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OPEN PEER REVIEW

The Risk Factors of Early Biliary Infection After ^{125}I Particles Stent Implantation in Patients with Malignant Biliary Obstruction

Fei Song, Youquan Niu, Xuelin Li, Jiayin Che, Hao Huang, Yingying Xiang, Ming Huang

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

5 comments · 31 Dec 2023 – 7 Feb 2024

Referee 1 Reviewer

MAJOR REVISION 31 Dec 2023

Thank you for submitting your manuscript to IJR. After carefully reviewing your work, I believe that it requires major revisions before it can be considered for publication. I kindly request that you take the following points into consideration for your next revision:

Abstract

1. Limited Methodology Description: The abstract methods section lacks details about the inclusion/exclusion criteria and data collection methods employed.
2. Lack of Study Design Description: The abstract states that the study is retrospective, but it does not provide any further details about the specific study design, such as a retrospective cohort design.
3. Incomplete Sample Selection Information: The abstract does not provide information about the inclusion and exclusion criteria.
4. Insufficient Description of Data Collection: The abstract does not provide information on how the data were collected and recorded. It is important to describe the specific variables collected, the methods used for data collection (e.g., medical records review, patient interviews), and any measures taken to ensure data accuracy and reliability.
5. Limited timeframe for EBI occurrence monitoring: The abstract mentions that EBI occurrence was monitored within the first 30 days following stent implantation. However, it does not explain the rationale for selecting this timeframe or provide any justification for why events occurring beyond this period were not considered.
6. Incomplete Results Presentation: The abstract results section does not provide the corresponding effect sizes, confidence intervals, or p-values.
7. Clinical implications: While the abstract conclusion mentions the identification of risk factors for early biliary infection (EBI), it does not elaborate on the clinical implications of these findings. Including a brief discussion on how the identified risk factors can impact patient management, guide treatment decisions, or inform preventive measures would make the abstract more informative for clinicians and researchers in the field.
8. Use of jargon and abbreviations: The abstract includes several abbreviations, such as EBI, MBO, PTBD, and ^125I, without providing their full forms or explanations.

Methods

9. Lack of clear study design description: The methods section should provide a clear description of the study design, including the retrospective cohort design.
10. Inadequate description of sample size and selection: The methods section mentions a total of 231 patients who had undergone 125I particle stent implantation, but it does not provide details on how the sample size was determined or how the patients were selected for inclusion in the study.
11. Insufficient details on data collection: The methods section briefly mentions the baseline data collected. However, it lacks information on how these data were collected, including the specific measurements or assessments used.
12. Lack of normality assessment for continuous data: The methods section does not mention whether the assumption of normality was assessed for the continuous data before performing the independent t-test.
13. Insufficient information is provided in the methods section regarding the multivariate logistic regression analysis. The section lacks details about the selection of dependent, independent, and covariate variables for inclusion in the analysis. It is important to clarify how these variables were chosen and which ones were

ultimately included in the model.
Furthermore, the assessment of assumptions such as linearity, independence of observations, and absence of multicollinearity is not described. It is crucial to explain how these assumptions were evaluated and addressed to ensure the validity of the analysis.
Additionally, the methods section should specify the goodness-of-fit measures used to evaluate the overall fit and complexity of the model. It is suggested that information about the Hosmer-Lemeshow test, Akaike information criterion (AIC), and Bayesian information criterion (BIC) and how these measures were utilized to assess the model's performance be included.

Tables
14. Insufficient inclusion of adjusted factors: It is crucial to mention the adjusted variables below the table presenting the multiple logistic regression analysis. Therefore, it is necessary to add the variables below Table 3 to provide a comprehensive understanding of the adjusted factors in the study.

Discussion
15. Lack of clear organization: The discussion section lacks a clear structure and organization. It jumps between different risk factors without providing a cohesive flow of information. It would be beneficial to organize the discussion section into subsections based on each risk factor to improve readability.

I appreciate your attention to these suggestions and look forward to reviewing your revised submission.

Shahram Akhlaghpour Reviewer

MAJOR REVISION 1 Feb 2024

Title:
Reasonable

Abstract:
Acceptable

Introduction:
Too long; unnecessary paragraphs need to be removed, such as:
P3L36-37: Malignant Obstructive Jaundice (MOJ) is not a common term and needs to be removed.
P3L41-47: The description is obvious and not necessary (remove).
The author should explain why the infection rate could differ between I125 seed stenting and regular stenting. No data are provided for this theory or problem. (P4L66-67)

Method:
P4L96: DSA angiography is not used for biliary visualization, and maybe the author means that this work was done in a DSA angiography suite.
P5L97-99: How are the I125 particles attached to the stent? Or do they place an order for manufacturing?
P5L100: Which planning system is used (name, manufacturer)?
The technique is not well described. Fig S2 shows that two stents were placed: one with I125 particles and one bare stent inside it. However, no description of the method was provided, and it's confusing.

Discussion:
Not well structured and needs to focus on what the article tries to say. Needs to be revised.

Fig S1: Not necessary and not informative. Instead, a photograph of a Particle Stent would be more informative.

Mahyar Mohammadifard Reviewer

ACCEPT 5 Feb 2024

Very good article.

Associate Editor

MAJOR REVISION 7 Feb 2024

Reviewer #1:
Title:
Reasonable
Abstract:
Acceptable
Introduction:
Too long; unnecessary paragraphs need to be removed, such as:
P3L36-37: Malignant Obstructive Jaundice (MOJ) is not a common term and needs to be removed.
P3L41-47: The description is obvious and not necessary (remove).
The author should explain why the infection rate could differ between I125 seed stenting and regular stenting. There are no data for this theory or problem. (P4L66-67)
Method:
P4L96: DSA angiography is not used for biliary visualization, and perhaps the author means that this work was done in a DSA angiography suite.
P5L97-99: How are the I 125 particles attached to the stent? Or are the stents ordered from a manufacturer with the particles attached?
P5L100: Which planning system is used (name, manufacturer)?
The technique is not well described. Fig S2 shows that two stents were placed: one with I 125 particles and one bare stent inside it. However, no description of the method was provided, and it is confusing.
Discussion:
Not well structured and needs to focus on what the article tries to say. Needs to be revised.
Fig S1: Not necessary and not informative. Instead, a photograph of a particle stent would be more informative.

Reviewer #2:
This is a retrospective descriptive manuscript about "The risk factors of early biliary infection after 125I particles stent implantation in patients with malignant biliary obstruction". The study has interesting points, but some limitations and defects are noted.
1- This manuscript is more suitable for gastroenterologists, infectious disease specialists, and IR specialists. It has few radiologic points and does not fully fit the scope of the Iranian Journal of Radiology.
2- There is not enough novelty in this study. It is clear that more foreign bodies and more stents carry a greater risk of infection, especially in diabetic patients and with more traumatic interventional procedures.
3- The study is retrospective, with a limited number of cases.
5- It is not clear whether prophylactic antibiotics were used for patients.
6- It is not clear whether patients with previous PTBD were evaluated for wound infection at the skin insertion site and silent infection in the catheter.
7- Many other important risk factors for EBI are ignored in this study, such as the time of onset of malignancy, patient weight loss and malnutrition, immunosuppression, previous chemotherapy, and any other treatment before PTBS.

Reviewer #3:

Thank you for submitting your manuscript to IJR. After carefully reviewing your work, I believe that it requires major revisions before it can be considered for publication. I kindly request that you take the following points into consideration for your next revision:

Abstract

1. Limited Methodology Description: The abstract methods section lacks details about the inclusion/exclusion criteria and data collection methods employed.
2. Lack of Study Design Description: The abstract states that the study is retrospective, but it does not provide any further details about the specific study design, such as a retrospective cohort design.
3. Incomplete Sample Selection Information: The abstract does not provide information about the inclusion and exclusion criteria.
4. Insufficient Description of Data Collection: The abstract does not provide information on how the data were collected and recorded. It is important to describe the specific variables collected, the methods used for data collection (e.g., medical records review, patient interviews), and any measures taken to ensure data accuracy and reliability.
5. Limited timeframe for EBI occurrence monitoring: The abstract mentions that EBI occurrence was monitored within the first 30 days following stent implantation. However, it does not explain the rationale for selecting this timeframe or provide any justification for why events occurring beyond this period were not considered.
6. Incomplete Results Presentation: The abstract results section does not provide the corresponding effect sizes, confidence intervals, or p-values.
7. Clinical implications: While the abstract conclusion mentions the identification of risk factors for early biliary infection (EBI), it does not elaborate on the clinical implications of these findings. Including a brief discussion on how the identified risk factors can impact patient management, guide treatment decisions, or inform preventive measures would make the abstract more informative for clinicians and researchers in the field.
8. Use of jargon and abbreviations: The abstract includes several abbreviations, such as EBI, MBO, PTBD, and ^125I, without providing their full forms or explanations.

Methods

9. Lack of clear study design description: The methods section should provide a clear description of the study design, including the retrospective cohort design.
10. Inadequate description of sample size and selection: The methods section mentions a total of 231 patients who had undergone 125I particles stent implantation, but it does not provide details on how the sample size was determined or how the patients were selected for inclusion in the study.
11. Insufficient details on data collection: The methods section briefly mentions the baseline data collected. However, it lacks information on how these data were collected, including the specific measurements or assessments used.
12. Lack of normality assessment for continuous data: The methods section does not mention whether the assumption of normality was assessed for the continuous data before performing the independent t-test.
13. Insufficient information is provided in the methods section regarding the multivariate logistic regression analysis. The section lacks details about the selection of dependent, independent, and covariate variables for inclusion in the analysis. It is important to clarify how these variables were chosen and which ones were ultimately included in the model.

Furthermore, the assessment of assumptions such as linearity, independence of observations, and absence of multicollinearity is not described. It is crucial to explain how these assumptions were evaluated and addressed to ensure the validity of the analysis.

Additionally, the methods section should specify the goodness-of-fit measures used to evaluate the overall fit and complexity of the model. It is suggested that information be included about the Hosmer-Lemeshow test, Akaike information criterion (AIC), and Bayesian information criterion (BIC) and how these measures were

utilized to assess the model's performance.
Tables
14. Insufficient inclusion of adjusted factors: It is crucial to mention the variables adjusted for below the table presenting the multiple logistic regression analysis. Therefore, it is necessary to add the variables below Table 3 to provide a comprehensive understanding of the adjusted factors in the study.
Discussion
15. Lack of clear organization: The discussion section lacks a clear structure and organization. It jumps between different risk factors without providing a cohesive flow of information. It would be beneficial to organize the discussion section into subsections based on each risk factor to improve readability.
I appreciate your attention to these suggestions and look forward to reviewing your revised submission.

Editor-in-Chief MAJOR REVISION 7 Feb 2024

Dear authors,
Your article needs Major Revision.
Regards

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Response to reviewers

Thank you for giving us the opportunity to submit a revised draft of the manuscript “The risk factors of early biliary infection after 125I particles stent implantation in patients with malignant biliary obstruction” for publication in the Iranian Journal of Radiology. We appreciate the time and effort that editor and reviewers dedicated to providing feedback on our manuscript and are grateful for the insightful comments on and valuable improvements to our paper. We have incorporated most of the suggestions made by the reviewers. Those changes are highlighted in red within the revised manuscript. Please see below, in red, for a point-by-point response to the reviewers’ comments and concerns. All line numbers refer to the revised manuscript.

Reviewers' Comments:

Reviewer 1:

Thank you for submitting your manuscript to IJR. After carefully reviewing your work, I believe that it requires major revisions before it can be considered for publication. I kindly request that you take the following points into consideration for your next revision:

Abstract

1. Limited Methodology Description: The abstract methods section lacks details about the inclusion/exclusion criteria, and data collection methods employed.

Response: Thank you for your feedback. Due to abstract word constraints, details on inclusion/exclusion criteria and data collection methods are provided in the Methods section (line 93-98).

2. Lack of Study Design Description: The abstract states that the study is retrospective, but it does not provide any further details about the specific study design such as retrospective cohort.

Response: We appreciate your feedback. The study design has been clarified including retrospective cohort in the revised abstract (line 11-14).

3. Incomplete Sample Selection Information: The abstract does not provide information about the inclusion and exclusion criteria.

Response: Thank you for your feedback. Due to abstract word constraints, details on inclusion/exclusion criteria and data collection methods are provided in the Methods section (line 93-98).

4. Insufficient Description of Data Collection: The abstract does not provide information on how the data were collected and recorded. It is important to describe the specific variables collected, the methods used for data collection (e.g., medical records review, patient interviews), and any

measures taken to ensure data accuracy and reliability.

Response: Thank you for your feedback. In response, we have added detailed information on data collection in the Methods section (line 101-108) due to abstract word constraints.

Patients included in the study underwent routine preoperative comprehensive assessments, including blood cell analysis, coagulation function tests, electrocardiography, liver and kidney function assessments, electrolyte analysis, abdominal computed tomography, magnetic resonance imaging, and magnetic resonance cholangiopancreatography. The baseline data, including sex, age, liver function (TBIL, DBIL, AST, ALT, and ALB), blood routine (WBC, HGB, and PLT), coagulation function (PT and APTT), comorbidity (DM and gallstones), obstruction location, and tumor types were collected.

5. Limited timeframe for EBI occurrence monitoring: The abstract mentions that EBI occurrence was monitored within the first 30 days following stent implantation. However, it does not explain the rationale for selecting this timeframe or provide any justification for why events occurring beyond this period were not considered.

Response: Thank you for the valuable feedback. The decision to monitor EBI within the initial 30 days post-stent implantation is consistent with clinical norms, emphasizing the critical early period when infectious complications are most prevalent. This timeframe was selected to enable a focused assessment of immediate postoperative events, optimizing the potential for timely intervention. Corresponding explanation has been mentioned in the abstract (line 14-15) and methods (line 140-142) sections.

6. Incomplete Results Presentation: The abstract results section does not provide the corresponding effect sizes, confidence intervals, or p-values.

Response: Thank you for your constructive feedback. In response, we have included the corresponding confidence intervals and p-values in the revised results section of the abstract (line 19-31).

7. Clinical implications: While the abstract conclusion mentions the identification of risk factors for early biliary infection (EBI), it does not elaborate on the clinical implications of these findings. Including a brief discussion on how the identified risk factors can impact patient management, guide treatment decisions, or inform preventive measures would make the abstract more informative for clinicians and researchers in the field.

Response: Thank you for your insightful feedback. In response, we have expanded the abstract conclusion to include a brief discussion on the clinical implications of the identified risk factors for EBI (line 36-38).

These risk factors can offer guidance to minimize post-^{125}I particle stent implantation biliary infection, thereby shortening hospitalization for affected

patients.

8. Use of jargon and abbreviations: The abstract includes several abbreviations, such as EBI, MBO, PTBD, and ^125I, without providing their full forms or explanations.

Response: Thank you for highlighting this. We have included explanations for abbreviations like EBI, MBO, PTBD, and ^125I in the abstract (line 6-38).

Methods

9. Lack of clear study design description: The methods section should provide a clear description of the study design, including the retrospective cohort design.

Response: Thank you for your feedback. We have clarified the study design, specifically highlighting the retrospective cohort design, in the revised methods section (line 90-100). A visual representation is also provided in Figure 1 for better clarity (line 447-450).

10. Inadequate description of sample size and selection: The methods section mentions a total of 231 patients who had undergone 125I particles stent implantation, but it does not provide details on how the sample size was determined or how the patients were selected for inclusion in the study.

Response: Thank you for your feedback. We have clarified the rationale for sample size determination and the inclusion/exclusion criteria in the methods section (line 90-100). Additionally, a flow chart illustrating the retrospective cohort design is provided in Figure 1 for clarity (line 447-450).

11. Insufficient details on data collection: The methods section briefly mentions the baseline data collected. However, it lacks information on how these data were collected, including the specific measurements or assessments used.

Response: Thank you for the feedback. In response, we have provided additional details in the methods section, specifying that baseline data were collected through comprehensive preoperative analyses, including blood cell analysis, coagulation function tests, electrocardiography, liver and kidney function assessments, electrolyte analysis, abdominal computed tomography, magnetic resonance imaging, and magnetic resonance cholangiopancreatography (line 101-108).

12. Lack of normality assessment for continuous data: The methods section does not mention whether the assumption of normality was assessed for the continuous data before performing the independent t-test.

Response: Thank you for your feedback. In response, we have incorporated a normality assessment for continuous data in the methods section (line 155-157), and for normally distributed metric data, we conducted the independent

t-test, expressing the results as mean ± standard deviation.

13. Insufficient information is provided in the methods section regarding the multivariate logistic regression analysis. The section lacks details about the selection of dependent, independent, and covariate variables for inclusion in the analysis. It is important to clarify how these variables were chosen and which ones were ultimately included in the model.

Response: We appreciate your feedback. The methods section now includes additional details on the multivariate logistic regression analysis, specifying the criteria for variable selection and listing the included variables (line 158-172).

This study classifies risk factors associated with EBI into two categories: patient-related and surgical-related factors. Patient-related factors encompass sex, age, gallstones in the gallbladder or bile ducts, types of malignant tumor, obstruction location (low or high), comorbidities (such as diabetes), preoperative liver function, blood routine, prothrombin time (PT), activated partial thromboplastin time (APTT), and postoperative intrahepatic pneumobilia. Surgical factors include ^{125}I particle numbers, intraoperative biliary bleeding, PTBD, time from PTBD to ^{125}I sent implantation (days), time from jaundice to ^{125}I sent implantation (days), and drainage tube removal. Univariate logistic regression analysis was employed to identify potential risk factors influencing postoperative EBI, with those having $P < 0.05$ subsequently subjected to multivariate logistic regression analysis to identify independent risk factors for EBI after ^{125}I particle stent placement. IBM SPSS 25.0 statistical software was used for data analysis, considering $P < 0.05$ as statistically significant and reporting results with a 95% confidence interval.

Furthermore, the assessment of assumptions such as linearity, independence of observations, and absence of multicollinearity is not described. It is crucial to explain how these assumptions were evaluated and addressed to ensure the validity of the analysis.

Response: Thank you for your feedback. Observations exhibit independence. We employed both univariate and multivariate logistic regression analyses to identify potential risk factors influencing postoperative EBI, with detailed methods outlined in the Statistical analysis section (line 166-172).

Additionally, the methods section should specify the goodness-of-fit measures used to evaluate the overall fit and complexity of the model. It is suggested to include information about the Hosmer-Lemeshow test, Akaike information criterion (AIC), and Bayesian information criterion (BIC) and how these measures were utilized to assess the model's performance.

Response: This study mainly employed univariate and multivariate logistic regression analyses to identify independent risk factors for EBI following ^{125}I particle stent placement. As no model construction was pursued, goodness-of-

fit measures were not implemented. Subsequent investigations will delve into more extensive analyses.

Tables

14. Insufficient inclusion of adjusted factors: It is crucial to mention the adjusted variables below the table in multiple logistic regression analysis. Therefore, it is necessary to add the variables below Table 3 to provide a comprehensive understanding of the adjusted factors in the study.

Response: Thank you for your insightful suggestion. Table 3 presents the results of the multivariate logistic regression analysis, where only risk factors with a significance level of $P < 0.05$ in the univariate logistic regression analysis are included. This study classifies risk factors associated with EBI into two categories: patient-related and surgical-related factors. Patient-related factors encompass sex, age, gallstones in the gallbladder or bile ducts, types of malignant tumor, obstruction location (low or high), comorbidities (such as diabetes), preoperative liver function, blood routine, prothrombin time (PT), activated partial thromboplastin time (APTT), and postoperative intrahepatic pneumobilia. Surgical factors include 125I particle numbers, intraoperative biliary bleeding, PTBD, time from PTBD to 125I sent implantation (days), time from jaundice to 125I sent implantation (days), and drainage tube removal. Univariate logistic regression analysis was employed to identify potential risk factors influencing postoperative EBI, with those having $P < 0.05$ subsequently subjected to multivariate logistic regression analysis to identify independent risk factors for EBI after 125I particle stent placement.

Discussion

15.Lack of clear organization: The discussion section lacks a clear structure and organization. It jumps between different risk factors without providing a cohesive flow of information. It would be beneficial to organize the discussion section into subsections based on each risk factor to improve readability.

Response: Thanks for your feedback. We have organized the discussion section by introducing subsections for each risk factor (line 222-296).

I appreciate your attention to these suggestions and look forward to reviewing your revised submission.

Response: Thank you for your thoughtful suggestions. We have carefully addressed your suggestions in our revision and hope it meets with your approval.

Reviewer 2:

This is a retrospective descriptive manuscript about "The risk factors of early biliary infection after 125I particles stent implantation in patients with malignant biliary obstruction".The study have interesting points but some

limitations and defects are noted.

1- This manuscript is more suitable for gastroenterologist, infectious disease specialist and IR so for iranian journal of radiology, this subject has minor radiologic points and not completely correlate.

Response: Thank you for your feedback. The ^{125}I particles stent implantation belongs to the radiotherapy treatment planning system. This study explored the risk factors of early biliary infection after ^{125}I particles stent implantation in patients with malignant biliary obstruction. Therefore, our study aligns with the scope of the Iranian Journal of Radiology.

2- There is not enough novelty is this study. It is clear that more foreign bodies and more stents have more risk for infections esp. in diabetic patients and more traumatic interventional procedures.

Response: Thank you for your feedback. We acknowledge that our study relies on single-center data, which may limit the consideration of risk factors. However, we have analyzed the most significant risk factors, encompassing both patient-related (e.g., sex, age, gallstones, tumor types, obstruction location, comorbidities, preoperative liver function, blood parameters, and postoperative intrahepatic pneumobilia) and surgical-related factors (e.g., 125I particle numbers, intraoperative biliary bleeding, PTBD, time intervals, and drainage tube removal). We have discussed the relevant limitations in the Discussion section (line 293-296).

3- The study is retrospective with limited cases.

Response: Thank you for your constructive feedback. We acknowledge the limited cases of our study, which is based on data collected from a single center between January 2014 and December 2020. The limitation of a relatively small sample size has been mentioned in the discussion section (line 292-293).

4- It is not clear that prophylactic antibiotic was used for patients or not.

Response: Thank you for your feedback. The use of prophylactic antibiotics has been clarified in the methods section (line 143-152).

For patients who develop EBI after ^{125}I particle stent placement, if the PTBD drainage tube is not removed, biliary drainage can be performed through the PTBD drainage tube to control EBI. In cases of EBI, early administration of antibiotics is recommended. In our hospital, broad-spectrum antibiotics such as cefmetazole, cefoperazone-sulbactam, cefotiam, and piperacillin-tazobactam are used based on clinical experience until the results of drug sensitivity tests are available. Following the availability of sensitivity results, antibiotic therapy is adjusted accordingly. In cases where infection control is inadequate, and there is a tendency for worsening EBI, potent antibiotics like meropenem are employed. In this study, among 35 patients with EBI, appropriate anti-inflammatory treatment effectively controlled biliary infections.

5- It is not clear that for patients with previous PTBD, Wound infection at skin insertion point and silent infection in catheter were evaluated or not.

Response: Thank you for your comment. Patients with previous PTBD has been excluded from our study, as outlined in our exclusion criteria (line 94-98). Therefore, evaluations for wound infection at the skin insertion point and silent infection in the catheter were not applicable to the scope of this research.

7-Many other important risk factors for EBI are ignored in this study, such as Time of onset of malignancy, patient weight loss and malnutrition, immunosuppression, previous chemotherapy and any other treatment before PTBS.

Response: Thank you for your feedback. We acknowledge that our study relies on single-center data, which may limit the consideration of risk factors. However, we have analyzed the most significant risk factors, encompassing both patient-related (e.g., sex, age, gallstones, tumor types, obstruction location, comorbidities, preoperative liver function, blood parameters, and postoperative intrahepatic pneumobilia) and surgical-related factors (e.g., 125I particle numbers, intraoperative biliary bleeding, PTBD, time intervals, and drainage tube removal). We have discussed the relevant limitations in the Discussion section (line 293-296).

Reviewer 3:
Very good article

Response: Thank you for your positive feedback on the article. We appreciate your encouraging comments.

Reviewer 4:
Title:
Reasonable

Abstract:
Acceptable

Introduction:
Too long and needs to remove unnecessary paragraphs such as :
P3L36-37: Malignant Obstructive Jaundice (MOJ) is not a common term and needs to remove

Response: Thank you for your input. We have removed unnecessary sections, including the mention of "Malignant Obstructive Jaundice," as per your suggestion (line 44).

P3L41-47: Description is obvious and not necessary (remove)
Response: We have streamlined the description at line 48-53.

The author should explain why the infection rate could be different between I125 seed Stent with regular stenting. No data for this theory or problem. (P4L66-67)
Response: The difference in infection rates between ^{125}I seed stents and regular stenting may be attributed to the antimicrobial properties of the integrated ^{125}I and variations in stent composition, design, or material. Corresponding explanation has been described in the Introduction section (line 72-74).

Method:
P4L96: DSA angiography is not used for Biliary visualization and maybe the author wants to say that this work has been done in a DSA Angiography suit.
Response: Thank you for your feedback. PTBD was performed to determine the location and length of obstruction in the bile duct under the digital subtraction angiography suite, which has been clarified in the Methods section (line 110-111).

P5L97-99: How the I 125 particles are attached to the stent? Or do they order for manufacturing?
Response: Thank you for your inquiry. The ^{125}I particles stents were ordered from the manufacturer (Micro-Tech (Nanjing) Co., Ltd, Nanjing, China). We have mentioned the source of ^{125}I particles stents in the Methods section (line 125).

P5L100: Which planning system is used (name, manufacturer?..)
Response: The treatment planning system employed in our study is the radiotherapy treatment planning system (HGGR-2000; Hokai Medical Instruments, Zhuhai, China) (line 120-121).

The technique is not well described. Fig S2 describes that two stents were placed one with I 125 particles and one bare stent inside it. However, no description of the method was provided and it's confusing.
Response: Thank you for your input. We have added a detailed description of the ^{125}I particle stent implantation method in the Methods section to address the confusion highlighted in Fig S2 (line 110-134).

Discussion:
Not well structured and needs to focus on what the article tries to say. Need to be revised.
Response: Thank you for your feedback. We have restructured the Discussion

section and added subheadings to enhance clarity and focus (line 209-296).

Fig S1: Not necessary and not informatics. Instead, a photograph of a Particle Stent is more informatics.

Response: Thank you for your feedback. We have removed the original Fig S1 and replaced it with a photograph of the ^{125}I particles stent (line 468).

2 Revision 1

3 comments · 2 Apr 2024 – 21 Apr 2024

Referee 1 Reviewer

ACCEPT 2 Apr 2024

I have thoroughly reviewed the revised version of the manuscript, and it is evident that the authors have appropriately addressed all comments. The revised methodology section provides a more detailed explanation of the research design, data collection procedures, and statistical analysis, significantly enhancing the study's transparency and reproducibility.
Furthermore, the discussion section has been significantly improved, effectively addressing study limitations and suggesting avenues for future research. The conclusions drawn are well-supported by the data, and the implications of the findings are appropriately discussed.
Therefore, from a methodological standpoint, I believe this manuscript is suitable for publication in IJRadiology.

Associate Editor

ACCEPT 14 Apr 2024

accept

Editor-in-Chief

MINOR REVISION 21 Apr 2024

Dear authors,
Your article needs Minor Revision.
Regards

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear editor and reviewers,

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "**The risk factors of early biliary infection after ^{125}I particles stent implantation in patients with malignant biliary obstruction"** again. We are encouraged that Reviewer 1 believes that "this manuscript is suitable for publication in the IJRadiology". Moreover, Reviewer 2 and Associate Editor 2 provide some minor revisions to improve our paper. We have revised the manuscript as suggested by the reviewer/editor. The point-by-point answers to the comments are listed as below, and we hope it can be acceptable for publication in the journal.

Reviewers' comments

Reviewer 1:

Based on the methodology standpoint, I believe this manuscript is suitable for publication in the IJRadiology.

Response: Thank you for appreciating our study by a very positive opinion recommending the publication in the IJRadiology.

Reviewer 2:

Please cite references in sequential order in the manuscript. (the references 28,29 cited after 30).

Response: Thank you very much for your careful work. We have adjusted the order of the literature citations as requested. Please see the re-uploaded manuscript for details.

Please cite figures in sequential order in the manuscript. (the fig S1 cited after fig S2).

Response: We have modified it. Please see the re-submitted manuscript.

Thank you again for your input. We apologize for any errors, which were caused by an oversight in preparing the manuscript. We hope that this revision will meet the requirement of the journal.

Associate Editor's Comments

Associate Editor 1:

Accept.

Response: Thanks for your consideration and input. We are pleased to see this positive feedback.

Associate Editor 2:

Thanks to authors for sending their paper to IJR. please address following points:

Response: Thanks for your important suggestions to help us to enhance this work. Following are the point-by-point response to your comments.

1-it is better to mention the full term of abbreviations in abstract in first usage; for example, CI in line 21 of abstract.

Reply: We have modified it.

2-line 45, what is perbilirubinemia? I think it is hyperbilirubinemia.

Reply: Thanks for your hard work. We have changed it to "**hyperbilirubinemia**".

3-line 46, please correct meat analysis to meta-analysis.

Reply: We have revised it.

4-in line 64 and 281 and 289, please change MOB to MBO.

Reply: We have revised.

5-in line 68-9, I think better version is: "Since EBI is a driver of cholangitis, cholecystitis, liver abscess, and other hepatobiliary tract infections, it seriously threats the health and life of patients (12)" please correct if I am right.

Reply: We have corrected it as suggested.

6-what is MOG in line 71?

Reply: Thank you very much for your careful work. We have checked the cited literature and found that the "MOG" is wrong. The correct content is "malignant obstructive jaundice (**MOJ)**".

7-the following sentence has been added in a wrong place. It has interrupted two conceptually related sentences: "The difference in infection rates between 125I seed stents and regular stenting may be attributed to the antimicrobial properties of the integrated 125I and variations in stent composition, design, or material." This sentence should be transferred to another place. [for example such version: line 66: Early biliary infection (EBI) is a common early postoperative complication of PTBS, presenting the symptoms of shiver, fever, and even septic shock (11) that is lower in 125I seed stents compared to regular stents. The reason may be attributed to the antimicrobial properties of the integrated 125I and variations in stent composition, design, or material.]

Reply: Thanks for your kind comment. The rewritten sentences are as follows:

"Early biliary infection (EBI) is a common early postoperative complication after PTBS, which manifests as shiver, fever, and even septic shock, posing a serious threat to the health and life of patients (11). A previous study reported that ^{125}I particles stent implantation to be superior to conventional stents in reducing the risk of EBI, possibly due to the antimicrobial properties of the integrated ^{125}I and variations in stent composition, design, or material (12)."

8-please add objective part to paper before method section.

Reply: We have added this part. The new added contents are as follows:

"2. Objectives

This study aims to reveal potential risk factors of EBI after ^{125}I particles stent implantation, providing guidance for clinical treatment of MBO."

9-please change method title to patients and methods.

Reply: We have changed it.

10-please add sequential numbers to titles: 1-Backgrounds, 2-Objectives, 3-Patients and Methods, 3-1-Subjects, …..

Reply: We have changed the format of the article as requested.

11-it is better to mention full term of lab tests abbreviations [lines 105-8]

Reply: Thanks for your careful work. We have added the full name of abbreviations. As follows:

Liver function (total bilirubin [TBIL], direct bilirubin [DBIL], aspartate aminotransferase [AST], alanine aminotransferase [ALT], albumin [ALB]); blood routine (white blood cells (WBC), hemoglobin [HGB], and platelets [PLT]), coagulation function (prothrombin time [PT] and activated partial thromboplastin time [APTT]), comorbidity (diabetes mellitus [DM]).

12-line 170, this part is repetitive and could be deleted: “IBM SPSS 25.0 statistical software was used for data analysis”.

Reply: We have deleted this sentence.

13-thi spart seems wrong in writing: “….. tumor types were not significant different between non-EBI and EBI groups.”

Reply: We have modified this sentence to “**there were no significant differences** in … tumor types between non-EBI and EBI groups”.

14-what is the meaning of “high obstruction” in line 203-4.

Reply: Thank you very much for your valuable comment. In our article, high and low refer to the location of the obstruction. Specifically, obstruction that occurs above the opening of the cystic duct is considered high-level, while one below the opening of the cystic duct is considered low-level. To avoid confusion, we have modified it to “high-level obstruction”.

15-please delete sub-titles in discussion such as: “Diabetes as a risk factor for EBI after

125 I particle stent implantation" …..

Reply: We have deleted them.

16-in line 255 this part is unclear: "multiple branches of high obstruction …."

Reply: Thanks for your careful work. We have changed this sentence to "High-level biliary obstruction is characterized by insidious onset and special anatomical location, which may lead to an increased risk of stent implantation and predispose to a variety of complications, such as EBI".

17-line 263 please replace the word of elevate with increase.

Reply: As suggested, we have changed it.

18-you have used several times the word proactive that seems not to be meaningful. [for example in line 289]. I think it should be protective not proactive.

Reply: Thanks for your careful work. It is indeed "protective" and we have modified it.

19-in table 1 footnote, ATS is wrong. It is AST.

Reply: We have modified it.

20-Please cite references in sequential order in the manuscript. (the references 28,29 cited after 30)

Reply: We have adjusted the order of the cited references.

21-Please cite figures in sequential order in the manuscript. (the fig S1 cited after fig S2).

Reply: We have revised it.

Thank you again for your careful work. We apologize for any errors. We hope that the changes we made in this time will provide a more complete manuscript and meet the requirements of the journal.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we did not list the changes but used track changes in revised paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Sincerely,

3 Revision 2

1 comment · 20 May 2024

Editor-in-Chief

ACCEPT 20 May 2024

Dear authors,
Your article is acceptable for publication in IJR.
Regards