

Reviewer #1:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors: This is an interesting work that concerns Pancreaticoduodenectomy for Ampullary Adenocarcinoma in a South American. But there are several issues that need to be checked and completed prior to possible consideration for publication. The article is well written and very clear and easy to read, but for reviewer there is no pagination or line counting. Regarding the content of the article there are some major issues to be resolved before submitting it to the journal, this concerns the antibodies used. Authors should clearly cite the origin of the cited antibodies, and in the results section, give the results found, and also discuss the results obtained. Therefore much of the work is missing in the article. Consequently, the article as it stands is not acceptable for publication.

Answer

Dear Reviewer #1: We appreciate the suggestions and we have made the appropriate pagination. Regarding the use of antibodies, we have cited them in the manuscript as indicated. Unfortunately, the information regarding all the cases and the results regarding the immunohistochemistry of each case and the final percentage of positivity of a given antibody could not be retrieved. However, the intention of this study is not to show how this antibodies would make a specific profile in this specific South American population, we aim to present histopathologic predictors of OS and not the role of the antibodies in diagnosis. Once again, we are grateful for your comment and support by reviewing this study.

Reviewer #2:
Scientific Quality: Grade C (Good)
Language Quality: Grade A (Priority publishing)
Conclusion: Major revision
Specific Comments to Authors: Thank you to give a chance reviewing this interesting paper. I enjoyed reviewing this paper. The authors studied the predictors of lower survival rate after curative PD for ampullary adenocarcinoma in South America population. The authors should refer their operation criteria and preoperative diagnosis process. The authors had better describe the reason why these results in South America are important and the differences from other populations. The authors should give comments the future preoperative diagnosis or treatment strategy for T3 ampullary adenocarcinoma.

Answer

Dear Reviewer #2: Thank you for your review and comments. Regarding the criteria and preoperative diagnosis process you will find the information in the manuscript. We have also included more discussion related to the difference from other populations and added the appropriate references. As well, we included a proposal for treatment in patients with T3 AAC. Once again, we are grateful for your comment and support by reviewing this study.

Reviewer #3:
Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing)
Conclusion: Minor revision
Specific Comments to Authors: Manuscript ID: 68038 Manuscript Title: Survival after Curative

Pancreaticoduodenectomy for Ampullary Adenocarcinoma in a South American Population: A Retrospective Cohort Study Title is appropriate, and it reflects the main subject of the manuscript. Abstract – concise, informative, summarize and reflect the manuscript. Suggestions: proportion of intestinal type and pancreatobiliary type should better be stated as percentage, not as a number like it is written. Key words – adequate. Background – appropriate length, gives enough information to introduce a reader into the topic and significance of the study. Methods – properly described, well statistically analyzed. Suggestion: since the methodology is previously described, part of the text under subheading Panceratoduodenectomy (PD) after reference 28 (from third sentence until the end of the paragraph) could be removed. Results - in general are well presented, in an understandable manner. Rarity of this type of tumors makes results and given data significant and 10-year follow-up makes it reliable. Suggestions: Study population: - The patient selection flowchart is not necessary. Authors should in one or two sentences state the inclusion and exclusion criteria (listed in that chart). - They say that 25 patients died during the study, and that data should be represented as a percentage of initially included in the study (if they are a part of that initially selected 83 patients). - Table 2: As a subtype is listed Intestinal and data were given as “(m, %)” . I believe that this is typing error, and that it should be “(n, %)” , if not – explain what “m” means. Patterns of recurrence: - If it is possible to get those data, it would be informative to say when recurrence occurred, after what period of time postoperatively - in the text authors state that most common organ involved was the liver (n=8). I believe that this statement should be accompanied by total number of cases with liver recurrence (n=12), which is in the Table 3 given as A+B+C. The same goes for peritoneum and lungs - sentence “Lymph nodes around the superior mesenteric artery or the retroperitoneal space were found in one and two patients,, respectively.” Of course that there can be found lymph nodes, but this is about “positive” lymph nodes, or those with tumor tissue, so it should be indicated Overall survival and prognostic factors - Last sentence of this paragraph say: “No influence of time or residuals on the independent....” I do not recall that “residuals” were mentioned before, so it is not clear what does it mean? Residual tumor tissue? As authors stated these were R0 surgeries, meaning that no tumor tissue was left in the body... Try to clarify this term “residuals”. - Table 3 – “Locoregional recurrence” this is related to lymphonodal recurrence? Than it should be stated as such - Table 4 – I don’t know is this appearing just in mine version of Word manuscript, but after “Histopatological subtype/ Intestinal” there is number 1 and after that a square bracket saying reference “[Reference]”. Same is after T classification T1-T2 and Lymph node metastasis/No, and Differentiation grade/ Well differentiated. To the best of my knowledge this is not correct, but if I am wrong – please give some explanation. Effect of lymph node invasion – authors use abbreviations N+ and N0. Although it is common in pathology reports, in case of scientific paper available to less specialized users, it would be good to give explanation of those abbreviations somewhere in the text. Discussion – clear, well written, it follows results obtained in their research, and give proper comparison to literature, without unsubstantiated claims. The manuscript is highlighting the key points concisely, clearly and logically. The discussion is supporting paper’s scientific significance and relevance to clinical practice.

Answer

Dear Reviewer #3: We are thankful for your review and academic comments, we have meticulously addressed them and gave our best to solve them. We have made the corrections in terms of writing and spelling in some cases, including the ones your have indicated. Kindly find them in the revised manuscript.

Since the interest for the readers regarding how we operate patients and select them (one of our reviewers asked us to add information in this topic) we decided to keep the paragraph. We have also specified that 25 out of the 83 died during follow-up and represented them as percentage. Unfortunately, as this is a retrospective cohort, not all patients had information available regarding the recurrence or the time this happened. About the positive lymph nodes (including the definition of N0 and N+), this has been changed as advised. The term residuals and the

paragraph has been deleted to not induce any confusion to the reader. However, this term refers to the test used to evaluate the Cox regression model. Once again, we are grateful for your comment and support by reviewing this study.