

Biochemical Markers in Patients with Readmission for Congestive Heart Failure

RAZAN AL. NAMAT¹, MIHAI CONSTANTIN^{2*}, IONELA LARISA MIFTODE^{3*}, ANDREI MANTA¹, ANTONIU PETRIS¹, RADU MIFTODE¹, ALEXANDRU DAN COSTACHE¹, DAN ILIESCU¹, IRINA IULIANA COSTACHE¹

¹Grigore T. Popa University of Medicine and Pharmacy, Faculty of Medicine, 1st Medical Department, 16 Universitatii Str., 700115, Iasi, Romania

²Grigore T. Popa University of Medicine and Pharmacy, Faculty of Medicine, 3rd Medical Department, 16 Universitatii Str., 700115, Iasi, Romania

³Grigore T. Popa University of Medicine and Pharmacy, Faculty of Pharmacy, Department of Infectious Diseases, 16 Universitatii Str., 700115, Iasi, Romania

Repetitive or recurrent hospitalizations are a general major health issue in patients with chronic disease. Congestive heart failure, is associated with a high incidence and presence of early rehospitalization, but variables in order to identify patients at increased risk and also an analysis of potentially remediable factors contributing to readmission have not been previously reported and it remains still a difficult problem. We retrospectively assessed 100 patients aged between 48-85 years old, of which 75% were men, who had been hospitalized with documentation of congestive heart failure in St. Spiridon County Emergency Hospital. They were hospitalized between 2010-2017. Even if recurrent heart failure was the most common cause for readmission or rehospitalization, other cardiac disorders and noncardiac illnesses were also accounted for readmission. Predictive factors of an increased probability of readmission included prior patient's medical heart failure history, heart failure decompensation precipitated or accelerated by an ischaemic episode, atrial fibrillation or uncontrolled hypertension. Factors contributing to preventable readmissions included noncompliance with medications or diet, inadequate discharge planning or follow-up, failure of both social support system and the seek of a prompt medical attention when symptoms reappeared. We also identified an inappropriate collaboration with family doctors especially for the patients from rural areas. Patients were more likely to cite side effects of prescribed medications rather than nonadherence as a precipitating factor for readmission. Thus, we can appreciate that early rehospitalization in patients with congestive heart failure may be avoidable in up to 50% of cases. Identification of high risk patients is possible and also necessary shortly after admission in order to identify nonpharmacological interventions designed to decrease readmission frequency.

Keywords: congestive heart failure, ischemic heart disease, atrial fibrillation, dilated cardiomyopathy

Heart failure is associated and related with an enormous burden on both patients and health care systems. Several national policy initiatives have concentrated on improving the quality of heart failure care, including reducing readmissions following a first hospitalization, which are common, costly, and, at least in part, preventable or avoidable. The transition from inpatient to the ambulatory care setting in the immediate post-hospitalization period presents an opportunity to further optimize and ameliorate guideline-based medical therapy, to identify reversible problems related to worsening heart failure and to assess the prognosis. It can also provide opportunities for an optimized medication approach, taking into account the device-based therapies, and to evaluate adverse drug reactions that can increase the cardiovascular risk, the appropriate and accurate management of comorbidities, the identification of individual barriers to care, and a discussion of the aims of care based on prognosis [1-4].

Latest studies suggest that attention to details regarding patient comorbidities, barriers to care, optimization of both diuretic and neurohormonal therapies, and evaluation of prognosis would improve patient outcome. Despite the fact that the transition period appears to be an optimal time to address and treat these issues in a comprehensive manner, most patients are not referred to programs specialized in this approach of post hospital discharge. In the Cardiology Department, congestive heart failure is the most common

indication for hospitalization and readmission within 3 to 6 months from initial discharge. Moreover, both the recurrence and prevalence of congestive heart failure are increasing and the rate of risk is higher in patients over 75 years of age than in those 65 years old or younger [5-9].

The present survey was undertaken in order to determine retrospectively the readmission rate in patients with congestive heart failure and also to identify factors related to an increased likelihood of early rehospitalization; also, the research tried to determine the percentage of readmissions that are potentially preventable or avoidable and also to identify remediable factors which contribute to early readmission.

Experimental part

Study population

The study group was 100 patients admitted to the the 1st Cardiology Clinic of the St. Spiridon Emergency Clinical Hospital Iasi during 2010-2017, aged 48-85 years, of which 75% were men and 78% of them came from rural areas. The inclusion criteria were: patients who have been readmitted in the Cardiology Clinic or who have been able to show readmissions in other clinics with the same profile have been selected. 35% of the readmitted patients were hospitalized in the Internal Medicine Clinic while 65% in the Cardiology Clinic. Regarding the readmissions, 90% were performed in emergency while 10% were scheduled.

* email: mihaiconstantin89@yahoo.com, larisa.miftode@yahoo.com

All authors contributed equally to this work

For every patient, it was performed a clinical examination, blood pressure, heart rate, echocardiography investigation at admission and subsequently repeated during hospitalization, focusing on the parameters that assess the systolic function of the left ventricle (estimated by the ejection fraction).

Laboratory investigations

These included analysis of blood urea and creatinine level, electrolytes (Na, K), total cholesterol, triglycerides, lipid profile, hepatic enzymes (alanine transaminase: ALT; aspartate transaminase: AST), myocardial enzymes (creatine kinase- heart isoenzyme: CK-MB).

Data collection

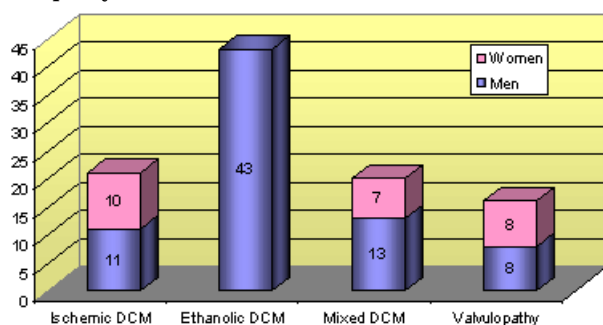
Informations on the general condition, medical history (hypertension, diabetes or coronary heart disease), personal history (smoking, alcohol ingestion) were obtained from all patients. Also, they were previously informed about the subject of the study, signing an informed consent.

Statistical analysis

Statistical analysis was performed using the IBM SPSS 20.0 software (Statistical Package for the Social Sciences, Chicago, Illinois). Data were expressed as mean \pm standard deviation or number of cases with percentage, for continuous and ordinal variables. Cross-tabulation and Pearson Chi-Square test were used for describing the relationship between two categorical variables. The one-way analysis of variance (ANOVA) was used to determine the significant differences between the means of continuous variables and an independent categorical variable. For all data, a two-sided p value < 0.05 was considered statistically significant.

Results and discussions

The etiologies of heart failure, as shown in figure 1, are as follows: ischemic dilated cardiomyopathy - 21 cases (11 men, 10 women); ethanolic cardiomyopathy - 43 cases (only men); mixed etiology (ischemic and ethanolic cardiomyopathy) - 20 cases (13 men, 7 women); valvulopathy - 16 cases (8 men, 8 women).



DCM= Dilated cardiomyopathy

Fig. 1. Etiology of the heart failure

Number of readmissions per patient ranged from 3 to 8 per year.

Among the readmission causes, patients presented with one or more complications (fig.2): left heart decompensation - 78%; global cardiac decompensation - 60%; anticoagulation accident - 52%; side effects of medication - 34%; arrhythmias (ventricular extrasystole or atrial fibrillation) - 26%; pulmonary embolism - 21%; amiodarone induced thyroid dysfunction - 9%; angina pectoris - 5%.

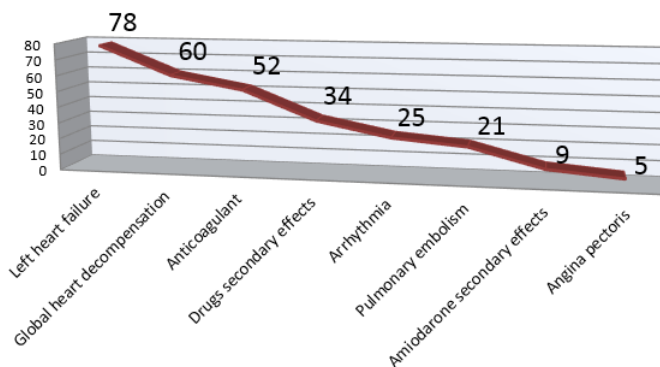


Fig. 2. Etiology of readmissions

Heart failure is the leading cause of hospitalization among adults > 75 years of age in the developed countries. Despite dramatic improvement in outcomes with medical therapy, readmission rates following heart failure hospitalization remain high, with $\geq 50\%$ of patients being hospitalized within 6 months after discharge. Associated complications or comorbidities, including atrial fibrillation, ischemic heart disease or uncontrolled arterial hypertension, determine higher risk for cardiovascular readmission. Beyond clinical and laboratory parameters, the overall level of disability as reflected in measures of functional limitation, frailty and patient-reported quality of life seems to be a particularly important predictor of the overall readmission rate. In our study readmissions were more frequently met in patients from rural areas (78%) and, regarding the heart failure etiology, in the case of dilated cardiomyopathy compared to valvular etiology. Since men were predominant in the study group, we can not say that there were major differences between the two sexes with regard to readmission. No correlation between the age of the patients and the increased frequency of re-hospitalisations could be established in our study, but we identified an inappropriate collaboration with family doctors especially for the patients from rural areas.

Discharge from a heart failure hospitalization is followed by a readmission within 30 days in $\approx 24\%$ of cases. Recurrent heart failure and related cardiovascular conditions account for only about half of readmissions in patients with heart failure. Although the proportion of noncardiovascular admissions is higher in those with preserved ejection fraction (EF), overall readmission rates for heart failure remain similar whether the heart failure occurs with reduced or preserved EF.

Another major cause for readmission was represented by the altered renal function, the further electrolyte imbalances (e.g. hyponatremia, hyperkalemia) being in the vast majority of cases a direct consequence of the diuretic medication. These complications were more common in patients with NYHA III/IV heart failure (fig.3), not being related to the age of the assessed patients (fig.4 and 5).

The treatment and management of heart failure is associated with high mortality rates and treatment costs. Poor medication adherence is a major barrier towards an improved medical care while traditional interventions addressing non-adherence have not consistently demonstrated improvement for the outcome, translated in the number of readmissions. The reasons for non-adherence are complicated and illustrate the broader challenges patients face when managing a complex disease like heart failure.

Studies have documented several factors contributing to hospital readmissions, including complications from in-hospital treatment, inappropriate coordination of care or

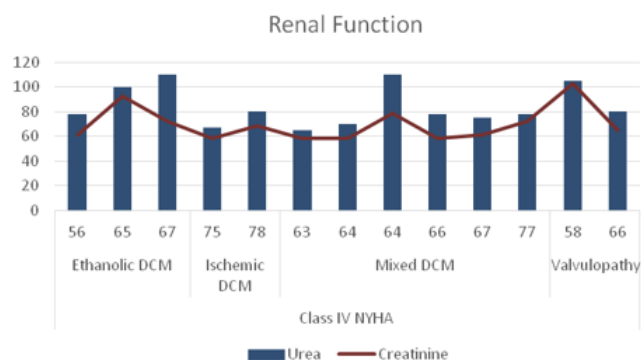


Fig. 3. Renal function in patients with NYHA Class IV Heart Failure dependent on etiology and age

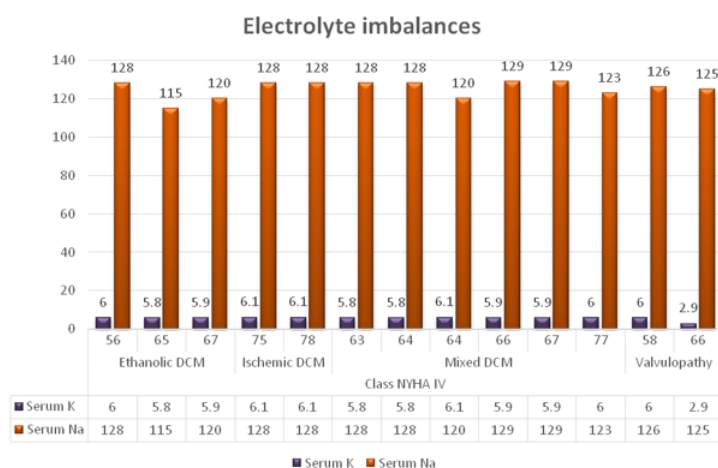


Fig. 4. Electrolyte imbalances in patients with NYHA Class IV Heart Failure dependent on etiology and age

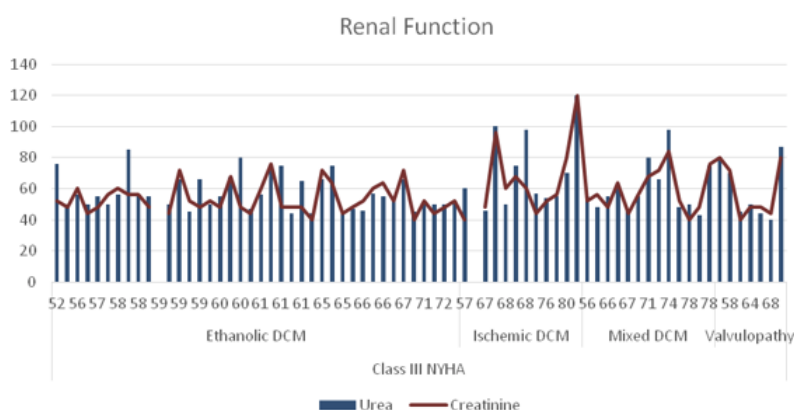


Fig. 5. Renal function in patients with NYHA Class III Heart Failure dependent on etiology and age

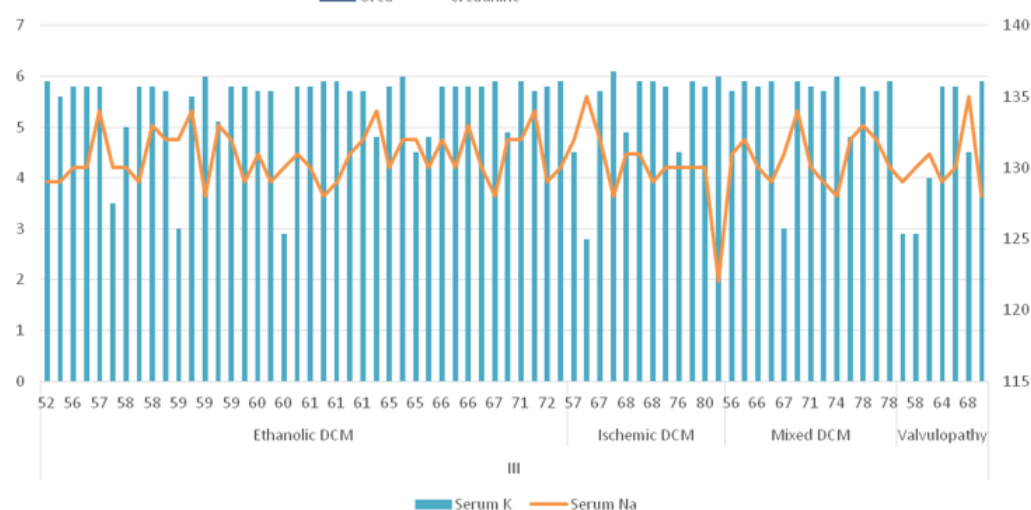


Fig. 6. Electrolyte imbalances in patients with NYHA Class III Heart Failure dependent on etiology and age

even the quality of medical services. Insufficient patient education and a poor follow-up should also be considered. The most beneficial strategy to reduce readmissions appears to be a coordinated care. Thereby, coordination between physicians and patient-centered approaches were far more successful in reducing readmissions than single physician approaches with disease-centered management

[10-14]. Dharmarajan et al reported that most readmissions among patients with CHF, pneumonia, and acute myocardial infarction were not attributed to the initial diagnosis. Although the main reason for 30-day readmission after CHF hospitalization was due to CHF, this accounted for only 35.2%, followed by renal disorders (8.11%), pneumonia (4.98%), arrhythmias and conduction disorders (4.04%), followed by septicemia and shock (3.55%) [15-

19]. Effective and successful strategies for preventing CHF readmissions should include interventions across a full continuum of care from hospital to outpatient clinic and home. Enhancing initial risk stratification in order to safely increase the emergency department discharges, or transitioning low-risk patients to alternative treatment pathways in order to avoid excessive hospitalizations, is paramount to preserving health care resources [20-23].

Risk stratification models were created in the past, being employed with varying degrees of effectiveness or success. Basoor et al conducted a prospective randomized controlled trial which involved 96 inpatients with CHF, of whom 48 patients were provided with a checklist at discharge that included relevant counseling, medication and dosage information, as well as follow-up instructions, while the other 48 patients were discharged without this checklist. Patients who received the CHF discharge checklist had higher rates of outpatient and medication compliance, as well as reduced 30-day (6 vs 19%, $P>0.05$) and 6-month (23 vs 46%, $P=0.045$) CHF readmission rates, compared to those who did not receive the above checklist [24]. Phillips et al conducted a survey including 18 studies and 3,304 inpatients with CHF, evaluating the use of comprehensive discharge planning and support, which included education and periodic follow-up visits. After an average observation period of 8 months, the use of comprehensive discharge planning was associated with an important reduction in readmission rates and a trend toward a reduction in all-cause with no significant difference in the length of hospitalization. The patients who received the comprehensive discharge plan also reported improved quality of life (25.7 vs 13.5%, $P=0.01$) [25-27].

Early readmissions after hospital discharge are often assumed to indicate an incomplete treatment in hospital, a deficit of coordination between services or poor communication of prescriptions at discharge. It can also imply inadequate access to medical care in early follow-up. The 30-day interval for readmission has increasingly compelled attention, emerging as a discrete time frame over which outcomes can be tracked or followed and potentially influenced by greater attention to improving in-hospital heart failure treatment and care transitions. Goals during the heart failure readmission include monitored decongestion and stabilization of fluid balance via oral diuretics, treatment of aggravating factors, and titration of neurohormonal antagonists for long-term benefit. Comprehensive discharge planning, including patient and caregiver education, nutritional advices like the limitation of sodium consumption and restriction of fluids, collaboration with visiting nurses and planned follow-up, are factors which may reduce early readmission rates by as much as 25%. Especially important may be the follow-up within 7 to 10 days, which was widely implemented after recognition that nearly half of heart failure readmissions occurred before the first ambulatory visit. Outcomes appear to be better when follow-up involves collaborative care between a cardiovascular specialist and the primary care physician [28-30].

Readmission rates are also higher when psychosocial and/or socioeconomic factors limit adherence, compliance and coordination with medication, self-monitoring, and follow-up. Patients with these risk factors tend to cluster according to the local geography of their hospitals. Resource limitations both for institutions and for individuals further influence the tendency for higher readmission in public hospitals, especially in those located in counties with low to medium income, with a limited number of cardiology specialists or with understaffed nursery. Local

practice patterns also appear to be important, because hospitals with high overall rates of admissions tend to have higher rates of readmissions after heart failure hospitalization. Readmission rates are similar with and without heart transplant capability. This is due to the fact that transplant programs focus on younger populations with more severe cardiac disease but fewer comorbidities. High adherence to guidelines does not predict in a reliable way lower readmissions, because the highest performing centers may also receive a more complex referral case mix [31-33].

Conclusions

The authors confirm that heart failure decompensation was the most common cause for readmission, being precipitated by an ischaemic episode, atrial fibrillation or medication side effects. HF hospitalization within one year prior to study enrollment, hyponatremia, renal dysfunction, hypotension and the degree of hyperkalemia were particularly important risk factors for cardiovascular readmission.

References

1. STEVENSON, L.W., PANDE, R. *Circulation*, no. 4, 2011, p. 390-392.
2. CUBBON, R.M., GALE, C.P., KEARNEY, L.C., et al, *Circulation*, no. 4, 2011, p. 396-403.
3. ROSS, J.S., CHEN, J., LIN, Z., et al, *Circulation*, no. 3, 2010, p. 97-103.
4. GAVRILESCU, C.M., FELEA, M.G., BARBU, R. ET AL, *Rev Med Chir*, 120, no. 1, 2016, p. 48-54.
5. KRUMHOLZ, H.M., MERRILL, A.R., SCHONE, E.M., et al, *Circ Cardiovasc Qual Outcomes*, no. 2, 2009, p. 407-413.
6. JOYNT, K.E., JHA, A.K., *Circ Cardiovasc Qual Outcomes*, no. 4, 2011, p. 53-59.
7. AURSULESEI, V., VASINCU, D., TIMOFTE, D., et al, *Gen. Physiol. Biophys.*, 35, 2016, p. 287-298.
8. CHUN, S., TU, J.V., WJEYSUNDERA, H.C., et al, *Circ Heart Fail*, 2012.
9. LINDENAUER, P.K., REMUS, D., ROMAN, S., et al, *N Engl J Med*, 356, 2007, p. 486-496.
10. ATHER, S., CHAN, W., BOZKURT, B., et al, *J Am Coll Cardiol*, 59, 2012, p. 998-1005.
11. BHATIA, R.S., TU, J.V., LEE, D.S., et al, *N Engl J Med*, 355, 2006, p. 260-269.
12. CINTRON, G., JOHNSON, G., FRANCIS, G., et al, *Circulation*, 87, no. 6, 1993, p. 17-23.
13. COSTACHE, I.I., AL NAMAT, R., MITU, E., CIOCOIU, M., AURSULESEI, V., MITU, O., COSTACHE, A.D., MARCU, D., BUBURUZ, A.M., *Rev. Chim. (Bucharest)*, 68, no. 12, 2017, p. 2967
14. PUNNOOSE, L.R., GIVERTZ, M.M., LEWIS, E.F., et al, *J Card Fail*, 17, 2011, p. 527-532.
15. ZILE, M.R., BENNETT, T.D., ST. JOHN SUTTON, M., et al, *Circulation*, 118, 2008, p. 1433-1441.
16. ZILE, M.R., BOURGE, R.C., BENNETT, T.D., et al, *J Card Fail*, 14, 2008, p. 816-823.
17. DATCU, M.D., DATCU, G., FERMESANU, I., AURSULESEI, V., *Acta Endo(Buc)*, 5, no. 2, 2009, p. 265-274.
18. STEVENSON, L.W., ZILE, M., BENNETT, T.D., et al, *Circulation*, no. 3, 2010, p. 580-587.
19. KANSAGARA, D., ENGLANDER, H., SALANITRO, A., et al, *JAMA*, 306, 2011, p. 1688-1698.
20. SOUCIER, R.J., MILLER, P.E., INGRASSIA, J.J., et al, *Curr Heart Fail*, 2018.
21. TALMOR, G., NGUYEN, B., KEIBEL, A., et al, *Trends Cardiovasc Med*, 2018.
22. RONALD, S.C., JASWINDER, S., KRISHNARAJ, M., et al, *Int J Gen Med*, 11, 2018, p. 127-141.
23. LU, N., HUANG, K.C., JOHNSON, J.A., *Int J Qual Health Care*, 28, no. 1, 2016, p. 53-58.
24. KOCHER, R.P., ADASHI, E.Y., *JAMA*, 306, 2011, p. 1794-1795.

25. AURSULESEI, V., BULUGHIANA, S., STOICA, B.A., ANISIE, E., Rev. Chim. (Bucharest), **68**, no. 5, 2017, p. 1014-1018.
26. GHEORMAN, V., MILITARU, F., CALBOREAN, V., Rev. Chim. (Bucharest), **69**, no. 4, 2018, p. 881
27. COSTACHE, LL., COSTEA, C.F., DANCIU, M., et al, Rom J Morphol Embryol, 58, no. **1**, 2017, p. 201-206.
28. DHARMARAJAN, K., HSIEH, A.F., LIN, Z., et al, JAMA, 309, no. **4**, 2013, p. 355-363.
29. SCOTT, K.W., JHA, A.K., N Engl J Med, 371, 2014, p. 3-5.
30. BASOOR, A., DOSHI, N.C., COTANT, J.F., et al, Congest Heart Fail, 19, no. **4**, 2013, p. 200-206.
31. COLLINS, S.P., PANG, P.S., FONAROW, G.C., et al, J Am Coll Cardiol, 61, no. **2**, 2013, p. 121-126.
32. PHILLIPS, C.O., WRIGHT, S.M., KERN, D.E., et al, JAMA, 291, no. **11**, 2004, p. 1358-1367.
33. CALBOREAN, V., GHEORMAN, V., ISTRATOIE, O., Rev. Chim. (Bucharest), **69**, no. 5, 2018, p. 1134

Manuscript received: 15.01.2018