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Original article

Nicardipine versus nitroglycerin for hypertensive acute heart failure syndrome: a single-center observational study

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Abstract

Objective: Nitroglycerin is a first-line treatment for hypertensive acute heart failure syndrome (AHFS). However, nicardipine is frequently used to treat hypertensive emergencies, including AHFS. In this study, we compared the effectiveness of nicardipine and nitroglycerin in patients with hypertensive AHFS.

Patients and Methods: This single-center, retrospective, observational study was conducted at the intensive care unit of a Japanese hospital. Patients diagnosed with AHFS and systolic blood pressure 140 mmHg on arrival between April 2013 and March 2021 were included. The outcomes were the time to optimal blood pressure control, duration of continuous infusion of antihypertensive agents, duration of positive pressure ventilation, need for additional antihypertensive agents, length of hospital stay, and body weight changes. Outcomes were compared between the nicardipine and nitroglycerin groups. We also compared these outcomes between the groups after excluding patients who received renal replacement therapy.

Results: Fifty-eight patients were enrolled (26 and 32 patients were treated with nitroglycerin and nicardipine, respectively). The nicardipine group had a shorter time to optimal blood pressure control (2.0 [interquartile range, 2.0–8.5] h vs. 1.0 [0.5–2.0] h), shorter duration of continuous anti-hypertensive agent infusion (3.0 [2.0–5.0] days vs. 2.0 [1.0–2.0] days), less frequent need for additional anti-hypertensive agents (1 patients [3.1%] vs. 11 patients [42.3%]), and shorter length of hospital stay (17.5 [10.0–33.0] days vs. 9.0 [5.0–15.0] days) than the nitroglycerin group. The duration of positive pressure ventilation and body weight changes were similar between the groups. The outcomes were similar after excluding patients who received renal replacement therapy.

Conclusion: Nicardipine may be more effective than nitroglycerin for treating hypertensive AHFS.

Key words: acute heart failure syndromes, nitroglycerin, calcium channel blocker, vascular failure, afterload mismatch

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Introduction

Heart failure is a syndrome caused by structural and/or functional compromise of the circulatory system[1]. Even in the modern era with advanced medical treatment, morbidity and mortality remain high in patients with heart failure[2–4], making this condition a major burden among the global elderly population[4, 5].

Acute heart failure syndrome (AHFS) is a life-threatening condition associated with rapidly deteriorating dyspnea. The pathophysiology of AHFS involves absolute intravascular fluid accumulation and/or excessive fluid influx into the central vasculature, which is sometimes associated with sympathoadrenal system activation[6], termed "central volume shift", followed by the rapid elevation of the left ventricle filling pressure, leading to increased hydrostatic pressure in pulmonary capillaries and severe pulmonary edema[7]. Once pulmonary edema occurs, patients' respiratory function is severely decreased, necessitating urgent or emergency medical interventions[8, 9]. AHFS has been categorized according to several aspects including duration (acute vs. chronic), preservation of ejection function (yes vs. no), and the affected side of the heart (left vs. right). Meanwhile, Mebazaa suggested a classification of AHFS consisting of five clinical scenarios covering systolic blood

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pressure (SBP), right heart failure, and acute coronary syndromes[10]. Because of its simplicity, this categorization of AHFS is useful for clinicians who treat patients in emergency settings. This report recommended nitrates, including nitroglycerin, as the main agents for treating patients with hypertensive AHFS.

Nitrates induce vascular smooth muscle cells to generate nitric oxide, which stimulates guanylate cyclase, resulting in the relaxation of smooth muscles. Low-dose nitrates mainly act on venous vessels, specifically dilating venous beds and reducing preload. Through these effects, nitrates are expected to relieve central volume shift and subsequently alleviate pulmonary edema[11]. In particular, nitroglycerin acts on coronary arteries at high doses, making it the preferred treatment for AHFS associated with myocardial ischemia[12]. Therefore, nitroglycerin is recommended as the first-line agent for AHFS in patients with coexistent hypertension in several guidelines[1, 13]. However, in a systemic review of nitrates in the treatment of AHFS, Wakai *et al.* concluded that nitrates were not more effective than other therapies regarding symptom relief and hemodynamic variables, although high-quality studies were not included in this review[14]. Therefore, therapies for patients with AHFS vary by region because the effectiveness of nitrates has not been sufficiently established[15–18].

Nicardipine belongs to the dihydropyridine class of calcium channel blockers. Because nicardipine acts quickly and safely, it is often used to treat hypertensive emergencies and postoperative hypertension[19–22]. Nicardipine mainly induces arterial relaxation, resulting in decreased blood pressure[23, 24]. Thus, nicardipine has been used to treat AHFS[19, 24], specifically to relieve symptoms by reducing afterload in patients with hypertensive AHFS.

The effectiveness of nicardipine and nitroglycerin in the treatment of hypertensive AHFS have not been compared, because only nitroglycerin has been recommended by several guidelines and is frequently used by cardiovascular experts as the first-line therapy. Thus, we conducted a retrospective observational study to compare the effectiveness of nicardipine and nitroglycerin in patients with hypertensive AHFS.

Patients and Methods

This was a single-center, retrospective, observational study conducted in the intensive care unit of an academic hospital in Japan. Patients diagnosed with AHFS and SBP >140 mmHg on arrival at the emergency room of the University of Miyazaki Hospital between April 2013 and March 2021 were included. AHFS was diagnosed according to the Framingham criteria[25]. We excluded patients with acute coronary syndrome, those who did not continuously receive anti-hypertensive agents (nitroglycerin or nicardipine), those admitted to other departments, and those who refused to participate.

We collected baseline information including age, sex, SBP and heart rate on arrival, history of hemodialysis among patients with end-stage renal failure, medical history, medication usage, laboratory variables (serum hemoglobin, serum creatinine, serum sodium, cardiac troponin T), and left ventricular ejection fraction (LVEF) on cardiac ultrasonography. We investigated the treatment after admission, including the maximum doses of antihypertensive agents, concomitant treatments (diuretics, human atrial natriuretic peptide, nitroglycerin sublingual spray, intravenous nicardipine), use of positive pressure ventilation, and induction of renal replacement therapy. Outcome measures were defined as follows: i) length of hospital stay, ii) time to optimal SBP control (<140 mmHg) without increasing the dose of nitroglycerin or nicardipine (blood pressure control time); iii) duration of continuous infusion of antihypertensive agents; iv) additional administration of the other antihypertensive agent to maintain optimal blood pressure after initially achieving blood pressure control (use of nicardipine in the nitroglycerin group or vice versa), v) duration of positive pressure ventilation (including noninvasive positive pressure ventilation), and vi) body weight changes. We compared the outcomes between the nicardipine and nitroglycerin groups. We also compared outcomes between the groups after excluding patients who received renal replacement therapy.

Statistical analysis was performed using SPSS software, version 23 (IBM Corporation, Armonk, NY, USA). Data are presented as the mean and standard deviation for normally distributed variables and as the median and interquartile range for other variables. Student's *t*-test was used for comparisons of normally distributed data; otherwise, we used the Mann–Whitney U test. We used the χ^2 test and Fisher's exact test to compare categorical variables. Statistical significance was defined as α <5% for all analyses.

Targeted patients were notified of the purpose of the study, and only patients who did not request exclusion were included in the analyses. The study protocol was approved by the ethics committee of the University of Miyazaki Hospital (O-0646).

Results

We enrolled 60 patients who visited the hospital during the study period. Of these, two patients (one with acute coronary syndrome and one who was hospitalized in another department) were excluded, and the remaining 58 patients (26 patients in the nitroglycerin group and 32 patients in the nicardipine group) were included. Overall, the patients' mean age was 75.2 ± 12.8 years, and 33 (56.9%) patients were male. A total of 18 (34.5%) patients received hemo-

dialysis for end-stage renal failure, and the mean SBP on arrival was 204.2 ± 31.6 mmHg. None of the patients died in the hospital.

SBP (208.1 ± 33.8 mmHg vs. 201.0 ± 29.9 mmHg, P=0.40) and heart rate on arrival (115.3 ± 24.7 beats/min vs. 108.4 ± 18.2 beats/min, P=0.22) were higher in the nitroglycerin group than in the nicardipine group, albeit without statistical significance. The nicardipine group had a larger change in body weight than the nitroglycerin group (−4.5 [3.2–5.6] kg vs. −4.4 [2.9-6.7] kg, P=0.70), although this difference was not statistically significant. Additionally, no differences were noted between the two groups with respect to baseline characteristics such as age, sex, use of renal replacement therapy, laboratory variables, medication usage, and medical history (Table 1). Table 2 presents the treatment after admission. The maximum dose was 0.70 ± 0.37 μg/kg/min for nitroglycerin and 4.0 (2.0–5.0) mL/h for nicardipine. There were no differences between the groups in the proportions of patients who received positive pressure ventilation, renal replacement therapy, and concomitant treatments (diuretics, human atrial natriuretic peptide). Nitroglycerin spray was used only in the nitroglycerin group (19.2%). Intravenous nicardipine was more frequently used in the nicardipine group than in the nitroglycerin group (14 [53.8%] vs. 29 [90.6%], P<0.01, Table 2).

Regarding outcomes, the nicardipine group exhibited a shorter time to optimal blood pressure control (1.0 [0.5–2.0] h vs. 2.0 [2.0–8.5] h, P<0.01) and a shorter duration of continuous infusion of anti-hypertensive agents (2.0 [1.0–2.0] days vs. 3.0 [2.0–5.0] days, P<0.05) than the nitroglycerin group. There were no differences between the two groups with regards to the duration of positive pressure ventilation (nitroglycerin vs. nicardipine: 2.0 [1.0–3.0] days vs. 2.0 [1.0–3.0] days, P=0.86). In total, 42.3% of patients in the nitroglycerin group required additional treatment with nicardipine, whereas only one patient in the nicardipine group required additional nitroglycerin therapy (P<0.01). The nicardipine group displayed a shorter length of hospital stay than the nitroglycerin group (9.0 [5.0–15.0] days vs. 17.5 [10.0–33.0] days, P<0.01).

We performed a subgroup analysis of 40 patients (20 patients in the nitroglycerin group and 20 patients in the nicardipine group) after excluding 18 patients who received renal replacement therapy. Compared with those in the nicardipine group, patients in the nitroglycerin group tended to be younger (75.6 ± 9.5 years vs. 80.8 ± 13.0 years, P=0.16) and were more likely to be male (11 [55.0%] vs. 9 [45.0%], P=0.53), albeit without statistical significance. Other baseline characteristics were similar between the two groups (Table 1). Regarding laboratory variables (serum hemoglobin, serum creatinine, serum sodium serum) on arrival, serum hemoglobin levels were higher in the nitroglycerin group than in the nicardipine group (13.0 ± 2.2 g/dL vs. 11.0 ± 1.6 g/dL, P<0.01), whereas serum creatinine, serum sodium, and cardiac troponin T levels were similar between the two groups (Table 1). There were no significant differences between the two groups in terms of medication usage and medical history (Table 1). We examined the LVEF using cardiac ultrasonography in 48 patients. A total of 13 (27.1%) patients displayed reduced LVEF (nitroglycerin [23] vs. nicardipine [25]: 8 [34.9%] vs. 5 [20.0%], P=0.25, Table 1).

Regarding outcomes after excluding patients who received renal replacement therapy, the nicardipine group had a shorter time to optimal blood pressure control than the nitroglycerin group (1.0 [0.5–1.8] h vs. 2.0 [2.0–6.3] h, P<0.01). The nicardipine group also had a shorter duration of continuous infusion of anti-hypertensive agents than the nitroglycerin group (2.0 [1.0–2.5] days vs. 3.0 [2.0–4.5] days, P=0.10), although this difference was not statistically significant. There was no difference in the duration of positive pressure ventilation between the groups (nitroglycerin vs. nicardipine: 2.0 [1.0–3.0] days vs. 2.0 [1.0–3.0] days, P=0.61). Meanwhile, seven patients (35.0%) in the nitroglycerin group required additional treatment with nicardipine, whereas one patient (5.0%) in the nicardipine group required additional nitroglycerin (P<0.05). In addition, the nicardipine group exhibited a shorter length of hospital stay than the nitroglycerin group (11.4 ± 6.2 days vs. 21.5 ± 14.1 days, P<0.01). No significant difference in body weight changes was noted between the groups (nitroglycerin vs. nicardipine: −4.0 [2.6–7.1] kg vs. −4.5 [3.2–6.2] kg, P=0.78) (Table 3). We conducted a subgroup analysis based on the ejection fraction (≤40% vs. >40%). In the ejection fraction >40% subgroup, nicardipine was more effective than nitroglycerin in terms of blood pressure control time, length of hospital stay, and duration of continuous infusion of antihypertensive agents (Table 4).

Discussion

We conducted a retrospective, observational study to compare the effectiveness of nicardipine and nitroglycerin in patients with hypertensive AHFS. The results demonstrated that compared to nitroglycerin, nicardipine was associated with a shorter time to optimal blood pressure control, shorter duration of the continuous infusion of antihypertensive agents, and shorter length of hospital stay, without the need for adjunctive nitroglycerin administration. After excluding patients who received renal replacement therapy, the time to optimal blood pressure control, duration of the continuous infusion of antihypertensive agents, and length of hospital stay were shorter in the nicardipine group than in the nitroglycerin group.

Our results indicate that nicardipine is more effective than nitroglycerin for treating hypertensive AHFS. In hypertensive AHFS, excessive fluid influx into a relatively

Table 1 Baseline characteristics of the patients

	All patients (N=58)			Excluding patients on renal replacement therapy (N=40)		
Characteristics on admission	Nitroglycerin (N=26)	Nicardipine (N=32)	*P* value	Nitroglycerin (N=20)	Nicardipine (N=20)	*P* value
Age, median (IQR), years	76.5 (69.0–82.0)	76.0 (66.5–86.5)	0.52	75.6 ± 9.5	80.8 ± 13.0	0.16¶
Male sex, no. (%)	16 (61.5%)	17 (53.1%)	0.52†	11 (55.0%)	9 (45.0%)	0.53†
Systolic blood pressure, mean ± SD, mmHg	208.1 ± 33.8	201.0 ± 29.9	0.40¶	203.8 ± 32.5	194.7 ± 24.9	0.33¶
Heart rate, mean ± SD, beats/min	115.3 ± 24.7	108.4 ± 18.2	0.22¶	118.4 ± 26.6	104.8 ± 19.6	0.07¶
Body weight change, kg	−4.4 (−2.9 to −6.7)	−4.5 (−3.2 to −5.6)	0.70	−4.0 (−2.6 to −7.1)	−4.5 (−3.2 to −6.2)	0.78
Laboratory values						
Serum hemoglobin, mean ± SD, g/dL	12.6 ± 2.1	10.9 ± 1.8	<0.01¶	13.0 ± 2.2	11.0 ± 1.6	<0.01¶
Serum creatinine, median (IQR), mg/dL	1.22 (0.89–4.86)	1.87 (1.12–7.54)	0.11	0.95 (0.80–1.41)	1.22 (0.95–1.81)	0.27
Serum sodium, median (IQR), mmol/L	140 (137–142)	141 (138–142)	0.91	140 (138–142)	141 (137–142)	0.80
Troponin T, median (IQR), ng/mL	0.06 (0.03–0.08) (N=25)	0.07 (0.05–0.08) (N=27)	0.14	0.05 (0.03–0.07) (N=20)	0.07 (0.03–0.09) (N=18)	0.33
Cardiac ultrasonography	(N=23)	(N=25)		(N=17)	(N=16)	
Reduced ejection fraction (≤40)	8 (34.9%)	5 (20.0%)	0.25†	7 (41.2%)	2 (12.5%)	0.07
Medical history						
Chronic heart failure, no. (%)	4 (15.4%)	10 (31.3%)	0.18†	3 (15.0%)	5 (25.0%)	0.35
Diabetes, no. (%)	13 (50.0%)	13 (40.6%)	0.48†	9 (45.0%)	6 (30.0%)	0.33†
Hypertension, no. (%)	20 (76.9%)	25 (78.1%)	0.91†	14 (70.0%)	13 (65.0%)	0.74†
Hyperlipidemia, no. (%)	7 (26.9%)	8 (25.0%)	0.87†	5 (25.0%)	2 (10.0%)	0.20
Atrial fibrillation, no. (%)	2 (7.7%)	1 (3.1%)	0.42	2 (10.0%)	1 (5.0%)	0.50
Renal failure, no. (%)	10 (38.5%)	15 (46.9%)	0.52†	4 (20.0%)	3 (15.0%)	0.50
Ischemic heart disease, no. (%)	3 (11.5%)	7 (21.9%)	0.25	3 (15.0%)	5 (25.0%)	0.35
Cancer, no. (%)	2 (7.7%)	0	0.20	2 (10.0%)	0	0.24
Cerebral vascular disease, no. (%)	1 (3.8%)	4 (12.5%)	0.25	1 (5.0%)	2 (10.0%)	0.50
Medications on admission						
ACE-I, no. (%)	1 (3.8%)	2 (6.3%)	0.58	1 (5.0%)	2 (10.0%)	0.50
ARB, no. (%)	13 (50.0%)	13 (40.6%)	0.48†	8 (40.0%)	6 (30.0%)	0.51†
Amlodipine, no. (%)	6 (23.1%)	12 (37.5%)	0.24†	3 (15.0%)	7 (35.0%)	0.14†
Aldosterone antagonist, no. (%)	3 (11.5%)	4 (12.5%)	0.62	2 (10.0%)	3 (15.0%)	0.50
Beta-blocker, no. (%)	5 (19.2%)	9 (28.1%)	0.43†	2 (10.0%)	6 (30.0%)	0.12
Loop diuretic, no. (%)	10 (38.5%)	9 (28.1%)	0.40†	8 (40.0%)	6 (30.0%)	0.51†
Digoxin, no. (%)	1 (3.8%)	0	0.45	1 (5.0%)	0	0.50
Aspirin, no. (%)	6 (23.1%)	9 (28.1%)	0.66†	5 (25.0%)	4 (20.0%)	0.50
Anti-arrhythmic, no. (%)	3 (11.5%)	1 (3.1%)	0.23	2 (10.0%)	0	0.24
Statin, no. (%)	7 (26.9%)	8 (25.0%)	0.87†	5 (25.0%)	2 (10.0%)	0.20
Warfarin, no. (%)	2 (7.7%)	0	0.20	2 (10.0%)	0	0.24
Oral hypoglycemic, no. (%)	6 (23.1%)	11 (34.4%)	0.35†	5 (25.0%)	4 (20.0%)	0.50
Insulin, no. (%)	4 (15.4%)	2 (6.3%)	0.24	2 (10.0%)	1 (5.0%)	0.50

Continuous variables are expressed as mean ± standard deviation for normally distributed variables and as median (interquartile range) for non-normally distributed variables. Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables, unless otherwise indicated. No patient received direct oral anticoagulants, hydralazine, or nitrates. ACE-I: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blocker. †: χ^2 test, ¶: Student's *t*-test.

small functional circulatory space causes hypertension[6, 7]. Theoretically, the treatment goals for hypertensive AHFS include reducing preload by dilating venous beds and reducing afterload via arterial dilation. Increased afterload depresses the Frank–Starling curve, resulting in reduced contractility[26, 27]. Our results suggest that nicardipine may resolve the pathological changes earlier than nitroglycerin in patients with hypertensive AHFS. Similar to nicardipine, the calcium channel blocker clevidipine has been reported as a novel antihypertensive agent for treating hypertensive AHFS[24]. Prior research has demonstrated that clevidipine reduces blood pressure and provides symptom relief more rapidly compared to conventional therapies, including nitroglycerin. In this report, nicardipine exhibited similar effects

Table 2 Treatment after admission

	All patients (N=58)			Excluding patients on renal replacement therapy (N=40)		
Variable	Nitroglycerin (N=26)	Nicardipine (N=32)	*P* value	Nitroglycerin (N=20)	Nicardipine (N=20)	*P* value
Maximum dose	0.70 ± 0.37 (μg/kg/min)	4.0 (2.0–5.0) (ml/h)	–	0.69 ± 0.36 (μg/kg/min)	3.0 (2.0–4.0) (ml/h)	–
Nitroglycerin spray (%)	5 (19.2%)	0	<0.05	5 (25.0%)	0	<0.05
Nicardipine IV (%)	14 (53.8%)	29 (90.6%)	<0.01†	11 (55.0%)	18 (90.0%)	<0.05†
PPV (%)	21 (80.8%)	25 (78.1%)	0.81†	18 (90.0%)	15 (75.0%)	0.20
Diuretics (%)	9 (34.6%)	13 (40.6%)	0.64†	9 (45.0%)	12 (60.0%)	0.34†
hANP (%)	3 (11.5%)	1 (3.1%)	0.23	3 (15.0%)	1 (5.0%)	0.30
Renal replacement therapy (%)	6 (23.1%)	12 (3.1%)	0.24†	–	–	

Continuous variables are expressed as mean ± standard deviation for normally distributed variables and as median (interquartile range) for non-normally distributed variables. Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables, unless otherwise indicated. IV: intravenous; PPV: positive pressure ventilation; hANP: human atrial natriuretic peptide. †: χ^2 test.

Table 3 Clinical outcomes

	All patients (N=58)			Excluding patients on renal replacement therapy (N=40)		
Variable	Nitroglycerin (N=26)	Nicardipine (N=32)	*P* value	Nitroglycerin (N=20)	Nicardipine (N=20)	*P* value
BPC time, hours	2.0 (2.0–8.5)	1.0 (0.5–2.0)	<0.01	2.0 (2.0–6.3)	1.0 (0.5–1.8)	<0.01
PPV time, days	2.0 (1.0–3.0)	2.0 (1.0–3.0)	0.86	2.0 (1.0–3.0)	2.0 (1.0–3.0)	0.61
Duration of continuous infusion antihypertensive agents, days	3.0 (2.0–5.0)	2.0 (1.0–2.0)	<0.05	3.0 (2.0–4.5)	2.0 (1.0–2.5)	0.1
Contra, no. (%)	11 (42.3%)	1 (3.1%)	<0.01†	7 (35.0%)	1 (5.0%)	<0.05
Length of hospital stay, days	17.5 (10.0–33.0)	9.0 (5.0–15.0)	<0.01	21.5 ± 14.1	11.4 ± 6.2	<0.01¶

Continuous variables are expressed as mean ± standard deviation for normally distributed variables and as median (interquartile range) for non-normally distributed variables. Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables, unless otherwise indicated. BPC: blood pressure control; PPV: positive pressure ventilation; Contra: administration of the opposite drug. ¶: Student's *t*-test, †: χ^2 test.

on blood pressure but not symptoms, although only a small number of patients received nicardipine. Calcium channel blockers may be more effective than nitrates in treating hypertensive AHFS. However, further research is needed to clarify which calcium channel blockers are most suitable for the treatment of hypertensive AHFS.

In our study, only one patient who received nicardipine required adjunctive antihypertensive agent infusion to maintain optimal blood pressure, whereas 42.3% of patients in the nitroglycerin group required adjunctive antihypertensive agent infusion. Because nitroglycerin induces resistance within 1 day[26–29], this result may reflect resistance to nitroglycerin. Although nicardipine induces hypotension and phlebitis as adverse effects, no patient who received nicardipine exhibited these adverse effects in our study. Nicardipine also appears to be more tolerable than nitroglycerin as a continuous infusion in patients with hypertensive AHFS. Nicardipine acts on coronary arteries to decrease arterial resistance, thereby increasing coronary blood flow and reducing the generation of lactate in left ventricular myocardial cells[30]. A similar effect may also be induced by high-dose nitroglycerin. These results provide additional evidence that nicardipine may be more beneficial than nitroglycerin in the treatment of hypertensive AHFS.

In this study, only 14 (24.1%) patients had a history of chronic heart failure, and 13 (27.1%) patients presented with reduced LVEF. In the subgroup analysis, nicardipine was more effective in patients without a reduced ejection fraction. Several studies have reported that patients with AHFS and preserved ejection fraction exhibit higher SBP than those with reduced ejection fraction[31, 32]. This finding indicates that nicardipine may be more effective in patients with hypertensive AHFS because vascular failure is the primary cause of heart failure without reduced ejection fraction.

Table 4 Subgroup analysis of clinical outcomes

	All patients			Excluding patients on renal replacement therapy		
EF ≤ 40	Nitroglycerin (N=8)	Nicardipine (N=5)	*P* value	Nitroglycerin (N=7)	Nicardipine (N=2)	*P* value
BPC time, hours	5.9 ± 5.8	1.5 ± 1.0	0.07¶	2.0 (2.0–5.75)	1.25 (0.5–2.0)	0.22
PPV time, days	1.0 (1.0–2.0) (N=5)	2.0 (1.5–3.5) (N=4)	0.36	1.0 (1.0–2.0) (N=5)	2.0 (N=1)	–
Duration of continuous infusion anti-hypertensive agents, days	2.4 ± 1.5	1.2 ± 1.3	0.18¶	2.0 (1.5–3.5)	2.0 (1.0–3.0)	0.65
Contra, no. (%)	3 (37.5%)	0%	0.23	2 (28.6%)	0%	1.00
Length of hospital stay, days	17.5 ± 16.1	14.2 ± 12.4	0.70¶	16.0 (6.0–33.5)	15.5 (12.0–19.0)	1.0
EF > 40	Nitroglycerin (N=15)	Nicardipine (N=20)	*P* value	Nitroglycerin (N=10)	Nicardipine (N=14)	*P* value
BPC time, hours	4.5 (2.0–12.8)	1.0 (0.5–1.3)	<0.01	5.3 (2.0–8.5)	1.0 (0.5-1.0)	<0.01
PPV time, days	2.0 (2.0–3.0) (N=13)	2.0 (1.0–3.0) (N=16)	0.63	2.0 (2.0–4.0) (N=10)	3.0 (2.0–4.0) (N=11)	0.89
Duration of continuous infusion anti-hypertensive agents, days	3.0 (2.5–6.0)	2.0 (1.0–3.0)	0.06	3.0 (3.0–6.0)	2.0 (2.0–4.0)	0.19
Contra, no. (%)	8 (53.3%)	1 (5%)	<0.01	5 (50.0%)	1 (7.1%)	0.05
Length of hospital stay, days	21.0 (12.5–29.0)	9.0 (6.5–15.0)	<0.01	24.2 ± 13.3	12.3 ± 6.1	0.02¶

Continuous variables are expressed as mean ± standard deviation for normally distributed variables and as median (interquartile range) for non-normally distributed variables. Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables, unless otherwise indicated. BPC: blood pressure control; PPV: positive pressure ventilation; Contra: administration of the opposite drug. ¶: Student's *t*-test, †: χ^2 test.

The main limitations of this study include its single-center, retrospective, and observational design. Because of the limited sample size, we cannot definitively conclude that nicardipine is superior to nitroglycerin in the treatment of hypertensive AHFS. Furthermore, half of the patients with acute hypertensive AHFS display reduced LVEF[33], whereas the LVEF was reduced in only 27.1% of the patients in this study. Thus, our results may have included a potential selection bias. We cannot discuss the long-term effects of nicardipine because this was a short-term study. Thus, further studies are needed to clarify the long-term efficacy of nicardipine, including assessments of mortality and recurrence of AHFS.

Conclusion

We performed a single-center, retrospective, observational study to compare the effectiveness of nicardipine and nitroglycerin for the treatment of hypertensive AHFS. Compared with nitroglycerin, nicardipine exhibited reduced time to optimal blood pressure control, duration of continuous infusion of antihypertensive agents, and length of hospital stay. No patient who received nicardipine required additional nitroglycerin to maintain blood pressure. Thus, nicardipine appears to be beneficial for treating hypertensive AHFS.

Conflicts of interest: None.

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