Editorial

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Identifying the optimal blood pressure target among Korean hemodialysis patients: current evidence and future directions

Young Su Joo[1,2], **Tae-Hyun Yoo**[1]

[1]*Department of Internal Medicine and Institute of Kidney Disease Research, Yonsei University College of Medicine, Seoul, Republic of Korea*
[2]*Division of Nephrology, Department of Internal Medicine, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Republic of Korea*

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Elevated blood pressure (BP) in patients with chronic kidney disease (CKD) is linked to CKD progression, cardiovascular events, and increased mortality. Therefore, BP management remains a major component of contemporary CKD care [1]. Several clinical guidelines have suggested BP targets to prevent adverse events in nondialysis patients with CKD, with evidence that individuals with systolic BP (SBP) higher than 120 to 140 mmHg have an increased risk of renal decline, cardiovascular events, and mortality [2]. The prevalence of hypertension is approximately 75% to 90% of hemodialysis patients undergoing hemodialysis [3]. Therefore, BP management in hemodialysis patients is crucial; however, a consensus on optimal BP targets remains elusive owing to limited evidence. BP management in hemodialysis patients requires careful balancing, as both persistent hypertension and intradialytic or postdialysis hypotension are independently associated with adverse outcomes, including falls and cardiovascular mortality. Most clinical trials in hemodialysis patients have focused on assessing the risk of cardiovascular events or death for a particular antihypertensive medication or hemodialysis modality and have not considered the target BP range in these populations. Previous observational studies investigating the association between BP categories and cardiovascular disease or mortality have demonstrated inconsistent findings, likely attributable to the reverse epidemiology in patients with kidney failure requiring renal replacement therapy (KFRT), variability in BP measurement timing (e.g., predialysis vs. postdialysis), hemodialysis treatment factors (hemodialysis vs. hemodiafiltration), and heterogeneous definitions of BP thresholds and outcomes of interest across studies (Fig. 1) [4–6].

In this issue of *Kidney Research and Clinical Practice*, Kim et al. [7] conducted a valuable study that addressed this gap using data from >70,000 hemodialysis patients in the Korea Renal Dialysis System (KORDS) to analyze the association between BP levels and mortality risk. This study investigated three critical research questions to advance our understanding of BP management in patients undergoing hemodialysis. First, which parameter, SBP or diastolic BP (DBP), exhibits a stronger association with mortality, addressing ongoing debates regarding risk stratification priorities? Second, what are the magnitudes and directionality of the

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Correspondence: Young Su Joo
Division of Nephrology, Department of Internal Medicine, Yongin Severance Hospital, Yonsei University College of Medicine, 363 Dongbaekjukjeon-daero, Giheung-gu, Yongin 16995, Republic of Korea. E-mail: jooys@yuhs.ac
ORCID: https://orcid.org/0000-0002-7890-0928

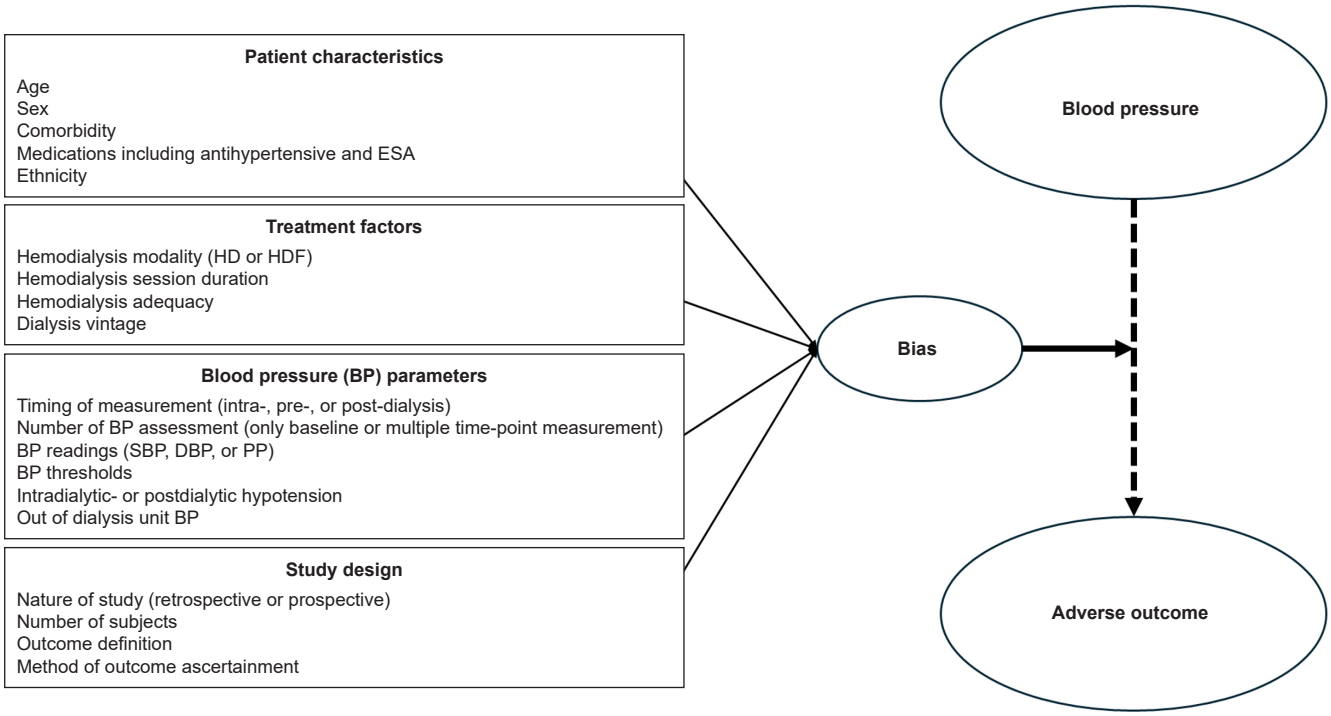

Figure 1. Attributable bias in optimal blood pressure studies for mortality among patients with hemodialysis.
ESA, erythropoietin-stimulating agent; DBP, diastolic blood pressure; HD, hemodialysis; HDF, hemodiafiltration; PP, pulse pressure; SBP, systolic blood pressure.

relationships between discrete BP strata and cause-specific mortality, particularly cardiovascular and all-cause mortality? Third, do specific patient subgroups, such as those stratified by age (<70 or >70 years) or diabetes status, derive differential prognostic benefits from specific BP ranges? To answer these questions, they utilized the KORDS dataset, which included Korean patients with KFRT maintained on hemodialysis and registered from 2001 to 2020. In addition to BP measurements, the analysis incorporated variables associated with clinical outcomes including demographic characteristics, dialysis-related treatment parameters, and laboratory data from the KORDS dataset. SBP and DBP were grouped at intervals of 20 and 10 mmHg, respectively. The main analysis evaluated all-cause mortality according to BP strata and separately assessed cardiovascular mortality according to BP categories. The strength of this study lies in its analysis of the association between BP and mortality, using a sufficiently large cohort and consistent outcome definitions.

The present study demonstrated that SBP, rather than DBP, is associated with all-cause and cardiovascular mortality. These findings align with the results from a study involving nondialysis patients with CKD, demonstrating that SBP exhibited a stronger association with cardiovascular outcomes and mortality than DBP [8]. The U-shaped relationship between SBP and all-cause mortality reinforces the findings of Jhee et al. [9], who utilized data from the Clinical Research Center for End-Stage Renal Disease (CRC for ESRD), a prospective observational study that enrolled Korean patients with KFRT. This study demonstrated that both the lowest and highest SBP groups were significantly associated with an increased risk of mortality [9]. Nevertheless, Kim et al. [7] demonstrated different values of increased mortality risk according to prespecified outcomes and subgroups. Specifically, the all-cause mortality risk increased at SBP >180 mmHg, whereas the cardiovascular mortality risk increased at SBP >160 mmHg within the same population. Notably, the cardiovascular mortality risk in the lower SBP range (<120 mmHg) was comparable to that observed in the reference SBP range (120–140 mmHg). In the subgroup analysis, a higher SBP was significantly associated with all-cause mortality among younger

(<70 years) patients and patients without diabetes mellitus, suggesting that factors other than SBP are significantly associated with mortality in elderly or diabetic patients. The discrepancy in the relationship between BP and all-cause or cardiovascular mortality observed in previous studies may be partly explained by the heterogeneity in the operational definitions of outcomes, such as cardiovascular and all-cause mortality, as well as variations in the associations between adverse outcomes and subgroups defined by factors such as age or comorbid conditions. Finally, variations in the causes of death across populations influenced by differences in race and ethnicity may have contributed to the observed inconsistencies. A meta-analysis integrating the findings with published literature on SBP categories and mortality in hemodialysis patients indicated that patients with extreme SBP readings (<120 mmHg or >180 mmHg) exhibited an elevated all-cause mortality risk [7].

However, significant gaps remain in defining optimal BP targets to mitigate adverse clinical outcomes in patients undergoing hemodialysis. First, the KORDS database lacks documentation on the timing of BP measurements relative to dialysis sessions (pre-, intra-, or postdialysis). Second, longitudinal BP assessments are imperative, as single-time-point measurements frequently fail to predict adverse outcomes such as CKD progression and mortality, whereas time-updated analyses reveal stronger correlations, as previously reported among nondialysis CKD patients [8,10]. Third, the absence of data on intradialytic hypotension (IDH) events is a potential confounding factor because IDH is independently associated with cardiovascular mortality. Further studies are required to address these limitations. Although prospective cohort studies are effective in establishing causal relationships, they are limited by their high costs and long timelines. Alternatively, electronic health records, which are available in modern dialysis systems, allow the aggregation of real-world BP data without requiring de novo collection. A multicenter collaborative study should provide sufficient participants to explore the link between optimal BP and clinical outcomes in patients undergoing hemodialysis. Standardized outcome definitions and comorbidity classifications such as those in the KORDS database can enhance retrospective study designs, help resolve discrepancies in observational evidence, and advance personalized management strategies in hemodialysis care.

In conclusion, the study by Kim et al. [7] contributes to the growing body of evidence on the association between BP and survival in Korean hemodialysis patients. This study underscores the necessity for large-scale data-driven epidemiological studies to further delineate the optimal BP target for enhancing survival among hemodialysis patients.

Conflicts of interest

Tae-Hyun Yoo is the Editor-in-Chief of *Kidney Research and Clinical Practice* and was not involved in the review process of this article. The authors declare no other conflicts of interest.

Data sharing statement

The data presented in this study are available from the corresponding author upon reasonable request from the corresponding author.

ORCID

Young Su Joo, https://orcid.org/0000-0002-7890-0928
Tae-Hyun Yoo, https://orcid.org/0000-0002-9183-4507

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