

Reply to the Reviewer #1' comments

Review #1

Q1: The review was not registered in a register for systematic review, such as PROSPERO.

R1: Thank you very much for your professional comments. Considering your kindly reminder, this review has been submitted for registration on PROSPERO and is awaiting review.

Q2: The search for eligible papers has to be updated. The last one was performed one year ago.

R2: We appreciate you for such careful comments. In order to further improve the reliability of the conclusion and include all relevant papers as much as possible, we also conducted a further search for relevant articles published in the past year. However, we found that there are no high-quality clinical studies that meet the inclusion criteria of this study. In our present study, we aimed to focus on the clinical efficacy and safety of intraluminal Iodine-125 (¹²⁵I) seeds brachytherapy for malignant biliary obstruction, and the diseases targeted by our study were clinically common, but the brachytherapy stent itself was a relatively small area, which led to fewer related clinical studies. In the follow-up work, we will continue to pay attention to this field, aiming to provide new effective treatment strategies for the clinical treatment of malignant biliary obstruction.

Q3: Many of the results of the review are based on forest plots consisting of very few studies. I can see forest plots with 5, or even 3 or 2 studies. One cannot draw strong conclusions as the authors did with such low level of evidence.

R3: Many thanks for such a professional comment. Indeed, as you said, there are fewer studies included in forest plots, which was largely due to the fact that there were fewer studies included in this study. At present, clinical studies focusing on the efficacy and safety of intraluminal Iodine-125 (¹²⁵I) seeds brachytherapy for malignant biliary obstruction are relatively limited. And not all of the included studies

contain the outcomes that we are interested in. In fact, our study has consisted all retrieved papers that meet the criteria for inclusion and exclusion. If other latest researches can be consisted later, it will be more helpful to draw stronger conclusions. In addition, we also find that many studies are similar to our present study^[1-3], and they draw the conclusion based on forest plots consisting relatively few studies for meta-analysis as well, and got reliable conclusions. We believe that our conclusions are based on strict standardized analyses, and the conclusions could play a certain role in clinical guidance. In order to obtain more reliable conclusions, we will continue to focus on this research field and consist more high-quality researches in the subsequent analysis. Thank you very much for your professional and careful review.

References

1. Crippa S, Cirocchi R, Partelli S, et al. Systematic review and meta-analysis of metal versus plastic stents for preoperative biliary drainage in resectable periampullary or pancreatic head tumors. *Eur J Surg Oncol*. 2016. 42(9): 1278-85.
2. Duan F, Cui L, Bai Y, Li X, Yan J, Liu X. Comparison of efficacy and complications of endoscopic and percutaneous biliary drainage in malignant obstructive jaundice: a systematic review and meta-analysis. *Cancer Imaging*. 2017. 17(1): 27.
3. Yu Q, Liu C, Raissi D. Balloon-occluded Retrograde Transvenous Obliteration Versus Transjugular Intrahepatic Portosystemic Shunt for Gastric Varices: A Meta-Analysis. *J Clin Gastroenterol*. 2021. 55(2): 147-158.