Author's response to reviews

Title: The risk for chronic kidney disease in patients with heart diseases: a 7-year follow-up in a cohort study in Taiwan

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Major

1. Estimated mechanism of developing CKD in this cohort Table 2 demonstrates the higher incidence of developing CKD in patients with DM and hypertension regardless of comorbid heart disease. Table 3 confirms the significance of DM and hypertension for developing CKD. These results suggest the importance of atherosclerotic risk factors for developing CKD and this is consistent with KDOQI clinical practice guidelines for CKD, regardless of heart disease. Moreover, additional analysis and table that authors made provide us very important information. Hypertensive heart disease, ischemic heart disease, and chronic heart failure, but not rheumatic or valvular heart disease, are the significant factors for developing CKD in patients with heart disease. These results remind us the importance of atherosclerotic risk factors, related heart disease, and chronic heart failure as their terminal stage, for developing CKD. As the authors insist, venous congestion might be one of the important factors for developing CKD. However the dataset of the present analysis have no hemodynamic data. Additional analysis is not enough for suggesting venous congestion as the risk for developing CKD. It’s better to discuss venous congestion as one of the possible mechanisms for developing CKD. As the authors mentioned, reciprocal direction between CKD and heart disease might be emphasized.

Ans: In discussion, third paragraph, we add the sentences to emphasize the point that you are pointed out as the follows: “Our results suggest the importance of atherosclerotic risk factors for developing CKD and this is consistent. Moreover, additional analyses that we made provide us more information. Hypertensive heart disease, ischemic heart disease, and chronic heart failure, but not rheumatic or valvular heart disease, are the significant factors for developing CKD in patients with heart disease. These results remind us the importance of atherosclerotic risk factors, related heart disease, and chronic heart failure as their terminal stage, for developing CKD. Growing evidence suggests that atherosclerosis has direct effects on the kidney, largely because of intrarenal microvascular and glomerular disease that precedes the onset and represents the silent phase of ischemic renal disease [16-18]. Renal function abnormalities may exist at the early stages of atherogenesis and in patients with evidence of only extrarenal atherosclerosis and may precede the onset of overt
ischemic nephropathy [18,19]. Indeed, nonobstructive atherosclerosis accelerates the decrease of renal size and the increased of serum creatinine level with age [18, 20], implying that deterioration of renal function is likely the result of direct parenchyma compromise, likely provoked by atherogenic factors.”

Minor

1. P10 Line4: The association between CKD and heart disease was significantly greater in men than women and the HR increased with age in the multivariable Cox model (Table 3 model 2 and model 3).

Ans: The sentence is revised as “The association of developing CKD was significantly greater in men than women and the HR increased with age in the multivariate Cox model (Table 3, model 2 and model 3).”

2. P10 Line 6: The hazard ratios of developing CKD associated with heart disease were augmented with age after adjusted for socioeconomic factors (Table 3, model 2). The statistical significance still existed even after additional adjustment for cardiometabolic risks such as diabetes, hypertension and hyperlipidemia (Table 3, model 3).

Ans: The sentence is revised as “The HR of developing CKD was augmented with age after adjusted for socioeconomic factors (Table 3, model 2). The statistical significance still existed even after additional adjustment for cardiometabolic risks such as diabetes, hypertension and hyperlipidemia (Table 3, model 3).”

3. P10 Line 8: The hazard ratio of CKD for patients with heart disease decreased to 2.37 (95% CI 2.05-2.74). This sentence is the main result of this study and should be more emphasized.

Ans: It is described more detail as the following: “In univariate analysis, the HR of developing CKD for patients with heart disease was 4.10 (CI = 3.61-4.66) (Table 3, model 1). In multivariate models, the HRs were 4.20 (CI = 3.70-4.78) after adjusted for baseline sociodemographic factors (Table 3, model 2) and decreased to 2.37 (95% CI = 2.05 - 2.74) after adjusted for baseline sociodemographic and cardiometabolic factors (Table 3, model 3).”

4. Low incidence rate of CKD: CKD diagnosis system used in this study might
based on the eGFR calculated by each physician, and diagnosed and registered as CKD in patients with eGFR < 60ml/min/1.73m2 or abnormally elevated serum creatinine. Thus, the majority of patients with slightly elevated serum creatinine likely not to be diagnosed as CKD if the physicians are not nephrologists. A low incidence of CKD might not only be the complete exclusion of CKD from baseline registry, but there might not have fully been captured the patients with developing CKD in a follow up period. If so, authors might mention about it in limitation.

Ans: In the part of limitation, these sentences had been existed to clarify the limitation that you point out. “Moreover, physicians other than nephrologists might diagnose CKD by the definition of abnormal serum creatinine concentration. It is possible that some patients with earlier stages (stage 1-2) of CKD were not identified. Although this coding is somewhat less sensitive for identifying CKD in its early stage, it is used as a measure of kidney function by physicians other than nephrologists. Thus, the diagnostic values of patients with early stage CKD have not yet been fully evaluated.”