

Peer Review File

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Reviewer Comments

The manuscript summarizes a single centre experience with pancreas graft biopsy sampling from 235 SPK transplantations performed between September 2016 and December 2021. 4 patients had a pancreas graft biopsy sampled with different methods. This is my concerns:

Comment 1: Who were the patients? Age and gender are listed, but what about comorbidity, BMI etc.

Reply 1: Thanks for reviewer. We will add information about the patients' comorbidity and BMI in the article.

Changes in the text 1: Comorbidity and BMI are added in Table 1 and marked in yellow.

Comment 2: Immunosuppressive protocols is relevant in the context of graft rejection; induction therapy, trough levels tacrolimus, tapering protocols of prednisolone etc.

Reply 2: Thanks for reviewer. We will add this information in this article.

Changes in the text 2: We add a paragraph about immunosuppressive regimens (see Page 4, line 71-81) and marked in yellow.

Comment 3: How were pancreas graft rejection suspected in the clinic? Amylase and lipase- but not glucose? If so- references to advocate the use of this laboratory parameters as rejection markers should be listed

Reply 3 : Thanks for reviewer. The elevation of serum lipase and amylase are the earliest and most typical laboratory parameter changes in acute rejection of transplanted pancreas. Animal experiments have confirmed that the inflammatory cells in acute rejection attack acinar cells first, leading to an increase in lipase and amylase, and then attack islet cells, leading to an increase in blood glucose. The references 5 and 6 are the supplement.

Changes in the text 3: We have added references 5 and 6 (see Page 8 and 15, line 157, 314-319) and marked in yellow.

Comment 4: Only 4 rejections in 235 SPK patients?

Reply 4: Thanks for reviewer. Probably we didn't describe it clearly. There were far more than 4 cases of rejection out of 235 SPK patients. Biopsies of transplanted pancreas were performed only in these 4 patients with suspected acute rejection at our center. It will be described more clearly at the time of modification.

Changes in the text 4: We made modifications for these 4 patients (see Page 3-4, line 65-67) and marked in yellow.

Comment 5: Which criteria was used to decide 1) if the biopsy sampling was representative 2) if rejection was present

Reply 5: That's a very good question. As mentioned in the previous question, inflammatory cells of acute rejection attacks acinar cells first and then islet cells. There is no clear regulation on the site of sampling and we hope it can include acinar cells, islet cells and blood vessels. Our pathologists follows the Banff criteria to determine if there is rejection.

Changes in the text 5: We have added the Criteria for histological determination(see Page 4, line 67-68) and marked in gray.

Comment 6: How was treatment success evaluated? Normalized amylase and lipase?

Reply 6 : The criteria for the success of anti-rejection treatment are not uniform at present. Successful treatment will reduce serum lipase and amylase, but the rate and degree of decline are different in each patient.

Changes in the text 6: We made modifications for the treatment effect (see Page 7, line 134-136) and marked in yellow.

Comment 7: Pancreas transplant biopsies are not new for the world- wide transplant society and there are more than one report for each of the different pancreas biopsy techniques which probably should be referred if a revision of biopsy techniques is intended

Reply 7: Thanks for reviewer. Different biopsy techniques for transplanted pancreas have been reported in some transplant centers, but they are less common than those that perform pancreatic transplantation. CT combined with color Doppler-guided needle biopsy mentioned in our article has not been reported. However, the purpose of this article is not to discuss this, but to explore which technique is safer and more effective according to the different location of the transplanted pancreas. The fact that the total number of cases is only 4 is our deficiency, but we hope it can explain the purpose of our article.

Changes in the text 7: None