Long-term mortality following bloodstream infection

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Abstract

Bloodstream infection is associated with significant short-term mortality, but less is known about long-term outcome. We describe factors affecting mortality up to 3 years after bloodstream infection in a cohort of patients reviewed at the bedside by an infection specialist. Patients seen by the bacteraemia service of our infectious diseases department between June 2005 and November 2008 were included in analyses. Routine clinical data collected at the time of consultation, together with laboratory, demographic and outcome data were analysed to identify factors predicting death at 30 days and 3 years after bloodstream infection. Cox regression models for both time-points were constructed, together with Kaplan–Meier survival curves. In all, 322 bloodstream infections were recorded in 304 patients. The 30-day mortality was 15%, with a 3-year mortality of 49%. At 30 days after bacteraemia, in the Cox regression model, increasing age (p 0.003) and lower serum albumin (p 0.014) were predictive of death. At 3 years, age (p <0.0001) and albumin (p 0.004) remained significant predictors of death, with the presence of vascular disease (p 0.05) also significantly associated with mortality. If temperature was treated as a continuous variable then urea was significant (p 0.044); however, if temperature was categorized into hypothermia and non-hypothermia, then the presence of hypothermia (p 0.008) and chronic renal disease (p 0.034) became significant. There is an appreciable and gradual increase in mortality after an episode of bloodstream infection. Although many factors may not be amenable to intervention, patients at high risk of long-term mortality might require further follow up and assessment for potentially modifiable factors.

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Introduction

Bacteraemia (bloodstream infection), whether associated with another site of infection or not, is a common cause of community and healthcare-associated infection and causes high early mortality in the range of 11–30% [1–8]. Most studies have concentrated on in-hospital or early mortality, few have looked at longer-term outcomes, particularly beyond 1 year. One study performed in Israel in the early 1990s showed a 1-year mortality of 48%, with a 4-year mortality of 63% [1]. A study from the same period, performed in Boston, USA, showed a 3-year mortality of 37% [2]. Both of these studies showed that patients who had had bacteraemia had a higher mortality than matched control people who had not. The reason for the apparent excess in longer-term mortality remains unclear, but possible explanations could be that bacteraemia is a marker of co-morbidity (e.g. in patients with renal impairment or malignancy) or it may trigger, for example, a long-term, low-grade inflammatory response, which subsequently leads to either destabilization of an existing co-morbidity or a new one, such as vascular disease. The latter, in particular, raises the possibility of early medical intervention following an episode of bacteraemia to reduce long-term mortality, although this approach is as yet unproven. Given the changes in patient demographics, co-morbidity and antibiotic resistance that have occurred over the last 20 years, little is known of the contemporary long-term mortality after bloodstream infection. We describe here the factors affecting mortality up to 3 years after bloodstream infection, in a UK teaching hospital bacteraemia service cohort.

Methods

Study population

The bacteraemia service at Hull and East Yorkshire Hospitals (a 1500-bed, two-site hospital trust, serving a population of approximately 1.2 million) has been described previously[6]. Briefly, between June 2005 and November 2008, patients with a presumed infecting pathogen isolated from blood cultures were reviewed at the bedside by an infectious diseases physician, either a consultant or a Specialist Trainee (Fellow), without previous solicitation by the patient's clinical team. Patients with haematological malignancy and those with solid organ tumours who were undergoing chemotherapy, patients already on the infectious diseases unit and children aged <16 years were not routinely reviewed because other existing infection services cover these areas. Initial antibiotic advice was provided by either a consultant or a Specialist Trainee (Fellow) in microbiology by telephone, with a structured and more detailed report provided following a bedside consultation by a consultant or Specialist Trainee (Fellow) in infectious diseases (a median of 3 days after blood cultures were taken).

Data collection

Data were recorded or dictated at the time of consultation, using a structured and pre-piloted, paper-based proforma, which also formed the report sent to the patient's clinical team as part of routine clinical practice. These included demographic data (gender and age), clinical observations (pulse, temperature, blood pressure and respiratory rate), relevant examination data (source of infection), microbiological and antibiotic data. These data were entered onto an Excel spreadsheet to which, via the hospital computer system, were added standard laboratory data from the time the blood culture was taken (or within 24 h), data regarding socio-economic deprivation (postal code of patient's address was used to derive the Index of Multiple Deprivation Score, using UK Office of National Statistics census data), co-morbidities and date of death. Data collection and analysis were approved for ongoing quality improvement, service evaluation and audit by the Hull and East Yorkshire Hospitals NHS Trust. No funding was required for this work.

Data analysis

Factors associated with mortality at both 30 days and 3 years were ascertained. Two separate analyses were performed; one using patients with a complete data set and subsequent analyses including patients with missing values, with the missing values imputed using the expectation-maximization method. Initial analyses were univariate, using Mann–Whitney and Fisher's exact tests as appropriate. Factors significant at a level of $p \leq 0.1$ in univariate analyses were entered into a Cox regression model, with backwards removal of variables until the final model was achieved, with co-morbidities being entered into the models to adjust for them. Kaplan–Meier survival curves for significant predictors of 3-year mortality were constructed and analysed using the log-rank test. Analyses were performed using GraphPad Prism 5 and SPSS (version 19.0).

Results

Patient cohort

Three hundred and twenty-two bacteraemic episodes were reviewed in 304 separate patients between June 2005 and November 2008. The median age of patients was 70 years (interquartile range 57–79) and 60.6% were women. The organisms isolated are shown in Table 1, with methicillin-sensitive *Staphylococcus aureus*, methicillin-resistant *S. aureus* and *Escherichia coli* being the commonest single isolates. Of the 322 patients, 263 (81.6%) were receiving effective antibiotic therapy, based on antibiotic sensitivity, before being reviewed by an infectious diseases physician at the bedside, increasing to 292 (90.7%) after review ($p < 0.0001$, McNemar's test). However, receipt of ineffective therapy was not associated with either 30-day (p 0.85) or 3-year (p 0.77) mortality. The overall mortality is shown in Figure 1, with a 30-day mortality of 15% and a 3-year mortality of 48.75%.

TABLE 1. Common organisms isolated

Organism	Number isolated
Methicillin-sensitive *Staphylococccus aureus* (MSSA)	94
Methicillin-resistant *Staphylococcus aureus* (MRSA)	51
Coagulase-negative staphylococci	47
Streptococci	44
Escherichia coli	36
Non-specified coliform	29
Enterococci	24
Candida spp.	9
Pseudomonas sp.	7
Klebsiella sp	6
Polymicrobial cases	40

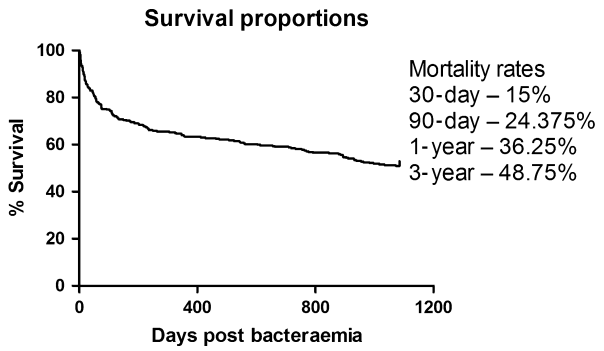

FIG. 1. Overall survival.