REVIEW

Predicting bacteraemia in validated models—a systematic review

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Abstract

Bacteraemia is associated with high mortality. Although many models for predicting bacteraemia have been developed, not all have been validated, and even when they were, the validation processes varied. We identified validated models that have been developed; asked whether they were successful in defining groups with a very low or high prevalence of bacteraemia; and whether they were used in clinical practice. Electronic databases were searched to identify studies that underwent validation on prediction of bacteraemia in adults. We included only studies that were able to define groups with low or high probabilities for bacteraemia (arbitrarily defined as below 3% or above 30%). Fifteen publications fulfilled inclusion criteria, including 59 276 patients. Eleven were prospective and four retrospective. Study populations and the parameters included in the different models were heterogeneous. Ten studies underwent internal validation; the model performed well in all of them. Twelve performed external validation. Of the latter, seven models were validated in a different hospital, using a new independent database. In five of these, the model performed well. After contacting authors, we found that none of the models was implemented in clinical practice. We conclude that heterogeneous studies have been conducted in different defined groups of patients with limited external validation. Significant savings to the system and the individual patient can be gained by refraining from performing blood cultures in groups of patients in which the probability of true bacteraemia is very low, while the probability of contamination is constant. Clinical trials of existing or new models should be done to examine whether models are helpful and safe in clinical use, preferably multicentre in order to secure utility and safety in diverse clinical settings.

Keywords: Bacterial bloodstream infections, blood cultures, prediction models, sepsis, validation

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Introduction

Among patients with infection, bacteraemia portends a poor prognosis, and clinicians' ability to predict it is low [1,2]. Bacterial bloodstream infections are associated with mortality of 14% to 37% [3–6]. Knowledge (or high suspicion) that a patient has a bloodstream infection can guide treatment—aggressively (or not) treating the patient, transferring the patient to an intensive care unit, empirically initiating appropriate antibiotic treatment and thinking of differential diagnosis.

Poses and Anthony [7], in a prospective cohort study, assessed inappropriate physicians' judgements of the probability of bacteraemia. They found that physicians significantly overestimated the likelihood of bacteraemia for most of their patients. Their receiver operating characteristic (ROC) curve for this diagnosis showed only moderate discriminating ability (area = 0.687, SE = 0.073). Generally only about 5% to 10% of blood cultures are positive, and of those that are positive, 30% to 50% represent contaminants—organisms inoculated from the skin into culture bottles at the time of sample collection [8–11]. The costs of performing and handling negative and false-positive blood culture results are significant. False-positive

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results lead to unnecessary investigations and treatment with unneeded antibiotic therapy. In one analysis, patients with falsely positive blood cultures were compared with those with truly negative blood cultures, and false-positive findings were associated with a 50% increase in total charges and a 64% increase in median length of hospitalization stay, along with higher pharmacy charges and laboratory charges [12]. Defining of a group of patients with a very low probability of bacteraemia, in which blood cultures are not necessary or not cost-effective, has the potential to reduce costs and prevent unnecessary antibiotic treatment. In addition, selection of a group with a high likelihood for bacteraemia caused by specific pathogens could assist physicians in choosing treatment or determining whether to perform new, costly tests such as PCR testing for bacterial and fungal DNA [13].

This is the logic for developing tools that can predict bacteraemia accurately in patients suspected of harbouring a moderate to severe bacterial infection. To be useful, such a tool should fulfil a few conditions. It should be able to define a group with a very low prevalence of bacteraemia, and this group should be of a useful size. We can be further reassured if the few truly positive blood cultures included in this group were expected and would have been covered by empirical antibiotic treatment so that the results of the positive blood culture would not have changed management. Definition of a group with a high prevalence of bacteraemia might also be useful for triaging patients for culture-free, expensive techniques of looking for bacteria or their products in the blood. The tool should use data that are readily available at the time of decision making, within the time frame of the decision whether or not to obtain blood samples for culture. It should be validated externally to assure its users that it performs well in multiple settings.

Many models for predicting bacteraemia have been developed. Some have been developed in specific populations of adult patients (e.g. elderly, hematology–oncology populations, neutropenic patients) or for specific settings (emergency room (ED), community or hospitalized patients). Models have also been developed for specific sources of infection (e.g. urinary tract, pneumonia, skin, soft tissue). However, not all models were validated, and even when the models were validated, the validation processes varied.

We reviewed the literature and asked which models for predicting bacteraemia have been developed; whether the models were successful in defining a group with a very low prevalence of bacteraemia and a group with a high prevalence; and whether they have been validated to such a degree that their use in clinical practice can be recommended. We also examined the components of the different models. Finally, we examined whether the models are being used in routine clinical practice.

Methods

We conducted a comprehensive search in an attempt to identify studies offering a model to predict bacteraemia. We searched the PubMed database (inception to September 2014), combining the terms (predict OR predicting OR prediction) AND (bacteraemia OR blood stream infection). The bibliographies of all included studies and pertinent reviews were scanned for additional references.

We included studies of adult populations where the model underwent internal or external validation. We extracted data on baseline study characteristics, whether the original study was prospective or retrospective, baseline study's population characteristics, which parameters were included in the model, whether the model underwent validation, and if so, which kind, and the probability of bacteraemia in the high- and low-risk group. We examined the cutoffs used in the studies against an arbitrarily chosen definition of high- or low-risk groups for bacteraemia: we defined high risk as >30% and low risk as <3%. We chose a low-risk cutoff that would be lower than the rates of contamination of blood cultures (which is approximately 3% to 5%) and a high-risk cutoff based on previous studies [14].

We addressed three types of validation: validation that is done in a single data set, with techniques such as jackknifing or bootstrapping, validation done in a second group of patients different from the original cohort but at the same centre and validation at a different centre. We defined internal validation as testing of the model on a group of patients, different than the derivation group, either from the same cohort or from a different cohort at the same centre. External validation was defined as testing of the model in a different group than the derivation group, in a different centre and at a different time. We searched for interventional studies that used the models to change the practice of obtaining blood cultures. We also wrote to the authors of validated models and asked whether, to their knowledge, their models are being used in routine clinical practice.

Results

Search results

We identified 710 records on electronic database searches and retrieved 36 publications for full-text inspection, of which 21 were excluded because they did not have any form of validation.

Description of included studies

Fifteen publications [2,8,14–26], conducted from 1990 through 2014 and including 59 276 patients, were included in the review (Table 1). All were published in journals; two were in Spanish