

Factors affecting rehospitalizations of heart failure patients

Czynniki wpływające na rehospitalizacje pacjentów z niewydolnością serca

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Abstract

Heart failure (HF) is at present an important clinical problem. Hospitalization of HF patients causes that they have a much less favorable prognosis, and their successive rehospitalizations significantly affect the course of the disease and further treatment. The main reason for readmission to hospital is HF exacerbation, which from the pathophysiological point of view is associated with an elevated pressure in the pulmonary circulation. Factors affecting rehospitalization can be divided into: cardiac-related factors such as ischemia, atrial fibrillation, and uncontrolled hypertension, non-cardiac factors including coexisting diseases (especially chronic obstructive pulmonary disease, infections), patient-related factors (nonadherence/noncompliance, self-care, frailty-syndrome, depression, cachexia) and healthcare system-related factors (nonadherence of physicians, therapeutic nihilism, insufficiency of interdisciplinary care system in the field of patients' therapy and education). Rehospitalization of HF patients is a complex, multifactorial and not fully understood problem. An integrated interdisciplinary care system, which covers patients' therapy, education, self-assessment and self-control may reduce the mortality rate and number of rehospitalizations for all reasons and for HF.

Key words: heart failure, rehospitalizations

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Introduction

Heart failure (HF) is an increasing epidemiological and clinical problem. The longer lifespan and higher survival rate of patients with acute coronary syndrome cause that the number of patients with this condition is growing. The incidence of chronic HF in Europe constitutes currently about 1–2% [1]; however, it noticeably increases with age – according to the report of the American Heart Association (AHA) of 2013 [2] HF affects 7.8% of men and 4.5% of women over 60 years of age, and 8.6% of men and 11.5% of women over 80. What is striking, more than 80% of HF patients are over 65-year-olds. The incidence of HF is believed to increase by about 25% by 2030 comparing to 2013.

Despite many available pharmacotherapy options and the use of implantable medical devices, hospitalization

of HF patients is still frequent. What is more, the survival rate in a group of patients with HFpEF (HF with preserved ejection fraction) has not improved, and only has slightly improved in patients with reduced ejection fraction [3].

The prognosis in chronic HF is unfavorable. One-year and five-year mortality rates have declined over recent years, but still remain high (according to epidemiological records, they are 11–30% and 41–65% respectively) [4]. A considerably worse prognosis and higher mortality rate are observed among hospitalized patients than those treated in outpatient clinics. Therefore, more and more attention is paid to the problem of rehospitalization for HF.

Hospitalizations due to HF can be divided into: hospitalizations with a newly diagnosed or so called *de novo* HF (about 15%), hospitalizations for exacerbation of the disease (about 80%), and hospitalizations of so called

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end-stage i.e. terminally ill patients (about 5%) [5]. As indicated by the statistics proposed by Jencks's team [6], every fifth HF patient of Medicare was rehospitalized during 30 days, and nearly every third – during 90 days since the last discharge from hospital. What is important, only 37% of rehospitalizations were associated with HF – the remainder was due to other diseases. It is also noticeable that about 50% of patients hospitalized for HF have a preserved left ventricular ejection fraction (HFpEF) [6].

In the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) registry [4] a proportion of readmissions to hospital during 60–90 days from the discharge was about 30%, and a death rate in this period was 10%. The report based on the EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan) [5] showed that 58% of the first-time rehospitalizations took place more than 60 days after the last discharge; moreover, during this time it was an estimated 70% of all recorded deaths during the study. It must be emphasized that about 40% of hospitalizations were due to HF, and cardiovascular diseases altogether caused about 60% of hospitalizations.

Reasons for rehospitalization (Table 1) can be divided into: cardiac-related factors such as ischemia, atrial fibrillation, and uncontrolled hypertension, non-cardiac factors including coexisting diseases (chronic obstructive pulmonary disease, infections), patient-related factors (nonadherence/noncompliance, self-care, frailty-syndrome,

depression, cachexia) and healthcare system-related factors (nonadherence of physicians, therapeutic nihilism, insufficiency of interdisciplinary care system in the field of patients' therapy and education).

Heart failure as a cause of readmission to hospital

One of the main reasons for rehospitalization of HF patients is exacerbation of the disease. Both in the OPTIMIZE-HF registry and in the EVEREST program, HF was the most common cause of readmission to hospital (18% and 28% respectively). In the ADHERE (Acute Decompensated Heart Failure National Registry) [7] 24% of admissions to hospital were due to newly-diagnosed heart failure, and as many as 76% were associated with exacerbation of the previously diagnosed HF. It is currently observed that the main reason for rehospitalizations associated with exacerbation of HF is pulmonary congestion but not a low cardiac output [8]. Aside from left ventricular ejection fraction, clinical symptoms observed on admission to hospital are caused by pulmonary congestion. As typical symptoms of HF exacerbation, the ADHERE and OPTIMIZE-HF registers mention dyspnea (about 90%), rales (about 65%), and peripheral edema (about 65%). Pathophysiological changes in HF exacerbation manifest themselves as an increased left ventricular filling pressure. This may be caused by various factors such as arrhythmia, hypertensive crisis, myocardial ischemia, and cardiac valve dysfunction. What is important, an increased left ventricular filling pressure may occur many days before admission to hospital and have a subclinical course up to the emergence of symptoms and the necessity of hospitalization [9]. It may happen that patients are discharged from hospital after their clinical symptoms have subsided or have been alleviated, but an increased left ventricular filling pressure is still present. This in turn may lead to frequent rehospitalizations. In the IMPACT-HF (Initiation Management Predischarge Process for Assessment of Carvedilol Therapy for Heart Failure) study [10], about 60% of patients still had HF symptoms (dyspnea, fatigue) at discharge from hospital. After 60 days from discharge about 45% of these patients had another HF exacerbation, and 25% required readmission to hospital.

An increased left ventricular filling pressure is marked by high levels of natriuretic peptides. It was found in EVEREST trial [11] that patients who had sudden medical events soon after discharge from hospital, had also high levels of natriuretic peptides when they were discharged from hospital for the first time. It may suggest that though the symptoms of congestion were absent or significantly reduced at discharge from hospital, 'hemodynamic congestion' or an increased left ventricular filling pressure was still present.

Table 1. Factors affecting rehospitalization of heart failure patients

Cardiac-related factors

Heart failure natural course and history

Exacerbating factors: ischemia, arrhythmias, especially atrial fibrillation, uncontrolled hypertension

Non-cardiac factors

Comorbidities (especially chronic obstructive pulmonary disease, infections)

Patient-related factors

Self-care

Nonadherence

Noncompliance

Frailty syndrome, cachexia, depression, cognitive disorders

Healthcare system-related factors

Nonadherence of physicians

Therapeutic nihilism

Insufficiency of interdisciplinary care system in the field of patients' therapy, education

Self-assessment and self-control

We currently lack appropriate diagnostic tests, which might be used to objectively confirm an increased left ventricular filling pressure. Indirect methods include Doppler echocardiography, measurement of the levels of natriuretic peptides, and imaging with X-rays to check for symptoms of congestion in the pulmonary circulation. An objective examination which enables us to confirm an increased left ventricular filling pressure is the measurement of pulmonary capillary wedge pressure (PCWP). Nevertheless, it is invasive and difficult to perform in a daily-routine clinical practice. Also serum biomarkers like impaired renal function, electrolyte metabolism disorders, anemia, high levels of natriuretic peptides, troponin and aminotransferases can be useful in determining patients with high risk of rehospitalization as they can show the beginning of the hemodynamic congestion. Hernandez et al. [12] showed that normal sodium levels (> 135 mmol/l) and reduction of N-terminal brain natriuretic peptide (NT-proBNP) at discharge (net reduction $> 23\%$ compared to admission levels) were predictive of a lower rate of 30-day readmission for HF. In turn, patients with decreased renal function, defined as carry out, therefore its clinical usage is very limited.

However there are some predictive factors for hospitalization of HF. Those factors include sex, age, psychosocial factors (depression, unemployment, low income, the level of education), coexisting diseases (which are mentioned glomerular filtration rate [GFR] less than 45 mL/min per 1.73 m²) were re-hospitalized more frequently than those with preserved renal function [13].

Comorbidities

Comorbidity is common among elderly people with chronic HF. The presence of many coexisting diseases delays and hinders a diagnosis of HF patients. What is more, additional health problems may affect the course and treatment of HF, through their contribution to hospitalizations and mortality rate in this group of patients.

Conditions which particularly contribute to hospital readmissions of HF patients are: chronic obstructive pulmonary disease, renal insufficiency, type 2 diabetes, depression and diseases of the lower respiratory tract. The study of Braunstein et al. [14] shows that the risk of hospitalization increases with the number of coexisting diseases. In the elderly HF population with a diagnosis of ≥ 5 coexisting diseases, 40% of patients required rehospitalization more frequently than their healthier counterparts.

The above-mentioned OPTIMIZE-HF registry shows that patients hospitalized for pneumonia, acute coronary syndromes/ischemia, and deterioration in renal function were at the highest risk of intrahospital death. The risk of death after discharge from hospital was the highest for patients admitted to hospital due to acute coronary

syndromes/ischemia and deterioration in renal function. What is important, all these conditions accompanying HF raise the risk of rehospitalization, which increases with their number [14].

Frailty syndrome

HF patients are mostly elderly people over 65 years of age. They are characterized by the coexistence of many diseases and clinical syndromes, including frailty syndrome (FS). Frailty syndrome is more common among HF patients than in the general population, and is an independent predictive factor for emergency interventions, hospitalization and mortality [15].

McNallan et al. [16] and Lupon et al. [17] demonstrated that patients with frailty syndrome were more often hospitalized and more often visited the hospital emergency department.

As indicated by the Cardiovascular Health Study, the incidence of HF in patients with frailty syndrome was higher than in patients who were only at the risk of developing such syndrome, and in the latter it was higher than in those without frailty syndrome (14% vs. 4.6% vs. 1.8%, $p < 0.001$) [18]. The results of the Women Health Initiative, on the other hand, showed that women with HF suffered from frailty syndrome six-seven times more often than those without HF [19].

The diagnosis of frailty syndrome in HF is of a great clinical importance, since it worsens the prognosis for the patients. In the study of Spanish population, the coexistence of HF and frailty syndrome contributed to a rise in one-year mortality rate (16.9% in the group with frailty syndrome vs. 4.8% in the group without frailty syndrome, $p < 0.001$), and rehospitalizations (20.5% in the group with frailty syndrome vs. 13.3% in the group without frailty syndrome, $p = 0.01$) [17]. Similar results were obtained in the 12-year observation of Italian patients, in whom frailty syndrome was a predictor of a higher mortality rate [20].

A frequent coexistence of HF and frailty syndrome results from a common pathological background consisting of metabolic inflammatory processes and autonomic disorders. As said by Afilalo et al. [21], frailty predisposes to myocardial damage, since it reduces stress resistance as a consequence of a decline in physiological reserve, and thus leads to HF decompensation and hospitalization. The research conducted by Pulignano et al. [22] demonstrated a significantly higher proportion of deaths (16.9% vs. 4.8%, $p = 0.001$) and a higher number of rehospitalizations (20.5% vs. 13.3%, $p = 0.01$) during one year.

The elderly with frailty syndrome and/or numerous coexisting diseases not always receive full treatment for HF, which results both from real contraindications and physicians' fear. The use of angiotensin converting enzyme (ACE)

inhibitors and angiotensin receptor blockers (ARBs) is limited by renal failure, beta-blockers – by chronic obstructive pulmonary disease, vasodilators – the risk of orthostatic hypotension, and diuretics – the fear of urinary incontinence, electrolyte disorders, progression of renal failure, and falls [23]. Additionally, patients with frailty syndrome are less mobile, and so they may encounter problems when getting to clinical centers. Impaired cognitive function, on the other hand, often results in worse adherence [23].

Cachexia

Cachexia is an important phenomenon in patients with HF and frailty syndrome. According to the Cachexia Consensus Conference in 2006, it is defined as a metabolic syndrome associated with the underlying disease and characterized by the weight loss $\geq 5\%$ within one year (or decreased body mass index [BMI] $< 20 \text{ kg/m}^2$), as well as at least three out of five following criteria: reduction of muscle strength, fatigue, a poor appetite, low fat-free mass index, and abnormal biochemical test results (inflammation, anemia, low sodium level in serum) [24]. Cachexia in general, and specifically cardiac cachexia entail a higher frequency of hospitalizations and a very high risk of death [25]. According to the European Society of Cardiology (ESC), cachexia is observed in 10–15% of HF patients, especially those with reduced ejection fraction. Furthermore, the mortality rate of patients with chronic cardiac cachexia is 2–3 times higher than in the case of people with cachexia in general population [1].

Depression

Another factor which plays a crucial role in HF is depression. Depressive disorders are an essential part of frailty syndrome [26], but even depression itself increases the frequency of rehospitalizations of HF patients – according to Johnson et al. [27], depressed HF patients are rehospitalized one-and-a-half times more often than those without depression, even if they cooperate with the doctors and take drugs regularly. Depression is significantly more common among people with HF and the New York Heart Association (NYHA) functional class III and class IV symptoms [28].

Cognitive function disorders

Impairment of cognitive function is common in elderly people. Its incidence is estimated at about 25% [29]. Cognitive disorders and comorbidity are closely related to a higher number of hospitalizations and higher mortality rate among elderly HF patients.

Factors associated with cognitive disorders arouse some controversy. In their study of cognitive deficits in HF,

Pressler et al. [30] demonstrated that age, sex and the severity of HF were significantly related to cognitive function. In another study, age, the level of hypertension, and depressive symptoms contributed to cognitive disorders in HF [31].

Patient-related factors

Self-care

An important aspect in all HF patients, and especially those with frailty syndrome is so-called self-care. It refers to patients' appropriate behaviors concerning their health and education. These behaviors are defined as those that are exhibited by patients to be healthy and function well. They include adherence to/compliance with pharmacological therapy, proper diet and regular exercises, as well as self-monitoring (everyday weighing and observing edema to check for increased fluid retention), reacting properly and searching for medical help when needed. Frailty syndrome affects all those behaviors, that is – the ability to self-care – especially in elderly patients with heart failure [32].

At present, there is little information about the influence of self-care on readmissions to hospital. As early as in 1994 Dracup et al. [33] claimed that proper education of HF patients may reduce the number of their rehospitalizations. According to other authors, this effect is associated with regular drug administration [34]. On the contrary, Jaarsma et al. [35], who in 1999 compared the influence of health education provided by nurses on 'self-care' in a group of 179 patients, did not demonstrate significant differences in the number or length of hospitalizations between educated and non-educated patients.

Numerous reports confirm that systematic education of HF patients plays an important part in the third-stage prevention, since it helps avoid decompensation and readmissions to hospital [36]. It was also found that education is most effective if it is self-care oriented. Self-care in HF includes such aspects as taking appropriate doses of prescribed medicines, modification of lifestyle (including diet and physical activity), and the ability to recognize the first symptoms of decompensation and react to them properly [37, 38]. Self-care level can be measured by appropriate scales, and those scales can show significant deficits in self-care behaviors which require to be optimized in future patient education [39].

Adherence

It is important to pay attention to non-adherence to medications and diet regimen, alcohol abuse, as well as overuse of over-the-counter (OTC) drugs (ex. non-steroidal anti-inflammatory drugs [NSAIDs]).

Both non-adherence to therapy and the lack of changes in the lifestyle, which are observed in one third of HF patients, considerably contribute to HF exacerbation and

increase the cost of therapy [40]. According to literature, non-adherence to the prescribed treatment affects 40–60% of HF patients.

Nieuwenhuis et al. [41] demonstrated that 72% of HF patients adhere to four out of six therapeutic recommendations. Those most often obeyed are pharmacological therapy (98%) and check-ups (95%), and the least – low-sodium diet regimen (79%), limitation of fluid intake (73%), and everyday weighing (35%).

Based on one of prospective studies, patients who adhered to nonpharmacological recommendations were less often hospitalized for HF, and their stays in hospital were shorter than it was in the case of patients who had not fully cooperated with medical professionals [42]. The number of rehospitalizations was also significantly related to regular physical exercises. Davies et al. [43] have shown that participation of HF patients in cardiac rehabilitation reduced the number of rehospitalizations for HF.

What is interesting, no relationship was observed between rehospitalizations or mortality rate and adherence to diet and fluid intake regimen. However, the randomized study [44] comparing low-sodium and normal-sodium diets followed by patients taking high doses of furosemide, revealed that those who limited sodium intake were more often hospitalized. It was associated with changes in the renin–angiotensin–aldosterone (RAA) system, occurring while being on a low-sodium diet.

In the study of Evangelista et al. [45], the risk of rehospitalization was higher for those HF patients who did not follow recommendations concerning smoking and alcohol consumption. Nonrandomized observations, on the other hand, demonstrated the relationship between more frequent hospitalizations and not getting a flu vaccination by patients over 65 years of age [46].

Murray et al. [47] noted a three times higher frequency of rehospitalizations among HF patients who did not follow a therapeutic regimen.

One of the most common causes of patients' non-adherence is their inability to keep to the doctor's orders. Patients claim that instructions given to them are too complicated and inapplicable (71%). The most common reason for not taking recommended medicines is their lack or problems with getting the next prescription (33%). Every fifth patient complains of adverse side-effects of therapy (20%), memory disorders (18%) and financial barriers [48].

According to World Health Organization (WHO), factors which hinder patients' compliance and adherence are physical disability and cognitive dysfunction, especially among elderly people. HF patients often suffer from depressive symptoms and cognitive disorders, and people with depression are less careful about taking drugs [49]. Patients with depressive symptoms miss doses of medications more frequently than those without depression (75% vs. 21%, $p < 0.01$) [50]. Studies also show that HF

patients more often adhere to pharmacological therapy than change their lifestyles. The most effective treatment and high levels of compliance are achieved in these patients who go for checkups or take part in HF treatment programs [51].

A lack of cooperation on the patient's part is common among elderly people and results in poor outcome [51]. Mockler et al. [52] demonstrated that discontinuation of the prescribed treatment was an independent predictor of rehospitalization for HF. Non-adherence to therapy was an independent factor associated with the higher mortality rate among the participants of the CHARM (Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity) trial program [34]. Old age, frailty syndrome and comorbidity may contribute to non-adherence among HF patients, consequently leading to more frequent rehospitalizations, stays in long-term care institutions and finally death [23].

Healthcare system-related factors

The analysis of the Euro Heart Survey (EHS) shows that only 50% of HF population receives pharmacotherapy recommended by the ESC [53]. On average, primary care physicians prescribe ACE inhibitors to 40% of those who should receive them in accordance with the ESC guidelines (from 18% in Netherlands to over 50% in Germany) [53]. In Poland, ACE inhibitors are prescribed by primary care physicians to 54% of HF patients, which is slightly less than in the IMPROVEMENT study performed in general practice, in which the use of ACE inhibitors was 65% [54].

Considering beta-blockers, according to the EHS, the therapy was initiated by primary care physicians only in one fifth of patients [53]. In the countries of Western Europe (Switzerland, France and Netherlands) these drugs belong to the least frequently used by primary care physicians (only in about 9% of patients), while in Germany and Hungary it is 70% and 71% respectively. In Poland it is 30%.

Therapeutic nihilism is responsible for a substantial number of hospitalizations for HF [55]. There is the need for continuous education of the medical environment on HF therapy related issues [56].

Modern methods of management of HF patients, based on the integrated healthcare system, have the task of improving the quality and comfort of patients' lives, slowing the progress of the disease, preventing frequent rehospitalizations, and cutting the huge costs of treatment. To achieve this goal, comprehensive health education is needed [57]. Integrated healthcare programs may be based on HF outpatient clinics, home visits, consultations by phone and telemonitoring. The majority of programs do not include all these elements, but using at least one of them may be of benefit to patients. Education of patients and interventions for supporting them reduce the number and cost of hospitalizations for HF [58]. The

multidisciplinary healthcare program for HF patients, carried out by McDonald et al. [59] in one of Irish clinics, demonstrated a decline in the number of rehospitalizations and deaths from HF during 90 days from discharge from hospital. The team included a cardiologist, a nurse and a dietitian.

Meta-analyses of randomized programs of care for HF patients, and the results of the multidisciplinary program implemented in Poznań, PL in 2002 confirm favorable effects of therapy based on new interdisciplinary care programs.

After one-year observation, Wierchowicki et al. [60] noted a decrease in the total and HF mortality rates, lower frequency of hospitalizations and improvement of the quality of life. Meta-analysis of 33 randomized studies conducted by Roccaforte et al. [61] revealed a decline in the total and HF mortality rates, as well as a reduction of the number of rehospitalizations for both HF and other health problems. The above mentioned programs also demonstrated that the cost of treatment decreased and the quality of life improved. Similar results were obtained by McAlister et al. [62] in their meta-analysis of 29 randomized studies. An integrated system of interdisciplinary care reduces mortality rate and the number of readmissions to hospital for both HF and other diseases.

As results from the above mentioned studies, interdisciplinary care programs noticeably improve the treatment process of HF patients. Comprehensive education of patients and their families is the most essential part of interdisciplinary care [63]. As part of such education, patients

should be informed about the nature of their disease, its symptoms, and the ways of monitoring decompensation symptoms. Education should be provided during patients' stay in hospital, and after discharge it should be continued in heart failure outpatient clinics. Education of patients and their families or caregivers should consist of individual and group conversations, interactive workshops, multimedia displays, lectures and printed materials. Van der Wal et al. [64] reported that out of 501 HF patients, 73% kept to fluid-intake regime, merely 35% weighed themselves regularly, as many as 80% believed that physical exercises were an important element of the lifestyle, but only 39% of them took physical activity. Education provided as a part of healthcare programs for HF patients should cover such issues as pharmacotherapy, diet, using alcohol and cigarettes, physical effort, sexual activity and obligatory vaccinations.

Summary

Rehospitalization of HF patients is a complex, multifactorial and not fully understood problem. An integrated interdisciplinary care system, which covers patients' therapy, education, self-assessment and self-control may reduce the mortality rate and number of rehospitalizations for all reasons and for HF.

Conflict of interest(s)

None declared

Streszczenie

Niewydolność serca (HF) jest obecnie ważnym problemem klinicznym. Rehospitalizacje chorych z HF są jedną z przyczyn gorszego rokowania, wpływają na przebieg choroby i dalsze leczenie. Główną przyczyną readmisji do szpitala jest zaostrzenie HF, które z patofizjologicznego punktu widzenia wiąże się z podwyższonym ciśnieniem w kapilarach płucnych. Czynniki wpływające na rehospitalizacje można podzielić na: związane z układem krążenia (takie jak niedokrwienie, migotanie przedsionków czy niekontrolowane nadciśnienie tętnicze), niezwiązane z układem krążenia (choroby współistniejące, w szczególności przewlekła obturacyjna choroba płuc czy infekcje), związane z pacjentem (takie jak współpraca i stosowanie się do zaleceń leczniczych, samokontrola, zespół kruchości, zaburzenia poznawcze, depresja, kacheksja), związane z systemem opieki zdrowotnej (takie jak niewydolność systemu opieki w zakresie edukacji i leczenia, nihilizm terapeutyczny). Rehospitalizacje chorych z HF są złożonym, wieloczynnikowym i nie do końca poznanym problemem. Zintegrowana wielodyscyplinarna opieka nad chorym, uwzględniająca także edukację pacjenta oraz jego samoocenę i samokontrolę, może zmniejszyć liczbę rehospitalizacji i śmiertelność ogólną chorych z HF.

Słowa kluczowe niewydolność serca, rehospitalizacje

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