Original Research

CLINICAL OUTCOMES OF HIGH-DOSE NITROGLYCERINE IN SYMPATHETIC CRASHING ACUTE PULMONARY EDEMA IN THE EMERGENCY DEPARTMENT: A RETROSPECTIVE INSTITUTIONAL STUDY

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ABSTRACT

Background: Sympathetic crashing acute pulmonary edema is a life-threatening form of acute heart failure characterized by severe hypertension, respiratory distress, and rapid clinical deterioration. Conventional low-dose nitroglycerine may be insufficient to counteract the extreme afterload. HDN (High-Dose Nitroglycerine), combined with NIV (Non-Invasive Ventilation), has been proposed to achieve faster hemodynamic stabilization. This study evaluates clinical outcome of HDN in SCAPE, with a focus on symptom resolution and emergency department length of stay.

Methods: This retrospective cohort study included 35 adult patients presenting with SCAPE (Sympathetic crashing acute pulmonary edema) between December 2023 and December 2025. All patients received HDN (bolus 800–1000 mcg and infusion >100 mcg/min) along with NIV. Clinical data were extracted from electronic health records. Primary outcomes included symptom resolution at 6 hours and ED length of stay. Secondary outcomes were the need for intubation, ICU admission, mortality, and hypotension. Statistical analysis involved a paired t-test/Wilcoxon test and a chi-square/Fisher's exact test, with $p<0.05$ considered significant.

Results: The mean age was 60.54 ± 12.86 years, with 57.2% patients above 60 years. Significant improvement was observed in all clinical parameters at 6 hours: respiratory rate (−11.54), systolic BP (−52.71 mmHg), MAP (−32.77), heart rate (−32.29), and SpO_2 (+13.51) ($p<0.001$). Symptom resolution was achieved in 88.6% of patients. The mean ED length of stay was 6.97 ± 1.89 hours. Intubation and ICU admission rates were 11.4% each, while mortality was 5.7%. No cases of hypotension were observed. Failure of symptom resolution was significantly associated with worse outcomes and prolonged ED stay.

Conclusion: High-dose nitroglycerine combined with NIV is an effective and safe strategy for rapid stabilization of SCAPE patients. It significantly improves clinical parameters, reduces ED length of stay, and is associated with low rates of complications, supporting its use as a first-line therapy in emergency settings.

Keywords: SCAPE, High-Dose Nitroglycerine, Acute Pulmonary Edema, Emergency Department, Non-Invasive Ventilation, Length of Stay.

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INTRODUCTION

Sympathetic crashing acute pulmonary edema represents a severe and rapidly progressive form of acute heart failure characterized by sudden onset respiratory distress, marked hypertension, and sympathetic overactivity.[1] Unlike traditional cardiogenic pulmonary edema, SCAPE

(Sympathetic Crashing Acute Pulmonary Edema) is primarily driven by acute redistribution of fluid into the pulmonary interstitium due to a surge in systemic vascular resistance rather than absolute fluid overload.[2] This distinct pathophysiology necessitates rapid afterload reduction as the cornerstone of management.

Conventional therapy for acute pulmonary edema has historically included oxygen supplementation, diuretics, and low-dose vasodilators such as nitroglycerine.[3] However, low-dose nitroglycerine (5–40 mcg/min) predominantly causes venodilation and may be insufficient to counteract the profound afterload elevation observed in SCAPE.[4] Delayed or inadequate treatment may lead to worsening respiratory failure, increased need for mechanical ventilation, and higher morbidity.

Recent literature has highlighted the role of high-dose nitroglycerine (HDN), administered as intravenous boluses (600–1000 mcg) followed by high-rate infusions (>100 mcg/min), in rapidly reducing both preload and afterload.[5] This approach facilitates improved cardiac output, reduces pulmonary congestion, and promotes faster clinical stabilization. Studies have demonstrated that HDN, especially when combined with NIV, can significantly decrease the need for endotracheal intubation and intensive care admission.[6] Furthermore, emerging evidence suggests that early aggressive vasodilation with HDN may improve patient-centered outcomes, including shorter emergency department length of stay and reduced hospital resource utilization.[7] Despite these promising findings, concerns regarding potential adverse effects such as hypotension have limited its widespread adoption in clinical practice.[8] Additionally, there remains a relative paucity of real-world data, particularly from institutional settings, evaluating both efficacy and safety outcomes of HDN in SCAPE. Given the increasing burden of SCAPE presentations and ED overcrowding, there is a critical need to identify therapeutic strategies that ensure rapid stabilization while maintaining safety.[9]

AIMS AND OBJECTIVES

This study aims to evaluate the clinical outcome of high-dose nitroglycerine in SCAPE patients, focusing on early symptom resolution and emergency department length of stay. Symptom resolution at 6 hours is defined by achieving at least two of the following: reduced respiratory rate (<24/min or ↓25%), controlled blood pressure (≤160/100 mmHg or MAP <120), and improved oxygen saturation (≥90% on room air or ≥95% on oxygen). Secondary objectives include assessing the need for mechanical ventilation, ED disposition and its length of stay.

MATERIALS AND METHODS

This retrospective institutional cohort study was conducted at SDM College of Medical sciences & Hospital, Shri Dharmasthala Manjunatheshwara University, Dharwad, Karnataka. The Study was carried out from December 2023 and December 2025 in the department of Emergency Medicine. Ethical approval was obtained from the Institutional Ethics Committee before conducting the study. The study included adult patients (>18 years) presenting with SCAPE who received intravenous nitroglycerine between 2023 and 2025. High-dose nitroglycerine is defined as an initial bolus of 800–1000 mcg over 2 minutes and/or infusion rates exceeding 100 mcg/min. Data will be collected from the institutional EHR (Electronic Health Record), including emergency department physician and nursing notes to assess clinical presentation and time of stabilization, medication administration records to obtain dosing details; and triage and admission-discharge logs to determine accurate timelines such as ED arrival, decision to admit, and ED length of stay.

Inclusion and Exclusion Criteria

Adult patients (≥18 years) with SCAPE were included if they presented with acute dyspnea (<6 hours), respiratory rate ≥30/min, SpO_2 <90% on room air, hypertension (SBP ≥160 mmHg, DBP ≥100 mmHg, or MAP ≥120 mmHg), features of sympathetic surge, and evidence of pulmonary edema by POCUS and chest radiographs. Patients were excluded if they had hypotension or shock, required immediate intubation before nitroglycerine, had contraindications to NTG, significant obstructive cardiac lesions, alternative diagnoses, or incomplete medical records.

Data Collection Procedure

Data for this retrospective study will be collected from the institutional EHR system by identifying adult patients (>18 years) presenting with clinical features of SCAPE between December 2023 and December 2025. Emergency department physician and nursing notes will be reviewed to confirm eligibility criteria and determine the time of clinical stabilization. Detailed information on nitroglycerine administration, including dosage, timing, and titration of high-dose boluses (800–1000 mcg) and infusions (>100 mcg/min), will be extracted from medication records. Triage and ER admission-discharge logs will be used to obtain precise timestamps for ED arrival, decision to admit, and departure to calculate ED length of stay. Clinical outcomes at 6 hours will be assessed based on predefined criteria for symptom resolution, and additional data will be collected regarding the need for mechanical ventilation, ED disposition, and its length of hospital stay.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using appropriate statistical software. Continuous variables were expressed as mean ± SD or median, and categorical variables as frequencies and percentages. Normality was assessed using tests such as the Shapiro–Wilk test. Comparisons between baseline and 6-hour clinical parameters were performed using a paired t-test or Wilcoxon signed-rank test as appropriate, while associations between categorical variables were analyzed using Chi-square or Fisher's exact test. A p-value <0.05 was considered statistically significant, and all tests were two-tailed.

RESULTS

Variable		Frequency	Percentage
Age Group	≤40 years	4	11.4%
	41–50 years	3	8.6%
	51–60 years	8	22.9%
	61–70 years	12	34.3%
	>70 years	8	22.9%
Gender	Male	19	54.3%
	Female	16	45.7%

Table 1: Age and Gender Distribution

Majority of patients belonged to the older age groups, with **57.2% above 60 years**. The mean age was **60.54 ± 12.86 years**, ranging from **32 to 82 years**. Males were slightly more common than females.

Parameter	Mean ± SD	Median	Range
Respiratory rate /min	35.83 ± 3.49	36	28–46
SBP mmHg	196.43 ± 16.15	190	180–230
DBP mmHg	113.00 ± 11.06	112	100–140
MAP mmHg	140.63 ± 10.42	137	127–170
SpO_2 on room air	81.03 ± 9.19	84	60–92
Heart rate /min	119.14 ± 11.65	120	80–140
BNP	1461.74 ± 953.54	1090	408–4000

Table 2: Baseline Clinical Parameters on Arrival

Patients presented with marked respiratory distress, severe hypertension, tachycardia, and hypoxia, consistent with SCAPE. Mean systolic BP was nearly **196 mmHg**, and mean room-air SpO_2 was only **81%**, confirming severe acute presentation.

Treatment Variable	Frequency	Percentage
NIV used	35	100.0%
High-dose NTG infusion >100 mcg/min	35	100.0%
NTG bolus 800 mcg	19	54.3%
NTG bolus 1000 mcg	16	45.7%

Table 3: Treatment Characteristics

All patients in the cohort (100%) received non-invasive ventilation (NIV) as well as high-dose nitroglycerin (NTG) infusion (>100 mcg/min), indicating a standardized treatment approach across the study population. This uniformity suggests that these interventions were part of a predefined protocol or first-line management strategy.

Regarding bolus dosing, there is a near-even distribution between 800 mcg (54.3%) and 1000 mcg (45.7%) NTG boluses.

Parameter	On Arrival Mean ± SD	At 6 Hours Mean ± SD	Mean Change	p-value
Respiratory rate /min	35.83 ± 3.49	24.29 ± 3.48	−11.54	<0.001
SBP mmHg	196.43 ± 16.15	143.71 ± 14.87	−52.71	<0.001
DBP mmHg	113.00 ± 11.06	89.60 ± 7.34	−23.40	<0.001
MAP mmHg	140.63 ± 10.42	107.86 ± 8.85	−32.77	<0.001
SpO_2	81.03 ± 9.19	94.54 ± 3.06	+13.51	<0.001
Heart rate /min	119.14 ± 11.65	86.86 ± 12.43	−32.29	<0.001

Table 4: Comparison of Clinical Parameters at Arrival and 6 Hours

There was statistically significant improvement in all clinical parameters at 6 hours. Respiratory rate, blood pressure, MAP, and heart rate reduced significantly, while oxygen saturation improved significantly. This indicates rapid clinical stabilization following high-dose nitroglycerine with NIV.

Outcome	Frequency	Percentage
Resolution achieved	31	88.6%
Resolution not achieved	4	11.4%

Table 5: Primary Outcome: Resolution of Symptoms at 6 Hours

Symptom resolution at 6 hours was achieved in **88.6%** of patients. This suggests high clinical efficacy of high-dose nitroglycerine in rapidly stabilizing SCAPE patients.

Variable	Mean ± SD	Median	Range
ED LOS in hours	6.97 ± 1.89	6	4–11

Table 6: ED Length of Stay

The mean ED length of stay was approximately **7 hours**, with most patients stabilized and shifted out of the emergency department within a relatively short duration.

Outcome	Frequency	Percentage
Intubation required	4	11.4%
ICU admission	4	11.4%
HDU admission	31	88.6%
In-hospital mortality	2	5.7%
Hypotension	0	0.0%

Table 7: Secondary Outcomes

The dataset reflects outcomes in a cohort of patients with a strong predominance of HDU (High Dependency Unit) admissions, accounting for 88.6% of cases. This suggests that most patients required close monitoring but not the highest level of critical care, likely reflecting effective early stabilization in the emergency department with high-dose nitroglycerin therapy.

Both intubation and ICU admissions were relatively uncommon, each occurring in 11.4% of patients. This indicates that only a small proportion progressed to severe respiratory compromise or required intensive life support.

The in-hospital mortality rate was 5.7%, which is relatively low, implying generally favourable outcomes within this population. Notably, no cases of hypotension (0.0%) were observed, suggesting stable hemodynamic status across the cohort.

Outcome	Resolution Yes n=31	Resolution No n=4	p-value
Intubation	0	4	<0.001
ICU admission	0	4	<0.001
Mortality	0	2	0.010
ED LOS, mean ± SD	6.55 ± 1.55	10.25 ± 0.50	<0.001

Table 8: Association of Symptom Resolution with Outcomes

Failure to achieve symptom resolution at 6 hours was significantly associated with intubation, ICU admission, mortality, and longer ED stay. Patients who improved at 6 hours had shorter ED stays and better outcomes.

In this retrospective cohort of **35 SCAPE patients**, high-dose nitroglycerine with NIV resulted in **88.6% symptom resolution at 6 hours** and significant improvement in respiratory rate, blood pressure, oxygen saturation, and heart rate, with **no documented hypotension**. The intubation rate and ICU admission rate were both **11.4%**, and mortality was **5.7%**. These findings support high-dose nitroglycerine as an effective and safe strategy for rapid stabilization of SCAPE patients in the emergency department.

DISCUSSION

In this retrospective cohort of 35 patients with SCAPE, the demographic profile showed a predominance of older individuals (mean age 60.54 ± 12.86 years) with slight male preponderance, which is consistent with prior studies on acute heart failure where elderly populations are disproportionately affected.[2,9] Similar observations have been reported in large registries and reviews, where advancing age and comorbid

hypertension are key contributors to acute pulmonary edema presentations.[3]

The baseline clinical characteristics in our study-marked hypertension (mean SBP ~196 mmHg), tachycardia, tachypnea, and hypoxia-closely resemble the classic SCAPE phenotype described in the literature.[2,8] Levy et al. demonstrated that patients with hypertensive acute pulmonary edema typically present with significantly elevated blood pressure and respiratory distress, driven by a sudden increase in afterload rather than fluid overload.[8] This pathophysiological mechanism has also been emphasized by Pang et al., highlighting the role of increased systemic vascular resistance and fluid redistribution in acute heart failure syndromes.[2]

A key finding of our study is the statistically significant improvement in all clinical parameters at 6 hours following treatment with HDN and NIV. There was a marked reduction in respiratory rate, systolic and diastolic blood pressure, mean arterial pressure, and heart rate, along with significant improvement in oxygen saturation ($p<0.001$). These results are consistent with previous studies by Mathew et al. and Siddiqua et al., which demonstrated rapid hemodynamic stabilization and symptomatic relief with HDN therapy.[5,6] The dual action of HDN in reducing both preload and afterload explains this rapid improvement and supports its use as a first-line intervention in SCAPE.

In our study, symptom resolution at 6 hours was achieved in 88.6% of patients, which is comparable to outcomes reported in observational studies and systematic reviews. Pranata et al., in a recent meta-analysis, reported that high-dose nitroglycerine is associated with improved clinical outcomes and faster symptom resolution compared to conventional dosing strategies.[7] Similarly, Stemple et al. reported high rates of clinical improvement with HDN, further supporting its efficacy.[1]

The mean emergency department (ED) length of stay in our study was approximately 7 hours, indicating rapid stabilization and early disposition. This aligns with findings from Long et al., who suggested that aggressive vasodilator therapy can reduce ED congestion by facilitating quicker clinical recovery.[4] In the current era of overcrowded emergency departments, such reductions in ED length of stay are clinically and operationally significant.

Secondary outcomes in our study further reinforce the benefits of HDN therapy. The rates of intubation and ICU admission were both 11.4%, which are relatively low compared to historical data. Previous studies have shown that early use of HDN combined with NIV reduces the need for invasive mechanical ventilation.[1,6] Notably, no cases of hypotension were observed in our study, addressing a common concern associated with high-dose nitrate therapy. This finding is consistent with prior research demonstrating that, when used appropriately, HDN is hemodynamically safe.[5,7]

An important observation in our study is the strong association between failure of symptom resolution at 6 hours and adverse outcomes, including higher rates of intubation, ICU admission, mortality, and prolonged ED stay. This highlights the prognostic significance of early clinical response, which has also been emphasized in other acute heart failure studies.[2,10]

The findings are in agreement with the growing body of evidence supporting the use of high-dose nitroglycerine in SCAPE. The combination of rapid symptom relief, improved hemodynamic parameters, reduced need for invasive interventions, and absence of significant adverse effects underscores its role as an effective and safe therapeutic strategy in emergency settings.

Limitations

This study is limited by its retrospective design, small sample size (n=35), and lack of a control group, which restrict causal inference and generalizability. Being a single-center study with reliance on electronic records, it is also prone to selection bias and unmeasured confounding factors that may have influenced the outcomes.

CONCLUSION

In conclusion, high-dose nitroglycerine combined with non-invasive ventilation appears to be an effective and safe treatment strategy for patients with sympathetic crashing acute pulmonary edema, leading to rapid clinical stabilization and high rates of symptom resolution within 6 hours. The study demonstrated significant improvement in hemodynamic and respiratory parameters, low rates of intubation and ICU admission, and no observed hypotension, along with a relatively short emergency department length of stay. These findings support the potential role of high-dose nitroglycerine as a frontline therapy in SCAPE management; however, larger prospective and controlled studies are needed to further validate these results and establish standardized treatment protocols.

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