Author's response to reviews

Title: Assessment of Arterial Stiffness Using Pulse Wave Velocity in Tacrolimus Users the First Year Post Kidney Transplantation: a Prospective Cohort Study

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Author's response to reviews: see over
Authors’ response to reviews

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Version: 2  Date: February 4, 2015

Authors’ response to reviews: see over
Reviewer's report
Title: Assessment of Arterial Stiffness Using Pulse Wave Velocity in the First Year Post Kidney Transplant: a Prospective Cohort Study

Version: 2
Date: 9 March 2015
Reviewer: Massimo Torreggiani

Reviewer's report:

In this paper, Birdwell and Colleagues aim to study the progression of cardiovascular disease by means of arterial stiffness in a population of kidney transplant recipients measuring aortic pulse wave velocity (PWV) one month after transplantation (baseline) and again after 12 months. Their results show that aortic arterial stiffness does not progress in the first year after a kidney transplant but increased age, diabetes and a higher baseline pulse wave velocity identify a group of patients at risk for increased arterial stiffness.

Most of the results of this study were already reported by previous investigations. Anyway, this work, although not completely original, is somewhat interesting.

Minor Essential Revisions

- There are a number of studies that deal with PVW and kidney transplant. I would suggest to cite and comment also the following papers:
  
  o Transplant Proc. 2012 Apr;44(3):684-6
  o Ann Transplant. 2011 Jul-Sep;16(3):30-5
  o Am J Transplant. 2011 Nov;11(11):2414-22

  Thank you for this list of references. They have now been included in the paper in the discussion and referenced.

- This is the first study with an entire population under a maintenance immunosuppression therapy with tacrolimus, thus I would stress this in the title of the paper.

  The title has been revised to read “Assessment of Arterial Stiffness Using Pulse Wave Velocity in Tacrolimus Users the First Year Post Kidney Transplantation: a Prospective Cohort Study,” and a sentence added to the discussion (line 195) to emphasize this.

- Page 2, line 45: please rephrase.

  The sentence has been rewritten to say “Further research that assesses patients for greater than one year and includes a control dialysis group would be helpful in further understanding the change in arterial stiffness post transplantation.” (now line 41)

- Page 3, line 61: please rephrase.
This sentence has been rewritten as “Though often used in the research setting, several studies support using PWV in the clinic based on its reported associations with cardiovascular risk and all-cause mortality…” (now line 57)

- Please correct format of reference number 9.

This has been corrected.

**Level of interest:** An article of importance in its field  
**Quality of written English:** Acceptable  
**Statistical review:** No, the manuscript does not need to be seen by a statistician. **Declaration of competing interests:**

I declare that I have no competing interests

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**Reviewer's report**  
**Title:** Assessment of Arterial Stiffness Using Pulse Wave Velocity in the First Year Post Kidney Transplant: a Prospective Cohort Study  
**Version:** 2  
**Date:** 22 March 2015  
**Reviewer:** Fabrizio Calliada  
**Reviewer's report:**

No revisions requested.

1 Is the question posed original, important and well defined?

The aim of the paper is to evaluate the arterial pulsed wave velocity behavior at baseline and one year after transplantation. The argument is new and original and the paper is well written and easily grasped.

2 Are the data sound and well controlled? Yes

3 Is the interpretation (discussion and conclusion) well balanced and supported by the data?  

Yes. The interpretation discusses the relevance of all the results in an unbiased manner.

Conclusions drawn from the study are valid and result directly from the data shown, with reference to other relevant works cited in the references.

4 Are the methods appropriate and well described, and are sufficient details provided to allow others to evaluate and/or replicate the work?
The methods are appropriate, well described and sufficiently detailed to permit to replicate the work by the reader. The statistical analysis, even if complex, seems clear and not need to be assessed specifically by an additional reviewer with statistical expertise.

5 What are the strengths and weaknesses of the methods?

The principal weakness of the research is the number of patients that, even if not exiguous, is limited to 66 patients, probably too few to draw absolute considerations on the effects of the transplantation on PWV and their implications. But the research methods are absolutely sound and the prospective results interesting.

6 Can the writing, organization, tables and figures be improved? No
7 When revisions are requested.
No revision is requested

8 Are there any ethical or competing interests issues you would like to raise? No

Level of interest: An article of importance in its field
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' below

Reviewer's report
Title: Assessment of Arterial Stiffness Using Pulse Wave Velocity in the First Year Post Kidney Transplant: a Prospective Cohort Study Version: 2 Date: 28 March 2015
Reviewer: Filippo Mangione
Reviewer's report:

Authors hypothesize that aortic stiffness, measured as carotid-femoral pulse wave velocity, may improve at one year after kidney transplantation. PWV is an accepted surrogate marker of cardiovascular morbidity and mortality, even in chronic kidney disease patients.

It has been already indirectly demonstrated that PWV could be ameliorated after kidney Tx compared to PWV measured in dialysis patients, at least in children (see Cseprekál O, Kis E, Schaffer P, Othmane Tel H, Fekete BC, Vannay A, Szabó AJ, Remport A, Szabó A, Tulassay T, Reusz GS: Pulse wave velocity in children following renal transplantation. Nephrol Dial Transplant 2009;24:309-315.). However, the present paper has the great advantage of a prospective assessment of PWV in the same cohort of transplanted patients.

- Major Compulsory Revisions

1. Selection of the population: did the authors select a population of well-functioning kidney graft, or transplant recipients were consecutively included? Distribution of serum creatinine values are very close to normal; no acute rejection or primary graft non-function or other early
complications were reported. Overall, the enrolled population should be considered at low-risk for renal and cardiovascular outcomes post-transplantation. I think that this observation should be specified in the paper.

Thank you for pointing this out. We have included this information as a limitation under the last paragraph of the Discussion. We also listed the low number of cardiovascular events (8) in the Results.

2. Conclusions, row 195 “we showed that there was no change in aortic PWV over the first year post kidney transplant, suggesting arterial stiffness does not progress during this time period”: again, I would stress the fact that the enrolled population was at low risk for cardio-renal outcomes (and no CV or renal events have been registered, indeed) and that results are referred only to well functioning kidney grafts.

We have rewritten the first sentence of the Conclusion to reflect the low risk population. It now reads “In a prospective study of new kidney transplant recipients treated with tacrolimus, we showed that there was no change in aortic PWV over the first year post kidney transplantation, suggesting arterial stiffness does not progress during this time period in a cohort of low risk individuals for cardio-renal outcomes.”

- Minor Essential Revisions

1. Affiliations must be checked: avoid repeating the same affiliation for different authors;

This has been corrected.

2. Please consider to use estimated GFR instead of or in addition or serum creatinine in results and table 1.

Estimated GFR results have been added to both the results and Table 1.

- Discretionary revisions

1. Consider to avoid publication of figure 1B: is it really useful?

We feel this is an interesting figure that allows one to see the individual level data more clearly. However, we will happily remove it if desired.

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

Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the

Declaration of competing interests:

I declare that I have no competing interests
Editorial Comments:
The manuscript by Birdwell and coworkers, although not novel, is quite interesting because
deals with a population of kidney transplant patients all treated with tacrolimus. As underlined by
the reviewers the paper is well written and the conclusions are supported by the results.
However the authors should underline that the sample is quite small and that the patients
enrolled in the study were at low risk of kidney rejection. The papers indicated by the reviewers
should be commented and included in the references

Thank you for allowing a revision of the manuscript. We have addressed the individual
reviewers' concerns above. We have emphasized all patients are on tacrolimus. We have
included the limitations of a small size and low risk study population. We have included the
additional references requested. Please let us know if we can do anything further. Thank you.