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SHORT TERM MORBIDITY AND MORTALITY FOLLOW UP OF NEWLY DIAGNOSED SYSTOLIC HEART FAILURE PATIENTS AFTER THEIR FIRST ADMISSION

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Contribution
All the authors contributed significantly to the research that resulted in the submitted manuscript.

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ABSTRACT

Objective: We aimed to follow up the clinical course of systolic heart failure patients for three months after their first admission because of heart failure, including morbidity and mortality.

Methodology: 49 patients were admitted to our police hospital in the period from 7th October 2008 to 7th March 2009 with verified heart failure depending on Framingham criteria and whose left ventricular ejection fraction < 45% evaluated echocardiographically within 24 hours of admission. They were prospectively followed up for 3 months.

Results: Coronary artery disease was the main cause of heart failure (75.6%). Hypertension was present in (67.3%). Mean length of stay during the first admission was 11.8 ± 5.5 days. Mitral regurge was highly prevalent and frequent premature ventricular contactions were the most common complication occurred. Atrial fibrillation was present in 24.5% of patients. The 1 and 3 months mortality rates were 4.1 and 6.1%, respectively. Mortality rate was higher in elderly patients > 70 years, low systolic blood pressure, low diastolic blood pressure, and high blood urea patients. 30.4% of the 46 survivors experienced at least one hospital readmission during follow-up. Readmission was associated more with the following variables; low left ventricular ejection fraction, poor compliance with diet and medication, and high RBS.

Conclusion: Despite the advances in treatment and diagnostic procedures, newly diagnosed heart failure still carries a grave prognosis. Morbidiy and mortality rates are still high.

Keywords: Heart failure, morbidity, mortality, first admission, follow up

INTRODUCTION

Heart failure is usually a progressive condition that begins with risk factors for cardiac dysfunction, proceeds to asymptomatic changes in cardiac structure and function. It then evolves into clinically overt heart failure, disability, and death.

It is commonly the result of acute or chronic cardiac injury that can be prevented with aggressive risk factor management. The aging of the population and the emerging pandemic of CVD in the developing nations of the world presage a rise in the incidence and prevalence of HF globally.

It is the leading cause of hospitalization in Medicare-eligible adults. Despite the mortality risk decreased by about 5%, patients with heart failure still have a three fold higher mortality compared with age-matched patients without heart failure.

Although survival in clinical trials is improving, heart failure remains a lethal condition in the community, with an estimated annual mortality of approximately 21% in men and 17% in women.

Data from Scotland collected in 1991 indicate that, with the exception of lung cancer, mortality in heart failure is as high as in many common types of cancer, with an approximately 25% five-year survival in men and women[17]. In previous studies 60 to 90 days mortality varies widely depending on the study, but is approximately 8 to 10 percent, increasing to about 30 percent at 1 year[6]. The prognosis of new cases of heart failure after their first admission remains relatively poor, despite recent advances in pharmacological therapy and medical care[1].

The risk of mortality in patients with a new diagnosis of heart failure seems to be higher in the first few weeks after the initial diagnosis. In a population-based cohort study of incident heart failure cases (either hospitalized or ambulatory) the authors found that survival was 81% at 1 month after the diagnosis, 75% at 3 months[18]. Also in a spanish study by F. Formiga, et al, the one and three months cumulative probability of survival was 90% and 95% respectively. In the Framingham study, the 3 months survival rate was 73%[19].

We aimed to assess the clinical context of newly diagnosed systolic heart failure Egyptian patients for three months after their 1st admission because of heart failure, including morbidity and mortality.

METHODOLOGY

This was a prospective observational study that included 69 patients newly diagnosed as systolic heart failure admitted to Police hospital with New York Heart Association (NYHA) functional class II or more. Heart failure was verified based on Framingham criteria in which diagnosis of heart failure is made if 2 major criteria (Paroxysmal nocturnal dyspnea, Neck vein distention, Rales, Radiographic cardiomegaly, Acute pulmonary edema, S3 gallop, Increased central venous pressure, Hepatojugular reflux, Weight loss >4.5 kg in 5 days in response to treatment) or 1 major and 2 minor criteria (Bilateral ankle edema, Nocturnal cough, Dyspnea on ordinary exertion, Hepatomegaly, Pleural effusion, Tachycardia more than 120 bpm) are present.

After discharge from the hospital, patients were followed up in the clinic 1 and 3 months. In addition they were instructed to contact the investigators for weight gain or symptomatic deterioration at any stage during follow up.

LV systolic function was assessed by echocardiography.

Newly diagnosed patients verified based on Framingham criteria as listed above (No previous history of heart failure diagnosis or admission.).

First admission to hospital and having EF of 45 % or less.

Patients with prior diagnosis of heart failure and patients who were suffering from another serious disease with a poor prognosis like cancer lung for example were excluded

All patients were subjected to detailed history taking, thorough clinical examination, 12 lead surface ECG, plain posteroanterior chest x-ray, laboratory investigations including random blood sugar, complete blood count, lipid profile, serum electrolytes (Na, K, Ca, Mg), liver functions, kidney functions.

A detailed transthoracic echocardiography was performed to all patients at hospital admission, one, and three months after discharge using a General Electric Vivid 7 ultrasound system equipped with 2.5 MHz probe. LV volumes and LVEF was measured using the biplane method of discs (modified Simpson's rule).

Ischemic heart disease was considered present if the patient had one of the following: (1) a documented previous admission for an ACS (Acute myocardial infraction or unstable angina), (2) prior coronary revascularization either surgically or percutaneously, (3) pathologic Q waves on the electrocardiogram, (4) reversible defects on a thallium stress test, or (5) greater than 70 % stenosis in one or more coronary arteries on coronary angiograms.

Valvular heart disease was denoted on the basis of the presence of long standing mitral or aortic valve involvement documented by physical examination and echocardiography.

Hypertension was defined by the criteria of the 7th report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. Persons were considered hypertensive if 2 or more blood pressure readings were greater than or equal to 140 mm Hg systolic and/or 90 mm Hg diastolic. Hypertensive heart disease was considered as an etiology of HF if there was a history of hypertension or if

the patient had been taking or needed, anti hypertensive medications to control the blood pressure.

DCM was diagnosed by the presence of global LV dilatation with impaired systolic function occurring in the absence of known cardiac or systemic causes.

Diabetes mellitus was considered if FPG ≥126 mg/dl (7.0 mmol/l) or 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) or if the patient has a history of diabetes and still on medical treatment.

Renal impairment was defined as serum creatinine level >1.5 mg/dl.

Peripheral vascular disease was established by intermittent claudication with an abnormal ankle brachial index, and confirmed by arterial duplex or a history of peripheral revascularization.

AF was considered to exist when there was electrocardiographic evidence of this condition, and includes the paroxysmal, persistent, and permanent types.

The diagnosis of anemia was based on the standard criteria of the World Health Organization: hemoglobin <13 g/L in men and <12 g/L in women.

Morbidity (readmission either due to heart failure or due to occurrence of complications such as ventricular tachycardia, cerebrovascular strokes, need for interventions as PCI, CABG, valvular interventions, ICD or multisite pacing) was reported.

Relation between poor outcome (mortality and morbidity) and the following multivariable predictors were evaluated.(1) Older age >70 years, (2) Gender, (3) Etiology of heart failure, (4) NYHA functional class at time of admission, (5) Decreased LVEF% at time of admission, (6) Poor compliance with medications, (7) Hyponatremia < 135 mEq/L , (8) Coronary artery disease, (9) Hypotension < 90/60 mmHg, (10) Peripheral vascular disease.

The use of ACE inhibitors, ARBs, beta blockers, aldosterone antagonists or combination of them was recorded.

Survival was estimated using the Kaplan-Meier method for all cause mortality. Normally distributed continuous variables were reported as mean ± SD. Categorical variables were reported as proportions.

The following variables were included in the univariate analyses: age, gender, etiology of heart failure, NYHA status upon admission, left ventricular systolic function, systolic and diastolic blood pressure, heart rate, sinus rhythm, hemoglobin, and serum creatinine. Categorical variables were compared using the Chi Square test and continuous variables were compared using the t-test. A P-value < 0.05 was considered significant. MedCalc v 9.2.1.0 for Windows software was used for the analyses.

RESULT

Of the 69 patients admitted for systolic heart failure, seven patients were excluded because they were missed during the follow up period. Five patients in whom previous assessments or treatments elsewhere could have been related to a prior diagnosis of heart failure were excluded. Three patients were excluded because they were suffering from other serious diseases with poor prognosis and five patients refuse to participate in the study. So, only 49 patients were included.

Sample characteristics:

Among the 49 patients hospitalized for the first time for systolic heart failure who were finally included, there were 15 (30.6%) women with a mean age of 61.6 years and 34 (69.4%) men with a mean age of 59.8 years. The overall mean age (±SD) was 60 (±12) years (range 27–84). Male prevalence was more in all age groups except those over 80 years. Mean length of stay during the first admission was 11.8 ± 5.5 days (range 5–25).

The mean (±SD) systolic blood pressure on admission was 141 (±36.9). The mean (±SD) diastolic blood pressure was 86.7 (±21.9). S3 was reported in 11(22.4%) patients. Pulmonary edema was present in 7 (14.3%) patients.

New York Heart Association (NYHA) functional class:

On admission, all patients were symptomatic: 13 (26.5%) patients were in NYHA functional class IV, 30 (61.2%) patients were in NYHA class III, and 6 (12.2%) patients were in NYHA class II. However, before discharge the majority of the patients had recovered well and had minimal or mild symptoms of CHF (26.1% in class I and 56.5% in class II, 17.4% in class III).

Risk factors:

The most common risk factor for congestive heart failure was systemic arterial hypertension, which was present in 33 (67.3%) patients, followed by diabetes mellitus, which was present in 21 (42.9%) patients. Dyslipedemia was present in 15 (30.6 %) patients. Peripheral vascular disease was present in 5 (10.2%) patients. 7(14.3%) patients were current smokers. Family history was positive in 3 (6.1%) patients.

Etiology: The most common underlying heart condition was ischemic cardiomyopathy, which was diagnosed in 37 (75.6 %) patients. Most patients underwent a coronary angiography to delineate their coronary anatomy and the results showed that LAD (40.7%) was the most common coronary artery affected in this group of patients, followed by LCX (29.6%) and RCA (3.7%).

Multi vessel disease was recorded in 14.8 % of the ischemic patients and all of them underwent CABG.

Valvular heart disease was recorded in 6 (12.2%) patients. Dilated cardiomyopathy was recorded in 7 (14.2%) patients and one patient (2%) had a peripartum cardiomyopathy.

On admission the mean (± SD) LVEF was 34.35 %(± 0.06%). The LV systolic dysfunction was mild (LVEF = 40-45%) in 13 (26.5%) patients, moderate (LVEF = 30-40%) in 24 (49%) patients, and severe (LVEF <30%) in 12(24.5%) patients.

After 3 months, the mean (± SD) LVEF was 36.41 %(± 7.47%).

PVCs was by far the most common complication and represents 43.6% of complications that occur in 34.7 % of patients.

VT and VF represent the most serious complications (10.3%) and have been occurred in 8.1 % of patients.

Survival:

During the follow-up period of 3 months, 3 patients (6.1%) died with sudden cardiac death. The cumulative survival was 93.9%.

Mortality rate was higher in elderly patients > 70 years (p = 0.0214), low systolic blood pressure below 90 mmhg (p = 0.0189), low diastolic blood pressure below 60 mmhg (p = 0.0186), and high blood urea patients more than 50 mg/dl (p=0.032).

All the 3 patients who died were ischemic and two of them have associated severe MR indicating that the presence of severe MR is associated with poor prognosis, but this was statistically insignificant.

The following variables was associated with increased mortality but did not reach the statistical significance; Admission NYHA IV (p = 0.343), Decreased ejection fraction below 30% (p = 0.148), Poor compliance with diet and medication (p= 0.2014), Presence of S3 (P=0.236), Increased heart rate more than 120 b/m (p = 0.4259), Decreased haemoglobin concentration below 12 % (p = 0.2182).

Statistically, neither ischemic etiology (p=0.936), hyponatremia <135 mEq/L (p=0.9027), serum creatinine > 1.5 mg/dl (p = 0.917), pulmonary edema on admission (p=0.902), hypertension > 140/90 (p=0.542), presence of diabetes mellitus (p=0.903), dyslipedemia (p= 0.589), smoking (0.093), nor PVD (P= 0.699) were associated with increased mortality.

Hospital readmissions related to decompensated heart failure:

At the end of the study, 14 (30.4%) of the 46 patients who survived experienced at least one unplanned admission because of worsening of their heart failure (23 admissions in 14 patients). The number of hospital readmissions was 1-3 with a mean ± (SD) of 1.5± (0.74)

Readmission was associated more with the following variables; low LVEF <30% (p<0.001), poor compliance with diet and medication (p= 0.045), and high RBS >200 mg/dl (p=0.035).

No association was found between readmissions and age (p = 0.420), gender (p = 0.597), etiology (p= 0.070), systolic blood pressure (p = 0.691), diastolic blood pressure (p = 0.411), heart rate (p = 0.757), creatinine (p = 0.143), hemoglobin (p = 0.410), hyponatremia (P=0.742), renal impairment (P=0.071).

The precipitating causes leading to the hospital readmission because of the decompensation of HF were identified in each patient; (1) lack of compliance with medical and dietary treatment was by far the most commonly identified factor for readmission (38%), (2) uncontrolled hypertension (23.8%), (3) systemic infection (14.3%), (4) arrhythmias (14.3%), (5) myocardial ischemia (9.5%).

Use of ACE inhibitors, ARBs, beta-blockers and aldosteron antagonists among patients who completed the follow-up:

At the time of admission, 24 patients were on ACE inhibitors. 6 patients were on ARBs, 22 patients on beta-blockers, and 2 patients on aldosterone antagonist. At discharge, there was a significant increase in the ACE inhibitor, beta-blocker, and aldosterone antagonist prescription rates (35 vs 24 patients, p = 0.0160), (31 vs 22 p = 0.0336), (21 vs 2 p<0.0001) respectively, but not for ARBs (10 vs 6 p=0.4116).

DISCUSSION

Our study population had a mean (± SD) age of 60 (± 12) and only 14 patients are older than 65 years. In the Euro Heart Failure Survey II (EHFS II), the mean age of de novo cases was 70.5 years[2]. In the US ADHERE study, the mean age was 71.[1] years[3]. In OPTIMIZE-HF study, the mean age was 72 years[4].

Like most of previous studies, the present study found that most patients were men (69.4%) and females were older than males[2,5].

The median length of stay for patients admitted for AHF in Europe ranges from 9 to 11 days and is 15 days for patients initially admitted to an ICU or CCU, where ICU/CCU length of stay ranged from 3 to 7 days. In the United States, median length of stay is 4.3 to 6.4 days, with a median ICU/CCU length of stay of 2.4 days[6].

In the current study, the mean (± SD) length of stay for stabilization during the first admission was 11.8 ± 5.5 days. This was shorter than that reported by Pereira Barretto, et al. 20087 which was 25.1±16.7 and longer than that reported in the EHFS II which was 9 days2, and than that reported in the ADHERE study, which was just 5.8 days[3].

The variation in the length of stay can be explained according to the seriousness of the disease, associated morbidity and the age of patients. In the present study, patients were younger and having less serious disease than those reported in the study reported by Pereira Barretto, et al 2008[7]. Also we excluded those patients with accompanying serious non cardiovascular disease that may influence morbidity or mortality.

Etiology and risk factors:

In the current study, coronary artery disease was the most common underlying causes of heart failure as ischemic cardiomyopathy was diagnosed in 37 (75.6 %) patients and 42.85% of cases had a previous myocardial infarction (MI). 67.3% of the patients were hypertensive.

In the Framingham Heart Study, hypertension was the most common precursor of the development of heart failure. 75% of patients were hypertensive.

Early identification of myocardial dysfunction associated with coronary artery disease is important, in view of the potential for reversal of dysfunction with effective management8. So most patients underwent a coronary angiography to delineate their coronary anatomy and multi vessel disease was recorded in 14.8 % of the ischemic patients and all of them underwent CABG.

Along with previous studies, diabetes mellitus was a common risk factor for heart failure as 42. 9 % of patients were diabetics.[9,10]

Echocardiography:

By the end of the study, systolic function was deteriorated in most patients (41.3%) like previous studies indicating that systolic heart failure is a progressive condition despite the recent advances in treatment and diagnostic procedures[13].

Function was preserved in 12 patients (26.1%), and was improved in 15 patients (32.6%). The later group was improved mostly due to revascularization of the ischemic patients.

Survival:

In the present study, the 3 months survival rate was 93.9% which is comparable to 92.6% in some studies13. And this difference is mostly due to the younger age in our group along with the great advances in diagnosis and treatment of heart failure that have been emerged after the Framingham study.

Previous studies have shown that renal dysfunction (usually elevated BUN), lower systolic blood pressure, greater age, and evidence of myocyte necrosis are predictors of increased mortality[6].

The largest analysis[20] found that BUN, systolic blood pressure, heart rate, and age were the main multivariate predictors, and using a different statistical approach with dichotomous variables, suggests that the best single predictor was an elevated admission blood urea nitrogen (BUN ≥ 43 mg/dl), followed by low blood pressure (systolic blood pressure < 115 mmHg), and then by increased concentrations of serum creatinine (≥ 2.75 mg/dl).

In the current study, it was found that older age ≥ 70, low systolic < 90 mmhg, low diastolic blood pressure < 60 mmhg, and high blood urea >50 mg/dl (not creatinine) to be associated with poor survival.

Age ≥ 70 years was the only demographic variable that was significant predictor of poor survival (P=0.021). And this goes in line with most of the previous studies[21].

Gender was not a significant predictor of survival.

An analysis of more than 48,000 hospitalized heart failure patients shows that systolic blood pressure (SBP) at admission is an important predictor of morbidity and mortality in patients with heart failure. Researchers found that patients with higher SBP levels at hospital admission had substantially lower in-hospital and post-discharge mortality rates compared with patients with lower SBP values[22].

The present study found that low systolic blood pressure was a significant predictor of death (p =0.019).

In contrast to many previous studies, the present study found also that low diastolic blood pressure < 60 mmhg was a significant predictor of poor prognosis(p=0.019).

Most of the previous studies found a strong correlation between serum creatinine and poor prognosis18 which we did not found (P=0.917). Instead we found a correlation between the blood urea level >50 mg/dl and such a poor prognosis (p=0.0321).

Against many previous studies, we found no relation between anemia, hyponatremia, diabetes and survival[12].

In contrast to a previous study done by Alon Barsheshet, that found that elevated admission blood glucose levels are associated with increased in-hospital and 60-day mortality in nondiabetic patients hospitalized because of HF, the current study did not show such a correlation[23].

The present study data are in line with F. Formiga, et al.[21] who reported that neither gender, ejection fraction , heart rate creatinine, haematocrit values,, admission NYHA status, nor etiology of heart failure were associated with increased mortality. Furthermore, no significant association was found between death and the prescription of ACE inhibitors or beta-blockers at the time of discharge.

Complications:

VT and VF represent the most serious complications (10.3%) that occurred in 8.1 % of patients. ICD was

implanted in half of these patients.

New hospital readmissions related to decompensated heart failure:

Rehospitalization within 60 to 90 days occurs in approximately 30 percent of patients[6].

Admission due to heart failure is frequently followed by readmission within a short period of time[18].

At the end of the 3 months of follow-up, 30.4 % of the 46 patients who survived experienced at least one unplanned admission because of worsening of their heart failure (23 readmissions in 14 patients). The number of hospital readmissions was 1-3 with a mean (± SD) of 1.64 ±1.69. This rate of readmission was much higher than that reported by Pereira Barretto, et al 2008 which was 30% at one year.

In contrast to F. Formiga, et al21 who did not identify any predictors associated with readmission, the present study found that readmission was associated more with the following variables; decreased LVEF < 30% (p<0.001), poor compliance with diet and medication (p= 0.045), and increased RBS > 200 mg/dl (p=0.035).

Like many previous studies[21], the present study did not found association between readmissions and age (p = 0.7), gender (p = 0.8), etiology (p= 0.070), comorbidity (p = 0.5), systolic blood pressure (p = 0.05), diastolic blood pressure (p = 0.1), heart rate (p = 0.9), creatinine (p = 0.9), haematocrit (p = 0.8), NYHA status (p = 0.1), sinus rhythm (p = 0.6).

Lack of compliance with medical and dietary treatment was by far the most commonly identified factor for readmission, and it represent more than one third of the causes of readmission (38%). And this also was reported in many previous studies[[29]].figure 1

In our study we found that uncontrolled hypertension is the second common cause for readmission (23.8%) and this may be also due to lack of compliance with anti hypertension medications and/or diet. Systemic infections are the next cause (14.3%) and mostly due to chest and upper respiratory infections during the study period which was mainly in winter. Arrhythmias were reported as a cause of readmission in about 14.3 % of cases. Ischemia was reported less than previous studies as a cause of readmission (only 9.5%).

Use of ACE inhibitors, ARBs, BB, and aldosterone antagonists:

Although in clinical trials, morbidity and case fatality related to heart failure has been significantly reduced by the implementation of therapies such as ACE inhibitors, ARBs, beta-blockers, and aldosterone antagonists; we didn't find such a reduction in hospital readmission mostly because of the short duration of follow up which does not give the chance for such therapy to give its full effect.

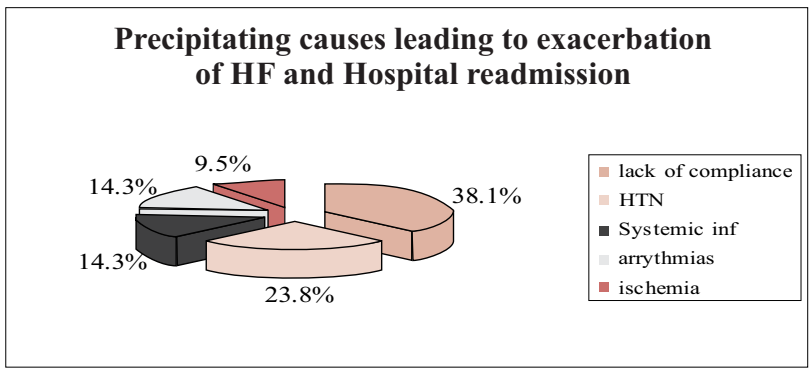
In the current study, The evidence based medications was used according to the major heart failure guidelines of the European Society of Cardiology (ESC)[26] which recommend the use of ACEIs and ß blockers. On admission 49 %, 12%, 45%, and 4% of our patients were taking ACE inhibitor, ARBs, BB, and aldosterone antagonists respectively mostly as antihypertensive and anti ischemic medications. At discharge and according to the recent guidelines, there was a significant increase in the ACE inhibitor (76%), beta blocker (67.4%), and aldosterone antagonist (45.7%) prescription.

The use of these two agents was much higher in this study (76% and 67.4% respectively) than in most reported studies. When such high percentage use is achieved, short-term survival may be very high as we re-ported (93.9% at 3 months).

The use of these medications are more than that reported by Komajda et al in the EuroHeart Survey who found ACEIs (61%), and ß blockers (36%) were the most commonly prescribed medications in heart failure[27].

Similarly, Cleland et al found that 60% of patients received ACEIs, 34% ß blockers[28] and in United States of America,

Figure 1 Precipitating causes for exacerbation of heart failure and hospital readmissions.



O'Conner et al reported percentage use of ACEIs and ß blockers in patients discharged after hospitalization for decompensated heart failure of 71% and 62% respectively. These rates are much closer to those achieved in this study[29].

Also Results similar to these were reported by Anguita for ACEI use but lower ß blocker use. This report from 62 heart failure clinics in Spain, found 87% ACEI/ARB and 59% ß blocker use [30].

In summary, medical treatment closely approached the recommended standards of major heart failure guidelines with high ACEI and ß blocker use comparable to recent heart failure trials so the short-term survival was high.

Limitations of the study:

This study was done at the police hospital where every patient is covered by health insurance including any medications or diagnostic or therapeutic procedures which is not the case in most of Egyptian hospitals.

CONCLUSION

Despite the advances in treatment and diagnostic procedures, the progression of systolic heart failure remains inevitable. Length of hospital stay for stabilization is still long. Morbidity and rehospitalization rates are still high.

Medical treatment closely approached the recommended standards of major heart failure guidelines with high ACE-I and B-blocker use comparable to recent heart failure trials and this resulted in high short-term survival.

Patient education is very important because most patients do not adhere to diet and drugs and this is the most common cause of readmission at least in our country.

Abbreviations:

ACE= angiotensin converting enzyme, ARBs= angiotensin II receptor blockers, AF= Atrial fibrillation, BB= beta blockers, CVD= cardiovascular disease, LVEF= left ventricular ejection fraction, VF= ventricular fibrillation, VT= ventricular tachycardia

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