Precipitant in acute heart failure in a multiethnic Asian urban cohort study

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ABSTRACT

Objectives To identify acute heart failure (HF) precipitants in patients with a history of chronic HF, and to analyse any relationship with early outcomes.

Background There are limited studies on acute HF precipitants and the relationship with outcomes, and determining this will help to identify the avoidable precipitants and may lead to better outcomes.

Methods Patients with a history of HF and admission to the authors' hospital in 2008, with a discharge primary diagnosis of HF, were enrolled. Diagnosis of HF was prospectively defined and reviewed by two cardiology teams. Patients' case records were reviewed, or families were interviewed for 1-month follow-up outcome information.

Results 242 admissions by 185 patients constituted our study cohort. Patients were older, and 36.8% were females. The ethnic Chinese, Malay and Indian composition of the cohort were 41.3%, 35.1% and 16.1% respectively. The mean left-ventricular ejection fraction was 34.0±17.5%. Preserved left ventricular ejection fraction (≥45%) constituted 35.1% of the cohort. Acute HF precipitants were identified in 62.8% of admissions and unidentified in 37.2% admissions. Non-compliance issues and infections constituted 27.2% and 13.6% of precipitants respectively. Cardiac precipitants accounted for 10.0% admissions. Multiple precipitants accounted for 8.3% admissions. There were no significant differences in patient profile, including ethnicity and gender, and outcomes between patients with identified precipitants and patients with unidentified precipitants.

Conclusion Non-compliance issues were a major precipitant of acute HF in patients with chronic HF. Precipitants were not determined in 37.2% of admissions. There were no significant associations between the different types of precipitants and early 30-day outcomes.

INTRODUCTION

Heart failure (HF) is the leading cause of mortality and morbidity in the USA and Europe[1] and in Singapore.[2] These exert considerable costs in the healthcare system. A major contribution to the burden of chronic HF is that of admissions to hospitals for acute decompensation episodes.[3]

Assessment for precipitants of HF exacerbation is recommended for evaluation of HF.[4] However, there are few published studies on the relationship between precipitants of acute HF and outcomes in USA and Europe, and no published studies on this subject in Asian cohorts. It would be useful to determine the precipitants of HF leading to hospital admissions, in patients with chronic HF. This will allow us to identify any avoidable precipitants and initiate a management plan, and may lead to better clinical outcomes.

The aim of this study is to identify the precipitants of acute HF in patients with a prior history of chronic HF, and to analyse the relationship, if any, of these precipitants with early outcomes.

METHODS

Singapore is an urban island city-state with a population of 4.8 million people and a total land area of 710 km^2, and situated at the southern tip of the Malayan peninsular. The population is multiethnic but predominantly Chinese, Malay, Indian and Eurasian.[5]

Changi General Hospital is a 790-bed tertiary hospital. It serves 800 000 residents living in the eastern part of Singapore. There is an HF programme in the hospital to manage patients with a primary diagnosis of HF. The HF programme consists of the HF team and a clinical pathway for the management of acute HF. The HF team is a multidisciplinary team. It consists of four dedicated cardiac care nurses, a HF cardiologist, a resident, a pharmacist, a physical therapist, an occupational therapist and a dietitian. The HF team reviews patients who are admitted with suspected HF. If the HF team confirms the diagnosis, the patient is managed according to the clinical HF pathway. Confirmation of HF diagnosis is based on Framingham's criteria[6] for clinical HF with objective evidence of structural or functional abnormality of the heart at rest.[7] The HF team, with the agreement of the attending cardiology team, will continue to supervise the management of the HF patient according to the clinical pathway. However, the patient is still under the management of the attending cardiology team, which is ultimately in charge of the management of the patient. This was an observational study. Therefore, a waiver of consent was obtained from the hospital's Institutional Review Board. Strict patient anonymity and confidentiality have been maintained.

Patients were eligible for the study if they were admitted between 1 January and 31 December 2008, with a discharge primary diagnosis of HF, and they had a previous history of HF. Patients with a new diagnosis of HF were excluded. There were no left-ventricular ejection fraction (LVEF) or serum creatinine exclusion criteria.

Patients' case records were reviewed for 1-month follow-up outcome information. If the patient had no contact with the hospital within 1 month, the study review team would telephone the patient or care giver for an update of the patient's status. One-month follow-up outcome information

included all-cause mortality, all-cause death or readmission, and heart failure readmission.

Statistics

Categorical variables are expressed as percentages and compared using the χ^2 test for analysis. Continuous variables are reported as mean±SD or median value with 25% and 75% IQR, depending on which is more clinically relevant or needed for comparison with historical studies. They are compared using the Student two-sample t test for analysis. Candidate co-variates for outcomes included those identified in univariable analysis with $p<0.1$ and those identified in previous studies to have an impact on mortality and morbidity.[8] Statistical significance was reached if $p<0.05$. All analyses were performed with the Statistical Package for the Social Sciences version 12.0 for Windows statistical software package.

RESULTS

During the enrolment period in 2008, there were 456 admissions by 373 patients for the primary diagnosis of HF. Of this group, 242 (53.1%) admissions were by 185 (49.6%) patients with a past history of HF. These 242 admissions by 185 patients constituted our study cohort of acute HF inpatients with a prior history of chronic HF.

See table 1 for the characteristics of the study population.

The median patient age was 70 years (IQR 59–78), and 36.8% were females. The Chinese, Malay and Indian composition of the cohort constituted 41.3%, 35.1% and 16.1% respectively. Common co-morbidities identified were hypertension, diabetes mellitus, hyperlipidemia, and cerebrovascular accidents.

The median LVEF was 30% (IQR 18.8–50.0%). Preserved LVEF (LVEF≥45%) and severely impaired LVEF (≤30%) were present in 35.1% and 52.1% of the cohort respectively.

Ischaemic heart disease was the aetiology in 75.6% of the HF admissions. Prior to admission, a high proportion of the patients were on appropriate anti-HF medication prescriptions.

Precipitants

Precipitants of acute HF were identified in 152 admissions (62.8%). They were not identified in 90 admissions (37.2%). Non-compliance with medications and non-compliance with fluid or diet restrictions were the precipitants of acute HF in 7.0% and 20.2% of admissions. Infections were the precipitants in 13.6% of admissions. Atrial fibrillation, poorly controlled hypertension and acute coronary syndromes were the precipitants in 5.4%, 2.5% and 2.1% of admissions respectively. Multiple precipitants were identified in 8.3% of admissions.

Outcomes

The outcomes are listed in table 1. The median length of stay was 4.0 days (IQR 2.0–6.0). The all-cause 30-day mortality, readmission, and combined mortality and readmissions were 2.1%, 28.5% and 30.6% respectively. Readmission in 30 days for HF constituted 11.2%.

There were no significant differences in patient profile between patients with identified precipitants (known precipitant group) and patients with unidentified precipitants (not known precipitant group). There was no significant difference in the prevalence of Chinese, Malays or Indians in either group (see table 2).

There were no significant differences in outcomes between the known precipitant cohort and the not known precipitant cohort (see table 3).

Table 1 Patient profile, comorbidities and outcomes

Characteristic	Frequency (%)/value
Profile	
Age	
Mean age±SD, years	68.3±12.8
Median age (IQR), years	70.0 (59–78)
Age≥65 years	162 (66.9)
Age≥80 years	43 (17.8)
Gender	
Female	89 (36.8)
Male	153 (63.2)
Ethnicity	
Chinese	100 (41.3)
Malay	85 (35.1)
Indian	39 (16.1)
Others	18 (7.4)
Cardiac function	
Mean left-ventricular ejection fraction±SD, %	34.0±17.5
Median left-ventricular ejection fraction (IQR), %	30.0 (18.8–50)
left-ventricular ejection fraction ≥45%	85 (35.1)
Left-ventricular ejection fraction ≤30%	126 (52.1)
Comorbidities	
Hypertension	198 (81.8)
Diabetes mellitus	155 (64.0)
Hyperlipidaemia	152 (62.8)
Cerebrovascular accident	28 (11.6)
Asthma or chronic obstructive pulmonary disease	32 (13.2)
Smoker	46 (19.0)
Laboratory values, mean±SD	
Serum creatinine, mmol/l	144.8±78.3
Na, mmol/l	136.3±4.1
Urea, mmol/l	9.0±5.7
Hb, g/dl	12.4±2.1
Aetiology	
Ischaemic heart disease	183 (75.6)
Hypertensive heart disease	8 (3.3)
Valve disease	17 (7.0)
Others	28 (11.6)
Not determined	6 (2.5)
Precipitant	
Non-compliance with	
Medications	17 (7)
Fluid or diet restrictions	49 (20.2)
Infection	33 (13.6)
Cardiac	
Acute coronary syndrome	5 (2.1)
Atrial fibrillation	13 (5.4)
Hypertension	6 (2.5)
Anaemia	5 (2.1)
Multiple precipitants	20 (8.3)
Others	2 (0.8)
Unable to determine	90 (37.2)
Outcomes	
Length of stay	
Mean±SD, days	4.7±4.0
Median (IQR), days	4.0 (2.0–6.0)
30-day outcomes	
All-cause death	5 (2.1)
All-cause readmission	69 (28.5)
All-cause death or readmission	74 (30.6)
Readmission for heart failure	27 (11.2)

Table 2 Known precipitants versus not-known precipitants characteristics

	Known PPT (n=152) frequency (%)	Not known PPT (n=90) frequency (%)	p Value
Age (years), mean±SD	67.4±13.3	70.0±11.9	0.13
Gender			
Female	51 (33.6)	38 (42.2)	0.21
Male	101 (66.4)	52 (57.8)	
Ethnicity			
Chinese	61 (40.1)	39 (43.3)	
Malay	54 (35.5)	31 (34.4)	
Indian	24 (15.8)	15 (16.7)	
Diabetes mellitus	94 9 (61.8)	61 (67.8)	0.41
Hypertension	122 (80.3)	76 (84.4)	0.49
Hyperlipidaemia	91 (59.9)	61 (67.8)	0.27
Cerebrovascular accident	18 (11.8)	10 (11.1)	1.00
Asthma or chronic obstructive pulmonary disease	21 (13.8)	11 (12.2)	0.85
Left-ventricular ejection fraction, %±SD	33.8±17.4	34.4±17.8	0.80
Serum creatinine, mmol/l			
±SD	142.2±80.9	149.2±74.0_	0.51
Na, mmol/l±SD	136.0±4.3	136.9±3.6	0.09
Urea, mmol/l±SD	8.80±6.1	9.30±4.9	0.51
Hb, g/dl±SD	12.5±2.2	12.2±1.8	0.22
Length of stay, days±SD	4.6±3.4	4.9±4.8	0.51

There were no significant differences in outcomes and the precipitant types-combined non-compliance with medications, fluid and diet restrictions, infection and atrial fibrillation (see table 4).

DISCUSSION

To date, there are no studies on the precipitants of acute HF in Asian cohorts. Publications on this topic in urban western populations are sparse.[9] The diagnosis criterion of HF in this study is strict. There is a definitive criterion for the diagnosis of HF, and there is a review of diagnosis by two teams, the primary cardiology team and the HF team. Thus, we propose that this study reveals an accurate profile of the precipitants of well-defined acute HF in our urban multiethnic Asian population with a past history of HF in a busy tertiary hospital.

The known HF cohort in this study is 53.1% of admissions. This is lower than the US-based Acute Decompensated Heart Failure National Registry[10] and EuroHeart Failure[11] registries figures of 75% and 65% respectively.

The mean age of this cohort at 68.3±12.8 years is younger than that of large acute HF registries in the US and Europe at 75 years and 71 years respectively, and similar to the mean age of 66±12 years observed in a previous Asian study by Lee *et al*.[12]

There were higher proportions of ethnic Malays and Indians in our HF cohort at 35.1% and 16.1%, respectively, compared with the general population at 13.9% and 7.9% respectively. The proportion of ethnic Chinese in the HF at 41.3% was lower than their proportion in the general population at 76.8%.[13] This ethnic composition is similar to that of a previous study in our institution[14] and to another study by Seow *et al* in the western part of Singapore.[15] More studies are needed to evaluate whether this observation is due to geographical demographics or cardiac pathology with genetic–social underpinnings.

The high prevalence of older people, patients with ischaemic heart disease, hypertension and diabetes mellitus in this cohort is consistent with the known epidemiology of HF.[1]

The proportion of patients with preserved LVEF is lower at 35.1% compared with 40% and 54% in the Acute Decompensated Heart Failure National Registry and EuroHeart Failure registries respectively. This is likely due to a stricter criterion for HF diagnosis described earlier.

Precipitants of acute HF were identified in 152 admissions (62.8%). They were not identified in 90 admissions (37.2%) (see table 1). This is similar to an analysis on precipitants of acute HF in the large US-based Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMISE-HF) cohort.[16] In that study, the precipitants of acute HF were not identified in 38.7% of admissions. In a German study by Michalsen *et al*,[17] with a study population of 179 patients with similar enrolment criteria to those in this study (patients with past history of HF) precipitants were not identified in only 14.5% of admissions.

Our study revealed that non-compliance issues accounted for 27.2% of precipitants. Non-compliance with medications and non-compliance with fluid or diet restrictions were the precipitants of acute HF in 17 (7.0%) and 49 (20.2%) admissions. This observation is similar to that in the Canadian study by Tsuyuki *et al*[18] where 22% of precipitants were due to non-compliance with diet restrictions. However, in the German study by Michalsen *et al*,[17] non-compliance with medications or diet constituted 41.9% of the precipitants. In an Italian study by Opasich *et al*[19] on precipitants in known HF patients, non-compliance was the precipitant in 15% of decompensation. In the larger US study on precipitants of hospital admissions for HF in the OPTIMISE-HF cohort by Fonarow *et al*,[16] non-compliance issues accounted for 14.1% of precipitants, cardiac issues accounted for 38.9% of precipitants, and pneumonia/respiratory process accounted for 15.3% of precipitants. However, this study by Fonarow *et al* also included new HF cases.

There could be several reasons for this significant prevalence of non-compliance as precipitants of acute HF in this study.

Table 3 Known versus not-known precipitants and outcomes

Outcome	30-day death	30-day death or readmission	30-day readmission for heart failure
Known precipitants (n=152)	4 (2.6)	44 (28.9)	14 (9.2)
Not-known precipitants (n=90)	1 (1.1)	30 (33.3)	13 (14.4)
p Value	0.65	0.48	0.21

Table 4 Precipitant (PPT) types and outcomes

Precipitant/outcome	30-day death	30-day death or readmission	30-day readmission for heart failure
Non-compliance PPT (n=87)	1 (1.1)	26 (29.9)	8 (9.2)
Not non-compliance PPT (n=155)	4 (2.6)	48 (31.0)	19 (12.3)
p Value	0.66	0.89	0.53
Infection as PPT (n=38)	2 (5.3)	13 (34.2)	5 (13.2)
Not infection as PPT (n=204)	3 (1.5)	61 (29.9)	22 (10.8)
p Value	0.18	0.7	0.59
Atrial fibrillation as PPT (n=15)*	1 (6.7)	3 (20.0)	0 (0)
Not atrial fibrillation as PPT (n=227)	4 (1.8)	71 (31.3)	27 (11.9)
p Value	0.28	0.56	0.39

*This includes the two cases of atrial fibrillation in the multiple precipitant groups.

Non-compliance with medications and dietary restrictions are known common precipitants in acute HF.[9] Second, in this study cohort, there is a very high prevalence of appropriate anti-HF medication prescription; thus non-compliance issues would assume a higher proportion of identified precipitant of acute HF admissions.

The variation in prevalence of non-compliance as a precipitant in acute HF could be due to different study cohorts in different environments: USA,[16] Germany,[17] Italy[19] and, in this study, Singapore.

Infections were the precipitants in 33 (13.6%) admissions. These were mainly respiratory and urinary-tract infections. This result is similar to previous US studies[20 21] on precipitants in acute HF, which ranged from 12% to 16%. More studies are needed on infectious precipitants in HF decompensation to assess if they are preventable.

Cardiac precipitants accounted for 10.0% of acute HF decompensation. This is low compared with the German study by Michalsen *et al*[17] (25.1%) and the Italian study by Opasich *et al*[19] (38%). It could be that our study cohort is already optimally treated medically. It has a very high prevalence of prescription of anti-HF medications.

The precipitants were not identified in 90 admissions (37.2%). This could be for several reasons. For example, it could be due to the progression of the disease, which was not identified as such. It could be due to a need for greater vigour in looking for precipitants by the clinicians. Language barrier is another likely reason for under-diagnosing non-compliance. The medical interview is crucial in diagnosing non-compliance. Many of the older Chinese and Indian patients could only converse in dialects: predominantly Hokkien, Cantonese and Teowchew for the Chinese, Javanese and Madura for Malays, and Malayam, Hindustani and Punjabi for the Indians. These dialects are not commonly spoken fluently by our younger clinicians.

There were no significant differences in patient profiles between patients with identified precipitants (known precipitant group) and patients with unidentified precipitants (Not Known Precipitant group).

There were no significant differences in outcomes between the Known Precipitant cohort and the Not Known Precipitant cohort. This is likely due to non-compliance, rather than cardiac problems being the major precipitant of acute HF.

There were no significant differences in outcomes and the different precipitants: combined non-compliance with medications, fluid and diet restrictions, infection and atrial fibrillation.

This observation contrasts with the study by Fonarow *et al* in the OPTIMISE-HF cohort.[16] In that study, precipitating factors were found to be independently associated with clinical outcomes. However, in the OPTIMISE-HF cohort, both new and old HF cases were included in the study cohort. In this paper, only patients with a past history or diagnosis of HF were included.

This study has several strengths. The diagnosis of HF is defined and rigorous. It has a strict criterion for HF, reviewed by the attending cardiology team, and an experienced HF team. It is not merely based on discharge diagnosis codes. This study attempts to look at the precipitant of acute HF in a real-world frontline situation, and not in a more ideal setting of a clinical trial, where enrolled patients may not reflect the patient profile in the 'real' world.

This study has several limitations. It is a small retrospective observational study in a single tertiary centre. Thus, it has the usual limitations that are associated with small, retrospective observational studies. The study sample size is small, as patients were recruited in one calendar year in 2008. The clinical diagnosis of comorbidities was carried out by the attending teams based on standard clinical criteria, and not by a central authority. This may potentially give rise to errors. There was no structured protocol to obtain information on non-compliance while taking the medical history. This was dependent on the individual clinicians' skill and enthusiasm. A structured interview of patients is a good way to assess compliance[22] and may have increased the pick-up rate of non-compliance.

In conclusion, this study reveals that in a multiethnic Asian, well-defined HF cohort, residing in an urban Asian society, non-compliance (to medication, diet and fluid restriction) is a major precipitant of acute decompensated HF inpatients with a prior history of HF, and that precipitants are not determined in about a third of admissions. There were no significant associations between the different types of precipitants and early 30-day outcomes. Greater efforts are needed to search for a patient's precipitant of acute HF. We need to do more to improve patient compliance so as to improve clinical outcomes in HF.

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