Acta Diabetologica (2019) 56:381–382
https://doi.org/10.1007/s00592-018-1250-8

LETTER TO THE EDITOR

Serum bilirubin concentrations, type 2 diabetes and incident coronary heart disease

Tomoyuki Kawada[1]

Received: 5 October 2018 / Accepted: 29 October 2018 / Published online: 22 November 2018

Dear Editor,

I have read the research article "Serum bilirubin concentrations and incident coronary heart disease risk among patients with type 2 diabetes: the Dongfeng-Tongji cohort" by Wang et al [1]. The authors conducted a prospective study to investigate the effect of serum bilirubin levels on incident coronary heart disease (CHD) among type 2 diabetes patients. Adjusted hazard ratio (HR) [95% confidence interval (CI)] of serum indirect bilirubin for incident CHD was 0.74 (0.56–0.99). In addition, drinking status affected the association between serum total, direct and indirect bilirubin and incident CHD. I have a concern about the study.

Uludag et al. conducted a prospective study to examine the effect of serum total bilirubin level on subsequent decline in renal function or new-onset of chronic kidney disease (CKD) in patients with type 2 diabetes mellitus [2]. Adjusted HR of lower serum total bilirubin level for the development of CKD stage 3 significantly increased. Li et al. also conducted a retrospective cohort study to investigate the effect of serum bilirubin on the progression of renal function in CKD patients [3]. Adjusted HR of serum indirect bilirubin for renal replacement therapy or death in CKD patients with hyperuricemia significantly decreased, and they speculated a high serum indirect bilirubin level was protective for the progression of renal function in patients with CKD and hyperuricemia. Although these two reports did not evaluate events of coronary heart disease, serum bilirubin level was closely associated with subsequent progression of CKD. In addition, hyperuricemia had an interaction on the association. Wang et al. did not use these factors for the adjustment, and I think that comprehensive analysis is required for the risk assessment of CHD.

As one of the mechanisms of the association, antioxidant actions of bilirubin for the protection of endothelial cells would be partly associated with protection for incident CHD [4]. In addition, inhibition of xanthine oxidase activity was correlated with attenuation of oxidative stress [5], and antioxidant actions of bilirubin would be observed in patients with hyperuricemia. Hyperuricemia is closely related to type 2 diabetes via insulin resistance, and I speculate the association between serum bilirubin levels and incident CHD by these mechanisms.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

Research involving human and/or animal participants This article does not contain any studies with human or animal subjects performed by the any of the authors.

Informed consent For this type of study formal consent is not required.

References

1. Wang J, Wu X, Li Y et al (2017) Serum bilirubin concentrations and incident coronary heart disease risk among patients with type 2 diabetes: the Dongfeng-Tongji cohort. Acta Diabetol 54:257–264
2. Uludag K, Oguzhan N, Arıkan T, Boz G (2018) Serum bilirubin level and its impact on the progression of chronic kidney disease. Int Urol Nephrol 50:1695–1701
3. Li M, Li X, Liu Y et al (2018) Relationship between serum bilirubin levels s and the progression of renal function in patients

Managed by Massimo Porta.

This comment refers to the article available at doi:https://doi.org/10.1007/s00592-016-0946-x.

Reply to this comment is available at doi:https://doi.org/10.1007/s00592-018-1251-7.

✉ Tomoyuki Kawada
kawada@nms.ac.jp

[1] Department of Hygiene and Public Health, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-Ku, Tokyo 113-8602, Japan

with chronic kidney disease and hyperuricemia. Clin Chim Acta 486:156–161
4. Jansen T, Hortmann M, Oelze M et al (2010) Conversion of biliverdin to bilirubin by biliverdin reductase contributes to endothelial cell protection by heme oxygenase-1-evidence for direct and indirect antioxidant actions of bilirubin. J Mol Cell Cardiol 49:186–195
5. Gliozzi M, Malara N, Muscoli S, Mollace V (2016) The treatment of hyperuricemia. Int J Cardiol 213:23–27