Reviewer's report

Title: Risk factors for acute kidney injury following orthotopic liver transplantation: the impact of changes in renal function while patients await transplantation

Version: 1 Date: 8 July 2010

Reviewer: Phuong Chi Pham

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In the current manuscript, the authors examined pre-operative factors that may be predictive of AKI post-OLT using the NIDDK Liver Transplantation Database. The authors specifically focused on the impact of pre-OLT changes in renal function on AKI post-OLT. Data analysis suggested a correlation between improving renal function pre-OLT and AKI within 48 hour post-OLT. In addition, the authors reported that increased body mass index, increased Childs-Pugh-Turcott score, decreased urine output during cross-clamp, improved renal function while awaiting OLT, increased post-operative stroke volume, non-Caucasian race, and post-operative use of tacrolimus to be independent predictors of AKI post-OLT.

Overall, the manuscript was well-written and the findings are interesting. However, I have the following major concerns:

Major compulsory revisions:

1. Renal function in the current study was measured by the MDRD estimated GFR. Any method of measuring renal function based on serum creatinine in cirrhotic patients has been well-documented to give an overestimate of true glomerular filtration rates. It must be cautioned that any study that is based on an inaccurate measurement of renal function may render any finding invalid.
   a. Urine output should have been included in the definition of post-operative AKI. This is especially important in patients with advanced liver disease because they are often overloaded and small fluctuations in serum creatinine may just reflect the extent of fluid administration.
   b. The changes in urine output and net fluid balance during the pre-operative period over which the authors determined pre-operative renal function improvement or deterioration would have added valuable supporting evidence for the claim of either renal function improvement or deterioration. Improved renal function can lead to a diuretic phase and an initial transient small increase in serum creatinine. An increase in serum creatinine alone therefore does not necessarily imply worsening renal function of "AKI" in these patients.

2. Exclusion of patients who required renal replacement therapy within the first day post-OLT. These patients could be in the "declining renal function prior to OLT" group who had worse renal outcome post-OLT. Exclusion of these patients...
may be a problem in the current study.

3. Volume overload is a major problem in patients with advanced liver disease. It is not uncommon for physicians to administer excessive fluids to these patients when their renal function deteriorates. A fall in serum creatinine in these patients may therefore not necessarily reflect an improvement in renal function, but a dilutional serum creatinine level. In the current study, patients in the AKI group who reportedly had “improved renal function” prior to their OLT also had higher BMI. Could the higher BMI reflect higher volume overload status? How was BMI calculated in these patients? Did body weights include ascites weight? Is it possible that the post-OLT AKI patients required and received higher IV fluids administration during the pre-OLT period because their hemodynamic parameters were consistent with worse circulatory failure (higher CO, lower SVR) compared to their “no AKI” counterpart. Their "improved renal function" pre-OLT could have just reflected a dilutional creatinine level.

4. Duration of follow-up: a 7-14 day follow-up in both AKI and no AKI groups would be helpful to determine if the post-OLT AKI during the first 48 hours was indeed clinically significant or just a reflection of transient changes in fluid and hemodynamic status.

**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.

**Declaration of competing interests:**

I declare that I have no competing interests.