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Correspondence

Reply to Tubiana et al

To the Editor—We thank Dr Tubiana, Dr Le Moing, and Dr Duval for their interest in our study [1]. They raise 3 issues about the analysis and reporting of our results that we would like to clarify.

The first point deals with the proportion of patients with enterococcal bacteremia that underwent a trans-thoracic echocardiogram. From the 1515 patients with enterococcal bacteremia, 388 (25.6%) had a transthoracic echocardiogram and 183 (12.1%) a transesophageal echocardiogram (TEE). All patients with enterococcal endocarditis had a TEE (65 episodes). We deeply regret that there was a typo in the text (TEE instead of echocardiogram) that led to this confusion, and we thank Dr Tubiana et al for pointing it out. Fortunately, the mistake does not affect the validity of the message. The proportion of patients with echocardiogram remains low despite our efforts to implement its systematic use. This proportion reflects real-life practice and the fact that it is not recommended in current guidelines [2]. We have not been able to find similar information from the literature [3–5].

Second, it is true that some of the independent predictors of infective endocarditis (IE) which compose the NOVA score (heart murmur, previous valve disease, persistent bacteremia) are endocarditis criteria. Maybe our description regarding the selection criteria chosen for the control patients was not clear enough. Controls were randomly selected among patients with enterococcal bloodstream infection (E-BSI) and a negative TEE result that finally were classified as not having IE. Some Duke-Li criteria were present in both populations (cases and controls) as stated in the original manuscript [1]

Table 1. Description of the Modified Duke Criteria, Present in Controls and Cases

Duke Criteria	Controls (65)	Cases (65)
MAJOR		
Blood culture		
Blood culture: All of 3 or a majority of >4 separate cultures of blood		
Yes	45 (69.2%)	62 (95.4%)
No	20 (30.8%)	3 (4.6%)
Community-acquired enterococci, in the absence of a primary focus		
Yes	0 (0%)	18 (27.7%)
No	65 (100%)	47 (72.3%)
Echocardiogram positive for IE		
Oscillating intracardiac mass		
Yes	0 (0%)	53 (81.5%)
No	65 (100%)	12 (18.5%)
Abscess or new partial dehiscence of prosthetic valve		
Yes	0 (0%)	13 (20%)
No	65 (100%)	52 (80%)
MINOR		
Predisposing heart condition		
Heart valve disease		
Yes	19 (29.2%)	41 (63.1%)
No	46 (70.8%)	24 (36.9%)
Heart murmur (worsening or changing of pre-existing murmur)		
Yes	19 (29.2%)	37 (56.9%)
No	46 (70.8%)	28 (43.1%)
Fever, temperature >38°C		
Yes	58 (89.2%)	59 (90.7%)
No	7 (10.8%)	6 (9.2%)
Vascular phenomena		
Conjunctival hemorrhages		
Yes	0 (0%)	6 (9.2%)
No	65 (100%)	59 (90.7%)
Septic emboli		
Yes	4 (6.2%)	8 (12.3%)
No	61 (93.8%)	57 (87.7%)
Intracranial hemorrhage		
Yes	0 (0%)	5 (7.7%)
No	65 (100%)	60 (92.3%))
Janeway lesions		
Yes	0 (0%)	7 (10.8%)
No	65 (100%)	58 (89.2%)
Immunologic phenomena		
Glomerulonephritis		
Yes	0 (0%)	1 (1.5%)
No	65 (100%)	64 (98.5%)

Table 1 continued.

Duke Criteria	Controls (65)	Cases (65)
Osler nodes		
Yes	0 (0%)	8 (12.3%)
No	65 (100%)	57 (87.7%)
Roth spots		
Yes	0 (0%)	7 (10.8%)
No	65 (100%)	58 (89.2%)
Rheumatoid factor		
Yes	0 (0%)	7 (10.8%)
No	65 (100%)	58 (89.2%)

Abbreviation: IE, infective endocarditis.

page 531, table 2. We did not exclude a control because it had heart murmur, valve disease, or continuous bacteremia. The potential overlap that might exist between predictor variables and the primary end point was overcome with the implementation of boot-strapping techniques that avoid overfitting. Final variables included in the model were selected using a backward stepwise approach and this logistic regression model was validated by 2 runs of 2000 bootstrap replications. Therefore, we do not consider it necessary to perform any further statistical analysis. In order to further clarify this issue, we include a table (Table 1) with the description of the Duke criteria present in cases and controls. If we excluded from the 65 IE cases all those patients who had 1 or more NOVA score factors, none would remain as stated in the original manuscript [1] page 533, figure 3.

Regarding the definition of "unknown origin of the bacteremia," it was not based at all in the results of the echocardiography. As mentioned above, all patients with bacteremia were prospectively evaluated by an independent investigator that searched with the attending physician for clinical microbiological or radiological evidence that explained the origin of the bacteremia. When no such source was demonstrated the case was classified as "unknown origin." It is well known that many bacteremias with a clear origin, such as catheter-related BSIs, are very commonly the origin of nosocomial endocarditis. So the classification of the origin was not established by considering the echocardiography results.

Finally, we concur with Dr Tubiana et al in the need to validate the NOVA score in larger and different populations. However, so far, our risk prediction score (NOVA) provides an easy to use system that could rapidly determine which patients with E-BSI may not require further studies to detect IE. We can anticipate that the NOVA score has already been validated in an Italian cohort of patients with enterococcal bacteremia (ECCMID 2015; poster number 2476) that will soon be published and that a prospective trial is on its way. We would like to take this opportunity to invite Dr Tubiana et al and any other group interested in endocarditis to participate in a prospective, multicentre validation of the NOVA score.

Note

Potential conflicts of interest. All authors: No potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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