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# Outcomes after attempted resuscitation for in-ICU cardiac arrest in septic shock: stratification by the 2026 Delphi consensus vasopressor threshold

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## Abstract

**Introduction:** Patients with septic shock may experience in-ICU cardiac arrest while receiving vasopressors, yet clinicians lack objective survival estimates following attempted resuscitation. The 2026 SCCM/ESICM Delphi consensus proposed norepinephrine-equivalent (NEE) >0.50 µg/kg/min as one criterion within the definition of refractory septic shock.

**Aim of Study:** To characterize outcomes after attempted resuscitation for in-ICU cardiac arrest in septic shock, stratified by the 2026 SCCM/ESICM consensus vasopressor threshold.

**Materials and Methods:** We conducted a retrospective cohort study using MIMIC-IV (2008–2022) involving adults with septic shock who received continuous vasopressors for ≥3 hours, regardless of dose, and subsequently experienced in-ICU cardiac arrest with attempted cardiopulmonary resuscitation (CPR). Patients were stratified by pre-arrest NEE dose (≤0.50 vs >0.50 µg/kg/min). The primary outcome was ICU survival; secondary outcomes were 2-hour, 24-hour, and hospital survival. Prespecified sensitivity analyses evaluated ≥1-hour and ≥6-hour vasopressor cohorts. Exploratory multivariable logistic regression adjusted for age, sex, and Charlson Comorbidity Index.

**Results:** Among 94,458 ICU admissions, 564 had in-ICU cardiac arrest with attempted CPR, of whom 213 had sepsis or septic shock. Of these, 118 received continuous vasopressors for ≥3 hours and constituted the final analytic cohort (51 with pre-arrest NEE >0.50 µg/kg/min and 67 with NEE ≤0.50). Among patients with pre-arrest NEE >0.50 µg/kg/min, 2-hour survival was similar to those with NEE ≤0.50 (49.0% vs 55.2%; P=0.50), but ICU survival was lower (2/51 [3.9%; 95% CI, 0.5–13.5]. vs 11/67 [16.4%; 95% CI, 8.5–27.5].; P=0.039), as were 24-hour (13.7% vs 41.8%; P=0.001) and hospital survival (1/51 [2.0%; 95% CI, 0.1–10.5]. vs 9/67 [13.4%].; P=0.042). After adjustment, NEE >0.50 µg/kg/min was associated with lower ICU survival (OR 0.18; 95% CI 0.04–0.85; P=0.031). No patient receiving ≥6 hours of vasopressors with pre-arrest NEE >0.50 µg/kg/min survived to hospital discharge (0/39; 95% CI, 0–9.0%).

**Conclusions:** Among patients with septic shock who underwent attempted resuscitation for in-ICU cardiac arrest, pre-arrest NEE >0.50 µg/kg/min was associated with substantially lower post-resuscitation ICU survival. Hospital survival was rare: only one patient receiving ≥3 hours of vasopressors survived, and none receiving ≥6 hours. These exploratory findings warrant validation in larger multicenter studies.

**Keywords:** Septic Shock; Cardiopulmonary Resuscitation; Cardiac Arrest; Intensive Care Units; Vasopressors; Prognosis

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## Introduction

Septic shock is a life-threatening syndrome characterized by profound circulatory and metabolic abnormalities that often require prolonged intensive care and life-sustaining therapies. With advances in antimicrobial therapy, hemodynamic resuscitation, and organ support, septic shock remains a potentially reversible condition, and many patients recover with continued

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aggressive treatment [1-3]. For those who fail to recover, however, in-ICU cardiac arrest often represents the terminal stage of progressive shock and is associated with substantially worse outcomes than cardiac arrest from other causes [4-7].

Vasopressor dose is widely recognized as an objective marker of shock severity, with higher norepinephrine-equivalent (NEE) doses associated with increasing mortality across the spectrum of septic shock [8–12]. Previous studies have described outcomes among patients receiving high-dose vasopressor therapy and, separately, outcomes following sepsis-associated in-hospital cardiac arrest [4–14]. However, these two bodies of literature have evolved largely in parallel, without examining patients in whom advanced vasopressor-dependent shock is complicated by cardiac arrest requiring attempted cardiopulmonary resuscitation (CPR).

This gap has important implications for prognostic communication and shared decision-making. Although the Surviving Sepsis Campaign guidelines recommend early discussions regarding prognosis and goals of care in patients with septic shock, clinicians and families currently lack evidence directly applicable to cardiac arrest occurring during advanced vasopressor-dependent shock [3]. Consequently, decisions regarding attempted resuscitation often rely on extrapolation from broader septic shock or in-hospital cardiac arrest populations.

Historically, studies have used heterogeneous definitions of high-dose or refractory vasopressor therapy, limiting comparisons across cohorts. In 2026, a joint Society of Critical Care Medicine and European Society of Intensive Care Medicine (SCCM/ESICM) Delphi consensus proposed a norepinephrine-equivalent dose >0.50 μg/kg/min as the vasopressor-dose criterion within the definition of refractory septic shock, providing a standardized threshold for describing advanced vasopressor-dependent shock [15]. Post-resuscitation survival among patients above this threshold, however, has not been systematically characterized.

We therefore used the MIMIC-IV database to characterize real-world survival following attempted resuscitation after in-ICU cardiac arrest among patients with septic shock receiving vasopressor therapy. Patients were stratified according to the NEE threshold (>0.50 μg/kg/min), corresponding to the vasopressor-dose criterion within the 2026 SCCM/ESICM consensus definition of refractory septic shock. We aimed to provide scenario-specific estimates of post-resuscitation survival using this consensus criterion.

## Materials and methods

### Study Design and Data Source

We conducted a retrospective observational cohort study using the Medical Information Mart for Intensive Care IV (MIMIC-IV, version 3.1), a publicly available database containing de-identified health records from adult patients admitted to six intensive care units at Beth Israel Deaconess Medical Center, Boston, Massachusetts, between 2008 and 2022. MIMIC-IV contains detailed information on demographics, physiologic measurements, medications, laboratory results, procedures, and clinical outcomes. Access to MIMIC-IV is governed by a data-use agreement, and separate institutional review board approval was not required because all data are fully de-identified [16,17].

### Patient Selection

Adult patients (≥18 years) were eligible if they met all of the following criteria: i) Septic shock identified using ICD-9 codes 785.52 and 995.92 and ICD-10 codes A40 and A41 (all subcodes) and R65.21; ii) In-ICU cardiac arrest with attempted cardiopulmonary resuscitation; and iii) Continuous vasopressor infusion for at least three hours immediately preceding cardiac arrest. ICD-coded sepsis or septic shock was used as a pragmatic screen, consistent with the exploratory intent of the study. In-ICU cardiac arrest with attempted CPR was identified using the 'Cardiac Arrest' (itemid 225466) event in the MIMIC-IV 'procedureevents' table, whose recorded start time was used as the 'CPR initiation' timestamp. The first such event per ICU stay was retained.

### Exposure Definition

The primary exposure was pre-arrest norepinephrine-equivalent (NEE) dose, categorized according to the 2026 SCCM/ESICM consensus vasopressor threshold (>0.50 μg/kg/min) [15].

NEE (μg/kg/min) = norepinephrine + epinephrine + (phenylephrine × 0.06) + (dopamine ÷ 100) + (vasopressin × 2.5) [18].

For each patient, all vasopressor infusion records active at any point within the 1-hour window immediately preceding cardiac arrest were identified. For each vasopressor agent, the maximum NEE contribution

observed within this window was retained, and these per-agent maxima were summed to derive the total pre-arrest NEE.

### NEE stratum and duration cohorts

As consensus on a specific vasopressor-duration criterion within the 2026 SCCM/ESICM Delphi definition has not been established [15], we defined the primary cohort as patients receiving ≥3 hours of continuous vasopressor infusion before arrest, selected a priori to identify patients with established vasopressor-dependent shock beyond the initial resuscitation period. The primary outcome was also analyzed in prespecified sensitivity cohorts at ≥1 hour and ≥6 hours. Within each cohort, patients were stratified by NEE at the time of arrest (≤0.50 vs >0.50 μg/kg/min), independent of prior dose trajectory. This stratification reflects the dose at arrest and does not imply sustained doses above the threshold for any specific duration beforehand.

### Outcomes

The primary outcome was ICU survival following attempted resuscitation after in-ICU cardiac arrest. Secondary outcomes included 2-hour survival, 24-hour survival, and hospital survival to discharge. Survival to 2 hours after cardiac arrest was used as a pragmatic early endpoint to capture the immediate post-CPR period, during which most re-arrests and early deaths occur. This endpoint reflects survival only and does not imply sustained ROSC or successful resuscitation.

### Covariates

Clinical variables extracted from MIMIC-IV included age, sex, race, Charlson Comorbidity Index, approximate Sequential Organ Failure Assessment (SOFA) score during the 24 hours preceding arrest, pre-arrest serum lactate, creatinine, platelet count, $PaO_2/FiO_2$ ratio, Glasgow Coma Scale score, mechanical ventilation, renal replacement therapy, pulmonary source of infection, malignancy, transplant status, and time from ICU admission to cardiac arrest.

An approximate SOFA score was reconstructed from available respiratory, coagulation, hepatic, cardiovascular, neurologic, and renal components. Because the vasopressor dose directly contributes to the cardiovascular SOFA component, SOFA was used for descriptive purposes only and was not included in the primary adjusted analyses.

### Statistical Analysis

Continuous variables were presented as median (interquartile range [IQR].) and compared using the Wilcoxon rank-sum test. Categorical variables were presented as counts (percentages) and compared using Pearson's chi-square or Fisher's exact test, as appropriate. Exact 95% confidence intervals were calculated using the Clopper-Pearson method.

Multivariable logistic regression was performed as an exploratory analysis to evaluate whether observed differences in ICU survival persisted after adjustment for baseline characteristics. Prespecified covariates included age, sex, and Charlson Comorbidity Index. A sensitivity model additionally adjusted for mechanical ventilation and renal replacement therapy and used Firth's penalized likelihood method. To assess the robustness of the NEE exposure definition, additional sensitivity analyses used the time-weighted mean NEE over standardized 60-, 30-, and 15-minute pre-arrest windows in place of the peak-based definition. In a further sensitivity analysis, the primary cohort was restricted to patients meeting the official Sepsis-3 criteria before cardiac arrest, defined as suspected infection and SOFA occurring on or before the time of arrest within the index ICU stay. In an exploratory analysis, NEE was also modeled as a continuous variable. Analyses were performed using Stata/SE version 19 (StataCorp, College Station, TX). All tests were two-sided, and a p-value <0.05 was considered statistically significant.

## Results

### Cohort Characteristics

Between 2008 and 2022, the MIMIC-IV contained 94,458 ICU admissions, of which 564 patients experienced an in-ICU cardiac arrest. Among these, 213 had a diagnosis of sepsis or septic shock, and 118 had received continuous vasopressor therapy for at least 3 hours before cardiac arrest, comprising the primary analytic cohort (Figure 1). The cohort included 67 patients with a pre-arrest NEE dose ≤0.50 μg/kg/min and 51 with NEE >0.50 μg/kg/min. Predefined sensitivity cohorts requiring at least 1 hour and at least 6 hours of continuous vasopressor therapy before cardiac arrest included 125 and 101 patients, respectively.

Table 1 summarizes baseline characteristics of the primary ≥3-hour cohort (≥3 hours of continuous vasopressor infusion before arrest, regardless of dose;

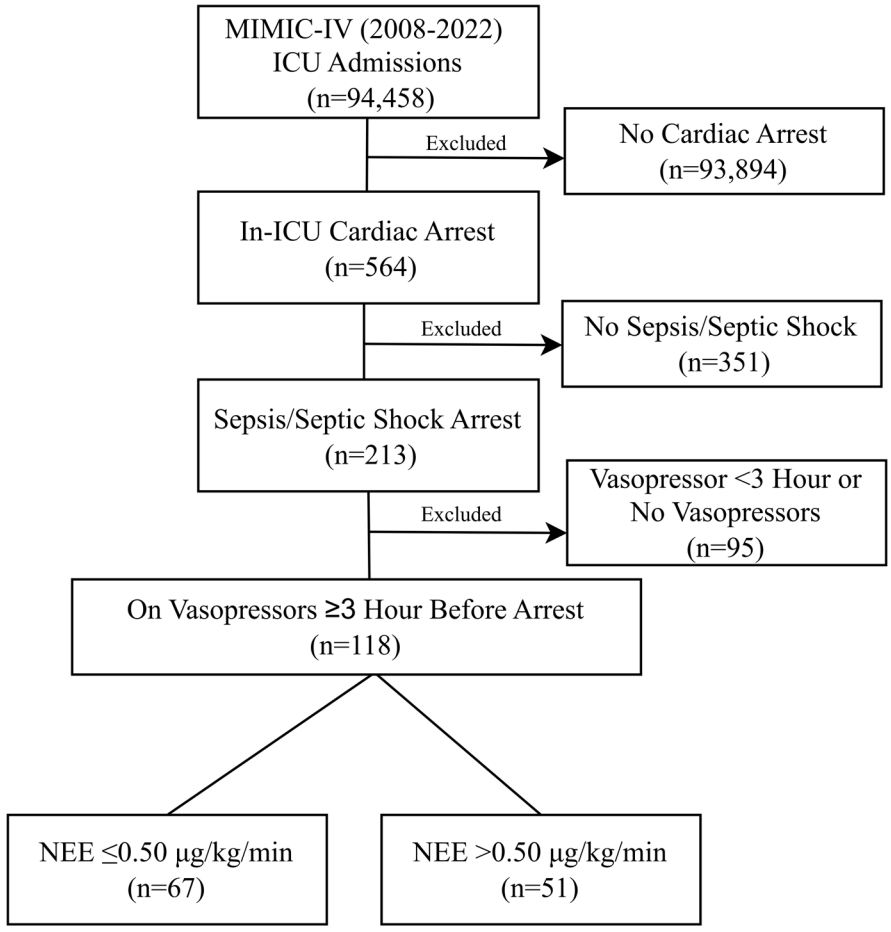



**Figure 1. Patient selection flow diagram. From 94,458 MIMIC-IV ICU admissions, 118 patients with septic shock and in-ICU cardiac arrest while receiving vasopressors for at least 3 hours formed the primary analytic cohort, stratified by pre-arrest norepinephrine-equivalent dose (NEE) stratum. NEE = norepinephrine-equivalent vasopressor dose; ICU = intensive care unit.**

**Table 1. Baseline Characteristics of the ≥3-Hour Vasopressor-Exposed Cohort by NEE Stratum**

| Characteristic | ≤0.50 (n=67) | >0.50 (n=51) | p value |
|---|---|---|---|
| Demographics | | | |
| Age, years, median [IQR] | 66 [54–73] | 63 [52–69] | 0.32 |
| Male, n (%) | 40 (59.7) | 36 (70.6) | 0.22 |
| Race, n (%) | | | |
| White | 39 (58.2) | 22 (43.1) | 0.11 |
| Black | 8 (11.9) | 8 (15.7) | |
| Hispanic | 4 (6.0) | 1 (2.0) | |
| Asian | 0 (0.0) | 3 (5.9) | |
| Other/Unknown | 16 (23.9) | 17 (33.3) | |
| Comorbidity and pre-arrest severity | | | |
| Charlson Comorbidity Index, median [IQR] | 4 [2–6] | 4 [2–6] | 0.96 |
| Approximate pre-arrest SOFA score, median [IQR] | 14 [11–16] | 15 [13–18] | 0.003 |
| Closest pre-arrest lactate, mmol/L, median [IQR]* | 2.8 [2.1–5.2] | 7.5 [4.8–10.7] | <0.001 |
| $PaO_2/FiO_2$ ratio, median [IQR] | 93 [46–179] | 59 [43–97] | 0.055 |
| Minimum GCS, median [IQR] | 6 [3–10] | 3 [3–7] | 0.013 |
| Creatinine, mg/dL, median [IQR] | 2.1 [1.3–3.7] | 2.5 [1.7–4.1] | 0.17 |
| Platelets, $\times 10^3/\mu L$, median [IQR] | 157 [82–250] | 109 [50–175] | 0.029 |
| Time from ICU admission to arrest, h, median [IQR] | 99.9 [24.8–251.0] | 28.6 [9.6–89.6] | 0.001 |

| Characteristic | ≤0.50 (n=67) | >0.50 (n=51) | p value |
|---|---|---|---|
| NEE at arrest, µg/kg/min, median [IQR] | 0.23 [0.11–0.37] | 0.75 [0.60–1.18] | <0.001 |
| Organ support before arrest | | | |
| Mechanical ventilation before arrest, n (%) | 55 (82.1) | 47 (92.2) | 0.11 |
| Renal replacement therapy before arrest, n (%) | 27 (40.3) | 21 (41.2) | 0.92 |
| Infection source and special populations | | | |
| Pulmonary source, n (%) | 44 (65.7) | 27 (52.9) | 0.16 |
| Malignancy, n (%) | 9 (13.4) | 5 (9.8) | 0.55 |
| Transplant, n (%) | 2 (3.0) | 4 (7.8) | 0.23 |

Values are median [interquartile range] or n (%). Race p-value is across all categories combined. Approximate pre-arrest SOFA was reconstructed from available variables within 24 hours before arrest. *Excluding the final 30 minutes before arrest to minimize inclusion of peri-arrest lactate measurements. NEE = norepinephrine-equivalent vasopressor dose; SOFA = Sequential Organ Failure Assessment; GCS = Glasgow Coma Scale; ICU = intensive care unit.

NEE stratified at arrest). Demographic characteristics and chronic comorbidity burden were similar between groups. Age, sex, race, Charlson Comorbidity Index, serum creatinine, mechanical ventilation, renal replacement therapy, pulmonary source of infection, malignancy, and transplant status did not differ significantly. In contrast, patients with NEE >0.50 µg/kg/min demonstrated substantially greater physiologic derangement immediately before cardiac arrest. Median approximate SOFA score was higher (15 [IQR 13–18] vs 14 [11–16]; p=0.003), median pre-arrest lactate was markedly elevated (7.5 [4.8–10.7] vs 2.8 [2.1–5.2] mmol/L; p<0.001), minimum Glasgow Coma Scale score was lower (3 [3–7] vs 6 [3–10]; p=0.013), platelet count was lower (109 [50–175] vs 157 [82–250] $\times 10^3$/µL; p=0.029), and the interval from ICU admission to cardiac arrest was substantially shorter (28.6 [9.6–89.6] vs 99.9 [24.8–251.0] hours; p=0.001).

## Survival Following In-ICU Cardiac Arrest

Survival outcomes are summarized in Table 2. Although 2-hour survival following attempted resuscitation was similar between groups (49.0% [25/51; 95% CI, 34.8–63.4] vs 55.2% [37/67; 95% CI, 42.6–67.4]; p=0.50), survival diverged substantially thereafter. Twenty-four-hour survival was 13.7% (7/51; 95% CI, 5.7–26.3%) among patients with NEE >0.50 µg/kg/min compared with 41.8% (28/67; 95% CI, 29.8–54.5%) among those with NEE ≤0.50 µg/kg/min (p=0.001). ICU survival was likewise lower among patients with NEE >0.50 µg/kg/min (3.9% [2/51; 95% CI, 0.5–13.5] vs 16.4% [11/67; 95% CI, 8.5–27.5]; p=0.039), as was hospital survival (2.0% [1/51; 95% CI, 0.1–10.5] vs 13.4% [9/67; 95% CI, 6.3–24.0]; p=0.042).

These findings were consistent across the predefined sensitivity cohorts. In the ≥1-hour vasopressor cohort, 2-hour survival remained similar between

**Table 2. Survival Outcomes by Minimum Duration of Vasopressor Exposure Before Arrest and NEE Stratum**

| Minimum Vasopressor Exposure Before Arrest | NEE Stratum (µg/kg/min) | n | 2-Hour Survival n/N (%) [95% CI] | 24-Hour Survival After Arrest n/N (%) [95% CI] | ICU Survival n/N (%) [95% CI] | Hospital Survival n/N (%) [95% CI] |
|---|---|---|---|---|---|---|
| ≥3 hours | ≤0.50 | 67 | 37/67 (55.2%) [42.6–67.4] | 28/67 (41.8%) [29.8–54.5] | 11/67 (16.4%) [8.5–27.5] | 9/67 (13.4%) [6.3–24.0] |
| | >0.50 | 51 | 25/51 (49.0%) [34.8–63.4] | 7/51 (13.7%) [5.7–26.3] | 2/51 (3.9%) [0.5–13.5] | 1/51 (2.0%) [0.1–10.5] |
| | p-value | | 0.50 | 0.001 | 0.039 | 0.042 |
| ≥1 hour | ≤0.50 | 70 | 39/70 (55.7%) [43.3–67.6] | 29/70 (41.4%) [30.0–53.8] | 11/70 (15.7%) [8.1–26.4] | 9/70 (12.9%) [6.1–23.0] |
| | >0.50 | 55 | 28/55 (50.9%) [37.1–64.6] | 9/55 (16.4%) [7.8–28.8] | 4/55 (7.3%) [2.0–17.6] | 2/55 (3.6%) [0.4–12.5] |
| | p-value | | 0.59 | 0.002 | 0.18 | 0.11 |
| ≥6 hours | ≤0.50 | 62 | 34/62 (54.8%) [41.7–67.5] | 27/62 (43.5%) [31.0–56.7] | 11/62 (17.7%) [9.2–29.5] | 9/62 (14.5%) [6.9–25.8] |
| | >0.50 | 39 | 18/39 (46.2%) [30.1–62.8] | 6/39 (15.4%) [5.9–30.5] | 1/39 (2.6%) [0.1–13.8] | 0/39 (0%) [0–9.0] |
| | p-value | | 0.40 | 0.003 | 0.026 | 0.012 |

Values are presented as n/N (%) with exact 95% confidence intervals unless otherwise specified. P-values were calculated using Pearson's chi-square test and Fisher's exact test, as appropriate. NEE = norepinephrine-equivalent vasopressor dose; ICU = intensive care unit.

groups (55.7% vs 50.9%; p=0.59), whereas 24-hour survival was significantly lower among patients with NEE >0.50 μg/kg/min (16.4% vs 41.4%; p=0.002). ICU survival (7.3% vs 15.7%; p=0.18) and hospital survival (3.6% vs 12.9%; p=0.11) demonstrated the same direction of effect but did not reach statistical significance. In the ≥6-hour cohort, 2-hour survival again remained similar (54.8% vs 46.2%; p=0.40), whereas 24-hour survival (15.4% vs 43.5%; p=0.003), ICU survival (2.6% vs 17.7%; p=0.026), and hospital survival (0% vs 14.5%; p=0.012) consistently favored patients with NEE ≤0.50 μg/kg/min. Notably, among patients who had received continuous vasopressor therapy for at least 6 hours and whose NEE at the time of arrest exceeded 0.50 μg/kg/min, none survived to hospital discharge (0/39; 95% CI, 0–9.0%).

Figure 2 illustrates the distribution of individual NEE values according to 24-hour, ICU, and hospital survival across the three prespecified vasopressor-duration cohorts, demonstrating progressively fewer sustained survivors above the Delphi threshold.

The primary findings were robust to the NEE exposure definition. Compared with the peak-based definition, the time-weighted mean NEE over standardized 60-, 30-, and 15-minute pre-arrest windows reclassified 4 of 118 (3.4%), 2 of 118 (1.7%), and 1 of 118 (0.8%) patients, respectively, across the 0.50 μg/kg/min threshold, with all four discordant patients dying before ICU discharge. Adjusted ORs for ICU survival were unchanged under each alternative definition (60-minute mean: adjusted OR 0.18; 95% CI 0.04–0.89; p=0.035; 30-minute mean: adjusted OR 0.19; 95% CI 0.04–0.90; p=0.037; 15-minute mean: adjusted OR 0.18; 95% CI 0.04–0.89; p=0.036), closely matching the primary adjusted analysis (adjusted OR 0.18; 95% CI 0.04–0.85; p=0.031).

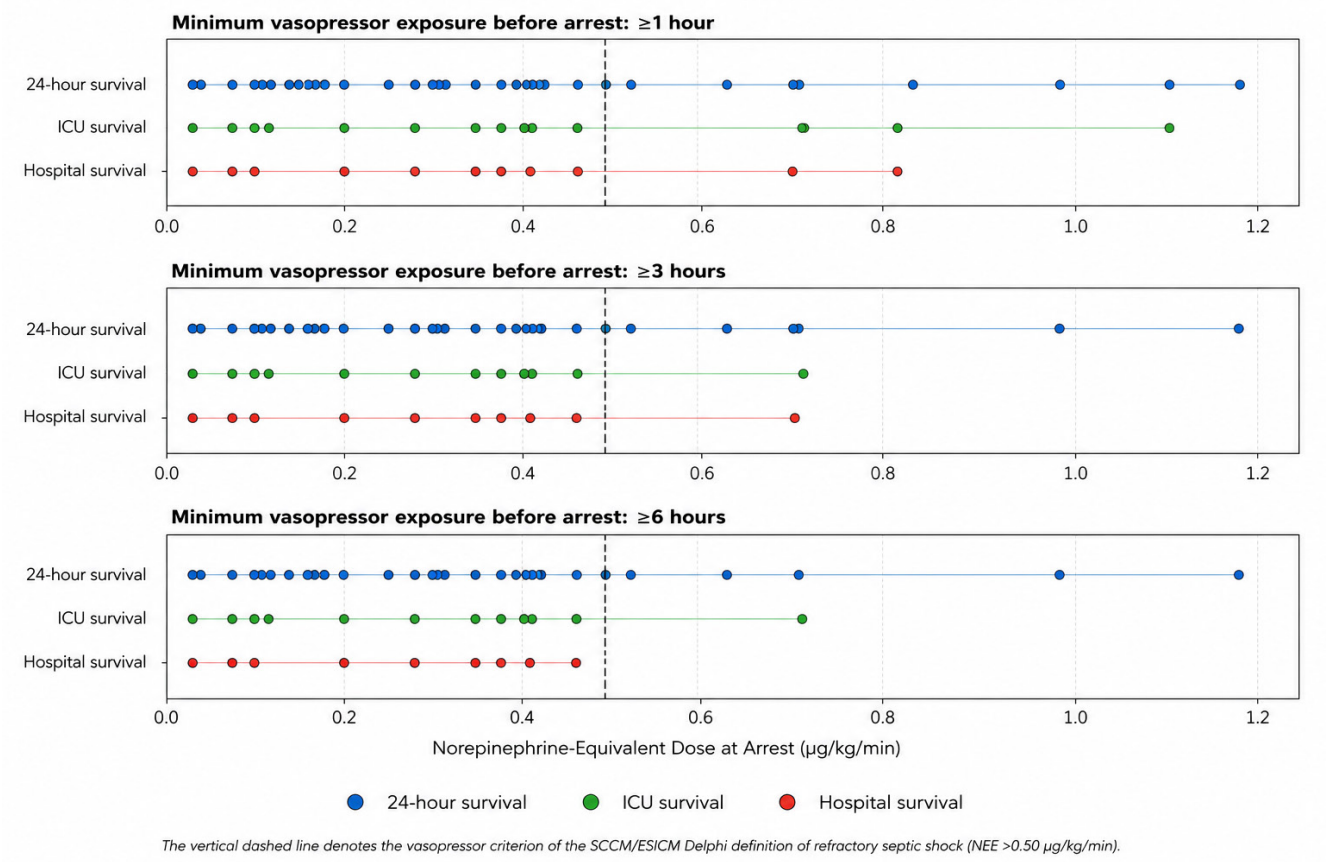



**Figure 2. Survivor norepinephrine-equivalent dose (NEE) distributions across three duration-defined cohorts (minimum vasopressor exposure before arrest: ≥1 hour, ≥3 hours, ≥6 hours). Each panel displays individual survivor NEE values at the time of ICU cardiac arrest, stratified by survival endpoint (24-hour, ICU, hospital). Horizontal lines connect minimum and maximum survivor values within each endpoint. Hospital survivors above NEE 0.50 μg/kg/min became exceedingly uncommon with prolonged vasopressor exposure before arrest, with only one survivor observed in the ≥3-hour cohort and none in the ≥6-hour cohort.**

In the exploratory analysis with NEE as a continuous variable, each 0.1 µg/kg/min increase was associated with lower odds of ICU survival (OR 0.86, 95% CI 0.732–0.998; p = 0.048), consistent with a gradual association across the NEE range. In the sensitivity analysis restricted to patients meeting Sepsis-3 criteria before cardiac arrest (105/118, 89.0%), findings were unchanged: 24-hour survival was 15.6% (7/45; 95% CI 6.5–29.5) in the NEE >0.50 group versus 43.3% (26/60; 95% CI 30.6–56.8) in the NEE ≤0.50 group; ICU survival 4.4% (2/45; 95% CI 0.5–15.1) versus 18.3% (11/60; 95% CI 9.5–30.4); and hospital survival 2.2% (1/45; 95% CI 0.1–11.8) versus 15.0% (9/60; 95% CI 7.1–26.6).

### Exploratory Logistic Regression Analyses

Exploratory logistic regression analyses of ICU survival in the primary ≥3-hour cohort are summarized in Table 3. In the unadjusted model, patients with NEE >0.50 µg/kg/min had significantly lower odds of ICU survival than those with NEE ≤0.50 µg/kg/min (OR 0.21; 95% CI, 0.04–0.98; p=0.048).

Because this was primarily a descriptive study, adjusted analyses were performed as exploratory sensitivity analyses. After adjustment for the prespecified baseline covariates of age, sex, and Charlson Comorbidity Index, the effect estimate remained essentially unchanged (adjusted OR 0.18; 95% CI, 0.04–0.85; p=0.031). Age, sex, and Charlson Comorbidity Index were not significantly associated with ICU survival. Results were similar using Firth's penalized likelihood method (adjusted OR 0.21; 95% CI 0.05–0.89; p=0.034). These adjustments, however, do not account for the substantial imbalance in pre-arrest acute illness severity between NEE strata; the reported association should therefore be interpreted as descriptive rather than independent of acute illness severity.

A sensitivity model additionally adjusted for pre-arrest mechanical ventilation and renal replacement therapy. This adjustment produced minimal change in the observed association (adjusted OR 0.18; 95% CI, 0.04–0.90; p=0.037), and neither mechanical ventilation nor renal replacement therapy was independently associated with ICU survival.

**Table 3. Logistic Regression Analysis of the Association Between NEE >0.50 µg/kg/min Vasopressor Exposure and ICU Survival (n=118)**

| Variable | OR (ICU survival) | 95% CI | p |
|---|---|---|---|
| *Unadjusted model* | | | |
| NEE >0.50 µg/kg/min | 0.21 | 0.04–0.98 | 0.048 |
| *Primary adjusted model* | | | |
| NEE >0.50 µg/kg/min | 0.18 | 0.04–0.85 | 0.031 |
| Age (per year) | 0.98 | 0.93–1.02 | 0.29 |
| Male Gender | 4.80 | 0.90–25.44 | 0.06 |
| Charlson CCI (per point) | 0.96 | 0.72–1.27 | 0.77 |
| *Sensitivity Model (+MV +RRT)* | | | |
| NEE >0.50 µg/kg/min | 0.18 | 0.04–0.90 | 0.037 |
| Age (per year) | 0.97 | 0.93–1.02 | 0.25 |
| Male Gender | 5.41 | 0.99–29.61 | 0.052 |
| Charlson CCI (per point) | 0.96 | 0.72–1.28 | 0.79 |
| Mechanical ventilation | 0.51 | 0.10–2.49 | 0.40 |
| Renal replacement therapy | 0.58 | 0.15–2.19 | 0.42 |

Reference group: NEE ≤0.50 µg/kg/min. The primary adjusted model included prespecified baseline covariates (age, sex, and Charlson Comorbidity Index). The sensitivity model additionally adjusted for pre-arrest mechanical ventilation and renal replacement therapy. OR = odds ratio; CI = confidence interval; NEE = norepinephrine-equivalent vasopressor dose; CCI = Charlson Comorbidity Index.

## Discussion

In this study, patients with septic shock receiving a pre-arrest norepinephrine-equivalent (NEE) dose >0.50 µg/kg/min had substantially lower 24-hour, ICU, and hospital survival following attempted resuscitation than those below this threshold, despite similar 2-hour survival. Over the 14-year study period, only one patient above this threshold survived to hospital discharge, and no patient survived after at least 6 hours of continuous vasopressor therapy. To our knowledge, these findings are among the first to provide real-world, scenario-specific estimates of post-resuscitation survival in patients undergoing attempted resuscitation for in-ICU cardiac arrest, using the vasopressor criterion from the 2026 SCCM/ESICM consensus definition of refractory

septic shock.

Previous studies of high-dose vasopressor therapy have reported hospital survival ranging from approximately 17% to more than 50%, reflecting heterogeneous populations in whom prognosis was assessed during ongoing septic shock rather than after cardiac arrest [8-12]. Conversely, studies of sepsis-associated in-hospital cardiac arrest have reported hospital survival of approximately 7%–17% but generally have not accounted for the severity of pre-arrest vasopressor support [4-7,13]. As a result, clinicians have had little objective evidence to estimate outcomes after CPR in patients receiving advanced vasopressor support. Hospital survival among patients above the SCCM/ESICM vasopressor criterion was substantially lower than reported in either body of literature. This likely reflects the intersection of advanced vasopressor-dependent shock and cardiac arrest, in which the physiological insult of cardiac arrest and reperfusion is superimposed on profound circulatory and metabolic failure [2-4].

An important observation was the divergence between early and sustained survival. Although approximately half of patients in both groups remained alive 2 hours after cardiac arrest, 24-hour, ICU, and hospital survival were substantially lower among patients receiving NEE >0.50 μg/kg/min. Despite similar age and baseline comorbidity burden, these patients demonstrated greater physiologic derangement before arrest, including higher SOFA scores, higher lactate concentrations, lower platelet counts, and a shorter interval from ICU admission to cardiac arrest. Together, these findings suggest that the severity of the underlying shock at the time of arrest may have contributed to the poorer post-resuscitation outcomes observed in this group, consistent with the progressive physiologic deterioration described in advanced septic shock [2,4,8]. However, because MIMIC-IV lacks detailed resuscitation and post-arrest variables, the relative contribution of pre-arrest illness severity and post-arrest factors cannot be determined.

Continuation of aggressive treatment and discussions regarding resuscitation are complementary aspects of caring for patients with septic shock. Septic shock remains a potentially reversible condition, and escalating vasopressor requirements alone should not imply that ongoing treatment is nonbeneficial [1–3,8–12]. Our study addresses a narrower question: what is the expected outcome should cardiac arrest occur while advanced vasopressor support continues? Notably, patients above NEE >0.50 μg/kg/min experienced cardiac arrest a median of only 28.6 hours after ICU admission, suggesting that opportunities for informed discussions may be limited once advanced vasopressor-dependent shock develops. Our findings do not define when CPR should be withheld and should not replace individualized assessment of prognosis, patient values, or resuscitation preferences. Rather, they provide scenario-specific survival estimates that may help clinicians and families discuss this possibility before cardiac arrest occurs, allowing resuscitation decisions to be informed by observed outcomes rather than extrapolation from broader septic shock or cardiac arrest populations. This approach is consistent with current resuscitation guidance emphasizing individualized decision-making and transparent communication regarding the expected benefits and burdens of CPR [14]. Importantly, these estimates reflect survival only; MIMIC-IV does not contain reliable neurological outcome data, and because survival without neurological recovery may not be considered an acceptable outcome, our findings should be interpreted in this context.

This study has several limitations. Its retrospective single-center design limits causal inference and generalizability. Septic shock was identified using ICD-based coding and misclassification is possible, though findings were unchanged in a sensitivity analysis restricted to patients meeting Sepsis-3 criteria. Cardiac arrest identification relied on a procedure-event item in MIMIC-IV; under-ascertainment is possible. MIMIC-IV lacks detailed cardiac arrest variables (rhythm, defibrillation, CPR duration, ROSC, neurological outcomes, and post-arrest management) that influence post-arrest survival and may differ between NEE strata. Although results were unchanged using time-weighted mean NEE over standardized pre-arrest windows, residual misalignment between infusion records and the documented arrest time cannot be excluded. With only 13 ICU survivors, the study was underpowered and logistic regression may not provide reliable inference, as reflected in wide confidence intervals for several covariate estimates; adjusted estimates should be interpreted as exploratory only, with residual confounding from unmeasured acute severity and the substantial pre-arrest physiologic imbalance between groups. The small number of ICU survivors also precluded stable nonlinear modeling of the NEE–survival relationship; the continuous association is therefore reported as a linear term. The wide 95% CI (0–9.0%) for the zero observed

hospital survivors in the ≥6-hour cohort does not exclude the possibility of survival. Finally, the SCCM/ESICM vasopressor criterion was used as a prespecified stratification threshold and should not be interpreted as an empirically derived biological threshold. These findings should therefore be considered descriptive and hypothesis-generating, requiring validation in larger multicenter cohorts.

## CONCLUSION:

In this 14-year retrospective cohort of patients with septic shock who underwent attempted resuscitation for in-ICU cardiac arrest, ICU survival was markedly lower among patients receiving a pre-arrest norepinephrine-equivalent dose >0.50 µg/kg/min. Above this threshold, hospital survival was rare, with only one survivor (1/51) among patients who had received at least 3 hours of continuous vasopressor therapy and none (0/39; 95% CI, 0–9.0%) among those who had received at least 6 hours. These hypothesis-generating findings provide scenario-specific estimates of post-resuscitation outcomes using the NEE >0.50 µg/kg/min criterion from the 2026 SCCM/ESICM consensus and require validation in larger multicenter studies.

## AUTHOR CONTRIBUTIONS:

I.K.: Conceptualization, Data curation, Formal analysis, Writing – original draft; M.I.: Methodology, Validation, Investigation, Writing – review & editing; R.I.: Formal analysis, Software, Visualization, Writing – review & editing; F.K.: Data curation, Validation, Investigation, Writing – review & editing; M.I.: Data curation, Validation, Investigation, Writing – review & editing; A.S.K.: Formal analysis, Software, Visualization, Writing – review & editing; M.S.D.: Investigation, Validation, Writing – review & editing, Visualization; I.M.I.: Data curation, Validation, Investigation, Writing – review & editing; I.T.M.: Investigation, Validation, Writing – review & editing, Visualization; B.G.A.: Data curation, Validation, Investigation, Writing – review & editing; T.J.K.: Supervision, Project administration, Validation, Writing – review & editing.

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