In-hospital management of heart failure, an Egyptian perspective

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Abstract

Aim

To define characteristics, management, and outcomes of hospitalized heart failure [HF] patients in a tertiary care hospital in Egypt.

Methods and results

107 Patients admitted with diagnosis of systolic HF [denovo or acute decompensation of chronic], between January 2006 and January 2008 were enrolled in this retrospective registry.

Mean age was 59.7 ± 11.7 years, 87% were males, and 23% had new onset HF. Coronary artery disease was the most common etiology [64%], with significant proportion of patients had myocardial infarction [30%] or undergone revascularization [47%]. Hypertension [57%], Diabetes mellitus [52%], significant valvular heart disease [43%], anemia [41%], and renal insufficiency [32%] were common.

80% were on ACEI/ARBs, 75% were on loop diuretics, 54% were on spironolactone, 40% were on Beta-blockers, and 30% were on hydralazine-nitrates, 4% were on intravenous vasodilators, 15% were on inotropic drugs, and 4.7% had CRT and ICD.

The mean length of stay was 6.3 ± 5.7 days. The re-hospitalization rate was 20%, while the in-hospital mortality was 12%.

Conclusion

Poor patients' profile, low rates of use of beta-blockers, and intravenous vasodilators, while maintaining high rates of use of inotropes appear to be associated with significant in hospital mortality for HF patients.

Keywords: heart failure, characteristics, treatment, outcome, mortality
Introduction

Heart failure [HF] is an increasing, global epidemic that results in significant health care expenditure, disability, and mortality.\(^1\) Since 1968, heart failure as the primary cause of death has increased fourfold.\(^2\)

In a systemic review of data from 12,763 heart failure and left ventricular dysfunction patients of five randomized trials, authors concluded that ACEI is associated with lower rates of morbidity, and mortality.\(^3\) Also, the beneficial effects of Beta-blockers on HF patients are well defined as in the U.S. Carvedilol Heart Failure Trials.\(^4\)

Similarly, in the Randomized Aldactone Evaluation Study (RALES), investigators enrolled 1663 patients with severe heart failure and LV systolic dysfunction to receive either spironolactone or placebo documenting a 30 percent reduction in all-cause mortality in patients receiving spironolactone.\(^5\)

Nevertheless, several device therapies were demonstrated to have a great beneficial impact on heart failure patients and were endorsed by European society of cardiology and American college of cardiology/ American heart association HF management guidelines.\(^6,7\)

Cardiac resynchronization therapy [CRT] has emerged as another evidence-based device treatment for heart failure. Biventricular pacing is accomplished through simultaneous pacing of both the left and right ventricles. The rationale for CRT is based on the presence of ventricular dyssynchrony, impairing the ability of the heart to function as a pump. Although a left bundle-branch block or prolongation of the QRS duration more than 120 millisecond [msec] has been used as a measure of dyssynchrony in clinical trials, LV mechanical dyssynchrony as evidenced by echocardiographic parameters has been historically shown to predict cardiac events.\(^8\)

The Multicenter InSync Randomized Clinical Evaluation (MIRACLE) trial was the first trial evaluating CRT with 453 NYHA class III and IV HF patients randomized. This study documented significant reduction in HF morbidity.\(^9\)

This positive impact of CRT on outcome of less symptomatic HF patients was documented in the preliminary data from the MADIT CRT trial. The current trial sought to determine the utility of CRT-D in reducing all-cause mortality and HF events in patients meeting criteria for an ICD, with NYHA class I/II symptoms, with a significant 29% reduction in death or HF interventions when compared to traditional ICD.\(^10\)
Similarly, the use of implantable cardioverter defibrillator [ICD] was documented to improve survival whether used for primary prevention of sudden cardiac death or for secondary prevention in patients who survived ventricular defibrillation or hemodynamically compromising ventricular tachycardia.

MADIT II was a large trial enrolling 1232 patients in which the risk of ventricular arrhythmias was based on the patients' history of MI and cardiac dysfunction, with an EF less than 30%. Patients were required to be at least 40 days post-MI. This study showed ICD a 31 percent reduction in all-cause mortality in the ICD group.11

Several registries around the globe have published data about management and outcome of HF patients in comparison to the published guidelines. The euro-heart failure survey I and II, aimed to assess the characteristics, etiology, management, and outcome of HF patients in European centers, in relations to the acute heart failure [AHF] guidelines published by the European society of cardiology.12, 13

Similarly, the acute decompensated heart failure national registry [ADHERE] defined the characteristics, management and outcomes for heart failure hospitalizations in the United States of America. This study enrolled 159, 168 patients from 285 centers between 2002 and 2004.14

Another important registry in this aspect was the more recent Get with the Guidelines Heart Failure trial [GWTG-HF] trial. The study cohort was comprised of 57,937 HF admissions. This study published several reports including a report about the management differences according to age.15

However, there is scanty data published about therapy and its impact on outcome on HF patients in Egypt.

One of the few published Egyptian studies was a retrospective study of patients with a diagnosis of CHF over a 3.5-year period in a general cardiology clinic. Demographics, ECG and echocardiography data for left ventricular systolic and diastolic functions were collected. The differential effect of systolic versus diastolic CHF was analyzed regarding hospitalization and mortality. It was found that 155 patients diagnosed with heart failure, 102 patients (66%) had systolic heart failure, and 53 (34%) had diastolic heart failure. Mean age was 60+/−10 and 63+/−11 years, respectively. Systolic CHF patients had significantly more CAD, while those with diastolic failure were mostly hypertensive. Patients with systolic failure required more hospitalization, and had a mortality rate of 17.6% vs. 11.3% for patients with diastolic heart failure.16

In our study, we aimed to cross this knowledge gap concerning the management and outcome in AHF patients in Egypt.
Methods

A] Patients selection

All patients admitted to a tertiary center in Egypt with a diagnosis of systolic heart failure between January 2006 and January 2008 were studied. This was a total of 107 patients. The study was conducted retrospectively from the patients’ medical records. HF was diagnosed clinically by dyspnea on ordinary activity, paroxysmal nocturnal dyspnea, acute pulmonary edema, rales, jagular venous distension, third heart sound gallop, etc.

Contraindications for the use or the up-titration of ACEI/ARBs were defined as renal impairment with creatinine above 2.5 mg/dl, hyperkalemia with serum potassium levels above 5.0 meq/L, or hypotension with systolic blood pressure less than or equal to 90 mmHg. Therefore, under dose of ACEI/ARBs is defined as a dose below the evidence based, target dose of ACEI/ARBs, when there is no documented contraindications for up-titration.

Eligibility for the aldosterone antagonist [Spironolactone] was defined as moderate to severe symptoms of HF and reduced ejection fraction. Creatinine should be less than or equal to 2.5 mg/dL in men or less than or equal to 2.0 mg/dL in women and potassium should be less than 5.0 mEq/L.7

Contraindications for the use or up-titration of BB were defined as evidence of decompensation in the form of bilateral basal rales or increased bronchovascular markings in chest x rays, Hypotension with a systolic blood pressure of 90 mmHg or less, documented history of reactive airway disease, or significant bradycardia. Therefore, under dose of BB is defined as a dose below the evidence based, target dose of BB, when there is no documented contraindications for up-titration.

CRT indications were defined according to the ESC cardiac pacing and CRT guidelines: For patients who have left ventricular ejection fraction (LVEF) less than or equal to 35%, a QRS duration greater than or equal to 0.12 seconds, and sinus rhythm, CRT is indicated for the treatment of NYHA functional Class III or ambulatory Class IV heart failure symptoms on optimal recommended medical therapy.17

Inclusion criteria

- Patients who presented with first manifestations of HF with systolic dysfunction [new onset HF].
• All patients with acute decompensation of chronic HF caused by systolic dysfunction. Systolic heart failure was defined by an ejection fraction, as measured by echocardiography, of 40% or less.\(^{18}\)

**Exclusion criteria**

• Patients with dyspnea of unknown etiology.
• Patients with ejection fraction above 40%.
• Patients presenting with acute coronary syndrome, complicated by HF, to exclude high risk ischemic heart disease patients, from this HF registry.
• Patients with right ventricular failure

**B] Statistics and Data management**

Data was collected, revised, verified, and then edited on personal computer. Data was then analyzed statistically using SPSS statistics package version (15). Quantitative data were presented in the form of mean ± standard deviation, while qualitative data were presented by number and percentage.

**Results**

**I] Demographics**

The mean age was 59.7 ± 11.7 years. The minimum age was 29 years and the maximum was 90 years. Male patients constituted 87.1% of the study population.

23% of the patients enrolled had new onset heart failure, while 73.8% had decompensated chronic heart failure.

Coronary artery disease was the most common etiology in 69 patients representing 64% of the patients' population.

61 patients had hypertension, 56 patients had diabetes mellitus, 31 patients sustained myocardial infarction, 49 patients had a history of revascularization, 41 patients had echocardiographically significant, moderate to severe, valvular heart disease, 34 patients had renal insufficiency, 31 patients had myocardial infarction, 25 patients had hyperlipidemia, 21 patients had a history of smoking, either as current smokers or ex-smokers, 20 patients had atrial fibrillation, 14 patients had COPD, 11 patients had peripheral vascular disease,
11 patients had concurrent chest infection, 9 patients had cerebro-vascular accident, 7 patients had valvular surgeries, and 6 patients had survived cardiac arrest.

![Co morbid conditions](image)

**Figure (1)** Co morbid conditions affecting these HF patients in percentage.

ACEI, ARBs, and BB were initiated in only 12% of patients before hospital admission.

Also, a high index for admission with most of the patients [83%] having NYHA class IV dyspnea on admission.

The mean EF was 30% ± 6.7%.

**II] Therapy**

**A] Oral Drug therapy during hospitalization**

66 patients were on ACEI, 18 patients were on ARBs, 42 patients were on BB, 57 patients were on low dose spironolactone, 79 patients were on diuretics, 31 patients were on the hydralazine and nitrates combination and 48 patients were on digitalis. The data was missing for 2 patients [1.9%].
Figure (2) Oral drug therapy, during hospitalization, in percentage

ACEI and ARBs

57 patients were on an under dose of ACEI, 9 patients were on a proper dose of ACEI, while 15 patients were on an under dose of ARBs, and 3 patients were on a proper dose of ARBs. 2 patients were on both ACEI and ARBs.

A total of 11 patients contraindications for the use of ACEI/ARBs, most commonly renal impairment (6 patients). Only 5 patients did not have documented contraindications and were not on ACEI/ARBS. There was no reported data for 2 patients [1.9%].

Figure (3) Use of ACEI and ARBs

- Use of ACEI, ARBs or both: 80%
- Contraindications: 10%
- Eligible, but no use: 5%
- Use of ACEI, ARBs or both: 5%
Use of spironolactone

57 patients were on spironolactone, 14 patients were not eligible to receive spironolactone, 18 patients had contraindications, and 16 patients had indications and no contraindications for spironolactone. The data was missing for 2 patients.

Figure (3) Use of ACEI and ARBs in percentage

Use of Beta-blockers [BB]

32 patients were on an under dose of BB, 10 patients were on proper dose of BB, 52 patients had contraindications for BB, mostly as decompensation (44 patients), and 11 patients had no contraindications for BB, but still were not on BB. The data was missing for 2 patients.

Figure (4) Use of Spironolactone in percentage
Figure (5) Use of BB in percentage

Use of Hydralazine and nitrates combination

31 patients [29.5%] were on the hydralazine and nitrates combination. This combination was used mostly as add on vasodilator for patients already on ACEI or ARBs (20 patients). The data was missing for 2 patients [1.9%].

Other drug therapy

There was an overlap in the drug therapy of these patients between the heart failure medication and the medications for ischemia or dyslipidemia. The other drug therapy can be demonstrated in the following table:

Table (1) Other, Oral drug therapy used, in numbers and percentage

<table>
<thead>
<tr>
<th>Drug Therapy</th>
<th>Frequency [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin only</td>
<td>35 [33.3%]</td>
</tr>
<tr>
<td>Aspirin and clopidogrel</td>
<td>32 [30.5%]</td>
</tr>
<tr>
<td>Statins</td>
<td>26 [24.8%]</td>
</tr>
<tr>
<td>Warfarin</td>
<td>20 [19%]</td>
</tr>
<tr>
<td>Fibrates</td>
<td>5 [4.8%]</td>
</tr>
<tr>
<td>Clopidogrel only</td>
<td>2 [1.9%]</td>
</tr>
<tr>
<td>No data</td>
<td>2 [0.9%]</td>
</tr>
</tbody>
</table>

B) I.V. Drug therapy
6 patients were on Nor-adrenaline, 5 patients were on Dobutamine, 4 patients were on Adrenaline, 4 patients were on intravenous Nitrates, and 1 patient was on Dopamine.

### C) Device therapy

4 patients [3.8%] had CRT, only 1 patient [0.9%] had ICDs, 2 patients [1.9%] had a dual chamber pacemaker. The data was missing for 2 patients.

#### Eligibility for CRT

13 [12.4%] patients had wide QRS complex, of these only 7 [6.6%] were eligible for CRT –prior to discharge- according to the ESC cardiac pacing and CRT guidelines.\(^{18}\)

#### Eligibility for ICD for secondary prevention

6 patients [5.7%] survived cardiac arrests that were indicated for implantation of ICD according to the ESC guidelines.\(^{18}\)

#### Eligibility for ICD for primary prevention

29 patients [27.6%] had indications for ICD, for primary prevention, according to guidelines.\(^{18}\)

#### Use of Intra-aortic balloon counter pulsation

9 patients [8.6%] were on intra-aortic balloon counter pulsation.

### II) Outcome

#### A) Morbidity

The mean hospital stay was 6.6 ± 5.3 days. The minimum hospital stay was 1 day and the maximum hospital stay was 34 days. 21 patients were readmitted during the 2 years period of the study.

#### B) Mortality

13 patients [12.1%] died during these 2 years follow up. 7 patients died with worsening heart failure, of which 6 patients died of cardiogenic shock; while 1 patient died of pulmonary edema. Sudden cardiac death was reported in 6 patients.
Discussion

The mean age of patients enrolled in this study was almost 10 years younger than the mean age of HF patients worldwide.[Mean 60 years versus about 70 worldwide], however, it seems that ischemic heart disease-with its complications including heart failure-occur at a younger age in Egypt. 13,14. This confirmed the earlier Egyptian demographic data.16

Drug therapy

A dramatic under use of BB was documented in this study with only 40% of patients being on it, while 50% of patients had contraindications, mostly in the form of decompensation.

This suggests that there are chances of practice improvement through initiation of BB in stable, compensated HF patients in the outpatient service and prior to hospital discharge, as evident in the CIBIS III trial. In this study, Initiating HF treatment with the BB, bisoprolol, was proven to be as effective and well-tolerated as initiating treatment with ACEI, enalapril, in patients with stable mild to moderate HF. 19

Figure (6) Morbidity and mortality Outcome data
SCD: sudden, cardiac death
The oral drug therapy in this study can be summarized versus the comparative data in the following table:

**Table (2)** Comparison of oral HF therapy use between our study and comparative data

<table>
<thead>
<tr>
<th>Drug name</th>
<th>This study %</th>
<th>EHFS II %</th>
<th>ADHERE %</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI/ARBs</td>
<td>79.9</td>
<td>80.4</td>
<td>81</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>75.2</td>
<td>90.1</td>
<td>79.6</td>
</tr>
<tr>
<td>Beta-Blockers</td>
<td>40</td>
<td>61.4</td>
<td>82.6</td>
</tr>
<tr>
<td>Spironolactone 25 mg</td>
<td>54.3</td>
<td>47.5</td>
<td>34.6</td>
</tr>
<tr>
<td>Digitalis</td>
<td>45.7</td>
<td>31</td>
<td>40</td>
</tr>
<tr>
<td>Oral nitrates/other vasodilators</td>
<td>29.5</td>
<td>37.4</td>
<td>-</td>
</tr>
</tbody>
</table>

However, the choices and the use of intravenous drug therapy showed several unbeneﬁcial and even harmful trends.

There was a significant underuse of intravenous vasodilators in an extreme minority of patients [4%] versus a remarkable overuse of inotropes [Dobutamine and Dopamine] and vasocative drugs [Adrenaline and Noradrenaline] in collectively 15% of patients.

Analysis from the ADHERE registry concluded that therapy with vasodilator was associated with signiﬁcantly lower in-hospital mortality than positive inotropic therapy in AHF patients.\(^{20}\)

However, it remains to be determined whether inotropic therapy caused increased mortality or was a marker of hemodynamic deterioration.

Importantly, the use of I.V. vasoactive drugs was not based on data from pulmonary artery catheter (PAC) and was dependant on physicians’ choice.

However, data from the ESCAPE trial [Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness] showed that there was no difference in the in-hospital or the 30 days mortality between patients treated by clinical decision only versus patients treated by clinical decision and PAC.\(^{21}\)

**Device therapy**

This study reported an underuse of the available device therapies in the form of CRT and ICD, since the data suggest that almost 40% of our patients were eligible for CRT and ICD, but did not receive it prior to discharge.

A recently published report about the real life use of ICD from GWTG HF showed that the overall use of ICD in-hospital or planned implantation rate was 20%. This rate ranged widely among hospitals, from 1% among the lowest tertile to 35% among the top tertile (\(p < 0.01\)). This study concluded that
there is significant, unexplained hospital variation in the use of ICD therapy among potentially eligible HF patients.\textsuperscript{22} This again highlights data about underuse of ICD in real life practice for heart failure patients.

Another report from the same study showed that 12.4\% of patients were discharged alive with CRT. The investigators concluded that although CRT is recent evidence-based therapies for heart failure, patterns of use differ significantly from clinical trials and published guidelines. Important variations also exist for CRT therapy based on race, geographic region, co morbidities, and age.\textsuperscript{23}

In this study, the economic burden associated with these lines of management in a developing country might have had an impact of the physicians’ decision not to pursue with these expensive lines of treatment.

Therefore, we can conclude that there is a dramatic, but rather financially justified underuse of these therapies.

**Outcome**

The mean length of stay in this study was 6.7 days, while in the EHFSII, it was 9 days. However, in the ADHERE registry; the mean length of stay was 5.8 days.

The re-hospitalization rate in this study, was only 20 \% in 2 years versus 23 \% for a 6 month follow up in the ADHERE registry.

However, the ADHERE was a nation wide registry in the USA versus this single centered study.

In this study, in-hospital mortality was 12\%; versus 17.6\% from the previously mentioned Ibrahim et.al. study.

These mortality rates might be explained by the following factors:
1. The high incidence of CAD, DM, HTN, anemia and renal insufficiency in these patients' cohort.
2. The long standing mismanagement of heart failure patients with a small proportion of them obtaining proper evidence – based medications.
3. Lower use of beta-blockers therapy.
4. Lower use of intravenous vasodilators.
5. Higher use of intravenous inotropes and vasoactive medications which is associated with poorer prognosis.
6. Lack of ventricular assist device and heart transplant programs which might be an ultimate solution for many patients.
Limitation

This study only included a total of 107 patients in only one tertiary, highly equipped referral center, so it does not reflect the general practice in Egypt.

This is a retrospective study that is affected with lack of documented data in some aspects e.g. HF precipitating factors, need for mechanical ventilation, length of intensive care stay, etc.

Also this study did not enroll patients with diastolic dysfunction which is a poorly studied cohort of patients.

Last, but not the least, this study did not include the intensive care stay and the need for mechanical ventilation as an endpoint to asses the outcome.

Conclusion

Low rates of use of beta-blockers, intravenous vasodilators and device therapy, while maintaining high rates of use of inotropes appear to be associated with significant in hospital mortality

Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AHF</td>
<td>Acute heart failure</td>
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<tr>
<td>CRT</td>
<td>Cardiac resynchronization therapy</td>
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<tr>
<td>ICD</td>
<td>Implantable cardioverter defibrillator</td>
</tr>
<tr>
<td>HF</td>
<td>Heart failure</td>
</tr>
<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
</tr>
<tr>
<td>LV</td>
<td>Left ventricle</td>
</tr>
<tr>
<td>I.V.</td>
<td>Intravenous</td>
</tr>
<tr>
<td>CHF</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>ACEI</td>
<td>Angiotensin converting enzyme inhibitor</td>
</tr>
<tr>
<td>ARBs</td>
<td>Angiotensin receptor blockers</td>
</tr>
<tr>
<td>BB</td>
<td>Beta blockers</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>HTN</td>
<td>Hypertension</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>CAD</td>
<td>Coronary artery disease</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>RI</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>HLP</td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>AF</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>PVD</td>
<td>Peripheral vascular disease</td>
</tr>
<tr>
<td>CVA</td>
<td>Cerebro-vascular accident</td>
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Conflict of interest
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**Figures legends**

**Figure (1)** Co morbid conditions affecting these HF patients in percentage.

**Figure (2)** Oral drug therapy in percentage

**Figure (3)** Use of ACEI and ARBs in percentage

**Figure (4)** Use of Spironolactone in percentage

**Figure (5)** Use of BB in percentage

**Figure (6)** Morbidity and mortality Outcome data
SCD: sudden, cardiac death

**Appendices**