Reviewer’s report

Title: Cost analysis and effectiveness of one-stage laparoscopic versus two-stage endolaparoscopic management of cholecystocholedocholithiasis: a retrospective cohort study

Version: 0 Date: 29 Apr 2017

Reviewer: Fabio Cesare Campanile

Reviewer’s report:

The manuscript "Success and costs of one-stage laparoscopic versus two-stage endolaparoscopic management of cholecystocholedocholithiasis" reports an observational study aiming at comparing the costs of laparoscopic vs two-stage endolaparoscopic treatment of choledocolithiasis. Therefore, the report should follow the standards of the STROBE Statement and also (for the economic aspect) those established in the CHEERS guidelines. This peer review is structured taking into consideration those standards.

Title and abstract: The title identifies the study as an economic evaluation (it does not, however, specifies which specific type of economic evaluation is done) and correctly describes the interventions compared (along with the CHEERS requirements). However, it does not indicate the study design (STROBE statement). The abstract is structured and informative; however, of course, it also reflects some of the methodological problems of the study.

Introduction: The background section explains the rationale of the study and states the aim of the study as "...to compare the success and costs of one-stage versus two-stage management for cholecystocholedocholithiasis". However, especially for an economic evaluation, it is extremely important to include informations about the study population (in this case patients with CBD and gallbladder stones to be treated electively) and the healthcare setting (private hospital, public health system, academic or not, community or tertiary care center); as a matter of fact, in many cases costs vary in different settings and different population and often results in one setting cannot apply to another and an economic evaluation is necessarily related to a specific setting and location. Also a description of the importance of the question should be given (could the results of the study have an impact on the hospital policy? National policies? Else?). Furthermore, it is not completely clear which is the intervention of interest and the comparator. In other words, do the authors consider one of the intervention as standard and mean to compare the other to it to assess its cost-effectiveness? What exactly is the hypothesis tested (for example "is the one stage laparoscopic treatment more cost effective than…")? Also in the economic evaluation is extremely important to specify the "point of view" from which the study is taken (see for example Drummond et al. Methods for the Economic Evaluation of Health Care Programmes, Second Edition, Oxford University Press 1997; and the item 6 of the CHEERS documentation itself at https://www.ispor.org/ValueInHealth/ShowValueInHealth.aspx?issue=3D35FDBC-D569-431D-8C27-378B8F99EC67), and it would be useful to indicate this aspect in the background section.
For example one can study the costs from the hospital administration or the "society" point of view; the items included in the study and the results may differ. For example in the present study (taken from the hospital administration point of view) it is shown that the "total mean cost" of the two alternatives "were similar". However, if this is true for the hospital administrator, it is not necessarily true from the patient point of view because the mean postoperative stay difference of 2.5 days or the different readmission rate may have an economic impact from the "patient point of view". This impact is considered in an economic evaluation from the "patient" or the "society" but not from the "hospital" point of view.

Methods: In the methods section should also be specified the details of the items already mentioned in the introduction (healthcare setting, study population and so on).

In addition, some of the key elements of the study design need to be clarified. It appears to be a case-control study; the study group and the control group (again, it is not clear which is which) are recruited in a consecutive manner and apparently all in the time frame between Jan 1999 and Dec 2014. What is the reason to collect the preoperative data of the one-stage group prospectively and those of the two-stage group retrospectively? Looks like the authors compared a new intervention (one stage) for which they started a new database collection, to a historical cohort of a standard intervention (two stage) for which they had to pull out the medical records. Again, if this is the case, it should be clearly stated both in the introduction/background and in the methods section. This design, of course, introduces several biases that should be acknowledged later in the discussion section (as a matter of fact, the prospective data collection is more accurate because the researcher know exactly what items they are supposed to include, while the retrospective (especially if paper medical record are utilized the researchers must rely on the completeness and accuracy of the data not included for the study specific purpose). Furthermore, the old group may have been treated in a time frame different from the new one (are the patients in the two groups distributed evenly between 1999 and 2014 or the two-stage patients are concentrated in the second part of the study period?) and this is a potential confounder. In any case, it should be specified the data sources for each study group (electronic or paper database? Clinical paper medical records?).

From the economic standpoint, this study appears as a "cost-analysis" study (and this should be stated both in the introduction and in the methods section) because the costs and outcomes of each alternative are studied but they are not put in relation between them (as in a cost-benefit or cost-utility analysis).

The authors indicate their outcome variables as: "The main measures of outcome were the success of CBD clearance and hospital costs per patient including readmissions. The secondary measures of outcome were 30-day morbidity and mortality and length of postoperative hospital stay."; given the stated aim ("...to compare the success and costs of one-stage versus two-stage management for cholecystocholedocholithiasis") the hospital cost should be the main measure of outcome, while the rest of the variables should be included in the measurements of effectiveness (see item 11 of the CHEERS checklist). However, I cannot quite understand the choice of CBD clearance as a "main" measure and the morbility and mortality items as "secondary" measures. Can the authors clarify their choice?
The cost calculations, and the items included in table 1, are not completely clear to me. The cost of the operating room resources include also the nursing costs (for ERCP there is an indication stating "3 nurses", what about LC?)? What are the costs of the surgical teams? It is specified that "the operating time charges vary by the amount of team members and expertise" but there is no indication of the calculated sums. The same applies for the items "reoperation price" and "reERCP price". How are the per day admission prices calculated?

Most of the data used for cost calculations are not made available. For example how do we define the surgical ward costs? Is the figure €602 per day an average cost that takes into consideration only the personnel or also the overhead costs? Is it calculated at a full occupancy of the ward or at an average occupancy rate? How were the fixed costs distributed?

Results:

The authors report a "similar" "overall" success of CBD stone clearance in both study groups; However they include in the "success" outcome the patients that were actually cleared by the examined method AND those who had to undergo open surgery for failure of the chosen treatment. Actually, table 3 shows a rate of conversion to open surgery almost double for the two stage (8.2 Vs. 13.3%). Also they claim that the 30-day morbidity (even if included in the secondary outcome measures) was similar in both groups, but actually the morbidity rate (the same applies to the surgical morbidity and the severity of the complications) for the one stage group was a little less than double of the two-stage group. Reoperation and readmission rate also favor the two-stage group. Most results are statistically not significant because of the small size of the groups, however this results cannot be ignored and should be included in the conclusion remarks that instead state that the costs are similar, the morbidity acceptable and the one stage treatment is attractive due to the shorter stay and the fewer procedures per patient.

Discussion:

The limitations and the possible biases suggested above should be included in the discussion. In particular the small sample sizes and their relation to the significance of the results, the particular study design and its reasons, the different distributions in the complication rate and the pitfalls of the design "cost-analysis" (instead of cost-benefit or cost-utility analysis) should be addressed. The last point is extremely important because cost-analysis is not a full economic evaluation and should not be used to examine resource allocations but have a very limited role in the decision-making.

Conclusions:

As stated above, the conclusions are only partially supported by the data of the study: the morbidity data are said to be "acceptable" but are not completely taken into consideration for the main conclusion statement ("one-stage management seems to be attractive").
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?
6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal