Outcomes and predictors of one-year mortality in patients hospitalized with Acute Heart Failure

Koravich Lorlowhakarn a, Suchapa Arayakarnkul a, Angkawipa Trongtorsak a, Thiratest Leesutipornchai a, Jakrin Kewcharoen a, Supanee Sinphurmsukskul b, Sarawut Siwamogsatham a,e, Sarinya Puwanant a,d, Aekarach Ariyachaipanich b,c,*

a Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
b Excellent Center for Organ Transplantation, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand
c Division of Cardiovascular Medicine, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
d Cardiac Center, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Pathum Wan, Bangkok, Thailand
e Chula Clinical Research Center (ChulaCRC), Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

ARTICLE INFO
Keywords:
Acute heart failure
Registry
Mortality
Predictor
Thailand

ABSTRACT

Background: Registries of patients hospitalized with acute heart failure (AHF) provided useful description of characteristics and outcomes. However, a contemporary registry which provides sufficient evidence on outcomes after discharge is needed.

Objective: The study aims to identify 1-year clinical outcomes and prognostic predictors of patients hospitalized with AHF.

Method: This is a retrospective registry which enrolled patients who were hospitalized due to a principal diagnosis of AHF in a tertiary care center in Thailand between July 2017 and June 2019. Baseline characteristics and hospital courses between the deceased patients and the survivors at 1 year were compared. Prognostic predictors for 1-year mortality were analyzed using Cox regression model.

Results: A total of 759 patients were enrolled (mean age of 68.9 ± 15 years, 49.8% men, mean ejection fraction of 47.1 ± 19.2%, 55.7% heart failure reduced ejection fraction (HFrEF)). Among these, 40.7% had no history of heart failure. The in-hospital and 1-year mortality was 5.8% and 21.5%, respectively. Patients with HFrEF had lower 1-year mortality compared to those without (HR = 0.57, p = 0.04). Age ≥ 70 years, the history of heart failure, prior heart failure hospitalization, cerebrovascular accident (CVA), reactive airway disease, cancer, length of stay > 10 days and NT-proBNP ≥ 10,000 pg/mL were associated with higher 1-year mortality (p < 0.05). The multivariate analysis showed age, CVA and NT-proBNP were independent predictors.

Conclusion: Patients with AHF had high mortality after discharge. Patients with poor prognostic predictors, such as elderly, may benefit from continuous care. The study is the most recent registry of patients with AHF in Thailand.

1. Introduction

For decades, heart failure (HF) has been a major health problem globally with an estimated prevalence of more than 37.7 million individuals worldwide [1]. In the USA, over 5.7 million people live with HF and approximately 915,000 patients are newly diagnosed with HF each year. Annually, approximately 65,000 people die from heart failure which cause over 30.7 billion dollars burden on the health care system [2].

Over the past 30 years, most randomized controlled trials (RCT) have been focusing on chronic HF patients. Evidence from RCT in AHF is significantly less partially due to inhomogeneous phenotypes of patients with AHF, causing challenges in conducting RCTs on these patients [3]. More recently, real word evidence from clinical registries is an important tool for advancing care and the majority of AHF studies are based on clinical registries. The current knowledge of AHF is obtained from multiple AHF registries have succeeded in providing comprehensive
outcomes of AHF patients [4]. In the USA, the largest AHF registry, the Acute Decompensated Heart Failure National Registry (ADHERE), enrolled a total of 105,388 patients hospitalized with acute decompensated heart failure. The registry reported the in-hospital mortality of 4% which increased to 10.6% for patients who received care in an intensive care unit [6]. Another large registry in Europe, the EuroHeart Failure Survey II (EHFS II), reported the in-hospital mortality of 6.7% and the 3-month mortality of 8.2% [7,8]. In Asia, the Korean Heart Failure Registry (KorHF) reported the in-hospital mortality of 6.4% [9,10]. These registries demonstrated that patients with AHF were associated with very high short-term mortality.

However, several registries reported very high mortality in patients with AHF even after hospitalization. Data from the United Kingdom demonstrates in-hospital mortality rates of around 10% with 1-year mortality of 30% in patients hospitalized with AHF [4]. In Asia, the Korean Acute Heart Failure Registry (KorAHF) reported the 1-year mortality of as high as 18.2% [10]. Thus, despite several medical therapies have been proven to improve survival in patients with HF over the past decades, the mortality after AHF hospitalization is still very high. A large number of literatures have identified post-discharge mortality predictors and proposed several predictive models for patients with AHF based on the past registries [11-13]. Due to the significant advancement of HF management, a contemporary registry is needed to provide evidence on clinical outcomes and prognostic predictors in patients hospitalized for AHF, especially in Thailand where the evidence relies on a registry conducted over a decade ago.

Therefore, this study is the most recent clinical registry of patients hospitalized for AHF in Thailand that aims to evaluate 1-year outcomes and identify independent prognostic predictors for 1-year mortality in AHF patients.

2. Methods

2.1. Criteria and enrolment

This is a retrospective registry which enrolled patients age ≥18 years who were hospitalized due to a principal diagnosis of AHF in a tertiary care center in Thailand between July 2017 and June 2019. The diagnosis of AHF was identified by International Classification of Diseases, Tenth Revision (ICD-10) and confirmed by the Framingham criteria. The accessibility to electronic medical record (EMR) and study design were approved by institutional review board and ethics committee before beginning the registry.

The patients were admitted to the medical wards or the critical care unit if needed and clinically managed by internists and internal medicine residents. Cardiology service including advanced heart failure cardiologists were consulted as needed. The patients were managed according to judgement of the providing physicians who were familiar with the international and local guidelines including 2013 ACCF/AHA Guideline for the Management of Heart Failure [14,15], 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure [16], and Heart Failure Council of Thailand (HFCT) 2019 Heart Failure Guideline: Acute Heart Failure [17].

2.2. Data collection

The clinical information of the patients was obtained from EMR using case report form (CRF). Data including patient characteristics, comorbidities, clinical presentations, initial investigations, hospital courses, medications at admission and discharge, in-hospital treatments, procedures, discharge status and clinical outcomes was collected.

2.3. Outcome

Clinical outcomes included length of stay and in-hospital mortality. Every patient’s EMR was reviewed up to 1 year from discharge. Post-discharge outcomes included 30-day and 1-year mortality and rehospitalization. If outcome information is not available in EMR, the patients were contacted by telephone.

2.4. Statistical analysis

The continuous variables were reported in means ± standard deviation and compared using independent sample t-test. The categorical variables were expressed in percentages and compared using Chi-square test. Survival analysis was conducted using the Kaplan-Meier method for survival function of 1-year mortality. The differences in mortality between subgroups were tested using the log-rank test. Predictors of 1-year mortality from discharge were identified using univariate and multivariate Cox proportional hazard regression model. The Statistical Package for the Social Sciences (SPSS) version 28.0 software (IBM Corp. Armonk, NY) was used to analyze all data.

We compared baseline characteristics, hospital courses and medications between the deceased patients and the survivors at discharge and 1 year follow-up period. All potential prognostic predictors of interest for 1-year mortality were analyzed for univariate Cox regression model. The criterion for multivariate Cox regression analysis were for those variables which exhibited p-value < 0.2. As medications, devices, investigations and procedures were not considered as potential risks, these variables were not included in Cox proportional hazard regression model.

3. Results

3.1. Patient characteristics

A total of 759 patients hospitalized with the diagnosis of AHF were enrolled. The mean age was 68.9 ± 15 years and 373 patients (49.8%) were men. Among these, 59.3% had a previous history of HF and 35.7% had a history of prior HF hospitalization. Left ventricular ejection fraction (LVEF) had been documented in 474 patients (62.5%) with the mean LVEF of 47.1 ± 19.2%. Heart failure reduced ejection fraction (HFrEF), heart failure mildly reduced ejection fraction (HfmrEF) and heart failure preserved ejection fraction (HfPEF) were accounted for 55.7%, 9.9% and 34.4% of patients with documented LVEF, respectively.

The common comorbidities were hypertension (67.1%), dyslipidemia (50.1%), diabetes mellitus (49.8%) and coronary artery disease (40.7%).

The averages of initial laboratory results were hemoglobin 11 g/dL, blood urea nitrogen (BUN) 32.5 mg/dL, creatinine 1.8 mg/dL and sodium 135.2 mEq/L. The mean N-terminal pro B-type natriuretic peptide (NT-proBNP) level was 10,711.2 pg/mL.

Medications were the patients taking included beta blockers (BB), angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blocker (ARB), mineralocorticoid receptor antagonists (MRA) and loop diuretics. BB, ACEI or ARB and MRA taken at admission were 53.4%, 36.7% and 14% respectively. Implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy (CRT) were used in 3.2% and 2.8% of the patients, respectively.

The baseline characteristics and medication prior to admission are summarized in Table 1.

3.2. Hospital course and patient management

The mean length of stay (LOS) was 11.9 days. During hospitalization, electrocardiogram and chest radiography were performed in almost all patients. Echocardiography was done in only half of the patients.

Intravenous inotropes were used in 212 patients (27.9%), including dobutamine, milrinone, levosimendan, epinephrine and norepinephrine. Mechanical ventilation was required for 21.6%. Renal replacement therapy was initiated in 5.9% of the patients. Of all patients, 19.1%
The overall in-hospital mortality was 5.8%. In respect of clinical outcomes in patients who survived to discharge, the 30-day and 1-year mortality was 3.1% and 21.5%, respectively (Fig. 1). The 30-day and 1-year rehospitalization was 24.2% and 63.9%. The 1-year composite outcome of mortality and rehospitalization was 66.6%.

3.4. Comparison between the survivors and the deceased patients at discharge and 1 year follow-up period

As shown in Table 1-2, baseline characteristics, comorbidities, laboratory results, hospital courses and medications were compared between the survivors and the deceased patients at discharge and 1 year follow-up period. The deceased patients at discharge and 1 year were significantly older and had the history of HF (p < 0.001 all). There were also significant differences in subtypes of HF between the deceased patients at discharge and 1 year (HFpEF 44.4% vs 60.2%, HFmrEF 11.1% vs 9.4%, HfPeF 44.4% vs 30.1%), despite there was no difference in the mean LVEF between groups. There were no differences in comorbidities except for chronic kidney disease, which was likely seen in the in-hospital deceased group, and cerebrovascular accident (CVA) also significant differences in subtypes of HF between the deceased patients at discharge and 1 year and the survivors at 1 year (HFpEF 44.4% vs 60.2%, HFmrEF 11.1% vs 9.4%, HfPeF 44.4% vs 30.1%), despite there was no difference in the mean LVEF between groups. There were no differences in comorbidities except for chronic kidney disease, which was likely seen in the in-hospital deceased group, and cerebrovascular accident (CVA) and reactive airway disease (RAD), which were likely seen in the deceased patients at 1 year.

Systolic and diastolic blood pressure were lower in the deceased patients and the survivors at 1 year (Systolic and diastolic blood pressure were lower in the deceased patients and the survivors at 1 year (p < 0.001 all). There were also significant differences in subtypes of HF between the deceased patients and the survivors at 1 year (HFpEF 44.4% vs 60.2%, HFmrEF 11.1% vs 9.4%, HfPeF 44.4% vs 30.1%), despite there was no difference in the mean LVEF between groups. There were no differences in comorbidities except for chronic kidney disease, which was likely seen in the in-hospital deceased group, and cerebrovascular accident (CVA) and reactive airway disease (RAD), which were likely seen in the deceased patients at 1 year.

Systolic and diastolic blood pressure were lower in the deceased patients. In terms of laboratory values, the deceased patients were hyponatremic and had a lower level of serum albumin. In contrast, BUN, NT-proBNP and hs-Tropl levels were significantly higher compared to the survivors. During hospitalization, mechanical ventilation, renal replacement therapy, advanced cardiac life support, intravenous

required intensive care unit admission.

Medications taken at discharge were 48.5% BB, 26.9% ACEI or ARB, 12.3% MRA and 75.7% loop diuretics.

Hospital courses and medications at discharge are summarized in Table 1-2.

### 3.3. Clinical outcomes

The overall in-hospital mortality was 5.8%. In respect of clinical outcomes in patients who survived to discharge, the 30-day and 1-year mortality was 3.1% and 21.5%, respectively (Fig. 1). The 30-day and 1-year rehospitalization was 24.2% and 63.9%. The 1-year composite outcome of mortality and rehospitalization was 66.6%.

| Table 1 | Comparison of baseline characteristics and medication at admission between the deceased patients and the survivors at 1 year from admission. |
|---------|------------------------------------------------------------------------------------------------------------------------------------|
| **Total** | **Dead in hospital** | **Survive to discharge** | **Dead at 1 year** | **Survive at 1 year** |
| n = 759 (%) | n = 44 (%) | n = 715 (%) | n = 154 (%) | n = 561 (%) |
| **Baseline characteristics** | | | | |
| Age (years) | 68.9 ± 15 | 75.5 ± 14.6 | 68.4 ± 14.9 | 71.2 ± 14.5 | 67.77 ± 15.0 | 0.004 |
| Male | 373 (49.8) | 25 (56.8) | 348 (49.4) | 80 (52.3) | 268 (46.8) | 0.41 |
| LVEF (%) | 47.1 ± 19.2 | 39.7 ± 22.1 | 47.5 ± 19.0 | 0.04 | 46.9 ± 48.6 | 47.7 ± 19.1 | 0.39 |
| **Known ejection fraction** | 474 (62.5) | | | |
| **HF subtypes** | | | | |
| HFrEF | | | | |
| HfmrEF | | | | |
| HfPeF | | | | |
| **Device Therapy** | | | | |

### Table 1

**Comparison of baseline characteristics and medication at admission between the deceased patients and the survivors at 1 year from admission.**

| Medication at Admission | p-value | p-value |
|-------------------------|---------|---------|
| Systolic blood pressure (mmHg) | 0.001 | 0.006 |
| Diastolic blood pressure (mmHg) | 0.001 | 0.006 |
| Heart rate (bpm) | 0.001 | 0.006 |
| Hemoglobin (g/dL) | 0.001 | 0.006 |
| Serum sodium (mEq/L) | 0.001 | 0.006 |
| BUN (mg/dL) | 0.001 | 0.006 |
| Serum creatinine (mg/dL) | 0.001 | 0.006 |
| Albumin (g/dL) | 0.001 | 0.006 |
| NT-proBNP (pg/mL) | 0.001 | 0.006 |
| hs-Tropl I (ng/L) | 0.001 | 0.006 |

### 3.4. Comparison between the survivors and the deceased patients at discharge and 1 year follow-up period

As shown in Table 1-2, baseline characteristics, comorbidities, laboratory results, hospital courses and medications were compared between the survivors and the deceased patients at discharge and 1 year follow-up period. The deceased patients at discharge and 1 year were significantly older and had the history of HF (p < 0.001 all). There were also significant differences in subtypes of HF between the deceased patients and the survivors at 1 year (HFpEF 44.4% vs 60.2%, HFmrEF 11.1% vs 9.4%, HfPeF 44.4% vs 30.1%), despite there was no difference in the mean LVEF between groups. There were no differences in comorbidities except for chronic kidney disease, which was likely seen in the in-hospital deceased group, and cerebrovascular accident (CVA) and reactive airway disease (RAD), which were likely seen in the deceased patients at 1 year.

Systolic and diastolic blood pressure were lower in the deceased patients. In terms of laboratory values, the deceased patients were hyponatremic and had a lower level of serum albumin. In contrast, BUN, NT-proBNP and hs-Tropl levels were significantly higher compared to the survivors. During hospitalization, mechanical ventilation, renal replacement therapy, advanced cardiac life support, intravenous

required intensive care unit admission.

Medications taken at discharge were 48.5% BB, 26.9% ACEI or ARB, 12.3% MRA and 75.7% loop diuretics.

Hospital courses and medications at discharge are summarized in Table 1-2.

### 3.3. Clinical outcomes

The overall in-hospital mortality was 5.8%. In respect of clinical outcomes in patients who survived to discharge, the 30-day and 1-year mortality was 3.1% and 21.5%, respectively (Fig. 1). The 30-day and 1-year rehospitalization was 24.2% and 63.9%. The 1-year composite outcome of mortality and rehospitalization was 66.6%.
inotrope use were highly seen among the deceased patients during hospitalization but were not different between the 1-year deceased and survivors.

At discharge, loop diuretics were likely to be prescribed in the deceased patients at 1 year period. There were no differences in neurohormonal blocking agents including BB, ACEI or ARB nor MRA prescribed at discharge.

### 3.5. Prognostic predictors

Table 3 shows unadjusted mortality for single predictors and adjusted mortality for independent predictors of 1-year mortality in multiple Cox regression model. Univariate Cox regression analysis revealed that age $\geq$ 70 years, the history of HF and prior HF hospitalization, CVA, cancer, RAD, LOS $>$ 10 days and NT-proBNP $\geq$ 10,000 pg/mL were associated with higher 1-year mortality ($p < 0.05$). The worst prognosis was associated with the history of HF with the hazard ratio (HR) of 2.76 ($p < 0.001$).

Multivariate analysis revealed that age, CVA and NT-proBNP were independent predictors for 1-year mortality. Moreover, patients with HFrEF independently had lower mortality compared to HFpEF (HR = 0.57, $p = 0.02$). Surprisingly, hypertension independently showed protective effect on 1-year survival (HR = 0.42, $p = 0.003$).

### 3.6. Time-to-event analysis

The survival curves of patients hospitalized with AHF are shown in Fig. 2. The overall survival curve was shown in figure A. The survival curves between subgroups were shown in figure B-F. In every subgroup, the curves started to separate clearly before 3 months from discharge. Among patients with different HF subtypes, the survival rates were significantly different and the curves separated at less than a month. HFpEF had higher mortality compared to HFrEF with the mortality rates of 34.2% vs 20.6% at 1 year ($p = 0.005$). Hypertension showed protective effect in 1-year survival (mortality 19.2% vs 26.3%, $p = 0.02$). The patients with and without CVA showed comparable short-term survival, but the 1-year mortality rates were significantly higher in the patients with CVA (32.4% vs 20.7%, $p = 0.003$).

*Fig. 1.* The in-hospital, 30-day and 1-year mortality of patients hospitalized with acute heart failure.

### Table 2

Comparison of hospital courses and medications at discharge between the deceased patients and the survivors at discharge and 1 year follow-up period.

| Investigation | Total n = 759 (%) | Dead in hospital n = 44 (%) | Survive to discharge n = 715 (%) | p-value | Dead at 1 year n = 154 (%) | Survive at 1 year n = 561 (%) | p-value |
|---------------|------------------|-----------------------------|---------------------------------|---------|--------------------------|-------------------------------|---------|
| Electrocardiogram | 742 (97.8) | 42 (95.5) | 700 (97.9) | 0.29 | 150 (97.4) | 550 (98) | 0.63 |
| Chest radiography | 757 (99.7) | 44 (100) | 713 (99.7) | 0.73 | 153 (99.4) | 560 (99.8) | 0.33 |
| Echocardiography | 435 (57.3) | 25 (56.8) | 410 (57.3) | 0.95 | 85 (55.2) | 325 (57.9) | 0.54 |
| Coronary angiography | 98 (13) | 3 (6.8) | 95 (13.3) | 0.21 | 22 (14.3) | 73 (13.1) | 0.70 |
| Right heart catheterization | 49 (6.5) | 5 (11.4) | 44 (6.2) | 0.18 | 11 (7.1) | 33 (5.9) | 0.58 |
| Procedure | n (%) | n (%) | n (%) | p-value | n (%) | n (%) | p-value |
| Mechanical Ventilation | 164 (21.6) | 30 (68.3) | 134 (18.7) | <0.001 | 37 (24) | 97 (17.3) | 0.06 |
| IABP and other MCS | 15 (2) | 3 (6.8) | 12 (1.7) | 0.02 | 2 (1.3) | 10 (1.8) | 0.68 |
| RRT | 45 (5.9) | 11 (25) | 34 (4.8) | <0.001 | 6 (3.9) | 28 (5) | 0.57 |
| ACLS | 17 (2.2) | 13 (29.5) | 4 (0.6) | <0.001 | 0 (0) | 4 (0.7) | 0.29 |
| ICU stay | 145 (19.1) | 19 (43.2) | 126 (17.6) | <0.001 | 22 (14.3) | 104 (18.5) | 0.22 |
| Intravenous medication | n (%) | n (%) | n (%) | p-value | n (%) | n (%) | p-value |
| Furosemide | 712 (93.8) | 41 (93.2) | 671 (93.8) | 0.86 | 148 (96.1) | 523 (93.2) | 0.19 |
| Nitroglycerine | 235 (31) | 11 (25) | 224 (31.3) | 0.38 | 38 (24.7) | 186 (33.2) | 0.04 |
| Dobutamine | 81 (10.7) | 16 (36.4) | 65 (9.1) | <0.001 | 20 (13) | 45 (8) | 0.06 |
| Milrinone | 27 (3.6) | 4 (9.1) | 23 (3.2) | 0.04 | 5 (3.2) | 18 (3.2) | 0.98 |
| Levosimendan | 2 (0.9) | 1 (6.3) | 1 (0.5) | 0.02 | 0 (0) | 1 (0.5) | 0.71 |
| Norepinephrine | 214 (7.2) | 10 (45.5) | 14 (4.5) | <0.001 | 4 (8.5) | 10 (3.8) | 0.15 |
| Epinephrine | 14 (4.2) | 9 (40.9) | 5 (1.6) | <0.001 | 2 (4.3) | 3 (1.1) | 0.11 |

Medication at Discharge

| n (%) | n (%) | n (%) | p-value |
| Loop diuretics | 569 (75.7) | 135 (87.7) | 434 (77.1) | 0.004 |
| BB | 351 (48.5) | 68 (45.3) | 282 (52.6) | 0.12 |
| ACEI or ARB | 194 (26.9) | 37 (24.7) | 157 (29.5) | 0.25 |
| ARNI | 6 (0.8) | 0 (0) | 6 (1.1) | 0.20 |
| MRA | 92 (12.3) | 121 (34.1) | 71 (12.8) | 0.80 |

Table abbreviations: IABP: intra-aortic balloon pump, MCS: mechanical circulatory support, RRT: renal replacement therapy, ACLS: advanced cardiac life support, ICU: intensive care unit, BB: beta blocker, ACEI: angiotensin converting enzyme inhibitors, ARB: angiotensin receptor blocker, ARNI: angiotensin receptor-neprilysin inhibitor, MRA: mineralocorticoid receptor antagonists
hypertension, dyslipidemia, diabetes mellitus and coronary heart disease, the mean age was older but the common comorbid diseases were management across registries are shown in Table 4. In the presented study, the mean age was older but the common comorbid diseases were hypertension, dyslipidemia, diabetes mellitus and coronary heart disease were highest among registries, although the lowest in-hospital mortality of 4% was reported in the US [6]. The utilization of medical treatments was more optimal in western countries compared to Asia [6,7,10,24]. However, this may result from the higher percentages of HFpEF patients in the western registries. Therefore, prioritization of optimal medical treatment in HF patients is highly recommended among physicians around the world.

During hospitalization, chest radiography and electrocardiogram were performed in almost all AHF patients across registries. The EHFS II registry reported much higher use of echocardiography and coronary angiography in Europe compared to the presented registry, in which the use was comparable to the Thai ADHERE and the US ADHERE registry [7,18,24]. Interestingly, the EHFS II registry reported the highest ICU stay percentages of 51% with the mechanical ventilation rate of only 5.1% compared to the ICU stay percentages of 19.1% and the mechanical ventilation rate of 21.6% reported in the presented registry [7]. This may indicate that more medical resources were used for AHF patients in Europe compared to Asia. Moreover, the significantly higher rates of mechanical ventilation in the presented study as well as the Thai ADHERE registry compared to the western registries [6,7,10,24] were possibly due to unfamiliarity to the use of non-invasive ventilation and high incidence of advanced cardiac life support performed in Thailand.

### 4. Discussion

The presented registry demonstrated that age, CVA and NT-proBNP ≥ 10,000 pg/mL were independently associated with higher 1-year mortality after discharge in patients hospitalized for AHF in Thailand. This registry is the most recent clinical registry of patients hospitalized for AHF in Thailand over the past decade.

Three largest HF registries were conducted in the USA and Europe [6–8,18–21]. In Asia, there are limited numbers of heart failure registries [5]. A few nationwide HF registries were conducted in Asia [9,10,22,23]. In Thailand, the first national heart failure registry published a decade ago was the Thai Acute Decompensated Heart Failure Registry (Thai ADHERE) registry which enrolled patients with the discharge diagnosis of HF excluding patients with cardiogenic shock [24]. The presented study is the most recent AHF registry in Thailand which identified patients with the diagnosis of AHF and demonstrated post-discharge outcomes. The description of patient characteristics and management across registries are shown in Table 4. In the presented study, the mean age was older but the common comorbid diseases were hypertension, dyslipidemia, diabetes mellitus and coronary heart disease which are comparable to the Thai ADHERE registry. The LVEF was assessed in 62.5% of enrolled patients prior to admission and the percentage of patients with HFrEF was 55.7%, which is higher than reported in the previous registry. However, the mean systolic blood pressure at admission in the presented registry is lowest among the past registries as the presented study is one of a few registries that included all patients with the diagnosis of AHF regardless of shock.

### 4.1. Patient characteristics

The profile of patients in the presented registry are comparable to the Korean registry. Our registry reported that 67.1% of the patients had hypertension as a comorbid condition, which is higher than reported in the KorAHF registry but comparable to 60–70% in the western registries [6,7,9,10,24]. The KorAHF registry revealed that fewer patients had a history of HF compared to our study [10]. Even though the percentage of patients with HFrEF was comparable, the use of ACEIs and MRAs in Korea was higher than reported in Thai registries [10,24].

In the western registries, the mean age was older and more patients had poor LVEF (LVEF ≤ 40–45%), but the common comorbidities were similar to the presented registry [6,7]. The US ADHERE revealed the percentages of patients who had hypertension and coronary heart disease were highest among registries, although the lowest in-hospital mortality of 4% was reported in the US [6]. The utilization of medical treatments was more optimal in western countries compared to Asia [6,7,10,24]. However, this may result from the higher percentages of HFpEF patients in the western registries. Therefore, prioritization of optimal medical treatment in HF patients is highly recommended among physicians around the world.

The presented registry demonstrated that age, CVA and NT-proBNP ≥ 10,000 pg/mL were independently associated with higher 1-year mortality and 1-year mortality. Clinical outcomes in AHF patients across registries were shown in Table 5. In some recent registries, outcomes from discharge were reported with the follow-up period ranging from 1 [2], 3 [19,26], and 6 to 12 months [2,8,27].

The presented registry showed the longest length of stay among registries with the mean duration of 11.9 days and reported the in-hospital mortality of 5.8%. In the USA, the US ADHERE registry reported the mean length of stay of 4.3 days and the in-hospital mortality of 4% [6]. In Europe, the EHFS II registry reported the mean length of stay of 9 days with the very high in-hospital mortality of 6.7% [7]. In Asia, the KorAHF also reported the mean length of stay of 9 days but showed the in-hospital mortality of only 4.8% [10]. Data from Switzerland and Finland registry revealed 30-day mortality of 11%, which was very high compared to only 3.1% reported in the presented study [27]. The very high mortality in Europe supported that the European patients hospitalized with AHF were likely to be more severe than the Asian patients, despite the comparable length of stay. Therefore, the disproportion between the length of stay and the mortality seen in the Asian registries may not be explained only by the severity of AHF but also partially explained by the difference in the Asian and the Western health care system that could affect the duration of hospitalization.

Regarding data on 1-year prognosis of AHF patients, the Thai ADHERE registry demonstrated that although the patients were younger and patients with cardiogenic shock were excluded, the mortality was higher with the 30-day and 1-year mortality of 8.1% and 28% compared
to 3.1% and 21.5% reported in our registry, respectively [25]. The five-year and ten-year mortality in the Thai ADHERE registry were also very high. This could be explained by the advancement in medicine over a decade and the availability of resources that could enhance the quality of patient care in the single center tertiary care hospital registry.

The western registries demonstrated high mortality in AHF patients. The 1-year mortality of 22% and 20.5% were reported in the Atherosclerosis Risk in Communities study, a population-based study conducted in the USA [28], and the EHFS II registry, respectively [8]. Data from Switzerland and Finland registry reported very high mortality of 29% at 1 year after discharge [27]. These data reflect that even though many medications have been shown to improve survival in HF patients, the 1-year mortality remains high across various countries.

4.3. Prognostic predictors

Prognostic predictors of patients hospitalized with AHF varied across registries. The US ADHERE registry reported that the best predictor for in-hospital mortality was high blood urea nitrogen level, followed by low systolic blood pressure and high serum creatinine level [18]. In the EHFS II registry, data showed that increasing age, the history of HF, prior MI, diabetes, anemia, high creatinine, low sodium levels, lower systolic blood pressure on admission and a hospital stay longer than 1 week were independent prognostic predictors for 1-year mortality [8]. The data is consistent with the presented study as we found that the deceased at 1 year after hospitalization were older and had poorer laboratory values at admission. Thus, poorer clinical characteristics at admission may not only be concerning for higher in-hospital death but can also reflect higher mortality even after discharge. However,
hypertension was associated with better long-term survival in the presented study as well as in the EHFS II registry [8].

In terms of prognostic predictor in Thai population, the presented registry reported that age ≥ 70 years, CVA and NT-proBNP ≥ 10,000 pg/mL were independently associated with higher 1-year mortality. In the Thai ADHERE registry, independent factors predicting long-term mortality included older age, history of HF, stroke, use of cardiac electronic devices, edema, low LVEF, anemia and not receiving ACEIs or ARBs [25]. Both registries demonstrated that CVA is an independent mortality predictor in Thai patients with AHF. Although there is plenty of evidence that HF increases the incidence of CVA due to the risk of thromboembolism from LV dysfunction [29], the presented study further revealed that patients with AHF who had concomitant history of CVA are independently associated with higher mortality. Therefore, patients hospitalized for AHF, especially in Thailand, who has the history of CVA may be both associated with higher risk of recurrent CVA and higher mortality after HF hospitalization.

5. Limitation

Our study has several limitations. Firstly, this is a single center study with a relatively small sample size and enrolled only the patients who were hospitalized in the tertiary care hospital. Some patients were partially treated prior to hospitalization and referred to the hospital for further management. Therefore, the sample could not well represent the clinical characteristics of general Thai population in other hospitals.

Secondly, the data was collected from the EMR in medical wards and critical care units. Thus, it did not include the patients with milder signs and symptoms of AHF who were treated and discharged from the emergency room. Since the EMR was reviewed from a single hospital, there was lack of data on cause of death and patient readmission in the different hospitals. There was also lack of post-discharge data regarding the follow-up intensity and patient compliance in out-patient management. Moreover, almost half of the patients had no record of LVEF prior to hospitalization available on the EMR which may affect the assessment of optimal guideline-directed medical therapy among different HF subtypes.

Finally, the presented registry was conducted before the introduction of newer treatments such as angiotensin receptor blocker-neprilysin inhibitor (ARNI) and sodium glucose co-transporter type 2 (SGLT-2) inhibitors, which now have been recommended in guidelines and shown to improve survival in patients with chronic stable HF. The long-term mortality is likely to be altered with these novel treatments.

6. Conclusion

Our registry demonstrated the 30-day and the 1-year mortality of 6.7% and 22.9%, respectively. More than half of the patients had LVEF<40%. Still, there was underutilization of optimal medical treatments, including ACEIs, ARBs and MRAs, excluding BBs which were
optimally prescribed in more than half of the patients.

In terms of mortality predictors, multivariate analysis revealed that age, CVA and NT-proBNP > 10,000 pg/mL were independent predictors for 1-year mortality. Hypertension independently showed protective effects in 1-year survival. Elderly patients who have comorbidities of CVA may benefit from continuous care after AHF hospitalization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] B. Ziaieian, G.C. Fonarow, Epidemiology and aetiology of heart failure, Nat. Rev. Cardiol. 13 (6) (2016) 368–378.
[2] F. Zannad, A. Mebazaa, Y. Juilliard, A. Cohen-Solal, L. Guize, F. Alla, P. Rouge, P. Blin, M.-H. Barlet, L. Paolozzi, C. Vincent, M. Desnos, K. Samii, Clinical profile, contemporary management and one-year mortality in patients with severe acute heart failure syndromes: The EFICA study, Eur. J. Heart. Fail. 8 (7) (2006) 697–705.
[3] L.H. Lund, J. Oldgren, S. James, Registry-Based Pragmatic Trials in Heart Failure: Current Experience and Future Directions, Curr. Heart. Fail. Rep. 14 (2) (2017) 59–70.
[4] S. Kurmani, I. Squire, Acute Heart Failure: Definition, Classification and Epidemiology, Curr. Heart. Fail. Rep. 14 (5) (2017) 385–392.
[5] Y. Sakata, H. Shimokawa, Epidemiology of heart failure in Asia, Circ. J. 77 (9) (2013) 2209–2217.
[6] K.F. Adams, G.C. Fonarow, C.L. Emeram, T.H. Lejtemel, M.R. Costanzo, W. T. Abraham, R.L. Berkowitz, M. Galvao, D.P. Horton, Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE), Am. Heart. J. 149 (2) (2005) 209–216.
[7] M.S. Nieminen, D. Brutsaert, K. Dickstein, H. Drexler, F. Follath, V.-P. Harjola, M. Hochadel, M. Komajda, J. Lassus, J.L. Lopez-Sendon, P. Ponikowski, L. Tavazzi, EuroHeart Failure Survey II (EHS II): a survey on hospitalized acute heart failure patients: description of population, Eur. Heart. J. 27 (22) (2006) 2725–2736.
[8] V.-P. Harjola, F. Follath, M.S. Nieminen, D. Brutsaert, K. Dickstein, H. Drexler, M. Hochadel, M. Komajda, J.L. Lopez-Sendon, P. Ponikowski, L. Tavazzi, Characteristics, outcomes, and predictors of mortality at 3 months and 1 year in patients hospitalized for acute heart failure, Eur. J. Heart. Fail. 12 (3) (2010) 229–248.
[9] D.-J. Choi, S. Han, E.-S. Jeon, M.-C. Cho, J.-J. Kim, B.-S. Yoo, M.-S. Shin, L.-W. Seong, Y. Ahn, S.-M. Kang, Y.-J. Kim, H.S. Kim, S.C. Chae, B.-H. Oh, M.-M. Lee, K.-H. Ryu, Characteristics, outcomes and predictors of long-term mortality for patients hospitalized for acute heart failure: a report from the Korean heart failure registry, Korean. Circ. J. 41 (7) (2011) 363.
[10] S.E. Lee, H.-Y. Lee, H.-J. Cho, W.-S. Cho, H. Kim, J.O. Choi, E.-S. Jeon, M.-S. Kim, J.-J. Kim, K.-R. Kwang, S.C. Bae, S.-M. Baek, S.-M. Kang, D.-J. Choi, B.-S. Yoo, K.-H. Kim, K.Y. Park, M.-C. Cho, B.-H. Oh, Clinical Characteristics and Outcome of Acute Heart Failure in Korea: Results from the Korean Acute Heart Failure Registry (KORAHF), Korean. Circ. J. 47 (3) (2017) 341.
[11] J. Trump, S. Bunlada, J.G.C. Cleland, C.E. Angermann, U. Dahlstrom, W. Osunwerker, W.T. Tay, K. Dickstein, G. Ertl, M. Hasnain, S.V. Perrone, M. Ghadfanfar, A. Schweizer, A. Obergfell, C.S.P. Lam, G. Filipatos, S.P. Collins, Post-discharge prognosis of patients admitted to hospital for heart failure by world region, and national level of income and income disparity (REPORT-HF): a cohort study, Lancet. Glob. Health. 8 (5) (2020) e411–e422.
[12] W. Kim, J.J. Park, H.-Y. Lee, K.H. Kim, B.-S. Yoo, S.-M. Kang, S.H. Baek, E.-S. Jeon, J. J. Kim, M.-C. Cho, S.C. Chae, B.-H. Oh, W. Kook, D.-J. Choi, Prediction of mortality in heart failure: a risk score based on machine-learning and change point algorithm, Clin. Res. Cardiol. 110 (8) (2021) 1321–1333.
[13] T. Tohyma, T. Ide, M. Ikeda, H. Kaku, N. Enzan, S. Matsushima, K. Funakoshi, J. Kishimoto, K. Todaka, H. Tsutsui, Machine learning-based model for predicting 1 year mortality of hospitalized patients with heart failure, ESC. Heart. Fail. 8 (5) (2021) 4077–4085.