Is timing everything?
A Bayesian meta-analysis of the prognostic and diagnostic utility of bloodculture time-to-positivity (TTP) and differential time-to positivity (DTP) for bloodstream infections

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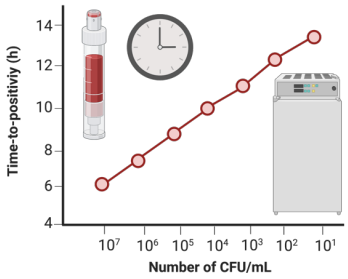
Abstract 01824

INTRODUCTION

- TTP defines the time from the start of incubation of blood cultures in an automated blood culture system to the detection of bacterial (or fungal) growth
- DTP defines the difference in time to positivity between central line and peripherally- drawn bloodcultures
- TTP and DTP are surrogate indicators for microbial inoculum and frequently investigated as a prognostic or diagnostic markers in patients with bloodstream infections (BSIs)
- Data concerning the prognostic or diagnostic utility of TTP and DTP are conflicting



- The objective of this study was to systematically review and better define the relationship between (i) TTP and patient survival; (ii) DTP and diagnosis of central-line associated bloodstream infection (CLABSI).

METHODS

- We performed a systematic review of published articles from 1980-2021 using PubMed, Google Scholar and SCOPUS databases
- Articles were reviewed to determine if (i) TTP data were reported in relation to patient survival from BSI; and (ii) DTP was reported in relation to the diagnosis of central line associated BSI using established definitions[1]
- Bayesian hierarchical summary receiver operating characteristic models[2] to analyze identified studies to generate pooled sensitivity and specificity estimates and summary receiver operating characteristic curves (SROCs)
- Sensitivity analysis was performed using different TTP cut-offs, by pathogen group, and by comparing prospective vs. retrospective study design

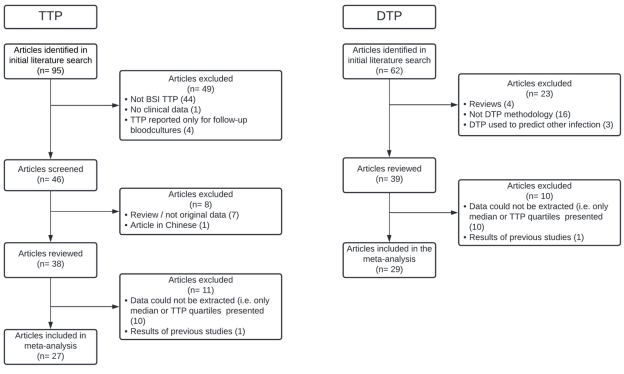
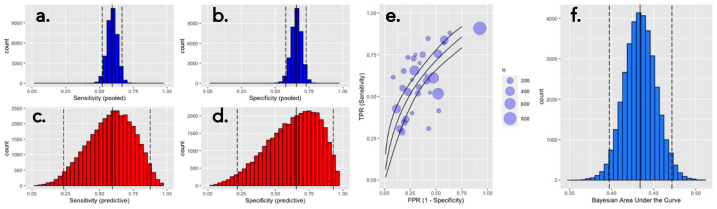


Fig 1. Systematic literature review of bacterial and fungal BSI studies. Studies were included that reported the association between: (i) TTP and patient survival; (ii) DTP and diagnosis of central-line associated bloodstream infection (CLABSI).

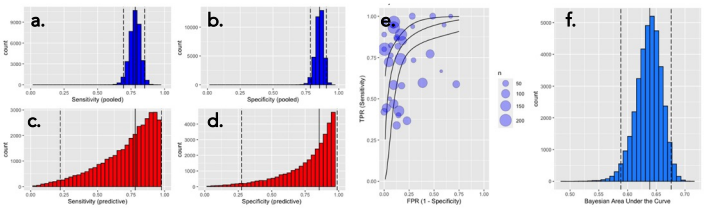
RESULTS

Fig 2. TTP exhibited low sensitivity and specificity for BSI mortality. Posterior distribution of the pooled **(a)** sensitivity and **(b)** specificity estimates and their predictive posteriors **(c,d) for** all BSI TTP vs. mortality; (e) Bayesian SROC curve. The size of bubbles is proportional to number of patients per study. The central line corresponds to the posterior median and the upper and lower curves correspond to the quantiles of the 2.5 % and 97.5 % respectively; **(f)** Posterior distribution of the area under the BSROC curve.



- Pooled sensitivity and specificity estimates for TTP and patient mortality were low (Fig. 1a-d)
- TTP did not differentiate non-surviving BSI patients from survivors, SROC 0.43, 0.39-0.47; (Fig 2a-b)
- The prognostic utility of TTP did not significantly change by patient subgroup analysis or at different TTP cutpoints.

Fig 3. DTP has higher sensitivity and specificity for CRBSI diagnosis. Posterior distribution of the pooled (a) sensitivity and (b) specificity estimates and their predictive posteriors (c,d) for DTP and CLBSI diagnosis; (e) Bayesian SROC curve. The size of circles is proportional to number of patients per study. The central line corresponds to the posterior median and the upper and lower curves correspond to the quantiles of the 2.5 % and 97.5 % respectively; **(f)** Posterior distribution of the area under the BSROC curve.



- Pooled sensitivity and specificity estimates for DTP for the diagnoses of CLABSIs were acceptable (Fig 3a-d)
- DTP discriminated between non-CLABSI vs. CLABSI with a pooled SROC of 0.63, 0.59-0.67; (Fig 3a-b)
- A "negative" DTP would be predicted to achieve negative predictive values > 90% when the prevalence of CLABSI is ≤ 25%.

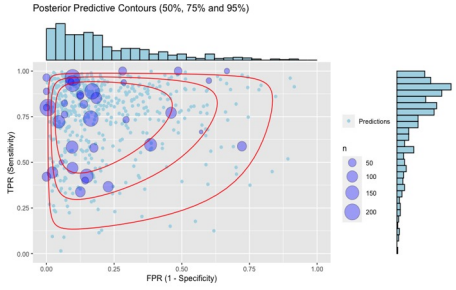


Fig 4. DTP can differentiate CLABSI from non- CLABSI. Bayesian predictive surface contours at different credibility levels compared with observed data for DTP diagnosis of CLABSI. The size of bubbles is proportional to the number of patients per study

CONCLUSIONS

- The cumulative evidence does not support use of TTP as a prognostic indicator for mortality in bacterial or fungal bloodstream infections
- DTP has moderate sensitivity and specificity for the diagnosis of CLABSI.
- DTP may be clinically useful for "ruling out" CLABSI for pathogens with a low pretest prevalence of catheters infections (i.e. < 25%) , as the negative predictive value of negative NPV result would exceed 90%
- Additional studies are needed to further explore the prognostic relationship of TTP for other clinical endpoints such as treatment failure or relapse.

1. Mermel et al. Clin Infect Dis, 2009;49:1–45,
2. Pablo Emilio Verde (2018). Bamdit: An R Package for Bayesian Meta-Analysis of Diagnostic Test Data. Journal of Statistical Software, 86(10), 1-32.