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Prehospital factors predicting mortality in patients with shock: state-wide linkage study

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ABSTRACT

Background Patients with shock treated by emergency medical services (EMS) have high morbidity and mortality. Knowledge of prehospital factors predicting outcomes in patients with shock remains limited. We aimed to describe the prehospital predictors of mortality in patients with non-traumatic shock transported to hospital by EMS.

Method This is a retrospective cohort study of consecutive ambulance attendances for non-traumatic shock in Victoria, Australia (January 2015–June 2019) linked with government-held administrative data (emergency, admissions and mortality records). Predictors of 30-day mortality were assessed using Cox proportional regressions. The primary outcome was 30-day all-cause mortality.

Results Overall, 21 334 patients with non-traumatic shock (median age 69 years, 54.8% female) were successfully linked with state administrative records. Among this cohort, 9 149 (43%) patients died within 30-days. Compared with survivors, non-survivors had a longer median on-scene time: 60 (35–98) versus 30 (19–50), p <0.001. Non-survivors were more likely to be older (median age in years: 74 (61–84) vs 65 (47–78), p<0.001), had prehospital cardiac arrest requiring cardiopulmonary resuscitation (adjusted HR (aHR)=6.26, 95% CI 5.87, 6.69) and had prehospital intubation (aHR=1.07, CI 1.00, 1.14). Reduced 30-day mortality was associated with administration of epinephrine (aHR=0.66, CI 0.62, 0.71) and systolic blood pressures above 80 mm Hg in the prehospital setting.

Conclusion The 30-day mortality from non-traumatic shock is high at 43%. Independent predictors of mortality included age, prehospital cardiac arrest and endotracheal intubation. Interventions that target reversible causes of short-term mortality in patients with non-traumatic shock are a high priority.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with non-traumatic shock have a high morbidity and mortality; however, knowledge of prehospital factors predicting mortality is limited.

WHAT THIS STUDY ADDS

⇒ The 30-day mortality for non-traumatic shock remains high, independently predicted by age, prehospital cardiac arrest and endotracheal intubation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Further research is needed to target reversible causes of short-term mortality in patients with non-traumatic shock.

BACKGROUND

Shock is a clinical syndrome characterised by inadequate tissue perfusion of oxygen and other nutrients, resulting in cellular injury and oxygen debt.[1 2] Cell death, end-organ damage and multi-system organ dysfunction are cascading events that can cause significant morbidity and mortality if not interrupted.[3] Persistent hypotension defined as systolic blood pressure (SBP) <90 mm Hg is a widely accepted hallmark of possible circulatory failure that can define shock.[4 5] Despite enhanced systems of care (such as resuscitative and supportive measures, prompt administration of antibiotics and reperfusion therapies) that have improved clinical outcomes in patients, mortality from shock remains high.[6 7]

The management of patients with shock within the hospital environment is well characterised; however, knowledge of prehospital factors predicting mortality from shock remains limited. Furthermore, patients presenting with shock in the prehospital setting represent a heterogeneous population with varying prognosis based on severity of illness, aetiology and comorbidities. The aim of this study was to describe the prehospital predictors of mortality in patients with non-traumatic shock using a population-based linkage analysis of patients admitted to hospitals arriving via emergency ambulance.

METHOD

Study design and setting

This was a retrospective, population-based cohort study using emergency medical service (EMS) electronic patient records (Victorian Ambulance Clinical Information System, VACIS) linked with data from government-held administrative datasets (emergency presentations, hospital admissions and death records). Details of the data linkage and the datasets are provided in the online supplemental material and described previously.[6]

Ambulance Victoria is the sole provider of EMS in the state of Victoria, covering a land mass of 227 038 square kilometres with an estimated population of 6.7 million.[8] The EMS operates on a two-tiered response system consisting of advanced life support (ALS) and mobile intensive care (MICA) paramedics. The ALS paramedics are capable of laryngeal mask airway insertion and medication administration (eg, intravenous fluid administration, analgesics, bronchodilators and aspirin) while the MICA scope of practice includes endotracheal intubation and a wider scope of medications, including intravenous epinephrine infusion and antiarrhythmic drugs. During the period of this study, epinephrine was the only vasopressor protocolised for patients experiencing severe cardiovascular compromise, such as those in cardiac arrest, or profound hypotension unresponsive to initial fluid resuscitation. Paramedics record electronic patient records (such as demographics, case time series information, vital signs, pre-existing conditions, paramedic diagnoses and clinical management) during patient care.

Data sources

We identified patients with non-traumatic shock who were attended by EMS personnel from the ambulance records. The VACIS is an in-field electronic data capture system that allows paramedics to record clinical data as electronic patient care records that are stored in an integrated data warehouse. Data from the VACIS were linked with government-held administrative and clinical datasets (hospital admissions; *Victorian Admitted Episodes Dataset (VAED),* emergency presentation; *Victorian Emergency Minimum Dataset (VEMD*) and death records; *Victorian Death Index*) from the Victorian Department of Health. The department captures information on emergency presentations to public hospitals, hospital admissions to public and private hospitals and date and cause of death occurring in Victoria. The admissions data include demographic information, dates of admission and discharge, International Classification of Diseases, 10th Revision, Australian, Modification (ICD-10-AM) diagnosis codes, procedure codes and transfer information.[9] The emergency presentation data include demographic information, mode of arrival, date and time of presentation, urgency of presentation, triage category and diagnoses.[10]

Selection of participants

Records for adult patients (18 years or older) with non-traumatic shock who were attended by EMS personnel in Victoria, Australia were identified from the VACIS between January 2015 and June 2019. Patients were excluded if (1) they had a known traumatic aetiology of shock; (2) were identified for palliative management only, (3) were transferred to a private hospital, (4) transferred between hospitals, (5) were normotensive and (6) their data were unable to be linked between datasets.

Definitions

Shock was defined as sustained hypotension (SBP <90 mm Hg sustained for greater than 30 min) or EMS administered intravenous epinephrine. Final diagnosis was defined according to ICD-10-AM coding as the VAED primary diagnosis if discharge occurred following an inpatient admission or the VEMD primary diagnosis if discharge was directly from the emergency department. Further details relating to the ICD-10-AM diagnostic codes used to classify shock aetiology are described in the online supplemental material. Patients were included in the primary analysis if they survived to hospital and had their information successfully linked to VEMD or VAED. Socioeconomic status of patients was estimated using the Index of Relative Socio-Economic Disadvantage (IRSD) which ranks residential postcodes into quintiles of relative disadvantage. Higher IRSD scores (fifth quintile) indicated greater relative socioeconomic advantage.[11] Geographical remoteness was determined through the residential area postcode of each event using the Accessibility and Remoteness Index of Australia—a geographical accessibility index that divides Australia into five classes of remoteness (‘Major City’, ‘Inner Regional’, ‘Outer Regional’, ‘Remote’ and ‘Very Remote’) to reflect relative access to services in non-metropolitan Australia.[12] Due to low numbers of patients from ‘remote’ or ‘very remote’ regions, these groups were combined with the ‘outer regional’ group for the purposes of this study.

Outcomes

The primary outcome of this study was 30-day mortality (including short term and in-hospital). The secondary outcome was to determine rates of in-hospital interventions including the use of mechanical circulatory support, coronary angiography and revascularisation procedures, length of hospitalisation and discharge destination.

Statistical analysis

Patients were categorised according to their vital status at 30-days from index presentation as survivors (alive after 30-days) and non-survivors (died within 30-days). Differences between survivors and non-survivors were assessed using Mann-Whitney U or Kruskal-Wallis test for continuous variables and Pearson’s χ^2 test for categorical variables. We used frequencies and percentages for categorical variables and medians and IQRs or mean and SD for continuous variables to describe the cohort’s

Table 1 Characteristics of patients with non-traumatic shock arriving at hospital by ambulance

Characteristics and clinical profile	Total n=21334	Survivors n=12185	Non-survivors n=9149	P value
Age (years), median (IQR)	69.0 (53.0–81.0)	65.0 (47.0–78.0)	74.0 (61.0–84.0)	<0.001
Female	11688 (54.8%)	6206 (50.9%)	5482 (59.9%)	<0.001
ARIA				0.414
Major cities of Australia	15197 (71.8%)	8669 (71.7%)	6528 (72.0%)	
Inner regional Australia	4781 (22.6%)	2764 (22.8%)	2017 (22.2%)	
Outer regional Australia	1191 (5.6%)	665 (5.5%)	526 (5.8%)	
Socioeconomic disadvantage (IRSD)				0.328
1, most disadvantaged	5280 (28.1%)	3043 (28.7%)	2237 (27.4%)	
2	4157 (22.1%)	2335 (22.0%)	1812 (22.2%)	
3	3683 (19.6%)	2063 (19.4%)	1620 (19.8%)	
4	3241 (17.2%)	1823 (17.2%)	1418 (17.3%)	
5, least disadvantaged	2433 (12.9%)	1346 (12.7%)	1087 (13.3%)	
Pre-existing comorbidities				
Hypertension	6461 (33.4%)	3408 (30.9%)	3053 (36.6%)	<0.001
Dyslipidaemia	3723 (19.2%)	2053 (18.6%)	1670 (20.0%)	0.012
Diabetes	3606 (18.6%)	1930 (17.5%)	1676 (20.1%)	<0.001
Coronary artery disease	3623 (18.7%)	1869 (16.9%)	1754 (21.1%)	<0.001
Cardiac failure	2311 (11.9%)	1021 (9.3%)	1290 (15.5%)	<0.001
Chronic kidney disease	1145 (5.9%)	560 (5.1%)	585 (7.0%)	<0.001
Peripheral vascular disease	280 (1.4%)	138 (1.3%)	142 (1.7%)	0.009
Cerebrovascular disease	1418 (7.3%)	686 (6.2%)	732 (8.8%)	<0.001
Chronic obstructive pulmonary disease	2040 (10.5%)	966 (8.8%)	1074 (12.9%)	<0.001
Prehospital observations and interventions				
Initial systolic blood pressure, mean (SD), mm Hg	81.6 (26.7)	82.5 (27.1)	78.7 (25.1)	<0.001
Initial heart rate, mean (SD), beats/min	94.9 (35.7)	95.1 (35.8)	94.3 (35.4)	0.20
Epinephrine infusion commenced	4985 (23.2%)	3007 (24.7%)	1978 (21.6%)	
Prehospital intubation	4517 (21.2%)	1425 (11.7%)	3092 (33.8%)	<0.001
Prehospital cardiac arrest (yes/no)	8135 (38.1%)	2001 (16.4%)	6134 (67.0%)	<0.001
If arrest, shockable rhythm (VT or VF)	2037 (25.4%)	748 (38.3%)	1289 (21.2%)	<0.001
Prehospital time metrics				
Time at scene, median (IQR), min	40.0 (23.0–70.0)	30.0 (19.0–50.0)	60.0 (35.0–98.0)	<0.001
Transport time, median (IQR), min	15.0 (7.0–25.0)	17.0 (10.0–28.0)	10.3 (0.0–20.0)	<0.001

Socioeconomic disadvantage presented as quintiles according to patient's residential address in regards to the Index of Relative Socioeconomic Disadvantage (IRSD) scores (as obtained from the Australian Bureau of Statistics Census data) where a score of 1 represents most and 5 is least disadvantage.
ARIA, Accessibility and Remoteness Index of Australia; IQR, interquartile range; SD, standard deviation; VF, ventricular fibrillation; VT, ventricular tachycardia.

demographic characteristics, pre-existing comorbidities, in-hospital interventions and patient outcomes.

To identify independent factors predicting 30-day mortality and patient outcomes, we used Cox proportional hazard regression to estimate HRs and 95% CIs to assess prehospital factors predicting 30-day mortality. We adjusted the Cox proportional hazard regression for potential covariates, including baseline characteristics (age and sex), initial SBP and heart rate, prehospital cardiac arrest, prehospital intubation, prehospital epinephrine infusion, area of residence, socioeconomic status and pre-existing comorbidities. We adjusted for covariates to enhance the predictive model's accuracy, ensuring that the identified factors reflect their association with the outcome, independent of other influencing variables. Statistical analyses were conducted using Stata V.16.1 for Windows.

RESULTS

Between January 2015 and June 2019, there were 2 857 760 calls made to EMS, resulting in 2 485 311 ambulance

Table 2 In-hospital intervention for patients with non-traumatic shock

Intervention performed	Total n=21334	Survivors n=12185	Non-survivors n=9149	P value
Inpatient coronary angiography	971 (4.6%)	625 (5.1%)	346 (3.8%)	<0.001
Inpatient percutaneous coronary intervention	471 (2.2%)	321 (2.6%)	151 (1.6%)	<0.001
Inpatient mechanical ventilation	2072 (9.7%)	1038 (8.5%)	1034 (11.3%)	<0.001
Inpatient dialysis	502 (2.4%)	287 (2.4%)	215 (2.3%)	0.980
Inpatient coronary artery bypass surgery	19 (<1%)	15 (<1%)	4 (<1%)	0.054

attendances for any reason (online supplemental file 1). Of the attended cases, 21 334 patients met the inclusion criteria of sustained hypotension or epinephrine administration in the prehospital setting and were successfully linked with administrative datasets. This analysis includes 21 334 patients with non-traumatic shock.

Characteristics of the study cohort are presented in table 1. The overall median age of the cohort was 69 years (IQR: 53–81) and 55% were female. Among this cohort, 9149 (43%) patients died within 30-days (median age in years: 74, IQR: 61–84 and 60% females). Pre-existing comorbidities—hypertension (37%), diabetes (20%), chronic kidney disease (7%), prior cardiac failure (16%) and coronary artery disease (21%)—were higher among non-survivors. Non-survivors were more likely to have sustained prehospital cardiac arrest requiring cardiopulmonary resuscitation (67%, n=6134) compared with survivors (16.4%, n=2001), p <0.001. Prehospital endotracheal intubation was more common among non-survivors (33.8%, n=3092) compared with survivors (11.7%, n=1425), p<0.001. Those who died within 30-days had a longer on-scene time (median minutes: 60, IQR: 35–98) and a shorter transport time (median minutes: 10, IQR: 0–20) compared with survivors (on-scene median minutes: 30, IQR: 19–50 and transport median minutes: 17, IQR: 10–28). Survivors were more likely to have higher SBP.

In-hospital interventions and patient outcomes are presented in tables 2 and 3. Less than 5% of the patients (4.6%) underwent inpatient coronary angiogram (p<0.001) and only 2.2% received percutaneous coronary intervention (p<0.001, table 2). Survivors were less likely to receive inpatient mechanical ventilation (8.5%) compared with non-survivors (11.3%, p<0.001, table 2). Approximately 28% (n=5874) of the patients died within 24 hours of transport to hospital, representing 64% of those who died within 30 days (table 3). Non-survivors had shorter time in ICU (medium hours: 49.0, IQR: 17.0–112.0) and shorter median in-hospital length of stay (median days: 2.0, IQR: 1.0–5.0) compared with survivors (median time in ICU in hours: 64.0, IQR: 33.0–116.5, p <0.001 and in-hospital lengths of stay in days: 4.0, IQR: 1.0–8.0, p<0.001).

The adjusted analysis of factors predicting 30-day mortality is presented in figure 1 and was generally consistent with the univariable analysis. The strongest independent predictors of 30-day mortality were age above 50 years (adjusted hazard of death (aHR)=1.58, 95% CI 1.46, 1.72 for age 50–75 years and aHR=2.45, 95% CI 2.25, 2.67 for age >75 years) and cardiac arrest requiring cardiopulmonary resuscitation (aHR=6.26, 95% CI 5.87, 6.69). Those with previous cardiac failure, chronic kidney disease, peripheral vascular disease and chronic obstructive pulmonary disease (COPD) had a higher hazard of 30-day mortality. 30-day mortality was inversely associated with high SBP (aHR=0.84, 95% CI 0.78, 0.91 for 80–120 mm Hg and aHR=0.52, 95% CI 0.43, 0.62 for >120 mm Hg); administration of epinephrine (aHR=0.66, 95% CI 0.62, 0.71) and heart rate between 50 and 100 beats/min).

DISCUSSION

In this large population-wide study of shock, our findings reveal further insights into the predictors of 30-day mortality in the prehospital setting. We found that 30-day mortality was predicted by cardiac arrest requiring cardiopulmonary resuscitation, age and prehospital endotracheal intubation. More importantly, reduced risk of 30-day mortality was associated with receiving

Table 3 Outcomes for patients with non-traumatic shock

Outcome	Total n=21334	Survivors n=12185	Non-survivors n=9149	P value
All-cause mortality 24 hours	5874 (27.5%)	0 (0.0%)	5874 (64.2%)	<0.001
Time in ICU, median (IQR), hours	59.0 (26.0–115.0)	64.0 (33.0–116.5)	49.0 (17.0–112.0)	<0.001
In-hospital lengths of stay, median (IQR), days	3.0 (1.0–7.0)	4.0 (1.0–8.0)	2.0 (1.0–5.0)	<0.001
ED lengths of stay, median (IQR), minutes	271.0 (172.0–444.0)	276.0 (177.0–458.0)	265.0 (161.0–421.0)	<0.001

ED, emergency department; ICU, intensive care unit; IQR, interquartile range.

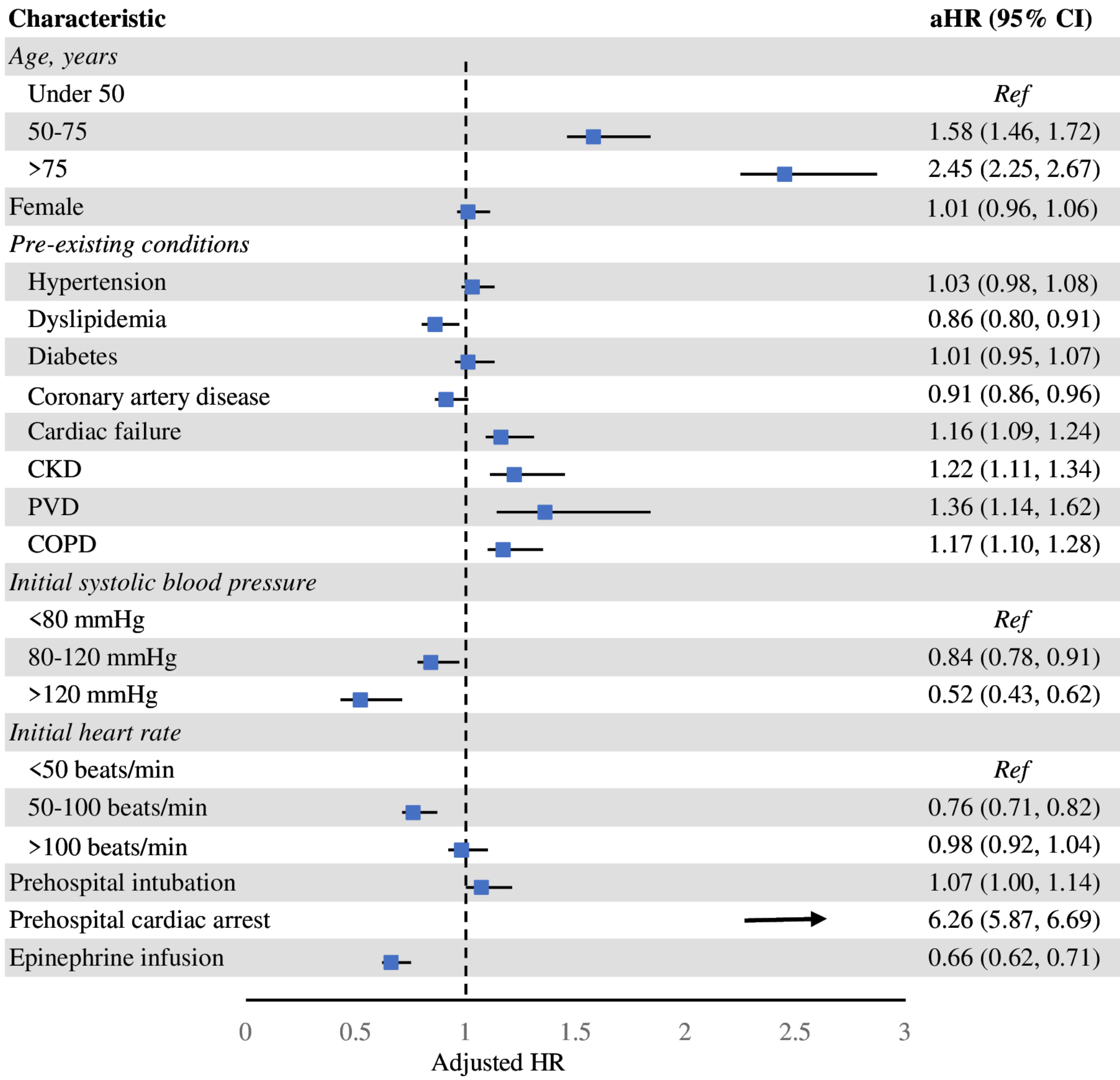

Figure 1 Prehospital factors predicting mortality in patients with non-traumatic shock. CKD, chronic kidney disease; PVD, peripheral kidney disease; COPD, chronic obstructive pulmonary disease; aHR, adjusted HR and 95% CIs which represent time-to-death analysis using a Cox regression model.

epinephrine in the prehospital setting and SBP above 80 mm Hg. Our findings also highlight an increased hazard of death among patients with pre-existing conditions such as cardiac failure, chronic kidney disease, peripheral vascular disease and COPD.

Authors of previous studies have found age as an independent predictor of mortality in patients with shock similar to the present study.[13 14] In this study, we report that older patients (above 75 years) have approximately a threefold increased risk of mortality. We previously reported a stepwise increase in incidence of non-traumatic shock with the risk of shock increasing with advancing age.[6] Other authors have also reported that advancing age is associated with worse outcomes in many critical illnesses.[15] Unsurprisingly, mortality remains high among older patients with shock despite the use of contemporary management strategies such as percutaneous coronary interventions in cases with ST-elevation myocardial infarction.[16] The higher mortality among older patients might be due to several factors. For instance, authors of a large comprehensive study from the USA reported poor survival after cardiac arrest with advanced age.[17] In the present study, we found that those who had a cardiac arrest were 6 times more likely to die within 30 days compared with those who did not have a cardiac arrest. Other authors have reported a high risk of death in older patients with more severe shock.[18] These outcomes are exacerbated with reduced rates of invasive interventions as previously reported in older patients with cardiogenic shock[19] or in those with sudden cardiac death.[20]

We found that patients who received prehospital endotracheal intubation had a higher 30-day mortality rate compared with those who did not. Endotracheal intubation has long been considered the optimal method for protecting the airway, preventing hypoxia and controlling ventilation prior to hospital arrival.[21] In Victoria, like elsewhere, patients with out-of-hospital cardiac arrest routinely undergo prehospital endotracheal intubation during cardiopulmonary resuscitation for airway management. Therefore, our finding of the higher 30-day mortality among intubated patients is likely confounded by out-of-hospital cardiac arrest as the proportion of patients with cardiac arrest among the non-survivors was significantly higher than the survivors. Nevertheless, several authors have reported significantly higher chances of survival to hospital admission in patients who received prehospital intubation compared with those who did not after out-of-hospital cardiac arrest.[22 23] Prehospital airway management remains paramount, and current guidelines recommend intubation in patients with shock.[24] Our data support robust prehospital randomised controlled trials (RCTs) into optimal airway management in critically unwell patients.

We report that administration of epinephrine was associated with lower mortality. The use of epinephrine for patients with prehospital hypotension is likely to result in improvements of blood pressure and allows sufficient time to initiate resuscitative measures with vasopressors and volume resuscitation.[25] Authors of small observational studies have reported the effectiveness of epinephrine in augmenting hypotension in the prehospital setting similar to our study.[26 27] However, the effectiveness of epinephrine use in the prehospital setting has been controversial. Some authors report worse outcomes or no benefit with epinephrine administration with regards survival to discharge or neurological outcomes[25 28] while others report the benefits of epinephrine to be time dependent[29] or dose dependent.[30] Prospective, RCT are needed to determine the efficacy of epinephrine in reducing mortality and improving clinical outcomes in the prehospital setting. One such trial, underway in the state of Victoria, Australia is the *Paramedic Randomised Trial of Noradrenaline versus Adrenaline in the Initial Management of Patients with Cardiogenic Shock (PANDA Trial: ACTRN 12621000805875*). This trial aims to compare the efficacy of norepinephrine and epinephrine in the prehospital setting in a population experiencing cardiogenic shock. The trial commenced recruitment in January 2024 and is expected to enrol 1155 patients (578 patients per group) by end of 2026. The efficacy endpoint of the PANDA trial is all-cause mortality while the safety endpoint is the development of refractory shock during prehospital care. This clinical trial will provide real-world evidence that is crucial for the management of the patients with cardiogenic shock in the prehospital setting.

LIMITATIONS

Our study findings need to be interpreted with the acknowledgement of limitations. First, there are several unmeasured confounders (such as age-related factors including frailty) that we were unable to adjust for in the analysis that are likely to influence survival. Second, we were also unable to capture those who self-presented to hospital or developed shock after hospital arrival. Third, our selected definition of shock may also result in an underestimation of the presence of prehospital hypovolemic shock or other shock aetiologies that were fluid responsive as is often difficult to determine the cause of shock in this setting. The final diagnosis of shock was guided by the inclusion and exclusion criteria listed in the study definitions, but ultimately determined by the hospital diagnosis ICD-10-AM codes from VAED/VEMD linkage. Finally, there also exist limitations in the data linkage process, where a number of eligible patients in the cohort were excluded from analysis due to data unlinked to VAED/VEMD.

CONCLUSION

In this large population-wide study, older patients, those with prehospital cardiac arrest and those who received prehospital endotracheal intubation had increased rates of 30-day mortality. 30-day mortality was inversely associated with prehospital epinephrine administration and SBP above 80 mm Hg. Further research is needed that focuses on interventions to reduce short-term mortality and optimisation of systems of care to improve patient outcomes.

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Patient consent for publication Not applicable.

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Data availability statement The data that support the findings of this study are available from the corresponding author, DS, upon reasonable request.

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