jugular veins (31 cases), involvement of the internal jugular vein (6 cases), involvement of the thyroid gland (6 cases), involvement of the submandibular gland (5 cases), polytraumas due to traffic accidents or falls from a height with complex thoracic, abdominal, craniofacial and limb injuries (11 cases) (Fig. 3.1.)

From the total number of vascular lesions of the anterior, external, and internal jugular veins, the following lesions were identified: contusions, adventitial lesions, and complete or partial sections, to which is added a case of penetrating wound involving the thoracic duct. These injuries required parietal reconstruction and vascular ligature to perform hemostasis, depending on the case, through specific techniques (Fig. 3.2.)

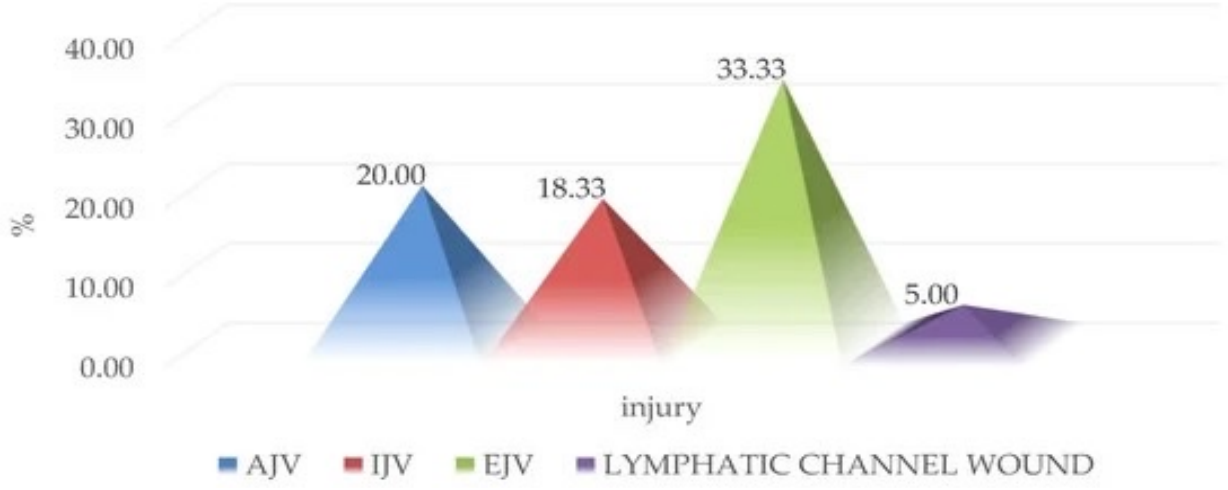


Figure 3.2. Distribution of venous lesions that required surgical treatment. (AJV = anterior jugular vein, IVJ = internal jugular vein, EJV = external jugular vein).

Regarding the arterial lesions of the carotid system, adventitious contusion-type lesions of the common and external carotid arteries and pseudoaneurysm-type lesions at the level of the common carotid artery were identified in our study (Fig.3.3.)

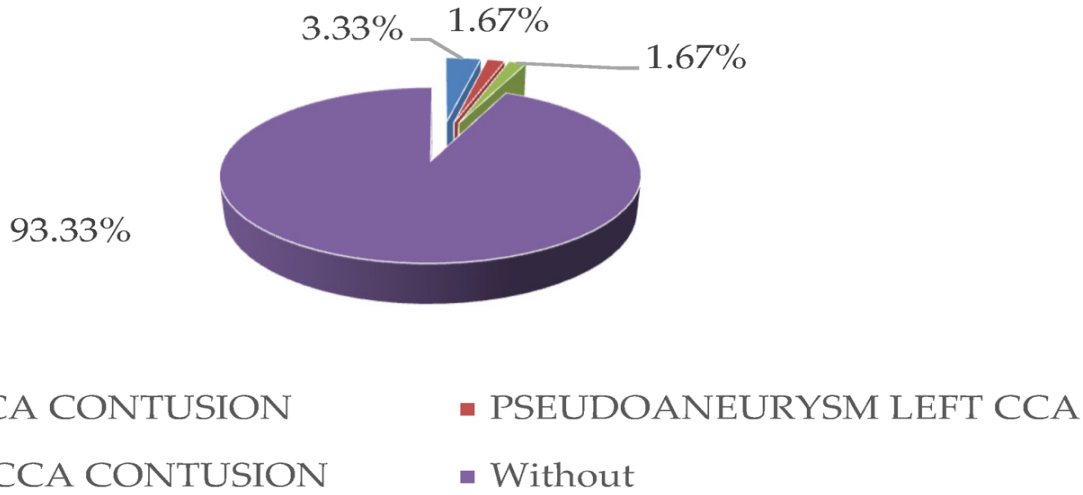


Figure 3.3. Distribution and characteristics of carotid lesions that required specific surgical treatment.

As for the penetrating hypopharyngeal lesions, in the entire study group, penetrating lesions of the pharyngeal wall were identified only at the level of the piriform sinuses with the development of parapharyngeal hematomas that had a posterior prevertebral extension and determined compressive phenomena with the onset of acute upper respiratory insufficiency and dysphagia (Fig. 3.4.)

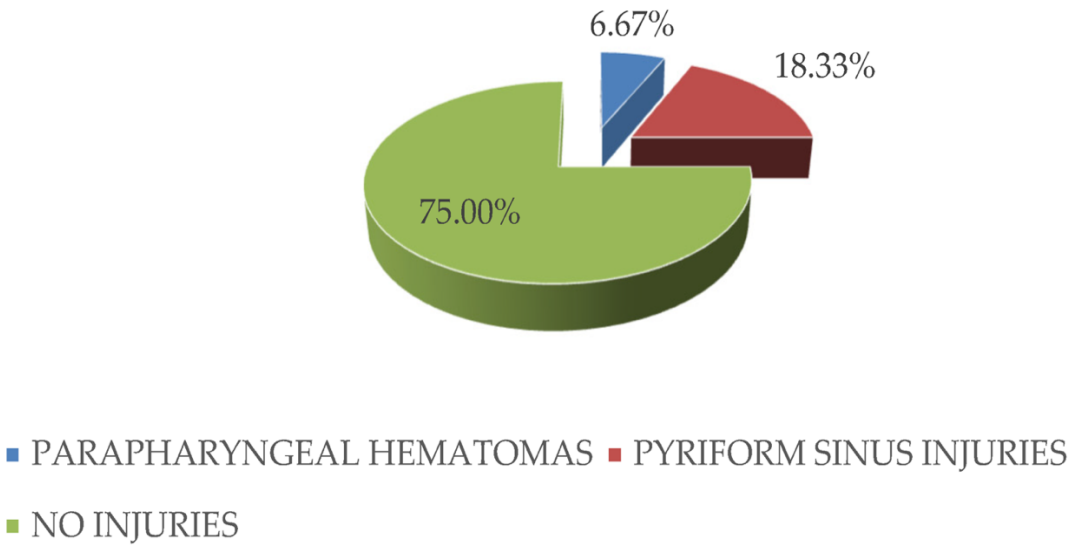


Figure 3.4. Distribution and characteristics of hypopharyngeal and parapharyngeal lesions that required surgical therapeutic management.

The appearance of traumatic laryngeal lesions identified both clinically, paraclinical, and intraoperatively is very diverse, including lesions of the mucosa, vocal cords, laryngeal cartilages, thyrohyoid and cricothyroid membrane, as illustrated in Fig. 3.5. and on which specific therapeutic intervention was performed, both surgically and medically.

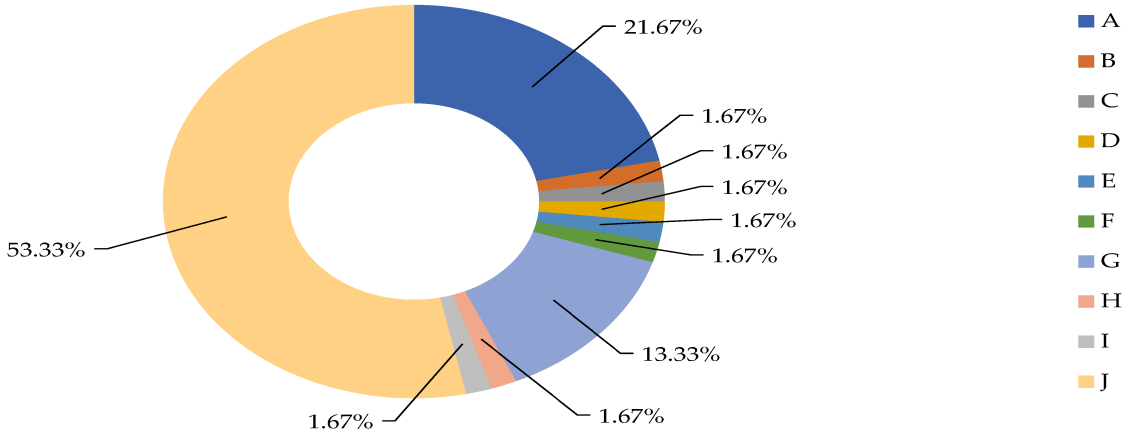


Figure 3.5. Distribution and characteristics of traumatic laryngeal injuries that required a surgical therapeutic approach. A—vocal cord injuries. B—arytenoid cartilage injuries. C—cricoid cartilage fracture. D—cricotracheal membrane section. E—section thyroyidian membrane. F—paralaryngian hematoma. G—total or partial thyroid cartilage fractures. H—section thyrohyoid membrane, epiglottic exposure, and laryngeal continuity solution. I—continuity solution at the laryngeal level with the appearance of cervical emphysema. J—no laryngeal injuries.

Surgical exploration under general anesthesia was performed in 42 of the 103 patients in the study group (39.6%), more frequently in males (44.1% vs. 27.3%; p = 0.656), age group under 45 years (40.7% vs. 38.3%; p = 0.803) and with a rural background (37% vs. 41.7%; p = 0.623) (Figure 3.6).

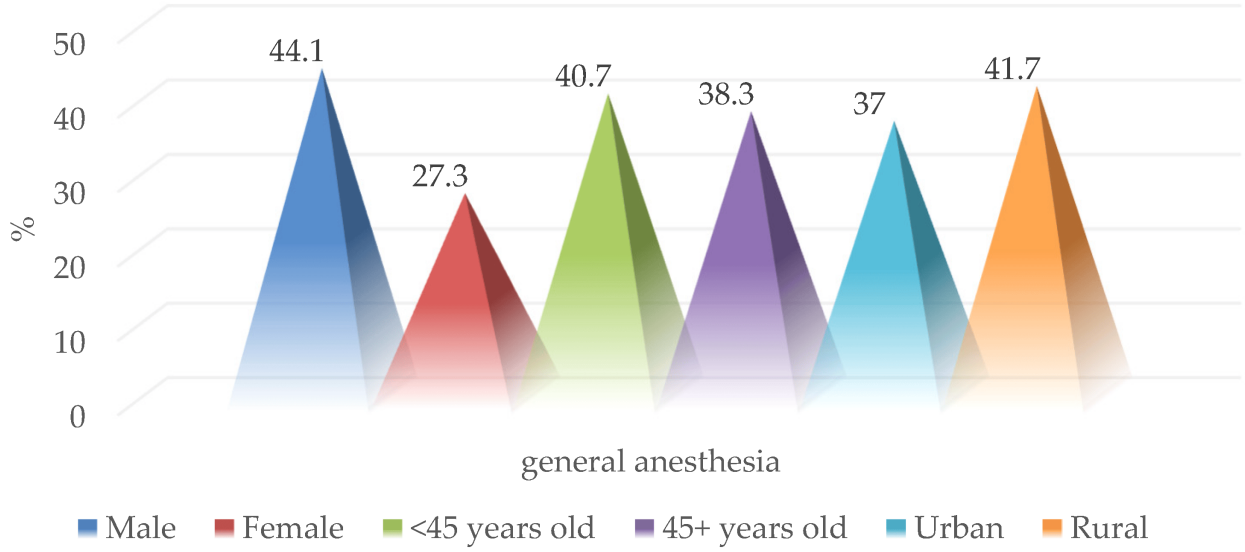


Figure 3.6. Epidemiological characteristics of patients with surgical exploration performed under general anesthesia.

Regarding the mechanism of production of traumatic injuries, the statistical analysis shows that the use of surgical exploration through general anesthesia was more common in patients with penetrating injuries produced by aggression and accidentally (27.5% vs. 45.2% and 50%; p = 0.05) (Fig. 3.7).

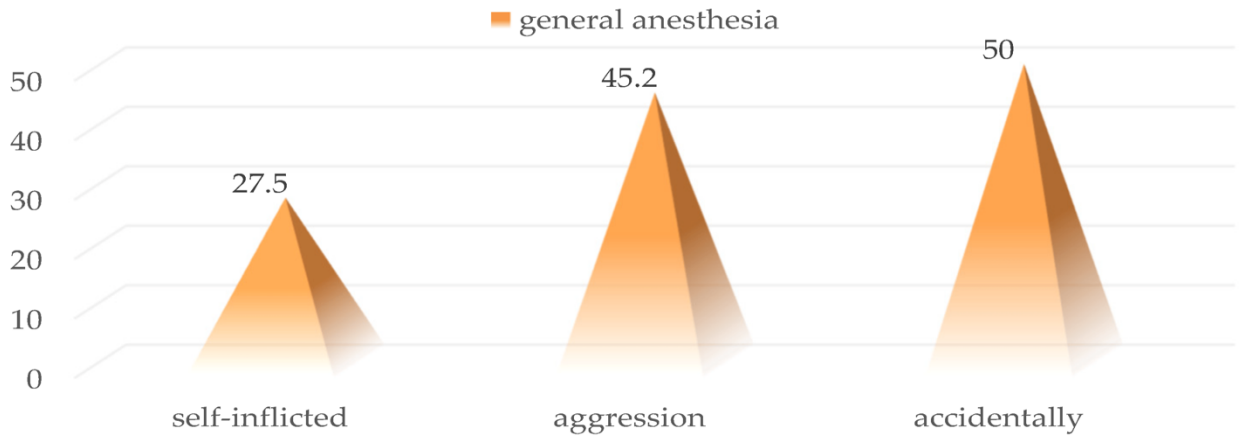


Figure 3.7. Distribution of cases surgically explored under general anesthesia according to the injury mechanism.

Surgical exploration of penetrating wounds under local anesthesia was performed in 28 of the patients in the study group (26.4%), more frequently in females (36.4% vs. 28.3%; p = 0.443), age group over 45 years (23.7% vs. 29.8%; p = 0.483) and the urban environment (34.8% vs. 20%; p = 0.688) (Fig. 3.8).

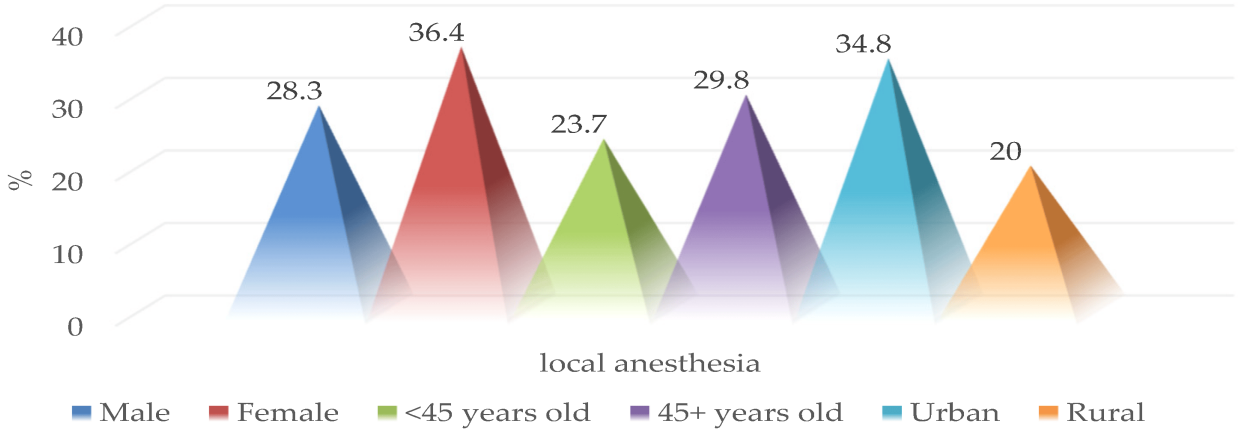


Figure 3.8. Epidemiological characteristics of patients with surgical exploration performed under local anesthesia.

Tracheostomy was performed in 17 patients included in the study (16%) without significant differences between sexes, age groups, or place of residence (Fig. 3.9). In addition, the need to secure the airway by performing a tracheostomy was not statistically significantly correlated with a specific injury mechanism determining cervical trauma (7.5% vs. 23.8% and 16.7%; p = 0.117) (Fig. 3.10).

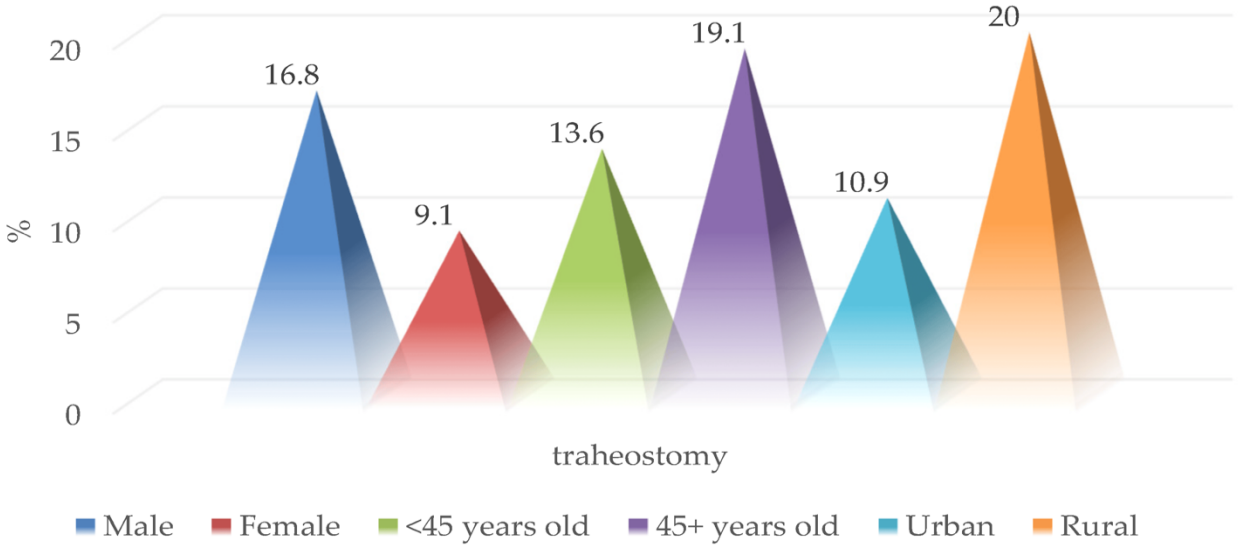


Figure 3.9. Epidemiological characteristics of patients who underwent tracheostomy

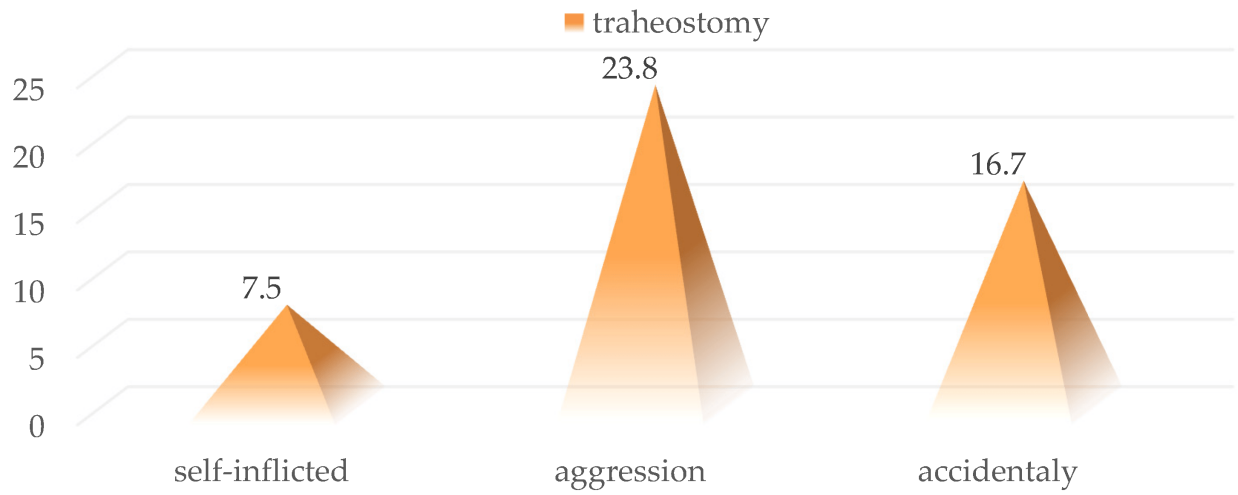


Figure 3.10. Distribution of cases in the batch in which tracheostomy was performed according to the lesion mechanism.

Complex penetrating traumatic injuries of the aero-digestive tract require local digestive rest and the application of a nasogastric tube. However, the recommendation to apply the nasogastric tube was not statistically significantly correlated with the lesion mechanism, which produced the penetrating traumatic injury (15% vs. 14.3% and 12.5%; $p = 0.961$) (Fig. 3.11).

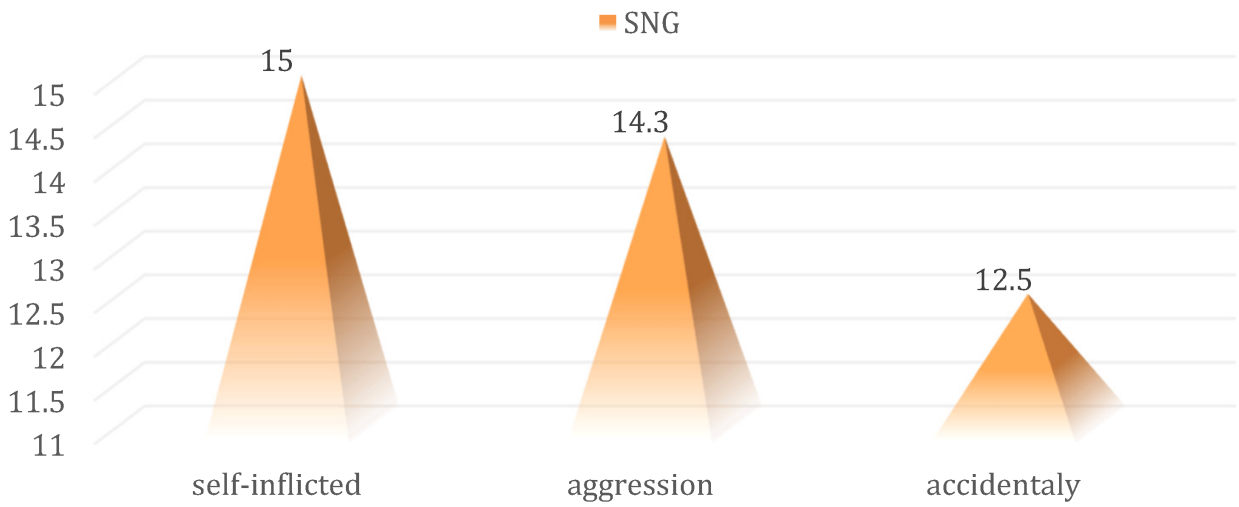


Figure 3.11. Distribution of cases in the batch to which SNG was applied according to the lesion mechanism.

Conservative therapeutic management, consisting of observation, serial clinical examination, paraclinical explorations, and supportive drug treatment, was carried out in 38 of the selected patients (35.8%) without significant differences between sexes, age groups, or the place of residence (Fig. 3.12).

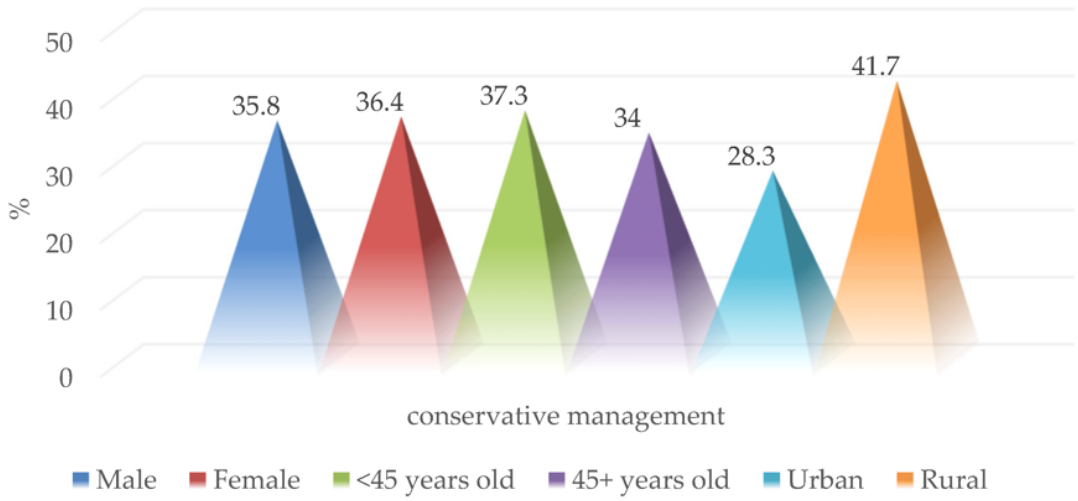


Figure 3.12. Epidemiological characteristics of patients with conservative management.

The conservative therapeutic approach correlated statistically significantly with the self-inflicted mechanism (60% vs. 26.2% and 12.5%; $p = 0.001$) (Fig. 3.13)

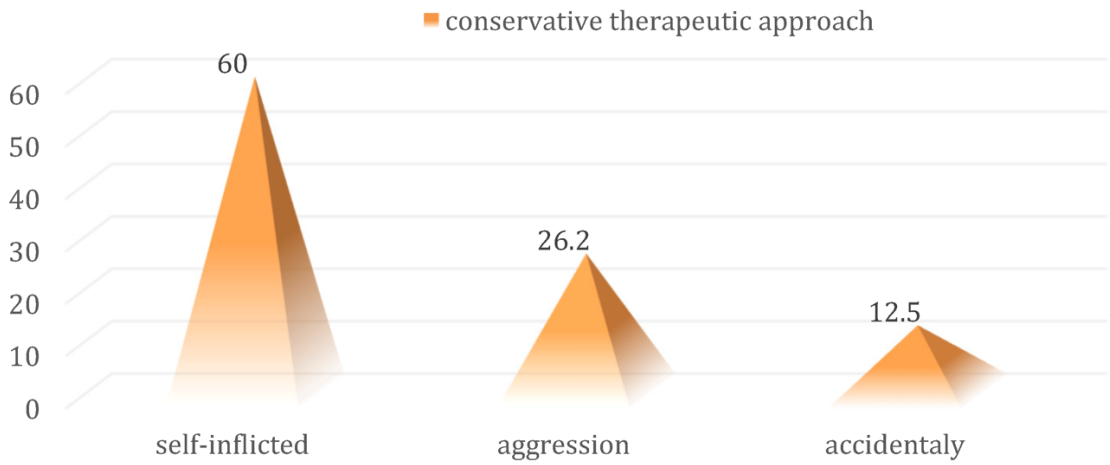


Figure 3.13. Distribution of cases in the batch with indications for conservative management according to the lesion mechanism.

The need for the administration of supportive drug treatment was identified in 102 patients from the group (96.2%), without significant differences between sexes, age groups, or the place of residence (Fig. 3.14).

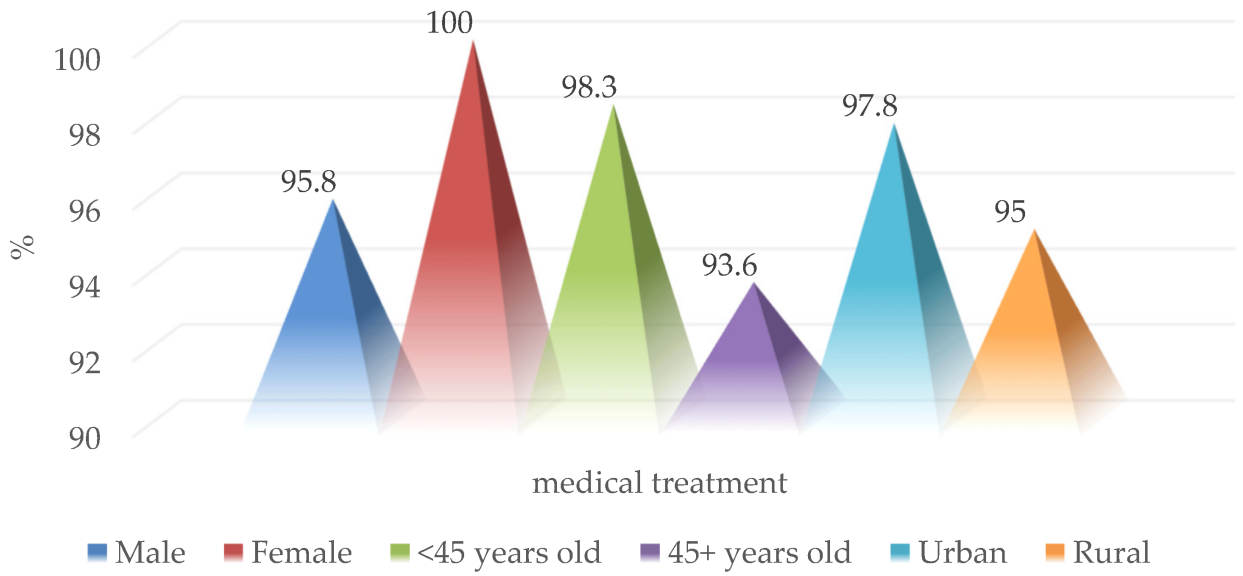


Figure 3.14. Epidemiological characteristics of patients who received medical treatment.

Postoperative complications were noted in 6 patients (5.7%), all male, five aged over 45 years, and five from rural areas. The postoperative complications identified were the following: partial dehiscence of the postoperative wound, parotid salivary fistula, postoperative wound infection with Enterobacter, stroke, pneumococcal pneumonia, post-traumatic left genial edema, dysphonia, and torticollis.

3.2.4. Discussions

The essential therapeutic attitude in complex cervical trauma is ensuring the airways' safety through orotracheal intubation or emergency tracheostomy and hemostasis control, followed by clinical and paraclinical investigations, then exploration and reconstructive surgical treatment. In cases where the hemodynamically unstable patient could not be investigated paraclinical and presented traumatic injuries with a penetrating character, urgent surgical exploration is required. This exploration can be performed under general anesthesia with orotracheal intubation, tracheostomy, or local anesthesia.

The importance of first aid, as well as emergency therapeutic measures in other health facilities, must include primary hemostasis and the proper support of cardio-respiratory parameters. Transport must be ensured in safe conditions and as soon as possible, considering the complications that can occur in the first hours after the trauma. In emergencies, the airway was secured (freeing the oral cavity of secretions and blood, possibly intubating the patient or tracheotomy), immobilizing the cervical spine, accessing the venous lines, and obtaining a correct anamnesis regarding the circumstances of the accident, the associated diseases, the state of consciousness. Intubation through the cervical area is indicated when there are injuries to the oral cavity, pharynx, or larynx. Orotracheal intubation can accentuate pharyngolaryngeal lesions, causing the extension of some lesions from the level of the piriform sinus to the mediastinum. In lesions with significant

cervical tissue destruction, intubation was performed through the continuity solution at the level of the sectioned thyrohyoid membrane.

According to the European Manual of Medicine, Otorhinolaryngology, Head and Neck Surgery, the standard of investigation and exploration procedures in the case of cervical traumatology is applied depending on the presence or not of the hemodynamic and neurological stability criteria. The unstable patient will be provided with an airway simultaneously with the treatment of shock and cervical surgical exploration; postoperative achievement of hemodynamic stability and neurological will allow additional endoscopic and imaging investigations to be performed. The symptomatically stable patient is subjected to endoscopic, imaging and interventional angiographic investigations to determine the lesion balance and establish subsequent to the therapeutic conduct.

Depending on the symptomatology and clinical examination of the patients with cervical trauma selected for this study, the following methods of paraclinical exploration were used: cervical and thoracic X-ray, Doppler cervical and soft part ultrasound, craniocerebral, cervical and thoracic computed tomographic scan, computed tomographic angiography, naso-pharyngo-laryngeal and upper digestive endoscopic exploration.Cervical and chest X-rays identify cervical soft tissue emphysema, fractures, tracheal lacerations, foreign body retention, hemothorax, pneumothorax, mediastinal emphysema. Computed tomography, ultrasound of the cervical soft parts and Doppler, angiography, or pharyngoesophageal transit with contrast material are performed when complex lesions are suspected. Panendoscopic exploration (laryngeal, pharyngo-esophageal and tracheo-bronchoscopy) are used in the case of complex lesions of the aerodigestive axis. The use of the rigid endoscope is superior to the flexible one in upper esophageal lesions.

For patients with aero-digestive lesions depending on the severity of the symptoms and the injury complexity, the therapeutic attitude involved a medical treatment associated with the surgical one. Patients with mild laryngeal and tracheal injuries, without respiratory changes or signs of laryngeal fractures, were hospitalized and kept under observation for at least 24–48 h (since there is a potential risk of further respiratory dysfunction, through the expansion of edema, in the interval of time, which follows the trauma). The treatment was conservative, with medicinal support, and consisted of administering antibiotic therapy, steroid anti-inflammatories, aerosols, oxygen therapy, and air humidification. During hospitalization, it is indicated to carry out serial evaluations clinically and through naso-pharyngo-laryngeal fiberoscopy.

In the case of patients with variable respiratory disorders associated with laryngeal mucosa lesions, edema, and hematomas, the intervention was performed by performing a tracheotomy under local anesthesia and an endoscopic lesion assessment after the induction of general anesthesia. 3–5 days postoperatively, the tracheotomy was suppressed, during which the patient received supportive drug treatment. The presentation at admission with signs and different degrees of acute respiratory insufficiency associated with extensive laryngeal lesions of the mucosa, edema, and endolaryngeal hematomas, alteration of the mobility of the vocal cords or different degrees of comminution of cartilaginous fractures required the surgical therapeutic approach. This was performed in the following sequence: tracheotomy, endolarynx exploration through direct laryngoscopy, cervical wound exploration, and laryngeal approach through

thyrotomy or the thyroid cartilage fracture path. Lesions of the laryngeal mucosa were repaired by sutures with absorbable 4-0 or 5-0 threads without exposing cartilaginous areas. Depending on each case's lesion, the foot of the epiglottis, the ventricular band, or the vocal cords were reinserted, the aryepiglottic fold was restored, and the laryngeal fractures were reduced by suturing with non-absorbable threads. Anchorage of the superior and inferior retrocricoid ends was required. In cases with significant loss of substance, the larynx was restored with different muscles plasties. Anchorage of the hyoid with separate wires to the external laryngeal perichondrium was performed to achieve adequate laryngeal tightness and statics. Surgical therapeutic management was associated with antibiotic treatment, steroid anti-inflammatories, aerosols, and oxygen therapy. Suppression of the tracheal cannula was performed after 10–12 days.

The most severe cases with poor prognosis were characterized by extensive destructive lesions, loss of soft and cartilaginous substance, vocal cord disinsertion, or crico-tracheal disjunction associated with severe acute respiratory failure. These required emergency surgical exploration, laryngeal reconstruction, and recalibration. Recalibration was performed by fitting and maintaining a Montgomery tube for two weeks. Again, appropriate laryngeal calibration is recommended, with scar management in major debridement and mucosal restoration to avoid stenoses.

In cases with hypopharyngeal lesions of varying degrees of complexity, a careful clinical examination was performed, digestive rest was indicated with the application of a nasogastric tube, and depending on the severity of the lesion, surgical reconstruction as quickly as possible (ideally within the first 6–8 h from trauma) associated with performing a tracheotomy. The suturing of the pharyngeal wall was performed in two planes, serous and mucous. Hypopharyngoesophageal injuries are severe and require immediate recognition and treatment. A muscle flap can be used as a sleeve and isolates the upper digestive tract to avoid the formation of pharyngo-cutaneous or eso-tracheal fistulas. Pharyngeal plastic surgery was performed with prevertebral aponeurosis and subhyoid muscles. They are ideal for preventing post-operative suppurative or stenotic complications. Significant is the prompt correction of metabolic and hydro-electrolytic imbalances in the pre-, intra-, and post-operative periods, such as the administration of correct broad-spectrum antibiotic therapy, anti-inflammatories, and proton pump and H2 receptor inhibitors to prevent regional complications and sequelae. Maintaining the nasogastric feeding tube is indicated in cases where pharyngeal sutures were performed and in the remission of fistulas for 3–4 weeks.

Depending on the complexity of the traumatic aero-digestive injury, digestive rest through a nasogastric tube and respiratory rest through tracheotomy for 7–14 days are necessary conditions for resuming normal swallowing, breathing, and phonation. In addition, aspiration drainage is applied and maintained to avoid the formation of postoperative hematomas and seromas to smooth the tissue planes.

Cervical wounds involving various tissues and the cervical visceral aerodigestive axis require an established protocol for a multidisciplinary team approach. This team consists of the otolaryngologist, anesthesia and intensive care physician, emergency physician, and other specialties depending on the injuries associated with different body segments.

Vascular lesions in the zone I required collaboration with the thoracic surgery department, with the performance of mediastinotomy and thoracotomy to perform hemostasis. The identification following the radiological examination of hemothorax, pneumothorax, or pneumomediastinum required proper drainage of air and blood collections. In one case with plurivisceral involvement and basicervical venous vascular section, the thoracic duct was also involved, along with anterior mediastinal lesions in the left half. This case also involved collaboration with the thoracic surgeon. In zone III, the lesions required the performance of a median mandibulotomy to expose the parapharyngeal space to evacuate hematomas with an obstructive dyspneic character or to have access to the vasculo-nervous structures at the base of the skull. In the case of cases involving the submandibular gland, excision of the torn tissues, suturing of the glandular body, or total or partial excisions of it were necessary.

Cervical venous injuries (jugular vein and thyro-lingo-facial venous trunk) were resolved by ligation and adventitial sutures except when both internal jugular veins were involved when an attempt was made to restore the continuity of one of them. In the case of the carotid artery injury, it was important to fix it by adventitial sutures, end-to-end anastomosis, or by applying a graft with the help of vascular surgery colleagues (two cases).

In the case of complex cervical trauma produced by a closed or penetrating mechanism, which involved the thyroid, the following aspects were identified: expansive anterior cervical hematoma, compressive on the respiratory axis with phenomena of acute respiratory failure, which required its emergency drainage; cervical wounds with thyroid and laryngeal involvement with bleeding, which flood the respiratory tract, causing the exacerbation of respiratory failure phenomena and which required the performance of protective tracheotomy and the securing of the airway associated with the removal of crushed glandular tissues or different degrees of subtotal thyroidectomy. In addition, in 7 of the cases included in the study group, the glandular suture of the suture type with slow resorbable thread was performed.

The postoperative occurrence of fever, tachycardia, chest pain, widening of the radiographic mediastinum, subcutaneous emphysema, bleeding wound, the onset of neurological deficits, or the development of a hematoma requires imaging and surgical re-exploration.

All cervical aero-digestive traumas, regardless of complexity, were carefully recorded in terms of local examination, the evolution of symptoms and vital or biological constants, imaging and endoscopic examination, and exploratory and surgical reconstruction protocols.

The clinical management of complex cervical trauma has changed over time towards a conservative approach. Even so, the need for surgical exploration in patients with traumatic penetrating injuries of the aerodigestive tract or great vessels should be based on clinical elements and reliable indicators for indicating an open exploration.

The number of medical and medical-surgical specialties involved and the diagnostic assessment of patients with traumatic neck injuries requires developing and implementing a multidisciplinary institutional protocol with national applicability. In addition, it could support the ways of indicating paraclinical diagnostic procedures, such as flexible naso-pharyngo-laryngeal fiberoscopy, plain radiography, and esophagography, as well as computed tomography, but also the clear indications of surgical versus conservative treatment.

Since Ambroise Pare ligated both carotid arteries and the jugular vein of a soldier with polytrauma of the neck in 1552, the therapeutic approach to complex penetrating cervical trauma has been one of the controversial topics in trauma surgery. There has not yet been a consensus on this. Surgical exploration of all neck injuries beyond the platysma muscle significantly reduced mortality during World War II (Monson et al., 1969), but 89% of interventions did not identify deep visceral injuries (Azuaje et al., 2003). In 1969, Monson et al. divided the cervical region into the three zones used in the management of trauma diagnostic protocol (Merion et al., 1991). Legerwood et al. in 1980 and Narrod et al. in 1984 showed that the absence of severe clinical signs of hemodynamic instability in penetrating limb trauma quite clearly excludes arterial injuries, which require surgical treatment (Narrod et al., 1984, Sekharan et al., 2000). They extrapolated this reasoning to the diagnosis and treatment algorithm of cervical trauma with vascular involvement, revealing that some arterial lesions may be missed in the diagnosis and may result in potentially life-threatening vascular accidents.

In the 1990s, two studies focused on clinical examination to identify severe signs of vascular involvement in zone II cervical trauma and the need for an indication for reparative surgical exploration (Das 2018, Pakarinen et al., 2006). In addition, the clinical examination is more than 99% accurate in diagnosing these lesions with a false-negative rate comparable to angiography. Furthermore, clinical examination is faster, less expensive, and involves few medical staff. Even so, it is less likely to be able to detect minor lesions such as intimal vascular irregularities, pseudoaneurysms, and arteriovenous fistulas compared to angiographic exploration. Most of these lesions are of no clinical significance (Ahmed et al., 2009). Therefore, routine angiography's additional costs and morbidity are difficult to justify.

Some studies even promote mandatory surgical exploration of all penetrating cervical wounds based on low morbidity and reduced hospital days. This approach has been described as cost-effective and characterized by higher accuracy than contrast-enhanced imaging studies (Ahmed et al., 2009).

For patients with high suspicion of penetrating laryngotracheal injury, detailed clinical examination is mandatory. Trauma of the upper aerodigestive tract is suspected in face of dysphonia or stridor, subcutaneous emphysema appearance, or blowing wound presence, and the main objective is to ensure and maintain the upper airway patency. In a retrospective study including 748 patients with this type of injury, only 11% of cases required immediate airway control, raising questions about the importance of conservative measures (Tallon et al., 2007). Surgical wound management is indicated if there is a significant change in the laryngotracheal anatomy. In such cases, orotracheal intubation may worsen the existing injuries; therefore, tracheostomy under local anesthesia is recommended, even at the site of the accident.

Metheny et al. believe that nasogastric tube placement and feeding is more effective than parenteral nutrition in most patients with critical aero-digestive traumatic injury because it preserves the integrity of the bowel and causes fewer infectious complications. However, nasogastric tube feeding has been associated with risks like other therapies. The most serious potential complication is the tracheobronchial aspiration of gastric contents, with the risk of developing a series of clinically silent microaspirations (Fox et al., 2006).

As we emphasized before, starting with WWII, the main recommendation was to surgically explore the neck for any traumatic lesion that involves the platysma (Nason et al., 2001). Over the years, various research showed that this may be associated with a significant number morbidity. An article from the late 1970s showed that 56% of surgical neck explorations were non-therapeutic (Biffl et al., 1997). The modernization of imaging technologies made the selective approach of neck exploration more common. In this matter, an important study showed that 207 of 312 patients (66%) presenting with penetrating neck injuries were able to be managed conservatively, due to a thorough physical examination, along with angiography/esophageal exploration. Only one patient appeared to have an esophageal lesion missed on the initial examination and required repeat exploration (Ahmed et al., 2009).

Nowadays, the advantages of a selective nonoperative management for penetrating cervical trauma have been established, but there remain some circumstances when immediate operative exploration is mandatory, such as significant airway or major vascular injuries (Ahmed et al., 2009). In 2012, Burgess et al. reviewed the specialized literature regarding managing traumatic cervical injuries with a penetrating character and the institution of mandatory or selective surgical treatment.

In the case of our study, all cervical traumas beyond the platysma were surgically explored under general or local anesthesia with the identification and surgical reconstruction of the lesion. The indication of paraclinical imaging studies was influenced by the hemodynamic status and the need to secure the airway by orotracheal intubation or tracheostomy. In addition, complex aero-digestive lesions required digestive rest and the placement of a nasogastric tube, with the administration of food through this route or the association with the parenteral administration of the necessary nutrients. In cases of reduced complexity, conservative management and supportive drug treatment of traumatic and associated pathology were associated, as appropriate.

Early recognition and management of the complications of penetrating cervical wounds are essential in reducing the mortality and morbidity of these injuries. Prevention of these complications depends on the initial therapeutic actions of securing the airway by intubation or tracheostomy, prompt control of bleeding, protection of the head and neck, accurate and rapid lesion diagnosis, and surgical treatment according to the indication. Additionally, in this study, 89.7% of selected patients were identified with uncomplicated healing, while in our study, the rate was 94.3%, close to other studies (Aich et al., 2011, Teng et al., 2014).

3.2.5. Conclusions

The first evaluation of complex cervical trauma is part of the standard Advanced Trauma Life Support (ATLS) protocol, an essential element on which the vital prognosis depends: securing the airways by orotracheal intubation or tracheostomy. The prehospital period should not be prolonged by performing the ATLS protocol and involves simultaneously balancing vital signs. These elements can dramatically change the patient's prognosis, transforming him from dying to savable. An unstable hemodynamic status and an airway, which requires emergency stabilization, determined the performance of the lesion balance by performing emergency surgical exploration

and involves multidisciplinary therapeutic management, followed by reconstructive surgical treatment at the same operative time or a second time. Optimizing a multidisciplinary emergency medical system will lead to improving global statistics regarding this pathology's mortality and morbidity.

3.3. Remaping the facial trauma

3.3.1. Introduction

Traumatic pathology is the main cause of mortality in adults under 40 years of age, and a significant part of trauma cases are in the maxillofacial area (Salentijn et al., 2013, Gassner et al., 2003).

Of all the injuries that can result after trauma to the cephalic extremity, midface fractures represent an important medical and social problem due to the frequency, complexity and, socio-economic impact they involve. They can have multiple consequences, both aesthetic and functional. In addition to facial deformity, they can cause a malocclusion, difficulty mobilizing the mandible with masticatory problems, diplopia, epiphora, nasal obstruction, respiratory disorders, but also sensory disorders or paresthesia (Yamamoto et al., 2014).

Midface fractures are a common type of injury that can occur due to various causes, such as falls, interpersonal violence, car accidents, and sports injuries. These fractures can affect the nose, cheekbones, and maxillary bone and can cause significant physical and emotional distress for the affected individuals, including facial deformities, functional impairment, and long-term scarring.

In the northeastern part of Romania, midface fractures are a significant health concern, with a high incidence rate among the population. This is likely due to a combination of factors, including the prevalence of high-risk activities and certain factors in the region, such as a high rate of alcohol consumption.

Understanding the epidemiology of midface fractures in the northeastern part of Romania is essential for developing effective prevention and treatment strategies to address this health issue. In the last years, there has been an increasing interest in understanding the prevalence and patterns of midface fractures in different populations. Therefore, it was considered necessary to carry out a retrospective descriptive statistical study that aims to update the epidemiological characteristics of midface trauma between the years 2015 and 2020, also including the general lock-down period during the COVID-19 pandemic in the northeastern area of Romania.

Midface fractures represent a significant medical and social problem due to their frequency, complexity, and socio-economic impact. It was stated that severe midface fractures protect the brain and torso from major traumatic injuries by dissipating the energy of the impact. A study conducted in the United States over the period 1989–2013, including 20,971 patients with trauma, concluded that severe midface fractures were associated with lower rates of hemorrhagic

brain injuries and lower rates of thoracic and abdominal post-traumatic complications (Woriax et al., 2018).

In most cases, a multidisciplinary approach is required, as well as modern diagnostic methods and innovative surgical techniques. In the era of technological medicine and permanent advances, the three-dimensional reconstruction of affected structures based on advanced medical imaging is being discussed, with the aim of more thorough and efficient preparation of operative steps (Satish et al., 2017).

In the present study, the authors aimed to investigate the prevalence of midface fractures in the northeastern part of Romania. This region has a diverse population with a mix of urban and rural areas, and previous studies have shown that the incidence of midface fractures can vary significantly between different regions. Therefore, this study aims to contribute to a better understanding of the epidemiology of these injuries and to aid the development of preventive measures and treatment strategies.

3.3.2. Materials and Methods

Within the Emergency Clinical Hospital "Sf. Spiridon" Iași, a retrospective study, aims to establish the epidemiological data from 2015 to 2020 related to midface fractures. Thus, the data on the background, environment, sex, and age of the patients who were treated in the hospital for fractures of the middle third of the face was collected, as well as the type of fracture, the etiology, the need for surgical treatment and the necessary hospitalization period.

Laterofacial fractures interest the zygoma and the zygomatic arch. Centrofacial fractures affect the nasal skeleton and the upper frontomaxillary processes. Oclusofacial fractures are also known as LeFort fractures. LeFort type I fracture affects the anterior maxilla, lateral nasal wall, and pterygoid plates. The LeFort type II fracture line passes through the nasal bones, causing fractures along the nasal bridge, frontal maxilla, lacrimal bones, orbital floor and inferior rim near the inferior orbital foramen, through the anterior wall of the maxillary sinus, and through the pterygoid plates. Lefort type III fractures determine the separation of the midface from the base of the skull, and the fracture line affects the nasal bridge, the medial orbital wall, the orbital floor, passes along the lateral orbital wall, through the zygomatic arch, ethmoid bone, and pterygoid processes.

A number of 651 subjects aged between 3 and 95 were included, patients of both sexes who suffered a midfacial trauma.

This study was carried out with the approval of the "Sf. Spiridon" Iași Emergency Clinical Hospital ethics committee, as well as of the "Grigore T. Popa" University of Medicine and Pharmacy Iași, in compliance with the European General Data Protection Regulation (GDPR) convention and the legislation in force on the protection of personal data.

The data was analyzed statistically using IBM SPSS Statistics 26 (IBM Corp. Released 2019, IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY, USA: IBM Corp.) and Microsoft Excel 2023 (Microsoft Corporation. (2023), Microsoft Excel for Mac, Version 16.70, Redmond, Washington, United States. Retrieved from https://office.microsoft.com/excel, accessed

on 21 January 2023) using descriptive statistic (average values, maximum values, 25th and 75th percentiles respectively), the ANOVA test, chi-square test and the study of the correlation between different phenomena was carried out using the correlation coefficient r (Pearson).

3.3.3. Results

Out of the total number of patients included in the study, 87 were females, representing 13.36%, and 564, respectively 86.63%, were males; with a distribution of 6.48 to 1 in favor of the male sex with the mean age for female participants being 46.83 (min—5 years, max—95 years) and 40,49 for the male group (min—3 years, max—89 years)

Additionally, the age groups 21–30 years (140 patients), 31–40 years (133 patients), and 41–50 years (117 patients) prevailed in the case of midface traumas. Additionally, 45.01% (mean age 40.97; CI 38.82–43.11; Min 5; Max 95) of subjects were from an urban environment, with 38.25% being male and 6.76% female, while 54.99% (age mean 41.33; CI 39.52–43.13; Min 3; Max 89) were from the rural area, of which 48.39% males and 6.51% females (Fig. 3.15). From the studied lot, a total of 462 (70.81%) patients admitted to our service required surgical treatment, while 189 (29.19%) were treated conservatively (Table 3.1).

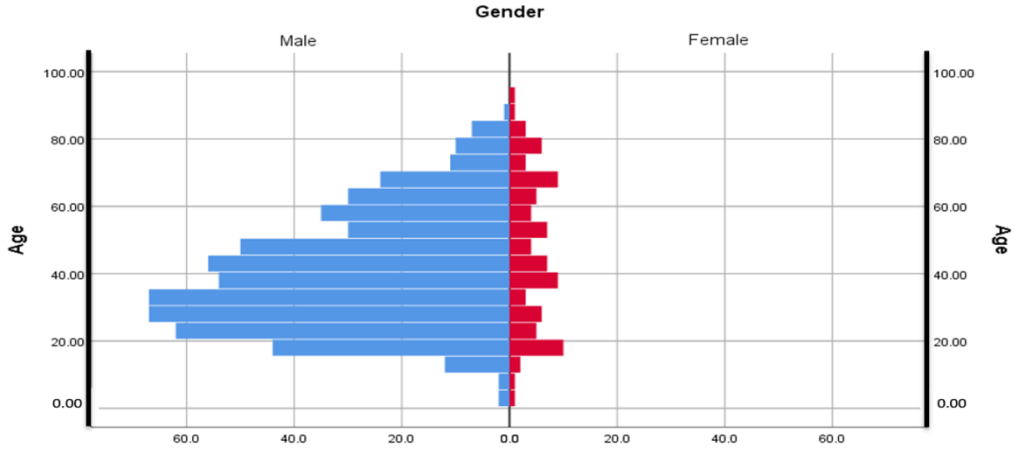


Figure 3.15. Distribution of the studied lot according to gender and age.

Table 1. Descriptive indicators depending on the type of treatment.

	Gender	N	%	Mean Age	Std. Dev.	Min.	Max.	*p*
medical treatment	female	32	11.90	47.75	24.20	5	89	0.513
	male	157	88.10	40.19	17.00	3	85	
	TOTAL	189	100.00	41.47	18.53	3	89	
surgical treatment	female	55	16.93	46.30	21.55	13	95	0.102
	male	407	83.07	40.33	17.05	8	89	
	TOTAL	462	100.00	41.04	17.72	8	95	

Regarding the etiology of midface trauma, the first place was occupied by interpersonal violence, representing 46.85% of cases, followed by traffic accidents. In the last places, we found work and sports-related accidents (Fig. 3.16.). When the lot was divided according to gender, the

predominance of interpersonal violence was maintained in the case of male participants. In contrast, for most female participants, midface trauma was caused by traffic accidents (Fig. 3.17).

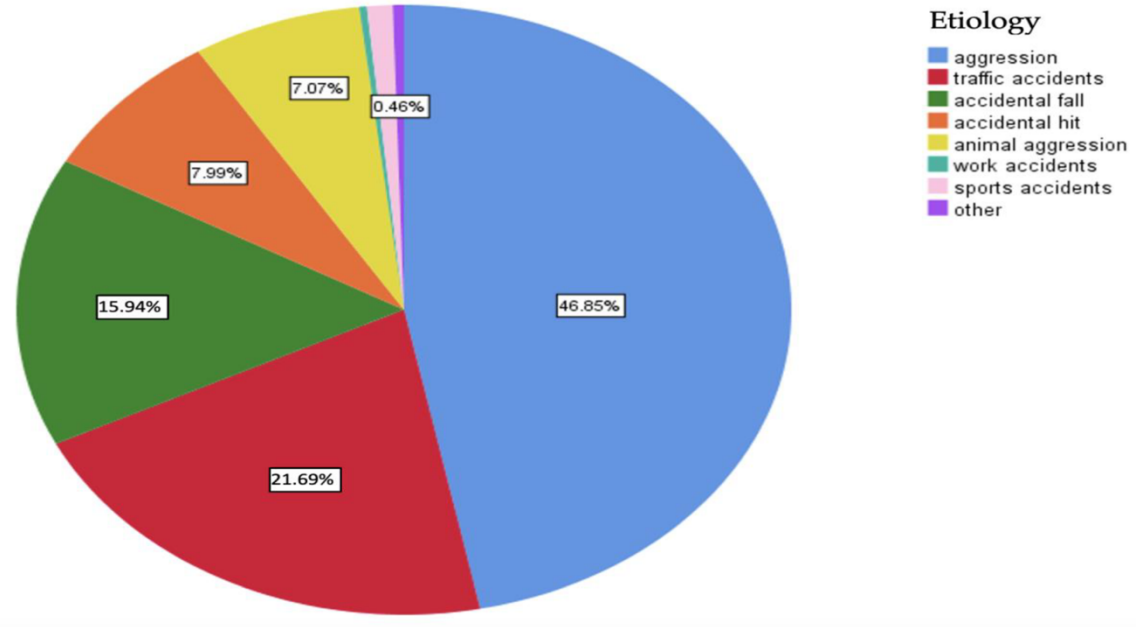


Figure 3.16. Chart reflecting the etiology of midface trauma in the studied lot.

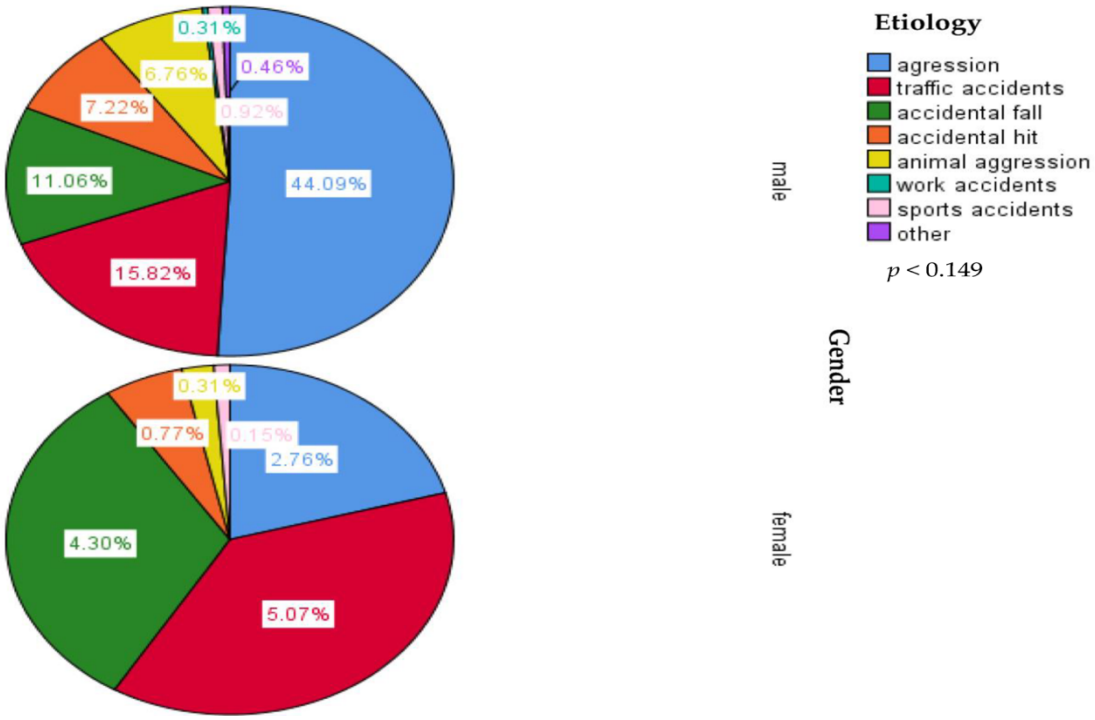
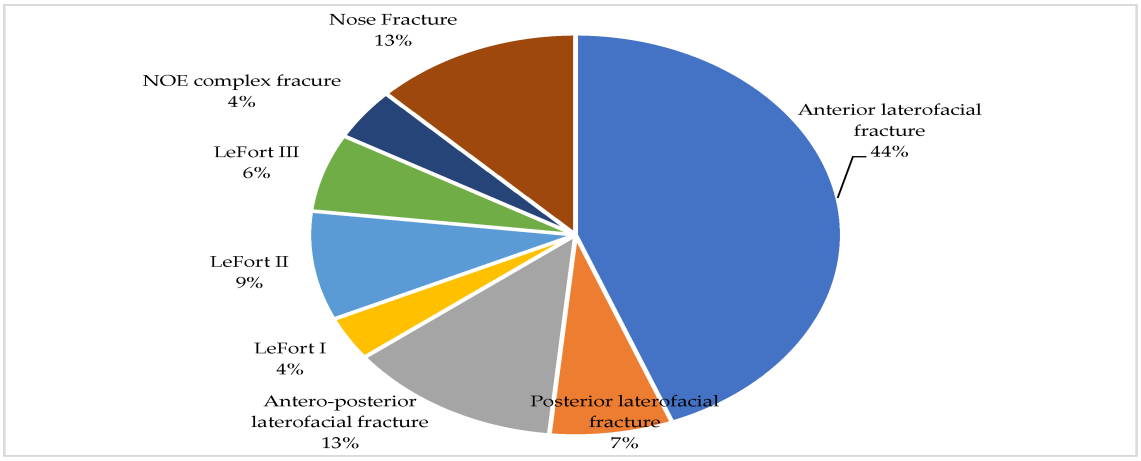


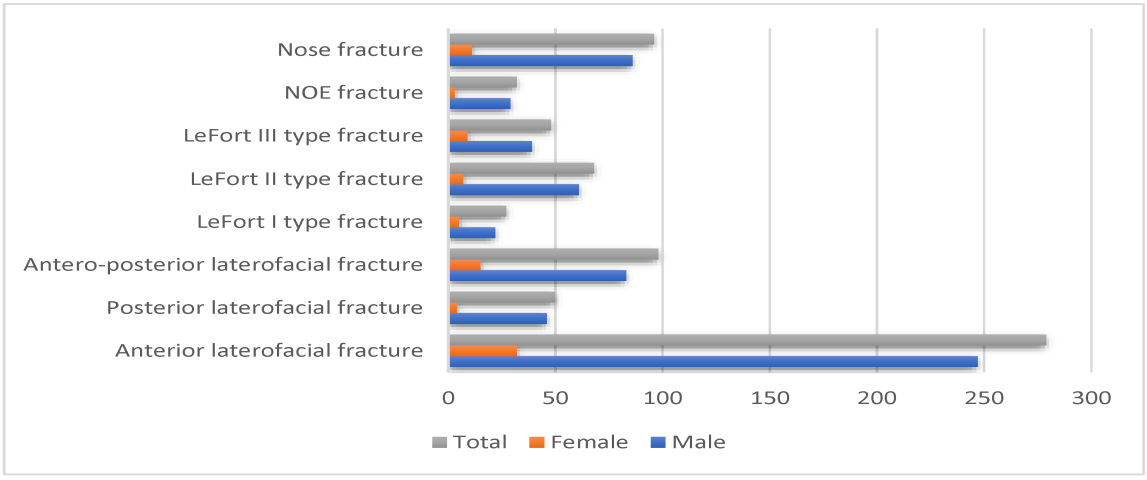
Figure 3. 17. Etiology for midface trauma between gender.

When comparing the number of hospital attendance by gender for the COVID-19 pandemic lock-down period with the same period from the previous year, the authors found no significant differences between female and male patients that were admitted to the hospital (p = 0.886) with a total number of patients of 16 admitted between march and may 2019 and 14 for the same period in 2020.

As for the different types of midface fractures, our study found that the most frequent, representing 44% of the total cases, were anterior laterofacial fractures, followed by anteroposterior laterofacial fractures and nose fractures, each representing 13%. On the other hand, the least encountered types of midface fractures were NOE (naso-orbio-ethmoidal) complex and LeFort type I fractures (Fig. 3.18. A,B). In addition, this study found that hospital admission for midface fractures had a continuous drop over the studied period, although the number of female patients was similar for each year in the documented period (Fig. 3.19).



(A)



(B)

Figure 3.17. (A)Types of midface fractures represented as a percentage, (B) Types of midface fractures according to gender.

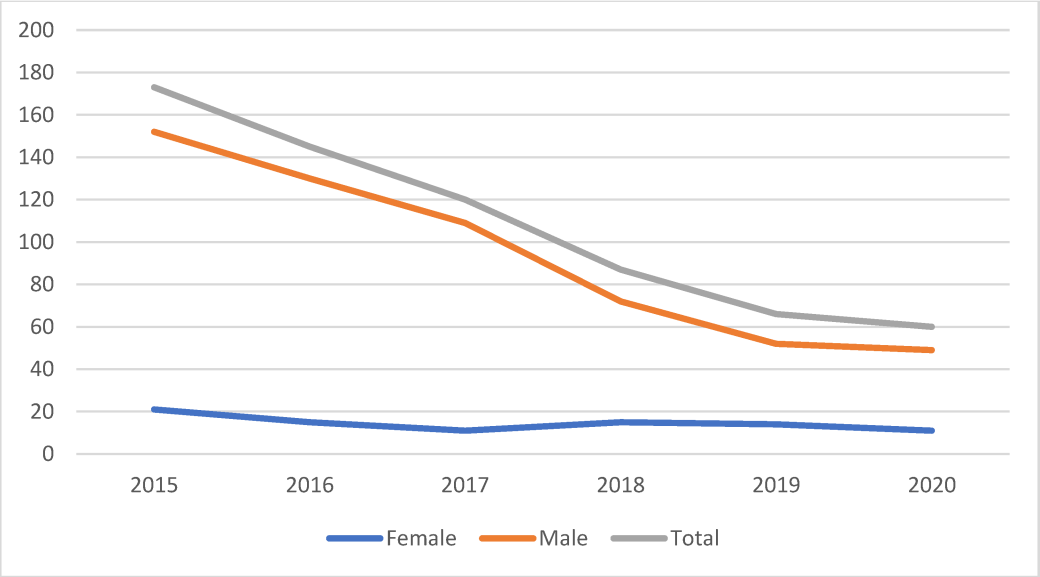


Figure 3.18. The number of cases of midfacial trauma over the years of the studied period.

3.3.4. Discussion

Our study found that most of the midface trauma cases were anterior laterofacial fractures representing 44%, followed by anteroposterior laterofacial fractures and nose fractures, each representing 13%. LeFort type II and LeFort type III fractures expressed 9% and respectively 6% of the total studied lot, with LeFort type I and NOE complex fractures each representing 4% of the cases. Men were especially at risk, surpassing the female patients, with a ratio of 6.48 to 1, with adults between 21 and 50 years old comprising more than 80% of the total patients included in this study.

The values of male to female ratio differ greatly in the specialized literature, depending on the area where the studies were conducted. Thus, a lower value of only 1.8:1 was recorded in Italy in 2017 in a study that followed trauma in the maxillo-facial region over a period of 15 years and included 1720 patients in the research (Bonavolonta et al., 2017). Another study carried out in Europe, this time in Austria in 2003, reported a ratio of 2.1:1 (male: female) (Gassner et al., 2003); in Amsterdam, in 2013, the stated ratio was 2.6:1 (Salentijn et al., 2013), and in China, the male: female ratio was 3.5:1 (Zhou et al., 2015). A ratio similar to that obtained in our study (6.4:1) was reported by a survey conducted in the Arab countries around the Persian Gulf in 2021, which included more than 19,000 patients (Al Qahtani et al., 2020). Higher values with a ratio of 8:1 were reported by India (Satish et al., 2017), but also in Africa, where this ratio reaches 12:1 in certain areas (Jaber et al., 2021). These large differences between the number of men and women with facial fractures could be explained by socio-economic, cultural, and educational factors.

A study realized in 2015 comparing data from multiple centers enrolled in the European Maxillofacial Trauma project about the demographics, cause, and characteristics of maxillofacial trauma showed a male-to-female ratio of 3.6:1 overall. Still, the ratio varied from center to center,

with the highest ratio (9,4:1) present in Kyiv, Ukraine, and the lowest in Amsterdam, The Netherlands (2.2:1). Additionally, the mean age varied from 29.9 years in Dundee, Scotland, UK to 43.9 in Ljubljana, Slovenia. Interpersonal violence (39%) was the most incriminated etiology, followed by falls (31%), traffic accidents (11%), sport-related injuries (11%), and work-related injuries (3%) (Boffano et al., 2015).

Regarding the etiology of midface traumas, for the entire studied group, the first place was occupied by interpersonal violence with 46.85% of cases, followed by traffic accidents at 21.69%, accidental falls at 15.94%, accidental hits at 7.99%, and aggression caused by animals with a percentage of 7.07%. In the last places, we found accidents at work and those resulting from sports activities. After dividing the group according to gender, we noticed that, for male participants, the situation reflected the global trend, with aggression being by far the most frequent etiology, followed by traffic accidents, falls, and accidental hits, while for female patients, the most cases of midface trauma were caused by traffic accidents, followed by accidental falls and, in 3rd place, by assault. Regarding the etiology of these fractures in the general population and, subsequently, by gender, numerous studies have been conducted worldwide at different time periods. We can thus try to outline an etiological hierarchy of midfacial fractures, although the results of the studies are extremely varied from one geographic region to another.

In European countries, interpersonal violence is also the most incriminated etiology, but with a lower percentage than that objectified by our study (39% vs. 46.85%), followed by falls (31%), traffic accidents (11%), sports-related injuries (11%) and work accidents (3%) (Boffano et al., 2015). Other countries reported different results, as follows: in the Netherlands (2013), the most frequent etiology was represented by traffic accidents, regardless of the patient's gender, followed by interpersonal violence for men, respectively, by falls in the case of women. For those who consumed alcohol, aggression was most frequently incriminated. On the other hand, in Italy in 2017, in a study carried out over a period of 15 years on 1720 patients, the hierarchy of etiologies looked like this: in first place were road accidents (57.1%), followed by interpersonal violence (21.7%), falls (14.2%), work accidents (3.5%), respectively sports accidents (3.3%) (Bonavolonta et al., 2017). Another study from Italy conducted in 2013 also mentions road accidents as the main etiology of facial fractures (Roccia et al., 2012). We find that there are differences depending on the specifics of the area; thus, in Austria in 2003, a study carried out on a group of 9543 patients described a completely different order of etiologies: initially, daily activities were incriminated (38%)—including falls, followed by sports accidents (31%), then interpersonal violence and traffic accidents, each with 12%, 5% work accidents, and 2% other causes. 19% of the patients included in the study were foreigners, with the Austrian Alps being a highly frequented area for winter sports (Gassner et al., 2003). In Croatia, authors reported falls as the main etiology, followed by aggression for men and traffic accidents for women (Siber et al., 2015). The same study also describes a difference regarding age, with interpersonal violence more frequent among young people, with falls being the prerogative of adults over 50.

A study that analyzed the clinical patterns and characteristics of midfacial fractures over a period of 10 years, this time in the western Romanian population, found that the most common types of fracture were laterofacial (50%) and nasal bone fractures (22.93%), with LeFort type

fractures being the least encountered, representing 0.83% for LeFort type I, 1.03% for LeFort Type II and 0.83 for LeFort type III from a total of 397 patients (Tent et al., 2019). Another study from the same part of the country found that midface fractures affect most commonly the male sex and patients from the urban area (54.35%) aged between 20 and 29 years old, with the most incriminated etiology being assault, followed by fall trauma and road traffic accidents (Tent et al., 2018). The fact that the second most incriminated etiology from the north-eastern part of the country is road traffic accidents, and for the western part is accidental falls could be explained by a more developed transport infrastructure in the western part of the country.

Regarding the background, the current study mentions that 45.01% of the subjects are from urban areas, while 54.99% are from rural areas. Another interesting observation would be the similar percentage of women from both backgrounds (6.76% in the urban environment versus 6.51% in the rural environment), thus not supporting the statement that domestic violence is more frequent in the rural environment. On the other hand, there is a greater number of men coming from the rural environment, 48.39% of the whole lot, compared to 38.25% from the urban environment. This can be explained by the level of education, the more frequent consumption of alcoholic beverages, but also their involvement in raising animals or other activities within the household.

Our study's results showed a continuous drop of the hospital attendance rate for midface fractures over the studied period. This can be attributed to a better implementation of public safety rules, better management of alcohol consumption and stricter traffic regulations, the implementation of a better diagnostic protocol utilizing cone beam computer tomography instead of conventional radiographic studies, and the cases of maxillofacial trauma being directed to other healthcare centers in the region. This phenomenon may also be explained by the lawmaker's concern for citizens' safety, whcih led to tougher sentences for acts of aggression (including interpersonal violence and road traffic accidents) directed to members of the family or for those committed by inebriated authors.

The authors compared the data regarding hospital attendance for midfacial trauma during the COVID-19 general lockdown with the same period of the previous year, but the results showed no significant difference. In contrast, another recently published study concerning the effect of the COVID-19 pandemic on midface fractures found a decrease in hospital admissions for facial trauma, approximately seven times lower, comparing the number of patients from March to April 2019 with the same period in 2020 (Kasem et al., 2022).

Interpersonal violence was the most incriminated cause of midface trauma, followed by traffic accidents and accidental falls. It must be noted that men were more affected by violence, while the leading cause for women was traffic accidents. Other studies in the literature show a different predominance in the etiology of facial fractures: an Indian study conducted in 2019 on 944 patients with facial trauma, with 19% midface fractures, found that the leading cause was by far road traffic accidents (Abhinav et al., 2019). The same predominance of road traffic accidents is mentioned in another study from Saudi Arabia (2019) (Al-Bokhamseen et al., 2018) and India (2022) (Menon et al., 2022).

The current study also underlines the predominance of young male adults, with a peak incidence between the 2nd and 3rd decade of life. Most studies report the same conclusions, with

young people in their 20s and 30s having an active lifestyle and engaging in many outdoor activities (AlQahtani et al., 2020). The average age for female patients was 46.83 years (minimum age—5 years, maximum age—95 years) and 40.49 years for male patients (minimum age—3 years, and maximum age—89 years). In general, most studies on the epidemiology of fractures in the oro-maxillo-facial region describe an older average age for female patients, something also highlighted in a study from Italy from 2017, where the average age for women with facial fractures is 59.5 years. For Europe, a varying average age of the whole lot can be observed, regardless of sex, from 29.9 years in Dundee, Scotland, UK, to 43.9 in Ljubljana, Slovenia (Boffano et al., 2015). Reviewing data from the literature, we find that the predominance of young adults in the group of patients with facial trauma has not changed over time, being described in Sweden in 1980 (Afzelius et al., 1980) and in Scotland (1985) (Cole et al., 2009).

Although children are more prone to craniofacial trauma, the absence of sinus pneumatization, the bone elasticity, the thickness of the periosteum, and the retruded position of the face in relation to the neurocranium offer a greater degree of protection (Cole et al., 2009). In our study, only 58 patients were children (maximum age of 18 years), representing 8.91% of the entire lot. A total number of 38 children received surgical treatment, representing 65,51%. A smaller percentage was mentioned in a study conducted in Indianapolis, Indiana, in 2019, on 218 pediatric patients, showing that only a quarter (25.2%) of the hospitalized children needed surgical intervention, the rest receiving conservative treatment (Kao et al., 2019).

Craniofacial trauma is common in all age groups. The cause is closely related to age, sex, and alcohol consumption, and it determines the type and severity of the injury. Hussain states that accidental falls are the primary cause of injuries in elderly patients, while interpersonal violence and traffic accidents are responsible for injuries in patients between 15 and 50 years of age. Physical violence most often involves young adults, and fights usually occur between strangers who have consumed excessive amounts of alcohol. Women are assaulted by people known to them, in most cases, their life partners; pedestrians are prone to skull fractures, vehicle occupants involved in traffic accidents suffer midfacial fractures, and cyclists have mandibular fractures (Hussain et al., 1994).

Our study found that the most common types of fractures affecting the midface were those involving the zygomatic complex, namely laterofacial fractures (75.58%) followed by oclusofacial fractures (LeFort type fractures) (21.81%) and centrofacial fractures (19.66%). Other authors reported that fractures of the zygomatic complex accounted for 62.5% of the total number of midface fractures, followed by LeFort II type fractures (23%), multiple fractures of the midface (10%), LeFort I type fractures (6%), LeFort III fractures (4.5%), and naso-orbito-ethmoid complex fractures (4%) (Bulgaru et al., 2021).

Fractures of the NOE complex are the result of forces applied to the middle third of the face. Due to the violence of the impact required to cause these fractures, other facial, cranial, or body lesions may be present. Traffic accidents, more often those involving an occupant not wearing a seat belt at the time of impact, are the most common causes of trauma affecting the NOE complex, representing 4% of all adult skull fractures (Kelley et al., 2005, Cabalag et al., 2014) , the most frequently affected being young male adults. This corresponds with the results of our study.

Midface fractures' treatment follows similar principles to the treatment of other systemic fractures but presents a series of particularities due to the complexity of the facial anatomy (Wusiman et al., 2020), with authors stating that the restoration of the facial vertical buttresses restores the load-bearing structure of the midface, while the rehabilitation of the horizontal buttresses recovers the aesthetic aspect.

The authors of this study found that 461 (70.81%) required and received surgical treatment consisting of open reduction and internal fixation with titanium miniplates and/or mesh for selected cases of laterofacial or nose fractures, while 189 (29.19%) patients admitted in our center were treated conservatively. Our results are similar to other studies. Manodph et al. found that 73.56% of the entire lot (3611 patients) required surgery (Manodh et al., 2016), while Wouter et al. reported similar percentages in a tertiary trauma center from the Netherlands where, over a period of 5 years, 293 (74%) patients received surgical treatment for midface fractures (Van Hout et al., 2013). A higher percentage of 85.4% was mentioned in a study from Nepal in 2021 (Chaurasia et al., 2021) and in Berlin, Germany, where 89.5% of patients with midface fractures were treated surgically in 2019 (Goedecke et al., 2019).

3.3.5. Conclusions

The present study regarding midfacial fractures shows similar results compared to the medical literature, with certain particularities: a male predominance with more than 80% of the current lot, a high incidence of interpersonal violence and traffic accidents, as well as high frequency of anterior laterofacial fractures, compared to other types. In addition, we observed a continuous descending trend in the total number of hospitalizations.
Most of the patients received surgical treatment.

Given the increasing esthetic and functional demands, a continuous update of available resources is necessary for a better outcome for midface fracture cases.

Reviewing the literature shows an extremely high variability of etiological agents, influenced by numerous factors such as socio-economic status, cultural background, life habits, or level of education. These findings could help promote a different lifestyle, with awareness campaigns to prevent aggression, accidents, and domestic violence. Further studies are needed for dynamic observation of changes in the epidemiology of midface fractures, to establish the effectiveness of preventive strategies, and also to note the impact of lifestyle on facial traumatic pathology.

3.4.Approaching the frontal sinus trauma

3.4.1. Introduction

Compared to other anatomical areas of the cranial vault, the frontal sinus is exceptionally resistant upon infliction of external forces, making a fracture less likely to occur when following major trauma (Chen et al., 2004). This fact is owed to the particular anatomy of the frontal bone, which evolved, in homo sapiens, primarily for containing the encephalon and secondarily for his protection. Sinus development is a result of anterosuperior pneumatization of the frontal recess into the frontal bone. Development begins late in intrauterine life or may start after birth (from one to twenty years), initially in the vertical segment. Pneumatization develops between ages 1-12 years.

This pneumatic cavity is bordered anteriorly and posteriorly by two bony tables. The structure of the anterior table is composed mainly by a thicker layer of cortical bone, than the posterior one, thus making it more resistant to external trauma. It can withstand between 800 to 2000 pounds of force before fracturing (Nahum 1975). Consequently, fractures in this area, represent only 5-15% of all cranio-facial fractures (Gerbino et al., 2000). The most common mechanism of injury is the application of an excessive and high velocity force, with a vector of direction perpendicular to the median sagital line. Very often the patients are victims of an aggression or an automobile accident and they frequently associate other injuries, thus making management difficult and raising significant medico-legal considerations. The management of frontal sinus fracture patients is controversial and dependent on the type of fracture and the involvement of surrounding anatomical structures. The main concerns are aesthetics and the prevention of acute and delayed complications, which occur often and can be life-threatening or with significant loss of quality of life. The main complications are represented by cerebrospinal fluid leaking, meningitis, epidural abscess, brain abscesses, mucopyocele, osteomyelitis. Complications can appear years or decades after the initial traumatic episode and therefore the therapeutic algorithm is not straight forward, and it heavily relies on the sound judgement of the surgeon. In many cases, fast decision making based on scarce clinical and imagistic data, is required in the operating theatre. We believe that a standard and safe pathway in the management of this serious pathology is a must have in the “panoply” of a neurosurgeon.

The anatomic particularities that make these fractures prone to complications are caused by the structure of the posterior bone table. A relatively thin osseous barrier, between the colonized mucous membrane of the paranasal sinus cavities and the sterile meninges and brain, once compromised, can give rise to numerous infectious complications. Also once fractured, favored by its proximity to with the superior sagittal sinus, in rare circumstances, can cause the tearing of the venous sinus which will result in a very serious intracranial hemorrhage (Donald 2008).

Specific bioinert materials, such as titanium meshes, aids us in the treatment of these types of severely comminuted fractures. We present our 5 year experience in frontal sinus fractures treatment and particularly, our experience of using titanium meshes in the surgical repair of the frontal bone defect.

3.4.2. Material And Methods

We present our experience in the treatment of frontal sinus fractures in a 5 year period and a review of the current management strategies offered by the literature.

Etiology of frontal sinus fractures

The most common etiology factor cited in the literature is represented by motor vehicle impacts. For an anterior table fracture to happen, because it's tensile strength, it requires a great amount of energy applied directly. Motor vehicle accidents frequently can produce those types of forces. In a large series of patients treated for frontal sinus fractures (857 patients) Rodriguez et al. (2008) reported motor vehicle collision as the cause in 42%, assaults in 14%, motorcycle collisions in 10% and pedestrian hit by a car while crossing the road in 8%. An interesting statistical fact of that study was the percentage of the passengers involved in car collisions which were unrestrained (not wearing seat-belt) – 60%.

In our statistical retrospective data on a five-year period (2014-2019) we hospitalized 665 patients with cranial fractures, and we diagnosed 78 patients with frontal sinuses fractures (11,72% of all cranial fractures). We noticed a difference regarding the etiology. In our series 22 patients (28.2%) were the victims of an human assault, 14 (17.94%) had motor vehicle accidents, 8 (10.25%) were the victims of a falling from heights, 7 (8.97%) of a falling from their own level, and 7 (8.97%) were victims of an animal assault. Most of the patients were male – 71(91%), and the average age in the series was 34.6 years.

Clinical presentation and diagnosis

Clinical examination of these patients is impaired by facial hematomas, lacerations, edema, ecchymosis. Inspection and palpation of a depression of the frontal bone or other facial bone deformities is important, but mandatory is to establish the presence of the cerebrospinal fluid fistula, confirmed by the presence of CSF in an laceration or in the nose cavity (CSF rhinorrhea) which is a direct sign of posterior table breaching and tearing of the dura mater (Tiwari et al., 2005). We believe that in the initial evaluation of a trauma patient a clinician identifying the presence of a CSF leak, even if it's time consuming, is a key objective. The presence or absence of a CSF leak is a must have data needed for guiding the correct management protocol. Sometimes, in isolated cases of trauma patients presenting with clear rhinorrhea, quantifying glucose and beta-2 transferrin in the exudative fluid, is useful for distinguishing CSF from normal nasal discharge (Tiwari et al., 2005). In our series 12 (15.38%) patients had a CSF leak at their initial presentation. Other common clinical findings in frontal bone fractures are represented by the ability to feel or see bony fragments during laceration examination (Rohrich and Hollier 1996), supra-orbitary anesthesia and conjunctival ecchymosis. We consider that conventional plain skull radiographs even with specific sinus incidences are not useful for patients with suspected frontal sinus fracture. In our experience which align to the current standards reported in the literature, the preferable imaging used for the assessment of craniofacial traumatized patient is computed tomography (CT) (Stanwix et al., 2010). It will provide, practically, almost all the information we need regarding bony elements of the face, the state of the nasofrontal ducts, and will confirm any intracranial associated lesions. Modern CT scanning allows multiplanar reconstructions, with detailed description of the type of

fracture, structures involved, and therefore significantly influencing the management decision algorithm.

One of the most important structure to observe is the nasofrontal tract, it's patency being of extreme importance in preoperative planning. Following a sound examination of scans, it is imperative to appreciate the type of fracture, the discontinuity of the sinus floor, the presence of CSF in the sinus, and note the degree of the displacement of the anterior and posterior table. Lastly, we must try not to overlook the intracranial and cervical spine lesions, which are associated frequently.

Classification of frontal sinus fractures

There were many classifications proposed for the frontal sinus fractures. However, the most accepted one, with the agreement among numerous authors (Luce, 1987; Wolfe and Johnson, 1988; Stanley, 1989; Rohrich and Mickel, 1995; Gonty et al., 1999) (Olson et al., 1992, Luce 1987, Wolfe and Johnson 1988, Rohrich and Mickel 1999, Gonty et al., 1999) divides the fractures in:

- Anterior table fractures;
- Posterior table fractures;
- Anterior and posterior tables fractures;
- "Through and through" fractures (skin to anterior cranial fossa);
- Fractures involving the nasofrontal duct.

In our series we had 42 (53.84%) isolated fractures of the anterior table, 2 cases (2.56%) of isolated posterior table fractures and 34 (43.58%) with combined fractures of anterior and posterior tables.

In their large series, Rodriguez et al. (2008) reported 38.3% anterior table fractures, 6.9% isolated posterior table fractures and 54.9% combined anterior and posterior tables fractures.

The problem of nasofrontal duct injuries is that they are not easily identified in head CT scans, and are often missed by the radiologist. This fact leads to under-reporting. In our database only 4 patients, had a fracture of this structure, mentioned in the initial radiology report, but, when we reanalyzed all the cases, we appreciated that the involvement of the nasofrontal duct was present in 51 cases (65.38%). A very important finding, as it influences the management, surveillance and outcome of sinus fractures.

Associated lesions and complications

Frontal sinus fractures, being the result of the exertion of high energy, makes the presence of cerebral associated lesions common, rather than an unusual finding. In our series, in 30 (38.46%) patients we diagnosed cerebral lesions: focal cerebral hematomas and contusions in 7 cases (8.97%), epidural hematomas in 10 cases (12.82%), subdural hematomas in 7 cases (8.97%), subarachnoid hemorrhage in 6 cases (7.69%), pneumoencephalus in 14 cases (17.94%). Six patients were admitted in a coma state (GCS $\leq$ 8).

The complications in our series included: CSF fistulas in 12 patients (15.38%), meningitis in 2 patients (2.56%), diplopia in 3 patients (3.84%), frontal osteomyelitis in 1 case (1.28%). Other possible complications, not encountered in our series, include: frontal sinusitis, intracerebral

abscess, empyema, cavernous sinus thrombosis, persistent CSF fistulas, limitation of extraocular motions, mucocele/mucopyocele, frontal contour defects.

3.4.3. Results

Management of frontal sinus fractures, as previously stated, is controversial. There are, however, several principles of which the medical team must have strictly adherence, in order to successfully treat these patients:

- Prevention of early or delayed complications;
- Restoration of normal sinus function when is possible;
- Restoration of normal frontal bone shape and contour.

In the literature, treatment options described include observation, various types of reconstruction of the sinus walls, osteoneogenesis, ablation/exenteration, cranialization (Strong et al., 2006, Bell et al., 2007, Gossman et al., 2006).

In cases with anterior wall involvement, the primary purpose is often the cosmetic aspect. Fractures of the anterior wall may be without displacement or they can have various degrees of it. Most often, undisplaced fractures do not require surgical treatment, the only management consists in suturing skin defects and active surveillance to prevent potential complications. The same conservative treatment is recommended for the fractures with little displacement (1-2 mm).

If there is severe displacement of the bony fragments (2-6 mm) or significant comminution a surgical reduction may be necessary, and most of the authors recommend correction with various types of fixations, in order to correct facial deformities and to prevent late complications as mucocele (Figs. 3.19. 3.20).

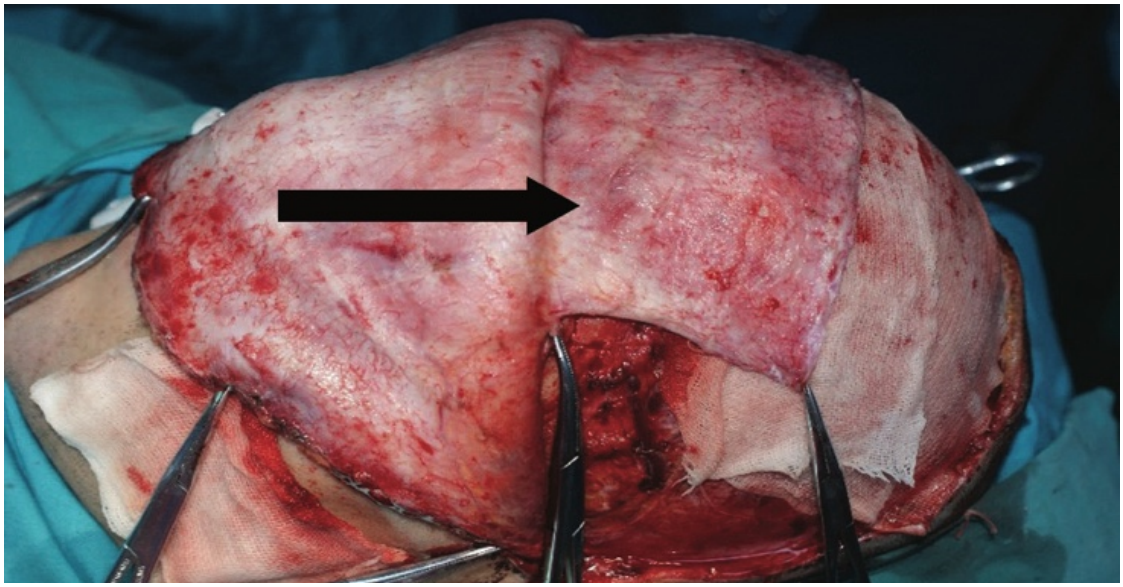


Figure 3.19. Exposure of epicranial flap after harvesting it.

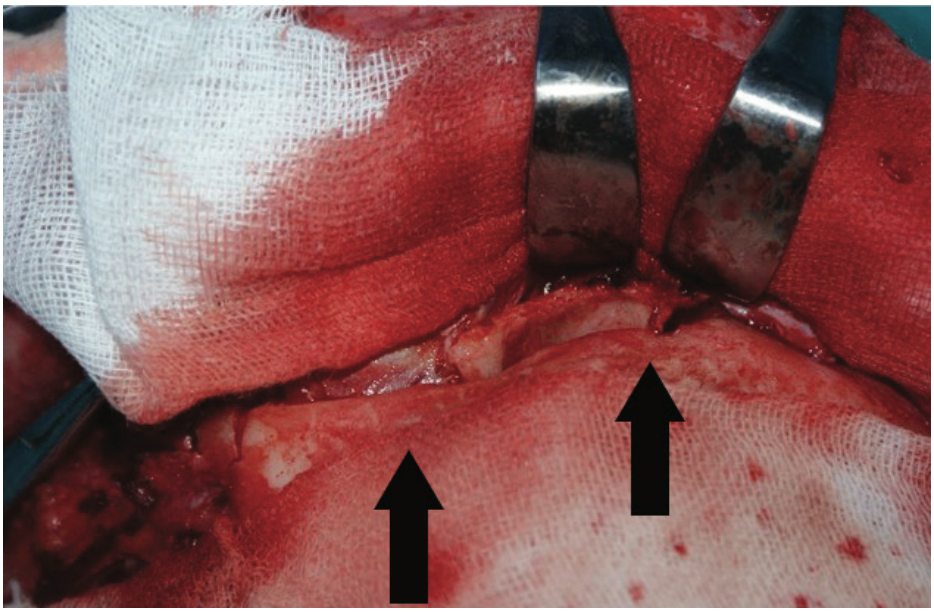


Figure 3.20. Exposure of anterior frontal wall fracture sites.

However, the risk of mucocele formation in isolated frontal sinus fractures is low, so, in our series we treated 9 patients with no reconstruction of the anterior wall, even comminuted, but, for cosmetic reasons, we performed cranioplasty with titanium mesh and left all the displaced fragments in place, with good results (Fig. 3.21).

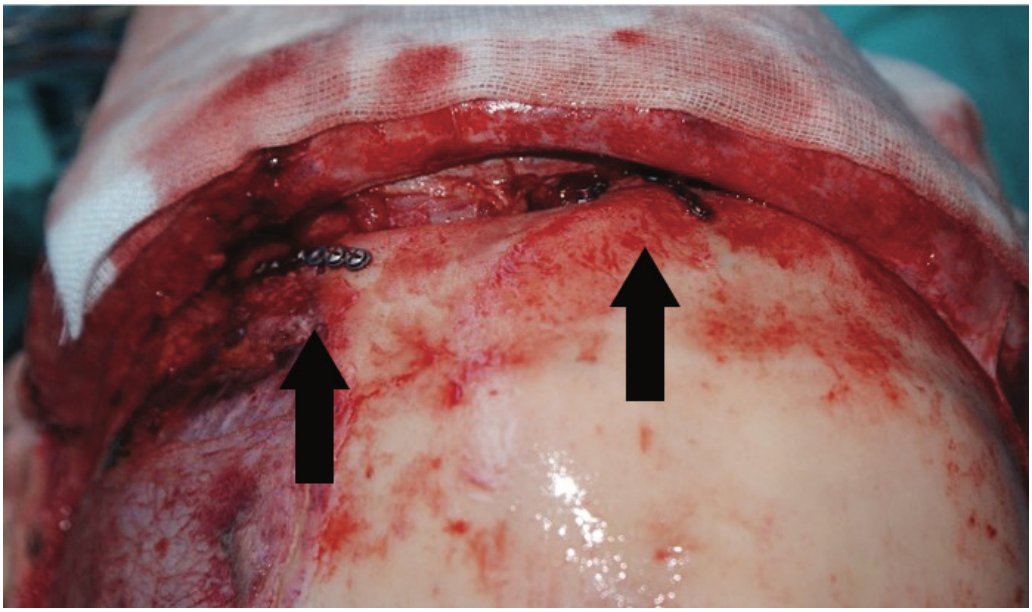


Figure 3.21. Reduction of the fracture using titanium plates.

The cosmetic result was excellent, and we encountered no infectious complications. All the patients had 5 days of antibiotic protection.

Another possible issue is the involvement of the nasofrontal duct; various authors report an incidence of 25-50% 9Bell et al., 2007), especially when there is an association with orbital-ethmoidal fractures.

It is quite rare to have an isolated sinus of the posterior wall, most often there is a complex fracture involving also the anterior wall, ethmoid cells, nasofrontal duct, cribriform lamina. In a classic study, Nahum et al. (1975) estimated the forces needed to fracture the posterior table, vary between 362 and 997 kg per square m2. In as many as a third of cases, a dural tearing accompanies the fracture, creating a communication between the intracranial space and the nasal mucosa which increases the risk of meningitis. We experienced 12 cases of CSF leak and in only 2 cases we used a surgical approach to close the fistula; all the other patients had conservative treatment, in 7 cases a lumbar drainage was necessary. The goal of the surgery, used in patients carefully selected in which the CSF leak persisted more than 10-14 days despite all conservative measures, was the restauration of dural integrity and protection of the intracranial space by cranialization of the sinus and obliteration of the nasofrontal duct.

Obliteration of the frontal sinus consists in complete removal of the sinus mucosa, cauterisation of the walls, obliteration of the nasofrontal duct and filling the aeric space with various materials. There are autologous and alloplastic materials which can be used. Autologous materials may be fat, muscle, bone and alloplastic bio-inert materials such as hydroxyapatite cement, methyl methacrylate, calcium phosphate bone cement, oxidized regenerated cellulose, bioactive glass (Fattahi et al., 2005, Kang et al., 2009). In our series, when the cranialization/ obliteration of the sinus was necessary, we used autografted bone fragments for filling the nasofrontal duct, after which we sealed it firmly with fat and fibrin glue and obliterated the rest of the sinus with autologous fat graft. The floor of the anterior cranial fossa is covered with a pedicled pericranial flap or lyophilized dura.

3.4.4. Discussions

Frontal sinus fractures raise important issues from the perspective of medical-legal activity. They are usually a consequence of an aggression or a vehicle accident, as in our series, where most of the patients (28.2%) were the victims of a human assault. The patients are relatively young (34.6 years in our series) but other authors reported even younger series between 21-30 years (Bell et al., 2009, Marzola et al., 2008).

Isolated fractures of the anterior wall are the most frequent ones (53.84%) but there are studies which reported even a larger incidence of this type of fracture (Bell et al., 2009, Marzola et al., 2008).

Frequently associated with esthetic issues, they can severely lower the quality of life. Thus, the repair of the frontal bone shape is in most of the cases, imperative, even when complex associated bony and skin lesions exists. In difficult to treat cases, from the aesthetic point of view, a multidisciplinary approach is recommended, preferably from a team formed by a plastic surgeon, a neurosurgeon, a ophthalmologist and a ENT surgeon.

Posterior table involvement, it is the result, in the majority of cases, of a high energy force of impact. An important medical-legal consideration, because, those forces occur especially in blunt weapon assault or shootings, and lesions can be used to quantify the severity of the aggression.

Also due to the frequent association of cerebral lesions and local complications (CSF leak, meningitis, abscesses, mucoceles) that have to be prevented or treated implying a longer hospitalization, high treatment costs, and a longer convalescence. In our series the involvement of the anterior and posterior wall was 43.58% and the global rate of associated cerebral lesions was 38.46%. The prevalence is similar to that reported in literature statistical data 9Gerbino et al., 2000).

We believe the future of treatment relies on the formulation of a standard management protocol, rooted in evidence-based medicine, being it conservatively or surgical, of frontal sinus fractures. Significant steps, on this pathway are made by the CMF branch of AO Foundation. S Fusetti et al., recently uploaded a digital library with summarized management guidelines, which can be accessed freely and readily by a surgeon in need. Therefore greatly aiding in clinical decision making and subsequently improving the outcome of treatment (Stoian et al., 2019).

3.4.5. Conclusions

Surgical repair of comminuted frontal sinus fractures is not always easy to perform. The scattering of small bone fragments makes it difficult and time consuming to attempt a reconstruction with plates or wires and the result is often unstable, non-aesthetic and posing a high risk of postoperative complications.

Sinus frontal fractures are rare, in comparison to other fractures of the cranial vault, are resultant of high energy of high impact trauma and raise significant socioeconomic and medicolegal considerations.

Frequently, these fractures are associated with intracranian injuries and crippling complications. There isn’t a single general strategy of management, so developing one based on systematic review and meta-analysis of the literature is mandatory.

SECTION C - NEW RESEARCH DIRECTIONS

In the context of the rapid evolution of society and in a competitive market of different opportunities, universities must adapt to the needs of the labor market and carry out an educational management, which will allow their further development and ranking in the top of the best higher education institutions. This can be achieved with the help of high-performing teaching staff, who must train competitive specialists adapted to the labor market.

The academic activity obliges both to teaching activity and to scientific research. European policy and research management cause a fault between the two directions, by the fact that institutional and individual evaluation are largely determined by the achievement of research performance parameters/indicators. Thus, while the didactic activity evolves on a linear plateau, the research activity develops exponentially.

Advances in anesthesia and surgery have made it so that almost any patient with a surgically resolvable pathology is now a candidate for intervention, be it elective. In any situation like this the most important thing is to fully understand the risks and do the appropriate investigations.
This situation requires a paradigm shift that anesthesiologists use for preoperative assessment. Understanding and stratifying perioperative risks allows the anesthesiologist to develop a focused systematic approach to these patients at the time of initial contact and immediately prior to induction, which can be used to guide anesthetic management.

For these reasons, my main future research direction refers to the verification, standardization and implementation of surgical patient evaluation protocols, especially elective ones in the field of rhino-sinus oncological surgery. Thus, together with the team I coordinate, I closely observe a series of risk factors whose evaluation can give us a more accurate perspective on the general risk of patients. Thus, we consider personal data: age, gender, personal and hereditary medical history.

The assessment of the surgical patient requires a special effort from the entire surgical team. First of all, the attending physician must evaluate both the patient's general condition and that of the surgical disease for which he is being referred. The anesthetist must make a clinical assessment as accurate as possible of the cardiovascular and respiratory factors and, as a novelty in our area, an assessment of the ent status. We intend to communicate the results of our proposed cohort studies in this direction as well as the co-opting of new university centers in this research direction. Another important aspect is the identification of the main risk factors according to the patient's pathology and the required surgical technique. In the case of oncological patients, the preoperative evaluation by the oncological commission is necessary to evaluate each case separately, according to the national and international protocols.

The main measure leading to a decrease in perioperative risk, which depends on the surgical team, is the decrease in operative time. This can be done in several ways:
- formation and training of standardized surgical teams,
- the use of modern surgical equipment: LigaSure, minimally invasive surgery etc.

- standardization of operating protocols for both elective and emergency interventions.

A second direction of research concerns the methods and techniques of training a surgical ENT team through what is called a convergent cluster. Current surgical training programs and the system of specialization are archaic, cumbersome, cost-inefficient, and for the most part endless calculations and permutations of intellectual antiquity and stultification processes devised more than a hundred years ago. years. Indeed, the old notion of surgery and medicine as mutually exclusive disciplines, which encompassed diagnosis and therapy as divergent events, must be thrown aside to facilitate the development of a new (organ-specific) model of disease management. Specifically, training programs must be shortened (educational mode) and reconfigured (focusing mode) to ensure the creation of a homogeneous group of specialists, each one being an interface in providing a certain (component-specific) skill. In this way, an effective training program can be implemented that produces teams of surgeons, rather than individual specialists, to provide effective care in a short time and in the most cost-effective manner possible, with the maximization expertise and full interdisciplinary integration of knowledge, experience and skills (cluster care module). As such, surgery itself should cease to be considered an end in itself or a separate entity, but rather as a teamwork, providing new multifaceted ways of health care.

It is necessary to create a simulation center in ENT, in order to train on different interventional techniques. This requires an intensive exchange of experience with similar centers in the country and abroad.

Another direction of our efforts is in the direction of research in general surgery. ENT surgery must and can generate research directions. We want to reach a new level of continuing medical education by integrating researchers and laboratory technicians into our surgical teams. We call this concept experimental and evolutionary integrated surgery. Research in ENT surgery has advanced tremendously in parallel with the accelerated progress in medical sciences. The ability to understand and apply theoretical concepts in practice is fundamental to the clinical sciences and has become more important than ever for ENT surgeons to advance research into clinical practice. The number of medical graduates with a background in scientific research who choose to pursue careers in ENT is small. Therefore, it is important to include a core of research education during residency training to ensure continued advancement of clinical practice. Some of the challenges of a comprehensive research experience during residency must be examined, including poor prioritization, inadequate institutional infrastructure, financial stress on residency budgets, limited time, and an insufficient number of mentors to encourage and guide residents to become clinicians- scientists. Strategies to overcome these challenges include developing and expanding residency programs with clinician-researcher pathways, promoting funding sources, and improving opportunities for residents to interact with mentors who can serve as role models. Successful integration of research education into residency programs will stimulate future ENT surgeons to develop the critical skills to conduct academic research, understand related findings, and translate them into patient care. Lessons learned from incorporating research training into ENT surgery residency programs will have broad application across medical specialties, both in primary care and across subspecialties.

Another direction of research refers to the phenomenographic approach of the "one day surgery" concept. This refers to engaging in Home Recovery Conditions, which include preparation for surgery as well as preparation to act on post-operative self-care needs. Patients' knowledge and personal traits mattered in the recovery process, and their sense of confidence was affected. The patients had these conditions in common but were related to them in different ways. To facilitate recovery, patients will be trained individual, regarding their specific requirements. These include completing or postponing tasks in their personal or professional lives, ensuring the expected supply of pain relievers, dressings at home for the day of discharge, emotional preparation focused on the intention of the surgery and its consequences after discharge.

The impact of personal traits during the recovery process refers to a positive mood and an optimistic attitude about the outcome of the surgery, together with confidence in the situation, were perceived as benefiting the recovery process. Motivational and fatalistic approaches might be different recovery management strategies. Useful knowledge for recovery management is related to what passes for normal biological recovery. Patients want guidance on safe ways to deal with tissue trauma from surgery, as well as guidance on normal recovery time. Wound management and hygiene aspects may be difficult. Surgical procedures and anesthesia are not clear to them, and patients want to be more informed about this. To set reasonable expectations about recovery upon their discharge, patients sought realistic and truthful information.

Individual strategies for post-discharge, management of body self-care, interventional wound management, and everyday problems should also be noted. His symptomatology and perception will be used as directions to decide on relevant self-care actions. Self-care means taking care of yourself, eating, drinking and exercising in the right way. Wound care is a substantial part of self-care: the patient will need to change dressings, assess healing and intervene if needed. Self-care also includes practical solutions to everyday problems, for example personal hygiene, food intake and getting around the house.

We also aim to research the managerial approach to day surgery. If we assume such a perspective, day surgery can be considered a different method of organizing patient care and not just an alternative surgical procedure to the traditional ones that require hospitalization of the patient. Taking a managerial approach to day surgery does not mean exclusively focusing on the potential benefits of reducing patients' average length of stay. All this means understanding:

- how and when same-day surgery can improve the overall performance of healthcare providers, both in terms of clinical effectiveness and financial outcomes, and
- how to organize it and integrate it with the other hospital activities to make it work.

Thus, day surgery must be considered as a managerial model decision and must be consistent with the long-term strategic goals of the hospital. Day surgery is generally defined as a surgical procedure that is performed when the patient is able to be safely discharged on the same day or after a short stay. It is also referred to as "same day services", "single surgical service" or "office surgery". We can distinguish two main models of one-day surgery:

- ambulatory surgery, i.e. surgical procedures performed without hospitalization;

& actual day surgery, that is, when the patient is admitted and discharged within 24 hours, with or without an overnight stay.

Day surgery can be performed in many different places. However, almost all day surgical procedures are performed in:

& independent units i.e. an independent unit or
& integrated units, i.e. a ward or unit within a hospital or
& dedicated beds, i.e. hospital beds reserved for day surgery in conventional hospital units.

A comprehensive and widely adopted definition of day surgery is still lacking. This makes it difficult to collect data on day surgery services and compare them on an international basis. Therefore, there is a lack of criteria for collecting statistically comparable uniform data. In fact, sometimes day surgery data does not include routine hospitalization and refers only to dedicated facilities. Day surgery is often performed as part of conventional interventions and not only in dedicated interventions. Day surgery services may end with same-day discharge, but patient discharge may occur the following day. Sometimes the last case is not taken into account in the statistics of one-day surgery.

As uniform data collection criteria are still lacking, the figures on the diffusion of day surgery may differ considerably. An additional problem is the poor quality of the data collected. In fact, what exists is only raw data taken from hospital discharge forms. This data says nothing about the organizational structure of the day-to-day operation and the different business models behind them. What we are actually aiming for in this direction is to do a cohort study, with the exact recording of cases that were amenable to being resolved by surgery that allowed them to be discharged on the same day. This means making admission forms for outpatient interventions as well, not just for those in the operating room.

The post-interventional follow-up of these patients, with the recording of standardized parameters, can be done through home visits, telephone monitoring or collaborations with family doctors and home care companies.

Endoscopic ultrasound is one of these diagnostic methods that is being developed to overcome the current problem of limited intraoperative access. It can visualize the wall of the explored cavity organ in more detail than any other method.

Currently, the main applicability of endosonography is preoperatively, in the local staging of tumors in the esophagus, pharynx, thyroid gland, tonsils and nasal passages, in the localization of specific endocrine tumors and in the differential diagnosis of submucosal tumors. This technique is accurate for tumor staging T (depth of primary tumor invasion) and, to a lesser extent, N (spread of cancer to regional lymph nodes), but not for detecting distant metastases, as the high ultrasonic frequency limits its depth of maximum penetration of 5-6 cm.

Thus, only the gastrointestinal wall and neighboring organs can be visualized. In this regard, other imaging modalities, such as computed tomography (CT), should be used as a complement to endoscopic ultrasonography to detect extensive local spread and distant metastases.

The accuracy of detecting the local stage of esophageal tumors by endosonography proved to be superior to CT. This is especially evident when differentiating between Tl and T2 tumor

stages. Although a tumor-induced stenosis restricts the accuracy of endoscopic ultrasound for staging, it can still achieve an accuracy of 92% in predicting T stage, although the rate of passing the obstacle was only 74%. In fact, most stenotic cancers are advanced to at least stage T3, and endosonography can stage them correctly by scanning toward the base of the stenosis. In esophageal motor disorders with primary morphological abnormalities, ultrasound can play an important role in detecting any underlying tumors.

Head and neck surgical oncology Although surgery plays a prominent role in the multidisciplinary management of most head and neck cancers, the definition of the surgical oncologist remains debatable. To some it is the surgeon who practices exclusively in the field of tumour management, with surgical oncology being the operative management of one or more body systems. To others it is a person who has particular operative skills and knowledge of surgical pathology, and is prepared to embark on what that pre-eminent of all head and neck surgeons, John Conley, would call 'The big cutout'.

However, just as surgery is not merely operating, so surgical oncology is not just treating cancer patients by operations, but rather the total care as part of a multidisciplinary team. The head and neck oncologist will therefore require special training, and because of the anatomical complexities of this region, may come from a variety of clinical back- grounds.

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