



Commentary on 'the predictors of daytime blood pressure, nighttime blood pressure, and nocturnal dipping in patients with chronic kidney disease'

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Elevation of nocturnal blood pressure(BP) is associated with increased risk of cardiovascular disease and progression of renal disease [1–4]. In the Dublin outcome study, nocturnal BP was the strongest predictor of cardiovascular disease compared to daytime BP and office BP [5]. Previously, studies have shown that chronic kidney disease(CKD) is associated with high prevalence of nocturnal hypertension and nocturnal hypertension has been shown to be a significant predictor of cardiovascular events and renal disease progression in patients with CKD [2, 6]. Therefore, determining clinical factors associated with nocturnal BP elevation in CKD will have clinical significance. The study by Motiejunaite et al. has clinical significance in that it determined the risk factors associated with nocturnal hypertension and non-dipping in a cohort of patients with CKD [7]. The strength of the study was that they analyzed eGFR and volume status using the gold standard method of using tracer $^{51}\text{CrEDTA}$. The study cohort also consisted of satisfactory number of sub-Saharan Africans to determine the racial difference of risk factors of nocturnal BP elevation. The important finding was that sub-Saharan African origin, BMI, lower eGFR, diabetes, albuminuria, lower serum potassium and extracellular water status were significantly associated with nighttime blood pressure while sub-Saharan African origin, measured eGFR and diabetes was associated with non-dipping. An interesting finding

was that in subjects with eGFR of $\geq 45 \text{ ml/min}/1.73 \text{ m}^2$, male gender, age, BMI, lower serum potassium and albuminuria were associated with nocturnal BP while extracellular water had no significant association. On the other hand extracellular water showed a tendency for association with nocturnal BP in subjects with eGFR $< 45 \text{ ml/min}/1.73 \text{ m}^2$. These results suggest that the association of volume status and nocturnal blood pressure may differ according to the degree of renal impairment, with excess volume being a more important determinant in those with advanced CKD. As excess volume is one of the major factors for poor prognosis and poor BP control in advanced CKD, adequate use of diuretics is important for BP control, as demonstrated in the CLICK trial [8, 9]. There was also a stronger association between the association of extracellular water and nighttime BP in sub-Saharan Africans, reaffirming the importance of volume status as a major determinant of hypertension in sub-Saharan Africans.

As was reported in previous studies, diabetes mellitus and proteinuria are known to be significantly associated with nocturnal hypertension and non-dipping [10–12]. However, this study had a limited number of diabetic nephropathy cases to confirm this association. Of note, albuminuria originating from different diseases may each have a distinct relationship with BP dipping status. Moreover, as stated by the authors, the data collection was done before the widespread use of SGLT2 inhibitors for treatment of proteinuria. In the future, it would be interesting to see the effect of SGLT2 inhibitors on nocturnal BP and its impact on the progression of CKD.

Masked hypertension is prevalent and contributes to poor cardiovascular and renal outcomes in CKD [13–16]. The results from the study by Motiejunaite et al. suggest that a significant portion of the cohort may have masked hypertension, based on the proportion of controlled blood pressures by either office measurements or ambulatory blood

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pressure monitoring (ABPM). Previous study by Drawz et al. using the CRIC cohort has shown that masked hypertension is associated with poor target organ damage, which is prominent in elevated nocturnal BP in CKD patients [17]. However, there is limited evidence on the factors influencing nocturnal BP and dipping patterns in CKD patients with masked hypertension. This study's findings on factors such as sub-Saharan Africans, low measured GFR, and diabetes warrant further investigation to determine if they are also applicable to the masked hypertension subgroups of CKD patients.

Lastly, one of the surprising findings from this study was that lower serum potassium was associated with elevated nocturnal hypertension. Primary aldosteronism is highly prevalent in hypertension and long standing primary aldosteronism is associated with kidney injury [18, 19]. Also, studies have shown that primary aldosteronism is associated with high prevalence of nocturnal hypertension and non-dipping status [20, 21]. However, primary aldosteronism is highly underdiagnosed due to masking of hypokalemia and limitations for using diagnostic imaging studies. The results from this study signals a possible hidden association between primary hyperaldosteronism and nocturnal BP elevation in patients with CKD. Future studies to determine this association is warranted.

Compliance with ethical standards

Conflict of interest JHH has nothing to declare. SP received honoraria from Viatris, Organon, Boryoung, Hanmi, Daewoong, Donga, Celltrion, Servier, Daiichi Sankyo, Chong Kun Dang, and Daewon, and a research grant from Daiichi Sankyo. SP has received consultation fee from Skylab. Also, SP has received stock option from Mediwhale. Others have nothing to declare.

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