Peer Review File

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Reviewer A

It is interesting to publish this paper.
I propose that the authors re-edit the test.
They should also include a brief summary about the indications that are accepted/ done for Domino LT.
Reply: Thank you for your feedback, we will add a brief summary regarding the indications for DLT.

Proposal to make a small table mentioning all indications for which DLT has been done and indicating if still advisable or not.
Reply: Good suggestion, thanks. We will add a table mentioning the indications for which DLT has been done and include if this is still acceptable or not.

The ref FURTADO must come in such paper at the beginning of the paper.
Reply: Furtado reference has been mentioned earlier.

Donor and recipient info must be grouped together for each case. will be clearer for the reader.
When revising the paper more info should be given about the metabolic results in both donors and recipients.
Reply: Thank you for the feedback, we rework this section.

The discussion about FAP DLT is insufficient and not completely right …see literature.
Reply: Thank you for this comment, more correct and in depth discussion about FAP has been added.

Reviewer B

Chorley w et al report 2 new domino LT where the domino donor was a patient with MMA.
The cases are interesting with case receiving a part of a liver from an unaffected sib. This MMA patient had a complicated course with post op hyperammonemia and what sounds like rapidly progressive kidney failure and the need for a kidney transplant. His labs are stated to be "improved".
Reply: Thank you for your comment, this has been corrected.

What were the mutations in which gene in this patient?
Reply: The gene mutations for these patients have been added.

What was the cystatin C eGFR or measured GFR in this case? Why was the patient not offered a combined LKT? Clearly this is the preferred procedure for this patient and a donor lobe seems nonsensical to this reviewer as now the patient will need dialysis or another transplant.
Reply: Thank you for these questions, cystine C levels (where available) have been included in table 1, and an explanation regarding our decision to opt for LT alone rather than combined LKT has been added.

Case 1 recipient is equally vexing from the metabolic medicine transplant perspective. The recipient clearly was critically ill and not an ideal candidate for an LT. The recipient of the MMA liver also has now developed MMAemia/uria.
Case 2 received a living liver donor (Cr Cl 35 ml/min) and was stable, then developed AKI and a depressed eGFR. This pt will indeed also require renal replacement at some point in the future. An LKT would have been preferred in this patient. The recipient of the MMA in this second case appears to have developed severe MMA related complication in the opinion of this reviewer as the plasma MMA value is now 635 uM which is massive. A renal syndrome has evolved and whether the very high pMMA might be causative is unknown.
Table 1 is not formatted properly. I note that the FGF21 in the second recipient is massively elevated showing that the MMA liver in this patient is severely affected by the mitochondriopathy of MMA.
Reply: Thank you for this feedback, table 1 has been reformatted.

Pros: I agree the recipients of the MMA livers have lived longer with some improvement in case 1. In case 2, it looks less beneficial. The use of living donors in MMA is under studied and this paper might help some select patients benefit from elective LT.
Cons: Both MMA patients would have benefited from an LKT. The mutations must be reported in the MMA patients. CrCl eGCR is inaccurate in MMA and cystatin C values should be reported - see PMID: 23639900. A more accurate measure of the GFR might have led to an LKT in these patients. The second recipient now has a severe MMA syndrome and might be symptomatic from it based on the pMMA and FGF21. Why a donor procedure was used vs waiting for the MMA pts for an LKT needs to be discussed. There is no meaningful discussion of the very high FGF21 in the second recipient. See PMID: 37243446 and PMCID: PMC6328030.
Reply: Thank you for your comment, cystine C values have been added where available, and a discussion has been added regarding our decision go ahead with LT alone rather than combined LKT. A discussion regarding the FGF21 results has been added, with references.

These cases are interesting but the descriptions of the patients and pathophysiology are poorly developed. There should be mention that there are no careful studies on the MMA recipients, and such patients might need to be treated as if they have MMA - with diet ? carnitine? Metabolic monitoring? Ammonia levels? Therefore MMA livers can be used in the domino procedure with many disclaimers.
Reply: Thank you for your feedback on this point, more information regarding their pre transplant workup, treatment prior to transplant, and metabolic status before transplant has been included. More emphasis has been placed on our overall perspective, which is that MMA livers

can be used for DLT with caution, and that further studies here are needed to assess safety and efficacy.