Author’s response to reviews

Title: Renal Resistive Index as an Indicator of the Presence and Severity of Anemia and its Future Development in Patients with Hypertension

Authors:

Muneyoshi Tanimura (m-tanimura@clin.medic.mie-u.ac.jp)
Kaoru Dohi (dohik@clin.medic.mie-u.ac.jp)
Masumi Matsuda (mandms@clin.medic.mie-u.ac.jp)
Yuichi Sato (sato0726@clin.medic.mie-u.ac.jp)
Emiyo Sugiura (emyogw@gmail.com)
Naoto Kumagai (kuma_cuma@yahoo.co.jp)
Shiro Nakamori (n-shiro@clin.medic.mie-u.ac.jp)
Tomomi Yamada (t-yamada@doc.medic.mie-u.ac.jp)
Naoki Fujimoto (naokifujimo@hotmail.com)
Takashi Tanigawa (t-tanigw@clin.medic.mie-u.ac.jp)
Norikazu Yamada (n-yamada@clin.medic.mie-u.ac.jp)
Mashio Nakamura (mashio@clin.medic.mie-u.ac.jp)
Masaaki Ito (mitoka@clin.medic.mie-u.ac.jp)

Version: 2 Date: 25 March 2015

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

Title: Renal Resistive Index as an Indicator of the Presence and Severity of Anemia and its Future Development in Patients with Hypertension

Authors:
Muneyoshi Tanimura, (m-tanimura@clin.medic.mie-u.ac.jp)
Kaoru Dohi, (dohik@clin.medic.mie-u.ac.jp)
Masumi Matsuda (mandms@clin.medic.mie-u.ac.jp)
Yuichi Sato (sato0726@clin.medic.mie-u.ac.jp)
Emiyo Sugiura (emyogw@gmail.com)
Naoto Kumagai (kuma_cuma@yahoo.co.jp)
Shiro Nakamori (n-shiro@clin.medic.mie-u.ac.jp)
Tomomi Yamada (t-yamada@doc.medic.mie-u.ac.jp)
Naoki Fujimoto (naokifujimo@hotmail.com)
Takashi Tanigawa (t-tanigw@clin.medic.mie-u.ac.jp)
Norikazu Yamada (n-yamada@clin.medic.mie-u.ac.jp)
Mashio Nakamura (mashio@clin.medic.mie-u.ac.jp)
Masaaki Ito (mitoka@clin.medic.mie-u.ac.jp)

Version: 3
Date: 25 March 2015

Author's response to reviews: see over
Hayley Henderson, MD

Executive Editor, *BMC Nephrology*

Dear Dr. Henderson,

Object: MS: 1276831905159199- Renal Resistive Index as an Indicator of the Presence and Severity of Anemia and its Future Development in Patients with Hypertension. Dr. Muneyoshi Tanimura et al.

Thank you for consideration of our manuscript for publication in your journal. We have reviewed the above manuscript according to your reviewer’s comments.
Reviewer #1 (Dr. Sugiura)

Major Comments:

1. While the correlation between RI and anemia is a new interesting finding, the hemoglobin levels are much higher than those expected from GFR (Fig.2). There are many patients whose hemoglobin levels are above normal range despite CKD. This makes it difficult to apply the results to the general CKD population.

As the reviewer pointed out, there are many patients whose hemoglobin levels are above normal range despite having CKD. Several factors including obesity-related obstructive sleep apnea, current smoking and COPD may contribute to persistent or intermittent hypoxia that lead to red cell production via EPO stimulation. Indeed, body mass index was positively related to hemoglobin level in the present study. Unfortunately, the presence and severity of sleep apnea and their contribution to hemoglobin level were not assessed in the present study. We added above sentences in the section of the limitation.

2. Concerning the above described issue, the end point accepted in this study, a decrease in hemoglobin > 1g/dL, can be clinically insignificant. For example, change in hemoglobin from 15 to 14 g/dL will have no clinical impact.

The description about the study end-point was insufficient and inaccuracy in the original manuscript.

The study end-point was 1) new anemia (<12.0 g/dl for women and <13.0 g/dl for men) for
non-anemic patients, and 2) decreased hemoglobin levels greater than 1 g/dl and/or initiation of treatment including iron supplementation and EPO-stimulating agents for anemic patients. We modified the above sentence in the section of the method (page 7, lines 15-18). Therefore, a patient in whom hemoglobin level decreased from 15 to 14 g/dL does not reach the study end-point.

3. It is hard to believe that RI can predict a development of anemia. The hazard ratios of RI are 1.05 (univariate) and 1.03 (multivariate) (Table 3). These values are not clinically and practically significant. In addition, the multivariate analysis showed 95% RI of 1.00-1.06 and P-value of 0.05, which is not statistically significant.

We found that renal RI per 0.05 rises was associated with the future development of anemia with hazard ratio of 1.18 and 95% CI of 1.02-1.37 (p =0.03) after correcting for confounding factors. Therefore, we modified Table 3 and the sentences in the abstract, the section of the results and discussion of the main text.
Reviewer # 2 (Dr. Moranne)

No Additional Comments:

Thank you for your acceptance of our 2nd revision.