LETTER TO THE EDITORS

Reply to "Association between donor age and risk of graft failure after liver transplantation: an analysis of the Eurotransplant database"

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Dear Editors,

We read with great interest the study by Pratschke *et al.* [1] "Association between donor age and risk of graft failure after liver transplantation: An analysis of the Eurotransplant database." The study analyzed a large dataset from Eurotransplant and included a final sample of 8351 patients undergoing liver transplantation between January 2000 and July 2014, of whom 252 (3.0%) were transplanted with octogenarian, brain-dead donor grafts.

Unfortunately, the paper raises several concerns from a methodological point of view. Although the initial population consisted of 26 294 subjects, a total of 68.2% was eventually excluded from analysis. Approximately, 7000 cases were removed due to data inconsistencies or missing values (e.g., MELD scores), while any attempt at resolving incongruent or missing information (i.e., negative or very long cold ischemia times) might have strengthened the study statistical validity. In addition, the decision to remove from analysis more than 1500 donors with very abnormal liver function tests (transaminases, γ GT \geq 1000 U/l) or ICU stay \geq 100 days has reduced the possibility to assess the impact of younger grafts with worse clinical variables and might have biased the study results.

Overall, the study focuses on the negative effect of combining older donors with well-known, independent risk factors of poor post-transplant outcomes, such as a recipient HCV-positive status, higher MELD scores, and long cold ischemia. However, the authors' conclusions do not seem to be built on solid ground. Several donor comorbidities have not been investigated, and variables such as donor height [2], diabetes mellitus [3,4], or hemodynamic instability are lacking [5]. The search for a donor age upper limit to be used in clinical practice is rather controversial, since age should not be viewed as a contraindication per se, and agerelated comorbidities should lay the basis for a more granular score to serve for higher to unacceptable risk liver grafts [2,6].

Finally, not balancing younger versus older donors on these risk factors is a major statistical drawback: a propensity score matching or weighing for the inverse probability of treatment are possible methodological solutions to mitigate this initial unbalance [4,7].

Aged donors are more prone to ischemic injury as a result of long-standing arteriolosclerosis, and clinical experience with management of older donors (i.e., the center effect) is a qualitative variable which is difficult to assess even with sophisticated statistical analyses [8]. Based on the above statistical limitations and the relatively small number of octogenarian donors reported this series (only 3% of the analyzed sample), we are convinced that the authors' conclusions should undergo scrutiny and be reexamined.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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