The Editor in Chief

World Journal of Clinical Oncology

Dear Sir or Madam,

We would like to thank the reviewers for their time and effort to review our manuscript 77700. We have read the constructive criticisms and made the necessary corrections. We wish to submit a revised version with the changes in bold type and also in point form below"

- Reviewer #1 commented: "As we know, the Whipple's procedure, even the LPD procedure, is a routine surgery in many high-volume centers. The authors did a lot of efforts in Whipple's procedure in a low-volume center and achieved a good short-term outcomes with a low complications for these patients. Because of this, the authors confirmed that Whipple's procedures should only be performed in high-volume centers. However, I do not agree the authors' opinion in the part of INTRODUCTION line 3-5: "Because these facilities are often in high income nations, patients in poor countries cannot access them easily". Firstly, what the authors said is the truth, but the patients in poor country always needs to be treated in a relative high-volume hospital."

  We note the reviewer's concern. The reviewer does state that what we have said "*is the truth*" and on-the-ground, it is indeed difficult for patients in low volume centers to access these high-volume centers in developed countries. Simply put, this is the reality on the ground that surgeons and patients in low and middle-income nations have to deal with. We agree that patients should be treated in what the reviewer has called a "relative high-volume hospital" but this is simply not available anywhere in our region.

  Nevertheless, I believe that we are all stating the same things in different ways. Therefore, in an attempt to strike a balance, we have re-worded this sentence to state: "*Most of these high-volume facilities are located in high income nations*". The next sentence: "*Therefore, undergoing resections in local hospitals are often the only options these patients have*" has been deliberately removed. We hope that this satisfies the reviewer.

- Reviewer 1 commented: "Secondly, how to become a high-volume hospital? I think this need a hard and repeated work in learning, training and operation like the authors did. After you can achieve a very good outcomes for these patients, more and more patients might come and ask for your help, and then it will be a high-volume center. Therefore, I think the major problems of this manuscript is that the

authors should provide more detailed data in the part of RESULTS since we should know whether the author's team did a better and better work in this procedure based upon the time from 2013 to 2021. For example, how many procedures performed in every single year from 2013 to 2021, how many complications occurred in every single year from 2013 to 2021, and so on."

We thank the reviewers for this comment. We do agree with the reviewer's comment that hard work and repetition will lead to increased volumes, with time. In our setting patients do not choose to attend this facility. Instead, we have to treat any and all patients who present for care. This explains the high proportion of high-risk patients in our study. But, more to the point, the year-by-year delineation is provided in a new paragraph that has been inserted at the results section, morbidity / mortality sub-section, paragraph 4.

Please note: The volumes will be significantly skewed due to institutional changes during the COVID pandemic. This is explained in the results section, morbidity / mortality sub-section, paragraph 4, line 2-3.

We have also added a table to show the morbidity / mortality that will help the reviewer to view the outcomes at a glance.

- Reviewer 1 commented: "The minor issues: 1. The author recruited a high portion of patients with ASA more than 3 and ECOG more than 2, whether the complications occurred more often in this group of patients?"

  We thank the reviewer for this comment. This is a public (general community) hospital and patients do not choose to attend this facility. Instead, we have to treat any and all patients who present for care. This explains the high proportion of high-risk patients in our study.

  We have included an analysis of patients stratified by their risk as it relates to performance ECOG scores and ASA scores. This now appears in a new paragraph that has been inserted at the results section, morbidity / mortality sub-section, paragraph 5. We have also added a new table (table 5) to show the morbidity / mortality stratified by patient risk that will help the reviewer to view the outcomes at a glance.

- Reviewer 1 commented: "The minor issues: "2. The authors should compare the results in your center to a high-volume center."

  Thank you for this comment. This report comes from the center in the region with the highest volume of pancreatico-duodenectomies. Therefore, any comparisons within the region would be with a lower-volume center. This would not be instructive.

Therefore, we could only compare the results in our center to those in published literature from high-volume centers. In order to do this, we have inserted a new paragraph in the discussion section (discussion section, paragraph 5) that compares our results with published results from high volume centers.

The new paragraph reads: "The 30-day mortality in high-volume centers ranged widely, but most high-volume centers maintained 30-day mortality rates between 4-6%. At 5.5%, our 30-day mortality compared favorably. Similarly, our major morbidity rates compared favorably with high-volume centers reporting figures that ranged from 16% to 26%. Several authors have advocated documentation of procedure-related complications that include pancreatic fistula, delayed gastric emptying, intra-abdominal sepsis and intra-abdominal haemorrhage. In our series the incidence of these procedure-specific complications was acceptable (1.4%, 1.4%, 2.8% and 2.8% of cases respectively).

- Reviewer 1 commented: "The minor issues: "3. The authors mentioned the ICU stay. The patient without complication need a ICU stay of 8 days?"

  We are happy that the reviewer asked this question. This query exactly exemplifies the difficulty working in a resource-poor system.

  Due to institutional limitations in our facility, there is no High Dependency Unit / Step Down Care ward. Therefore, patients discharged from the ICU have to go directly to the general surgical floor. However, in this case, the difference in nursing care and support services between ICU and the general surgical floor is striking. And, to put it bluntly, we do not have confidence that these critical patients will be properly cared for. Therefore, to overcome this limitation, our patients stay in the ICU for a longer period of time to ensure proper support services / nursing care is provided. We are NOT arguing that this is ideal, but it is the reality on-the-ground.

  We have added a sentence to explain this in the results section, clinical outcomes sub-section , paragraph 4, lines 1-3.

  The reviewer made the point that "becoming a relatively high-volume center" requires repeated experience and learning. And, this is exactly what is happening in this hospital. Therefore, one of the purposes of publishing this paper is to highlight these issues so that there is progress. For this reason, we have not changed this comment in the revised version.

- Reviewer #2 commented: 1- Paper needs a good introduction, the introduction section of the manuscript is weak, authors are advised to improvise the introduction section.

  This reviewer has suggested a revised introduction, but they have not voiced any specific concerns. In the absence of specific concerns, we have revised this

section. The introduction clearly states that Whipple's operations should be done ideally in high volume centers, and makes the point that in the West Indies all centers are low volume centers. We then state that the purpose of the paper is to document the clinical outcomes when Whipple's procedures were performed at small numbers in these limited-resource environments. The authors collectively think that this introduction is clear, well-presented and succinct. If the reviewer has a specific objection / concern, we would be happy to address it.

- Reviewer #2 commented: 2- The contributions presented in this manuscript are not sufficient for possible publication in this journal. I highly suggest authors to clearly define the contributions.

  We understand that this reviewer is of the opinion that our work is not sufficient for publication in this journal. While we understand that this is the reviewer's opinion, we respectfully disagree with this assessment.

  This paper documents outcomes when Whipple's procedures were done in a low-volume and resource poor setting. We have made the point that hospital volumes alone should not be used to judge facilities performance. This data adds to the increasing volume of work in the medical literature in support of a facility-specific and audit-based outcomes instead of a case-volume-only assessment.

  The reviewer suggested that we define the contributions. We have clearly defined the contributions in the discussion section at paragraph 9 which reads: "*Whipple's procedure is a complex operation that depends heavily on surgeon experience. At the same time, there is more to experience than technical facility. For example, the experienced surgeon would know how to resect and reconstruct the portal vein when required to achieve negative margins, when not to operate on patients, to recognize aberrant anatomy, how to get out of trouble when complications occur intra-operatively. These can only be learned with experience and proper mentorship."*

  We have also clearly defined the contributions in the discussion section at paragraph 11 which reads: "*multiple factors contributed to the outcomes in our setting: (1) training of unit staff, (2) developing an intimate knowledge of the hospital, (3) fostering teamwork, (4) diligent administration of care, (5) continued audit of outcomes and (6) knowledge of population-based data. We also advocate two experienced surgeons operating to maximize experience. Also, if one surgeon is more experienced it speeds up the learning curve for the second surgeon. The key is overall team experience because, in addition to reducing intraoperative complications, effectively managing post-operative complications is important."*

  Finally, the contributions are further defined in the conclusion which reads: "*This paper adds to the growing body of evidence that volume alone should not be used as a marker of quality for patients requiring Whipple's procedures. Low volume centers in resource poor nations can achieve good short-term outcomes. This is largely due to the process of continuous, adaptive learning by the entire hospital*

and includes: good teamwork, appropriate staff training, due diligence in care administration, continued audit of outcomes and knowledge of the population-based data for the patients you serve."

Collectively, the authors collectively think that this data is clear and well-presented. We stand by the validity of our data and the value of their presentation for publication. If the reviewer has a specific objection / concern that they would like us to consider, we would be happy to address it.

- Reviewer #2 commented: 3- Result and Discussion section is inadequate. Need more attention and better explanation.

  This reviewer has suggested a revised result and discussion section, but they have not voiced any specific concerns. In the absence of specific concerns, we have revised this section to clearly discuss the results of our study. The authors collectively stand by our work. We would be happy to address any concerns if the reviewer has a specific objection and/or suggestion.

- Reviewer #2 commented: 4- I suggest extending the conclusions section to focus on the results you get, the method you propose, and their significance. Overall, I don't think this manuscript is qualified to be published at this time.

  We understand that this is the reviewer's opinion. Our conclusions have been revised to clearly discuss our interpretation of the data in the study. We cannot "extend the conclusions" as the reviewer suggests because this would require extrapolation beyond the data we have collected and presented.

  Collectively, the authors collectively think that this data is clear and well-presented. We stand by the validity of our data and the value of their presentation for publication. If the reviewer has a specific objection / concern that they would like us to consider, we would be happy to address it.

- The editorial office commented: Title: Abbreviations are not permitted. Please spell out any abbreviation in the title.

  Thank you for these comments. There are no abbreviations in the title and so no change has been made.

- The editorial office commented: Running title: Abbreviations are permitted. Also, please shorten the running title to no more than 6 words.

  Thank you for these comments. There are no abbreviations in the running title and the running title is now shorter than six words.

- The editorial office commented: Abstract: Abbreviations must be defined upon first appearance in the Abstract.

  Thank you for these comments. Three abbreviations in the abstract have now been defined upon first appearance in the abstract: ICU, ASA and ECOG.

- The editorial office commented: Key Words: Abbreviations must be defined upon first appearance in the Key Words.

  Thank you for these comments. There are no abbreviations in the key words therefore no changes have been made in response to this comment.

- The editorial office commented: Core Tip: Abbreviations must be defined upon first appearance in the Core Tip.

  Thank you for these comments. There are no abbreviations in the core tip therefore no changes have been made in response to this comment.

- The editorial office commented: Main Text: Abbreviations must be defined upon first appearance in the Main Text.

  Thank you for these comments. We confirm that all abbreviations have been defined upon first appearance in the main text.

- The editorial office commented: Article Highlights: Abbreviations must be defined upon first appearance in the Article Highlights.

  Thank you for these comments. There are no abbreviations in the core tip therefore no changes have been made in response to this comment.

- The editorial office commented: Figures: Abbreviations are not allowed in the Figure title. For the Figure Legend text, abbreviations are allowed but must be defined upon first appearance in the text. For any abbreviation that appears in the Figure itself but is not included in the Figure Legend textual description, it will be defined (separated by semicolons) at the end of the figure legend.

  Thank you for these comments. There are no abbreviations in the figure titles, figure legends or in the figure itself. Therefore, no changes are required in response to this comment.

- The editorial office commented: Tables: Abbreviations are not allowed in the Table title. For the Table itself, please verify all abbreviations used in tables are defined (separated by semicolons) directly underneath the table.

  Thank you for these comments. The abbreviations in the table titles have been removed and the words spelt out in their entirety.

- Science editor commented: "The manuscript has been peer-reviewed, and it' s ready for the first decision. Language Quality: Grade A (Priority publishing). Scientific Quality: Grade C (Good)"

  Thank you for this comment. No changes or corrections are required in response to the Science Editor's comments.

- Company editor-in-chief commented: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

  We thank you for these comments. No change is needed in response to the comments.

- Company editor-in-chief commented: Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

  The original figure documents are provided. The files are arranged in power point, ensuring that all graphs or arrows can be reprocessed by the journal as necessary.

- Company editor-in-chief commented: In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights.

  We confirm that the figure included in this manuscript is an originally generated figure by the authors. Thus, no copyright holder authorizations are needed. We agree with the journal indicating the author's copyright as you see fit.

- Company editor-in-chief commented: Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022.

  We confirm that the figures in this manuscript are original figures generated by the authors. Therefore, I have added the copyright information at the bottom hand right side of the power point file.

- **Company editor-in-chief commented:** Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

  We have provided standard three-line tables that only have a top line, bottom line and column line. All other lines are hidden.

- **Company editor-in-chief commented: Requirements for Article Highlights:** If your manuscript is an Original Study (Basic Study or Clinical Study), the "Article Highlights" section is required. Detailed writing requirements for the "Article Highlights" can be found in the Guidelines and Requirements for Manuscript Revision.

  Thank you. Article highlights have been added as requested.

- Company editor-in-chief commented: Please revise the references according to the Format for References Guidelines, and be sure to edit the reference using the reference auto-analyser.

  All references have been checked so that they are in compliance with the reference guidelines for this journal.

- Company editor-in-chief commented: Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file, and submit as "77700-Figures.pptx" on the system. The figures should be uploaded to the file destination of "Image File". Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Please click to download the sample document:

We have uploaded decomposable figures in which all components are movable and editable and organized them into a single PowerPoint file named77700-Figures.pptx. We confirm that the figures in this manuscript are original figures generated by the authors. Therefore, I have added the copyright information at the bottom hand right side of the power point file.

- Company editor-in-chief commented: Requirements for Tables: Please provide decomposable Tables (in which all components are movable and editable), organize them into a single Word file, and submit as "77700-Tables.docx" on the system. The tables should be uploaded to the file destination of "Table File".

  We have provided decomposable tables in which all components are editable. The tables have been saved in a single word file and names 77700-tables.docx on the system.

- The editorial office commented: please download all the uploaded documents to ensure all of them are correct.

  We have prepared and uploaded the following documents as instructed:

  (1) 77700-Answering Reviewers
  (2) 77700-Audio Core Tip
  (3) 77700-Biostatistics Review Certificate
  (4) 77700-Conflict-of-Interest Disclosure Form
  (5) 77700-Copyright License Agreement
  (8) 77700-Institutional Review Board Approval Form or Document
  (9) 77700-Non-Native Speakers of English Editing Certificate
  (11) 77700-Image File
  (12) 77700-Table File

- The editorial office commented: All authors should accept and sign the Copyright License Agreement (CLA), following the link sent in individual emails to each author. After all authors have accepted and signed their respective CLA, the Corresponding Author is responsible for downloading the signed CLA by clicking on the "Download" button in the CLA page, re-storing it as "PDF", and then uploading it to the file destination of "Copyright License Agreement". If any of the authors do not accept to sign the CLA, the manuscript will not be accepted for publication.

  All co-authors have signed the copyright license agreement. A PDF version of the signed copyright document has been uploaded with the resubmission.

- The editorial office commented: Please click and download the fillable ICMJE Form for Disclosure of Potential Conflicts of Interest (PDF), and fill it in. The Corresponding Author is responsible for filling out this form. Once filled out completely, the Conflict-of-Interest Disclosure Form should be uploaded to the file destination of 'Conflict-of-Interest Disclosure Form'.

  Thank you. We have completed the Disclosure of Potential Conflicts of Interest form and uploaded the form as instructed.

Thank you for the opportunity to submit a revised manuscript.

Best regards
Shamir cawich