External validation of bloodstream infection mortality risk score in a population-based cohort

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Abstract

A risk score was recently derived to predict mortality in adult patients with Gram-negative bloodstream infection (BSI). The aim of this study was to provide external validation of the BSI mortality risk score (BSIMRS) in a population-based cohort. All residents of Olmsted County, Minnesota, with *Escherichia coli* and *Pseudomonas aeruginosa* BSI from 1 January 1998 to 31 December 2007 were identified. Logistic regression was used to examine the association between BSIMRS and mortality. Area under receiver operating characteristic curve (AUC) was calculated to quantify the discriminative ability of the BSIMRS to predict a variety of short-term and long-term outcomes. Overall, 424 unique Olmsted County residents with first episodes of *E. coli* and *P. aeruginosa* BSI were included in the study. Median age was 68 (range 0–99) years, 280 (66%) were women, 61 (14%) had cancer and 9 (2%) had liver cirrhosis. The BSIMRS was associated with 28-day mortality ($p < 0.001$) with an AUC of 0.86. There was an almost 56% increase in 28-day mortality for each point increase in BSIMRS (OR 1.56, 95% CI 1.40–1.78). A BSIMRS ≥ 5 had a sensitivity of 74% and a specificity of 87% to predict 28-day mortality with a negative predictive value of 97%. The BSIMRS had AUC of 0.85, 0.85 and 0.81 for 7-, 14- and 365-day mortality, respectively. BSIMRS stratified mortality with high discrimination in a population-based cohort that included patients of all age groups who had a relatively low prevalence of cancer and liver cirrhosis.

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Introduction

Bloodstream infection (BSI) is a major cause of morbidity and mortality in Europe and North America with 1.8 million episodes of BSI and 250 000 deaths annually [1]. Gram-negative bacilli account for nearly one-half of the cases of BSI [2]. A risk score was recently derived to predict the prognosis of patients at the time of diagnosis with Gram-negative BSI based on acute severity of illness as summarized in the Pitt bacteraemia score, source of infection and two major comorbid medical conditions that were independently associated with mortality (Table 1). The BSI mortality risk score (BSIMRS) had high prognostic ability to predict mortality in adult patients with Gram-negative BSI that were treated at tertiary care medical centres [3].

The aim of the current study was to provide external validation for the BSIMRS in a population-based cohort to account for the potential limitations of the derivation cohort that were related to the referral sample, including under-representation of patients at the extremes of age and relatively high prevalence of cancer and liver cirrhosis. We used a population-based cohort of patients with BSI due to *Escherichia coli* and *Pseudomonas aeruginosa*, the most common Gram-negative bacilli among *Enterobacteriaceae* and

TABLE 1. Bloodstream infection mortality risk score

Variable	Point allocation
Malignancy	3
Liver cirrhosis	4
Source of infection other than urinary tract or central venous catheter	4
Pitt bacteraemia score[a]	
0–1	0
2–3	2
≥4	5

[a]Pitt bacteraemia score was calculated based on temperature (35.1–36°C or 39.0–39.9°C: 1 point, ≤35 or ≥40°C: 2 points), blood pressure (hypotension: 2 points), mental status (disorientation: 1 point, stupor: 2 points, coma: 4 points), respiratory status (mechanical ventilation: 2 points) and cardiac status (cardiac arrest: 4 points). The worst reading was recorded on the day the first positive blood culture was obtained or the day before for nosocomial bloodstream infections.

lactose non-fermenters, respectively. The primary aim was to evaluate the ability of the BSIMRS to predict 28-day mortality in this population-based cohort. Secondary aims included examination of other short-term (7-day and 14-day mortality) and long-term outcomes (1-year mortality).

Methods

Setting

Olmsted County is located in southeastern Minnesota and has a population of 124 277 according to the 2000 census (US Census Bureau, Olmsted County QuickFacts—http://quickfacts.census.gov, accessed 1 October, 2012). The population characteristics of Olmsted County residents are similar to those of USA non-Hispanic whites [4,5]. The Rochester Epidemiology Project is a unique medical records-linkage system that encompasses healthcare delivered to Olmsted County, Minnesota, residents. The microbiology laboratories at Mayo Medical Center and Olmsted Medical Center are the only two laboratories in Olmsted County. These two medical centres are geographically isolated from other urban centres as previously described [4,6], which increases the likelihood that residents get their healthcare at the local facilities rather than seeking care at a distant geographic location.

Definitions

The primary source of BSI was defined using the Centers for Disease Control and Prevention criteria [7]. Patients with cancer were defined as those with current diagnosis of malignant tumour, excluding skin basal and squamous cell carcinoma. Liver cirrhosis was defined based on clinical, laboratory, ultrasonography or histopathology results, when available [8].

Case ascertainment

All residents of Olmsted County, Minnesota, were eligible for inclusion as we used complete enumeration of the Olmsted County population from 1 January 1998 to 31 December 2007. After the institutional review boards of Mayo Medical Center in Rochester, Minnesota, and Olmsted Medical Center had approved the study, we used the microbiology laboratory databases at both institutions to identify all patients with *E. coli* and *P. aeruginosa* BSI during the study period. All patients were considered for inclusion in the study, regardless of the status of hospitalization, site of infection acquisition, admission location during hospitalization, or primary admitting service. Using the Rochester Epidemiology Project tools, we identified residents of Olmsted County, Minnesota, for inclusion in the study and excluded those who lived outside Olmsted County at the time of BSI. The primary investigator (MNA) reviewed the medical records of all patients to confirm the diagnosis, determine patient residency status and obtain clinical features and outcome. The detailed case ascertainment methods are described elsewhere [9,10]. As both the derivation and validation cohorts were located in the same geographic area, we excluded patients who were previously included in the derivation cohort to avoid potential overlap.

Blood cultures were processed using standard microbiology techniques according to the CLSI. The detailed blood culture methods used are described elsewhere [2,11]. The microbiology laboratories at the Mayo Medical Center in Rochester, Minnesota, and Olmsted Medical Center are certified by the College of American Pathologists.

Statistical analysis

BSIMRS was calculated by adding the allocated points for variables present in each patient (Table 1). Logistic regression was used to examine the association between BSIMRS and 28-day mortality. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to indicate the strength of association between BSIMRS and mortality.

The area under a receiver operating characteristic curve (AUC), was used to quantify the discriminative ability of the BSIMRS, with a value of 0.5 denoting random predictions and a value of 1.0 denoting perfect predictions. To visually assess calibration, deciles of predicted risk of mortality were plotted from the risk score model by the actual fraction of patients who died within 28 days. Predicted probabilities obtained directly from the scoring model were plotted by risk score values to visualize the estimated risk of mortality. The sensitivity, specificity and negative predictive value (NPV) were calculated from the receiver operating characteristic curve for the best cut point in the BSIMRS for 7-, 14-, 28- and 365-day mortality. Only patients who were followed for the