Author's response to reviews

Title: Adjuvant radio-chemotherapy for extrahepatic biliary tract cancers

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Version: 3 Date: 2 May 2011

Author's response to reviews: see over
Dear Prof. Dr. Zhao-Chong Zeng,

We would first thank you for your comments, concerns and requests that have improved the quality of our paper.

We resubmit a revised version where we have applied the corrections purposed by the editor and reviewers. We have as well made an English language revision paying particular attention to the abstract. References are now also well shown according to BMC style.

Following, we attach our replies to reviewer’s comments and concerns point-by-point highlighted in blue. We reference as well the changes in the text to make it easier for the editors.

We are looking forward for hearing for you,

Sincerely,

Dr. Marta Bonet Beltrán
(Corresponding author)
Editor's comment

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Version: 2 Date: 22 March 2011

Editor's comment:
Even though many relative papers had been published in the past, this study reports the first retrospective data on Swiss population treated with postoperative radiotherapy after radically surgical procedures in patients with EHBDC. The reviewers have gave authors good comments. I have some comments after read this manuscript and reviewers comments.

Some mistake in Figures. No figure 1 and 2. Figure 1 is figure 3 according to the text. Due to lacking figure 1, we do not know the dose range. We apologize; it was a mistake because no figures 2 and 3 were included in the submitted version of the paper. It is now corrected (the reference of figure 1 is on the top of page 8).

The authors collected clinical data from 1998 to 2004. Why there were not recent data? The authors must explain. Is now justified (Methods, page 5).

The authors must list the reference about RTOG/NCI-CTCAE V3.0 toxicity criteria. Is now listed (Results, page 7).

The authors concluded that “some patients seem to have benefited from adjuvant treatment”. This study did not have non-EBRT group, they did not compare two groups. This conclusion is not reasonable. We agree there is not a control group to make this statement; we have rectified the sentence in the abstract and the conclusions.

Minor comments: page 6 line 5 from bottom, 50,4 Gy should be changed to be 50.4 Gy. Is now corrected.

Page 10 1st line more than an a half should be changed to be more than one half. Is now corrected.
Reviewer's report
Title: Adjuvant radio-chemotherapy for extrahepatic biliary tract cancers
Version: 1 Date: 22 November 2010
Reviewer: yerko borghero

Reviewer's report:
Type of Study: retrospective, single institution
Number of patients: 23
The authors describe their experience treating a cohort of patients who suffered an unusual disease. The exclusion and inclusion criteria are appropriate, the manuscript well written, data analysis coherent showing results that supports the stated conclusions, within the stated limitations of the study.

Typo:
In the section “Authors' contributions” Line 5: says “appropriately”, should read appropriately. Is now corrected (page 14).

A FINAL RECOMMENDATION CANNOT BE MADE SINCE THE PDF FILE DOES NOT SHOW FIGURE 2 AND 3. It was a mistake that has been corrected (no figures 2 and 3 were included in the last version of the paper).

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests
YB
Reviewer's report
Title: Adjuvant radio-chemotherapy for extrahepatic biliary tract cancers
Version: 2 Date: 14 March 2011
Reviewer: Liu Houbao

Reviewer's report:
Doctor Marta Bonet Beltrán and his co-operator have done a good job and
displayed a constructive conclusion that the patients with extrahepatic biliary duct
cancers (EBDC) could benefit from postoperative adjuvant radiotherapy. EBDC are
uncommon malignancies characterized by a poor prognosis with high rates of loco-
regional recurrence as well as has been considered the cancers that show no
activity on radiotherapy in the past. Though the patients involved in this study were
only 23 patients (4 gallbladder, 7 ampullary and 12 cholangiocarcinoma), the
authors had performed long-term follow up, investigated and evaluated the
effectiveness of the radiotherapy and its toxicities and made analysis precisely.
So much so that the conclusion that postoperative radiotherapy with 50-60 Gy was
safe and effective for the patients with EBDC could be trusted and be useful for
clinical practice. The study depicted meanwhile that the positive surgical margins
had a lower loco-regional control, hence the surgeons must do their damnedest to
make surgical margins negative.
Fewer work has undertook on this area. The scholars in France, Netherlands,
South Korea and China have obtained similar conclusion that postoperative
radiotherapy could improve the survival of the patients with EBDC in a way. Hope
more institute participate the work and more patients with EBDC involve in the
series. Then the more compelled conclusion will come.

Declaration of competing interests:
I declare that I have no competing interests
Reviewer's report:
 Basically, this is a small sample retrospective analysis of the adjuvant chemoradiotherapy of extrahepatic duct cancer. The data collected spaned about 7 years. There are three categories of cancer which actually possess different tumorous biological behavior and prognosis. The conclusion is that "Postoperative radiotherapy with 50-60 Gy is feasible with acceptable acute and late toxicities; some patients seem to have benefited from adjuvant treatment.

1. Major Compulsory Revisions
   (1) Whether there is survival difference among patients of different stages, which is a more crucial data on the prediction of prognosis of patients.

   In table 1 we show patient and tumor characteristics. A 78% of patients were had advanced stages III-IVA (AJCC 5th ed.). Due to the small number of patients we faced a statistical weakness by attempting to assess this endpoint (as shown in the following figure). While patients with stage II survived 52 months compared to 22 months for patients with stage IA, the differences were not statistically significant (p=0.27).

   ![Survival Functions](image)

   (2) The time interval between surgery and the onset of adjuvant therapy? Is now shown in the text (page 7).

   (3) The average lymph nodes collected of patients? Is now shown in the text (page 5).
The relationship between lymph node status and survival? It was not directly assessed. According to AJCC 5th staging system, patients with positive lymph nodes were classified on stages III-IVA. A 78% of our patients were on these locally advanced stages and survival was analysed according to tumor stage. Unfortunately, and linking to the subject of question 1, our small series and stage distribution was not enough powerful to statistically answer it.

2. Minor Essential Revisions

#1#The physical status of patients before adjuvant therapy? Is now shown in the text (page 6).

(2)Is there any data of tumor marker before and after adjuvant therapy? There is data on tumor markers CEA and/or CA 19.9 for some patients that helped to promptly detect some tumor relapses. However, no comprehensive efforts were made to assess this endpoint.

Level of interest: An article of limited interest
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.