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Sepsis-related mortality in 497 cases with blood culture-positive sepsis in an emergency department

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SUMMARY

Objective: Few studies have sought to establish how often death after sepsis is related to the sepsis and how often underlying diseases have a major role in case fatality.
Methods: In this retrospective cohort study, data were collected on 497 cases with blood culture-positive sepsis in an emergency department (ED).
Results: Sepsis was categorized as severe in 31% of cases; 7% had septic shock. The quick Sepsis-related Organ Failure Assessment score was positive in 136 out of 473 cases (29%). Ninety-eight patients died by day 90; in 16 of these cases (16%) the death was sepsis-related in a patient without a rapidly fatal underlying disease, in 45 cases (46%) the death was sepsis-related in a patient with a rapidly fatal underlying disease, and in 37 cases (38%) the death was unrelated to sepsis. Sepsis-related death occurred in 58 out of 61 cases (95%) by day 28.
Conclusions: Underlying diseases were found to have a considerable role in the death of patients suffering from blood culture-positive sepsis in an ED of a developed country, as only 16% of the deaths by day 90 occurred where death was sepsis-related and the patient had a life-expectancy of more than 6 months. Improving the outcome of sepsis with new treatments is thus challenging. It is possible that day 7 + day 28 mortality is a more appropriate endpoint than day 90 mortality when studying the outcome of sepsis, as this time-span includes most of the patients whose death was related to sepsis.

Introduction

Sepsis is one of the leading causes of death worldwide. It has been ranked as the eleventh most common cause of death in the USA.[1] Advanced age, immunosuppression, diabetes, and cancer are major risk factors for sepsis.[2–6] Prognostic factors for the severity and outcome of sepsis include advanced age, type of infection (e.g., methicillin-resistant *Staphylococcus aureus* (MRSA), polymicrobial), number of organ dysfunctions, and adequacy of antimicrobial therapy.[7–9]

Studies have been performed on sepsis patients in emergency departments (EDs) and intensive care units (ICUs) in order to determine risk factors for mortality[9–13] and the aetiology of illness.[14] Less attention has been paid to the questions of how often these patients actually die of sepsis, how often sepsis is a contributory factor in the death of a patient with an advanced underlying disease, and how often the death is independent of sepsis.

In this retrospective cohort study, data were collected on 497 adult cases of blood culture-positive sepsis in the ED of Tampere University Hospital (TAUH). A categorization of causes of death was developed in order to establish how often death was related to sepsis in patients without a rapidly fatal underlying disease (group 1), was related to sepsis by weakening of a patient with a rapidly fatal underlying disease (group 2), and was independent of sepsis but caused by the underlying disease (group 3). It was also sought to determine the best cut-off among the commonly used days for mortality used in sepsis research, i.e. day 7, day 28, or day 90, for mortality related to sepsis (deaths in groups 1 and 2).

Materials and methods

TAUH is a tertiary hospital with a catchment population of approximately 524 700 inhabitants in Pirkanmaa County. The ED of

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the hospital handles patients requiring both basic and specialized emergency care. In specialized care, the majority of patients are internal medicine and surgical patients. Blood cultures are taken routinely from patients with signs or symptoms of systemic infection. The population of the present study comprised 497 adult patients admitted to the ED of TAUH and treated in specialized care, who had blood culture-positive sepsis during the period March 1, 2012 to February 28, 2014. The study was approved by the Ethics Committee of Tampere University Hospital. The need for informed consent was waived, as no additional blood sampling was needed and routine patient care was not modified.

TAUH has a 24-bed ICU which includes a seven-bed high dependency unit (HDU). In this article, 'ICU' refers to both of these. There are four other HDUs (cardiology, pulmonary, surgical, and internal medicine), all taking care of sepsis patients; these are referred to as 'HDUs'.

Blood cultures were collected in BacT/Alert Aerobic (FA Plus) and Anaerobic (FN Plus) blood culture bottles and placed in the automated microbial detection system BacT/Alert 3D (bioMérieux, Marcy l'Etoile, France). All patients with a positive blood culture obtained during specialized care in the ED were identified in the microbiology laboratory serving TAUH (Fimlab Laboratories plc). Patient details, the name of the organism, and the date of blood culture were collected by clinical microbiologists (T.S. and J.A.). Cultures positive for coagulase-negative Staphylococcus, Propionibacterium, Micrococcus, Bacillus, and Corynebacterium, with detection in a single blood culture bottle and without clinical relevance, were considered to be contaminants and were excluded.

Patients whose routine blood samples taken on admission were no longer available for further studies were also excluded. This could be due, for example, to the fact that the blood culture became positive later than 72 h after the day of admission.

The clinical data for the patients included in the study were gathered retrospectively from the patient records by the principal investigator (J.R.). The site of infection was decided retrospectively by the principal investigator based on clinical judgement. Sepsis was deemed to be healthcare-associated if the symptoms had started more than 48 h after admission to a healthcare institution, or the bacteraemia was related to a surgical operation within the preceding 30 days or some other invasive procedure within the previous 10 days.[15] Data on cause of death were gathered from patient records (and autopsy records when applicable) by two clinicians (J.R. and R.H.) independently. In cases of discrepancy, a meeting was held together with a third clinician (J.S.) and a final decision was made.

Cause of death by day 90 was classified into three different categories: (1) group 1 included cases of sepsis-related mortality in patients without a rapidly fatal underlying disease. The immediate cause of death in this group was sepsis, or sepsis was a factor in a chain of events leading to death, and the patient had a life-expectancy of more than 6 months. (2) Group 2 included cases of sepsis-related mortality in patients with a rapidly fatal underlying disease. In this group, the patient died of sepsis (immediate cause of death, or sepsis was a factor in a chain of events leading to death) by weakening of a patient with a rapidly fatal (<6 months) underlying disease. (3) Group 3 included cases of mortality related to underlying disease. In this group, sepsis was not an immediate cause of death or a factor in a chain of events leading to death.

The categorization was based on clinical decision and the judgement was based on the severity of the patient's underlying disease, the patient's pre-performance, severity of the sepsis, and recovery after the infection. The main underlying disease associated with death was determined retrospectively by the principal investigator.

Diagnoses of sepsis, severe sepsis, and septic shock were made according to consensus definitions.[16] Further, the quick Sepsis-related Organ Failure Assessment score (qSOFA) was calculated post-hoc according to recently published definitions.[17] The qSOFA score was positive if at least two of the following three criteria were fulfilled in the ED: respiratory rate ≥22/min, altered mentation, and systolic blood pressure ≤100 mmHg. The McCabe classification was determined as reported by McCabe and Jackson.[18] The Pitt bacteraemia score was calculated as presented by Korvick et al.[19] IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA) was used for the statistical analyses. Categorical data were analyzed by Chi-square test, or Fisher's exact test when appropriate. Odds ratios (OR) with 95% confidence intervals (95% CI) are also presented.

Results

There were 800 consecutive positive blood cultures in adult patients during the study period. One hundred and thirty-six of these were considered to be contaminants and 167 were excluded for other reasons. A total 497 cases of positive blood culture among 484 patients were thus included. All 497 cases had sepsis. During the study period, 11 patients had sepsis twice on different admissions and one patient had sepsis three times. Of the total study population, 262 (53%) were male and 235 (47%) were female; they ranged in age from 16 to 95 years (median 68 years).

Table 1 provides the demographic data, data on the causative organisms, and data on the underlying diseases stratified into six different categories: groups 1, 2, and 3 (as noted in the Materials and methods section), all patients who died, all patients who survived, and all cases. For 16 out of 98 patients (16%) who died by day 90, death was related to sepsis and the patient did not have a rapidly fatal underlying disease (group 1), i.e. 3% of all 497 sepsis cases. For 45 patients (46% of all deaths by day 90), death was related to sepsis in that it weakened the patient leading to the death, which was in any case expected as the patient had a rapidly fatal underlying disease (group 2). For 37 patients (38%), death by day 90 was unrelated to sepsis and was caused by an underlying disease(s) in the patient (group 3).

Of the group 1 patients, four (25%) had alcohol abuse as an underlying disease (Table 1). One was without any underlying disease. Four of the patients in group 1 were over 80 years of age (25%). Three group 1 patients (19%) were found lying at home with a low level of consciousness and were transferred to hospital. In group 2 patients, the rapidly fatal underlying disease was a solid tumour with metastasis in eight cases (18%) and a haematological malignancy in nine (20%). In group 3 patients, the cause of death was a solid tumour with metastasis in 19 patients (51%) and a haematological malignancy in two (5%). Thus, malignancies were associated with death in 46% of patients in groups 2 and 3 combined. Other common rapidly fatal underlying diseases associated with death among the patients in groups 2 and 3 were liver disease (11%), heart disease (11%), and neurological/neurosurgical disease (10%).

The case fatality rate by day 7, day 28, and day 90 was 9%, 14%, and 20%, respectively. Death occurred by day 7 in 94% of group 1 patients, in 56% of group 2 patients, and in 11% of group 3 patients (Figure 1). All except two cases in group 2 died before day 28. The deaths in group 3 occurred most often between day 29 and day 90 (68%). Ninety-five per cent of all sepsis-related deaths occurred within 28 days after sepsis.

Table 2 gives data on the severity of sepsis stratified into the same categories as used in Table 1. The qSOFA was positive in 136 out of 473 cases (29%). Group 1 had the highest Pitt bacteraemia scores. Forty-eight (10%) cases were transferred from the ED to the ICU and 52 (11%) to HDUs. Thus, the majority of sepsis patients and the majority of qSOFA-positive cases were taken care of in general wards. Out of 449 cases who were treated outside the ICU, 104