

March 3, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Manuscript_20131231013023.docx).

Title: *Management of Renal Artery Stenosis: What does the Experimental Evidence Tell Us?*

Author: Al-Suraih, Mohammed (Al-Suraih.mohammed@mayo.edu) and Grande, Joseph Peter (grande.joseph@mayo.edu)

Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 8632

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated as requested by the editor. In particular, we have reformatted the citations, have added a running title, author contributions, corresponding author address, and key words.

2 Revision has been made according to the suggestions of the reviewer

(1) Reviewer #1 had no specific comments.

(2) Reviewer #2 requested that we describe the management of renal artery stenosis for reducing the inflammatory response in order to prevent kidney damage. We have made several revisions. In the last paragraph of our discussion on "development of chronic renal disease in RAS: what does the experimental evidence tell us" we introduce the concept that blockade of CCL2-CCR2 signaling may prevent the development and/or progression of chronic renal disease in RAS. We indicate that additional studies are required to address this issue. In the section on "management of renal artery stenosis" we have added a statement indicating that therapeutic approaches that target inflammation may have a role in the management of patients with renal artery stenosis. In our "conclusion" section, we indicate that treatment of the inflammatory response to tissue injury may have therapeutic benefit. The next logical step is to better understand pro-inflammatory signaling pathways in RAS so that more targeted therapies can be developed. We mention blockade of CCL2-CCR2 signaling as one such example.

Thank you again for publishing our manuscript in the *World Journal of Cardiology*.

Sincerely,

A handwritten signature in black ink that reads "Joseph P. Grande". The signature is written in a cursive, flowing style.

Joseph P. Grande, M.D., Ph.D.

Professor of Laboratory Medicine and Pathology