Response to reviewers' comments

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Manuscript Title: **Male gender and increased body mass index independently predicts clinically relevant morbidity after spleen-preserving distal pancreatectomy**

First, I would like to thank the reviewers and editor for their interest and assessment of our manuscript. The provided comments and suggestions will help us to improve our manuscript. Furthermore, we have tried to do our best to provide a point by point response to all the concerns raised by reviewers and editorial staff.

Reviewer 1:

Comment:

This study evaluated risk factor of morbidity after SPDP and detected that the male gender and high BMI were independent risk factors for severe morbidity after SPDP. Though, these factors are well known as risk factors of morbidity after any types of pancreatectomy. Therefore, I could not understand that these factors are specific for SPDP. The author should demonstrate the risk factors of severe morbidity after ordinary distal pancreatectomy in the same era and the difference between SPDP and ordinary distal pancreatectomy.

Answer:

Indeed the above-mentioned factors are widely considered as risk factors for different types of pancreatectomies including distal pancreatectomy. Our scope for this study was not to explore potential predictors of morbidity after distal pancreatectomy because many studies in the literature assessed potential predictors of morbidity after distal pancreatectomy. However, to the best of our knowledge, this is the first study including only patients with SPDP. SPDP is widely considered to be sometimes technically challenging. Furthermore, our previous studies did not identify any significant

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differences of outcomes between distal pancreatectomy with and without splenectomy in adults (Dumitrascu T et al, J Hepatobiliary Pancreat Sci, 2014; 21(9):654-62. doi: 10.1002/jhbp.110). Thus, the risk factors identified in our study are not specific for SPDP but may have clinical value, and may be useful for clinical decision-making in the selection of patients suitable for spleen-preservation or not, mainly when preservation of the spleen is technically challenging. Noteworthy, no previous studies are exploring such factors in patients with SPDP and, thus, we do consider that our study worth to be published and would be of interest to pancreatic surgeons.

Reviewer 2:

Comment 1:

The authors should list the risk factors they used in the univariate and multivariate analysis model in a distinct table comprehensively and extensively. The table should contain the odds ratio (or hazard ratio), 95% confidence interval, and P values individually. The risk factors should include the comorbidity of the patients, such as the Charlson Comorbidity Index or Elixhauser comorbidity measure.

Answer 1:

For the univariate analysis, we have provided the requested data in Table 1. All the potential predictors of clinically relevant morbidity were included in Table 1 (for the univariate analysis).

For the multivariate analyses, we have provided the data in the text, not in a table, including hazard ratio, 95% confidence interval, and p value.

For co-morbidities, we have used the ASA score. However, as the reviewer suggested, we have introduced the Charlson Comorbidity Index to assess the co-morbidities of the patients better. No significant differences were observed between the groups for the Charlson Comorbidity Index.

Thus, Table 1 was modified introducing the following data:

Charlson Comorbidity Index	All Patients	No complications	Clinically relevant complications	P value
	0 (0 – 4)	0 (0 – 4)	1.5 (0 – 3)	P = 0.157

Comment 2:

The authors had presented the risk factors of complications as hazard ratio (HR). However, the most reports usually used HR as the results of survival analysis. The authors should clarify their statistic method for analyzing HR (such as Cox regression model, etc.). In addition, the authors may present the survival curve of risk factors in figures if using a survival analysis model.

Answer 2:

Indeed HR is more commonly used for survivals while Odds ratio or Relative Risk is used for risk factors not related to survivals. However, in papers published in the literature HR is frequently used for risk factors too (see Goh BKP et al, Arch Surg, 2008; 143(10):956-65 etc). Our statistical method for multivariate analysis was stated in Statistical analysis and is a binary logistic regression model with a stepwise forward method. There was no survival analysis in our study. Nevertheless, to avoid any confusions, we have replaced HR with Odds ratio (OR).

Comment 3:

For analysis of body mass index (BMI), I recommend the authors analyzing the risk factor according to BMI subgroup rather than BMI directly. The authors may categorize BMI subgroups as underweight, normal, and overweight, etc. They may select the cut-off values of BMI subgroups according to the definition of the World Health Organization (WHO) or local variation.

Answer 3:

We have stratified the patients according to the World Health Organization definitions for underweight (BMI < 18.5 kg/ m^2), normal weight (BMI = 18.5 – 24.9 kg/ m^2), overweight (BMI = 25 – 29.9 kg/ m^2) and obesity (BMI ≥ 30 kg/ m^2). No patients were in the group with underweight. As shown in Table 1, we have made a subgroup

analysis for overweight and obesity (all together and separate for each subgroup). However, in the multivariate analysis, the BMI value was introduced because it is the base for the definition of any of these subgroups. In the manuscript it was introduced in Materials and Methods the following statement: "The patients were stratified according to the World Health Organization definitions for underweight (BMI < 18.5 kg/ m^2), normal weight (BMI = 18.5 – 24.9 kg/ m^2), overweight (BMI = 25 – 29.9 kg/ m^2) and obesity (BMI ≥ 30 kg/ m^2)".

Comment 4:

The authors should also focus on the positive findings of the discussion. They had found male gender and increased BMI as risk factors for complication. Is there any hypothesis or mechanism to explain the findings and address this concern?

Answer 4:

To the best of our knowledge, there is no strong hypothesis to explain the fact that increased BMI or male gender is risk factors for complications after distal pancreatectomy. In obese patients, it was suggested that distal pancreatectomy might be more technically challenging and potentially associated with increased blood loss. However, this is not particular for distal pancreatectomy, and it might be true for any pancreatectomy or other complex surgical procedure.

On behalf of all authors,

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Bucharest, September 23rd, 2018