

References

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Risk Scores and Long-Term Mortality Prediction After Aortic Valve Replacement

To the Editor:

I would like to congratulate Dr Barili and colleagues [1] for their elegant article published in your journal. Prediction of mortality beyond the operative period to 1 year or more is important for several reasons. Patients are interested to know about their long-term prognosis and not just short-term outcomes. Long-term prediction is even more important in high-risk patients in decision making of treatment modality and comparison with outcomes after transcatheter aortic valve implantation. Such models may also aid cost-effectiveness analyses. Despite these advantages, there is a paucity of data in this area and an absence of risk models designed to predict long-term mortality.

The article found that contemporary risk scores being moderately prognostic of long-term mortality after aortic valve replacement (AVR; C-statistics, 0.69 to 0.71 for 1 or 5 years), inferior to predicting 30-day mortality in terms of discrimination (C, 0.76 to 0.79) and calibration [1]. The reason is clear, because these scores were derived to predict operative mortality rather than long term. However, it should be cautioned that about 40% of 1-year mortality occurred within 30 days, and perhaps if these early deaths were excluded as a late mortality outcome, the discriminative ability of risk scores is even more modest or absent. Are the authors able to provide these figures? In our study, which we were grateful was cited, C equaled 0.71 to 0.75 of EuroSCORE, EuroSCORE II, and the Society of Thoracic Surgeon's (STS) scores found for operative mortality [2]. Although C was 0.67 to 0.71 for 1-year mortality, if early mortality up to 30 days was excluded, this was reduced to 0.60 to 0.61 for the two EuroSCOREs but remained at 0.70 for the STS Score.

Similarly, hazard ratios of 1.08 to 1.34 ($p < 0.0001$) were found for the risk scores in univariate Cox models for long-term mortality in the Barili and colleagues article [1]. The corresponding figures for our cohort were hazard ratios of 1.04 for EuroSCORE, 1.07 for EuroSCORE II, and 1.15 for STS score (all $p < 0.001$). Our study was underpowered, however, to report adjusted-models for long-term mortality, but with results from both studies it seems that STS score was the best score for predicting mortality during follow-up beyond

30 days. Hopefully, this will be the start of more studies evaluating long-term mortality prediction after cardiac surgery.

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Reply

To the Editor:

We read with great interest the comment on our manuscript by Dr Wang [1] and we completely agree with its thoughts [2]. The performance evaluation of the scores in predicting 1- and 5-year mortality represented only the first part of the study and was designed to understand if scores could be used as direct predictors of long-term outcomes. The results of this preliminary analysis were not unexpected, as an algorithm developed to predict perioperative mortality is unlikely to be also suitable for predicting long-term mortality, without any adjustments. Nonetheless, both Society of Thoracic Surgeons (STS) score and EuroSCORE have been previously reported to have good performance even for estimating long-term outcomes [3], although calibration has been tested with the Hosmer-Lemeshow test, which has been demonstrated to be of limited usefulness and misleading [4]. Hence, we focused on analyzing calibration with more suitable methodologies in order to unmask the potential lack of calibration of all models. Moreover, the performance analysis has been conceived to give a rationale to the second part of the study, as a good performance in predicting long-term outcomes does not need further recalibrations or modeling. The unsurprising lack of calibration of the 3 scores in predicting long-term outcomes justified the development of a time-to-event model based on perioperative mortality scores, which was the novel message of the study.

The evident lack of calibration led us not to deepen the performance analysis. However, As Dr Wang suggested [1], we also checked the discriminative power at 1-year follow-up excluding perioperative deaths. As shown in Figure 1, the discriminative power excluding perioperative deaths decreased for all scores, from 0.69 (confidence interval [CI], 0.63 to 0.75) to 0.62 (CI, 0.54 to 0.70) for EuroSCORE II; from 0.70 (CI, 0.64 to 0.76) to 0.63 (CI, 0.55 to 0.72) for STS score; and from 0.70 (CI, 0.63 to 0.77) to 0.66 (CI, 0.57 to 0.76) for age, creatinine, ejection fraction (ACEF) score. These data confirmed the outcome previously reported [5], although in our study group the discriminative power decrease was similar for all scores, including STS score.

PREDICTION OF 1-YEAR MORTALITY EXCLUDING 30-DAY MORTALITY: DISCRIMINATION

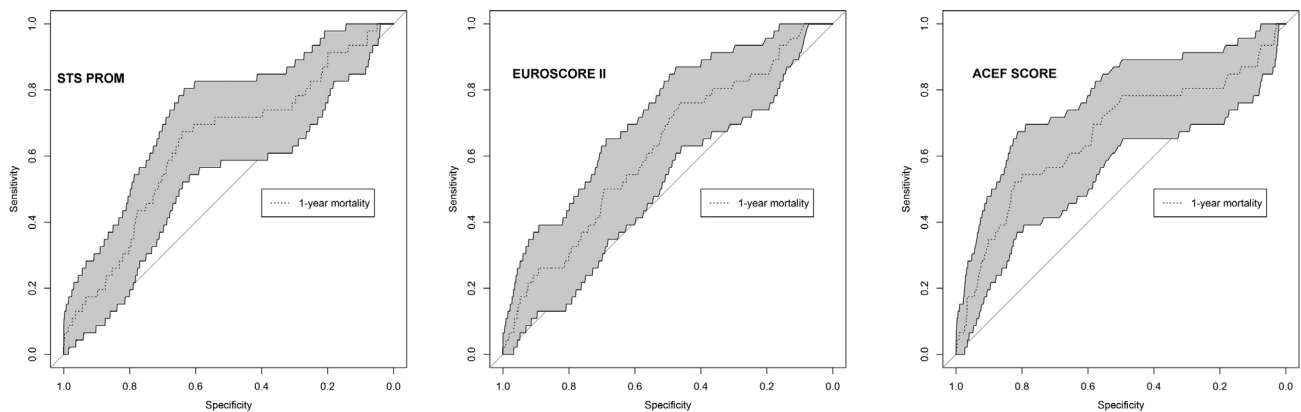


Fig 1. Receiver-operating characteristic curves of EuroSCORE II, Society of Thoracic Surgeons (STS) score, and age, creatinine, ejection fraction (ACEF) score in predicting 1-year mortality, excluding perioperative deaths. (PROM = predicted risk of mortality.)

The evaluation of discrimination excluding perioperative deaths confirms that predicted risk generated by EuroSCORE II, STS, and ACEF scores cannot be also considered a direct estimate of the long-term risk for death.

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Internal Thoracic Artery Histologic Characteristics Clarify Its High Performance in Coronary Bypass

To the Editor:

We have read with interest the article by He and Taggart concerning the functional characteristics of the internal thoracic artery (ITA) fitting well with coronary artery bypass operations [1]. We have performed histologic research on fresh discharged segments of ITAs, corresponding to their distal parts, in 20 patients (68–77 years) who underwent operation for atherosclerotic coronary artery disease [2]. Our results agree with and clarify the conclusions of the these authors [1].

First, the skeletonized ITA preserves a small amount of adipose tissue around its tunica adventitia. S-100 protein immunohistochemical evaluation, aimed at detecting sympathetic nervous fibers, demonstrates only vegetative fibers around the vasa vasorum, without evidence of real plexuses. Moreover, we have not found nervous fibers among the smooth muscle cells of the muscular tunica.

Second, all around the skeletonized ITA, we have observed that the vasa vasorum are able to protect it against external wall ischemia.

Third, the tunica media of ITA is characterized by several circumferential elastic laminae, which explain its elastic capacities. In elderly patients, this elastic apparatus can encounter an elastotic degeneration, followed by a proliferation of smooth muscle cells. Positive immunolabeling for smooth muscle actin and caldesmon, together with a lack of reactivity for desmin, indicates an unspecialized smooth muscle phenotype, whereas the CD34 immunonegativity excludes a vascular origin. These new cells also spread toward the subintimal space, probably in an attempt to repair the internal elastic membrane. When this event occurs, the subintimal space thickens, but without endothelial damage or a significant narrowing of ITA lumen. The particular nature of these cells, not completely developed toward proper muscular elements, corresponds with their poor responsiveness to vasoconstrictor agents. Their origin can be referred to a primitive mesenchymal cell, located in the adventitia, or to a transdifferentiated cell from the endothelium [3].