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Case Report

Multidisciplinary Approach for a Patient with Advanced Heart Failure: A Case Report

Diego José Rodriguez Torres*, Silvia Lopez-Fernandez, Mario Verdugo Marchese and Montserrat Puga Vilchez

Department of Cardiology, Complejo Hospitalario Universitario de Granada, Spain

***Corresponding author**

Diego José Rodríguez Torres, Cardiology Department, Complejo Hospitalario Universitario de Granada, Avenida de las Fuerzas Armadas 2, 18014 Granada, Spain; Email: diegojrodrigueztorres@yahoo.es

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Keywords

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Abstract

Background: Patients with a history of advanced heart failure (HF) and repeated hospitalizations place a heavy financial burden on health systems in western countries. Although multidisciplinary HF management programs are recommended for patients at high risk of hospital readmission, not many studies of their benefits in individual cases have been reported.

Case Presentation: In this report, we present the case of a 79-year-old man with highly symptomatic advanced stage D heart failure corresponding to NYHA functional Class IV and with frequent re-hospitalizations despite optimized guideline-directed medical therapy and cardiac resynchronization treatment. He joined our heart failure management program for follow-up. The specialized multidisciplinary strategy reduced both the number and duration of his HF re-hospitalizations and improved his quality of life at this so-called end-stage phase of the disease.

Conclusions: A multidisciplinary approach, including nurse-based interventions, for patients with advanced heart failure included in a heart failure management program is an important tool for improving their quality of life and for reducing costly hospital readmissions.

ABBREVIATIONS

ACE: Angiotensin Converting Enzyme; BNP: Brain Natriuretic Peptide; COPD: Chronic Obstructive Pulmonary Disease; CRT: Cardiac Resynchronization Therapy; ECG: Electrocardiogram; EPO: Recombinant Human Erythropoietin; ESC: European Society of Cardiology; ESS: European Heart Failure Self-Care Behavior Scale; FEV: Forced Expiratory Volume; GDMT: Guideline-Directed Medical Therapy; GI: Gastrointestinal: HF: Heart Failure; ICD: Implantable Cardioverter Defibrillator; IV: Intravenous; LVEF: Left Ventricular Ejection Fraction; MDRD: Modification of Diet in Renal Disease; MQ: Minnesota Living with Heart Failure Questionnaire; NEI: Nurse-Based Educational Intervention; NYHA: New York Heart Association; YS: Yessavage's Geriatric Scale; 6MWT: 6 Minute Walk Test.

INTRODUCTION

Heart failure (HF) is a major high prevalence healthcare problem. The prevalence of HF in Europe is estimated to be approximately 2.3%, increasing to 16% in people over 75 years old [1,2]. 26 million people are estimated to suffer from HF worldwide, with up to 6 million sufferers in the United States and a similar number in Europe. One million people are newly diagnosed with HF in the USA and the European Union every year [3].

Heart failure consumes enormous quantities of health care resources, accounting for 2% of total healthcare costs in western countries [4]. It is the most common cause of hospitalization in persons aged 65 years and over [5], with the percentage of 30-day readmissions after hospital discharge reaching 20% to 25% [6].

Advanced end-stage heart failure is associated with substantial morbidity, mortality and frequent hospital readmissions.

Clinical factors need to be considered carefully before determining whether patients are in Stage D of Heart Failure.

Patient co-morbidities worsen prognosis and quality of life and sometimes limit the use of some guideline-directed medical therapy (GDMT).

Barriers to effective palliative care include difficult prognosis at the end stage due to unpredictable disease behavior.

Multidisciplinary HF disease-management programs have been assigned a class I recommendation for this group of patients

in the latest European [7] and American guidelines [8].

Clinicians and specialized HF nurses involved in heart failure management programs can assist in dealing with the complex end-stage patients and their family context by focusing on both improving patients quality of life and reducing hospital readmissions.

In this study, we describe the case of a 79-year-old man with stage D HF (NYHA class IV functional classification) and multiple re-hospitalizations despite optimized guideline-directed medical therapy and cardiac resynchronization treatment. The patient was assigned to our heart failure management program for follow-up.

CASE DESCRIPTION

79-year-old male patient, former smoker, with a medical history of arterial hypertension, non insulin-dependent diabetes mellitus, repeated deep vein thrombosis episodes, severe chronic obstructive pulmonary disease (COPD), bronchiectasis, frequent respiratory infections and right lung pachypleuritis from a previous tuberculosis infection, peripheral vascular disease with diffuse aorto-iliac involvement, abdominal aortic aneurism measuring 3 cm, bilateral carotid atherosclerosis and a transient ischemic attack in 2012.

His first episode of initial congestive HF occurred in 2003 which required hospitalization, when dilated cardiomyopathy due to hypertensive heart disease with severe left ventricular dysfunction was diagnosed; 30% left ventricular ejection fraction (LVEF) was detected by echocardiography. Coronary angiography showed diffuse atheromatosis without significant coronary stenosis. An electrocardiogram (ECG) showed sinus rhythm with left bundle branch block. He was admitted to hospital (Pneumology department) in 2006 suffering from pneumonia.

Still highly symptomatic (NYHA Class III) despite optimized medical treatment consisting of aspirin, furosemide, eplerenone, β blockers and ACE inhibitors in maximum tolerated doses, a CRT+ICD was implanted in 2007. The patient failed to respond positively to CRT (non-responder) so when a left ventricular electrode dysfunction was detected due to electrode displacement In 2011, it was decided just to program the CRT pacemaker in pacing mode VVI with minimal right ventricular stimulation. At the end of 2011 he began with paroxystic atrial fibrillation and antiagregation was changed to oral anticoagulation.

The most recent echocardiogram (2013) showed a severely dilated left ventricle with hypertrophic walls (eccentric hypertrophy); marked asynchrony with severely depressed LVEF, augmented filling pressures, mild dilatation of left atrium, normal right chambers, mild mitral regurgitation secondary to left ventricular dilatation, mild aortic regurgitation and normal right valves (see Figure 1). Pulmonary artery systolic pressure (PASP) was estimated to be 70 mm Hg, and sildenafil treatment (20 mg t.i.d.) was started [10,11].

The patient was hospitalized and re-hospitalized twelve times between 2003 and 2013 due to decompensated HF with fluid overload symptoms; twice in the Internal Medicine department and eleven times in the Cardiology department, with hospital length of stays of 90 days in 2011, 61 days in 2012 and 27 days in 2013 (see Figure 2). He also visited the Emergency department several times suffering from congestive HF during this period. During these visits, his condition improved following short courses of intravenous (IV) diuretic administration and he could be discharged. His functional status could be classified as "Intermacs 4", frequent flyer [9], as shown in Table 1.

Following his last hospital admission to Cardiology in 2013, the patient was assigned to our heart failure program for follow-up. He was first visited by our specialist HF nurse two weeks after discharge from hospital. At this early follow-up visit, he was examined using the following standardized tests to measure performance: 1. The Barthel index of activities of daily life, 2. The Pfeiffer cognitive impairment test and 3. The Charlson Co-morbidity Index. Self-care, quality of life and presence of depression were also determined with the aid of 4. the European Heart Failure Self-Care Behavior Scale (ESS), 5. the Minnesota Living with Heart Failure Questionnaire (MQ) and 6. Yessavage's Geriatric Scale (YS), respectively.

The patient still was able to lead an independent daily life style, (Barthel test score of 100) without any significant cognitive impairment (Pfeiffer test score of 0,94). He presented poor quality of life (MQ score of 90), signs of intense depression (YS score of 5) and a Charlson co-morbidity index score of 11.

Medication doses were reviewed and increased when possible, with adherence to treatment being checked by our nurse. The patient and his caregiver were offered a place on a nurse-based educational intervention (NEI) program. This consisted of four consecutive sessions per week involving brochures and audio-

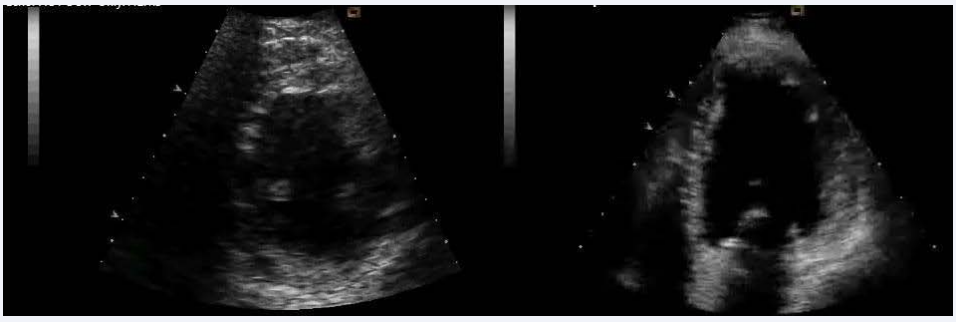

Figure 1 Transthoracic echocardiogram. Parasternal short axis and parasternal long axis showing a dilated left ventricle with a severely reduced ejection fraction.

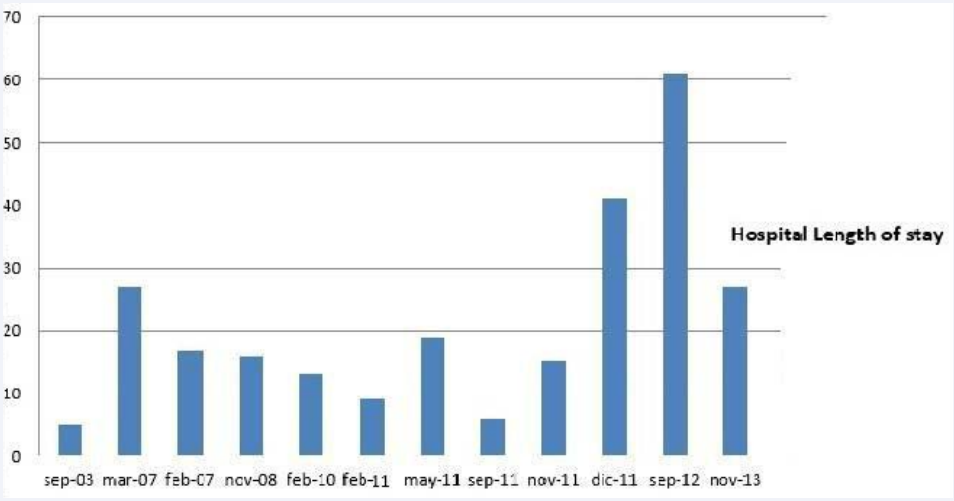

Figure 2 Length of hospital stay due to decompensated HF from 2003 to 2013.

Table 1: INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) Scale for Classifying Patients with Advanced Heart Failure. Modified from [9].

Profile	Definition	Description
INTERMACS 1	*"Crash and burn"*	Hemodynamic instability in spite of increasing doses of catecholamines and/or mechanical circulatory support with critial hypoperfusion of target organs (severe cardiogenic shock)
INTERMACS 2	*"Sliding on inotropes"*	Intravenous inotropic support with acceptable blood pressure but rapid deterioration of kidney function, nutritional state, or signs of congestion
INTERMACS 3	*"Dependent stability"*	Hemodynamic stability with low or intermediate, but necessary due to hypotension, doses of inotropics, worsening of symptoms, or progressive kidney failure
INTERMACS 4	*"Frequent Flyer"*	Temporary cessation of inotropic treatment is possible, but the patient presents frequent symptom recurrences and typically with fluid overload
INTERMACS 5	*"Housebound"*	Complete cessation of physical activity, stable at rest, but frequently with moderate water retention and some level of kidney dysfunction
INTERMACS 6	*"Walking wounded"*	Minor limitation on physical activity and absence of congestion while at rest. Easily fatigued by light activity
INTERMACS 7	*"Placeholder"*	patient in NYHA functional class II or III with no current or recent unstable water balance

visual support on topics such as self-care, recognition of alarm signals and symptoms, a flexible diuretic regimen, diet/regular exercise advice, pharmacological treatment and emphasis on the importance of psychological factors.

In the 4th week following discharge, he received a clinical visit from a specialist HF cardiologist. Oral medication consisted of dabigatran (110 mg bid), digoxin (0.25 mg qd), eplerenone (50mg qd), atorvastatin (20mg qd), ivabradine (7.5 mg bid), furosemide (40 mg bid), sildenafil (20 mg tid), hydrochlorothiazide (50 mg qd), telmisartan (40 mg qd), nebivolol (5 mg qd), amiodarone (200mg qd), tiotropium (5 mcg qd), salmeterol (50 mcg), tamsulosin (400 mcg qd) and omeprazole (20mg qd).

Despite CRT, he presented LVEF<30%, and was clinically in NYHA Class III-IV (6 minute walk test (6MWT) of 150 m) so he was considered for heart transplantation and left ventricular assist devices as destination therapy (Tables 2 and 3). We ruled out these options due to the patient's age, advanced diabetes mellitus with significant peripheral arterial disease and severe respiratory disease (FEV1<40%) [12].

His co-morbidities included mild-moderate renal dysfunction (Glomerular filtration rate 4-MDRD: 45.2 mL/min/1.73 m^2), mild normocytic anemia (hb=12 g/dL) and iron deficiency: Ferritin<100 ng/mL, Transferrin Saturation Index <20%. As the patient was undergoing anticoagulant therapy with dabigatran 110 mg bid for paroxystic AF, we ruled out digest bleeding given a negative gastrointestinal (GI) evaluation before starting iron treatment. Intravenous iron in an outpatient setting was started with the administration of 200 mg IV iron sucrose every 2 weeks until the patient reached hb=13 g/dL and a ferritin level >300 ng/mL.

Following his frequent and lengthy readmissions over the previous 2 years, totaling 178 days of hospitalization, the administration of intermittent and repeated doses of IV levosimendan in an outpatient setting was considered. A 6h infusion of levosimendan at a rate of 0.1 μg/kg/min without a loading dose was administered at 4-week intervals for 3 consecutive months in addition to standard care therapy. When necessary, diuretic IV shots of furosemide (40-60 mg) were carried out by a primary care nurse at the patient's home.

The palliative care unit was contacted to regulate analgesic treatment due to intense sciatic pain caused by the patient's

Table 2: Indications and contraindications for cardiac transplantation. Modified from ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012 [7].

Patients to consider	End-stage heart failure with severe symptoms, a poor prognosis, and no remaining alternative treatment options
	Motivated, well informed, and emotionally stable
	Capable of complying with the intensive treatment required post-operatively
Contraindications	Active infection
	Severe peripheral arterial or cerebrovascular disease
	Current alcohol or drug abuse
	Treated cancer in previous 5 years
	Unhealed peptic ulcer
	Recent thrombo-embolism
	Significant renal failure (e.g. creatinine clearance <50mL/min)
	Significant liver disease
	Systemic disease with multiorgan involvement
	Other serious co-morbidity with poor prognosis
	Emotional instability or untreated mental illness
	High, focused pulmonary vascular resistance(>4-5 Wood Units and mean transpulmonary gradient > 15mm Hg)

Table 3: Indications for left ventricular assist devices as destination therapy. Modified from [42].

Patients are not candidates for cardiac transplantation
Ejection fraction of <25% although optimal treatment
New York Heart Association (NYHA) functional class IV symptoms for ≥3 months before (all patients had been treated with maximally tolerated doses of angiotensin-converting enzyme inhibitors, beta blockers, digoxin, diuretics, and/or other vasodilators)
Peak oxygen consumption<12ml/kg/min exceeding anaerobic threshold or need for inotropic therapy 14 days before

previous prolonged hospitalization. Once the pain was under control, he began a program of physiotherapy.

Following our multidisciplinary HF program interventions, the patient's profile changed from "Intermacs 4" to "Intermacs 5": housebound. Up to now, he has remained in a hemodynamically stable condition at home without any further readmissions for 380 days with an advanced NYHA Class IV functional status. However, his 6MWT distance has increased from 150 to 230 m, his quality of life improved (MQ score from 90 to 75) and his depression level has decreased (YS=3).

DISCUSSION

Patients with severe left ventricular dysfunction (stage D) and an advanced functional class (NYHA III-IV) present a high mortality rate (in-hospital mortality of 8-10% and 50% at the five-year follow-up) [13,14], with frequent and long hospitalizations for HF.

Multidisciplinary HF disease management programmes are recommended for patients with advanced HF stage in order to reduce the risk of subsequent rehospitalization [7,8]. These programmes have proven to be cost-effective [15-17].

The recommended characteristics and components of management programs for patients with HF are described in the 2012 ESC guidelines (see table 4). These programs should target high-risk symptomatic patients and facilitate access to advanced treatment options [7].

Specialist HF doctors play an important role in establishing when a patient with heart failure is in Stage D (Table 5). It is important to ensure that patients are on an optimized GDMT and that advanced therapeutic options, such as cardiac device therapy, heart transplantation, left ventricular assist devices and a MitraClip system for mitral regurgitation percutaneous repair, have been considered.

As mentioned above, it is important to adopt a holistic approach to patient care in order to offer an integrated multidisciplinary management to the patient that can improve clinical results.

Patients with advanced HF suffer significant impairment of all aspects of their quality of life in both physical and mental health [18]. This impairment caused by HF is more pronounced than in other severe illnesses such as hemodialysis [19]. It is therefore important to evaluate psychological factors, to focus on non-pharmacological interventions and to promote self-education. As previously demonstrated by our group [21], specialist HF nurse interventions in these areas improve quality of life, self-care and depression levels.

More than half of all hospitalizations are associated with non-cardiovascular causes [20-22] which highlights the importance of treating co-morbidities.

Anemia, iron deficiency, chronic kidney disease, chronic obstructive pulmonary disease and depression are the most common co-morbidities in HF patients [23].

Anemia is associated with increased risk of mortality in both HF with reduced and preserved ejection fraction [24,25]. Although the causes of anemia in congestive HF are multi-

Table 4: Characteristics and components of management programs for patients with heart failure with reduced ejection fraction and heart failure with preserved ejection fraction. Modified from ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012 [7].

Characteristics	Should employ a multidisciplinary approach (cardiologists, primary care physicians, nurses, pharmacists, etc.)
	Should target high risk symptomatic patients
	Should include competent and professionally educated staff
Components	Optimized medical and device management
	Adequate patient education with special emphasis on adherence and self care
	Patient involvement in symptom monitoring and flexible diuretic use
	Follow up after discharge (regular clinic and/or home-based visit, possibly telephone support or remote monitoring)
	Facilitated access to care during episodes of decompensation
	Assessment of (and appropriate intervention in response to) an unexplained increase in weight, nutritional status, functional status, quality of life, and laboratory findings
	Access to advanced treatment options
	Provision of psychosocial support to patients and family and/or caregivers

Table 5: Clinical events and findings useful for identifying patients with advanced HF. Modified from ACCF/AHA Guidelines for the Management of Heart Failure: [8].

Repeated (>2) hospitalizations or ED visits for HF in the past year
Progressive deterioration in renal function (eg., rise in BUN and creatinine)
Weight loss without other cause (e.g., cardiac cachexia)
Intolerance to ACE inhibitors due to worsening HF or hypotension
Frequent systolic blood pressure <90 mmHg
Persistant dyspnea with dressing or bathing requiring rest
Inability to walk 1 block of the level ground due to dyspnea or fatigue
Recent need to escalate diuretics to maintain volume status, often reaching daily furosemida equivalent dose > 160 mg/d and/ or use of supplemental metolazone therapy
Progressive decline in serum sodium, usually to < 133 mEq/L
Frequent ICD shocks

factorial, iron deficiency was found to be the most common cause by the Nana study [26].

Iron deficiency is regarded as playing an important role in HF. Cells with high-energy demands such as cardiac myocytes are particularly sensitive to depleted iron supply and/or abnormal iron utilization. This is an important factor in HF, as abnormal energy generation and utilization in the myocardium and peripheral tissues such as skeletal muscles contribute to HF pathophysiology [27].

Several recent studies have targeted iron deficiency with iv iron as therapeutic approach [28,29]. Treatment of patients with chronic HF and iron deficiency (anaemic and non anaemic patients) with 24-week therapy of iv iron increased the distance walked on the 6MWT, improved NYHA class and overall quality of life at 6 months follow-up in the FAIR-HF trial [29].

As in the case of the patient described in this report, we always recommend a thorough evaluation and correction of the iron status of end-stage chronic HF patients. Although the patient presented type 2 cardiorenal syndrome, darbepoetin alfa, which did not show positive results in the latest trial [30], was not prescribed.

Levosimendan is a calcium-sensitizing agent which has a combined positive inotropic and vasodilator effect [31]. Extensive scientific evidence exists on its effectiveness and utility in the treatment of patients with acutely decompensated HF [32,33]. In the REVIVE II study [34], the mean duration of the initial hospitalisation was almost 2 days shorter in the levosimendan group (7 days) than in the placebo group (8.9 days) and significantly more patients treated with levosimendan were discharged within 5 days (p=0.008).

The effects of long-term, intermittent treatment with levosimendan (based on the existence of an active metabolite that reaches peak plasma concentration 80–90 h after administration of the parent drug) in patients with end-stage HF have been reported in a number of small-scale studies [35,36] Results suggest that levosimendan improves hemodynamics, neurohormones and clinical outcomes. However, an optimal dosing scheme has not yet been established [37]. The LevoRep study is the largest randomised trial with pulsed infusions of levosimendan in outpatients with advanced HF [38]. The treatment group has not shown any significant improvement in functional capacity or quality of life as compared with the placebo group. However, Levosimendan administration has been safe and there have been less cardiac events on the treatment group than in the placebo group.

Long-term inotropic support strategies are not included in current treatment guidelines for acute HF (Class III recommendation) [8]. As was also the case with the patient described in this report, many groups working with HF and heart

transplantation patients continue to administer levosimendan in intermittent doses in their clinical practice based on their own positive experiences while awaiting positive results from the following ongoing clinical studies: 1. Intermittent Intravenous Levosimendan in Ambulatory Advanced Chronic Heart Failure Patients study (LION-HEART, NCT01536132), 2. The Randomized, Double-Blind, Placebo Controlled, Multicenter Trial to Study Efficacy, Security and Long Term Effects of Intermittent Repeated Levosimendan Administration in Patients with Advanced Heart Failure (LAICA) [39] and 3. Early Levosimendan Vs Usual Care in Advanced Chronic Heart Failure (ELEVATE, NCT01290146). Sometimes, as in palliative care, individualized non-evidence-based therapies can be effective in providing this high-risk population with symptom relief and hemodynamic stabilization [40]. Repetitive use of levosimendan for treatment of chronic advanced HF has been recently established by an expert panel consensus [41].

In conclusion, HF management programmes for patients with advanced HF allow closer follow-up procedures and multidisciplinary approaches resulting in positive clinical outcomes. Accurate diagnosis, optimized GDMT including advanced therapeutic options and co-morbidity treatment are essential components for achieving hemodynamic stabilization, improving clinical situations and avoiding hospital readmissions of these patients. This HF Management approach is cost-effective. As shown in this case report, holistic evaluations and a nurse-based intervention considering psychological aspects, non-pharmacological treatment and promoting self-care are key-points to improve quality of life at this end stage disease. Sometimes, as in the case of palliative care, clinical practice and tailored therapies have to run a "little" ahead of scientific evidence based treatments in this group of patients.

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