

## Format for ANSWERING REVIEWERS

February 12, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 16491-review.doc).

**Title:** Early renal failure as a cardiovascular disease: Focus on lipoprotein(a) and prothrombotic state

**Author:** Cristiana Catena, GianLuca Colussi, Francesca Nait, Francesca Pezzutto, Flavia Martinis, Leonardo A Sechi

**Name of Journal:** *World Journal of Nephrology*

**ESPS Manuscript NO:** 16491

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

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewers as follows:

**Reviewed by 00503228**

Good article

**Author:** Thank you.

**Reviewed by 00503207**

In their manuscript, Catena et al. try to focus on two surrogate markers of cardiovascular disease in chronic renal failure. However, these topics could have been interesting, but the exposition of them is quite poor. This is especially true for the second part, the prothrombotic state, where authors cite only two papers from 1994 and 2000. What did happen in this field since that time? But also in case of Lp(a) part, more data for example about the pathophysiological involvement in atherosclerosis, or some information about ongoing follow-up studies of this field would be worth to be discussed. The summary in one sentence about this minireview is: many authors, few messages. Other comment: In table 1 from the list of emerging non-traditional risk factors arterial stiffening and endothelial dysfunction are missing. In summary, in this form I do not recommend this paper for publication. It requires more work to increase the quality.

**Author:** We thank the Reviewer for his comments. Although the medical literature of recent years on these topics is rather poor and in particular in subjects with early impairment of renal function that are the subject of the article, we have updated the manuscript with further citations on the role of lipoprotein(a) and the prothrombotic state in early renal failure as requested (page, lines). As also requested, arterial stiffening and endothelial dysfunction have been added in the revised Table 1.

**Reviewed by 00503233**

Excellent review, no changes required.

**Author:** Thank you.

**Changes in the revised manuscript** (red character)

Page 5, lines 19-28: the following sentences have been added: "The association of GFR with Lp(a) levels was investigated in the 7,675 participants of the Third National Health and Nutrition Survey (NHANES) [25]. In this population study, a moderate impairment of GFR was associated with greater Lp(a) levels although this association was more prominent in non-Hispanic blacks and Mexican Americans than non-Hispanic whites. Despite this association of elevated Lp(a) levels with early decrease of GFR, other studies demonstrated that this lipoprotein does not contribute to progression of chronic kidney disease [26]. The mechanisms through which Lp(a) promotes atherosclerosis in patients with or without renal failure are not clearly understood. Proposed mechanisms include and increased Lp(a)-associated cholesterol capture in the arterial intima, inflammatory cell recruitment, and carrying of proinflammatory oxidized phospholipids [27]."

Page 5, lines 31-32: the following sentence has been added: "Also, elevated Lp(a) levels have been found to be frequently associated with hyperhomocysteinemia in patients with pre-dialysis renal failure [28]."

Page 6, lines 20-26: the following sentences have been added: "Consistently, in 50 patients with stage 2-3 renal failure plasma fibrinogen was significantly increased possibly contributing to the high cardiovascular morbidity of these patients [35]. In the 3,758 patients with GFR of 20 to 70 ml/min 1.72 m<sup>2</sup> of the Chronic Renal Insufficiency Cohort (CRIC) Study, a prothrombotic state was associated with increased prevalence of peripheral artery disease [36]. In a prospective study of 4,029 men aged 60-79 years who were followed for an average period of 6 years, mild-to-moderate renal failure was associated with increased plasma levels of hemostatic markers and caused significantly increased cardiovascular mortality [37]."

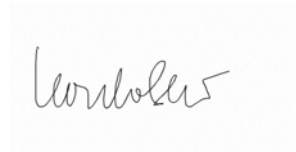
Table 1: endothelial dysfunction and arterial stiffening have been added in the revised manuscript

References 25, 26, 27, 28, 35, 36, 37 have been added

3 References and typesetting were corrected

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

Sincerely yours,



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