Prognostic roles of time to positivity of blood cultures in patients with *Escherichia coli* bacteremia

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Abstract

The time to positivity (TTP) of blood cultures has been considered a predictor of clinical outcomes for bacteremia. This retrospective study aimed to determine the clinical value of TTP for the prognostic assessment of patients with *Escherichia coli* bacteremia. A total of 167 adult patients with *E. coli* bacteremia identified over a 22-month period in a 3500-bed university teaching hospital in China were studied. The standard cut-off TTP was 11 h in the patient cohort. The septic shock occurred in 27.9% of patients with early TTP (<11 h) and in 7.1% of those with a prolonged TTP (>11 h) (P = 0.003). The mortality rate was significantly higher for patients in the early than in the late group (17.7% vs. 4.0%, P < 0.001). Multivariate analysis showed that an early TTP (OR 4.50, 95% CI 1.70–11.93), intensive care unit admission (OR 4.20, 95% CI 1.55–11.40) and neutropenia (OR 4.34, 95% CI 1.22–15.47) and a Pittsburgh bacteremia score ≥2 (OR 4.34, 95% CI 1.22–15.47) and a Charlson Comorbidity Index ≥3 (OR 11.29, 95% CI 2.81–45.39). Overall, a TTP for blood cultures within 11 h appears to be associated with worse outcomes for patients with *E. coli* bacteremia.

*Escherichia coli* bacteremia is a common clinical presentation that may at times be transient but on occasion, can lead to septic shock or even death [1]. Established risk factors for mortality include underlying diseases, the severity of systemic inflammatory response syndrome, inadequate antibiotic treatment, nosocomial acquisition, age over 65 years, non-urinary tract source and multi-drug resistant infections [2, 3]. However, such data and other sepsis indicators, specifically elevated levels of C-reactive protein and procalcitonin have limited prognostic precision [4] and some clinical scoring systems may not provide sufficiently timely data or may require intricate calculations not readily appropriate for daily routine use. Therefore, it is very important to identify and utilise a simple and practical indicator to guide clinical treatment. The purpose of this study was to evaluate the prognostic value of the time-to-positive (TTP) interval of blood cultures for patients with *E. coli* bacteremia.

An retrospective observational study was conducted from January 2014 to November 2016 at the Xiangya Hospital Central South University, a 3500-bed comprehensive tertiary hospital located in Changsha, China. Adult inpatients (⩾18 years old) were considered eligible if they had a bloodstream infection with one or more blood culture positive for *E. coli*. Each patient was included only once at the time of the first positive blood culture result, but if multiple blood culture proved positive, the shortest TTP value was recorded. Patients were excluded if they had polymicrobial infections or were treated with antimicrobials prior to blood culture.

Clinical data included age, gender, underlying diseases as per the Charlson Comorbidity Index [5], neutrophil count <1.5 × 10⁹/L, primary site of *E. coli* infection prior to, or coincident with, the onset of bacteremia. The latter was classified as primary in a patient if a specific body site of the acquisition was not evident [6], they had previous surgery or interventional therapy during hospitalisation, had received steroids (prednisolone 10 mg/daily or equivalent dose for a minimum of 2 weeks) and/or other immunosuppressive therapy within 2 months prior to bacteremia. The adequacy of antimicrobial therapy was based on in vitro susceptibility of an isolate and whether antibiotic treatment was started within 24 h after blood cultures were taken. The Pittsburgh bacteremia score [7], presence of septic shock [8] and mortality rates were used to assess clinical outcomes.

At least two sets of blood samples, 20 ml each, were taken from separate venous sites and inoculated into aerobic and anaerobic culture bottles. These were loaded on a BACTEC 9120 automated detection blood culture system (Becton Dickinson, Sparks, MD, USA). All bottles were inoculated into aerobic and anaerobic culture bottles. These were loaded on a BACTEC 9120 automated detection blood culture system (Becton Dickinson, Sparks, MD, USA). All bottles...
Bacteremia was defined as the presence of viable bacteria in the blood cultures. The TTP was defined as the time interval from the onset of symptoms to the detection of bacteria in the blood cultures. The TTP was used as a diagnostic tool to predict septic shock and in-hospital mortality. Variables with $p$ < 0.1 were included in the multivariable logistic regression analysis. The ROC curves were used to determine the optimal cut-off value for TTP, which was 11.42 h. The AUC for TTP was 0.71 (95% CI 0.61–0.80), indicating a moderate predictive capability for this condition. The maximum Youden index was used as a criterion for selecting the optimum cut-off point for TTP. Univariate analysis was performed for associations between risk factors, the incidence of septic shock and in-hospital mortality. Variables with $p$ < 0.1 in univariate analysis were entered in multivariable logistic regression models with forward selection. Odds ratio (OR) and corresponding 95% confidence interval (CI) were calculated by standard formulae.
found to have a moderate predictive capability for septic shock, which is similar to the result of an earlier study [14]. However, both the median (12.5 h) and cut-off values of TTP which were indicative of poor prognosis in our patient cohort proved to be substantially longer than those reported by others for *E. coli* bacteremia [15,16]. Such differences might have been due to both patient and strain characteristics as well as the specific methodology of the laboratory assays and clinical diagnostic criteria. Several studies have shown that the shorter the TTP interval, the higher the incidence of septic shock and mortality in bacteremia caused by different bacterial species [16,17] and some have also reported correlations between short TTP intervals and severity of clinical presentation [14–16]. Indeed, our patient cohort with a TTP ≤11 h had higher Pittsburgh bacteremia scores and an increased risk of septic shock as well as greater in-hospital mortality than those with a TTP >11 h, which was consistent with other studies [14–16]. Our patients with TTP ≤11 h had almost five and fourfold higher risk of septic shock and in-hospital mortality than those with TTP >11 h, respectively, which supports the view that the chosen cut-off value can be used as a prognostic factor for patients with *E. coli* bacteremia and is therefore of value, in combination with standard diagnostic signs and symptoms, for the assessment of such patients.

We also observed a good correlation between TTP values and clinical outcomes. Notably, neutropenia and intensive care unit admission were independent risk factors for septic shock. Likewise, the Charlson Comorbidity Index, Pittsburgh bacteremia score and intensive care unit admission, which together reflect the severity of underlying diseases and bacteremia, were independently associated with in-hospital mortality in our cohort and was consistent with earlier findings [3].

There are some limitations to our study. Firstly, due to its retrospective nature, our ability to identify clinical variables as significant predictors of mortality was limited. Secondly, TTP is known to be influenced by various factors, such as the sampling time, the blood volume used and the interval from sampling to incubation. Lastly, the sample size of 167 patients is relatively small and the findings need to be validated by prospective studies in a larger series of subjects. In conclusion, we consider that this study has added data which underlines the use of a short TTP is a valuable and clinically relevant index for predicting the occurrence of septic shock, or death, in patients with *E. coli* bacteremia.

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**Ethical standards.** Not required.

**References**


**Fig. 1.** ROC curve of TTP for predicting septic shock.