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Invited response to "MELD calibration"

To the Editor:

We thank the authors for their interest in our study.[1,2] As stated in the manuscript, the MELD-Na score as proposed by Kim et al[3] was validated, not the score as currently used by the OPTN/UNOS. Our goal was to show that the MELD-Na score as proposed by Kim et al already improved prediction of waitlist mortality as compared to MELD. By using the exact same formula, external validation could be achieved and results could be compared. Because the UNOS and ET regions differ, the exact specifications of the MELD-Na formulae are likely to differ. The final formula will depend on evaluation of population characteristics, evidence-based weighing of regression coefficients and expert-based opinion.

Indeed, ideally R_0 and $S_0(t)$ are drawn from the derivation study. However, neither were reported by Kim et al and thus we used the values from our own sample. The mean MELD-Na (R_0) was 19 and the corresponding 90-day survival probability ($S_0(t)$) was 0.110, as reported in the study supplement 6. The provided calibration plot gives a good impression of the slope and calibration in-the-large, which are very good for 90% of the population, as discussed. These were not formally tested, as the R_0 and S_0t from Kim et al would have been needed. Moreover, as MELD-Na is used to prioritize waitlist patients, the excellent discrimination (c-index 0.847) is most important.

D'Amico and Maruzelli express their concerns over selection bias through the large number of excluded patients. This is of course a valid concern, which was clearly addressed in the manuscript. In supplement 1, the characteristics of the patients with and without serum sodium (Na) at listing were analyzed. We found significant differences between the groups, which were discussed. Also, between 2007 and 2012, more Na data were missing as compared to recent years, which implies that our results are more applicable to the current and future ET population. Thus, the missingness is related to some of the observed data, that is, not MCAR. We found no evidence that missing values in patients who died within 90 days were different from the values in those who were censored. Therefore, we expect to have minimized the potential for biased conclusions given the size of the available sample, absence of clinically relevant differences, comparable missingness of Na per patient outcome and missing at random data. However, there is no exact way of knowing as long as data are missing.

The study interpretation naturally depends on the population it is based on. Possible predictors not included in the MELD-Na score are, for example, some of the baseline characteristics (Table 1) that influence patient survival. Basic differences between the ET and UNOS regions can easily be clinically interpreted and compared.[3,4] It is evident that the MELD-Na score does not capture all factors that influence patient waitlist survival, only those that relate to the four laboratory measurements and dialysis dependency. A model considering more factors would be useful, but was not the goal of this study.

KEYWORDS

clinical research/practice, editorial/personal viewpoint, liver transplantation/hepatology, liver transplantation: auxiliary, organ allocation, organ procurement and allocation, recipient selection, waitlist management

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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