Reviewer’s report

Title: The prognostic importance of jaundice in surgical resection with curative intent for gallbladder cancer

Version: 2 Date: 11 June 2014

Reviewer: Perry Shen

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This is one of the largest series evaluating the prognostic importance of jaundice in surgical resection with curative intent for gallbladder cancer. The conclusion that jaundice is indicative of worse prognosis but not a surgical contraindication corroborates findings from other studies 9 (Reference 4).

However, we would recommend some minor essential revisions as listed below:

Introduction, paragraph 2 (line 20, page 4): Need to cite reference

Methods, paragraph 2 (line 7, page 5): Not sure if we can make the deduction from the reference (4) cited

Under operative procedure, paragraph 3 (line 18, page 6): “The surgical resection was considered…” is inconsistent with the comment above regarding R0, R1 resections being considered curative resection (in the Materials and Methods section).

For extrahepatic bile duct resection (Operative procedure, line 70), do you perform intraoperative frozen section of cystic duct margin to determine if extrahepatic bile duct resection is needed?

Operative procedure, paragraph 4 (line 24, page 6): Please elaborate on intraoperative chemotherapy

Under Results, Table 1 and Table 4, please change p= 0.000 to p<0.001

Results paragraph 5 (line 15, page 8): Please classify/grade classifications using Clavien-Dindo classification etc.

Results paragraph 5 (line 21, page 8): Change “mortality” to morbidity

Results paragraph 7 (line 2, page 9): Change “mortality” to morbidity

Results paragraph 8 (line 27, page 9) “Patients who underwent RO resection had a longer 5-year survival than those undergoing R1 resection (p<0.001). This statement is inconsistent with the comment above regarding R0, R1 resections being considered curative resection (in the Materials and Methods section).

Would recommend including a table comparing demographics such as bilirubin level, perioperative morbidity and mortality, survival etc. between jaundiced patients with and without preoperative biliary drainage

Under Discussion, paragraph 1(line 26, page 10) “Jaundiced patients had poorer 5-year survival than non-jaundiced patients “. This was only true on univariate analysis but not on multivariate analysis.
Under discussion, paragraph 2 (line 9,10; page 11) “Postoperative mortality was not significantly different between jaundiced patients with and without PBD.” Based on table 1, we know three jaundiced patients died peri-operatively and one of which died of liver failure who did not have PBD. Do we assume the other two patients had PBD? Again, a table comparing jaundiced patients with and without PBD will help.

Under discussion, paragraph 4 (line 20, page 11) “Some researchers showed a significant relationship between PBD and an increase in intra-abdominal abscesses.” Please cite reference.

Under discussion, paragraph 6 (line 12, page 12): “Preoperative jaundice was the only independent predictor of mortality in GBC patients.” Again, on univariate analysis, jaundice was found to be a prognostic factor for survival but not on multivariate analysis.

Under discussion, paragraph 7 (line 22-24, page 12): “In this study….favorable outcome could be expected after resection in locally advanced (T3,4) GBC. Not sure if that conclusion can be drawn from the dataset especially since Reference 4 clearly showed T stage impacts survival.

Under discussion, paragraph 9 (line 22, page 13) “Extended resection carries high surgical mortality rate.” Don’t think the data set proves that statement. Additionally, what percentage of patients with combined resection of adjacent organs/extended resection had R0 resection?

Change the heading in Table 2 and 3 to morbidity from mortality

Patients with preoperative jaundice in this series had a 5 yr OS of 6% compared to D’Angelica series of 20%. Can the authors truly justify resection in this group with such a poor prognosis?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.