นิพนธ์ต้นฉบับ

ผลของการรักษาด้วยยาขับปัสสาวะอย่างรวดเร็วในห้องฉุกเฉินต่อผลลัพธ์ทางคลินิกในผู้ป่วยหัวใจล้มเหลวเฉียบพลัน

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บทคัดย่อ

บทนำ: ภาวะหัวใจล้มเหลวเฉียบพลันเป็นภาวะที่พบได้บ่อยในผู้ป่วยที่มารับการรักษาที่ห้องฉุกเฉิน การรักษาหลักของภาวะหัวใจล้มเหลวเฉียบพลัน คือ การรักษาด้วยยาขับปัสสาวะซึ่งการให้ยาขับปัสสาวะทางหลอดเลือดดำอย่างรวดเร็วอาจช่วยบรรเทาอาการ และส่งผลต่อผลลัพธ์ทางคลินิกที่ดีขึ้นได้

วัตถุประสงค์: เพื่อศึกษาผลของระยะเวลาที่เริ่มให้ยาขับปัสสาวะนับตั้งแต่ผู้ป่วยมาถึงห้องฉุกเฉิน (door-to-diuretic time: D2D time) ต่ออัตราตายในโรงพยาบาล และผลลัพธ์ทางคลินิกอื่น ๆ ในผู้ป่วยที่มีภาวะหัวใจล้มเหลวเฉียบพลันที่ได้รับการรักษาในโรงพยาบาลแบบผู้ป่วยใน

วิธีการศึกษา: การวิจัยนี้เป็นการวิจัยเชิงสังเกตแบบย้อนหลัง (retrospective cohort study) โดยใช้ข้อมูลจากระบบฐานข้อมูลโรงพยาบาลนครพิงค์ ในผู้ป่วยที่เข้ารับการรักษาในโรงพยาบาลด้วยภาวะหัวใจล้มเหลวเฉียบพลัน และได้รับยาขับปัสสาวะทางหลอดเลือดดำภายใน 24 ชั่วโมงหลังมาถึงห้องฉุกเฉิน ระหว่างวันที่ 1 มกราคม 2563 ถึง วันที่ 30 กันยายน 2565 เพื่อหาความสัมพันธ์ของระยะเวลาที่เริ่มให้ยาขับปัสสาวะนับตั้งแต่ผู้ป่วยมาถึงห้องฉุกเฉิน กับอัตราตายในโรงพยาบาลจากทุกสาเหตุ คำนวณกลุ่มตัวอย่างได้ 726 ราย จำแนกผู้ป่วยเป็นกลุ่มที่ได้รับยาขับปัสสาวะอย่างรวดเร็ว (early treatment group; D2D time ≤ 60 นาที) และกลุ่มที่ได้รับยาขับปัสสาวะล่าช้า (non-early treatment group; D2D time > 60 minutes).

ผลการศึกษา: ผู้ป่วยเข้าเกณฑ์การศึกษา 750 ราย ค่ามัธยฐานของเวลาที่เริ่มให้ยาขับปัสสาวะ คือ 65 นาที พิสัยระหว่างควอไทล์ 43.75 ถึง 108 นาที จากจำนวนผู้ป่วยทั้งหมด พบว่า 343 ราย (45.7%) อยู่ในกลุ่มที่ได้รับยาขับปัสสาวะอย่างรวดเร็ว ในขณะที่ 407 ราย (54.3%) อยู่ในกลุ่มที่ได้รับยาขับปัสสาวะล่าช้า อัตราการเสียชีวิตในโรงพยาบาลจากทุกสาเหตุ คือ ร้อยละ 4.7 (16 ราย) และ ร้อยละ 5.9 (24 ราย) ตามลำดับ ($p = 0.454$) การวิเคราะห์ในผู้ป่วยที่มีระดับความเร่งด่วนสูงสุด (triage level 1) กลุ่มที่ได้รับยาขับปัสสาวะอย่างรวดเร็วพบแนวโน้มอัตราการเสียชีวิตที่ต่ำกว่าร้อยละ 5.0 เมื่อเทียบกับกลุ่มที่ได้รับยาขับปัสสาวะล่าช้า ร้อยละ 10.9, $p = 0.029$

สรุปผลการศึกษา: ในการศึกษานี้การให้ยาขับปัสสาวะทางหลอดเลือดดำอย่างรวดเร็วแม้ไม่พบว่าช่วยลดอัตราการเสียชีวิตอย่างมีนัยสำคัญทางสถิติ แต่พบแนวโน้มว่าอาจช่วยลดอัตราการเสียชีวิตในกลุ่มผู้ป่วยที่มีอาการรุนแรง จำเป็นต้องมีการศึกษาวิจัยเพิ่มเติมเพื่อยืนยันผลลัพธ์นี้และประเมินถึงประโยชน์ที่อาจเกิดขึ้นในการจัดการภาวะหัวใจล้มเหลวเฉียบพลัน

คำสำคัญ: ยาขับปัสสาวะ, ห้องฉุกเฉิน, ภาวะหัวใจล้มเหลว,อัตราตาย, กระบวนการคัดกรอง

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Original Article

The effect of early diuretic therapy in the emergency department on clinical outcomes in patients hospitalized with acute heart failure

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ABSTRACT

Introduction: Acute heart failure (AHF) is a common condition among individuals who need medical attention at the emergency department (ED). The mainstay treatment of acute heart failure is diuretic therapy. Early intravenous (IV) diuretics may rapidly improve symptoms and clinical outcomes.

Objective: The study explored the effect of door-to-diuretics (D2D) time on mortality and other clinical outcomes in patients hospitalized with AHF.

Method: A retrospective cohort study was conducted at Nakornping Hospital, using data from the hospital's database center to evaluate the association between D2D time and all-cause in-hospital mortality as the primary outcome. Patients hospitalized with AHF and treated with IV diuretics within 24 hours of ED arrival between January 1, 2020, and September 30, 2022, were included, targeting a calculated sample size of 726. After applying the predefined exclusion criteria, eligible patients were categorized into an early treatment group (D2D time ≤60 minutes) and a non-early treatment group (D2D time >60 minutes).

Results: A final analysis of 750 patients, the median D2D time was 65 minutes (IQR 43.75-108). Of the total number of patients, 343 (45.7%) were in the early treatment group, while 407 (54.3%) were in the non-early treatment group. All-cause in-hospital mortality was 16 cases (4.7%) and 24 cases (5.9%) respectively ($p = 0.454$). In a subgroup analysis for triage level 1, there was a trend toward a lower mortality rate in the early treatment group (11 out of 221, 5.0%) compared to the non-early treatment group (18 out of 165, 10.9%), $p = 0.029$.

Conclusions: In summary, early IV diuretic therapy showed no significant mortality benefit but suggested a trend toward lower mortality in severe cases. Further research is needed to confirm and explore its potential benefits in AHF management.

Keywords: diuretics, emergency department, heart failure, mortality, triage.

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Introduction

Acute heart failure (AHF) is a complex clinical syndrome with symptoms and signs that result from any structural or functional impairment of ventricular filling or ejection of blood.[1] It is regarded as a common condition among individuals who need medical attention at the emergency department (ED). Furthermore, they are frequently hospitalized, resulting in patient morbidity and mortality.

Intravenous (IV) diuretics are the cornerstone of AHF treatment, as they increase renal excretion of salt and water[2], providing the most rapid and effective treatment for signs and symptoms of congestion.[1] The European Society of Cardiology (ESC) and the American Heart Association, American College of Cardiology, and Heart Failure Society of America (AHA/ACC/HFSA) guidelines recommend prompt administration of IV loop diuretics for all patients hospitalized with AHF presenting with signs and symptoms of fluid overload as a Class I recommendation. In Thailand, the Heart Failure Council of Thailand (HFCT) Heart Failure Guideline aligns with international recommendations, endorsing diuretic administration as an essential step to AHF treatment.[3]

Recent studies have demonstrated that rapid diuretic administration will reduce mortality[4-7] and the length of hospital stay.[5] However, the mentioned observational studies are subject to several limitations, and some research gives conflicting results.[8] Real practices vary among countries and areas, and only a few published research studies on this topic are available in Thailand. Our objective is to explore the effect of door-to-diuretics (D2D) time on mortality and other clinical outcomes in patients hospitalized with acute heart failure as more supporting evidence is necessary to conform it to a strong recommendation on guidelines.

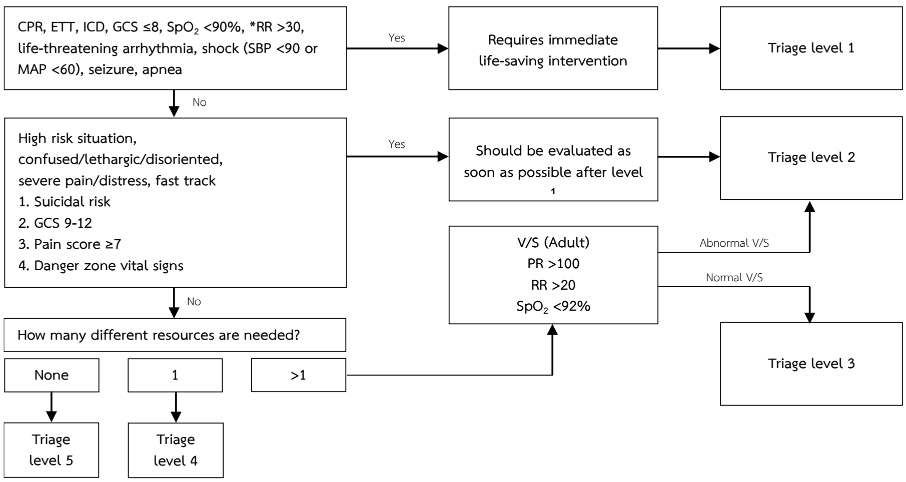
Methods

A retrospective cohort study was conducted using data from the Nakornping Hospital database center to evaluate the association between D2D time and all-cause in-hospital mortality as the primary outcome. D2D time was defined as the duration from when a patient arrived at the ED to the time of first receiving intravenous (IV) furosemide. The early treatment group was a patient with D2D time ≤ 60 minutes[4] otherwise, the non-early treatment group. The secondary outcomes were the length of hospital stay (LOS) and the length of mechanical ventilation (LOMV).

The Inclusion criteria were patients with 1) age ≥ 20 years; 2) AHF, diagnosed based on Framingham criteria[9]; and 3) patients who were hospitalized. The exclusion criteria were 1) patients not obtained medical attention in ED; 2) the final diagnoses at discharge were not heart failure; 3) no IV diuretics administration within 24 hours from ED arrival; 4) no definite D2D time record; 5) pre-ED arrival IV diuretics (pre-hospital and referral from other hospitals); 6) end-stage renal disease (ESRD) patients on routine peritoneal or hemodialysis (CAPD or HD);

7) out-of-hospital cardiac arrest (OHCA); 8) ST-elevation myocardial infarction (STEMI); 9) COVID-19 infection; 10) major surgery in admission; and 11) patients were discharged against advice.

Patients' data were retrieved from the Nakornping Hospital database center based on the International Classification of Diseases, 10th Revision (ICD-10) diagnoses, and subsequently reviewed. Following inclusion and exclusion from the specified criteria, essential data were documented, including basic information, past medical history, physical findings, laboratory examination, and outcomes. The triage level was determined by a registered nurse or emergency nurse practitioner using the Ministry of Public Health of Thailand Emergency Department Triage (MOPH ED Triage)[10] derived from the Emergency Severity Index (ESI)[11] with an additional parameter per local protocol (Figure 1). Echocardiography results were received from the official report done by cardiologists. Get With the Guidelines–Heart Failure (GWTG-HF) risk score[12], which predicted all-cause in-hospital mortality in patients admitted with AHF, was calculated based on age, systolic blood pressure, heart rate, blood urea nitrogen, serum sodium levels, and history of chronic obstructive pulmonary disease (COPD).



*Additional parameter of RR >30 /min indicating severe respiratory distress; adapted from Ministry of Public Health of Thailand Emergency Department Triage (MOPH ED Triage)[9] and the Emergency Severity Index (ESI)[10]; CPR = cardiopulmonary resuscitation; ETT = intubated patient or requiring intubation; GCS = Glasgow coma scale; ICD = intercostal drainage; MAP = mean arterial pressure; PR = pulse rate; RR = respiratory rate; SBP = systolic blood pressure; SpO_2 = peripheral oxygen saturation; V/S = vital signs.

Figure 1 Triage algorithm used at the emergency department, Nakornping Hospital

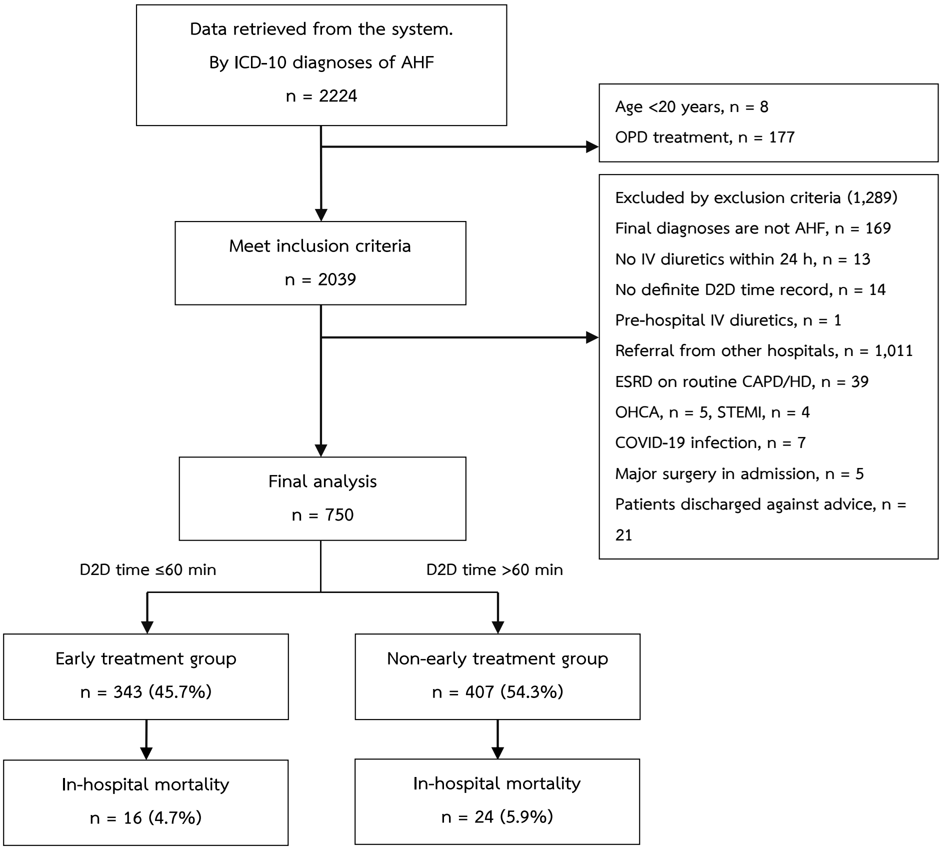
The sample size was calculated using the mortality rate of AHF patients in Nakornping Hospital from the first observed 200 samples. The mortality rate among the early treatment group was 3.8% (3 out of 79), while in the non-early group was 9.1% (11 out of 121). The sample size was 726 to achieve a power of 80% and a two-sided alpha level of 0.05.

The continuous data were presented as mean ± standard deviation (SD) for normally distributed and as median (interquartile range, IQR) for non-normally distributed variables. Categorical data were presented as numbers (%). Group differences were analyzed using Student's t-tests or Mann-Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. Subgroup analyses were done according to 1) triage level from level 1 to level 5; 2) left ventricular ejection fraction (LVEF), which was categorized into three groups, ≤ 40% = heart failure with reduced ejection fraction (HFrEF), ≥ 50% = heart failure with preserved ejection fraction (HFpEF), >40 to <50% = heart failure with mildly reduced ejection fraction (HFmrEF); and 3) GWTG-HF risk score divided into quartile groups (Q1 to Q4). Multivariable logistic regression and generalized linear model analyses were performed to study the simultaneous effect of multiple factors on primary and secondary outcomes, respectively. Significant covariates, with p-value < 0.10 in univariable analyses, were included in the multivariable models. Statistical analyses were performed using the IBM SPSS Statistics version 29.0.2.0 and Stata version 16.1.

The study was conducted in accordance with the ethical principles in the Declaration of Helsinki and was consistent with the Good Clinical Practice guidelines. The study protocol was approved by the Nakornping Hospital Ethics Committee, with approval number 066/65, granted on September 12, 2022.

Results

A total of 2,224 patients with acute heart failure were admitted to Nakornping Hospital between January 1, 2020, and September 30, 2022. 2,039 patients fulfilled the inclusion criteria. 1,550 patients were excluded by exclusion criteria, giving a final analysis of 750 patients. Of the total number of patients, 343 (45.7%) were in the early treatment group, while 407 (54.3%) were in the non-early treatment group (Figure 2).



AHF = acute heart failure; COVID-19 = Coronavirus Disease 2019; D2D = door-to-diuretics; CAPD = Continuous Ambulatory Peritoneal Dialysis; ESRD = end-stage renal disease; HD = hemodialysis; IV = intravenous; OHCA = out-of-hospital cardiac arrest; STEMI = ST-segment elevation myocardial infarction.

Figure 2 Study Flow

The median D2D time was 65 minutes, with an interquartile range from 43.75 to 108 minutes (not shown in the table). The baseline characteristics of the patients in the early treatment group were more likely to have higher respiratory rates, lower peripheral oxygen saturation, more obvious signs of congestion (orthopnea and crepitations/rales), a history of previous heart failure, and a reduced left ventricular ejection fraction. Baseline laboratory data significantly differed for blood urea nitrogen, creatinine, and cardiac troponin. Therefore, they were more likely to be triaged to level 1 and had higher GWTG-HF risk scores (Table 1).

Table 1 Baseline characteristics between groups

	Early treatment n = 343 (45.7)	Non-early treatment n = 407 (54.3)	p-value	Missing data
Age (years), median (IQR)	72 (61-80)	69 (58-79)	0.099	0
Male, n (%)	162 (47.2%)	180 (44.2)	0.411	0
Arrived by EMS, n (%)	79 (23.0)	82 (20.1)	0.338	0
Symptom onset (hours), median (IQR)	24 (4-48)	24 (5-60)	0.070	0
Vital signs, median (IQR)				
Systolic blood pressure (mmHg)	138 (118-157)	136 (115-159)	0.858	0
Diastolic blood pressure (mmHg)	80 (67-95)	78 (68-93)	0.758	0
Heart rate (beats/min)	96 (80-111)	93 (78-110)	0.158	0
Respiratory rate (/min)	30 (26-34)	26 (22-32)	<0.001	1 (0.001)
Peripheral oxygen saturation (%)	95 (90-98)	96 (93-98)	<0.001	1 (0.001)
Triage level, n (%)				
Level 1	221 (64.4)	165 (40.5)	<0.001	0
Level 2	104 (30.6)	205 (50.4)	<0.001	
Level 3	17 (5.0)	37 (9.1)	0.029	
ECG rhythm, n (%)				0
Sinus rhythm	244 (71.1)	279 (68.6)	0.442	
Atrial fibrillation	90 (26.2)	120 (29.5)	0.324	
Others	9 (2.6)	8 (2.0)	0.546	
LVEF, n (%)				
HFrEF	153 (46.9)	141 (37.3)	0.010	48 (6.4)
HFmrEF	24 (7.4)	42 (11.1)	0.089	
HFpEF	149 (45.7)	195 (51.6)	0.120	
NYHA III/IV at admission, n (%)	339 (98.8)	389 (95.6)	0.008	0
Past medical history, n (%)				
Heart failure	219 (63.8)	213 (52.3)	0.001	0
Hypertension	246 (71.7)	278 (68.3)	0.310	0
Diabetes mellitus	156 (45.6)	157 (38.6)	0.052	0
Chronic kidney disease	103 (30.0)	108 (26.5)	0.289	0
Coronary artery disease	85 (24.9)	89 (21.9)	0.335	0
Atrial fibrillation	83 (24.2)	104 (25.6)	0.669	0
Valvular heart disease	58 (16.9)	73 (17.9)	0.712	0
Cerebrovascular disease	20 (5.8)	32 (7.9)	0.280	0
Chronic obstructive pulmonary disease	45 (13.1)	39 (9.6)	0.126	0
Cancer	10 (2.9)	16 (3.9)	0.449	0
Physical examination, n (%)				
Orthopnea	263 (76.7)	272 (66.8)	0.003	0
Crepitation/rales	324 (94.5)	328 (80.6)	<0.001	0
Peripheral edema	213 (62.1)	247 (60.7)	0.693	0
Laboratory data, median (IQR)				
Hemoglobin (mg/dl)	11.3 (9.8-13)	11.5 (9.8-13.2)	0.316	0
Capillary blood glucose (mg/dl)	136 (110-178.75)	131 (106-183)	0.459	95 (12.6)
BUN (mg/dl)	22.7 (16.6-38.7)	20.6 (14.9-31.8)	0.012	0
Creatinine (mg/dl)	1.3 (1.0-2.19)	1.25 (0.91-1.99)	0.047	0
Serum sodium (mmol/l)	138 (135-141)	138 (135-140)	0.397	0
Serum potassium (mmol/l)	4.06 (3.6-4.5)	4.05 (3.65-4.50)	0.642	0
Serum bicarbonate (mmol/l)	20 (18-24)	21 (18-24)	0.671	0
Venous blood gas				
pH	7.436 (7.365-7.48)	7.440 (7.37-7.482)	0.670	330 (44)
pCO2 (mmHg)	38 (32-45.25)	38.2 (31.7-44.8)	0.790	330 (44)

Table 1 Baseline characteristics between groups (Cont.)

	Early treatment n = 343 (45.7)	Non-early treatment n = 407 (54.3)	p-value	Missing data
Troponin T (ng/ml)	41.46 (27.76-79)	37.72 (22.6-65)	0.020	0
NT-proBNP (pg/ml)	3378 (1761.75-9918.5)	5660 (2265.5-14799.5)	0.417	708 (94.4)
GWTG-HF risk score, mean ± SD and n (%)	41.43 ± 8.24	40.01 ± 8.58	0.022	0
Q1	66 (19.2)	106 (26.0)		
Q2	90 (26.2)	104 (25.6)		
Q3	88 (25.7)	88 (21.6)		
Q4	99 (28.9)	109 (26.8)		
Mechanical ventilator use, n (%)	99 (28.9)	96 (23.6)	0.101	0

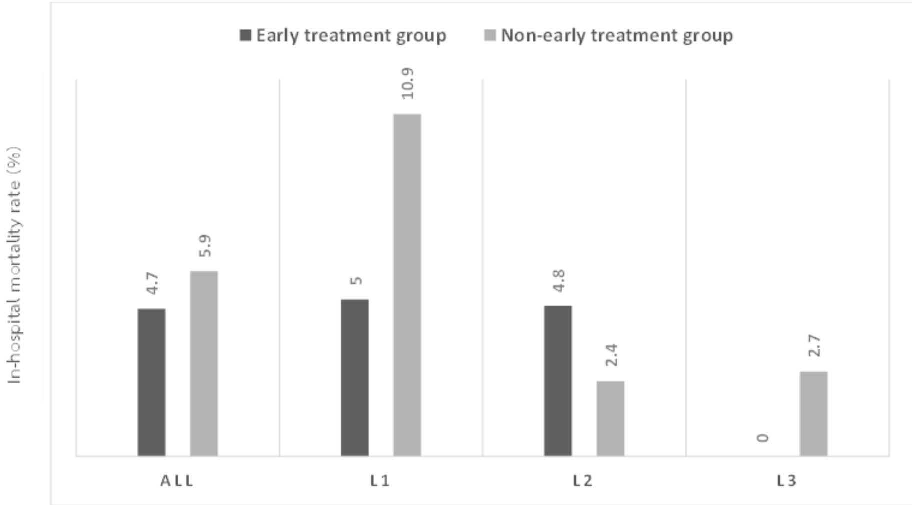
Variables are presented in mean ± SD, median (interquartile range), or n (%). BUN = blood urea nitrogen; ECG = electrocardiogram; EMS = emergency medical services; LVEF = left ventricular ejection fraction; GWTG-HF = Get With the Guidelines-Heart Failure; HFrEF = heart failure with reduced ejection fraction; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserve ejection fraction; NT-proBNP = N-terminal pro-BNP; NYHA = New York Heart Association; pCO2= partial pressure of carbon dioxide.

All-cause in-hospital mortality was 16 (4.7%) in the early treatment group and 24 (5.9%) in the non-early treatment group (p = 0.454). We performed three subgroup analyses focusing on triage level, LVEF, and GWTG-HF risk score for the primary outcome (Table 2). There was a trend toward a lower mortality rate in the early treatment group in triage level 1 (11 out of 221, 5.0%) compared to the non-early treatment group (18 out of 165, 10.9%), p = 0.029 (Table 2 and Figure 3).

Table 2 Clinical outcomes and group differences analyses

	Early treatment	Non-early treatment	p-value
Primary outcome			
All-cause in-hospital mortality, n (%)	16 (4.7)	24 (5.9)	0.454
Subgroup analyses			
Triage level, n (%)			
Level 1	11 (5.0)	18 (10.9)	0.029
Level 2	5 (4.8)	5 (2.4)	0.315
Level 3	0	1 (2.7)	1.000
LVEF, n (%)			
HFrEF	8 (5.2)	7 (5.0)	0.918
HFmrEF	1 (4.2)	5 (11.9)	0.404
HFpEF	5 (3.4)	5 (2.6)	0.751
GWTG-HF risk score, n (%)			
Q1	4 (6.1)	2 (1.9)	0.205
Q2	0	8 (7.7)	0.008
Q3	3 (3.4)	2 (2.3)	1.000
Q4	9 (9.1)	12 (11.0)	0.647
Secondary outcome			
Length of hospital stay (days), median (IQR)	4 (3-6)	4 (3-6)	0.519
Length of mechanical ventilation (hours), median (IQR)	39 (28-74)	46.5 (22.25-92.25)	0.816

Variables are presented in the median (interquartile range) or n (%). LVEF = left ventricular ejection fraction; GWTG-HF = Get With the Guidelines-Heart Failure; HFrEF = heart failure with reduced ejection fraction; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; Q = Quartile.



In-hospital mortality rates are presented in percentages. L1 = triage level 1; L2 = triage level 2; L3 = triage level 3

Figure 3 In hospital mortality rates (subgroup analysis by triage level)

Multivariable logistic regression analyses were performed by adjusting significant covariates, e.g., underlying hypertension, diabetes mellitus, systolic blood pressure, respiratory rate, crepitation on physical examinations, blood urea nitrogen, serum bicarbonate, triage level 1, and mechanical ventilator use. The results showed that patients in the early treatment group tended to have a lower in-hospital mortality, but it was not statistically significant. (Odds ratio (OR) = 0.65, 95% confidence interval (CI) 0.30 to 1.42 (p = 0.280)). Similarly, after adjusting for the GWTG-HF risk score, the results remained consistent, showing a non-significant trend toward lower in-hospital mortality in the early treatment group (Table 3).

Table 3 Effects of early diuretics treatment on in-hospital mortality

Adjustment	In-hospital mortality		
	OR	95% CI	p-value
Univariable logistic regression analysis	0.78	0.41-1.50	0.455
Multivariable adjusted for significant covariates*	0.65	0.30-1.42	0.280
Multivariable adjusted for GWTG-HF risk score	0.69	0.36-1.35	0.280

CI = confidence interval; GWTG-HF = Get With the Guidelines-Heart Failure; OR = odds ratio. *Significant covariates, e.g., underlying hypertension, diabetes mellitus, systolic blood pressure, respiratory rate, crepitation on physical examinations, blood urea nitrogen, serum bicarbonate, triage level 1, and mechanical ventilator use.

For the secondary outcomes, the median length of hospital stay (LOS) was 4 days (IQR 3–6) in both groups, with no significant difference (p = 0.519). The median length of mechanical ventilation (LOMV) tended to be shorter in the early treatment group (39 hours; IQR 28–74) compared to the non-early treatment group (46.5 hours; IQR 22.25–92.25), although this difference was not statistically significant (p = 0.816) (Table 2).

A generalized linear model (GLM) with a gamma distribution and log link was used to assess the effect of early diuretic treatment on secondary outcomes. In the univariable analysis, early treatment showed no significant association with the length of hospital stay (LOS) (adjusted rate ratio (aRR) = 0.96, 95% CI 0.84 to 1.10, p = 0.545). This result persisted after adjusting for significant covariates and the GWTG-HF risk score. For the length of mechanical ventilation (LOMV), the early treatment group tended to have a shorter duration on mechanical ventilation. However, this association was not statistically significant (aRR = 0.83, 95% CI 0.60 to 1.13, p = 0.235) and remained non-significant after adjusting for significant covariates and the GWTG-HF risk score (Table 4). Notably, LOMV analyses were restricted to intubated patients, excluding those without mechanical ventilation.

Table 4 Effects of early diuretics treatment on secondary outcomes

Adjustment	aRR	95% CI	p-value
Length of hospital stay			
Univariable GLM analysis	0.96	0.84-1.10	0.545
Multivariable adjusted for significant covariates*	0.93	0.83-1.04	0.232
Multivariable adjusted for GWTG-HF risk score	0.94	0.82-1.08	0.382
Length of mechanical ventilation			
Univariable GLM analysis	0.83	0.60-1.13	0.235
Multivariable adjusted for significant covariates**	0.86	0.64-1.15	0.301
Multivariable adjusted for GWTG-HF risk score	0.83	0.61-1.12	0.226

aRR = adjusted rate ratio; CI = confidence interval; GLM = generalized linear model; GWTG-HF = Get With the Guidelines-Heart Failure. *Significant covariates for the length of hospital stay, e.g., gender, underlying chronic obstructive pulmonary disease (COPD), heart rate, respiratory rate, peripheral oxygen saturation, orthopnea, peripheral edema on physical examinations, blood urea nitrogen, serum sodium, triage level 1, and mechanical ventilator use. **Significant covariates for the length of mechanical ventilation, e.g., underlying atrial fibrillation, systolic blood pressure, diastolic blood pressure, orthopnea on physical examination, and blood urea nitrogen.

Discussion

The median of door-to-diuretics (D2D) time in our study is 65 minutes, which is less than the durations reported in prior studies (90 and 128 minutes[4,8]). Additionally, we discovered that D2D time ≤60 minutes in almost half (45.7%) of cases, a higher proportion compared to previous studies (37.3% and 24%[4,8]).

The baseline characteristics of our study population appeared to be younger and had slightly higher GWTG-HF risk scores compared to the Registry Focused on Very Early Presentation and Treatment in Emergency Department of Acute Heart Failure (REALITY-AHF)[4], with a median age of 72 years (IQR 61-80) in the early and 69 years (IQR 58-79) in the non-early treatment group, compared to 79 ± 11 and 78 ± 13 years respectively. The mean GWTG-HF risk scores of our study population were 41.43 ± 8.24 in the early and 40.01 ± 8.58 in the non-early treatment group, compared to 37 ± 8 and 38 ± 8 in REALITY-AHF consecutively.

Although most of the data has been ultimately collected in this research, NT-proBNP, which is considered valuable, particularly in heart failure research, was compiled by only 5.6% of our study population (Table 1). Due to the local practice of Nakornping Hospital, we exclusively use NT-proBNP when the diagnosis is questionable. This is because it has a high negative predictive value[13], making it helpful for ruling out heart failure. Additionally, it is a cost-effective option. In this study, we enhanced the accuracy of heart failure diagnoses by including the final diagnoses from specialists, addressing this constraint.

Current acute heart failure (AHF) treatment guidelines advocate the timely initiation of diuretic therapy.[14] Our study investigated the impact of D2D time on clinical outcomes and demonstrated that the early treatment group (D2D ≤ 60 minutes) had potentially lower mortality rates. Although it was not statistically significant, the results were consistent with several previous studies.[4-7] Systematic review and meta-analysis might help us reach a conclusion soon.

Rapid and accurate sorting of patients in ED is a critical component of emergency practice. MOPH ED Triage[10], derived from ESI[11], is Thailand's most widely used triage algorithm due to its efficacy and familiarity among ED personnel. Although several research on heart failure have conducted subgroup analyses based on the New York Heart Association (NYHA) classification[15], most patients in our study were in NYHA classes 3 and 4. Therefore, we omitted this classification and instead applied a triage approach as an effective tool to categorize the patients' severity. There was a trend toward lower mortality rates in the early treatment group in the subgroup analysis for triage level 1, which identified patients with severe respiratory distress (requiring intubation, respiratory rate (RR) > 30 /min, and/or peripheral oxygen saturation (SpO2) < 90%). This finding highlights the need to prioritize the administration of IV diuretics as a crucial component of the treatment process for patients with severe symptoms, which carries important clinical implications for emergency department (ED) practice.

GWTG-HF risk scores were calculated to predict in-hospital mortality, and subgroup analysis by quartile group demonstrated that the early treatment group potentially had a lower mortality rate in Q2 (p = 0.008) (Table 2). However, the effect was not uniform across all quartile groups. A multivariable logistic regression analysis adjusted for GWTG-HF risk score resulted in an odds ratio of 0.69 (95% CI 0.36-1.34), p = 0.280. This indicates that early treatment with IV diuretics had a potentially protective effect despite GWTG-HF risk scores.

Although not statistically significant, these findings align with previous results and multiple studies.[4-8]

As for the secondary outcome, early IV diuretic treatment tended to be associated with shorter length of mechanical ventilation (LOMV) (Tables 2 and 4). Still, the effects were not statistically significant because the sample size was not calculated for these outcomes directly, and only 26% of patients had mechanical ventilator use. Expanding the sample size may potentially reveal the difference.

Limitation

Due to the observational character of the study, it is essential to emphasize that only an association, not causality, was identified. Nevertheless, assigning patients to a delayed treatment group using randomization is ethically unfeasible. Furthermore, the sample size was calculated primarily to assess the primary outcome, which may have limited the statistical power to detect significant associations in the secondary outcomes. Additional data and more extensive prospective studies are required to establish a strong relationship between door-to-diuretic (D2D) time, in-hospital mortality, and other clinical outcomes.

Conclusion

The study focused on the management of patients hospitalized with acute heart failure. While no statistically significant association was found between early IV diuretic therapy and all-cause in-hospital mortality, the findings suggest a trend toward lower mortality rates in the early treatment group, particularly in patients with severe symptoms classified as triage level 1. These findings highlight the potential clinical importance of prioritizing early IV diuretic administration in the management of acute heart failure.

Conflict of interest

The author has no conflicts of interest to declare.

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