Reviewer's report

Title: Do statins modify the risk of delayed graft function in renal transplantation?

Version: 4 Date: 14 June 2012

Reviewer: marcelo santos sampaio sampaio

Reviewer's report:

The changes done in the manuscript have improved the quality of the paper; however further changes may be done.

Please this time indicate in the new version the applied changes (e.g. underline the new text) so it would be easy to the reviewers to identify them.

Major Concerns:

1. Authors' definitions of delayed graft function are not usual.

The most accepted definition of delayed graft function is the need of dialysis in the first week after transplant. Authors used the need of dialysis in the 72h after transplant. Using an unusual definition brings difficulty when comparing authors’ data to other studies. Also, redefining the outcome definition may change study results.

Moreover, non-dialysis delayed graft function has no common definition in literature, and just a few studies have used it. Authors should discuss the different ways do define the outcome based on creatinine reduction, so the readers may not get the impression that this is the common definition. One of the best definitions of delayed graft function based in the creatinine decrease was the one used by Boom H (Kidney Int.) and Moore J (transplantation) in their manuscripts. These authors defined delayed graft function as failure of serum creatinine to decrease by at least 10% daily on 3 successive days during the first week post-transplantation. The one day definition may include an isolate and transient intercurrence.

I would suggest the use of these commonest definitions, and recheck outcome ratios and association with statins. Otherwise, at least include a comment in the discussion about the different definitions in the literature.

2. I insist that authors should try to analyze in separate deceased and living donor (item 1 of the previous revision). Results should be shown in table 4 and 5. It is very difficult to adjust results in a similar way to deceased and living transplants. By doing like this no interaction term is needed. Kidney donated after cardiac death can be pooled together with brain death, or just add a note that deceased analysis included only brain death donor transplant as the few number of donation cardiac death do not allow a adjusted analysis.

3. Authors define OR by multivariable logistic regression analysis. They describe backward stepwise model elimination until the most parsimonious model was identified. The stepwise model may include in the final model some of the
co-variables used in the initial model according to a pre-defined p-value, or it can be done by excluding variables according to its significance after running the initial model and re-running the new model. This last model has the interference of the researcher, as he can choose variables and can keep the ones he feels are important for the adjustment despite of the p-values. It has to be better specified in the methods how authors did it. Also, in either way, variables may change when studying different outcomes (D-DGF, ND-DGF). The final variables used to adjust the OR in each model have to be specified. I suggest including a line in the bottom of table 4 and 5. I just could find in methods (page 8)the variables initially included in the model, not actually the description of the variables used in the final model (please refer to minor revisions #3 in my previous revision).

4. Still regarding the variables used to adjust the model, the length of hospitalization cannot be used here. Length of hospitalization is in general an event defined by delayed graft function, and not vice-versa. Authors acknowledge it in their introduction section of the manuscript. Also, as the objective of the study is to define risk of using statin the variable for it should not be dropped from the model even if not significant in univariate analysis.

5. On tables 4 and 5 the following should be revised:
   a. N from table 5 (249) is smaller than in table 4 (252), please verify and explain. Maybe create a figure showing the intersection between the different definitions (e.g. as done in Moore J et al in Transplantation). It may be related to the inclusion of variables in the mode with missing values.
   b. In BMI OR cannot be zero. <18.5 group has probably not enough N to be analyzed. Please explain the inclusion of p-value of 0.23 in table 4. In table 5 p-value or CI is wrong in <18.5 group. Also, explain 0.02. As explained above use of length of hospitalization as a cofounder should not be used.
   c. I am very surprised that the cold ischemia was not a risk factor for delayed graft function. I believe that is was caused by analyzing in the same group living and deceased donors. Please verify and comment.

6. Missing data cited in the methods should be specified in methods and not only in table 1. Authors can mention that X% of data from age is missing.

7. Table 2 is not necessary.

I suggest adding in page 9 median dose of statin used in deceased, living donor and overall recipients, in the place of the sentence “97% of ….or less Table 2”. I think it would be equally informative, and avoid inclusion of one more table to the manuscript.

8. Title: use “delayed graft function” instead of “graft function”

Minor Concerns:

1. I suggest adding in the background percent of DGF in living and deceased donor found in the literature and comment the different risk factors associated with increased risk of delayed graft function according to donor type.
2. As a consent form was collected, please mention IRB approval.

3. In statistical analysis change “number” to “percent” and exclude % in parenthesis. Define interquartile range. 25-75percentile? As it is a non-randomized study it is difficult to believe that a variable can have a normal distribution. Maybe the age, race? Please indicate the test used to calculate the p-values in table 1. Use a symbol as an indicator and give the test name in the bottom of the table.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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'