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Editorial

Predicting bacteremia in the Emergency Room: How and why

Pronosticando bacteriemias en Urgencias: cómo y porqué

Bacteraemia is associated with high morbidity and mortality. Recognising patients at risk for bacteremia in the Emergency Room (ER) may conduct to a prompt adequate treatment and better outcomes. As a consequence of this concern, ER clinicians order blood cultures liberally among patients in whom bacteremia is suspected, though a small proportion of blood cultures are truly positive. In this context, ordering blood cultures inappropriately may be wasteful when ordering too many otherwise harmful when no performed if indicated.

The consideration of bacteremia as an important clinical problem in ER as well as the knowledge that getting a positive result in a blood culture is commonly unsuccessful, have promoted the development of several bacteremia prediction rules in the last decades. Most of them included clinical and laboratory data with different predictive capacity. In a metanalysis of bacteremia predictive models published by Eliakim-Raz and cols.[1] the predictivity ranged from 0.60 to 0.83 according to the area under de curve value. Most common used variables in these models were: chills, temperature over or equal to 38.3 °C, systolic blood pressure < 90 mmHg, tachycardia, tachypnea, vomiting, specific suspected sources (as urinary, catheter or endocarditis), age over 65 years, comorbidities according to Charlson score, and laboratories results as white blood cells count, C reactive protein (CRP) or procalcitonin (PCT).[2–6] As commented by the authors, those models were quite heterogenous in predictivity and factors included. That variability could be explained because of studding different patient populations and also because they may have been performed in settings with differences in clinical practice.[1] In many of these models, population was classified according to the risk of presenting a bacteremia. A low risk was defined when probability was lower than 3% and high when it was higher than 30%. Defining a group of patients with low probability of bacteraemia, in which blood cultures would not be useful or cost-effective, has the potential to reduce prevent unnecessary antibiotic treatment and costs. In the other hand, selection of a group with a high likelihood for bacteraemia caused by specific pathogens can assist physicians in choosing treatment or determining whether to perform new, costly tests such bacterial and fungal polymerase chain reaction tests.[7] But, as remarked by Eliakim-Raz and cols.,[1] this is a consensus stratification that have been widely used although its description is absolutely arbitrary and had not been related to clinical or financial outcomes in clinical trials. Another important point to be noted is that most of these models had not been validated, and even when they were, the validation processes was heterogenous.

In this issue of Enfermedades Infecciosas y Microbiología Clínica, Julián-Jiménez and cols. presented a validation of a bacteremia prediction rule[8] including the following items: temperature over 38.3 °C (one point score), a Charlson index score equal or higher to 3 (one point score), a respiratory rate equal or higher to 22 (one point score), leukocytes count over 12,000/mm^3 (one point score), and PCT value equal or higher to 0.51 ng/ml (4 points score). The validation was performed in a prospective and multicentre observational cohort study of blood cultures (BC) ordered in 74 Spanish ER. A total of 3843 blood samples were cultured and true-positive results were confirmed in 839 (21.83%).[9] The low risk for bacteremia was indicated by a score of 0–2 points, intermediate risk by 3–5 points, and high risk by 6–8 points. Bacteremia in these 3 risk groups was predicted for 1.5%, 16.8%, and 81.6%, respectively. The prognostic performance with a cut-off value of equal or higher to 5 points achieved 94.76% (95% CI: 92.97–96.12) sensitivity, 81.56% (95% CI: 80.11–82.92) specificity, and negative predictive value of 98.24% (95% CI: 97.62–98.70). According to these results, the authors concluded that the 5MPB-Toledo score is useful for predicting bacteremia, that may be useful to decide whether to perform BC or not in the ER and also may help to take clinical decisions.

Some features are really valuable in the present study. First, the model was validated in a multicentre cohort including 74 different hospitals and a high number of BC which conferred it an important external validity. This sample size also permits to explore application of the model in important subgroups of patients as immunosuppressed, those previously receiving corticosteroids or antibiotics. Second, different score cut-off have been explore achieving a high predictive capacity (as previous mentioned equal or higher to 5 points achieved 94.76% of sensitivity and a negative predictive value of 98.24%) that really improve the predictivity of previous published studies.[1,10–13] As a limitation, the important weight of PCT in the model (4 points score) may difficult its implementation in low-income resources where biomarkers may not be easily available. By other hand, in those patients with low PCT, no matters the presence of the other variables described, the risk of bacteremia was very low. That supports the idea that if available, PCT test should be performed in most patient with moderate and severe infection in ER.

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This study invites to a reflection about questions that different researchers tried to solve when through bacteremia predicting rules: are they useful to decide whether to take or not a BC from patients with infections in ER?; May them help the physician to conclude admitting or not the patient to the hospital?; Is this approach safe enough to decide starting or delaying an antibiotic treatment?; Is this model (and those previously published)[10–13] feasible to be implemented in clinical practice in an ER?. An accurate answer of these questions may involve important clinical and financial consequences.

To perform or not a BC in ER, the question to be resolved. Most of these studies analysed populations of patient with suspected infections in which a BC had been already taken. Factors related to positivity were interpreted as predictors to differentiate a population in which performing a BC was cost-effective. But, what about those patients which infection in which a BC was never performed? That might have occurred because of availability in different settings, or because a low grade of bacteremia suspicion in less trained physicians. The real population in which an ER physician confronts to decide taking a BC or not certainly include a wider population not considered in most studies. In the study of Julián-Jiménez and cols.[9] patients were selected "according to opportunity" that means at discretion of the physicians working in ER, and those physicians resulted to be site investigators of the study. That might have incurred in selection bias and might have influenced the higher predictivity of the concluded model in comparison with those previously published.[10–13] In this sense, Eliakim-Raz and cols.,[1] proposed to use public population health records as historic cohort, where multiple variables can be analysed and selection bias easily avoided.

Are those models useful to decide where to treat the patient or whether starting antibiotic or not?. Knowledge (or high suspicion) that a patient has a bloodstream infection can guide treatment, admitting the patient to a clinical ward (or intensive care unit), empirically initiating appropriate antibiotic treatment, and guiding new diagnostics or therapeutics interventions. Most of those decisions may be timing-conditioned. In regards to models including laboratory results, might a physician intervention be delayed until those results are available?. Of course, this option should not be acceptable when confronting a severe patient. Therefore, can be concluded that models are only useful in mild or moderate clinical presentations?. One of the mean strengths of the validation cohort presented by Julián-Jiménez and cols. is the high predictive negative value obtained with a cut-off of 5 points. In those patients scoring less than 5 points seems reasonable not to take a BC or to decide treating the patient in ambulatory care, as better outcome is expected (although not proven through this study). According to the described score, most patients with a normal PCT value may preclude the intake of a BC.

Also, an important consideration is to evaluate the feasibility to implement the predictive rule in clinical practice. We have already mentioned the implications of including biomarkers in regards of low-income settings. None of most validated models analysed in the study of Eliakim-Raz and cols.[1] was used in routine clinical practice after validation. Reasons are not fully explained but common barriers in implementing new intervention in ER are mostly lack of time and structural resources. One of the mentioned advantages of 5MPB-Toledo model is that the factors included can be easily fulfilled, as they are considered to be routine clinical and laboratory data. For instance, is a Charlson score usually calculated in an ER initial evaluation? It should be but it is not. Variables implicating an extra clinical evaluation may difficult its implementation in daily ER clinical work. Even though, all other variables are simple to record apart from the PCT in certain settings. Nowadays, automatic physical signs records of host sensors have been shown to globally impact on hospital mortality.[14] This information when linked to communication tools and used with analytics, may present substantial potential for implementing predictive bacteremia rules. In relation to it, Paul et al.[15] constructed a system based on a causal probabilistic network (TREAT) including different clinical and laboratory results. The area under the curve for prediction of bacteraemia was 0.68 in the derivation cohort, and 0.70 in the validation cohort. The prevalence of bacteraemia was 2.4% in the low-risk group and 29.9% in the high-risk group. The TREAT system performance was validated in different settings (both internal and external validation). So, incorporating these predictive models with information technology in different health care settings as ER may improve the applicability of predictive rules.

Biomarkers and information technology, would those really in combination be more accurate than physicians' ability of suspecting a bacteraemia? For sure not always but may complete and perfect the physician capability of prediction in many clinical scenarios,[16] so in bacteremia. The important question is that if this approach is translated into outcomes improvement.

As we have been mentioned throughout the text, no answer concerning safety, clinical outcomes, and cost-effectiveness can be concluded of these studies. Clinical trials of existing or new models should be done to test whether they are helpful and safe in clinical use, preferably in multicentre designs in order to secure utility and safety in diverse clinical settings. 5MPB-Toledo model[8] was validated in an important number of ER and also in specific subgroups. In both general population and subgroups, the 5MPB_Toledo presented an unbeatable sensitivity and predictivity. Two important next steps in this context should be to integrate it in information technology resources so to make it use really feasible and to demonstrate outcomes and cost-effectiveness impact in a cluster randomised trial in which this approach is compared to routine clinical deliberation.

Conflicts of interest

LELC has served as scientific advisor for Angelini, speaker for Angelini, ViiV, Gilead and Correvio, and has served as trainer for ViiV. PRG has served as scientific advisor for Shionogi, speaker for MSD, Pfizer, and Gilead and has served as trainer for MSD.

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