Reviewer's report

Title: Number of cholangitis episodes as a prognostic marker to predict timing of liver transplantation in biliary atresia patients after Kasai portoenterostomy

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Reviewer: Steven Martin

Reviewer's report:

General comments:
This is a well written paper concerning a subject of important clinical interest. The data-set is of particular interest as the Taiwanese experience in biliary atresia is extensive and well regarded. The data capture in Taiwan is very complete and the numbers are significantly large to enable conclusions to be made.

The main drawback of the paper is the confusing description of the proposed analyses and their subsequent presentation in the results. Other important flaws include: given that the database does not permit, as the authors do acknowledge in the discussion, any analysis of the other factors that may have led to early transplant (eg restoration of bile flow) it would seem prudent after describing the whole population to only include for analysis the patients who underwent Kasai at <60 days as this group has a better overall prognosis and would provide a more uniform patient group. Furthermore as indicated below, patients need to have at least 2 years of follow-up (perhaps at least 1 year) to make any sense of the effects of episodes of cholangitis on transplantation. Statistical analyses in general are appropriate (with a few comments below).

Specific comments:

Abstract: The first sentence is very difficult to understand and should be re-written.

Introduction: line 19 The aim should be made more clear - is it incidence, number of episodes, cumulative incidence (or all three) that is hypothesized to be a prognostic factor? The word "episodes" alone does not give the reader an understanding of the uniqueness of this study.
Patients and methods:

Line 44: ICD-9_CM code 51.67 does not appear in any of my sources. This should be re-checked for accuracy.

line 54: The study period is defined as 1989-2011. It is not indicated how patients entering the study near the end (2011) are treated. This is of particular importance as insufficient follow-up time may have occurred to make any conclusions about cholangitis or about transplantation. The authors should consider only analyzing patients with at least 2 years of follow up. This is particularly important for determining "cumulative incidence" which requires that the time-frame be clearly defined and that the population is "at risk" during that time period.

line 69-72: The authors introduce the concept of "cumulative duration" as the sum of annual cholangitis episodes throughout the study for non-transplant patients and up until transplant for the others. This is not the same as cumulative number of episodes in the first 1 or 2 years depicted in figure 3. This needs clarification or should be removed if the results are not presented.

Line 74-76: what are "both groups of BA patients with cholangitis who survived without receiving LT"? The study only refers to one group.

RESULTS:
Table 1: I would prefer to see age data expressed as median rather than mean to better illustrate any outliers. The age at study end shows the youngest in the transplant group at 8.4 months and in the non-transplant group at 2.4 months. This illustrates the problem of insufficient follow-up for a study exploring the effect of cholangitis episodes on LT.

Line 110. The overall percentage of cholangitis in the population should be stated here rather than in line 156 of the discussion
Line 110: It is not clear what information the authors wish to express with these data which can be expressed in different ways. This again relates to problems with defining the study population of interest. It may be advantageous to provide a section on overall data and a separate section looking specifically at those within 2 years post KP.

Cholangitis occurred in 77/96 (80.2) LT vs. 171/270 (63%) non-LT (P<0.002); cholangitis occurred within 2 years after KP in 56/96 (58.3%) of the LT patients vs 116/270 (42.9%) non-LT; in those who had cholangitis, it occurred within 2 years in 56/77 (72.7%) LT vs 116/171 (67.8%) non-LT. Statistics were not provided.

Line 116: This is a repetition of the last sentence of the preceding paragraph (line 111-113)

DISCUSSION:

The discussion related to corticosteroids is outside the scope of this study and should be removed. However, it would be beneficial to describe the standard treatment used in Taiwan during the study period in the Methods section.

Figure 3: The figure shows the mean number of episodes per person in the two years specified. It does not actually show cumulative data for the study groups although this seems to be presented in the legend (116 vs 66 in year 1; 154 vs 40 in year 2?)

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.
Yes
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