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Reply to the reviewers' comments

Reviewer Number	Original comments of the reviewer	Reply by the author(s)
1	Reviewer 1: General comment: The effectiveness of plasmapheresis remains undefined for the acute graft dysfunction in the patient with liver transplantation. This case report	We thank the reviewer for his/her analysis and constructive criticism of our manuscript.

	describes the patient that was successfully treated with plasmapheresis for the graft dysfunction of the transplanted liver. The patient recovered from the graft dysfunction following liver transplantation upon several cycles of plasmapheresis. The report suggests that plasmapheresis represents one of the treatment options for the cases with acute graft failure of liver transplantation. This is a good report that can be shared by the physicians that involve in the liver transplantation. Specific comment Minor In the figure, the Y axes on both sides need to be specified for their unit. The left axis appears to represent bilirubin whereas the right one must be AST.	We have made the changes in the figure as mentioned by the reviewer
2	1) The case report introduced the role of plasmapheresis in early allograft dysfunction following deceased donor liver transplantation. It is better guidance to treat the early allograft	We sincerely thank the reviewer for the comments.

	dysfunction after liver transplantation . 2) I suggest that the manuscript can be published in the form of case report.	
3	Accept as it	We sincerely thank the reviewer for the comments.
4	The paper is good, although it doesn't seem to get different conclusion from the larger case series already published. INTRODUCTION should be more detailed about early graft dysfunction characteristics (such as incidence, percentage of mortality, possible alternative treatments). CASE REPORT: - please detail immunosuppressive treatment (drugs and doses) - please detail the diagnosis of allograft dysfunction (transaminases, INR, albumin...) - please detail the hystology of the liver biopsy - which steroid was used? can you confirm the doses (20 mg/kg/day)? - please detail	We thank the reviewer for his/her analysis and constructive criticism of our manuscript. As advised by the reviewer, we have rewritten the Introduction section to incorporate details of allograft dysfunction In the Case Report section, we have also ensured the clinical details have been appended as appropriate, including the details of immunosuppression. We have added the details of infection and the antibiotic used.

	blood exams on the day in which plasmapheresis was started - the bloodsteram infection by K. Pneumoniae must be better explained: which clinical manifestations did it have? which were the antibiotics employed? - please better detail the patient's conditions and exams at discharge. DISCUSSION - the role of plasmapheresis before and after hepatic allograft should be distinguished and needs a more detailed explanation - also the previous studies on plasmapheresis in early allograft disfunction should be described more extensively.	We have also detailed the patient's condition at discharge. In the discussion section, we have reviewed other studies on plasmapheresis and allograft dysfunction, and have added these to the revised manuscript. The modified sections of the manuscript have been highlighted in yellow.
5	The manuscript entitled "The Role of Plasmapheresis in Early Allograft Dysfunction Following Deceased Donor Liver Transplantation" provides a short case report of the treatment of a patient with early allograft dysfunction (EAD) after liver transplantation. This case report is	We sincerely thank the reviewer for his/her comments and constructive criticism.

	generally in line with the previous reports/articles of this kind published elsewhere. The potential benefits of this work are the age of the patient combined with positive outcome, which means that high-volume exchange plasmapheresis can be successfully used while treating young patients. I also think it is useful to remind doctors not to disregard a simple but very effective procedure such as plasmapheresis. However, the report does not bring anything specifically new about the clinical utility of plasmapheresis in allograft dysfunction. Furthermore, I am highly concerned by the fact that the authors did not analyze the references well enough and therefore were unable to describe both procedures executed by them and the outcomes thereof to provide a clear explanation of their study. Major comments:	We have added a more comprehensive paragraph on early allograft dysfunction. As rightly pointed out by the reviewer, the incidence is variable. However, in most large volume liver transplant centres, the incidence of allograft dysfunction has fallen to single digits.(reference added)

	1) A number of statements in the text are not supported by references. For example: a) Page 3: "Early allograft dysfunction is not an uncommon entity, especially in transplantation with organs from marginal donors.1" The paper that the authors refer to claims the opposite: "Early allograft dysfunction (EAD) is a rare but serious complication […] The incidence has been reported to be 5% to 10% for liver grafts with a downward trend…" (Camci et al., 2004). However, the additional search that I executed showed the occurrence of early allograft dysfunction of 2-23%: therefore, it is probably better to refer to this numbers. b) Page 3: "Plasmapheresis has been used in acute liver failure, but its role in supporting dysfunctional liver grafts remains unclear.5,6" Both reference articles 5 and 6 state nothing about the	The references have been updated to make this section of the manuscript more comprehensible. The references quoted are to reinforce the fact that plasmapheresis is an integral part of the

	plasmapheresis utility in EAD. Paper 5 (Akdogan, 2006) investigates fulminant hepatic failure and states "Total plasma exchange has been shown to be a useful treatment modality for early allograft dysfunction after liver transplantation"), paper 6 (Hwang, 2006) is a case report of Hepatic Failure after Major Hepatectomy also stating that "plasmapheresis can be a useful liver support for post-hepatectomy liver failure". Thus, the origin of the "unclear role of plasmapheresis" remains incomprehensible.	"acute liver failure algorithm". While the same cannot be said for EAD, where there are no clear published guidelines for management.
	c) Page 5: "Prothrombin time is readily affected by the plasma infusion and is also not a predictable marker of the effectiveness of plasmapheresis." As far as I could understand from the context, plasmapheresis is a synonym to plasma infusion. If it is so, then the phrase remains unclear. If PT is affected by plasmapheresis, why cannot it be a	As the reviewer has rightly pointed out, plasmapheresis will affect the PT, giving a false low value due to the plasma infusion. While this trend of PT is heartening to see, it is not a true improvement in PT consequent to graft recovery. Thus PT remains a poor marker to assess actual benefit of plasmapheresis- which is recovery of the allograft. Reference has been added for the same in the manuscript(3,10)

	marker of plasmapheresis? I guess that in case if coagulation factors are consumed and/or not produced by the liver, plasma infusion should affect PT. Please clarify the statement and provide the reference if possible.	
	2) In general, the article contains 7 references, of which 5 refer to only 2 different scientific groups: this makes the references look unbalanced and biased. I would recommend adding more variable references. Moreover, the latest article cited by the authors was published in 2012. I would recommend including some more up-to-date publications, for example, a recent paper by W. Choe et al. (J Clin Apher, 2016) can be taken into consideration while it describes broadly the same idea as the authors.	We appreciate the reviewer's concern. Following a comprehensive re-review of literature, we could come upon only one other team (Johns Hopkins) which has published on this topic. This reiterates our previous statement, that the role of plasmapheresis remains a grey area, with only few centres having explored this option. Thus highlighting the importance of our casereport. We thank the reviewer for the reference, which has been updated and quoted in the discussion section.
	3) What was the possible cause of noted portal vein thrombosis? Could this thrombosis be the possible cause of further	The most common cause of early portal vein thrombosis is technical. The incidence of PVT following LT is 1-2%. While routine thromboprophylaxis was employed. As per

	graft dysfunction? How common are thrombotic complications after such surgeries? Was any antithrombotic prophylaxis and monitoring done?	protocol no specific additional measures were taken, apart from a meticulous surgical technique during the reexploration.
	4) The description of plasmapheresis is poor and unclear for a non-expert, I would recommend completing and clarifying it. Please explain which device, regime, and anticoagulant were used. Were any additional fluids administered? Why this particular volume of fluids was chosen for replacement? When were the tests (bilirubin, AST, INR) performed in relation to plasmapheresis: before each procedure, shortly after it, or each test was performed without correlation with the time of plasmapheresis?	This has been updated comprehensively in the manuscript in the casereport section
	5) What was the aim of the INR test? Was it performed to evaluate the liver condition or the patient's hemostasis? Were any anticoagulants used during the	This has been mentioned in the previous sections. The figure has been updated to include the

	treatment (especially after the thrombosis was noticed) and how they were monitored (if any)? The article figure provides poor information about INR: the INR presentation scale is incorrect, please revise it. Which axes correspond to which parameters? Also please provide normal ranges for bilirubin, AST, and INR on the graph so the critical values would be clearly visible. What are the units used on each side of the figure, for vertical axes?	values and parameters.
	6) One of the effects of plasmapheresis after liver transplantation is removal of antibodies from the recipient's blood plasma. High antibodies titer, antibodies level control and monitoring can often be an issue. Thus, if the antibodies level was monitored during the study, I would recommend including this into the paper. Minor comments:	Antibodies were not monitored.

	1) Pages 2 and 3: please correct "in situ" uniformly within the text. 2) Page 2: please correct "Fogarty endothrombectomy". 3) Page 4: please give definitions of LFT and OLT. 4) Page 5, references: please provide uniform references ("et al:" vs "et al", "Transplant Proc 2004" vs "Transplant Proc2010" (without space); also please correct "molecular adsorbent" (ref.4).	They have been corrected in the appropriate sections. We once again thank the reviewer for taking the time in pointing out the areas improvement, thereby helping us improve our manuscript.