Reviewer’s report

Title: Outcome comparison between percutaneous cholecystostomy and cholecystectomy: a 10-year population-based analysis

Version: 1 Date: 21 Oct 2017

Reviewer: Fabio Cesare Campanile

Reviewer's report:

Would like to congratulate you for the impressive dataset and the excellent work of revising the previous manuscript. I think that the paper is now substantially improved. In particular, the new table 4 presents unique data that certainly deserved publication and, in my opinion, well contribute to the understanding of the role of percutaneous cholecystostomy.

Still, a few remarks are necessary and a few further revisions could add more value to the paper. I will start with the most trivial to finish with what I believe is the main methodological critical aspect, that concerns the new conclusions

1. p. 6 lines 17-20 (the reference is to the numbers on the left column of the pdf, it corresponds to the 6th line of the "Data Definition" paragraph): "When patients initially had undergone PC before CCS, they were classified as PC patients, and the reverse was also true" I do not understand how a PC can be carried out on a patient who already had the gallbladder removed by a CCS. Probably you did not mean it.

2. p. 12 line 28: "Fabio et al. [28] conducted a survey of the literature..."; I really appreciate your acknowledgement of this paper; please note that the correct mention of it should be "Campanile et al. [28] conducted a survey of the literature..."

3. In table 4 legend should be specified that the relative risk is expressed in Odds ratio.

4. In the methods section: "30-day mortality referred to patients who died within one month after discharge, and did not include the patients who died during hospitalization". The current definition of 30-day mortality includes, and not excludes the patients who died during hospitalization, as in your original version. My remark #5 only meant to bring your attention to the fact that your reported definition was mis-typed, not that it was wrong. I am sorry I was not clear enough! In other words you had given the same definition ("patients who died during hospitalization") to both your indexes, but, of course, it was a simple writing mistake. In your table 4 the use of the correct 30-day mortality (i.e. with the inclusion of the patients who died in the hospital) would make clearer your results and more evident the difference in risk between the two procedures.
5. Your data show, more clearly than in any other paper in the literature, that the mortality risk is far higher for PC than CCS, even if examined in subgroups stratified by age or co-morbidity and cause of procedure. I think that this is the most valuable finding of your study and it should be emphasized. PC carries a mortality risk that is increased from a minimum of 1.4 fold to a maximum of 34.2 fold. Even in the most serious scenario (patients of age 70 or more with a CCI>3 and an acute cholecystitis) the CCS, when possible, carries a lower risk of death. But your conclusions are not consistent with your own data and I believe that some methodological aspect should be underlined. In fact, in the conclusions (and in the discussion on p. 13) you state "However, due to the general conditions were far worse in the average PC patients than in the average CCS patients". Unless I misunderstood the data, your results are stratified by general conditions as far as possible; I do not understand the assumption that the average general condition were different between the two groups. Of course, you acknowledge that the particular dataset you worked on may not disclose complete details on the patient general conditions (and this should be stated in the "discussion" limitations section) but still, to the best of your knowledge, the patients are grouped in rather homogeneous groups (for example patients with CCI score of 3 or more) and the comparison of those homogeneous groups shows that PC mortality is worse. Furthermore, "some patients who underwent PC could not have tolerated any surgery" this is an important selection bias that has to be specified in the limitation section; but, again, this bias alone cannot justify a conclusion that appears to be contradictory with the data ("so we could not conclude that PC was inferior to CCS based on a simple comparison"), certainly you are right to be cautious, but your data are something more than a simple comparison and you should really stand up by them and conclude that, based on your data, PC is not as safe as suggested and actually its mortality rate is higher than CCS.

6. P 16 lines 28-34: "Therefore, we posit that being elderly and critically ill may cause patients to be more likely to die during hospitalization or within 30 days after both types of operations and that the operation itself may not play a major role as a cause of death" Of course being elderly and critically ill increase your mortality. Still, even in the worst scenario (elderly patients with acute cholecystitis and a CCI score of 3 or more) you show that RR of death is 1.4 fold higher for PC.. I do not think that a role of the operation itself can be excluded. Your data show that that role is real (of course after consideration of all the possible limitations of your dataset).

7. "The Tokyo guidelines considered the use of PC mandatory for "severe" cases and strongly suggested the use of this procedure even in most moderate-grade cholecystitis cases; our study confirmed that the Tokyo guideline recommendations were adequate and current." You correctly state that the Tokyo guidelines suggested the use of PC even in most moderate grade cholecystitis. This corresponds to those patients with acute cholecystitis without organs/systems dysfunction. The group includes most of the patients with AC and CCI of 0; their relative risk (PC Vs. CCS) must be rather high, according to your data. Even the RR of
the "severe" group (AC + CCI of at least 1) cannot be disregarded. Do you think that your data support the conclusion that the Tokyo guidelines are adequate and current. It appears to me that your paper is particularly interesting also because it is the first clear evidence that the role of PC in the Tokyo guidelines is overstated.

8. The in-depth subset analysis very interesting as it shows that gap between the in-hospital and 30-day mortality rates narrowed in the most compromised patients. The relative risk of death is higher in the less compromised patients (or, if you prefer, lower in the most serious patients). This important aspect means, in my opinion, that the indication for PC should be limited only to the sicker patients, because in everybody else the risk seems to be excessive.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

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