Characteristics and Factors Associated With the Mortality of Hypotensive Patients Attending the Emergency Department

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Abstract

Background: The prevalence of hypotension in emergency departments (EDs) is approximately 1-2%, but is associated with a mortality rate of 8-15%. There has never been a study in Thailand examining the epidemiology or the risk factors for early mortality of patients presenting with hypotension in the ED. Therefore, this study aimed to define the characteristics, mortality rate within 48 h and associated factors of hypotensive patients at ED.

Methods: Data of patients with hypotension attending the ED of Thammasat University Hospital (TUH) were retrospectively studied.

Results: Of the 9,000 patients seen in the TUH ED, 233 were hypotensive for a prevalence of 2.5%. Patients were old, with a mean age of 61 ± 20 years. The most common presenting symptom was fever, and sepsis was the most common cause of hypotension. The mean systolic blood pressure (SBP) was 78 ± 8 mm Hg. Isotonic crystalloid volume resuscitation in first hour was 758 mL (interquartile range (IQR), 500 - 1,000) and the total volume to achieve a mean arterial pressure (MAP) ≥ 65 mm Hg was 1,142 mL (IQR, 500 - 1,500). Twenty-seven percent of patients needed vasopressor support. Nineteen patients died ≤ 48 h, giving a case fatality rate of 8.2%. Three independent factors associated with 48-h mortality were initial pulse rate > 100 beats/min (odds ratio (OR), 4.21; 95% confidence interval (CI), 1.05 - 16.88; P = 0.042), diagnosis of shock (OR, 13.74 (1.49 - 126.61); P = 0.021) and recurrent hypotension (OR, 6.91 (1.54 - 30.99); P = 0.012).

Conclusions: Hypotension in the ED was common and associated with high mortality rate. Better triage, patient monitoring and treatment may improve outcomes in these patients.

Keywords: Hypotension; Shock; Systolic blood pressure; Emergency department; Hypoperfusion

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Introduction

Hypotension, defined as either a mean blood pressure (MBP) < 65 mm Hg, a systolic blood pressure (SBP) < 90 mm Hg or a > 40 mm Hg decrease in the SBP [1, 2], is associated with a high mortality rate of 8-15% [3] in patients presenting to emergency departments (EDs). When hypotension progresses to shock or circulatory failure, there is an imbalance between tissue oxygen delivery and oxygen consumption that results in signs of poor perfusion, end-organ dysfunction and, if untreated, death [4].

In the USA, approximately 5.6 million hypotensive patients per year are seen in EDs, representing 1% of all ED attendances [5]. The main causes of hypotension are infection, hypovolemic, cardiogenic, neurogenic, and drug induced hypotension. However, the etiological characteristics and mortality rates in patients who develop shock in the ED are not well described.

The rapid diagnosis and treatment of hypotension is important because if shock develops, it may become irreversible and delayed treatment is associated with an increasing mortality of 35-56% for cardiogenic shock, and 40-60% for sepsis-related shock [6]. Defining the clinical characteristics and epidemiology of hypotension are important to inform triage and management policies in EDs.

There are few data on the causes, clinical characteristic and prognosis of hypotension in the ED. We, therefore, set out to ascertain these and report the findings herein.

Materials and Methods

Study design and patient population

This was a retrospective cohort study of hypotensive patients presenting to the ED of Thammasat University Hospital (TUH) between June 1 and August 31, 2016. TUH is a tertiary referral center situated in the northern outskirts of Bangkok with 700 beds and sees approximately 45,000 patient ED visits per year.

The study was approved by Human Research Ethics Committee of Thammasat University, and funding was obtained from the Thammasat Research Fund.

The study inclusion criteria were one of: 1) an SBP < 90 mm Hg, 2) a mean arterial blood pressure (MAP) < 65 mm Hg,

or 3) a decrease in SBP > 40 mm Hg from baseline [5, 6]. The exclusion criteria were patient who aged < 17 years old and/or who had an out of hospital cardiac arrest.

Using the hospital information system, all notes were retrieved of patients with a diagnosis of hypotension. Data were extracted using a standard case report form and included demographic data, major symptoms, serial pulse, blood pressure and oxygen saturation measurements, laboratory parameters, including serum lactate, clinical diagnoses and outcomes at 24 and 48 h. The SIRS criteria were used to select patients, comprising at least two of the following criteria: HR > 90/min, RR > 20/min, body temperature < 36 °C or > 38.3 °C, and white blood cell count > 12,000/μL or < 4,000/μL [2, 7]. We calculated the quick sequential organ failure assessment (qSOFA) score ranges from 0 to 3 with one point awarded for each of the following clinical signs: SBP ≤ 100 mm Hg, RR ≥ 22/min, and altered mental status from baseline [7].

The sample size was estimated (STATA v14, Stata Corporation, USA) according to the previous report [8] and our pilot study, and the 48 h mortality rate of patients with hypotension was 8%. Providing a power of 80% and two-side alpha of 0.05, the calculated sample size was 223.

Statistical analysis

Descriptive statistics are reported as frequencies, 95% confidence intervals, mean (standard deviation (SD)) and median (interquartile range (IQR)). Proportional data between groups were analyzed by Chi-squared or Fisher's exact test; continuous data were analyzed by Student's *t*-test or the Wilcoxon-Mann-Whitney U test for normally distributed and skewed data, respectively. Factors associated with mortality within 48 h were analyzed by multivariable logistic regression. All analyses (STATA v14) were two sided and a statistically significant P-value was defined as < 0.05.

Results

A total of 9,000 patients were seen in the TUH ED during the 3 months study period. Of these, 250 patients presented with hypotension, including 17 patients who were referred to other hospitals. Therefore, the final number of included patients was 233. Patient's characteristics are shown in Table 1. The mean age was 61.4 ± 20.2 years, and there was a slightly higher proportion (53.7%) of male patients.

The majority of patients had an underlying disease (69.1%), including hypertension (40.3%) and diabetes mellitus (DM, 26.2%). Most patients (88.8%) had been brought to hospital by their families; the rest came by ambulance, and the emergency medical service (EMS, 11.2%). A minority of patients, 2.2%, were at the critical triage level, according to TUH triage criteria. The median times to receive initial IV fluids, to achieve an MAP ≥ 65 mm Hg, and admission times were 29 min, 103 min, and 21 h, respectively.

The chief complaints were fever (18.5%), dyspnea (16.7%), and abdominal pain (8.6%). On admission to the ED,

the mean SBP was 78 mm Hg, the mean diastolic (DBP) was 48 mm Hg, the mean pulse rate was 96/min, and 7.3% of patients had an oxygen saturation ≤ 90%. The mean shock index (heart rate/SBP) and modified shock index (heart rate/MAP) were 1.3 and 1.7, respectively. Of patients, 36.5% had ≥ 2 of the SIRS criteria and 21.9% met qSOFA score ≥ 2. The most common cause of hypotension was infection (50.2%) followed by hypovolemia (40.8%). The initial median serum lactate concentration was 3.5 mmol/L (IQR 1.6 - 4.4).

The median volume of fluid required to achieve an MAP ≥ 65 mm Hg was 1,142 mL (IQR 500 - 1,500) and 27.0% of patients received a vasopressor. Of patients, 40.3% had recurrent hypotension, 16.7% of patients were intubated, and 8.2% died within 48 h.

By univariable analysis, the factors associated with mortality within 48 h are shown in Table 2. The main factors were: 1) being bed ridden, 2) initial pulse rate > 100 beats/min, 3) initial pulse oximetry ≤ 90%, 4) altered mental status, 5) qSOFA score ≥ 2, 6) diagnosis of shock, 7) total fluid in first hour ≥ 1,500 mL, 8) intubation, 9) recurrent hypotension, and 10) those who needed a vasopressor. By multivariable logistic regression, there were three independent factors associated with death ≤ 48 h (Table 3); these were initial pulse rate > 100 beats/min, diagnosis of shock, and recurrent hypotension.

Discussion

In our retrospective study, we have shown that hypotensive patients account for less than 3% of all ED attendances, but they suffered a 48-h mortality of just over 8% and half of those deaths were associated with a final diagnosis of infection.

The baseline characteristics of our ED patients presenting with hypotension were similar to those reported in previous studies, i.e. older patients with underlying morbidities [8-10]. Waiting times to see the doctor and receive treatment were 10 and 28 min, respectively, which compare favorably to the times reported by the US CDC in 2010 - 2011 of 10 and 30 min, respectively. Our ED is busy and sees some 45,000 patients per year and overcrowding and long waiting times are significant challenges we face.

The prevalence of hypotension in EDs varies depending on where the study took place and the definition used of hypotension. Moreover, definitions of sepsis and septic shock have evolved over time with changing definitions of hypotension and shock. Holler et al from Denmark reported an ED prevalence of hypotension of 1% with a 7-day mortality of 12% [1]; this contrasts with a higher rate of 19% reported by Jones et al whose patients suffered an in-hospital mortality of 8% [8].

Although the most common complaint was fever, it was only reported in a little under 20% of patients; interestingly a similar proportion also had a measured fever of ≥ 38 °C. This should alert physicians to a diagnosis of possible sepsis even if the measured temperature is within the normal range. In our series, 113 of 233 patients had sepsis according to qSOFA score, of which 45% had septic shock. This score has been accepted as a screening tool to identify patients who may have early sepsis in the EDs [7, 11].

Table 1. Baseline Characteristics and Clinical Outcomes of 233 Hypotensive Patients

Characteristics	n (%)	Characteristics	n (%)
Male gender	125 (53.7%)	SIRS criteria ≥ 2	85 (36.5%)
Age (year)*	61.4 ± 20.2	qSOFA score ≥ 2	51 (21.9%)
BMI (kg/m^2)*	22.2 ± 3.9	Suspected cause of hypotension	
Underlying diseases	161 (69.1%)	Hypovolemic	95 (40.8%)
Diabetes mellitus	61 (26.2%)	Infection	113 (50.2%)
Hypertension	94 (40.3%)	Cardiovascular	33 (14.2%)
Other	6 (3.7%)	Anaphylaxis	7 (3.0%)
Patient status bed ridden	46 (19.7%)	Neurogenic	1 (0.4%)
Mode of transportation		Hemorrhagic	23 (9.9%)
EMS	26 (11.2%)	Adrenal insufficiency	7 (3.0%)
Family	207 (88.8%)	Diagnosis of shock	93 (39.9%)
Type of illness		Suspected type of shock	
Trauma	10 (4.3%)	Hypovolemic	21 (22.3%)
Non-trauma	223 (95.7%)	Cardiogenic	15 (15.9%)
Chief complaint		Septic shock	51 (54.3%)
Fever	43 (18.5%)	Anaphylactic shock	7 (7.4%)
Dyspnea	39 (16.7%)	Time to IV fluid administration (min)†	29 (9 - 28)
Abdominal pain	20 (8.6%)	Resuscitation time until MAP ≥ 65 mm Hg (min)†	103 (30 - 120)
Triage level, critical	5 (2.2%)	ED admission time (h)†	21 (6 - 25)
Vital signs		Initial serum lactate concentration (mmol/L)†	3.5 (1.6 - 4.4)
Pulse rate (/min)*	96 ± 26	Management	
SBP (mm Hg)*	78 ± 8	Intubation	39 (16.7%)
DBP (mm Hg)*	48 ± 8	Total fluid in first hour (mL)†	758 (500 - 1,000)
MAP (mm Hg)*	58 ± 7	Total fluid until MAP ≥ 65 mm Hg (mL)†	1,142 (500 - 1,500)
Respiratory rate (/min)*	23 ± 5	Vasopressor administration	63 (27.0%)
Pulse oximetry ≤ 90%	17 (7.3%)	Recurrent hypotension	94 (40.3%)
Body temperature > 38.3 °C	38 (16.3%)	Mortality outcome	
Altered mental status	51 (21.9%)	Death in ED	9 (3.9%)
Shock index*	1.3 ± 0.4	Death within 24 h	10 (4.3%)
Modified shock index*	1.7 ± 0.5	Death within 48 h	19 (8.2%)

*Data are expressed as mean ± SD. †Data are expressed as median (IQR). BMI: body mass index; EMS: emergency medical service; ED: emergency department; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure. Shock index = heart rate/systolic blood pressure. Modified shock index = heart rate/MAP. SIRs: systemic inflammatory responses; qSOFA score: quick sequential organ failure assessment score; IV: intravenous.

We found that the qSOFA score was related to hospital mortality in the univariable analysis but it was not a significant factor in the multivariable analysis, which accords with Askim et al and Tusgul et al who found that the qSOFA failed to be a risk stratification tool for predicting 7- and 30-day mortality [12, 13]. The shock and modified shock index may be good markers of a patient's hemodynamic status and have been found to be associated with increased mortality in the ED [14, 15]. We did not show that either index was a significant mortality factor. This difference could be explained by heterogeneity in patients' characteristics and clinical settings among studies.

Within the first hour, the mean volume of isotonic crystalloid fluid resuscitation given to our patients was approximately 750 mL. This amount is in accordance to the survival sepsis campaign, which recommends fluid replacement of 30 mL/kg in the first 3 h [16].

The three independent factors associated with death within 48 h were initial pulse rate > 100 beats/min, shock diagnosis, and recurrent hypotension; these are consistent with the findings of Barfod et al who reported that the SpO$_2$, respiratory rate, SBP and Glasgow coma score were all significantly associated with in-hospital mortality [17]. Factors that we found to be unrelated to increased mortality include serum lactate level

Table 2. Univariable Analysis of Factors Associated With 48 h Mortality in Hypotensive Patients

Characteristics	Odds ratio	95% CI	P value
Male gender	1.53	0.58 - 4.04	0.389
Age ≥ 65 years	1.11	0.43 - 2.84	0.826
Underlying disease	1.28	0.44 - 3.68	0.652
Patient status bed ridden	3.37	1.27 - 8.94	0.015
Body temperature > 38.3 °C	3.76	0.49 - 29.07	0.204
Initial pulse rate > 100 beats/min	5.58	1.79 - 17.39	0.003
Initial pulse oximetry ≤ 90%	8.33	2.84 - 24.49	< 0.001
Altered mental status	7.69	2.84 - 20.80	< 0.001
Shock index > 0.9	4.53	0.59 - 34.85	0.147
Modified shock index > 1.3	5.77	0.75 - 44.33	0.092
qSOFA score ≥ 2	7.69	2.84 - 20.79	< 0.001
Traumatic patient	1.27	0.15 - 10.56	0.828
Diagnosis of shock	33.36	4.37 - 254.80	0.001
Time to initial IV fluid < 30 min	1.50	0.42 - 5.37	0.532
Time to target BP (MAP ≥ 65) < 60 min	1.16	0.40 - 2.64	0.965
Total fluid in first hour ≥ 1,500 mL	4.74	1.50 - 14.94	0.008
Vasopressor administration	2.66	1.03 - 6.91	0.043
Intubation	7.09	2.66 - 18.92	< 0.001
Recurrent hypotension	9.30	2.63 - 32.92	0.001
WBC (/µL) > 12,000 or < 4,000	1.65	0.63 - 4.36	0.311
Serum lactate concentration ≥ 4 mmol/L	1.86	0.68 - 5.09	0.224
ED admission time > 8 h	1.09	0.41 - 2.87	0.868

EMS: emergency medical service; MAP: mean arterial pressure; CI: confidence interval; ED: emergency department; SBP: systolic blood pressure; IV: intravenous. Shock index = heart rate/systolic blood pressure. Modified shock index = heart rate/MAP. qSOFA score: quick sequential organ failure assessment score; WBC: white blood cell count.

and shock index which contrast to a number of other studies [14, 18-22], and could be due partly to our heterogeneous population. Interestingly, a recent meta-analysis found that delayed antibiotic treatment was not associated with an increased risk of death in sepsis [22].

Our study had some limitations. This was a single hospital study with a relatively small number of patients. In addition, this was retrospective, with some incompleteness of data. Larger prospective studies are needed to validate our findings, which could contribute to developing a predictive score of

Table 3. Multivariable Analysis of Factors Associated With 48 h Mortality in Hypotensive Patients

Characteristics	Odds ratio	95% CI	P value
Patient status bed ridden	2.24	0.63 - 8.00	0.214
Initial pulse rate > 100 beats/min	4.21	1.05 - 16.88	0.042
Initial pulse oximetry ≤ 90%	2.94	0.68 - 12.74	0.149
qSOFA score ≥ 2	3.13	0.94 - 10.30	0.061
Altered mental status	2.20	0.60 - 8.04	0.235
Diagnosis of shock	13.74	1.49 - 126.61	0.021
Intubation	1.88	0.52 - 6.82	0.337
Total fluid in first hour ≥ 1,500 mL	3.79	0.72 - 20.00	0.117
Vasopressor administration	0.53	0.15 - 1.86	0.322
Recurrent hypotension	6.91	1.54 - 30.99	0.012

CI: confidence interval; qSOFA score: quick sequential organ failure assessment score.

mortality among these patients.

Conclusions

Hypotension is a common problem in the ED, with sepsis being the most common cause. Our 48-h mortality rate of all causes hypotension was high. In our setting, initial pulse rate > 100 beats/min, diagnosis of shock, and recurrent hypotension were risk factors for death. This knowledge should help ED personals to better triage these patients, and initiate treatment promptly.

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Conflict of Interest

None.

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