Soluble CD14, a marker of endotoxemia, associates with progression of CKD

Ruben Poesen[1], Pieter Evenepoel[1] ,Ali Ramezani[2], Kathleen Claes[1], Allen Jian[2] ,Björn Meijers[1], Dominic Raj[2]

[1]Division of Nephrology, Department of Microbiology and Immunology, University Hospitals Leuven, Leuven, Belgium

[2]Division of Renal Diseases and Hypertension, George Washington University, Washington, USA

INTRODUCTION AND OBJECTIVES

Endotoxemia has been linked to sepsis-related AKI. Although gut microbial dysbiosis and a disturbed gut barrier may promote endotoxin exposure in CKD, data to support this are scarce. In addition, whether endotoxemia is a risk factor for progression of pre-existing renal disease is unknown. Endotoxin activates the innate immune system after binding to toll-like receptor-4 and its co-receptor CD14. As half-life of systemic endotoxin is very short, soluble CD14 (sCD14) has been proposed as a better marker of endotoxin exposure. In this study, we explored the interaction between sCD14 and renal function.

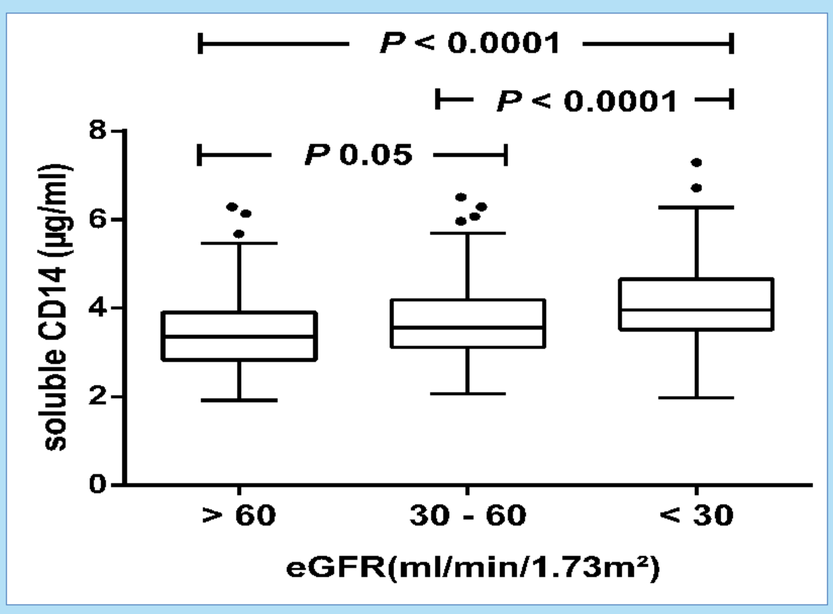
METHODS

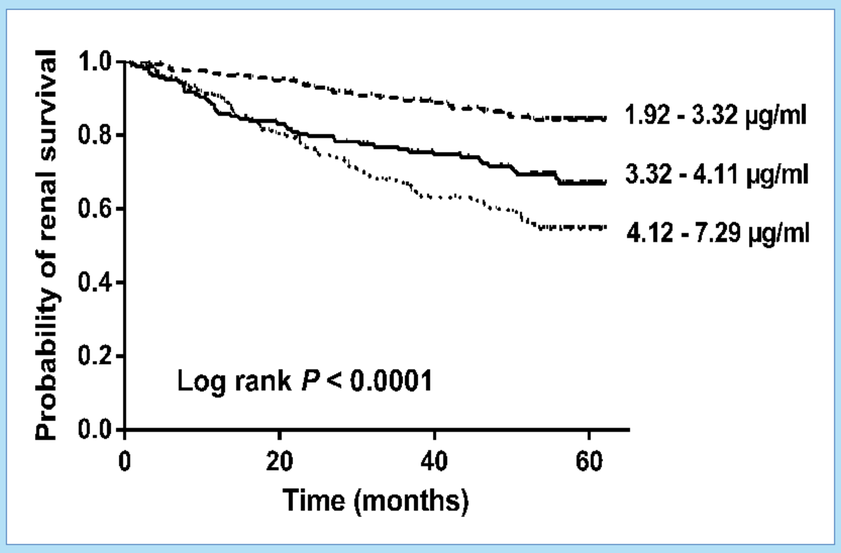
We performed a prospective study in patients with CKD stage 1-5 (NCT00441623). Plasma levels of sCD14 were determined using ELISA (sCD14 Quantikine Kit, R&D Systems). The relationship between renal function and sCD14 was investigated using ANOVA and regression analysis. For outcome analysis, we explored the role of sCD14 with respect to CKD progression, using Kaplan Meier estimates and Cox proportional hazard analysis. CKD progression was defined as doubling of serum creatinine or progression to dialysis during follow-up.

RESULTS

- 499 CKD patients were followed from November 2005 until December 2010
- Median plasma level of sCD14 was 3.72 µg/mL (IQR 3.15 – 4.40)
- Significant relationship between kidney function and sCD14 (see figure)
- 132 CKD progressors with a gradually increased risk with higher tertiles of plasma sCD14 (Log rank P < 0.0001) (see figure)
- Cox proportional hazard analysis:

sCD14 remained a significant predictor of CKD progression (univariate HR per SD increase of 1.659 (1.385 – 1.987), P < 0.0001), even after adjustment for renal function, anemia, calcium-phosphate metabolism, use of ACEI/ARB, Framingham risk factors, inflammation and nutritional parameters (HR 1.659 (1.385 – 1.987), P 0.04)





CONCLUSIONS

Higher plasma levels of sCD14 are observed in patients with advanced CKD, indicating increased exposure to endotoxins, sCD14 is independently associated with CKD progression, pointing to a causative and/or prognostic role for sCD14 in patients with renal dysfunction.

UZ Leuven | Herestraat 49 B - 3000 Leuven | www.uzleuven.be tel. 0032 (0)16 33 22 11

UNIVERSITY HOSPITALS LEUVEN

52 ERA 269--FP

J2) Chronic Kidney Disease. Pathophysiology, progression & risk factors.

Ruben Poesen

DOI: 10.3252/pso.eu.52era.2015

ePosters supported by F. Hoffmann- La Roche Ltd.

52nd ERA-EDTA CONGRESS London 2015 UNITED KINGDOM MAY 28TH -31ST

PosterSessionOnline.com