

Response:

We thank the reviewers for their valuable comments and suggestions for improving our manuscript. We have carefully corrected the manuscript following reviewers' suggestions. We provide point-to-point response to their questions below.

Reviewer 1

Review of the ms "Is Endoscopic Papillary Balloon Dilatation (EPBD) Really a Risk Factor for Post-ERCP Pancreatitis?" by Toshio Fujisawa et al. The aims of this review paper were to summarize the literature data on the efficacy of endoscopic papillary balloon dilatation / endoscopic papillary large balloon dilatation, and to re-evaluate the incidence of post-ERCP pancreatitis following EPBD. The manuscript presents a well-stated hypothesis and its clear debate: the authors suggest that balloon dilatation itself does not cause PEP, but the procedures accompanying insufficient dilatation of the papilla can indeed induce PEP. In this respect the work is timely and reasonably discussed, I found that it read quite well, was well organized/presented and well cited.

Response:

We appreciate the reviewer for carefully reviewing our manuscript. We are very glad for you to understand the meaning of our manuscript.

Reviewer 2

The paper by Fujisawa et al on technical aspects of endoscopic papillary balloon dilatation (EPBD) and its pros and cons, is a well written, analysed and detailed review. The authors convince us that EPBP is an effective method to remove bile stones without sphincterotomy. The authors suggest that if the papilla is dilated sufficiently (ballooning size > stone size, at least 8 mm with sufficient pressure for opening the waist; and ballooning time > 60 seconds) and a prophylactic pancreatic stent is placed, the post ERP pancreatitis is prevented and other complications of ERCP are decreasing. I have some minor comments Page 8 "A total of 13 RCTs was included in the analysis". References of 13 RCT are needed Page 9 "3 RCT", "3 RCT" etc References of 3 RCT are needed Page 9

Response:

We thank the reviewer for his/her valuable suggestions. We added all references that the reviewer suggested on page 8, 9, and 10.

"There was no obvious difference in EPBD procedures between the significant group

and the non-significant group” Please define the significant and the non significant groups.

Response:

The definition of “the significant and the non-significant groups” was stated on page 9, line 1. “one group that showed significant differences in the PEP rate between EPBD and EST (significant group)^[2, 33, 34], and another group that did not (non-significant group)^[13, 22, 25, 35-41]”

Page 14 “Among the 10 EPLBD studies in Table 3, six and four studies used the stone size and waist disappearance approaches, respectively” Which studies?

Response:

We added the references that the reviewer suggested on page 15.

Six studies using the stone size are ref. 42, 44, 45, 47, 50, and 51.

Four studies using the waist disappearance are ref. 43, 46, 48, and 49.

Reviewer 3

There’s a lot of debate about whether EPBD could be used for the prevention from early complications of ERCP. The safety of EPBD has been widely questioned because of a high incidence of PEP. Thus, how to improve the safety and efficacy of EPBD becomes particularly important. In this review, the authors compared EPBD with EST in 13 randomised control trials, and direct EPLBD with EST in 10 studies, separately. They found that the incidence of PEP in EPBD was higher than that in EST in 3 RCT. But longer and higher-pressure inflation of balloons might decrease the incidence of PEP. This review investigated an interesting medical problem. Overall, the article has been selected carefully. However, there are still some defects. First, in the authors’ opinion, EPBD could decrease the early complications of ERCP, including bleeding, biliary infection and perforation. But, the effects on the incidence of biliary infection and perforation are not consistent.

Response:

We appreciate the reviewer for valuable comments. We admit what the reviewer suggested. Table 1 contains several controversial points. Therefore, they have “?” at the end in the table, and especially for biliary infection and perforation, we have directly stated “Effects on the rates of perforation and biliary infection, however, are not consistent among the reports^[9-12]” on page 6, line 14-15.

Second, EPBD with small-calibre balloons increases the incidence of PEP while EPLBD

does not. The possible mechanisms of the paradoxical results should be discussed more. The authors speculated the reason is insufficient papillary dilatation. Is there any other probable reason?

Response:

We added the statement about the reasons generally suggested on page 11, line 2-6. "In the past reports, three reasons were suggested^[4]. First, frequency of MLT use is decreased in EPLBD. Second, patients who receive EPLBD are relatively older. Younger age is supposed to be a risk factor of PEP^[52]. Third, EPLBD makes selective cannulation into the bile duct easier and decreases incorrect cannulation and injection into the pancreatic duct."