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Original Contribution

Use of nitroglycerin by bolus prevents intensive care unit admission in patients with acute hypertensive heart failure☆,☆☆

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ABSTRACT

Objectives: The purpose of this study was to compare health care resource utilization among patients who were given intravenous nitroglycerin for acute heart failure (AHF) in the emergency department (ED) by intermittent bolus, continuous infusion, or a combination of both.
Methods: We retrospectively identified 395 patients that received nitroglycerin therapy in the ED for the treatment of AHF over a 5-year period. Patients that received intermittent bolus (n = 124) were compared with continuous infusion therapy (n = 182) and combination therapy of bolus and infusion (n = 89). The primary outcomes were the frequency of intensive care unit (ICU) admission and hospital length of stay (LOS).
Results: On unadjusted analysis, rates of ICU admission were significantly lower in the bolus vs infusion and combination groups (48.4% vs 68.7% vs 83%, respectively; $P < .0001$) and median LOS (interquartile range) was shorter (3.7 [2.5-6.2 days]) compared with infusion (4.7 [2.9-7.1 days]) and combination (5.0 [2.9-6.7 days]) groups; $P = .02$. On adjusted regression models, the strong association between bolus nitroglycerin and reduced ICU admission rate remained, and hospital LOS was 1.9 days shorter compared with infusion therapy alone. Use of intubation (bolus [8.9%] vs infusion [8.8%] vs combination [16.9%]; $P = .096$) and bilevel positive airway pressure (bolus [26.6%] vs infusion [20.3%] vs combination [29.2%]; $P = .21$) were similar as was the incidence of hypotension, myocardial injury, and worsening renal function.
Conclusions: In ED patients with AHF, intravenous nitroglycerin by intermittent bolus was associated with a lower ICU admission rate and a shorter hospital LOS compared with continuous infusion.

1. Introduction

Vasodilators are considered one of the mainstay therapies for acute heart failure (AHF) management. For hypertensive patients with AHF, existing guidelines recommend the use of vasodilators to provide preload and afterload reduction [1-4]. Although vasodilators improve hemodynamics and symptoms in such patients, they provide no apparent benefit on mortality or hospital readmissions [5-7]. For hypertensive AHF, nitroglycerin is the vasodilating agent of choice, and when given intravenously (IV), is typically administered as a continuous infusion (dose range, 5-400 μg/min). However, continuous infusions of nitroglycerin have been associated with increased health care costs and hospital length of stay (LOS) leading to questions about their utility in management of AHF [6].

When administered in higher doses by intermittent bolus, nitrates result in greater arterial dilation and more substantial reduction in cardiac afterload leading to favorable changes in central pressure dynamics [8,9]. Existing trial data on the use of bolus, high dose nitrates suggest that such hemodynamic effects may be accompanied by lower rates of endotracheal intubation, myocardial infarction, and intensive care unit (ICU) admission [10-12] but the real-world impact of this approach on resource utilization has not been evaluated.

Based on prior work by our research group supporting the use of bolus nitroglycerin therapy [12], its use has become routine in clinical

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practice as part of the management of dyspneic, emergency department (ED) patients with hypertensive AHF at our institution. Accordingly, we designed the present study to examine the impact of intermittent bolus nitroglycerin therapy on resource utilization, specifically ICU admission rate and hospital LOS. We hypothesized that administration of nitroglycerin by intermittent bolus would be associated with a lower rate of ICU admission and shorter hospital LOS when compared with continuous infusion.

2. Methods

2.1. Study design

This was a retrospective observational cohort study of IV nitroglycerin use in ED patients with AHF. This study protocol was approved by Wayne State University institutional review board before initiation with waiver of need for informed consent.

2.2. Study setting and population

All included patients were treated in the ED of Detroit Receiving Hospital, a university-affiliated, urban teaching hospital and is part of the Detroit Medical Center and serves a predominantly African-American population in the metropolitan area of Detroit, Michigan for AHF between January 1, 2007 and July 31, 2011. During the study period, Detroit Receiving Hospital had an annual ED census of approximately 100 000 visits, and an average of 1400 yearly AHF admissions.

2.3. Study protocol

Patients older than 18 years who were treated in the ED for AHF as documented in the treatment note and received IV nitroglycerin were included. Potentially eligible patients were identified by a query of electronic pharmacy orders, enabling comprehensive capture of every patient that received IV nitroglycerin during the study period, regardless of the manner of administration. Once identified, ED treatment notes were reviewed and complete records for those patients with a final primary ED diagnosis of AHF who had specific documentation of AHF as the reason for treatment with nitroglycerin were abstracted. Patients were included only if IV nitroglycerin was started in the ED as documented in the electronic medication administration record (eMAR). Patients were excluded if they were pregnant, had IV nitroglycerin orders but not documented as given on the eMAR or received nitroglycerin for other indications such as acute coronary syndrome, blood pressure management, or hypertensive emergency not related to AHF. Although there is no clinical protocol for treatment of AHF with IV nitroglycerin at our facility, it is typically reserved for patients with elevated blood pressure (>160 mm Hg) who have marked dyspnea. When administered by bolus, 10 mg of nitroglycerin is prepared in a 10 mL syringe and given by IV push in increments up to 2 mg every 3 to 5 minutes. Nitroglycerin infusions are prepared and administered in a usual clinical manner, with starting dose and titration parameters set by the treating physician. Hospital policy mandates ICU admission for any patient on a titratable vasoactive infusion (nitroglycerin included) at the time of disposition; patients who received IV boluses or who were on infusions in the ED that were discontinued could be admitted to non-ICU settings.

Electronic medical records were reviewed and study variables including demographic information, comorbidities, baseline medications, hemodynamic data, and laboratory values were abstracted. Ejection fraction was recorded if documented in the treatment note or available via echocardiography report within the 12 months preceding the index visit. Nitroglycerin use variables were abstracted from the eMAR and nursing care flow sheets. Information collected included the dose and number of nitroglycerin boluses given as well as starting rate and maximum rate for continuous infusions. Hemodynamic variables such as blood pressure measurements and heart rate along with respiratory rate, and pulse oximetry during the first 180 minutes of presentation were also collected.

Data on disposition from the ED (admission to ICU or non-ICU setting), LOS (ED, ICU, total hospital), and need for airway management in the ED (bilevel positive airway pressure [BiPAP] or endotracheal intubation) were recorded. Length of stays was abstracted from the hospital's bed tracking status application. Heart failure specific hospital readmission rates through 30 days were also tracked using the electronic medical record (which captures visits to any of 4 hospitals that comprise the Detroit Medical Center system in the metropolitan area of Detroit, MI), using date of discharge as time 0. The investigators were not blinded to the purpose of the study. Records were reviewed by a resident physician, a pharmacist, and a medical student. All data abstracted by the medical student were then reviewed by the pharmacist investigator. All discrepancies between the medical student and the pharmacist abstractions were adjudicated by consensus of all 3 reviewers. Abstractors were trained by the principal investigator using a single data dictionary that contained definitions for each variable and coded response to be entered on the standardized abstraction form to ensure uniform data collection and accuracy. Abstractors were trained by the principal investigator using a single data dictionary that contained definitions for each variable and coded response to be entered on the standardized abstraction form to ensure uniform data collection and accuracy. Missing data were coded as not available and any uncertainty regarding data variables or coding was reconciled by the principal investigator.

2.4. Outcome measures

All patients in the study were analyzed for characterization of the treatment course in the ED. The primary outcome variables of interest were the need of ICU admission, defined as admitted to the ICU from the ED, and hospital LOS. Patients who were evaluated by the ICU team but not admitted to the ICU were classified as not requiring ICU admission. The main secondary outcomes were the ED and ICU LOS, and the incidence of adverse events including hypotensive episodes, defined as systolic blood pressure (SBP) more than 90 mm Hg at any time during the first 180 minutes post nitroglycerin administration; incidence of acute myocardial injury, defined as an increase in cardiac troponin of at least 0.25 ng/mL within the first 24 of presentation; and interval development or worsening of renal dysfunction, determined by an increase in serum creatinine by 0.5 or more during the first 24 and 48 hours of presentation. Other outcomes included the rates of mechanical ventilation and BiPAP use in the ED.

2.5. Data analysis

Included patients were categorized into the following 3 groups: (1) bolus nitroglycerin group (bolus), which included patients who received 1 or more intermittent bolus doses at least 0.5 mg of IV nitroglycerin; (2) continuous infusion of nitroglycerin group (infusion), which included those who received a continuous infusion of IV nitroglycerin without any administration of intermittent nitroglycerin bolus doses; and (3) combination of intermittent bolus and continuous infusion of IV nitroglycerin group (combination), which included those that received both bolus followed by continuous dosing of IV nitroglycerin. Baseline characteristics were analyzed using descriptive statistics and reported as proportions, mean (standard deviations) or median (interquartile range [IQR]) when appropriate. Categorical variables were analyzed χ^2 test. Analyses of continuous variables were compared using an unpaired t test, Wilxocon test, Kruskal-Wallis test, or 1-way analysis of variance as appropriate. All tests were 2-tailed, and a P value less than .05 was considered statistically significant. Stata 14.1 (StataCorp, College Station, TX) was used for all analyses.

As this study was observational (ie, patients were not randomly assigned to treatment), standard methods to compare the 3 groups could not be used because of potential bias in treatment assignment. To approximate the causal effect of differing treatments on ICU admission and hospital LOS, we used a treatment-effects estimator. Stata offers 6 different treatment-effects estimators to address nonrandom treatment assignment. Under correct model specification, all the estimators generally produce similar results. Regression adjustment uses contrasts of averages of treatment-specific predicted outcomes to estimate treatment effects and was chosen here as it is a natural base-case estimator when one knows some of the determinants of the outcome. Unlike propensity score matching and nearest neighbor matching, regression adjustment can also handle more than 2 groups making it appropriate for a 3-group comparison. The following covariates were used in our regression adjustment as they may influence the decision to use different treatments and both primary outcome measures: age, sex, race, initial troponin, initial brain natriuretic peptide, initial SBP, initial heart rate, initial respiratory rate, initial oxygen saturation, medical history of chronic HF, medical history of hypertension, use of BiPAP, and use of mechanical ventilation. As ICU admission was a binary outcome, logistic regression was used as the functional form. Length of stay was treated as a count variable with use of a Poisson functional form.

Based on our 2007 paper that showed an absolute reduction in the ICU admission rate of approximately 40% with bolus IV nitroglycerin (12), a minimum of 71 patients per group were needed to have 90% power to detect an equivalent or greater effect size, with a 0.05 2-sided significance level.

3. Results

A total of 1227 patients were identified from our pharmacy electronic medication orders. Of these, 395 patients (124 in bolus, 182 in infusion, and 89 in combination) met the eligibility criteria based on review of ED treatment records and were included in the study (Figure). The most common reasons for exclusion were non-AHF indication for nitroglycerin and IV nitroglycerin ordered but not documented as given on the eMAR. Demographics and baseline clinical characteristics of study patients are summarized for all 3 study groups in Table 1. There were no significant differences among all 3 groups with respect to age, sex, or race with most study patients being African American. Initial SBP and diastolic blood pressure were significantly higher in the combination group. There were a total of 4 patients that had initial SBP 100 mm Hg or less that received nitroglycerin therapy (2 in bolus group, 1 in infusion group, and 1 in combination group). Patients that received continuous therapy of nitroglycerin alone had significantly lower baseline respiratory rate than the other 2 groups. Bolus patients were more likely to have a history of chronic HF, chronic obstructive pulmonary disease (COPD), and atrial fibrillation, and were more likely to be on guideline directed medical therapy for chronic HF (Table 2).

In the bolus group, the median (IQR) total dose of nitroglycerin was 2 (1-2) mg; 79% of patients received 1 dose, 14.6% received 2 doses, 4% received 3 doses, and 3 patients received at least 4 doses of bolus nitroglycerin. One patient received 10 repeat doses of bolus nitroglycerin for a total of 20 mg. The median (IQR) starting rate of nitroglycerin infusion in the infusion group was 20 (10-30) μg/min with a maximum rate of 35 (20-50) μg/min. In the combination group, the median (IQR) dose of the boluses was 2 (2-4) mg, with 40.5% received 1 dose, 28.1% received 2 doses, 9% received 3 doses, and 12.4% received 4 or more nitroglycerin boluses. The median (IQR) starting rate of nitroglycerin infusion was 20 (10-40) μg/min and the maximum rate was 60 (30-100) μg/min in these patients. The median (IQR) duration of nitroglycerin infusion therapy was 16 (5.2-41.5) hours in the infusion group and 16.5 (5-38.9) hours in the combination group. Similar proportions of patients received at least 1 dose of IV furosemide (70.2% bolus vs 75.8% infusion vs 73% combination; $P = .54$) with a median (IQR) initial furosemide dose of 60 (40-80) mg in the bolus vs 60 (40-80) mg in the infusion group vs 60 (40-80) mg in combination ($P = .76$). Hemodynamic and respiratory effects over the first 180 minutes post nitroglycerin administration.

Primary and secondary outcomes are presented in Table 3. In the unadjusted analysis, patients who received nitroglycerin bolus therapy alone were significantly less likely to require ICU admission (48.4% bolus vs 68.7% infusion vs 83% combination; $P < .0001$) and median (IQR) total hospital LOS was significantly shorter: bolus = 3.7(2.5-6.2) days; infusion = 4.7 (2.9-7.1) days; and combination = 5.0 (2.9-6.7) days; $P = .02$. There were no differences in the duration of ED or ICU LOS among the study groups. The rates of mechanical ventilation were statistically similar but there was a trend toward higher rates in the combination group (16.9% combination vs 8.9% bolus vs 8.8% infusion,

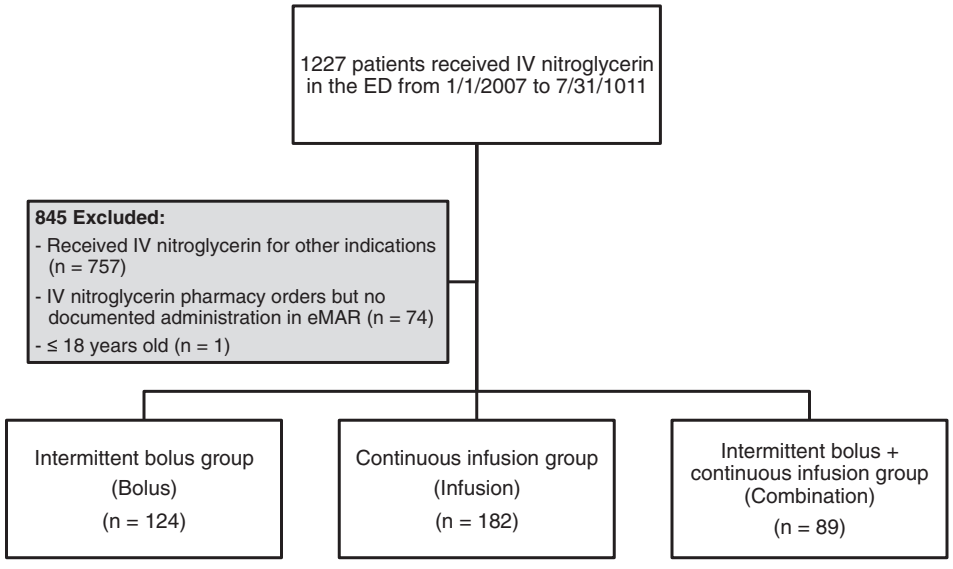

Figure. Flow diagram for patient inclusion.

Table 1
Demographic and baseline clinical characteristics

	Bolus (n = 124)	Infusion (n = 182)	Combination (n = 89)	*P*
Age (y)	56 (27-71)	56 (49-69)	57 (49-68)	.70
Male	61 (49.6)	99 (54.4)	42 (47.2)	.49
African American	109 (87.9)	161 (88.5)	79 (88.8)	.41
Ejection fraction on admission (%)	35 (20-55) (n = 98)	30 (20-50) (n = 131)	35 (20-55) (n = 70)	.23
Baseline brain natriuretic peptide (pg/mL)	1685 (618-4013) (n = 118)	1839 (840-3785) (n = 171)	2100 (784-2663) (n = 86)	.063
BUN, initial (mg/dL)	19 (14-28)	21 (15-32)	21 (13-42)	.73
Scr, initial (mg/dL)	1.2 (1.0-2.0)	1.3 (1.1-2.1)	1.4 (1.0-3.1)	.14
Troponin, initial (ng/mL)	0.11 (0.05-0.32)	0.06 (0.04-0.14)	0.09 (0.05-0.20)	.0018
Initial vital signs				
SBP (mm Hg)	186 (169-212)	184 (159-210)	206 (186-231)	<.001*
DBP (mm Hg)	110 (95-121)	110 (92-125)	120 (106-139)	.003*
Heart rate (bpm)	108 (92-128) (n = 119)	107 (94-120) (n = 179)	117 (98-128) (n = 89)	.13
Pulse oxygenation (%)	95 (88-98) (n = 122)	97 (92-99) (n = 168)	95 (89-98) (n = 81)	.17
Respiratory rate (breaths per min)	24 (20-32) (n = 119)	22 (18-28) (n = 175)	28 (21-34) (n = 85)	<.001†

Continuous data are presented as median (IQR); categorical data are presented as number (percentage).
Abbreviations: BUN, blood urea nitrogen; DBP, diastolic blood pressure; Scr, serum creatinine.
* No statistical difference between bolus and continuous infusion nitroglycerin groups.
† No statistical difference between bolus nitroglycerin and bolus + infusion groups.

$P = .096$). The use of BiPAP was also similar across all groups ($P = .21$). In-hospital mortality rate was similar as well (2 [1.7%] bolus group vs 7 [4%] infusion group vs 3 [3.5] combination group; $P = .52$) but hospital readmission within 30 days was significantly higher among the infusion group (65% infusion vs 33% bolus vs 28.5% combination group; $P = .001$).

Table 4 describes the incidence of adverse events. Overall, there were no differences in the rates of hypotension, myocardial injury, or worsening renal function between the 3 groups. None of the patients that had initial SBP 100 mm Hg or less experienced hypotension.

In the logistic regression model, probability of being admitted to the ICU was 48% in the bolus group, compared with 67% for the infusion group and 79% for the combination group. The difference between bolus and infusion groups was statistically significant ($P = .006$), but no difference was found between the combination and infusion groups ($P = .052$). In the Poisson regression model, patients in the bolus group had an average hospital LOS of 4.4 days compared with 6.3 days for the infusion group and 7.3 days for the combination group. Again, there was a statistically significant difference in hospital LOS between bolus and infusion groups ($P = .01$) but not between combination and infusion groups ($P = .27$). Because COPD prevalence was different between groups, we re-ran the models including adjustment for COPD. Although our logistic regression model for ICU admission failed to converge due to the low overall prevalence (19%) of COPD in our study cohort, the Poisson model evaluating LOS was stable, with no impact of COPD on outcome. We then analyzed our data excluding patients with a history of COPD and the unadjusted rate of ICU admission remained lower in the bolus group (43.7% bolus vs 68.2% infusion vs 83.1% combination; $P < .0001$). To enable convergence, we compared the bolus group with a pooled group including both infusion and combination patients, and found a statistically significant absolute reduction in the ICU admission rate among bolus patients of 25% ($P = .001$). Using the same approach, we did not find a significant difference in hospital LOS between bolus (5.1 days) and infusion/combination therapy (6.5 days); $P = .054$.

Table 2
Patient medical and medication history

	Bolus (n = 124)	Infusion (n = 182)	Combination (n = 89)	*P*
Medical history				
Atrial fibrillation	16 (13.0)	5 (2.7)	3 (3.4)	.001
Coronary artery disease	22 (17.7)	30 (16.5)	11 (12.4)	.55
Chronic kidney disease	14 (11.3)	19 (10.4)	6 (6.7)	.52
Chronic HF	89 (71.8)	96 (52.7)	40 (44.9)	<.001
COPD	37 (29.8)	28 (15.4)	12 (13.5)	.002
Diabetes mellitus	45 (36.6)	68 (37.4)	23 (25.8)	.15
End-stage renal disease	17 (13.7)	11 (6.0)	17 (19.1)	.004
Hypertension	101 (81.5)	136 (74.7)	78 (87.6)	.04
Myocardial infarction	16 (12.9)	16 (8.8)	9 (10.1)	.51
Stroke	3 (2.4)	8 (4.4)	4 (4.5)	.63
Home medications				
ACE inhibitor/ARB	54 (43.5)	71 (39)	28 (31.5)	.20
Aspirin	52 (41.9)	54 (29.7)	19 (21.3)	.005
β-Blocker	75 (60.5)	78 (42.9)	40 (44.9)	.007
Digoxin	10 (8.1)	10 (5.5)	1 (1.1)	.08
Hydralazine	20 (16.1)	22 (12.1)	13 (14.6)	.59
Isosorbide mononitrate/dinitrate	28 (22.6)	32 (17.6)	13 (14.6)	.31
Loop diuretic	55 (44.4)	60 (33)	21 (23.6)	.006
Nonloop diuretic	10 (8.1)	10 (5.5)	6 (6.7)	.67
MRA	11 (8.9)	11 (6.0)	3 (3.4)	.26

Data are reported as number (percentage).
Abbreviations: ACE inhibitor, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; MRA, mineralocorticoid receptor antagonist.

4. Discussion

Based on this retrospective analysis, intermittent bolus nitroglycerin is a viable alternative to continuous infusion in patients with AHF, providing similar clinical effectiveness with a 20% to 30% reduction in the need for ICU admission and a decrease in hospital LOS of 2 to 3 days. Because this was a retrospective study with unbalanced cohorts, we used the adjusted models to account for confounders that were clinically relevant such as age, sex, race, biomarkers of myocardial stress and injury, baseline blood pressure, oxygenation status, and use of accessory ventilatory support, as well as underlying history of chronic HF and found that the association between bolus nitroglycerin and improved resource utilization was maintained. Although we did not adjudicate the determination of AHF, relying instead on what was reported by the treating clinician in the medical record, there was stability in our findings related to both ICU admission rate and LOS with exclusion of (and accounting for) patients with COPD, making it less likely that group differences were due to misdiagnosis of undifferentiated dyspnea.

We acknowledge that at least some of this difference reflects the requirement for ICU admission in patients on titratable vasoactive infusions at our hospital. However, in institutions such as ours where a nitroglycerin or other vasoactive infusion mandates admission to

Table 3
Primary and secondary outcomes

	Bolus (n = 124)	Infusion (n = 182)	Combination	*P*			
				Overall	Bolus vs infusion	Bolus vs combination	Infusion vs combination
Primary outcomes:							
ICU admission	60 (48.4)	125 (68.7)	74 (83.0)	<.0001	<.0001	<.0001	.006
Hospital LOS (d)	3.7 (2.5-6.2)	4.7 (2.9-7.1)	5.0 (2.9-6.7)	.02	.006	.039	.84
Secondary outcomes:							
ICU LOS (d)	2.5 (1.6-3.9) (n = 56)	2.7 (1.3-4.9) (n = 124)	2.1 (1.2-4.0) (n = 75)	.60	.56	.71	.33
ED LOS (h)	6.4 (2.6-14.1)	6.3 (4.0-12.6)	5.9 (3.0-10.9)	.43	.40	.90	.21
BiPAP rate	33 (26.6)	37 (20.3)	26 (29.2)	.21	.20	.68	.10
BiPAP duration (h)	3.9 (2.01-13.6) (n = 33)	8.2 (3.5-22.1) (n = 37)	6.6 (3.6-14.3) (n = 26)	.38	.15	.37	.59
Mechanical ventilation rate	11 (8.9)	16 (8.8)	15 (16.9)	.096	.98	.079	.05
Length of mechanical ventilation (d)	1.1 (0.6-1.7)	1.1 (0.9-2.0)	1.2 (0.9-1.8)	.79	.98	.65	.53
Readmission for AHF within 30 d	17 (13.7)	43 (23.6)	4 (4.5)	.001	.001	.736	.01

Data are reported as number (percentage) or median (IQR).

the ICU, such admission could be avoided by the use of bolus administration rather than a continuous infusion of nitroglycerin. As nitroglycerin confers no direct benefit on mortality or other hard end points when used to treat AHF, our findings challenge the use of continuous nitroglycerin infusions, suggesting that they can be safely and effectively supplanted using a bolus approach.

These data support our earlier work that showed a reduction in ICU admission with intermittent bolus nitroglycerin; however, unlike that study, we did not find any clear benefit on the rates of mechanical ventilation or BiPAP with the use of intermittent bolus therapy [12]. Although this difference may be attributable to the lower total dose of bolus nitroglycerin used by clinicians in this analysis (median 2 mg vs median 6 mg), present results reflect real-world practice and a dosing regimen that was based solely on clinical need as determined by the treating physician.

Though not tracked in prior study, use of combination therapy with intermittent bolus followed by continuous infusion was also associated with a lower rate of AHF specific readmission within 30 days compared with the use of bolus nitroglycerin or infusion therapy alone. Whether this signals a true treatment effect or a consequence of treatment-propensity–related bias is not clear. Patients that received combination therapy were less likely to have a history of chronic HF and, as such, might inherently be at lower risk for postdischarge adverse events. That said, they were also more hypertensive and tachypneic at presentation than the other 2 cohorts, potentially indicating a more severe acute disease with a greater degree of respiratory distress, thus requiring a more aggressive therapy with combination of bolus and continuous infusion. Despite this, there was no significant difference in the rates of intubation or BiPAP compared with other groups, suggesting that intermittent bolus nitroglycerin may provide clinical benefit above and beyond an infusion alone approach in patients with more severe clinical manifestations without additional adverse events.

In addition to effectiveness signals, we found no statistical difference in adverse event rates, including the incidence of hypotension or myocardial injury with the use of intermittent bolus nitroglycerin, either alone or in combination with a continuous infusion. In fact, 2 patients in the bolus group had initial blood pressures of 84/55 and 96/69 received 1 and 2 mg of bolus nitroglycerin with no adverse events. This was potentially a concern with the use of high doses of nitroglycerin given that previous evidence indicated a decrease in myocardial blood flow in patients with coronary heart disease given sublingual nitroglycerin [13] Combined with prior literature [10,12], our results suggest that bolus nitroglycerin can be safely used alone or in combination with standard continuous infusion of IV nitroglycerin in patients with AHF.

4.1. Limitations

This study has several limitations. First, it was based on clinical data derived from a single institution that serves an urban population in the metropolitan area of Detroit. Therefore, our study, which was almost 90% African American, and related findings (especially the in-hospital mortality rate) may not be generalizable to a more heterogeneous HF population. Our institution also serves a predominantly under resourced community and many of our patients are unable to obtain prescriptions or describe their medications, which makes it difficult to accurately capture such data. As a result, patients in our study have lower reported usage of HF guideline directed medical therapy such as angiotensin-converting enzyme inhibitor, angiotensin II receptor blockers, β-blockers, and loop diuretics. However, as we focused on immediate interventions and in-hospital outcomes, home medications are

Table 4
Adverse events

	Bolus (n = 124)	Infusion (n = 182)	Combination (n = 89)	*P*
Incidence of hypotension	2 (1.9) (n = 108)	2 (1.3) (n = 159)	5 (6) (n = 82)	.068
Incidence of myocardial injury on serial troponin measurement	11 (12.4) (n = 89)	29 (17.2) (n = 169)	10 (12.8) (n = 78)	.49
24-h increase in Scr by ≥0.5	11 (11.7) (n = 94)	14 (9.2) (n = 152)	11 (1.3) (n = 82)	.59
48-h increase in Scr by ≥0.5	8 (8.5) (n = 94)	20 (12.9) (n = 155)	5 (6.7) (n = 75)	.28
RIFLE* criteria	(n = 54)	(n = 117)	(n = 46)	.13
0	46 (85.2)	109 (93.2)	37 (80.5)	
1	6 (11.1)	7 (6.0)	6 (13)	
2	2 (3.7)	1 (0.8)	3 (6.5)	

Data are reported as number (percentage).
* RIFLE = Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease.

less likely to have had an impact on our targeted end points. The retrospective nature of our study could pose bias as well as investigators were not blinded to outcome when extracting data. Misclassification for some data elements and the diagnosis of AHF itself may also have occurred because we relied solely on documentation as available in the electronic medical record. Similarly, the retrospective nature of our study limited our ability to perform complete data abstraction for some measures as information was incomplete or missing. Moreover, as we only had access to medical records from a single hospital system, 30-day readmission data may be an underestimate. Lastly, we only included patients who received nitroglycerin as part of routine AHF management, and thus cannot comment on the general effectiveness of nitroglycerin for AHF. However, our goal was not to compare nitroglycerin with other AHF therapies, focusing instead on the route of administration when such therapy is clinically indicated.

5. Conclusions

When IV nitroglycerin is used to treat AHF, administration by intermittent bolus is associated with fewer ICU admissions and shorter hospital LOS compared with standard infusion therapy. Safety and effectiveness with a bolus approach are similar as well, challenging the need for continuous nitroglycerin infusions in the management of AHF. Such findings warrant study in a future prospective, randomized, multicenter trial.

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None.

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