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One Scoring System Does Not Fit All Healthcare Settings

To the Editor—We read with interest the article by Peinado-Acevedo and coworkers [1] describing the validation of the Predicting Risk of Endocarditis Using a Clinical Tool (PREDICT) and VIRSTA scores in a large Colombian cohort of patients with *Staphylococcus aureus* bacteremia (SAB). PREDICT and VIRSTA are scoring systems intended to guide the use of echocardiography to detect infective endocarditis (IE) in patients with SAB [2, 3].

External validation of scoring systems is essential to evaluating their clinical usefulness. Therefore, the study by Peinado-Acevedo et al [1] is of interest. Importantly, it was performed in a healthcare system different from those used in the PREDICT and VIRSTA studies [2, 3]. The cohort studied was very different in composition from those used to generate the PREDICT and VIRSTA scores [2, 3]. Most importantly, SAB in this cohort was mainly a nosocomial complication of the use of central venous access, and only 16% of patients had community-acquired infection.

The main finding reported by Peinado-Acevedo et al [1] was that the VIRSTA score has high sensitivity (97%), while the PREDICT score has relatively low sensitivity (52%). The conclusion, therefore, was that transesophageal echocardiography could safely be omitted in patients with negative VIRSTA results, but not in those with negative PREDICT results. This conclusion is reasonable given the conditions in the Colombian cohort.

Different factors likely contribute to the low sensitivity of PREDICT in this study. First, PREDICT uses community acquisition as one variable in the score, and the low proportion of such patients partly explains the low sensitivity [2]. Second, a very large proportion of patients with IE were receiving hemodialysis, and among these patients PREDICT had an even lower sensitivity. Thus, PREDICT might be particularly unsuited to detecting IE in this subgroup. The sensitivity of PREDICT was higher among patients not receiving hemodialysis (65%).

Peinado-Acevedo and coworkers [1] stated that there is no external validation of PREDICT and VIRSTA, but Abu Saleh et al [4] and Kahn et al [5] have performed external validations of PREDICT. Their studies were from the United States and Sweden and demonstrated sensitivities of 100% and 81%–95%, respectively. VIRSTA was also validated in the Swedish cohort, showing high sensitivity (85%–100%) but moderate specificity (44%–55%) [5].

Time to blood culture positivity (TTP) is a feature readily available with automated blood culturing systems. A low TTP, indicative of a high bacterial concentration in blood, is a feature of intravascular infections [5–7]. Kahn et al [5] demonstrated that TTP could be included in a scoring system called POSITIVE, which had a high sensitivity and specificity for detecting IE in a cohort of patients with SAB, separate from the generation cohort [5]. It would be very interesting to evaluate the performance of POSITIVE in a different cohort of patient with SAB, such as that presented by Peinado-Acevedo and coworkers.

The results reported by Peinado-Acevedo et al [1] clearly demonstrate that scoring systems cannot be universally applied and that the performance of a given system needs to be validated before implementation. The performance of PREDICT is likely better in clinical settings other than that described by these authors.

Note

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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Reply to Karakonstantis, et al; Zervou and Zacharioudakis; and Rasmussen, et al

To the Editor—Reply to Karakonstantis, Zervou, Rasmussen and coworkers for reading our article and for their cogent comments [1–3]. Certainly, an always challenging issue is how to apply clinical research to daily clinical practice. This concern seems to be even more critical in the prediction models' scope, either for diagnosis or prognosis [4]. Therefore, updated, wide, and independent validation of any predictive model is just one step in a continuously evolving process.

Karakonstantis et al asked the very important question of how sure are we about the use of the VIRSTA score in clinical practice [1]. High discordance exists in selection criteria for echocardiography in patients with *Staphylococcus aureus* bacteremia (SAB), even in series with expert clinicians [5]. Risk stratification using scores to limit the use of echocardiography in low-risk patients with SAB is an innovative approach and a research gap that is present in the latest Infectious Diseases Society of America guidelines [6]. Thus, standardization of care is paramount to improve outcomes and optimize the use of resources for the healthcare system. Furthermore, we agree that the appropriate threshold to indicate echocardiography in patients with SAB is unclear, but the best available guidance comes from the publication of Heriot et al, which suggests that <1.1% risk of infective endocarditis (IE) is a reasonable cutoff point to omit the test [7]. Additional studies may further improve accuracy and precision in the estimation of the diagnostic accuracy of VIRSTA or any other scores. Unfortunately, in all others validation studies, the pretest probability of IE was >7% [8–10]. This finding, on the other hand, reinforces the importance of local validation of prediction clinical scores.

In addition, owing to the retrospective nature of our study, we agreed and acknowledged that a limitation is the absence of postdischarge follow-up with the risk of late endocarditis omission. Another limitation is the proportion of patients that did not undergo echocardiography in our study (65%). However, we carried out a sensitivity analysis [10] in which only patients who underwent any form of echocardiography were included; we did not find any change in the score performance, which is reassuring.

We agree with Zervou et al [2] that we faced a very particular study population, with several characteristics that are different from any previously analyzed cohort. However, we respectfully disagree with them regarding the true usefulness of subgroup analysis in this context. Instead, we believe that this issue supports the importance of a carefully defined study population, as well as the value of the local validation of prognostic models. In summary, the aim of the score is to omit unnecessary echocardiography (rule out IE), not to suggest or treat empirically IE. On the other hand, we agree with their statement that "the characteristics of the patient population should be taken into account when the scoring system is applied since the negative predictive value of the test is affected by the disease prevalence" and that in patients with VIRSTA score ≥3, transthoracic echocardiography should be considered as a first step only if patients are not candidates for immediate transesophageal echocardiography to guide early treatment decisions. An assumption that different strains of *Staphylococcus aureus* differ in abilities to cause IE and that this can be reflected in the performance of the prediction scores in different populations is an intriguing challenge.

Finally, we agree with Rasmussen et al [3] about the proportion of patients with community-acquired SAB on hemodialysis as a potential explanation for the lower performance of the Predicting Risk of Endocarditis Using a Clinical Tool (PREDICT) score. Needless to say, both scores were tested in the same study population and, consequently, it is fair to compare and assess their comparative accuracy. At the time of submitting our manuscript, the interesting articles of Abu Saleh et al [11] and Kahn et al [9] had not yet been published. Interestingly, we also analyzed time to blood culture positivity (TTP) in our cohort, because IE as a high-inoculum infection may lead to a shorter TTP. However, TTP is affected by a variety of factors such as previous antibiotic administration, blood volume for culture, and time to incubation. We found in our cohort a TTP of 12.6 hours (interquartile range [IQR], 8.6–12.6 hours) and 16.0 hours (IQR, 10.8–15.8 hours) in patients with and without IE, respectively. In patients with IE, the 99th percentile of TTP was 43 hours, which contrasts with the results of Kahn et al [9] who found no episodes of IE with TTP longer than 12 hours and 36 minutes. Additionally, in the derivation cohort of the VIRSTA study [12], the prevalence of IE was higher both in patients with short (quartile 1, <10 hours) and long (quartile 4, >18 hours) TTP, with a U-shape curve, calling into question the role of TTP for excluding IE. Certainly, the addition of TTP to any score might improve precision, but more studies are needed to define the true role of TTP.

Note

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