

## Deadline 2-08-2022

Reviewer #1:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** I would like to suggest you to present more discussion of different machine learning methods including the decision tree, the random forest and the artificial neural network.

Response: we thank you for your valuable comments.

We have included a more thorough discussion of different machine-learning methods in the text, under the section “artificial intelligence”.

Reviewer #2:

**Scientific Quality:** Grade D (Fair)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** This is a review article on role of AI in LT allocation. Multiple issues need to be addressed: 1. Introduction part is too long and has irrelevant information. Would recommend to make it more precise and concise. In addition the AI part is also very general, can be summarized and added to the introduction part to give the reader an idea on principles of AI. 2. Applications of Artificial Intelligence on Liver Allocation : it is very very brief, authors need to discuss all studies and criticize them in details with taking into consideration the clinical context, study design, sample size, model used, statistics done, limitations, implications ... 3. Would recommend adding a table to summarize the literature to make it easier for the reader to capture

Response: we thank you for your valuable comments.

We could not simply summarize the introduction and the AI part, because other reviewers asked us to add further comments on ethics, describe with more details the concepts of AI and add a discussion on the matter of hepatocellular carcinoma exception points. We did manage to cut out a few parts of the introduction and reorganized the text, dividing into different sections. The introduction became “Liver Allocation”. We divided AI applications on in two parts, “AI applied for the Prediction of Mortality in the Waiting List” and “AI applied for Liver Allocation”. We believe the text has become easier and more straightforward. We have included more studies on our text, as a request from other reviewer, enriching the discussion. Finally, we added a table to better summarize the studies on AI applied for liver allocation.

Reviewer #3:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** This was a minireview on artificial intelligence applied to organ allocation in the liver transplant setting. In the first section (i.e., Introduction) the Authors described the current state of the art on organ allocation around the world, introducing concepts as utility and urgency. In the second part, they briefly described some studies which applied artificial intelligence in the setting of organ allocation. On a general view, the paper is fluent, and the topic is of interest for the Journal. My comments. - There are some typos that should be carefully reviewed (e.g., morbimortality; usefulness instead of utility; receptor instead of recipient). - The first section describes principles as utility and urgency. I think that also the concept of transplant benefit should be added. - Hepatocellular carcinoma is one of the most important indications to liver transplantation, with an increasing trend over time. Patients with HCC usually undergo transplantation according to utility criterion (and not urgency). Notably, the topic of transplant benefit for HCC has been proposed. This point should be added and briefly discussed. - In the core tip, the Authors dealt with ethical aspects of liver allocation. In what way artificial intelligence can help these aspects? - The Authors described results of three papers which applied artificial intelligence in organ allocation. Nevertheless, there are other many (and recent) papers which investigated this point (i.e., PMID 34019601; 33428298; 32274856; 32073494). In my opinion this topic should be discussed more in depth, adding new references.

Response: we thank you for your valuable comments.

We have removed the term “morbimortality” and replaced all instances of the term “liver receptor” with “liver recipient”.

We have chosen not to replace the term “utility” for “usefulness”, because it was a term proposed by Keller et al in “Ethical Considerations Surrounding Survival Benefit-Based Liver Allocation”, reference 3 in our article. It is also repeatedly used in the article by Cholongitas and Burroughs (“The evolution in the prioritization for liver transplantation”), reference 16 in the revised version of our article.

We have made added some discussion of the matter transplant benefit, for which we thank you, because we believe the introductory text became more clear with it.

We added a short discussion regarding MELD exception points for HCC patients and commented on related findings in one of the cited works (reference 1 - Halliday et al, 2017)

We have included the suggested references in the text, enriching the review (PMID 34019601; 33428298; 32274856). Reference PMID 32073494 was not

included, because it did not seem to bring out additional relevant information, since it is an extension of the article cited by us in reference 35 of the revised version (Bertsimas et al, 2019), published by the same group.

We added further (in-depth) discussion regarding ethical aspects of liver allocation in the conclusion.