Early and long-term outcomes of decompensated heart failure patients in a tertiary-care centre in India

Sanjay Ganapathi, Pannyamakkal Jeemon, Rajasekharan Krishnasankar, Rajamoni Kochumoni, Purushothaman Vineeth, Krishna Kumar Mohanan Nair, Ajit Kumar Valaparambil and Sivadasanpillai Harikrishnan*

See Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum 695011, Kerala, India

Abstract

**Aim** Long-term outcome data of acute decompensated heart failure (HF) are scarce from India. The aim of the study was to collect in-hospital and long-term outcome data of HF patients admitted during 2001–10 in a tertiary-care centre in South India.

**Methods and results** Consecutive patients admitted with first episode of decompensated HF were part of the registry. Data regarding diagnosis, risk factors, treatment, early (in-hospital), and late (5 and 10 year) mortality outcomes were captured. During this period, 1502 patients were admitted with first episode of decompensated HF [37.7% of women, mean age of 51.1 (SD = 14.3) years]. Common causes were ischaemic heart disease (36.2%), rheumatic heart disease (34.3%), and cardiomyopathies (9.9%). HF with reduced ejection fraction (HFrEF) was present in 26.9% of patients, and 33.8% had atrial arrhythmias. Diabetes, hypertension, and renal dysfunction were prevalent in 27.4%, 28.6%, and 37.4%, respectively. Median duration of hospitalization was 6 days (interquartile range: 3–10), and 247 patients (16.4%) died during index admission. The total time at risk was 6248 person years, and 1051 patients died during the study period with a median survival time of 3.7 years. Overall mortality rate was 16.8 per 100 person years (95% CI: 15.8–17.9 per 100 person years). Older age [hazard ratio (HR) = 1.08, 95% CI: 1.02–1.14, \( P = 0.007 \)], anaemia (HR = 1.34, 95% CI: 1.08–1.65, \( P = 0.007 \)), renal dysfunction (HR = 1.38, 95% CI: 1.20–1.59, \( P < 0.001 \)), HFrEF (HR = 0.61, 95% CI: 0.52–0.73, \( P < 0.001 \) against HFrEF), and the use of guideline-directed therapies (GDT; beta blockers: HR = 0.57, 95% CI: 0.49–0.66, \( P < 0.001 \); and angiotensin converting enzyme inhibitor/angiotensin receptor blocker: HR = 0.59, 95% CI: 0.51–0.69, \( P < 0.001 \)) were important predictors of mortality. Patients with HF and mid-range EF also benefited from GDT.

**Conclusion** In our cohort, ischaemic and rheumatic heart diseases were the leading contributors for HF. Anaemia, renal dysfunction, poor ejection fraction, and suboptimal prescriptions of GDT were the main predictors of long-term mortality. Both patients with HFrEF and mid-range EF benefited from GDT.

**Keywords** Heart failure; Decompensated; Registry; Outcome; Ejection fraction

*Correspondence to: Dr Sivadasanpillai Harikrishnan DM, Professor, See Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum 695011, Kerala, India. Tel: +91-471-2524457. Email: dhharikrishnan@outlook.com

**Introduction**

Epidemiological data on heart failure (HF) from India are recently emerging. A few hospital-based cohort studies provide information regarding in-hospital and early outcomes of patients admitted with acute HF, while long-term outcomes are yet to be reported. Available data allude to equally bad or worse prognosis of HF in Indian population when compared with high-income countries. However, the patients with HF are younger by a decade or more in India in comparison to the patients from high-income countries. Additionally, patients in India develop HF due to a combination of new age diseases like coronary heart disease and persistence of traditional diseases like rheumatic heart disease (RHD). The health system in India is grappling with the dual burden of new age diseases and conditions like RHD in the same...
settings. In this context, management of HF becomes more complex in India. There is hardly any published data on long-term outcomes of patients with acute HF from India. We present the in-hospital and long-term survival of patients admitted with acute HF in a tertiary referral public hospital in India.

Methods

Study settings and population

The study [Chitra Heart Failure (CHF) registry] was conducted at Sree Chitra Tirunal Institute for Medical Sciences and Technology, a tertiary care, referral centre for cardiovascular and neurological illnesses under the Government of India, located in the southern state of Kerala. The records of all patients aged 18 years and above, belonging to the state of Kerala, admitted to our hospital between 1 January 2001 and 31 December 2010 with first episode of acute decompensated HF, were accessed retrospectively. We searched electronic records of our hospital (admission notes, in-hospital records, and discharge summaries) with keywords related to ‘heart failure’, ‘cardiac failure’, ‘left ventricular failure’, ‘pulmonary oedema’, ‘congestive heart failure’, and ‘congestive cardiac failure’.

Study variables

Demographic and clinical variables including diagnosis, treatment, and outcomes were obtained from electronic medical records by performing detailed chart review. A structured tool was used for uniform data collection based on chart review. Laboratory variables at the time of admission (haemoglobin and serum creatinine) were obtained directly from the electronic laboratory records. The diagnosis of HF was based on established clinical guidelines prevalent at the time of admission. Echocardiographic data were compulsory for diagnosis. Patients were classified on the basis of left ventricular ejection fraction; those with left ventricular ejection fraction <40%, 40–49%, and ≥50% were grouped into HF with reduced EF (HFrEF), mid-range EF (HFmrEF), and preserved EF (HFpEF), respectively. Guideline-directed therapy (GDT), defined as the use of a combination of either angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) and beta adrenoceptor blocker during index hospitalization, was assessed.

Follow-up data collection

Follow-up information was obtained either from medical records or telephonically in those who did not attend the routine follow-up clinic. All possible methods were used to contact patients who were lost to follow-up including contacting them through postal letters with reply cards, local civic body representatives, post offices, and local religious institutions. The study was approved by the Institute Ethics Committee of Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCT/IEC/373/Sept 2011).

Statistical methods and analyses

The demographic and clinical characteristics of patients with HFrEF, HFmrEF, and HFpEF are summarized using descriptive statistics. Continuous variables are presented as means with standard deviation or median with interquartile range for skewed data. Categorical variables are expressed as proportions. We estimated the in-hospital mortality as proportion of deaths over total enrolled patients. Mortality rate per 100 person years of follow-up was also estimated. We performed univariate survival analysis using Kaplan–Meier survival plots and compared the groups using log-rank tests. We created Cox proportional hazards model to assess the probable multivariate adjusted risks of all-cause mortality and included the following covariates with P < 0.20 in the univariate analysis: diabetes, hypertension, age > 65 years, sex, atrial arrhythmias, anaemia, renal dysfunction, prescription of ACEI/ARB during index hospitalization, the use of beta adrenoceptor blockers during index hospitalization, type of HF, and HF aetiology. Follow-up data for survival analyses were censored for a maximum period of 10 years since the first admission date. All analyses were performed using Stata 12 (StataCorp, College Station, TX, USA).

Results

Demographic and baseline clinical characteristics

In total, 1502 eligible patients with HF were enrolled in the database (Table 1). The mean age of the population was 51.1 (14.3) years. More than three fifths of the patients were men (62.3%). The proportions of patients who had HFrEF and HFpEF were 26.9% and 57.7%, respectively (Table 1). Patients with HFpEF were younger (mean age = 48.8 years) than patients with HFrEF (53.9 years) and HFmrEF (54.7 years). Nearly half (48.3%) of the patients with HFpEF were women, whereas the proportion of men was more than three fourth in the other two groups.

More than one fourth of the patients reported had diabetes (27.4%) and hypertension (28.6%). History of tobacco use was recorded among 42.3% of men. More than one third (37.4%) of the patients had co-morbid renal dysfunction (eGFR < 60 mL/min/m²) during hospitalization. Prevalence of renal dysfunction was the least (34.1%) in HFpEF. The
Table 1 General characteristics of the study population

| Variables                        | All patients (n = 1502) | HFrEF (n = 404) | HFmrEF (n = 231) | HFPF (n = 867) | P value |
|----------------------------------|-------------------------|-----------------|------------------|----------------|---------|
| Age in years (SD)                | 51.1 (14.3)             | 53.9 (12.8)     | 54.7 (13.8)      | 48.8 (14.7)    | 0.007   |
| Women, n (%)                     | 566 (37.7)              | 88 (21.8)       | 59 (25.5)        | 419 (48.3)     | <0.001  |
| Diabetes, n (%)                  | 411 (27.4)              | 174 (43.1)      | 87 (37.7)        | 150 (17.3)     | <0.001  |
| Hypertension, n (%)              | 430 (28.6)              | 156 (38.6)      | 82 (35.5)        | 192 (22.2)     | <0.001  |
| Atrial fibrillation/flutter, n (%)| 506 (33.8)              | 54 (13.4)       | 54 (23.5)        | 398 (46.0)     | <0.001  |
| Aetiology, n (%)                 |                         |                 |                  |                | <0.001  |
| Ischaemic                        | 545 (36.2)              | 260 (64.5)      | 129 (56.3)       | 156 (17.9)     |         |
| Rheumatic heart disease          | 515 (34.3)              | 39 (9.7)        | 55 (24.0)        | 421 (48.4)     |         |
| Non-RHD valve                    | 124 (8.3)               | 16 (3.9)        | 16 (7.0)         | 92 (10.6)      |         |
| Dilated cardiomyopathy           | 71 (4.7)                | 62 (15.4)       | 9 (3.9)          | 0              |         |
| Restrictive and hypertrophic cardiomyopathies | 53 (3.5) | 6 (1.5) | 4 (1.7) | 43 (5) |
| Other cardiomyopathies           | 24 (1.6)                | 7 (1.7)         | 2 (0.9)          | 15 (1.7)       |         |
| Grown-up congenital heart disease| 63 (4.2)                | 8 (2.0)         | 4 (1.8)          | 51 (5.9)       |         |
| Others                           | 107 (7.1)               | 6 (1.5)         | 12 (5.2)         | 89 (10.3)      |         |
| Haemoglobin in g/dL (SD)         | 12.8 (2.1)              | 12.9 (2.1)      | 12.5 (1.9)       | 12.6 (2.2)     | 0.235   |
| eGFR (SD)                        | 67.6 (30.8)             | 64.2 (28.8)     | 63.6 (28.6)      | 70.2 (32.1)    | 0.017   |
| Renal dysfunction, n (%)         | 561 (37.4)              | 167 (41.3)      | 98 (42.4)        | 296 (34.1)     | 0.111   |
| Duration of hospital stay, median (IQR) days | 6 (3–10) | 6 (3–9) | 6 (3–11) | 6 (3–10) | 0.44 |

P value for inter-group difference is provided.

eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced ejection fraction; HFPF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; RHD, rheumatic heart disease; SD, standard deviation; IQR, interquartile range.

The proportions of patients with diabetes and hypertension were also lower in HFPF group. However, atrial arrhythmias were commoner in patients with HFPF (46%, 38.6%, and 35.5%, respectively, in HFPF, HFrEF, and HFmrEF).

The common aetiologies were ischaemic heart disease (36.2%), followed by RHD (34.3%), cardiomyopathies (dilated, restrictive, hypertrophic, and others combined: 9.9%), non-rheumatic valvular heart diseases (8.3%), and grown-up congenital heart disease (4.2%). Endomyocardial fibrosis, a form of restrictive cardiomyopathy contributed to 1.7% of cases. Valvular heart disease was the commonest underlying disease in patients with HFPF, while ischaemic heart disease predominated in patients with HFrEF and HFmrEF (Table 1). Active infective endocarditis contributed to HF in 3.4% of patients. Anaemia, as defined by haemoglobin levels <10 g/dL, was seen in 5.1% of patients. Mean levels of haemoglobin did not differ between the different HF groups.

A small proportion of patients in this cohort had undergone invasive procedures like valve replacement surgery (7.8%), coronary artery bypass graft surgery (4.5%), and permanent pacemaker implantation (2.7%) before the index admission.

In-hospital outcomes and treatment

Median duration of hospital stay in the index admission was 6 days (interquartile range: 3–10) and did not differ between the groups. Overall, 18.4% of patients administered intravenous inotrope infusion; dopamine in 13.5%, epinephrine in 7%, norepinephrine in 5.3%, dobutamine in 6.3%, and others (vasopressin, milrinone, and levosimendan) in 1.3% of patients. A combination of these agents was required in 79% of patients needing inotropes. Intravenous vasodilators were used in 3% of patients, nitroglycerin being the commonly used agent. Mechanical ventilation was needed in 17.6% of patients. Other cardiovascular medications used during hospitalization are listed in Table 2.

About 10% (154) of the patients underwent invasive procedures during index hospitalization, which included percutaneous coronary intervention in 70 patients, percutaneous mitral commissurotomy in 26 patients, surgical valve replacement in nine patients, implantation of permanent pacemaker in 15 patients, coronary artery bypass graft in five patients, and placement of implantable cardioverter defibrillator in two patients.

In total, 247 patients (16.4%) died during index hospitalization. The proportions of deaths in the HFrEF, HFmrEF, and HFPF were 20.8%, 19%, and 13.7%, respectively (P < 0.001). Three fifths (61.9%) of the in-hospital deaths were due to refractory HF. Refractory ventricular arrhythmias and sepsis contributed to 13.8% and 24.3% of all in-hospital deaths, respectively. The proportions of deaths due to refractory ventricular arrhythmias were higher in patients with HFrEF (17.9%) and HFmrEF (20.5%) when compared with those with HFPF (8.4%) (P = 0.057).

Survival rates

Follow-up data of 1471 patients (97.9%) were available for analysis. The total time at risk was 6248 person years. During the study period, 804 patients died (excluding in-hospital death). The median survival was 3.7 years (range: 0–10 years). The total crude mortality rate was 16.8 per 100 person years (95% CI: 15.8–17.9 per 100 person years). The
Table 2  Cardiovascular medications and therapies used during hospitalization

| Medication, n (%) | All patients (n = 1502) | HFrEF (n = 404) | HfmrEF (n = 231) | HfPEF (n = 867) | P value |
|-------------------|-------------------------|-----------------|------------------|-----------------|---------|
| Antiplatelets     | 556 (37)                | 219 (54.2)      | 116 (50.2)       | 221 (25.5)      | <0.001 |
| Oral nitrates     | 338 (22.5)              | 139 (34.4)      | 80 (34.6)        | 119 (13.7)      | <0.001 |
| Intravenous nitrates | 45 (3)               | 19 (4.7)        | 9 (3.9)          | 17 (2)          | 0.019  |
| Calcium channel blockers—dihydropyridine | 119 (7.9) | 21 (5.2) | 23 (10) | 75 (8.7) | 0.049  |
| Calcium channel blockers—nondihydropyridine | 216 (14.4) | 11 (2.7) | 23 (10) | 182 (21) | <0.001 |
| Beta blockers     | 498 (33.1)              | 163 (40.3)      | 95 (41.1)        | 240 (27.7)      | <0.001 |
| Amiodarone        | 124 (8.3)               | 44 (10.9)       | 23 (10)          | 57 (6.6)        | 0.014  |
| Digoxin           | 762 (50.7)              | 209 (51.7)      | 95 (41.1)        | 458 (52.8)      | 0.006  |
| Loop diuretics    | 1115 (74.2)             | 300 (74.3)      | 162 (70.1)       | 653 (75.3)      | 0.277  |
| ACE inhibitor      | 400 (26.6)              | 164 (40.5)      | 81 (35.1)        | 155 (17.9)      | <0.001 |
| Angiotensin receptor blocker | 102 (6.8) | 44 (10.9) | 20 (8.7) | 38 (4.4) | <0.001 |
| Combination of ACEI or ARB and beta blockers | 240 (16) | 108 (26.7) | 60 (26) | 72 (8.3) | <0.001 |
| MRA               | 470 (31.3)              | 165 (40.8)      | 65 (28.1)        | 240 (27.7)      | <0.001 |
| Intravenous inotropes | 276 (18.4) | 102 (25.3) | 49 (21.2) | 126 (14.5) | <0.001 |
| Oral anticoagulation | 437 (29.1) | 69 (17.1) | 40 (17.3) | 328 (37.8) | <0.001 |
| Mechanical ventilation | 264 (17.6) | 85 (21.4) | 51 (22.1) | 128 (14.8) | 0.003  |

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; HFrEF, heart failure with mid-range ejection fraction; HfPEF, heart failure with preserved ejection fraction; HfPEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid antagonist.

crude mortality rates in the study population in percentages are provided in Table 3. Unadjusted mortality rates were lower for HfPEF when compared with the other two groups, with HFrEF having the highest 1 to 5 year mortality.

Overall, HFrEF reported the worst survival rates (Figure 1). However, the survival rates of HFrEF and on guideline-directed medications were similar to that of HfmrEF. Even among HfmrEF, those who are on medications acting on neurohormonal mechanisms (combination of beta blockers with either ACEI or ARB) reported better survival outcomes (Figure 2). Additionally, the survival of patients with HfPEF who were prescribed beta adrenergic blockers and either ACEI or ARB was better than those who were not on any of these medications.

In the multivariate Cox proportional hazards model (Table 4), older age (HR for an increment of 10 years of age = 1.08, 95% CI: 1.02–1.4, P = 0.007), haemoglobin levels <10 g/dL (HR = 1.34, 95% CI: 1.08–1.65, P = 0.007), presence of renal dysfunction during index hospitalization (HR = 1.38, 95% CI: 1.20–1.59, P < 0.001), poor LV ejection fraction (HfmrEF: 0.82; 95% CI: 0.67–1.01, P = 0.056; and HfPEF: 0.61; 95% CI: 0.52–0.73, P < 0.001), and the use of either ACEI/ARB (HR = 0.59; 95% CI: 0.51–0.69, P < 0.001) or beta blockers (HR = 0.57; 95% CI: 0.49–0.66, P < 0.001) were associated with time to all-cause mortality. Additionally, a diagnosis of valvular heart disease as the underlying cause for HF did not confer any survival advantage over others.

During the follow-up period, therapeutic procedures were performed in 408 patients (32.5%). The procedures included valve surgeries (replacement or repair) (n = 197, 15.7%), percutaneous mitral commissurotomy (n = 51, 4.1%), coronary revascularization (n = 145, 11.6%) (of all the coronary revascularization, nearly two thirds underwent percutaneous coronary intervention), and implantation of cardiac resynchronization–defibrillator device (cardiac resynchronization therapy/implantable cardioverter defibrillator) (n = 20, 1.6%).

Discussion

The CHF study provides long-term survival data of over 1500 patients with HF from Kerala, India. Coronary heart and

Table 3  Crude 1–5 year mortality rates in the study population

| Variables                  | Overall (n = 1502) | HFrEF (n = 404) | HfmrEF (n = 231) | HfPEF (n = 867) | P value |
|----------------------------|-------------------|-----------------|------------------|-----------------|---------|
| One year mortality rate    | 490 (32.6)        | 159 (39.4)      | 83 (35.9)        | 248 (28.6)      | <0.001 |
| Two year mortality rate    | 593 (39.5)        | 183 (45.3)      | 101 (43.7)       | 309 (35.6)      | 0.002  |
| Three year mortality rate  | 685 (45.6)        | 207 (51.2)      | 112 (48.5)       | 366 (42.2)      | 0.007  |
| Four year mortality rate   | 767 (51.1)        | 231 (57.2)      | 125 (54.1)       | 411 (47.4)      | 0.003  |
| Five year mortality rate   | 843 (56.1)        | 254 (62.9)      | 136 (58.9)       | 453 (52.3)      | 0.001  |

P values indicate inter-group difference.

HfmrEF, heart failure with mid-range ejection fraction; HfPEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

ESC Heart Failure 2020; 7: 467–473
DOI: 10.1002/ehf2.12600
valvular heart diseases were the predominant aetiologies reported in the CHF registry. In our middle-aged cohort of patients with HF (mean age of 51 years), the median survival time was 3.7 years. Despite relatively poor overall utilization of guideline-directed neurohumoral modifying therapy, it reduced the mortality and improved survival rate in HFrEF. Additionally, the benefits accrued from guideline-directed neurohumoral modifying therapies improved the survival

Figure 1 Kaplan–Meier curves of patients hospitalized with heart failure grouped by ejection fraction and the use of combination of renin-angiotensin blockers and beta blockers for mortality. HFrEF and not on guideline-directed therapy have the highest mortality. Patients with HFmrEF on GDT have lesser mortality than HFmrEF not on GDT. GDT was defined as prescription of combination of renin-angiotensin blocker and beta blocker during index hospitalization. Among 1502 patients, 10 had incomplete data on one of the components of GDT, who were excluded from this analysis. GDT, guideline-directed therapy; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; RASBB, combination therapy with renin-angiotensin blocker and beta blocker.

Table 4 Cox proportional hazards model for all-cause mortality

| Variable                              | Hazard ratios | 95% confidence interval | P value |
|---------------------------------------|---------------|-------------------------|---------|
| Diabetes                              | 0.97          | 0.81 - 1.15             | 0.69    |
| Hypertension                          | 1.03          | 0.87 - 1.22             | 0.72    |
| Age in years (each increment of 10 years) | 1.08          | 1.02 - 1.14             | 0.007   |
| Female sex                            | 0.99          | 0.86 - 1.22             | 0.88    |
| Atrial arrhythmias                    | 0.91          | 0.78 - 1.07             | 0.25    |
| Anaemia                               | 1.34          | 1.08 - 1.65             | 0.007   |
| Renal dysfunction                     | 1.38          | 1.20 - 1.59             | <0.001  |
| ACEI/ARB*                             | 0.59          | 0.51 - 0.69             | <0.001  |
| Beta blockers*                        | 0.57          | 0.49 - 0.66             | <0.001  |
| HFmrEFb                               | 0.82          | 0.67 - 1.01             | 0.056   |
| HFpEFb                                | 0.61          | 0.52 - 0.73             | <0.001  |
| Ischaemic heart disease^c             | 1.15          | 0.92 - 1.43             | 0.21    |
| Others^c                              | 1.08          | 0.90 - 1.30             | 0.41    |

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction.

*The use of ACEI or ARB and the use of beta adrenoceptor blockers during index hospitalization.

HFmrEF and HFpEF when compared with HFrEF.

When compared with valvular heart disease, for patients with ischaemic heart disease and other diagnoses.
rate in HFmrEF. Traditional risk factors such as older age, anaemia, renal dysfunction, and poor ejection fraction were the prominent predictors of mortality.

Long-term outcome data following hospitalization for acute HF are scarce from low and middle-income countries. The long-term follow-up in CHF registry patients helped us to estimate the median survival time of acute decompensated HF, probably for the first time in India. The median survival time of 3.7 years in CHF registry patients are comparable with that of corresponding data from high-income countries (2.1 years in the GWTG-HF registry linked with Medicare data in the US; patients >65 years of age). However, our study population was 1–1.5 decade younger than the population from high-income settings. Similar studies from India confirm that majority of patients with HF in India are in the middle-aged group, and HF in India mostly affects in the most productive age group of 35–64 years.

The disease aetiology pattern in our study population differs from that of high-income countries with disproportionately larger disease contribution from valvular heart disease. The ejection fraction of valvular heart disease patients in CHF was better than HF resulting from other disease conditions. The better ejection fraction of patients with HF and valvular heart disease in general would have resulted in better survival of the overall CHF cohort. However, patients with symptomatic RHD are known to develop HF rapidly and die young as evidenced in the Global Rheumatic Heart registry (the REMEDY study), which reported a median age of death of 28 years. Similar to other regional registries, male predominance was also noted in CHF registry (e.g. 62% of men among Indian patients in INTER CHF; 69% of men in THFR). However, registries from high-income countries report mixed patterns with a higher female preponderance in ADHERE registry (52% of women) to higher male proportion in ESC registry (63% of men).

The mortality rate during index hospitalization in our study is probably the highest reported in India. For example, the in-hospital mortality in THFR is lower (8.5%) than the in-hospital mortality rate of 16.4% in CHF registry. Being a premier referral centre in the public sector, it is likely that sicker patients are referred from elsewhere to our centre. The higher use of intravenous inotropes and mechanical ventilation during hospital stay in our study population probably also indicates the referral bias. Patients with RHD who reach our hospitals are mostly from low socioeconomic zones and they may present late in the course of the illness. The higher in-hospital mortality may be partly attributable to the referral bias of sick patients to our centre. Although the prevalence of cardiovascular risk factors such as diabetes and hypertension was higher in the THFR cohort (more than half of the patients had diabetes or hypertension), the parameters indicating advanced cardiovascular disease were more prevalent in the CHF registry. For example, the prevalence of atrial arrhythmias (14.7% in THFR and 33.8% in CHF study) and renal dysfunction (17.9% in THFR and 37.4% in CHF study) was higher in CHF registry as compared with THFR.

Despite being a referral centre, only one of four patients with HF received guideline-directed neurohumoral modulators during hospitalization. Additionally, many of them did not receive therapies at the optimal dose. Because of the retrospective nature of the study, the reasons for poor utilization of GDT were not available. Future studies should therefore investigate in detail the reasons for underutilization of optimal GDT at least in HFrEF. While neurohumoral modulating therapies are definitely beneficial for HFrEF and recommended in clinical guidelines, their impact on HFpEF has not been substantiated in clinical trials. The impact of these medications on the subset of HFmrEF is evolving. In CHF cohort, HFmrEF on neurohumoral modulating therapies had long-term survival outcomes similar to patients with HFrEF. Even among HFpEF, there was a trend of better survival in patients, who were on neurohumoral modulating therapies. Whether neurohumoral targets alter the prognosis in younger patients with HFpEF or HFmrEF in the subcontinent needs to be assessed in future studies with adjustment of all potential confounders.

Limitations of the study

The patients from our single centre study may not be representative of the HF patient population in Kerala, India. Additionally, the lack of data on the pharmacologic therapy titrations, risk factor control, and reasons for the non-optimal use of evidence-directed therapies are other major limitations. Additionally, re-hospitalizations especially that occurred outside our hospital could not be captured reliably due to lack of optimal tracking system.

Conclusions

We present long-term survival outcomes and median survival time of patients hospitalized for decompensated HF from India. When compared with the high-income settings, the patients admitted with decompensated HF in our study were younger and with male preponderance. Ischaemic heart disease was the leading individual contributor to the condition, while the burden due to RHDs was relatively higher than other HF registry patients in high-income settings. We report relatively higher in-hospital mortality rate as compared to data from high-income HF registries. However, the median survival time is higher, perhaps due to the younger age, and relatively higher prevalence of valvular heart disease in CHF cohort. Despite less than optimal use, both patients with HFrEF and HFmrEF benefited from GDT.
References

1. Harikrishnan S, Sanjay G, Agarwal A, Kumar NP, Kumar KK, Bahuleyan CG, Vijayaraghavan G, Viswanathan S, Sreedharan M, Biju R, Nair T, Suresh K, Rao AG, Dalus D, Huffman MD, Jeemon P and Trivandrum Heart Failure R. Clinical presentation, management, in-hospital and 90-day outcomes of decompensated heart failure patients in Trivandrum registry in Kerala, India: the Trivandrum Heart Failure registry. *Eur J Heart Fail* 2015; 17: 794–800.

2. Harikrishnan S, Sanjay G, Agarwal A, Kumar NP, Kumar KK, Bahuleyan CG, Viswanathan S, Sreedharan M, Biju R, Rajalekshmi N, Nair T, Suresh K, Jeemon P. One-year mortality outcomes and readmissions of patients admitted with acute heart failure: data from the Trivandrum Heart Failure registry in Kerala, India. *Am Heart J* 2017; 189: 193–199.

3. Sanjay G, Jeemon P, Agarwal A, Viswanathan S, Sreedharan M, Vijayaraghavan G, Bahuleyan CG, Biju R, Nair T, Prathakpumar N, Krishnakumar G, Rajalekshmi N, Suresh K, Park JP, Huffman MD, Harikrishnan S. In-hospital and three-year outcomes of heart failure patients in South India: the Trivandrum Heart Failure registry. *J Card Fail* 2018; 24: 842–848.

4. Dokainish H, Teo K, Zhu J, Roy A, AlHabibKF, ElSayed A, Palileo–Villanueva L, Lopez–Jaramillo P, Karaye K, Yusofi K, Orlandini A, Slawa K, Mondo C, Laras F, Prabhakaran D, Badr A, Elmaghawry M, Damasceno A, Tibazarwa K, Belley-Cote E, Balasubramaniam K, Islam S, Yacoub MH, Huffman MD, Harkness K, Grinvalds A, McKeilvieve R, Bangdiwala SI, Yusuf S, Investigators I-C. Global mortality variations in patients with heart failure: results from the International Congestive Heart Failure (INTER-CHF) prospective cohort study. *Lancet Glob Health* 2017; 5: e665–e672.

5. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GM, Ruilope LM, Ruschitzka F, Rutenberg FH, van der Meer P. Authors/Task Force M and Document R. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2016; 18: 891–975.

6. Ponikowski P, Voors AA, Anker SD, Bueno H, Caronna E, Coste J, Falk V, Filippatos G, Garcia D, Gooszen HG, Hamm WC, Jhund PS, Komajda M, Merx I, NP–ejection fraction spectrum. *Eur J Heart Fail* 2016; 18: 1334–1341.

7. Shah KS, Xu H, Matsouaka RA, Bhatt DL, Heidenreich PA, Hernandez AF, Devore AD, Yancy CW, Fonarow GC. Heart failure with preserved, borderline, and reduced ejection fraction: 5-year outcomes. *J Am Coll Cardiol* 2017; 70: 2487–2489.

8. Zuhlke L, Karthikeyan G, Engel ME, Ranganjan S, Mackie P, Cupido-Kaya, Mauff B, Islam S, Daniels R, Francis V, Ogedo S, Gitura T, Mondo C, Okello E, Lwabi P, Al-Kebsi MM, Hugo-Hamman C, Sheta SS, Haileamlak A, Daniel W, Goshu DY, Abdisa SG, Desta AG, Shasho BA, Begna DM, ElSayed A, Ibrahim AS, Musuku J, Bode-Thomas F, Yilgwan CC, Amusa GA, Ige O, Okeahialam B, Sutton C, Misra R, Abul Fadl A, Kennedy N, Damasceno A, Sani MU, Ogah OS, Elhassan TO, Mucumbitsi J, Teo K, Yusuf S, Mayosi BM. Clinical outcomes in 3343 children and adults with rheumatic heart disease from 14 low- and middle-income countries: two-year follow-up of the global rheumatic heart disease registry (the REMEDY study). *Circulation* 2016; 134: 1456–1466.

9. Dokainish H, Teo K, Zhu J, Roy A, AlHabibKF, ElSayed A, Palileo–Villanueva L, Lopez–Jaramillo P, Karaye K, Yusofi K, Orlandini A, Slawa K, Mondo C, Laras F, Prabhakaran D, Badr A, Elmaghawry M, Damasceno A, Tibazarwa K, Belley-Cote E, Balasubramaniam K, Islam S, Yacoub MH, Huffman MD, Harkness K, Grinvalds A, McKeilvieve R, Bangdiwala SI, Yusuf S, Investigators I-C. Global mortality variations in patients with heart failure: results from the International Congestive Heart Failure (INTER-CHF) prospective cohort study. *Lancet Glob Health* 2017; 5: e665–e672.

10. Akintunde AA, Opalijio OG. Late presentation of rheumatic heart disease: a justification for renewal of preventive methods? *Pan Afr Med J* 2009; 3: 22.

11. Okello E, Wanzhu Z, Musoke C, Twalib A, Kakande B, Lwabi P, Wilson NB, Mondo CK, Odoi-Adome R, Freers J. Cardiovascular complications in newly diagnosed rheumatic heart disease patients at Mulago Hospital, Uganda. *Cardiovasc J Afr* 2013; 24: 80–85.

12. Choi KH, Choi JO, Jeon ES, Lee GY, Choi DJ, Lee HY, Kim JJ, Chae SC, Baek SH, Kang SM, Yoo BS, Kim KH, Cho MC, Park HY, Oh BH. Guideline-directed medical therapy for patients with heart failure with mid-range ejection fraction: a patient-pooled analysis from the KorHF and KorAHF registries. *2018; 7: e009806.

13. Lund LH, Claggett B, Liu J, Lam CS, Jhung PS, Rosano GM, Svedberg K, Yusuf S, Granger CB, Pfeffer MA, McMurray JJV, Solomon SD. Heart failure with mid-range ejection fraction in CHARM: characteristics, outcomes and effect of candesartan across the entire ejection fraction spectrum. *Eur J Heart Fail* 2018; 20: 1230–1239.

14. Cielew JG, Bunton KV, Flather MD, Altman DG, Holmes J, Coats AJ, Manzano I, McMurray JJV, Ruschitzka F, van Veldhuisen DJ, von Lueder TG, Bohm M, Andersson B, Kjekshus J, Packer M, Rigby AS, Rosano G, Wedel H, Hjalmarson A, Wikstrand J, Kotecha D, beta blockers in heart failure collaborative G. Beta blockers for heart failure with reduced, mid-range, and preserved ejection fraction: an individual patient-level analysis of double-blind randomized trials. *Eur Heart J* 2018; 39: 26–35.