Hospitalization for worsening chronic heart failure

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The total number of admissions for heart failure (HF) in the United States is approaching 1 million/year. HF is the number one volume diagnosis in the Medicare health system. Readmission rates are as high as 30 to 60% within 3 to 6 months after discharge even in patients without renal failure, low blood pressure or significant arrhythmias.

Patients admitted with HF can be classified into three categories: new-onset HF (5% of total admissions), end-stage or refractory HF (5%), and worsening chronic HF (90%).

This review will focus on the epidemiology, prognosis, pathophysiology and pharmacological treatment of patients hospitalized for worsening chronic HF.

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The total number of admissions for heart failure (HF) in the United States is approaching 1 million/year[1,2]. If we take into account patients admitted for other conditions who also have a diagnosis of HF, the number reaches 3 millions/year[1,2].

Patients who have been admitted to a hospital for the treatment of HF have a readmission rate as high as 30 to 60% within 3 to 6 months after the initial discharge. Despite those patients appear to respond well to therapy, the event rate (readmission and mortality) is exceeding 35% within 60 days after discharge even in patients without renal failure, low blood pressure or significant arrhythmias[3].

In contrast to patients admitted with acute coronary syndromes there are no evidence-based guidelines on how to treat this condition (Table I).

Classification

Patients admitted with HF can be classified into three categories: new-onset HF secondary to an acute injury (e.g. a large anterior myocardial infarction [MI] or acute mitral insufficiency); advanced or end-stage or refractory HF that by definition is not responding or poorly responding to therapy; and the third group that constitutes more than 90% of all admissions with worsening chronic HF who appear to respond well to short-term therapy but have a high event rate within 60 days.

The present review will focus exclusively on this latter group of HF patients.

Epidemiology

The baseline clinical characteristics of those patients is mostly derived from the Acute Decompensated Heart Failure National Registry (ADHERE)[4] that enrolled > 100 000 consecutive patients admitted with worsening HF. This registry has shown that the majority of patients are older (> 75 years), 75% have a prior history of HF, > 50% are women and have a coronary artery disease, approximately 40% have a normal ejection fraction, atrial fibrillation, diastolic HF and/or diabetes mellitus. Half of the patients were hypertensive at the time of admission (mean systolic blood pressure of 110-130 mmHg) and < 3% presented with hypotension.

Prognosis and predictors of outcome

Although in-hospital mortality for patients with worsening chronic HF is very low (< 2-3%), the readmission rate within 60 days is as high as 30% and the mortality rate is 5-15%[5].

It is important to recognize factors that predict recurrent hospital admissions. Opasich et al.[6] studied 2701 outpatients

Table I. Comparison between heart failure and acute myocardial infarction (MI).

	Heart failure (≈970 000)	Acute MI* (≈1 000 000)
60-day readmission rate	High	Low
Placebo-controlled trials**	6	> 100
Citations Medline 1997-2002	100	5692
Guidelines	No	Yes

* ST-elevation MI and non-ST-elevation MI; ** published March 2002-February 2003.

with HF and found that 215 (8%) had short-term decompensation on average 2 months after the index outpatient visit. A multivariate analysis showed that previous hospitalization, duration of symptoms > 18 months, ischemic etiology, atrial fibrillation, high blood urea nitrogen, mild anemia, mild hyponatremia, a high functional class (NYHA class III-IV), a heart rate > 100 b/min, and a low systolic blood pressure were each independently associated with the exacerbation of HF[3,6]. Moreover, the presence of ischemia and a history of previous hospitalization predicted both recurrent hospitalization and the 1-year mortality rate[3,6]. Although erythropoietin and vasopressin antagonists are able to correct two risk factors, i.e. anemia and hyponatremia respectively, ongoing studies will determine if normalization or improvement of hemoglobin or serum sodium levels will translate into better outcomes.

In addition, changes in levels of B-type natriuretic peptide (BNP) after treatment may predict early readmission rates and mortality rates in patients hospitalized with HF[7,8]. In a trial conducted by Colucci et al.[9] patients whose discharge BNP levels fell below 430 pg/ml after treatment were less likely to be readmitted during follow-up than those who did not show a substantial change in BNP levels.

A role for cardiac troponins in the evaluation and risk stratification of patients with HF has recently emerged. In a study by Del Carlo and O'Connor[10], elevated cardiac troponin I levels were found in 10 of 34 patients (29%) hospitalized with HF and were a predictor of mortality at 3 months. A study of 98 patients hospitalized with class III and IV HF found that a cardiac troponin T level > 0.033 µg/l on admission was associated with an increased risk of cardiac mortality[11].

Because both BNP and cardiac troponins appear to provide independent prognostic information in patients with HF, an integrated approach of measuring both biomarkers would be expected to provide independent prognostic information and to further improve determination of mortality risk[12]. In fact, the combination of elevated cardiac troponin I and elevated BNP identified HF patients with a markedly increased mortality risk (12-fold increase)[13].

Pathophysiology

Worsening chronic HF is primarily associated with a deterioration in hemodynamic function which increases left and right ventricular filling pressures and/or decreases cardiac output (CO)[14] due to fluid overload or congestion and precipitated by different factors (e.g. diet indiscretion, poor compliance with medication as anti-inflammatory, diuretics or calcium channel blockers) that disrupt a previously stable clinical status[15].

The hemodynamic abnormalities associated with acute exacerbations may contribute to progressive ventricular dysfunction and dilation, which lead to symptoms of dyspnea at rest, orthopnea, fluid retention, and possibly myocyte loss. High left ventricular filling pressure and increased wall stress may lead to acute subendocardial ischemia/necrosis which may cause a release of cardiac troponin even in the absence of coronary artery disease[16,17]. In fact, evidence is emerging that a significant number of patients with worsening chronic HF have a myocardial injury at the time of admission or developing during hospitalization[5]. This is reflected by the fact that approximately 60% of those patients in whom MI is not suspected, a troponin I or T release could be present and has been correlated with poor long-term prognosis[18]. Accordingly, preventing and/or treating myocardial injury and improving diastolic filling pressure are major goals in the management of worsening chronic HF.

On the other hand, it is important to realize that approximately 50-60% of patients admitted with worsening chronic HF have coronary artery disease[19] and of these 60% have hibernating myocardium (firstly described[20] as viable but dysfunctional myocardium that is down-regulated secondary to a chronic reduction in coronary blood flow and repetitive episodes of ischemia). This down-regulation may be an adaptive and protective mechanism by which decreased myocardial oxygen demand resulting from decreased contractility can prolong the metabolic integrity of the ischemic myocardium.

Interestingly, when experimentally hibernating myocardium is stimulated by a relatively low dose of dobutamine, myocardial necrosis occurs[21]. This phenomenon is usually clinically silent unless troponin release is measured before, during or after dobutamine infusion.

Pharmacological treatment for worsening chronic heart failure

For patients with worsening chronic HF a large armamentarium of non-pharmacological, pharmacological, electrical, and/or surgical therapies is available but it is extremely underused (Table II)[4]. The immediate goal is to improve symptoms and signs of congestion

Table II. Procedures during hospitalization for heart failure.

Procedure	Rate (%)
Mechanical ventilation	5
Dialysis	5
Defibrillation	1.5
Coronary angiography (PCI)	10 (2)
EP studies	4
PA catheter	4
CABG	1
AICD	<1
CRT	2

AICD = automatic implantable cardioverter-defibrillator; CABG = coronary artery bypass grafting; CRT = cardiac resynchronization therapy; EP = electrophysiological; PA = pulmonary artery; PCI = percutaneous coronary intervention. Data from the ADHERE study[4].

that are related usually to hemodynamic improvement, preserving renal function without causing or preventing myocardial injury. Once stabilization has occurred, the goals are to implement long-term life-saving therapies that include: a) angiotensin-converting enzyme (ACE)-inhibitors, beta-blockers, and aldosterone antagonists; b) implantable cardioverter-defibrillators; c) for patients with coronary artery disease, antiplatelet agents, statins, and possibly revascularization-therapeutic strategy that is presently tested in the National Institute of Health funded Surgical Treatment for Ischemic Heart Failure trial (NIH-STICH).

Treating symptoms and improving the hemodynamic profile in this patient population can be guided by skilled clinical assessment alone. However, in addition to careful clinical assessment, patients may require invasive hemodynamic monitoring to help guide the specific course of therapy. Currently, the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE)[22] trial, that is examining the question of whether therapy guided by pulmonary catheter measurements and clinical assessment will lead to decreased readmission and mortality rates compared with therapy guided by clinical assessment alone, will further clarify these issues.

Intravenous diuretic therapy. None potassium-sparing diuretics are extremely useful in managing congestion and the efficacy and safety of the routine use of diuretics in the setting of worsening chronic HF have not been studied in prospective, randomized, placebo-controlled clinical trials. Moreover, they cause electrolytic imbalance, activate the neurohormones, decrease oncotic pressure, and decrease intravascular volume that result in kidney hypoperfusion.

If patients exhibit loop diuretic resistance, a distally active agent such as an oral thiazide diuretic or aldosterone antagonist may be combined with a loop diuretic for synergistic diuretic effects.

Patients who are congested and show evidence of volume overload that requires intravenous diuretics should be monitored for urine output, hypotension, electrolyte levels, and renal function. Treatment should be highly individualized based on response to therapy and the degree of fluid overload.

Although no definitive data support this hypothesis, the administration of furosemide by continuous infusion may be associated with less prerenal azotemia and fewer of the other side effects associated with intravenous diuretics, possibly because this method of administration avoids the high peak concentrations associated with bolus dosing. In a randomized cross-over study, Dormans et al.[23] compared the efficacy of continuous infusion of furosemide vs an equivalent dose of the agent given in a single bolus injection. Their study, which enrolled patients with NYHA class III or IV congestive HF who were taking oral doses of at least 250 mg of furosemide, demonstrated that patients receiving the agent by continuous infusion had a greater urine output compared with those receiving an equal dose administered as an intravenous bolus. The maximal furosemide plasma concentration was significantly lower in the patients receiving the continuous infusion, as was the incidence of adverse effects[23].

Digitalis. Digoxin given intravenously results in increased cardiac index and decreased heart rate, left ventricular filling pressure and right atrial pressure, as well as in acute attenuation of neurohormonal abnormalities, in patients with HF[24]. Its beneficial acute effects are sustained during chronic therapy particularly in patients with an ejection fraction < 25% or severe symptoms or cardiomegaly.

It appears that chronically a digoxin dose that results in serum concentration of < 1 ng/ml is likely to reduce total mortality and total hospitalization when added to ACE-inhibitors and diuretics[25].

In patients with chronic left ventricular dysfunction, the hemodynamic effects of intravenous digoxin and ACE-inhibitors are enhanced when these agents are given in combination[24].

Nesiritide. Recently approved by the Food and Drug Administration, nesiritide has shown to improve symptoms after 3 hours without any effect on long-term prognosis.

The Vasodilatation in the Management of Acute Congestive Heart Failure (VMAC) trial compared the effects of intravenous nesiritide to intravenous nitroglycerin and placebo in addition to standard chronic medications (ACE-inhibitors, beta-blockers and digoxin) and standard intravenous treatment (diuretics and, if needed, intravenous dobutamine and dopamine) in patients admitted with worsening chronic HF[26]. The addition of nesiritide significantly decreased the pulmonary capillary wedge pressure at 24 hours when compared to nitroglycerin or placebo. Moreover, nesiritide signifi-

cantly reduced dyspnea when compared with placebo.

The Prospective Randomized Evaluation of Cardiac Ectopy with Dobutamine or Natrecor Therapy (PRECEDENT) trial found that nesiritide was not proarrhythmic when compared with dobutamine[27]. Specifically, treatment with nesiritide for 24 hours did not aggravate preexisting ventricular tachycardia nor did it increase the frequency of premature ventricular beats when compared with patient measurements taken from a baseline 24-hour Holter recording. Low-dose nesiritide treatment was also associated with a lower readmission rate at 3 weeks (8 vs 20%) and 6-month mortality when compared with dobutamine (18 vs 31%)[28].

Other ongoing studies will better clarify the role of nesiritide in the management of these patients[15].

Nitrates. Although nitrates are known to decrease preload and improve HF symptoms primarily by reducing pressures through direct venodilation and indirectly by reducing afterload and increasing stroke volume, their use is limited by the development of tolerance within 48 hours and by the fact that there are no long-term efficacy and safety data.

Isosorbide dinitrate is another nitrate preparation effective for the treatment of HF. Cotter et al.[29] randomized 110 patients to repeated high-dose boluses of intravenous isosorbide dinitrate (3 mg every 5 min) plus a single 40 mg bolus of intravenous furosemide or repeated high-dose furosemide (80 mg every 15 min with continuous low-dose isosorbide dinitrate). Compared with repeated boluses of furosemide, repeated boluses of isosorbide dinitrate significantly reduced the requirement for mechanical ventilation within 12 hours of admission and the frequency of MI within 24 hours of admission.

Dobutamine. Although inodilators can improve hemodynamics in patients hospitalized for worsening chronic HF, their short-term use has been associated with an increase in long-term mortality, particularly if associated with coronary artery disease. It has been speculated that stimulating contractility of hibernating myocardium with dobutamine appears to increase short-term myocardial contractility at the expense of MI, myocyte necrosis, and myocardial recovery[21,30].

Despite the fact that dobutamine has been used for ≈20 years, the clinical evidence supporting the therapeutic value of dobutamine is scanty. No large-scale, prospective, randomized, controlled trial has investigated this agent for short-term therapy. Most evidence supporting its use is based on several small series that have suggested that it improved hemodynamic function and provided symptomatic benefits. Higher doses of dobutamine are associated with tachycardia, which produces increased myocardial oxygen demand. The PRECEDENT trial showed that dobutamine was associated with an increase in ventricular ectopy when compared with nesiritide[27].

The Levosimendan Infusion versus Dobutamine (LIDO) trial[31], which compared dobutamine to levosimendan, also found that dobutamine was associated with unfavorable outcomes. Retrospective data from the Flolan International Randomized Survival Trial (FIRST)[32] also showed an increased risk of clinical events for patients treated with dobutamine. These trials raise the possibility that the short-term deleterious effects of dobutamine may have adverse long-term outcomes.

Milrinone. The Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) study[3] was the first carefully designed randomized, placebo-controlled trial to assess the utility and safety of short-term use of intravenous milrinone in patients admitted with worsening chronic HF. The trial randomized 951 patients, who did not absolutely require inotropic support for low CO, to a 48-72 hour infusion of intravenous milrinone or placebo in addition to standard therapy that included diuretics, ACE-inhibitors, digoxin and beta-blockers. The results showed that the addition of milrinone to standard therapies did not decrease the median number of days hospitalized for cardiovascular causes (the primary endpoint) or the rate of readmission/death at 60 days. Milrinone use was also associated with an increased incidence of treatment failures (mainly due to hypotension) and new atrial fibrillation and with a trend in increased mortality. Based on these findings, the investigators concluded that milrinone should not be routinely used as an adjunct to standard therapy in patients admitted for worsening chronic HF.

Sodium nitroprusside. Sodium nitroprusside is a balanced direct arterial and potent venodilator which generally involves continuous blood pressure monitoring. Nitroprusside also dilates pulmonary arterioles and reduces right ventricular afterload. Although this effect may improve right ventricular function, there may be a worsening of ventilation-perfusion mismatch in patients with advanced chronic obstructive pulmonary disease or large pleural effusions and may worsen hypoxia in patients with HF.

Nitroprusside has been noted to increase mortality rates when given to patients with acute MI but without HF[33].

An important limitation of sodium nitroprusside is the potential production of two adverse metabolites: thiocyanate and cyanide which may reach toxic levels in patients with renal insufficiency or liver disease, respectively.

Beta-blockers and ACE-inhibitors. Although they are extremely useful for long-term therapy and should be continued in patients with worsening chronic HF, their acute affects are modest.

The acute use of beta-blockers is limited due to the fact that they transiently decrease ejection fraction and increase filling pressure. They may be particularly useful (e.g. esmolol) for patients in whom HF is precipitated by supraventricular arrhythmias, hypertension and/or ischemia.

ACE-inhibitors should be used with caution in patients with marginal CO or marginal blood pressure because they can decrease glomelular filtration by antagonizing the efferent arteriolar constriction mediated by angiotensin II. These effects may result in a rise in serum creatinine and deterioration in renal function. In the Cooperative North Scandinavian Enalapril Survival Study II (CONSENSUS II)[34], the intravenous administration of enalapril was associated with an early increase in mortality when given to patients hospitalized with acute MI. The postulated mechanism for the increased mortality rate seen in this study is related to hypotension and a drop in cardiac perfusion pressure in ischemic patients.

Intravenous ACE-inhibitors are primarily given only to patients who are unable to take oral medications and may be used when initiating treatment; they may also be used in patients who are on chronic maintenance ACE-inhibitor therapy but are unable to take oral medications while in the hospital. Enalaprilat, an intravenous ACE-inhibitor, inhibits the conversion of angiotensin I to angiotensin II. Intravenous enalaprilat reduces both supine and standing systolic and diastolic blood pressure, with minimal orthostatic hypotension. In a placebo-controlled, randomized study in 20 patients with congestive heart failure (NYHA class III or IV) with acute pulmonary edema, a single 2-hour infusion of enalaprilat demonstrated significant reductions in pulmonary capillary wedge pressure and mean arterial pressure with no effect on CO[35].

Newer pharmacological therapies

Recent trials examined the role of new medications, such as vasopressin antagonists, endothelin receptor antagonists and calcium sensitizers, in the management of patients hospitalized with worsening chronic HF.

The Acute and Chronic Therapeutic Impact of a Vasopressin Antagonist in Congestive Heart Failure (ACTIV in CHF) trial randomized 320 patients admitted for worsening HF to three doses of tolvaptan (a selective vasopressin 2 receptor antagonist) or placebo in addition to the best medical therapy[36]. Treatment was initiated within 72 hours of admission and was continued for 60 days. The primary objective was to determine whether therapy with tolvaptan further reduces body weight at 24 hours and the rate of worsening HF (death, readmissions, unscheduled visits for HF) within 60 days following discharge. The results of this study have shown improvement in body weight, normalization in serum sodium in patients with hyponatremia and a retrospective decrease in mortality at 60 days in patients with severe congestion and/or a mild renal failure. These results could be confirmed by the ongoing Effects of Vasopressin Antagonists in Heart Failure: Outcome Study with Tolvaptan (EVEREST) trial which is investigating the effects of 30 mg of tolvaptan on mortality in 3600 patients from North and South America, Australia and Europe.

Tezosentan is a dual endothelin-1 receptor antagonist that has demonstrated efficacy in improving cardiac index and reducing pulmonary capillary wedge pressure in patients with decompensated HF. Clinical trials have rendered mixed results for the efficacy and tolerability of this endothelin antagonist[37]. The recently published Randomized Intravenous Tezosentan (RITZ)-4 study was a multicenter, randomized, double-blind, placebo-controlled study of tezosentan in patients with acute decompensated HF associated with acute coronary syndromes[38]. A total of 193 patients were randomized to receive tezosentan (25 mg/hour for 1 hour, then 50 mg/hour for 23 to 47 hours) or placebo. At the doses studied, tezosentan did not result in a significant improvement in the composite primary clinical endpoint of death, worsening HF, recurrent ischemia, and recurrent or new MI within 72 hours[38].

The LIDO trial randomized 203 patients admitted for worsening HF who were judged to have low CO and require inotropic support to a 24-hour infusion of levosimendan (a novel calcium sensitizer) or dobutamine[31]. Although the number of patients who achieved hemodynamic improvement (the primary endpoint) was greater in the levosimendan group compared with dobutamine (28 vs 15%), there was little difference in the improvement in symptoms between the two groups. The hemodynamic effects of levosimendan, unlike those of dobutamine, were not attenuated with the concomitant use of beta-blockers. At 6 months, the mortality rate was also lower in the levosimendan-treated patients when compared with dobutamine (26 vs 38%).

In patients admitted with acute coronary syndromes complicated by HF, a 6-hour low-dose infusion of levosimendan did not result in significantly more episodes of ischemia and/or hypotension than placebo (13.4 vs 10.8%)[39]. The combined risk of death and worsening HF was lower in the levosimendan-treated patients during the first 24 hours after the start of the infusion. Fourteen-day and 6-month mortality rates were also lower in the levosimendan group.

Implementation of long-term therapies

A large treatment gap between guidelines and practice exists for HF patients. Therefore, another important goal in worsening chronic HF is the implementation of current life-saving therapies.

The hospital setting is the ideal opportunity to increase utilization and avoid delay in providing life-saving benefits of medication such as beta-blockers. In fact, despite the results from four major clinical trials[40-43] showing that beta-blockers decrease the mortality and readmission rates in HF patients, this life-saving therapy is used in only 30-40% of the eligible patients. The Initiation Management Predischarge: Process for Assessment of Carvedilol Therapy in Heart Failure (IMPACT-HF) trial was conducted to determine if starting carvedilol prior to hospital discharge in patients admitted with a primary diagnosis of HF and ejection fraction ≤ 40% is safe and improves the overall use of beta-blockers at 60 days after randomization as compared with usual care[44]. Three hundred and sixty three patients admitted with worsening HF were randomized to carvedilol started in hospital (3.125 mg bid and adjusted to target dose) or any beta-blocker initiated at physician discretion at least 2 weeks after the patients have been discharged. The results showed that significantly more patients randomized to carvedilol predischarge were receiving a beta-blocker at 60 days as compared to beta-blocker initiation at physician discretion. In addition, the predischarge initiation of carvedilol was not associated with an increased risk of worsening HF or other serious adverse events[44].

A strategy that targets the in-hospital initiation of these medications is likely to yield better results and to improve patient care and outcome. The Organized Program to Initiate Life-Saving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) is a hospital-based process of care improvement program and web based registry in HF. For this project, approximately 500 hospitals will work collaboratively to measure and improve the management of care for HF patients[45]. Up to 50 000 patients with HF as primary or secondary diagnosis will be included in this registry. The objectives are to improve medical care and education of patients hospitalized with HF and to accelerate initiation of HF evidence-based, guideline-recommended therapies by starting the life-saving therapies before hospital discharge in appropriate patients without contraindications[45]. OPTIMIZE-HF will be the largest HF quality of care improvement project ever undertaken and if successfully implemented, it will improve the standard of care in HF in the hospital and outpatient settings.

Conclusion

Hospitalization for worsening chronic HF has emerged as a major public health problem. Patients hospitalized with worsening chronic HF face a substantial risk of in-hospital mortality and rehospitalization.

Hemodynamic improvement might not correlate with symptomatic improvement which may occur even in patients who continue to have hemodynamic congestion.

None of the acute interventions tested so far improved post-discharge outcomes compared to placebo.

All these issues are now being discussed at the Acute Heart Failure Syndromes 1st International Meeting, Cannes, France, from a scientific committee from Europe, North and South America, industries, regulatory agencies and National Institute of Health. The three objectives to be discussed are to review the existing and new therapies, how to conduct clinical trials, how to conduct registry implementation program and to develop guidelines for HF.

Riassunto

Il numero totale di ricoveri per scompenso cardiaco (SC) negli Stati Uniti è di circa 1 milione l'anno con una percentuale di riospedalizzazione pari al 30% a 3 mesi e 60% a 6 mesi dalla dimissione. Inoltre, malgrado questi pazienti sembrino rispondere bene alla terapia medica, la percentuale di eventi (riospedalizzazione e mortalità) a 60 giorni dalla dimissione va oltre il 35%, anche escludendo i pazienti senza insufficienza renale, ipotensione o aritmie maggiori.

I pazienti ricoverati per SC possono essere classificati in tre gruppi: 1) quelli con SC di nuova insorgenza, secondario ad un danno acuto come un infarto miocardico anteriore o un'insufficienza mitralica acuta; 2) quelli con SC avanzato o "end-stage" o refrattario che per definizione non rispondono o rispondono poco alle terapie somministrate; 3) quelli con un peggioramento dello SC che costituiscono più del 90% di tutti i ricoveri per SC, che sembrano rispondere bene alla terapia a breve termine.

Sebbene la mortalità intraospedaliera dei pazienti con SC sia molto bassa (< 2-3%), a 60 giorni dalla dimissione la riospedalizzazione è del 30% e la mortalità raggiunge il 5-15%.

È importante riconoscere i fattori predittivi di riospedalizzazione. In uno studio su 2701 pazienti ambulatoriali con SC, 215 (8%) avevano un chiaro peggioramento delle condizioni cliniche a soli 2 mesi dalla dimissione. All'analisi multivariata una precedente ospedalizzazione, una durata dei sintomi > 18 mesi, l'eziologia ischemica, la fibrillazione atriale, alti livelli ematici di azotemia, l'anemia e l'iponatriemia, un'elevata classe funzionale NYHA, una frequenza cardiaca > 100 b/min e l'ipotensione erano indipendentemente associati ad un peggioramento delle condizioni cliniche dello SC. Inoltre la presenza di ischemia ed una storia di pregressa ospedalizzazione erano fattori indipendenti di riospedalizzazione e mortalità ad 1 anno.

Le riospedalizzazioni per SC sono principalmente dovute ad un peggioramento delle condizioni emodinamiche che conducono ad un aumento delle pressioni di riempimento ventricolare destro e sinistro ed una ridu-

zione della portata cardiaca. Tali alterazioni emodinamiche possono con il tempo contribuire ad una progressiva disfunzione e dilatazione ventricolare nonché ad un'ischemia/necrosi subendocardica, responsabile di un rilascio di troponine, anche in assenza di sindromi coronariche acute.

I presidi terapeutici attualmente disponibili per il trattamento acuto dello SC sono sicuramente sottoutilizzati nella pratica clinica. L'obiettivo principale è quello di migliorare i sintomi ed i segni di congestione preservando il danno renale e prevenendo il più possibile il danno miocardico. Una volta ottenuta la stabilizzazione delle condizioni emodinamiche, è importante prescrivere quelle terapie farmacologiche che, come dimostrato dai grandi trial clinici, hanno benefici effetti sulla sopravvivenza a lungo termine come gli ACE-inibitori, i betabloccanti e lo spironolattone. Sono anche a disposizione nuove terapie in studio per i pazienti ricoverati per SC come gli antagonisti della vasopressina, gli antagonisti recettoriali dell'endotelina ed i nuovi sensibilizzanti al calcio.

Purtroppo però esiste ancora un ampio gap tra il trattamento consigliato dalle linee guida e la pratica clinica. Di conseguenza un altro importante obiettivo nel trattamento dei pazienti con SC è implementare l'utilizzo delle terapie esistenti. A tale scopo è stato ideato un programma di "care improvement" (OPTIMIZE-HF) che arruolerà più di 50 000 pazienti in circa 500 ospedali allo scopo di migliorare il trattamento dei pazienti ricoverati con diagnosi di SC.

In conclusione, i pazienti ricoverati con diagnosi di SC hanno un rischio elevato di riospedalizzazione e mortalità ed è quindi necessario un maggiore impegno nell'adottare le terapie approvate e sperimentate in numerosi trial clinici controllati.

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