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Research paper

Intensive care patients receiving vasoactive medications: A retrospective cohort study

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ABSTRACT

Background: Vasoactive medications are high-risk drugs commonly used in intensive care units (ICUs), which have wide variations in clinical management.
Objectives: The aim of this study was to describe the patient population, treatment, and clinical characteristics of patients who did and did not receive vasoactive medications while in the ICU and to develop a predictive tool to identify patients needing vasoactive medications.
Methods: A retrospective cohort study of patients admitted to a level three tertiary referral ICU over a 12-month period from October 2018 to September 2019 was undertaken. Data from electronic medical records were analysed to describe patient characteristics in an adult ICU. Chi square and Mann–Whitney U tests were used to analyse data relating to patients who did and did not receive vasoactive medications. Univariate analysis and Pearson's r^2 were used to determine inclusion in multivariable logistic regression.
Results: Of 1276 patients in the cohort, 40% (512/1276) received a vasoactive medication for haemodynamic support, with 84% (428/512) receiving noradrenaline. Older patients (odds ratio [OR] = 1.02; 95% confidence interval [CI] = 1.01–1.02; $p < 0.001$) with higher Acute Physiology and Chronic Health Evaluation (APACHE) III scores (OR = 1.04; 95% CI = 1.03–1.04; $p < 0.001$) were more likely to receive vasoactive medications than those not treated with vasoactive medications during an intensive care admission. A model developed using multivariable analysis predicted that patients admitted with sepsis (OR = 2.43; 95% CI = 1.43–4.12; $p = 0.001$) or shock (OR = 4.05; 95% CI = 2.68–6.10; $p < 0.001$) and managed on mechanical ventilation (OR = 3.76; 95% CI = 2.81–5.02; $p < 0.001$) were more likely to receive vasoactive medications.
Conclusions: Mechanically ventilated patients admitted to intensive care for sepsis and shock with higher APACHE III scores were more likely to receive vasoactive medications. Predictors identified in the multivariable model can be used to direct resources to patients most at risk of receiving vasoactive medications.

1. Introduction

Vasoactive medications comprising inotropes and vasopressors are commonly used in intensive care units (ICU) to improve tissue and end-organ perfusion by supporting blood pressure, heart rate, and cardiac output in critically ill patients.[1] Management of vasoactive medications in the ICU is highly variable[2] with a scarcity of research evidence to support clinical decision-making. Vasoactive medications are high-risk agents with potential adverse effects including arrythmias, cardiac arrest, stroke, and tissue necrosis if used in error.[3–5]

Intensive care nurses manage patients receiving vasoactive medications with varying degrees of autonomy and with the support of the interdisciplinary ICU team. Interventions for patients receiving one or more vasoactive medications might include infusion preparation, administration, dose titration using continuous haemodynamic assessment, and weaning.[6] The population of patients receiving vasoactive medications while admitted to the ICU has not been fully described, and there are few published

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comparisons to the patient population who have not received vasoactive medications.[7–9]

It has been reported that between 10% and 54% of patients admitted to the ICU receive vasoactive medications for a variety of conditions including sepsis, cardiac failure, postoperative vasoplegia, and organ failure.[7,8,10] Research on vasoactive medications has largely focused on the choice of inotropes or vasopressors for specific physiological conditions,[2,11] with a number of studies exploring optimal blood pressure targets for various patient populations.[5,12,13]

Better Safer Care Victoria, an independent body working with healthcare clinicians and consumers to develop evidence-based resources and clinical guidelines, identified inotropes and vasopressor management in critical care as a priority area for improving patient safety in 2016. At that time, nine vasopressors and inotropes or vasoactive medications were identified as the most commonly used in Victorian ICUs, and these are the target medications for this study.[14]

The demographic and clinical characteristics and outcomes for patients who have received vasoactive medications in ICUs are not well understood. Establishing a knowledge base, including a predictive model, for patients likely to receive vasoactive medications may help identify patients at risk of clinical deterioration, prompt more timely treatment conversations with patients and families, and assist nurse workload planning and allocation.

2. Aim

The aim of this study was to describe the patient population, treatment, and clinical characteristics of patients who did and did not receive vasoactive medications during an ICU admission and to develop a predictive tool to identify which ICU patients are likely to receive vasoactive medications.

2.1. Design

A retrospective cohort study of all patients admitted to the study ICU over a 1-year period was conducted.

2.2. Methods

Over a 12-month period from October 1, 2018, to September 30, 2019, the medical records of all patients admitted to an adult tertiary, medical/surgical ICU in metropolitan Melbourne, Australia, were screened using inclusion and exclusion criteria. Inclusion criteria were all patients admitted to the ICU during the study period with exclusions applied when patients had more than one ICU admission. To ensure that the most recent patient characteristics were captured, only the last admission during the study period was included and each patient appeared only once in the data for calculation of ICU and hospital survival. The medical records of the resulting 1276 patients were then interrogated, collated, and analysed.

The term vasoactive medication was used to describe nine inotropes and vasopressor medications commonly used in the ICU. These are noradrenaline (norepinephrine), adrenaline (epinephrine), vasopressin, metaraminol, dobutamine, isoprenaline (isoproterenol), milrinone, dopamine, and levosimendan.[14] To avoid confusion, the Australian terms noradrenaline, adrenaline, and isoprenaline are used in this article.

2.3. Ethics

Collection and analysis of reidentifiable data was approved without the need for patient consent by the university (2019-406-191015) and the study site (E19/007/51675) human research and ethics committees.

2.4. Sample and setting

The study ICU is a 20-bed medical/surgical adult unit staffed to Australian ICU nursing workforce standards of 1:1 for ICU admissions and 1:2 for step-down or high-dependency patients. At the time of the study, there were 102 nurses employed across a variety of shifts with results likely to be applicable to other similar sized ICUs.[15]

2.5. Data collection

Eligible patients were identified from ICU admission lists generated by the third author, from October 1, 2018, to September 30, 2019. The lists were cross referenced by the first author to the health service electronic medical records (EMRs) (Cerner Electronic Health Record, North Kansa City, MO, USA) for confirmation of admission and discharge dates, and the medication summary was interrogated to identify all patients who received a vasoactive medication. Clinical, treatment, and outcome data were then extracted from the EMR and Australian and New Zealand Intensive Care Society (ANZICS) Centre for Outcome and Resource Evaluation (CORE) [40] data, by the third author.

While patients were admitted to the ICU, clinical data were automatically transferred into the EMR from monitoring equipment and ventilators or manually entered into EMR by clinicians at the bedside. In order to focus on variability in local clinical practices, only those vasoactive medications delivered as infusions were included. Data included the type of vasoactive medications delivered, maximum and total doses, and length of time that patients received the medications. For each patient admission, demographic characteristics collected included age, gender, ICU and hospital admission sources, diagnoses and length of stay, ICU and hospital survival, and discharge location. Predictive scores included the Critical Care Outcome Predictive Equation (COPE) [19] and Acute Physiology and Chronic Health Evaluation (APACHE III) [39]. Treatment modalities including mechanical ventilation, propofol prescriptions, and renal replacement therapy were also reported from ANZICS CORE data.

2.6. Statistical analysis

Microsoft® Excel® (Excel version 14.7.1. Redmond, Washington: MS Corp) was used to collate, clean, code, and store data. Coded data were then entered into IBM® SPSS® Statistics (IBM SPSS Statistics for Macintosh, Version 25.0. Armonk, NY: IBM Corp) for analysis. Descriptive statistics were used to summarise normally distributed data and to describe treatment characteristics of patients who received vasoactive medications. Where data were not normally distributed, medians and interquartile ranges (IQRs) were presented.

The demographic and clinical characteristics of patients who did and did not receive vasoactive medications were compared using the Chi-square test (categorical variables) and Mann–Whitney U test (continuous variables). Confidence intervals (CIs) set at 95% and p-values of <0.05 were reported as significant. Explanatory variables that were statistically significant in univariate logistic regression were considered for inclusion in multivariable logistic regression.[16,17]

3. Results

3.1. Characteristics of patients admitted to the ICU

Of 1276 included patients in the study, 46% (592/1276) were female and 83% (1058/1276) were admitted from a private residence.

The most common admission stream was from the emergency department (67.8%; 866/1276), and the most common hospital admission diagnoses were surgical (23%; 292/1276), cardiovascular (15%; 192/1276), and respiratory (13.4%; 172/1276). In all, 21.8% (279/1276) had a medical emergency team (MET) call prior to ICU admission and 10.5% (135/1276) had a documented treatment limitation. Treatment limitations are often implemented to minimise the burden of invasive and uncomfortable interventions for patients who have a poor prognosis due to extreme age and/or disease comorbidities. Insertion of central venous catheters, intubation, chest compressions in the event of cardiac arrest, and renal replacement therapy could all be considered invasive and uncomfortable interventions and possibly unlikely to contribute to quality of life or improve outcomes in this patient cohort.[18]

Shock was the most common ICU admission diagnosis (39.6%; 505/1276); 31% (393/1276) of patients received mechanical ventilation, 30% (379/1276) had propofol infusions for sedation, and 4.7% (61/1276) received renal replacement therapy.

3.2. Treatment characteristics of patients who received a vasoactive medication during their ICU admission

During the study period, 40% (512/1276) of patients received vasoactive medications (Table 1). In this cohort of patients, noradrenaline was the most commonly used vasoactive medication at 83.5% (428/512), with 34.3% (176/512) of patients receiving metaraminol, 13.8% receiving adrenaline (71/512), and 11.3% receiving vasopressin (58/512). Patients with an ICU admission of shock, who were mechanically ventilated (67.2%, $p < 0.001$) and sedated with propofol (58.6%, $p < 0.001$), were more likely to receive both noradrenaline and vasopressin. No patients received levosimendan or dopamine during the study period (Table 1).

3.3. Outcomes of patients admitted to the ICU

Overall survival to ICU discharge was 91.4% (1167/1276) and hospital survival was 87.4% (1116/1276). Post-ICU MET calls occurred in 15.2% of patients (195/1276) and cardiac arrests in 1% (13/1276) of patients after ICU discharge. Readmissions to the ICU occurred in 5.3% (68/1276) of patients with a length of ICU stay of 20–104 h and hospital length of stay of between 4 and 18 days once outliers where removed.

Table 1
Description of treatment characteristics of patients who received vasoactive medications.

Type of vasoactive medications received	n = 512	%	
• Noradrenaline	428	83.5	
• Metaraminol	176	34.3	
• Adrenaline	71	13.8	
• Vasopressin	58	11.3	
• Dobutamine	15	2.9	
• Isoprenaline	8	1.5	
• Milrinone	3	0.2	
Noradrenaline administered to	n = 428	%	p*
• patients admitted with shock	125	29.2	<0.001
Noradrenaline doses			
• <0.1 μg/kg/min	168	13.1	
• ≥0.11–0.99 μg/kg/min	256	20.0	
• ≥1.0 μg/kg/min	4	0.31	
Vasopressin administered to	n = 58	%	p*
• patients admitted with shock	21	36.2	<0.001
• patients who received mechanical ventilation	39	67.2	<0.001
• patients who received a propofol infusion	34	58.6	<0.001

IQR (#) = interquartile range; p* = chi-square; p** = Mann–Whitney U.
For all categorical variables, the reference = 0 (no) and 1 (yes).

3.4. Comparison of patients who did and did not receive vasoactive medications in the ICU

3.4.1. Patient characteristics

Univariate logistic regression showed there were no significant differences in gender or admission source when comparing the characteristics of patients who did and did not receive vasoactive medications (Table 2). Patients with a hospital admission diagnosis code of cardiovascular disease (odds ratio [OR] = 1.41; 95% CI = 1.04–1.93; $p = 0.026$) or sepsis (OR = 3.68; 95% CI = 2.43–5.59; $p < 0.001$) were significantly more likely to receive a vasoactive medication when in the ICU. Patients admitted to the ICU via the emergency department (OR = 2.10; 95% CI = 1.63–2.70; $p < 0.001$) or who triggered an MET call prior to ICU admission (OR = 1.54, 95% CI = 1.18–2.01, $p = 0.002$) were also more likely to receive vasoactive medications after ICU admission. Advancing age (OR = 1.02; 95% CI = 1.01–1.02; $p < 0.001$) increased the odds of patients receiving a vasoactive medication, and patients with a documented treatment limitation (OR = 1.94; 95% CI = 1.35–2.78; $p < 0.001$) had increased odds of receiving a vasoactive medication compared with patients with no documented treatment limitations.

On univariate analysis, patients with a higher APACHE III score were more likely to receive vasoactive medications (OR = 1.04; 95% CI = 1.03–1.04; $p < 0.001$). Patients who received vasoactive medications had a median APACHE III score of 68 (IQR = 52–83) compared with 49 (IQR = 35–61) for patients who did not receive a vasoactive medication. There were statistically significant differences between the groups on univariate analysis, for patients with an ICU admission diagnosis of shock (OR = 4.85; 95% CI = 3.47–6.77; $p < 0.001$).

3.4.2. Treatment characteristics

When assessed using univariate analysis, the odds of receiving a vasoactive medication increased if patients were mechanically ventilated (OR = 3.52; 95% CI = 2.75–4.51; $p < 0.001$) compared with those who were not mechanically ventilated and if patients received propofol for sedation (OR = 3.20; 95% CI = 2.50–4.11; $p < 0.001$) compared with those who were not sedated with propofol. Renal replacement therapy (OR = 4.50; 95% CI = 2.21–8.06; $p < 0.001$) and a positive COPE mortality prediction score (OR = 3.82; 95% CI = 2.14–6.81; $p < 0.001$) also increased the likelihood of patients receiving one or more vasoactive medications (Table 3).

3.4.3. Patient outcomes

ICU survival (OR = 2.35, 95% CI = 1.17–4.71; $p = 0.016$) and hospital survival (OR = 2.93; 95% CI = 2.08–4.14; $p < 0.001$) had increased odds for patients who did not receive a vasoactive medication while in the ICU. The adjusted median length of ICU stay was increased for patients who received vasoactive medications with 63.0 h (IQR = 39–104) compared with 31.9 h (IQR = 20–54) for patients who did not receive vasoactive medications. Median hospital length of stay was increased to 10 days (IQR = 5–18) for the vasoactive medication group compared with 6 days (IQR = 4–12) for the non–vasoactive medication group. Cardiac arrest after ICU discharge, ICU readmissions, and hospital discharge destination were not statistically significant explanatory variables on univariate analysis (Table 4).

3.5. Predictors of receiving vasoactive medications during an ICU admission

There were 19 statistically significant explanatory variables on univariate analysis, and 10 of these were entered as predictors into a multiple regression model. Shock, septic shock, circulatory shock,

Table 2
Univariate analysis comparing demographic characteristics of patients who did and did not receive vasoactive medications.

Patient variables	Received vasoactive medications (n = 512)		Did not receive vasoactive medications (n = 764)		OR	95% CI	P*
	n	%	n	%			
Gender							
• Female	226	44.1	366	47.9	0.85	0.68–1.07	0.186
Hospital admission source (most common)					1.13	0.84–1.53	0.406
• Private residence	430	84.0	628	82.2	0.77	0.56–1.07	0.129
• Transfer from acute hospital/rehab/geriatric	66	12.9	122	16.0	2.01	0.84–4.81	0.116
• Transfer from aged care facility	12	2.3	9	1.2	1.19	0.31–4.47	0.791
Hospital admission diagnosis (most common)							
• Surgical	96	18.8	196	25.7	0.66	0.50–0.88	0.004
• Cardiovascular	91	17.8	101	13.2	1.41	1.04–1.93	0.026
• Respiratory	62	12.1	110	14.4	0.81	0.58–1.14	0.241
• Sepsis	77	15.0	35	4.6	3.68	2.43–5.59	<0.001
• Gastrointestinal	45	8.8	65	8.5	1.03	0.69–1.54	0.861
Admitted to hospital via emergency department	395	77.1	471	61.6	2.10	1.63–2.70	<0.001
MET calls prior to ICU admission	135	26.4	144	18.8	1.54	1.18–2.01	0.002
Treatment limitations							
• Treatment limitations in place	74	14.5	61	8.0	1.94	1.35–2.78	<0.001
Age, y					1.02	1.01–1.02	
	Median	IQR#	Median	IQR			p**
Age, y	70	58–78	63	48–75			<0.001

CI = confidence interval; ICU = intensive care unit; IQR (#) = interquartile range; Mdn = median; MET = medical emergency team; OR = odds ratio; p* = chi-square; p** = Mann–Whitney U.
For all categorical variables, the reference = 0 (no) and 1 (yes).
Age is a continuous variable.

traumatic shock, hypovolaemic shock, and unspecified shock as ICU admission diagnoses were combined under a single heading of shock for use in the multivariable model. Variables that were significant in univariate analysis but not included in multivariable analysis were: the COPE score as it used parameters already included in multivariate analysis (age, mechanical ventilation, hospital category, and admission diagnoses);[19] and length of ICU and hospital stay as they were outcome variables, and not helpful when developing a predictive model.

Variables of admission to hospital with a diagnosis of sepsis (OR = 2.43; 95% CI = 1.43–4.12; p = 0.001), admission to the ICU with a diagnosis of shock (OR = 4.05; 95% CI = 2.68–6.10; p < 0.001), and receiving mechanical ventilation (OR = 3.76; 95% CI = 2.81–5.02; p < 0.001) were strongly predictive for patients receiving a vasoactive medication. Other statistically significant predictive variables were treatment limitations (OR = 1.99; 95% CI = 1.30–3.06; p = 0.002), higher APACHE III scores (OR = 1.03; 95% CI = 1.03–1.04; p < 0.001), and increasing age (OR = 1.02; 95% CI = 1.01–1.02; p < 0.001) with a positive association with patients receiving vasoactive medications (Table 5).

Receiving propofol (OR = 1.26; 95% CI = 0.81–1.95; p = 0.294), renal replacement therapy (OR = 1.12; 95% CI = 0.56–2.23; p = 0.735), MET calls prior to ICU admission (OR = 1.16; 95% CI = 0.83–1.61; p = 0.377), and hospital admissions via the emergency department (OR = 1.00; 95% CI = 0.72–1.39; p = 0.968) were not significant predictors within the multivariable model.

Table 3
Univariate analysis comparing clinical characteristics of patients who did and did not receive vasoactive medications.

Admission and treatment characterstics	Received vasoactive medication (n = 512)		Did not receive vasoactive medication (n = 764)		OR	95% CI	P*
	n	%	n	%			
ICU admission diagnosis of							
Shock	142	27.7	56	7.3	4.85	3.47–6.77	<0.001
Septic shock	82	16.0	20	2.6	7.09	4.29–11.73	<0.001
Circulatory shock	110	21.5	27	3.5	7.46	4.81–11.57	<0.001
ICU admission for cardiac arrest	14	2.7	11	1.4	1.92	0.86–4.27	0.108
Mechanical ventilation	240	46.9	153	20.0	3.52	2.75–4.51	<0.001
Propofol infusion	227	44.3	152	19.9	3.20	2.50–4.11	<0.001
Renal replacement therapy	45	8.8	16	2.1	4.50	2.21–8.06	<0.001
COPE mortality prediction	41	8.0	17	2.2	3.82	2.14–6.81	<0.001
APACHE III					1.04	1.03–1.04	
	Mdn	IQR	Mdn	IQR			P**
APACHE III	68	52–83	49	35–61			<0.001

APACHE = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; COPE = Critical Care Outcome Predictive Equation; ICU = intensive care unit; IQR (#) = interquartile range; Mdn = median; OR = odds ratio; p* = chi-square; p** = Mann–Whitney U.
For all categorical variables, the reference = 0 (no) and 1 (yes).
APACHE III is a continuous variable.

Table 4
Univariate analysis comparing outcomes for patients who did and did not receive vasoactive medications.

Discharge and outcome characteristics	Received vasoactive medication (n = 512)		Did not receive vasoactive medication (n = 764)		Odds ratio	95% CI	p*
	n	%	n	%			
Survived to ICU discharge	438	34.3	729	57.1	2.35	1.17–4.71	0.016
Survived to acute hospital discharge (study site)	411	32.2	705	55.3	2.93	2.08–4.14	<0.001
MET call after ICU discharge	104	8.2	91	7.1	0.53	0.39–0.74	<0.001
In-hospital cardiac arrest after ICU discharge	5	0.4	8	0.6	0.51	0.13–1.89	0.318
ICU readmissions	35	2.7	33	2.6	0.61	0.37–1.00	0.052
Hospital discharge destination							
• Private residence	246	19.3	500	39.2	1.19	0.89–1.58	0.237
• Transfer from acute hospital/rehab/geriatric care	108	8.5	137	10.7	0.81	0.61–1.08	0.160
• Transfer to aged care facility	19	1.5	18	1.4	0.62	0.32–1.20	0.161
• Statistical separation	30	2.4	26	2.0	0.99	0.49–1.70	0.794
• Left against medical advice	7	0.5	22	1.7	2.13	0.90–5.04	0.082
ICU length of stay (hours)					1.00	1.00–1.01	
Acute hospital length of stay (days)					1.00	0.99–1.01	
	Mdn	IQR	Mdn	IQR			p**
ICU length of stay (hours)	63.15	39.4–103.8	31.95	20.2–53.7			<0.001
Acute hospital length of stay (days)	10	5.0–17.75	6	4–12			0.396

IQR (#) = interquartile range; Mdn = median; p* = chi-square; p** = Mann–Whitney U.
For all categorical variables, the reference = 0 (no) and 1 (yes).
Hospital and ICU length of stay are continuous variables.

Table 5
Standard multivariable logistic regression for predictor variables associated with patients likely to receive vasoactive medications.

Predictor variables	OR	95% CI	P
ICU admission diagnosis – shock	4.05	2.68–6.10	<0.001
Mechanical ventilation	3.76	2.81–5.02	<0.001
Hospital admission diagnosis – sepsis	2.43	1.43–4.12	0.001
Treatment limitations	1.99	1.30–3.06	0.002
Patient received propofol	1.26	0.81–1.95	0.294
Renal replacement therapy	1.12	0.56–2.23	0.735
MET calls prior to ICU admission	1.16	0.83–1.61	0.377
APACHE III score	1.03	1.03–1.04	<0.001
Age	1.02	1.01–1.02	<0.001
Admitted to hospital via emergency department	1.00	0.72–1.39	0.968

APACHE = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; ICU = intensive care unit; MET = medical emergency team; OR = odds ratio.

4. Discussion

This study found that 40% of patients in an adult ICU received a vasoactive medication and of these, noradrenaline was the most common agent. On adjusted analysis, significant predictors for receiving a vasoactive medication were an ICU admission for shock, hospital admission for sepsis, mechanical ventilation, documented treatment limitations, higher APACHE III scores, and increasing age.

Noradrenaline was the most commonly used vasopressor in nearly 84% of the 40% of patients who received a vasoactive medication, and this reinforces that management and titration of noradrenaline is core business and a major part of the daily workload for ICU nurses.[6] Adoption of the Better Safer Care Clinical Guidelines for Inotropes and Vasopressors into practice in the study ICU has helped standardise infusion preparation concentrations; however, there are no evidence-based resources supporting nurse titration and weaning of noradrenaline.[14,20]

Hospital admission with sepsis and ICU admission diagnosis of shock were both significant predictors for patients receiving a vasoactive medication while in the ICU. Sepsis is characterised as the presence of organ dysfunction secondary to inflammatory host responses to infection and is chronically under diagnosed owing to the variation in patient presentations, and the lack of diagnostic tests to aid identification.[11] A national longitudinal study of all patients admitted to Australian public hospitals, from 2013 to 2018, reported more that 39% of patients had sepsis recorded as the principal diagnosis,[21] while only 8.7% of patients in our cohort had a hospital admission diagnosis of sepsis. However, reporting of vasoactive medication use was outside the scope of this epidemiological study.

The low rate of sepsis coding in our cohort may have resulted from reporting of localised infections as the principal diagnosis for hospital admission. Pneumonia, abscess, cholecystitis, infective myocarditis, and enterocolitis, for example, are all diagnoses with potential to escalate into sepsis. Other explanations for this disparity could be that sepsis was not recognised on hospital admission, that patients presented to hospital with other pathology before sepsis symptoms became obvious, or that patients developed sepsis and shock during their hospital stay.

A large number of patients were admitted to the ICU with a diagnosis of shock, which may indicate that guidelines implemented to aid detection of sepsis in ward patients and identification of patients who deteriorate on the ward were working well. There are challenges for clinicians recognising, responding, and managing sepsis due to heterogeneity of presenting symptoms, the potential for rapid deterioration and lack of specific treatments, with early recognition and intervention having significant impacts on improving patient outcomes.[38] Management variables of mechanical ventilation and having a documented treatment limitation significantly increased a patient's odds of receiving a vasoactive medication while in the ICU. Patients on mechanical ventilation are likely to be more acutely unwell and receive medications for sedation that have known hypotensive action, such as propofol and intravenous paracetamol.[22,23] A Colombian cohort study of 357 patients admitted to the ICU for mechanical ventilation found that 88% received inotropes or vasopressors, and these patients had a significantly reduced chance of ICU survival.[24]

Despite being a small subset of the study unit population (10.5%), patients having documented treatment limitations (OR = 1.996) were predictive for receiving noradrenaline to support blood pressure. We were unable to determine when during the hospital or ICU stay that treatment limitations were documented. Treatment limitations may have been implemented prior to initiation of treatment with vasoactive medication commenced as a short-term support as a purposeful delay while an end-of-life pathway was

actioned, and family assembled. Treatment limitations decided after commencement of the vasoactive medication infusion can reflect the dynamic decision-making pathways that evolve as discussions with families, diagnostic information, and responses to clinical interventions come to light.

A recent retrospective cohort study from the USA on the use of life-sustaining treatments for patients admitted to the ICU with limitation of treatment orders showed that this population of patients were significantly less likely to receive a vasoactive infusion than patients with no limitations documented. The disparity of data from this study and ours might be explained by differences in our health insurance models as Australian health services are largely publicly funded with no out-of-pocket expenses.[25]

Patients with high APACHE III scores and older age were more likely to receive vasoactive medications when in the ICU, and while this was statistically significant, the risk for receiving a vasoactive medication was small. While patients with higher APACHE III scores were only slightly more likely to receive vasoactive medications, there was a significantly increased risk for both ICU and hospital mortality for this group of patients, indicating the value of APACHE as mortality predictive scores.[26] The admission to the ICU of patients older than 85 y increases by 5.6% every year,[27] and while needing inotropic support was highly predictive of mortality in older patients,[28] there is little evidence of correlation between older age and ICU mortality in patients who do not require vasoactive medications.[27]

Patients who received a vasoactive medication (compared with no vasoactive medication) had longer median ICU length of stay (63 vs 32 h) and clinically significant hospital length of stay (10 days vs 6 days). There are many documented reasons for increased length of ICU stay for critically ill patients including nursing autonomy, ratios and workload, patient acuity, sedation choice and dose, duration of mechanical ventilation, bed blocking, and slow weaning of noradrenaline.[29–31] Patients in the study unit had almost half the length of ICU stay if they did not receive a vasoactive medication compared with those patients who did receive a vasoactive medication (32 h vs 63 h). Acuity of illness is implicated in increased length of ICU stay for this patient population as evidenced by the higher APACHE III scores and need for mechanical ventilation.

Noradrenaline weaning practices vary from nurse to nurse in the absence of an evidence-based weaning protocol or strategy. Our data indicated that patients with borderline low blood pressure can spend many days on 1 or 2 mg/minute of noradrenaline and are unable to be discharged from the ICU. Nurse-led weaning protocols and nursing autonomy have been shown to improve weaning rates from mechanical ventilation,[32,33] but a weaning protocol for vasoactive medications has not been developed. Hospital length of stay was greater for patients who received a vasoactive medication (10 days vs 6 days for patients who did not receive a vasoactive medication). While this variable was not statistically significant between the two groups, and hospital length of stay is a complex outcome measure, clinical impacts include higher risk of falls, risk for sepsis, and increased mortality.[34]

4.1. Strengths and limitations

The study provided clinical insights describing the population of patients who do and do not receive vasoactive medications and developed a novel predictive model for patients at risk of needing vasoactive medications that has not previously been reported in the literature. As a single-site retrospective analysis, there are limitations to internal and external validity that may temper generalisability of the study results including the subjectivity of hospital and ICU admission diagnoses. Although ubiquitous for all health services, hospital coding can be subjective and skewed by local culture and practices.[35,36] Documentation of treatment limitations is also not a standardised practice, so is highly reliant on personal preferences, local practices, and culture.[37]

4.2. Implications for practice

A predictive model was developed using multivariate logistic regression analysis that could be used to identify patients more likely to receive a vasoactive medication during their ICU admission. Using this predictive model could help clinicians flag patients at risk for deterioration, support allocation of nursing resources, and provide direction for ICU discharge planning. Many patients are likely to receive a vasoactive medication during their ICU stay and are also likely to have a longer ICU stay and higher rates of mortality.

5. Conclusion

This study comprises a comprehensive description of the population of patients who received a vasoactive medication while admitted to the ICU. Older patients admitted to hospital with sepsis, ICU with shock, who had high APACHE III scores, positive COPE scores, and were managed with mechanical ventilation, had higher odds of receiving a vasoactive medication during their ICU admission.

Unexpected results were the number of patients receiving vasoactive medications, especially noradrenaline, and the increased odds of patients receiving noradrenaline if they had documented a treatment limitation. If prospectively validated, our predictive model could be implemented as a clinical risk screening tool, identify patients likely to receive a vasoactive medication in the ICU, prompt timely consideration of treatment goals and limitations, and aid in allocation of nursing resources.

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Conflict of Interest

None.

CRediT authorship contribution statement

Stephanie Hunter: Conceptualisation, Formal analysis, Investigation, Writing – Original Draft, Writing -Review & Editing, Project administration. **Elizabeth Manias**: Conceptualisation, Formal analysis, Writing – Review & Editing, Supervision. **Steven Hirth**: Data curation, Writing – Review & Editing. **Julie Considine**: Conceptualisation, Formal analysis, Writing – Review & Editing, Supervision.

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