ETIOLOGY OF SHOCK IN THE EMERGENCY DEPARTMENT: A 12-YEAR POPULATION-BASED COHORT STUDY

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ABSTRACT—**Introduction:** The knowledge of the etiology and associated mortality of undifferentiated shock in the emergency department (ED) is limited. We aimed to describe the etiology-based proportions and incidence rates (IR) of shock, as well as the associated mortality in the ED. **Methods:** Population-based cohort study at a University Hospital ED in Denmark from January 1, 2000, to December 31, 2011. Patients aged ≥18 years living in the ED-catchment area (N = 225,000) with a first-time ED presentation with shock (n = 1,553) defined as hypotension (systolic blood pressure ≤100 mm Hg) and ≥1 organ failures were included. Discharge diagnoses defined the etiology and were grouped as follows: distributive septic shock (SS), distributive non-septic shock (NS), cardiogenic shock (CS), hypovolemic shock (HS), obstructive shock (OS), and other conditions (OC). Outcomes were etiology-based characteristics, annual IR per 100,000 person-years at risk (95% confidence intervals [CIs]), mortality at 0 to 7-, and 0 to 90 days (95% CIs) and hazard rates (HR) at 0 to 7, 8 to 90 days (95% CIs). Poisson and Cox regression models were used for analyses. **Results:** Among 1,553 shock patients: 423 (27.2%) had SS, 363 (23.4%) NS, 217 (14.0%) CS, 479 (30.8%) HS, 14 (0.9%) OS, and 57 (3.7%) OC. The corresponding IRs were 16.2/100,000 (95% CI: 14.8–17.9), 13.9/100,000 (95% CI: 12.6–15.4), 8.3/100,000 (95% CI: 7.3–9.5), 18.4/100,000 (95% CI: 16.8–20.1), 0.5/100,000 (95% CI: 0.3–0.9), and 2.2/100,000 (95% CI: 1.7–2.8). SS IR increased from 8.4 to 28.5/100,000 during the period 2000 to 2011. Accordingly, the 7-, and 90-day mortalities of SS, NS, CS, and HS were 30.3% (95% CI: 25.9–34.7) and 56.2% (95% CI: 50.7–61.5), 12.7% (95% CI: 9.2–16.1) and 22.6% (95% CI: 18.1–27.7), 34.6% (95% CI: 28.2–40.9) and 52.3% (95% CI: 44.6–59.8), 19.2% (95% CI: 15.7–22.7), and 36.8% (95% CI: 33.3–43.3). SS (HR = 1.46 [95% CI: 1.03–2.07]), and CS (HR = 2.15 [95% CI: 1.47–3.13]) were independent predictors of death within 0 to 7 days, whereas SS was a predictor within 8 to 90 days (HR = 1.66 [95% CI: 1.14–2.42]). **Conclusion:** HS and SS are frequent etiological characteristics followed by NS and CS, whereas OS is a rare condition. We confirm the increasing trend of SS, as previously reported. Seven-day mortality ranged from 12.7% to 34.6%, while 90-day mortality ranged from 22.6% to 56.2%. The underlying etiology was an independent predictor of mortality.

KEYWORDS—Emergency department, epidemiology, etiology, incidence rate, mortality, shock

INTRODUCTION

Circulatory shock is a life-threatening condition associated with substantial morbidity and mortality (1). Shock result from one, or a combination, of four different pathophysiological mechanisms (1). Internal or external loss of fluids (i.e., trauma or gastrointestinal bleeding) often cause hypovolemia, while intracardiac etiologies (i.e., myocardial infarction, myopathy, or a major arrhythmia) cause altered contractility and cardiogenic failure. Extracardiac etiologies of cardiac pump failure (i.e., pulmonary embolism, tension pneumothorax) cause obstruction. Effects of inflammatory agents (distributive, i.e., sepsis, anaphylaxis, poisoning, or other vasodilation effects) often mediate vascular permeability and loss of vascular tone and lead to distributive shock (1, 2).

Knowledge of the frequency and associated prognosis across etiologies of undifferentiated shock are limited, especially in the emergency department (ED) (3). The research available has mainly been limited to the post-ED period. The estimates reported are often based on highly selected patient populations (e.g., septic or cardiogenic shock) in the intensive care unit (ICU) and are of limited value for understanding the early

etiological characteristics of shock at the presentation in the ED. Clarification of the shock-related etiologies in the pre-ICU period could aid knowledge to clinical decision makers handling critically ill ED patients. We therefore carried out a population-based epidemiologic study in an area with a well-defined adult population.

The aims of the present study were to examine the etiology of shock in an ED setting in a well-defined Danish area as well as trends in the annual incidence and mortality across etiologies.

PATIENTS AND METHODS

Study design and setting

This is a secondary analysis of the clinical characteristics and outcomes of adult patients with shock enrolled in a population-based cohort study at the ED of Odense University Hospital, Denmark, between January 1, 2000, and December 31, 2011 (4). Odense University Hospital is a 1,000-bed university teaching hospital with all specialties represented. The ED, at Odense University Hospital, serves a mixed rural-urban population of 225,000 person (age $\geq$18). It is the only serving ED in this part of Denmark and provides primary 24-h acute medical care, with 37,000 annual adult visits (5). The basic prehospital assistance response is an ambulance staffed by two emergency medical technicians (EMTs) with competences restricted to such as initial treatment of patients with myocardial infarction (nitroglycerine, thrombolytic agents, defibrillation), fluid, and inhalation therapy (6). From 2006 and onward, a physician-staffed mobile emergency care unit manned with a physician specialist in anesthesiology and an EMT were added to the prehospital emergency medical system (6). This unit provides prehospital advanced medical treatment exceeding the competences of the EMTs (severe chest pain, sudden loss of consciousness, high-velocity car crash, dyspnea, etc.) (6).

At ED arrival patients are usually assessed in the ED and hereafter allocated and admitted to a specific specialty (orthopedic surgery, infectious diseases, etc.) or referred to primary care or ICU after primary ED evaluation. Patients are treated according to international standard algorithms (e.g., Advanced Trauma Life Support) program and the Injury Severity Score for trauma, Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock [from 2006 and onward], percutaneous coronary intervention for obstructive coronary artery disease). In 2009, the Adaptive process triage (ADAPT) was implemented in the ED at Odense University Hospital and is the most commonly used triage system in Denmark (7).

Participants

Patients aged $\geq$18 years presenting to the ED with a systolic blood pressure (SBP) $\leq$100 mm Hg registered within 3 h upon arrival during the study period were considered eligible. Recording of vital values and blood tests were performed based on a clinical judgment. Patients suffering minor complaints (e.g., sprained ankle, etc.) had not vital values measured or blood test analysis performed. The primary date of contact defined the index date. Patients were included the first time they presented with hypotension (SBP $\leq$ 100 mm Hg) during the study period. We excluded patients who had visited the ED with hypotension between January 1, 1998, and January 1, 2000, to minimize left-sided censoring. Patients without a Danish personal identification number and patients residing outside the hospitals catchment area at the time of contact were excluded. Patients were retrieved from the background population (N = 225,000) and were followed from index date until the date of death, emigration, December 31, 2011, or completion of 90 days follow-up, whichever came first.

Data sources and processing

Database—All patients' records from the ED were registered electronically. In the records, vital parameters are consistently stated and available as structured text format, including time of admission and time of measured SBP and heart rate (HR). By electronic screening it was possible to identify information on all patients with the unique recorded value of SBP and HR. The method of free-text search has been validated in the context of extracting numerical data, including blood pressure recordings (8). The data extraction process used has previously been validated in 500 random ED notes to have a sensitivity of 95.8% (95% CI: 91.2–98.5) and a specificity of 100% (95% CI: 99.0–100) for retrieving correct SBP (9). Data were supplemented with information from the hospitals' local and laboratory information systems to define organ dysfunction.

Population-based registers

In Denmark, the Danish National Health Service provides free individual ED services to every Danish citizen. At birth the Danish Civil Registration system assigns a unique 10-digit civil personal registry number (PRN-number) to each Danish citizen and to residents upon immigration since 1968. This unique PRN-number enables accurate linkage of the Danish national registers (10).

The Danish National Patient Registry—Since 1995 the Danish National Patient Registry has registered all in and outpatient clinic contacts at hospitals in Denmark assembling data regarding dates of admission, discharge, admitting departments, and all primary and secondary discharge diagnoses (*International Classification of Diseases*, version 10 [ICD-10] code system, since 1994) from hospitals (11, 12). At discharge every unique patient contact is assigned one primary diagnosis and secondary diagnoses classified according to the ICD-10 system. From The Danish Civil Registration System, we retrieved data on municipality of residence, migration, marital and vital status, and date of birth (10).

Outcome measures, exposure, and variables of interest

Shock was defined as the presence SBP $\leq$ 100 mm Hg (9) and $\geq$1 organ failures. We used the Shock Index (SI) as a measure of cardiovascular dysfunction (13, 14). SI is calculated as the ratio of heart rate to SBP and included as a categorical variable ($<$0.7, 0.7–1, $\geq$1) (13). The following organ failures were included: cardiovascular (SI $\geq$ 1), renal, coagulation, and hepatic. Biochemical variables (creatinine, bilirubin, platelets, and international normalized ratio [INR]) registered 180 days before and 1 day after the index date was used to identify renal ($>$100 μmol/L recent S-creatinine increase, hepatic (recent S-bilirubin $>$42 μmol/L) and coagulative failure (recent platelet count $<$101 $\times$ 10^9/L or recent INR $>$1.59) (see Appendix 1, http://links.lww.com/SHK/A522 for details). SBP was measured with either an automated oscillometric device or a manual cuff and sphygmomanometer. Heart rate was measured with ECG, palpation or pulse oximetry. The primary outcome was the etiology of shock. Secondary outcomes were the etiological trends in annual IRs and mortality proportions and the mortality within 7- and 90 days of the index date. The primary exposure variables were the first recorded SBP $\leq$ 100 mm Hg and HR at presentation, registered within 3 h upon arrival and the presence of $\geq$1 organ failures.

We used the primary discharge diagnose, assigned to each patient at discharge and grouped these into the classification of shock states proposed by Weil and Shubin (15) and latter updated by Vincent et al. (2). In brief, a discharge diagnosis suggesting an infectious pathophysiology (e.g., pneumonia) was grouped as "septic" (distributive), whereas non-infectious etiologies causing inflammation and vasodilation were grouped as "non-septic" (distributive) (e.g., poisoning, diabetes). Cardiovascular diagnoses (e.g., myocardial infarction, arrhythmia) were grouped as "cardiogenic," and diagnoses suggesting hemorrhage, trauma, or dehydration, were grouped as "hypovolemia." Conditions causing increased afterload (e.g., pulmonary embolus) where group as "obstructive." Finally, diagnoses that did not meet these criteria were grouped as "others." See Appendix 2, http://links.lww.com/SHK/A523, for full list of ICD-10 codes and classification (n = 1,170). For patients with primary unclassifiable diagnoses (n = 383) (see Appendix 3, http://links.lww.com/SHK/A524), two authors (JGH and HKJ) independently and in a blinded manner read and evaluated all discharge summaries for information indicating etiological characteristics and if such information was not clearly stated, the full medical record was reviewed.

We also included information on the additional covariates: sex, age, and Charlson Comorbidity Index (CCI). The latter, was used as a proxy for comorbid illness (16). We used discharge diagnoses from the previous 10 years to generate the CCI (0, 1–2, $>$2) for each enrolled patient upon the index contact date (16).

Statistical analysis

We presented continuous and categorical data as medians (interquartile range [IQR]) and numbers (%), respectively. We used the Pearson chi-square test for categorical variables and the Kruskal–Wallis equality-of-populations rank test for continuous variables.

Incidence rates—The crude annual IRs were calculated as the number of IRs per 100,000 person-years at risk (age $\geq$18 years) with the corresponding 95% confidence intervals (95% CI) assuming a Poisson distribution. The annual IRs were adjusted using direct standardization to the sex- and age distribution of the municipalities of the EDs catchment area midyear population in the year 2000. The population was defined as contributing to one person-year at risk per resident per year in the analyses (17). The incidence rates were estimated and analyzed using a Poisson regression model. Sex, age group, calendar time in years were used in the adjusted model. Calendar time was entered in the model as a continuous variable. Age was divided into two predefined age intervals: 18

to 64 years and ≥ 65 years. The Poisson model was assessed using the Hosmer–Lemeshow goodness-of-fit test.

Mortality analysis—Mortality for the different shock etiologies were presented in a Kaplan–Meier plot, and comparison between survival curves were tested using log-rank test. Mortality proportions were reported at 7-, and 90-day after the index date. Independent prognostics of mortality across etiologies were evaluated by Cox regression and presented as unadjusted and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for time periods 0 to 7 days and 8 to 90 days. The model was adjusted for the following predefined confounders: sex, age, CCI, and number of organ failures (1, 2, and ≥ 3). Model assumptions were checked using Schoenfeld residuals and model fit evaluated using Cox–Snell residuals. Cuzick test was used for trends in annual mortality and mortality trends in age intervals. Statistical analyses were performed using Stata version 13.1 (Stata Corporation LP, College Station, Tex).

Ethics committee approval

The study was approved by the Danish Data Protection Agency (j.nr. 2008-58-0035) and the Danish Health and Medicines Authority (j.nr. 3-3013-205/1). In accordance with Danish law, observational studies performed in Denmark do not need approval from the Medical Ethics Committee. The study was reported according to the *Strengthening the Reporting of Observational Studies in Epidemiology* statement (18).

RESULTS

Participants

Of 438,191 adult ED contacts, a total 1,553 (0.4%) patients met the criteria for shock and were included in the analysis. Reasons for exclusions are presented in Figure 1. The median age was 71 years (IQR 56–81) and 53.4% were male (Table 1). Further characteristics of the population have been presented in a previous paper (4). The most common etiology was hypovolemic (n = 479 [30.8%]), followed by septic (n = 423 [27.2%]), non-septic
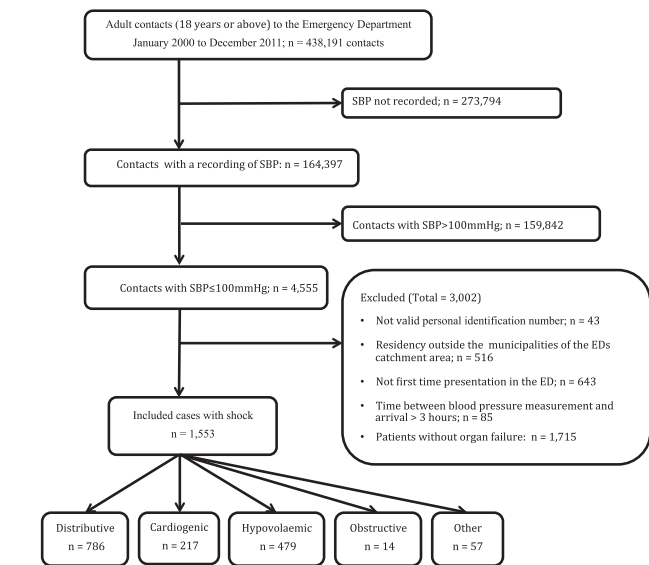

Fig. 1. **Flow chart of patients recruited to the study.**

(n = 363 [23.4%]), cardiogenic (n = 217 [14.0%]), obstructive (n = 14 [0.9%]) and other (n = 57 [3.7%]). Patients suffering septic shock had more comorbidity and a higher number of organ failure, compared with other etiologies.

The validation of the primary unclassifiable diagnoses (n = 383) found a general interrater agreement of 70.3% (κ,

Table 1. **Baseline characteristics at time of arrival to the ED***

Variable	Total (%)	Distributive (septic)	Distributive (non-septic)	Cardiogenic	Hypovolemic	Obstructive	Other
N (%)	1,553 (100%)	423 (27.2%)	363 (23.4%)	217 (14.0%)	479 (30.8%)	14 (0.9%)	57 (3.7%)
Age in years, median (IQR)	70 (56–81)	74 (63–83)	56 (43–72)	75 (65–82)	72 (57–81)	72 (66–77)	68 (54–80)
Sex (%)							
Male	830 (53.4%)	231 (54.6%)	183 (50.4%)	114 (52.5%)	267 (55.7%)	6 (42.9%)	29 (50.9%)
Female	723 (46.6%)	192 (45.4%)	180 (49.6%)	103 (47.5%)	212 (44.3%)	8 (57.1%)	28 (49.1%)
Age in age groups, yr (%)							
18–39	147 (9.5%)	18 (4.3%)	73 (20.1%)	6 (2.8%)	40 (8.4%)	1 (7.1%)	9 (15.8%)
40–64	468 (30.1%)	92 (21.7%)	167 (46.0%)	47 (21.7%)	141 (29.4%)	2 (14.3%)	19 (33.3%)
65–84	691 (44.5%)	220 (52.0%)	98 (27.0%)	127 (58.5%)	212 (44.3%)	11 (78.6%)	23 (40.4%)
85+	247 (15.9%)	93 (22.0%)	25 (6.9%)	37 (17.1%)	86 (18.0%)	0 (0.0%)	6 (10.5%)
CCI (%)							
0	477 (30.7%)	87 (20.6%)	148 (40.8%)	55 (25.3%)	155 (32.4%)	4 (28.6%)	28 (49.1%)
1–2	589 (37.9%)	180 (42.6%)	117 (32.2%)	85 (39.2%)	186 (38.8%)	4 (28.6%)	17 (29.8%)
>2	487 (31.4%)	156 (36.9%)	98 (27.0%)	77 (35.5%)	138 (28.8%)	6 (42.9%)	12 (21.1%)
Vital variables							
Systolic blood pressure, median (IQR)	88 (80–94)	88 (80–94)	90 (82–95)	88 (77–93)	86 (78–93)	89 (78–92)	87 (75–93)
Diastolic blood pressure, median (IQR)	52 (44–62)	51 (42–59)	53 (45–65)	52 (42–62)	52 (45–61)	56 (49–65)	56 (48–66)
Heart rate, median (IQR)[†]	101 (88–115)	104 (90–118)	100 (88–114)	104 (88–129)	100 (86–110)	111 (98–120)	100 (91–108)
Number of organ dysfunctions, n (%)							
1	1,160 (74.7%)	275 (65.0%)	290 (79.9%)	178 (82.0%)	355 (74.1%)	9 (64.3%)	53 (93.0%)
2	311 (20.0%)	106 (25.1%)	59 (16.3%)	34 (15.7%)	104 (21.7%)	4 (28.6%)	4 (7.0%)
3+	82 (5.3%)	42 (9.9%)	14 (3.9%)	5 (2.3%)	20 (4.2%)	1 (7.1%)	0 (0.0%)
Site of organ failure (%)							
Cardiovascular	1,245 (80.2%)	329 (77.8%)	299 (82.4%)	174 (80.2%)	378 (78.9%)	13 (92.9%)	52 (91.2%)
Renal	333 (21.4%)	133 (31.4%)	63 (17.4%)	50 (23.0%)	83 (17.3%)	2 (14.3%)	2 (3.5%)
Coagulation	387 (24.9%)	125 (29.6%)	70 (19.3%)	32 (14.7%)	149 (31.1%)	4 (28.6%)	7 (12.8%)
Hepatic	72 (4.6%)	30 (7.1%)	21 (5.8%)	5 (2.3%)	15 (3.1%)	1 (7.1%)	0 (0.0%)

*Values expressed as total number (fraction) and medians [25 percentile-75 percentile] as appropriate. Chi-squared test for categorical variables and Kruskal-Wallis test for continuous variables.
[†]35 Missing.
CCI indicates Charlson Comorbidity Index; ED, emergency department; IQR, interquartile range.
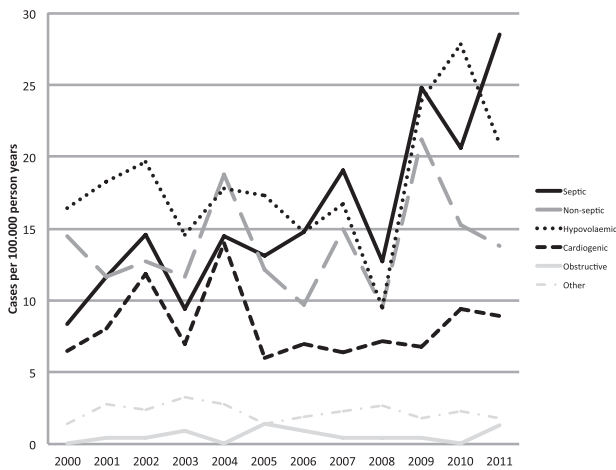
Fig. 2. **Crude annual incidence rates of shock from 2000 to 2011 stratified on etiology (septic, non-septic, hypovolemic, cardiogenic, obstructive, and other).**

Fig. 3. **Crude incidence rates stratified by age and etiology.**

0.62; 95% CI: 0.59–0.63), across all etiologies, corresponding to a substantial strength of agreement (19). When restricting to specific etiologies, the interrater agreement was between 33.3% (obstructive) and 82.4% (septic).

Incidence rates

The yearly mean crude IRs across etiologies are shown in Figure 2 and the IR stratified into age intervals (Fig. 3). Except for septic shock, there were no significant trends in the annual IR of the different etiologies during the period 2000 to 2011. IRs of septic, non-septic, cardiogenic, and hypovolemic shock all increased by age.

Septic shock—Of the 423 (27.2%) patients with septic shock, the corresponding IR was 16.2/100,000 person-years at risk (pyar) (95% CI: 14.8–17.9). The IR increased from 8.4 to 28.5/ 100,000 pyar, during the period 2000 to 2011, with an average adjusted annual increase of 8.5% (95% CI: 5.5–11.7).

Non-septic shock—Three hundred sixty three (23.4%) suffered non-septic shock. The IR of non-septic shock was 13.9/ 100,000 pyar (95% CI: 12.6–15.4).

Cardiogenic shock—Of the 217 (14.0%) with cardiogenic shock the IR was 8.3/100,000 pyar (95% CI: 7.3–9.5).

Hypovolemic shock—Four hundred seventy four (30.8%) suffered hypovolemic shock. The IR was 18.4/100,000 pyar (95% CI: 16.8–20.1).
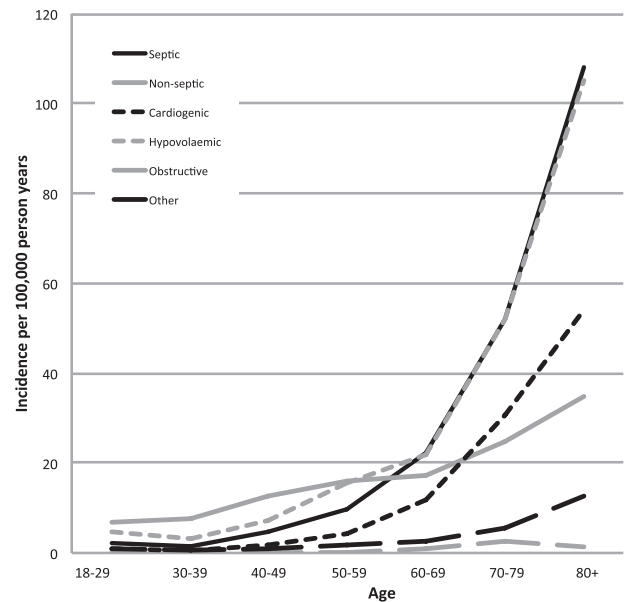
Obstructive shock—Fourteen (0.9%) suffered obstructive shock. The annual IR was 0.5/100,000 pyar (95% CI: 0.3–0.9).

Other causes—The IR of other causes was 2.2/100,000 pyar (95% CI: 1.7–2.8), based on 57 patients (3.7%).

Mortality

The 7-day mortality of the major groups, non-septic, septic, cardiogenic, and hypovolemic, were 12.7% (95% CI: 9.2–16.1), 30.3% (95% CI: 25.9–34.7), 34.6% (95% CI: 28.2–40.9), and 19.2% (95% CI: 15.7–22.7), respectively (Table 2). Accordingly, 90-day mortality was 22.6% (95% CI: 18.1–27.7), 56.2% (95% CI: 50.7–61.5), 52.3% (95% CI: 44.6–59.8), and 36.8% (95% CI: 33.3–43.3), respectively. Kaplan–Meier curves are shown in Figure 4 with the overall estimated probability of 90-day survival stratified into etiologies. Trend analysis of the annual 7-, and 90-day mortality proportions did not show a significant change during the entire observation period across etiologies of shock.

Mortality related to etiology

In the multivariate analysis (controlled for sex, age, CCI, and number of organ failure) patients with septic (HR = 1.46 [95% CI: 1.03–2.07]) and cardiogenic shock (HR = 2.15 [95%

TABLE 2. **Importance of etiology for death in patients presenting with shock at presentation to the ED—Cox regression**

	N, total (%)	0–7 days					8–90 days				
		N, died (%)	Crude HR (95% CI)	P^{**}	Adjusted HR (95% CI)*	P^{**}	N, died (%)	Crude HR (95% CI)	P^{**}	Adjusted HR (95% CI)*	P^{**}
Etiology											
Non-septic	363 (23.4)	46 (12.7)	1		1		41 (11.3)	1		1	
Septic	423 (27.2)	128 (30.3)	2.55 (1.82–3.57)	<0.001	1.46 (1.03–2.07)	0.036	104 (24.6)	3.13 (2.18–4.49)	<0.001	1.66 (1.14–2.42)	0.009
Cardiogenic	217 (14.0)	75 (34.6)	3.10 (2.15–4.47)	<0.001	2.15 (1.47–3.13)	<0.001	39 (17.8)	2.31 (1.49–3.58)	<0.001	1.33 (0.85–2.08)	0.216
Hypovolaemic	479 (30.8)	92 (19.2)	1.57 (1.10–2.23)	0.013	1.12 (0.78–1.60)	0.547	85 (17.8)	1.78 (1.23–2.59)	0.002	1.14 (0.78–1.67)	0.496
Obstructive	14 (0.9)	7 (50.0)	4.94 (2.23–10.93)	<0.001	3.04 (1.37–6.79)	0.006	2 (14.3)	2.41 (0.58–9.94)	0.226	1.61 (0.39–6.67)	0.512
Other	57 (3.7)	14 (24.6)	2.11 (1.16–3.83)	0.015	2.05 (1.12–3.75)	0.020	5 (8.8)	0.88 (0.35–2.22)	0.782	0.76 (0.30–1.92)	0.558

*Cox proportional hazard model adjusted for sex, age as a continuous variable, Charlson comorbidity level (0, 1–2, >2) and number of organ dysfunctions. Patients who died during the first 7 days after admission were excluded from the analyses of 8- to 90-day mortality.
**Log-rank test for equality.
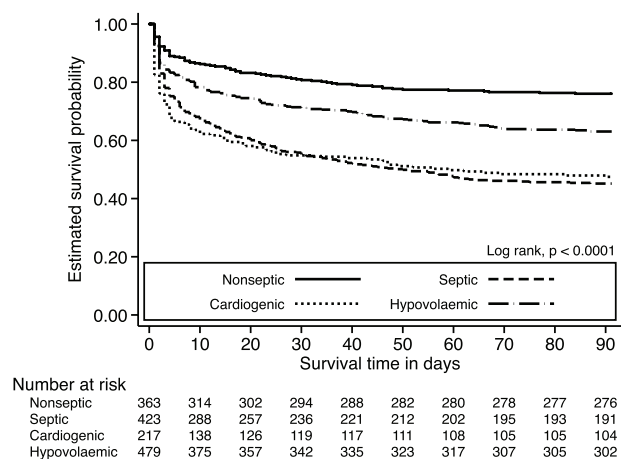CI indicated confidence interval; ED, emergency department; HR, hazard ratio.

FIG. 4. **Kaplan–Meier curves illustrating overall 90-day survival across etiologies of shock.** Below the curves are listed the number at risk at corresponding intervals in survival time.

CI: 1.47–3.13]), had a higher hazard rate as compared to the reference (non-septic shock) within 0 to 7 days. Conditional upon surviving 8 days or more, only septic shock was a significant etiologic independent predictor with an HR = 1.66 (95% CI: 1.14–2.42) as compared to the reference (Table 2).

DISCUSSION

In this population-based cohort study, we explored the etiological characteristics of undifferentiated shock at presentation in the ED. Hypovolemic and septic shock were the most common etiologies followed by non-septic and cardiogenic shock, whereas obstructive shock was a rare condition.

The published studies investigating the etiology of shock in the ED have been limited (3) while the frequency in the post-ED period has gained more attention. One-third of the ICU population has been reported to suffer shock (20). In a large randomized trial by De Backer et al. (21), septic shock occurred in 62% of the patients, cardiogenic shock in 16%, hypovolemic shock in 16%, obstructive shock in 2%, whereas other types of distributive shock counted 4%. As these studies often include patients from different settings, both the ED and local wards within the hospital, the estimates could be confounded by the premise of patients surviving to the ICU. These estimates are therefore a reflection of this selection making extrapolation to the ED difficult. In ED populations with undifferentiated symptomatic persistent hypotension, Jones et al. (22) identified 43% to suffer septic shock, 15% cardiovascular shock, 28% severe dehydration, and 7% toxicological causes. Less than 1% suffered anaphylaxis (22). Accordingly, Arendts et al. (23) described septic shock in 28%, cardiogenic in 27%, trauma in 14%, non-traumatic hemorrhage in 6%, and acute respiratory failure in 6%. Lastly, in a cohort of hypotensive shock patients, Kheng et al. (24) found hypovolemic shock 36%, septic shock 33%, cardiogenic shock 29%, and anaphylactic shock in 2%. Altogether the studies suggest septic, cardiovascular and hypovolemic shock to be common causes of shock. These findings are in line with our results.

Trend analysis of IRs across etiologies in our study did not exhibit significant trends, except for an increasing trend of

septic shock, which has been reported in all areas of the world where epidemiological studies of septic shock patients have been conducted (25). The IR of septic shock has previously been reported to be 31/100,000 pyar among in-hospital patients (wards and ICUs) (26). Although the incidence of acute myocardial infarction has decreased (27, 28), the incidence of cardiogenic shock complicating ST-elevation myocardial infarction (STEMI) paradoxically seem to be increasing (29). Due to our local prehospital structure, patients suffering STEMI are commonly triaged prehospitally and referred directly for primary percutaneous coronary intervention and thereby bypass the ED, which could explain the absence of an increase in the IR of cardiogenic shock in our study.

Of notion was the decline in IR during 2008 followed by an increase across several etiologies (Fig. 2). This trend could partly be explained by a decrease of 9.6% (3,637) during 2000 to 2008 of all adult ED contacts and a subsequent increase of 7.8% (2.897 contacts) from 2008 to 2011, and thereby a concordantly proportional change in the annual frequency of shock cases (Fig. 5). Moreover, we hypothesize a possible change in ED personal behavior concerning monitoring patients and increased awareness during 2009 to 2011 due to the implementation of the ADAPT triage algorithm in 2009 (especially among the older individuals).

Exploring mortality proportions revealed 90-day mortalities of septic and cardiogenic shock of 56.2% and 52.3%, respectively. These findings are in line with rates reported for septic (26) and cardiogenic shock (30), although the later has decreased (29). Non-septic shock had the lowest 90-day mortality (22.6%). This group of patients was younger (Fig. 3) and consisted of patients suffering mainly of disorders related to glucose homeostasis, poisoning, epilepsy, and use of alcohol (see Appendix 4, http://links.lww.com/SHK/A525). Finally, we found the underlying etiology an independent predictor of mortality, especially in patients suffering septic shock.

Study strengths and limitations

The strengths of this study were the large sample size and the accurate linkage between healthcare registries. Due to the Danish public healthcare system, it was possible to identify
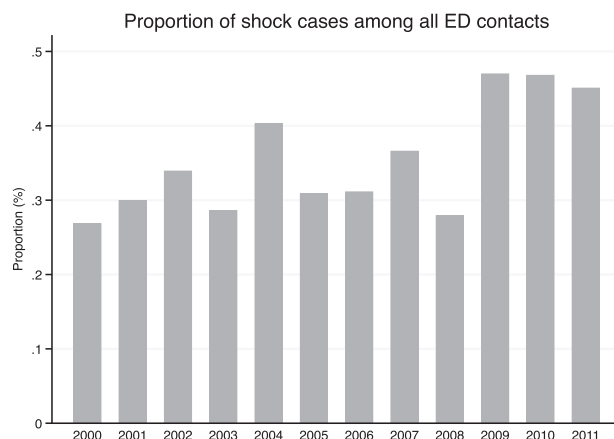

FIG. 5. **Annual proportion of shock patients based on the annual overall ED visits of adult patients (age ≥18 years).** ED indicates emergency department.

all patients in the population-based registries, allowing complete follow-up. Moreover, it was possible to follow each individual patient event throughout the study period. The blood pressure measurements were registered prospectively and as a routine documentation in the ED population. We used the first contact with shock within the study period to minimize bias from repeated measurements. Furthermore, we excluded patient with residency outside the catchment area and a previously reported admission with SBP $\leq$ 100 mm Hg in the years 1998 to 1999 to avoid possible overestimation of the incidence.

We derived a definition for etiological characteristics of shock based on hospital discharge data (see appendix 1, http://links.lww.com/SHK/A522), with a case definition that required both a diagnostic code indicating the etiology (e.g., "pneumococcal pneumonia" = septic, "Myocardial infarction" = cardiogenic) plus biochemical variables or SI $\geq$ 1 at presentation indicating organ failure. However, metabolic failure was not included, as arterial punctures were not systematically collected and registered. Moreover, respiratory frequencies and Glasgow Coma Scale were not consistently registered in the electronic records, whereby organ failures related to the respiratory system, and failure of the central nervous system were not included. Due to the design of the study and data availability (electronic administrative data), we are unfortunately not able to add the variables mentioned (arterial punctures, respiratory frequencies, use of vasopressors, mechanical ventilation, etc.). Including a higher number of organ failures would not only increase the IR but could also have a possible impact on the mortality estimates. Moreover, we used SBP $\leq$ 100 mm Hg based on increasing evidence supporting a higher threshold (9, 31–33). Traditionally, hypotension is defined as SBP $\leq$ 90 mm Hg. Using the traditional definition would exclude 608 (39.2%) patients (90 > mm Hg SBP $\leq$ 100 mm Hg) with shock from our cohort of which 6.4% (100/1,553) died within 7 days and 13.3% (206/1,553) died within 90 days. Details of patients with SBP < 90 mm Hg are given in Table 3. We used discharge diagnosis information to calculate the CCI, which means that for a comorbidity to be recognized it had to require hospitalization. Comorbidities such as diabetes could therefore be under reported.

Importantly, we acknowledge the limitation in our estimates of cardiogenic shock as these patients are likely to be underestimated due to possible referral bias by the emergency medical service operating in the prehospital setting during the period of observation. Moreover, the etiology of shock is not always solely restricted to one type, but can overlap, due to the underlying heterogeneity, and patients admitted with one type of shock can develop other types of shock (1).

The study was a single-center, retrospective study from an academic hospital. The large proportion of ED patients who were not eligible for study inclusion because SBP was not measured at all (n = 273,794) may be seen as an important limitation. However, most of these patients suffered minor complaints and based on a clinical judgment vital parameters were not measured.

The data we have access to were limited to the type of observation and investigations that the clinician found relevant to order—and register—for the specific patient who arrived at

Table 3. **Cohort characteristics stratified on systolic blood pressure thresholds**

	Systolic blood pressure threshold		
			>90 mm Hg SBP
	$\leq$100 mm Hg	$\leq$90 mm Hg	$\leq$100 mm Hg
Variable	n (%)	n (%)	n (%)
Male (1), Female (0)			
0	723 (46.6)	427 (45.2)	296 (48.7)
1	830 (53.4)	518 (54.8)	(312 (51.3)
Total	1,553 (100.0)	945 (100.0)	608 (100.0)
CCI (%)			
0	477 (30.7)	283 (29.9)	194 (31.9)
1–2	589 (37.9%)	352 (37.2)	237 (39.0)
>2	487 (31.4%)	310 (32.8)	177 (29.1)
Total	1,553 (100.0)	945 (100.0)	608 (100.0)
Number of organ dysfunctions			
1	1,160 (74.7%)	665 (70.4)	495 (81.4)
2	311 (20.0%)	218 (23.1)	93 (15.3)
3+	82 (5.3%)	62 (6.6)	20 (3.3)
Total	1,553 (100.0)	945 (100.0)	608 (100.0)
Etiology			
Nonseptic	363 (23.4)	194 (20.5)	169 (27.8)
Septic	423 (27.2)	254 (26.9)	169 (27.8)
Cardiogenic	217 (14.0)	133 (14.1)	84 (13.8)
Hypovolaemic	479 (30.8)	314 (33.2)	165 (27.1)
Obstructive	14 (0.9)	10 (1.1)	4 (0.7)
Other	57 (3.7)	40 (4.2)	17 (2.8)
Total	1,553 (100.0)	945 (100.0)	608 (100.0)
Overall 7-day mortality			
Alive	1,191 (76.7)	683 (72.3)	508 (83.6)
Dead	362 (23.3)	262 (27.7)	100 (16.5)
Total	1,553 (100.0)	945 (100.0)	608 (100.0)
Overall 90-day mortality			
Alive	915 (58.9)	513 (54.3)	402 (66.1)
Dead	638 (41.1)	432 (45.7)	206 (33.9)
Total	1,553 (100.0)	945 (100.0)	608 (100.0)

CCI indicates Charlson Comorbidity Index; SBP, systolic blood pressure.

the ED. In some instances, the clinician have omitted to order further investigations despite the fact that the patient had an SBP $\leq$ 100 mm Hg. Tables 4 and 5 aim to describe these patients. The tables show that most of these patients are 70 years or older, and that they are discharged directly from the ED. The ethical question of whether or not it is acceptable to omit further investigations of elderly patients is highly relevant and is probably the explanation of why so many patients had no further blood test ordered. The patients with missing laboratory values are a result of clinical decisions between 2000 and 2011. This is a culture that changes with time and geography, and the data have to be interpreted as such.

It is therefore possible that our local triage algorithm does not easily translate to other acute health care systems outside our ED, which limit the generalizability of the results. 3.5% (n = 22) died in the ED upon arrival or shortly after (majority suffered cardiac arrest) explaining the rather excessive 24-h mortality of "discharged" ED patients and the lack of blood test performed in these patients (Tables 4 and 5).

Also the differences between our estimates reported here and results from the United States and other centers in Europe could reflect different ways of defining etiologies of shock, place of setting and variability in demographics and health systems. Moreover, the use of different algorithms of case identification

TABLE 4. **Characteristics of hypotensive patients (non-shock) without blood tests performed (<24 h)**

Specialty/Department*	n (%)	Age (mean)	SBP (mean)	Heart rate (mean)	Overall mortality, n (%)		
					≤24 h[†]	7 days	90 days
Emergency Department	627 (91.3)	54 (31–73)	94 (90–97)	72 (63–81)	22 (3.7)	29 (5.1)	57 (9.3)
Cardiology	4 (0.6)	77 (55–84)	85 (74–97)	61 (50–80)	4 (100.0)	4 (100.0)	4 (100.0)
Endocrinology	1 (0.2)	50 (50–50)	92 (92–92)	80 (80–80)	0 (0.0)	0 (0.0)	0 (0.0)
General Internal Medicine	11 (1.6)	43 (36–86)	98 (89–99)	78 (62–82)	0 (0.0)	1 (3.7)	2 (18.2)
General Surgery	3 (0.4)	61 (31–85)	94 (87–99)	78 (56–84)	0 (0.0)	0 (0.0)	0 (0.0)
Geriatriology	1 (0.2)	79 (79–79)	87 (87–87)	70 (70–70)	1 (100.0)	1 (100.0)	1 (100.0)
Heart, Pulmonary and vascular Surgery	4 (0.6)	50 (29–71)	95 (87–97)	60 (56–67)	2 (50.0)	2 (50.0)	2 (50.0)
Nephrology	1 (0.2)	41 (41–41)	88 (88–88)	49 (49–49)	0 (0.0)	0 (0.0)	0 (0.0)
Neurosurgery	2 (0.3)	79 (78–79)	90 (82–97)	75 (58–92)	1 (50.0)	2 (100.0)	2 (100.0)
Orthopedic Surgery	33 (4.8)	49 (34–73)	93 (89–97)	70 (64–78)	1 (3.0)	2 (6.1)	5 (15.2)
Total	687 (100.0)	55 (34–74)	94 (90–97)	72 (63–80)	31 (4.5)	41 (6.2)	73 (10.6)

*Two missing variables.
[†]These 22 patients died while they were in the ED due to severe time dependent diseases.
ED indicates emergency department; SBP, systolic blood pressure.

TABLE 5. **Mortality characteristics stratified on age of unadmitted patients in the ED**

Age	n (%)	Overall mortality, n (%)		
		≤24 h*	7 days	90 days
18–29	137 (21.9)	1 (0.7)	1 (0.7)	1 (0.7)
30–39	78 (12.4)	1 (1.3)	1 (1.3)	1 (1.3)
40–49	70 (11.2)	0 (0.0)	0 (0.0)	1 (1.4)
50–59	86 (13.2)	1 (1.2)	2 (2.9)	4 (4.7)
60–69	69 (11.0)	2 (2.9)	2 (2.9)	6 (8.7)
70–79	85 (13.6)	6 (7.1)	6 (7.1)	15 (17.7)
80+	102 (16.3)	11 (10.8)	17 (16.7)	29 (28.4)
Total	627 (100.0)	22 (3.5)	29 (4.6)	57 (9.1)

*The patients died while they were in the emergency department due to severe time-dependent diseases.
ED indicates emergency department.

could explain the difference in estimates (e.g., sepsis-specific discharge codes or discharge codes of infection and organ dysfunction (34)).

Finally, the increasing incidence of septic shock could be, in part, a consequence of the initiation and implementation of the Surviving Sepsis Campaign in 2004 (35) (Denmark, 2006) as focus has increased on this condition.

CONCLUSION

Hypovolemic (30.8%) and septic shock (27.2%) are common etiological characteristics of shock at presentation in the ED, followed by non-septic (23.4%) and cardiogenic shock (14.0%), all increasing by age. Obstructive shock is a rare condition (0.9%). Septic shock increased during the study period. The 7-, and 90-day mortality of septic, non-septic, cardiogenic, and hypovolemic shock was 30.3%/56.2%, 12.7%/22.6%, 34.6%/52.3%, and 19.2%/36.8%, respectively. Independent etiologies of mortality were primarily septic and cardiogenic shock within 0 to 7 days and septic shock within 8 to 90 days.

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