



Pre-dialysis blood pressure and cardiovascular mortality in Japan: need for much stricter control?

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Keywords Dialysis · Cardiovascular mortality · DKD · Pre-dialysis blood pressure · Salt intake

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The kidney has an important role in the pathogenesis of hypertension; the prevalence of hypertension increases with the deterioration of kidney function [1, 2]. Cardiovascular disease (CVD) is a leading cause of mortality in patients with chronic kidney disease (CKD) undergoing dialysis therapy [3], and blood pressure (BP) control is thought to be extremely important in preventing major cardiovascular events and mortality in patients with CKD [4, 5]. However, among patients with maintenance hemodialysis, many studies consistently noted a U-shaped relationship between systolic BP (SBP) at the start of dialysis and various hard outcomes such as cardiovascular events and all-cause mortality [2, 6–8]. In fact, a minimum risk of the total mortality rate in hemodialysis patients in Japan was shown at a pre-dialysis SBP of 140–159 mmHg [8]. Furthermore, a number of studies indicated that a decrease in BP during dialysis (intradialytic hypotension) was involved in a risk of hard outcomes and mortality [9, 10]. Therefore, it is difficult to establish the numerical target of BP control in patients undergoing hemodialysis [1].

Hypertension associated with CKD is often resistant to drug treatment; the pathophysiology of hypertension in patients with CKD is considered to be multifactorial [11]. Among them, sodium/volume excess as well as the renin-angiotensin-aldosterone system activation are thought to be most important, although other alternative mechanisms have been proposed to be involved, including the increased sympathetic nervous system activity, the decreased availability or action of endothelium-derived vasodilators, and the decreased activity of natriuretic peptides [11]. In

addition, medications such as cyclosporine, steroids, erythropoietin, and nonsteroidal anti-inflammatory drugs may contribute to aggravating hypertension in CKD patients [11]. These factors altogether should make the proper management of BP quite difficult and complex especially in patients with advanced CKD.

In the latest issue of *Hypertension Research*, Sakuma et al. reported a nation-wide analysis of regional variation in pre-dialysis BP and risk of cardiovascular mortality rates in Japanese dialysis patients [12]. Using large-scale data extracted from the registry of the Japanese Society for Dialysis Therapy, they analyzed clinical data of more than 336,000 patients undergoing dialysis in Japan. They found that the prefecture-based mean pre-dialysis SBP values were all higher than 140 mmHg especially in those with diabetic kidney disease (DKD), and that, at the prefectural level, CVD mortality rate was positively correlated with pre-dialysis SBP among female patients [12]. They concluded that the positive association between pre-dialysis SBP and CVD mortality rate suggests an importance of optimal BP management at the prefectural level to reduce CVD mortality, especially in female patients. The reason why there was no significant correlation found among male patients was not clear at present. A recent report on sex differences in cause-specific mortality in Japanese dialysis patients showed that death from CVD was more common in males than in females (1.15-fold), especially from myocardial infarction (1.53-fold) and hyperkalemia/sudden death (1.36-fold) [13]. Further investigation on such sex differences should be important to reduce CVD mortality in male patients.

Another important information of the current study was that pre-dialysis SBP was higher in patients with DKD (~160 mmHg) than those with non-DKD (~140–150 mmHg), and that the CVD mortality rate was significantly higher in patients with DKD than those with non-DKD [12]. However, no significant association was found between pre-dialysis BP and CVD mortality rate among patients with DKD. Although

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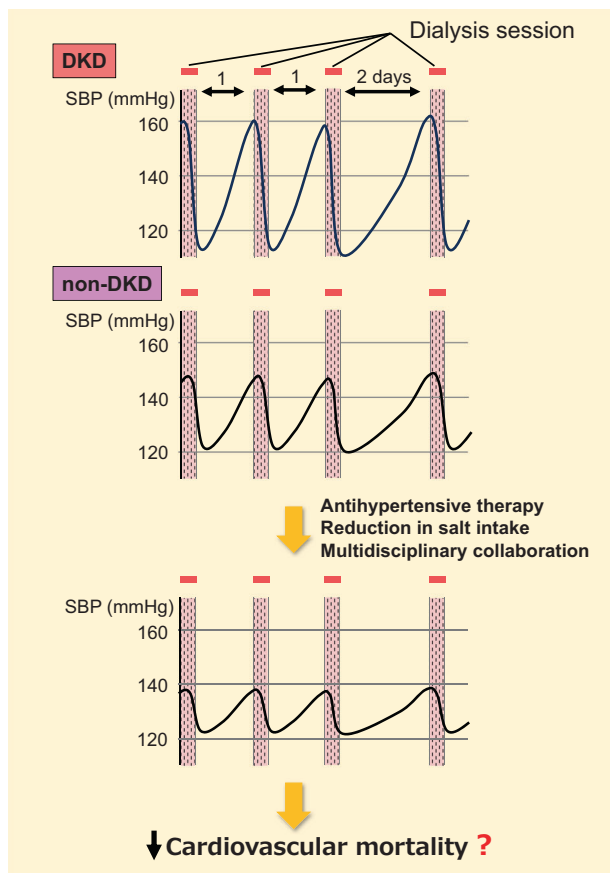


Fig. 1 A proposed scheme for better management of pre-dialysis blood pressure in patients to reduce cardiovascular mortality. DKD diabetic kidney disease, SBP systolic blood pressure

not clarified yet, this could be due to much complex hemodynamic states in patients with DKD, such as a large variety of BP values during a single dialysis session as well as a higher occurrence of intradialytic hypotension in those with DKD [14].

Of note, the present study showed that CVD mortality was relatively high in the Tohoku area [12], an area where salt intake is assumed to be high [15]. Although not investigated in this study, it is well conceivable that the reduction in salt intake in dialysis patients could lead to more favorable BP control, thus eventually decreasing CVD occurrence and cardiovascular mortality in those with high pre-dialysis BP (Fig. 1). Avoidance of intradialytic hypotension by managing interdialytic body weight changes is no doubt equally important to decrease cardiovascular mortality, especially in DKD patients. To achieve this goal, we should further proceed with multidisciplinary collaboration, at the prefectural level, including physicians, nurses, pharmacists, and certified educators for kidney disease with related professionals. We should also continue to investigate a large-scale analysis for defining optimal target BP levels to reduce CVD occurrence and mortality, in patients undergoing maintenance dialysis therapy.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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