Blood Pressure Variability and the Progression of Chronic Kidney Disease: a Systematic Review and Meta-Analysis

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BACKGROUND: Blood pressure variability (BPV) is a risk factor for poor prognosis including cardiovascular events, chronic kidney disease, and mortality, independent of elevated BP.

METHODS: We searched PubMed/Medline, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) from inception to November 23, 2022. Cohort studies reporting the association between BPV and chronic kidney disease (CKD) progression were selected. Hazard ratios were pooled using a random-effects model. Meta-regression, subgroup analyses, and sensitivity analyses were conducted.

RESULTS: A total of 23 studies were included in this systematic review and meta-analysis. Increased BPV was associated with progression of CKD (HR: 1.21, 95% CI: 1.09–1.33) and incidence of ESRD (HR: 1.08, 95% CI: 1.08–1.30). Among the different BPV metrics, high variation independent of mean (VIM), coefficient of variation (CV), standard deviation (SD), and average real variability (ARV) were indicated as predictors of CKD progression.

DISCUSSION: Increased BPV was associated with CKD progression.

KEY WORDS: blood pressure variability; chronic kidney disease; end-stage renal disease.

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BACKGROUND

Blood pressure variability (BPV) is defined as fluctuations in blood pressure (BP) occurring within periods of time, for example, hours, days, weeks, months, and even years. BP follows a circadian rhythm in some people. When nocturnal BP decreases by an average of 10–20% compared to daytime values, it is referred to as "dipping."[1] BPV is classified as very-short-term BPV (beat to beat), short-term BPV (within a 24-h period), and long-term BPV (day to day or visit to visit). In the past, BPV was thought to be due to error in BP measurement. However, recent studies have indicated that BPV is the result of interactions between the extrinsic environment and intrinsic regulatory mechanisms. The underlying mechanisms of BPV are complex. BPV may reflect fluctuations in neuromodulation, hormonal regulation, psychological factors, custom behavior, and even seasonal changes. Measurement of BPV varies and can include office blood pressure monitoring (OBPM), 24-h ambulatory monitoring (24-h ABPM), and home blood pressure monitoring (HBPM). Several metrics of BP could be used to assess BPV, including standard deviation (SD), coefficient of variation (CV), variation independent of the mean (VIM), average real variability (ARV), and weighted standard deviation (W-SD). While elevated BP is a universally known risk factor for poor prognosis and multiple organ damage, since the 1980s, BPV has been shown to increase cardiovascular events, renal damage, and even mortality, independent of elevated BP.[2–6]

Chronic kidney disease (CKD) is common, with 697.5 million cases of CKD globally in 2017.[7] CKD is often a slowly progressive disease, characterized by irreversible renal dysfunction leading to end-stage renal disease (ESRD). ESRD is associated with poor health outcomes.[8] In recent decades, treatment costs for CKD have risen sharply.[9] Approximately 2.3–7.1 million adults die from a lack of access to renal replacement therapy.[7] In recent years, growing evidence has indicated that increased BPV is independently associated with the development of CKD.[10] Moreover, several prospective cohort studies have investigated the relationship between BPV and CKD progression,[11] though some studies have failed to find an association.[14, 15] Given this inconsistent data, our study purpose was to conduct a meta-analysis to evaluate the relationship between BPV and CKD progression.

METHODS

Protocol and Guidance

This meta-analysis is reported in accordance with the Cochrane handbook and Preferred Reporting Items for Systematic

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Reviews and Meta-Analyses (PRISMA).[12] The study protocol was registered in PROSPERO (CRD42020215037).

Study Search

A search was conducted in PubMed/Medline, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) from inception to November 23, 2022. Complete search strategies for each database are provided in Supplementary Table 1. Searches were not limited by language, date, or study type. We also manually searched gray literature and references from the included studies.

Study Selection and Eligibility Criteria

After removal of duplicates, two reviewers (YLT and LJ) independently screened the titles and abstracts of all identified records. If studies were identified as potentially relevant in the abstract screen, a full-text review was conducted. Disagreement about study selection was resolved by discussion between the review team members (YLT, LJ, and ZYL). We included studies of adults (over 18 years of age) who had not had a transplant or were on dialysis and had CKD stages 1–5. Additionally, studies had to provide follow-up information on the association between BPV and progression of CKD. Studies were excluded for the following reasons: (a) BPV was the outcome and (b) the study was an abstract only. If multiple articles were derived from the same cohort, the study with the most information was included.

Data Extraction

Using a standardized data form, two reviewers (YLT and LJ) independently extracted the following data from all included studies: the study characteristics, BPV measurement, and research outcomes. These data were validated by another reviewer (ZYL). For studies performing more than one multivariate regression analysis, data from fully adjusted models were included. For studies reporting results from multiple BPV metrics, we chose the results according to the following hierarchy: standard deviation (SD) → weighted standard deviation (W-SD) → coefficient of variation (CV) → variation independent of mean (VIM) → average real variability (ARV) → other metrics. The definition and calculation of BPV metrics were summarized in Supplementary Table 2. Similarly, for multiple indicators of CKD progression in the same study, the following hierarchy was used: composite renal outcome → the development of ESRD → decrease of eGFR → elevation of serum creatinine. In addition, the results derived from systolic BPV in the form of a continuous variable were preferred to results from diastolic BPV as a categorical variable. If relevant details of interest were not sufficient, we emailed the corresponding author for assistance.

Quality Assessment

The risk of bias of all included studies was assessed using the Quality In Prognosis Studies (QUIPS) tool.[13] The quality of the included studies was assessed in the following six domains: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis, and reporting. According to the prespecified standard criteria, two reviewers (YLT and LJ) independently assessed and scored each study. Disagreements were resolved by group discussion.

Data Synthesis and Statistical Analysis

The outcome was the progression of CKD, including the development of ESRD (inception of dialysis or kidney transplant), a decrease in eGFR, and an increase in serum creatinine. In the meta-analysis, the pooled effects were expressed as standardized HRs and 95% CIs under a random-effects model to allow for heterogeneity. $P < 0.05$ was considered statistically significant. Heterogeneity was assessed among the included studies by using the $\chi 2$ test and I^2 statistics. Meta-regression of a single covariate was used to investigate the potential source of heterogeneity. Then, we performed subgroup analyses based on different BPV metrics and study characteristics that were considered to be clinically important or potential contributors to heterogeneity by meta-regression. Sensitivity analysis was conducted by sequentially deleting a single study each time in an attempt to identify the potential influence of the individual study. Statistical analysis was performed by two reviewers (YLT and LJ) independently, with adjudication by a third reviewer (ZYL). All analyses were performed in R software version 4.0.4 (R Development Core Team, Vienna, Austria).

RESULTS

Eligible Studies

The process of the literature search and selection are summarized in Figure 1. The initial search identified 6425 records. After duplicates were excluded, we screened the titles and abstracts of 2946 citations and removed 2877 irrelevant items. Then, the remaining 69 articles were eligible for full-text assessment. Six studies were reviews or comments. Eighteen studies investigated the association between BPV and the risk of CKD. One study focused on children with CKD. Two articles were derived from the same cohort, and we excluded those with less information. Nine studies assessed kidney injury rather than deterioration of renal function. Ultimately, 21 articles were included in the systematic review[8, 14–34] and 16 articles were included in the final meta-analysis.[8, 20–34]

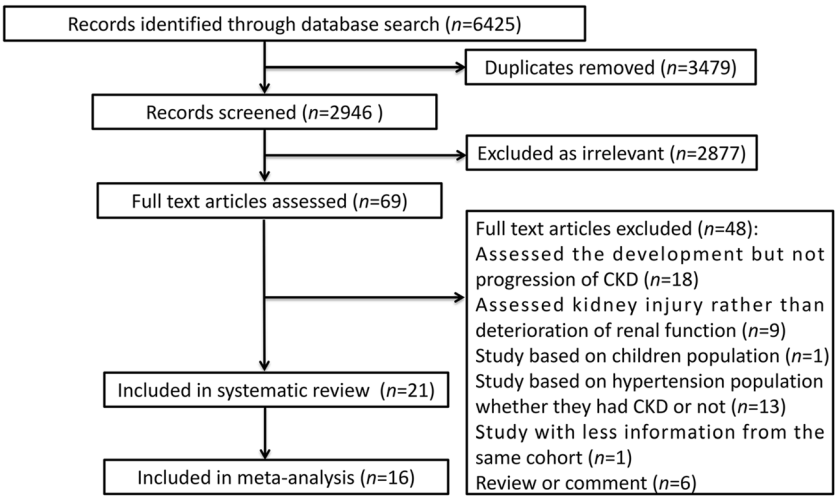

Figure 1 The flowchart of the study search and selection process.

Study Characteristics

Data from 746,744 patients were included in this meta-analysis. The sample size ranged from 29 to 537,313. Twenty-one studies were published from 2012 to 2022. There were 12 studies based on an East Asian population (China, Korea, and Japan) and 9 studies based on Western populations (the USA, Turkey, Greece, and Italy). The mean ages ranged from 37.1 to 77.4 years old. Thirteen studies enrolled patients with CKD regardless of the stage, while the other 8 studies enrolled patients with CKD with specific stages. The outcomes were variable in the eligible studies. Six studies reported on the incidence of ESRD. Eight studies reported on the decline in renal function. Seven studies reported the composite renal outcomes of ESRD or a decline in renal function. Study characteristics are shown in Table 1.

BPV Measurement

Thirteen studies measured long-term BPV (11 studies measured visit-to-visit BPV, and 2 studies measured day-to-day BPV), and 8 studies measured short-term BPV (within a 24-h period). Twenty studies reported SBP, and 7 studies reported DBP, with 6 studies reporting both. Variable metrics were used to assess BPV, including SD, CV, ARV, VIM, and W-SD. BPV was expressed as a categorical variable in 13 studies and as a continuous variable in 10 studies. The details of BPV measurement in each study are shown in Table 1.

Quality Assessment

Using the QUIPS tool, the methodological quality of each study was assessed (Supplementary Table 3). All studies were rated as low risk in the domain of prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. Most studies were rated as low risk in the domains of study participation (15/21, 71.43%). For the domain of study attrition, 10 studies (47.62%) were rated as low risk, and 11 studies (52.38%) were rated as moderate risk. No study was identified as high risk in any of these domains.

BPV and the Progression of CKD

Overall analysis of the 16 eligible studies indicated that increased BPV was significantly associated with the progression of CKD (HR: 1.21, 95% CI: 1.09–1.33, $P = 0.004$) (Fig. 2).

For 5 other eligible studies, a meta-analysis could not be performed due to lack of quantitative data or differences in methodology. Among them, 2 studies indicated BPV was negatively correlated with renal function in CKD patients using the correlation coefficient.[14, 17, 35] Sarafidis, P.A., et al. found within CKD stages an increasing trend from stage 1 toward stage 5, which was observed for variability of both SBP and DBP.[18] However, 2 studies reported opposite results. Okada, T., et al. enrolled 368 CKD patients and found that no significant difference in the change in eGFR was observed between the high-BPV group and the low-BPV group during the 2-year period.[19] In addition, Ryu, J., et al. also indicated that increased BPV could not predict the decline of eGFR.[16]

Meta-regression of a single covariate was used to examine possible sources of underlying heterogeneity ($I^2 = 72\%$, $P < 0.01$). The results showed that heterogeneity could be partially explained by year of publication (Supplementary Table 4).

When stratified by different indicators of CKD progression, increased BPV had a significant association with the incidence of ESRD (HR: 1.18, 95% CI: 1.08–1.30, $P < 0.001$) and composite renal outcome (HR: 1.36, 95% CI: 1.03–1.78, $P =$

Table 1 Characteristics and Blood Pressure Variability Measurement Methodology of Included Studies

Year	First author	Country	Sample size	Population	Age (years)	Gender (male, %)	Outcomes	BPV type	BP assessment	BP type	BPV metrics	Variable type
2019	Bae, E. H.	Korea	537,313	eGFR < 60 ml/min per 1.73 m^2	NA	NA	ESRD	Long-term	OBPM	SBP DBP	VIM	Categorical variable
2018	Borrelli, S.	Italy	465	Non-dialysis/ kidney transplant CKD	63.5 ± 14.2	267 (57.4)	ESRD Kidney function decline	Short-term	24-h ABPM	SBP DBP	W-SD CV	Categorical variable continuous variable
2016	Chang, T. I.	USA	114,900	CKD stages 3–4	74.4	47,477 (41.3)	ESRD	Long-term	OBPM	SBP	SD ARV	Categorical variable
2012	Di Iorio, B.	Italy	374	CKD stages 3–4	76 ± 11	232 (62)	ESRD	Long-term	OBPM	SBP	CV	Categorical variable
2021	Gregg, L. P.	USA	62,788	CKD stages 1–5	72.2	60,406 (96.2)	ESRD	Long-term	OBPM	SBP	CV	Categorical variable
2020	Jhee, J. H.	Korea	470	CKD stages 3–5	60.9 ± 12.0	259 (55.1)	Kidney function decline	Short-term	24-h ABPM	SBP	ARV	Categorical variable
2013	McMullan, C. J.	USA	908	eGFR of 20–65 ml/min per 1.73 m^2	55 (11)	562 (62)	ESRD Kidney function decline	Long-term	OBPM	SBP	SD	Categorical variable
2012	Okada, T.	Japan	135	Non-dialysis CKD stages 3–5	66.0 ± 10.0	98 (72.6)	Kidney function decline	Long-term	OBPM	SBP DBP	SD CV ARV	Categorical variable
2018	Sahutoglu, T.	Turkey	191	CKD stages 2–4	59.7 ± 12.4	105 (54.9)	Dialysis inception Kidney function decline	Short-term	24-h ABPM	DBP	CV	Categorical variable
2014	Takao, T.	Japan	664	Diabetic nephropathy	NA	NA	Kidney function decline	Long-term	OBPM	SBP	SD CV	Continuous variable
2020	Wang, Q.	China	1421	CKD stages 1–4	49.4 ± 13.6	798 (56)	Dialysis initiation Kidney transplantation	Short-term	24-h ABPM	SBP	W-SD	Continuous variable categorical variable
2013	Yokota, K.	Japan	56	Non-diabetic chronic kidney disease	69.5 ± 11.8	33 (59)	Dialysis initiation Kidney function decline	Long-term	OBPM	SBP DBP	SD CV	Continuous variable
2021	Pallikadavath, S.	UK	16,999	eGFR < 65 ml/min per 1.73 m^2	77.4	6812 (40.1)	ESRD	Long-term	OBPM	SBP	SD CV ARV	Continuous variable
2022	Tang, C.	China	1376	IgA nephropathy	37.1 ± 13.3	712 (51.7)	ESRD Kidney function decline	Long-term	OBPM	SBP DBP	SD	Categorical variable
2022	Wang, G.	China	245	Non-dialysis/ kidney transplant CKD	42.1 ± 12.7	141 (58)	Dialysis inception Kidney function decline	Short-term	24-h ABPM	SBP	VIM	Categorical variable
2017	Sethna, C. B.	USA	443	Glomerular diseases	43 (32, 57.8)	182 (61.5)	ESRD Kidney function decline	Long-term	OBPM	SBP DBP	SD ARV	Continuous variable
2008	Okada, T.	Japan	368	CKD patients	63 ± 13	253 (68.75)	Kidney function decline	Long-term	OBPM	SBP	CV	Categorical variable
2015	Nakano, C.	Japan	150	Non-dialysis/ kidney transplant CKD	62.7 ± 11.7	61 (40.6)	Kidney function decline	Long-term	OBPM	SBP	SD CV	Continuous variable
2017	Sarafidis, P.A.	Greece	6276	CKD patients	64.8 ± 12.3	2981 (47.5)	Advancing CKD stage	Short-term	24-h ABPM	SBP	SD wSD ARV	Continuous variable
2017	Isobe, S.	Japan	29	IgA nephropathy	42.7 ± 15.6	9 (31)	Kidney function decline	Short-term Long-term	OBPM	SBP	SD ARV	Continuous variable
2014	Ryu, J.	Korea	1173	Hypertensive CKD patients	56.6 ± 11.9	739 (63)	Kidney function decline	Short-term	24-h ABPM	SBP	ARV	Continuous variable

CKD chronic kidney disease, eGFR estimated glomerular filtration rate, ESRD end-stage renal disease, BPV blood pressure variability, BP blood pressure, OBPM office blood pressure monitoring, 24-h ABPM 24-h ambulatory blood pressure monitoring, SBP systolic blood pressure, DBP diastolic blood pressure, VIM variation independent of mean, W-SD weighted standard deviation, CV coefficient of variation, SD standard deviation, ARV average real variability

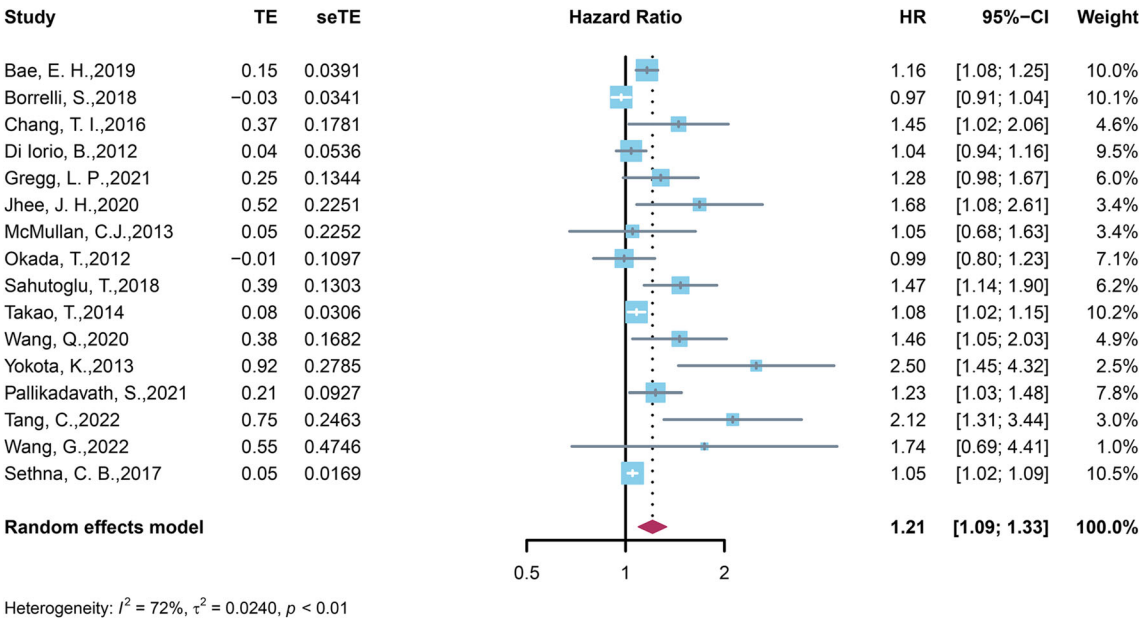

Figure 2 Meta-analysis of CKD progression in a random-effects model. HR: hazard ratio. CI: confidence interval.

0.004). However, increased BPV could not predict eGFR decline (HR: 1.27, 95% CI: 0.84–1.94, P = 0.005) or an increase in serum creatinine (HR: 0.99, 95% CI: 0.80–1.23, P = 0.927) (Fig. 3).

As shown in Figure 4, stratified analysis by BPV metrics indicated that increased CV (HR: 1.14, 95% CI: 1.02–1.28, P = 0.003), VIM (HR: 1.17, 95% CI: 1.08–1.26, P < 0.001), SD (HR: 1.24, 95% CI: 1.04–1.49, P < 0.001), and ARV (HR:

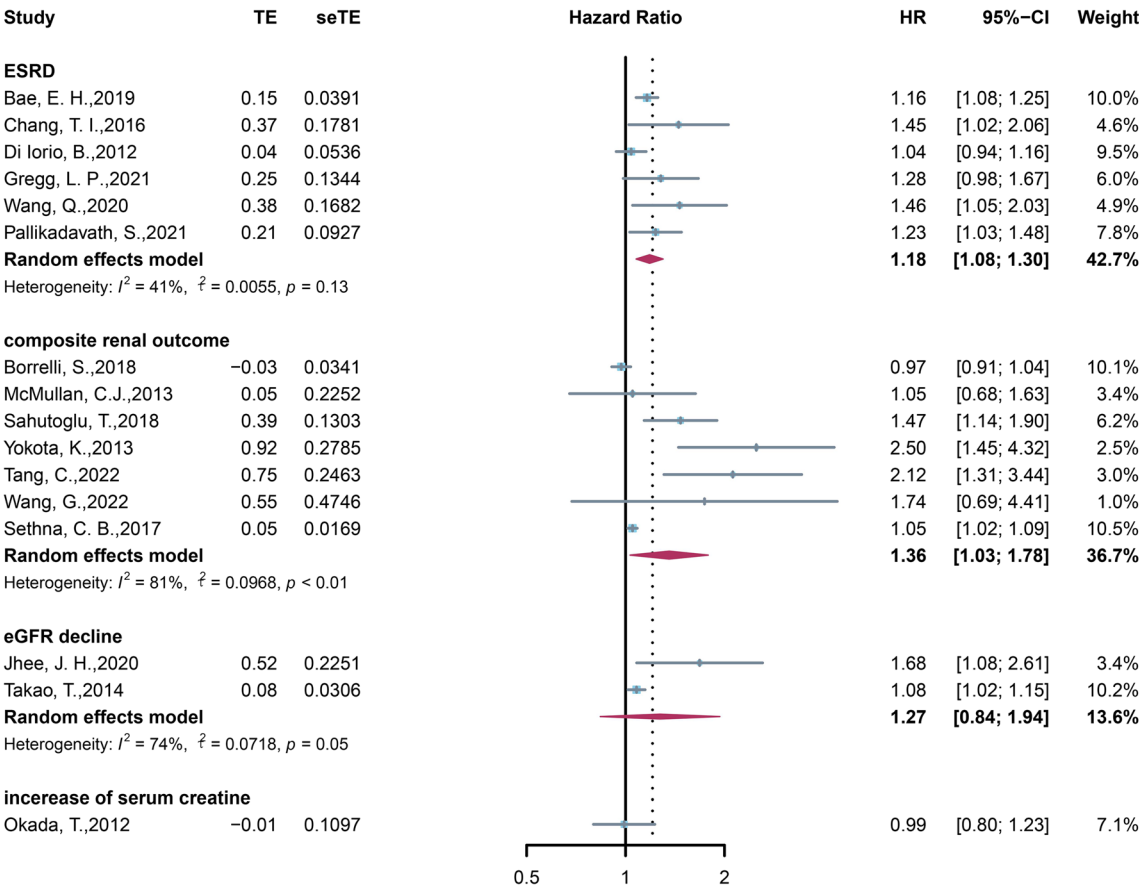

Figure 3 Meta-analysis of CKD progression by renal outcomes in a random-effects model. HR: hazard ratio. CI: confidence interval. ESRD: end-stage renal disease. eGFR: estimated glomerular filtration rate.

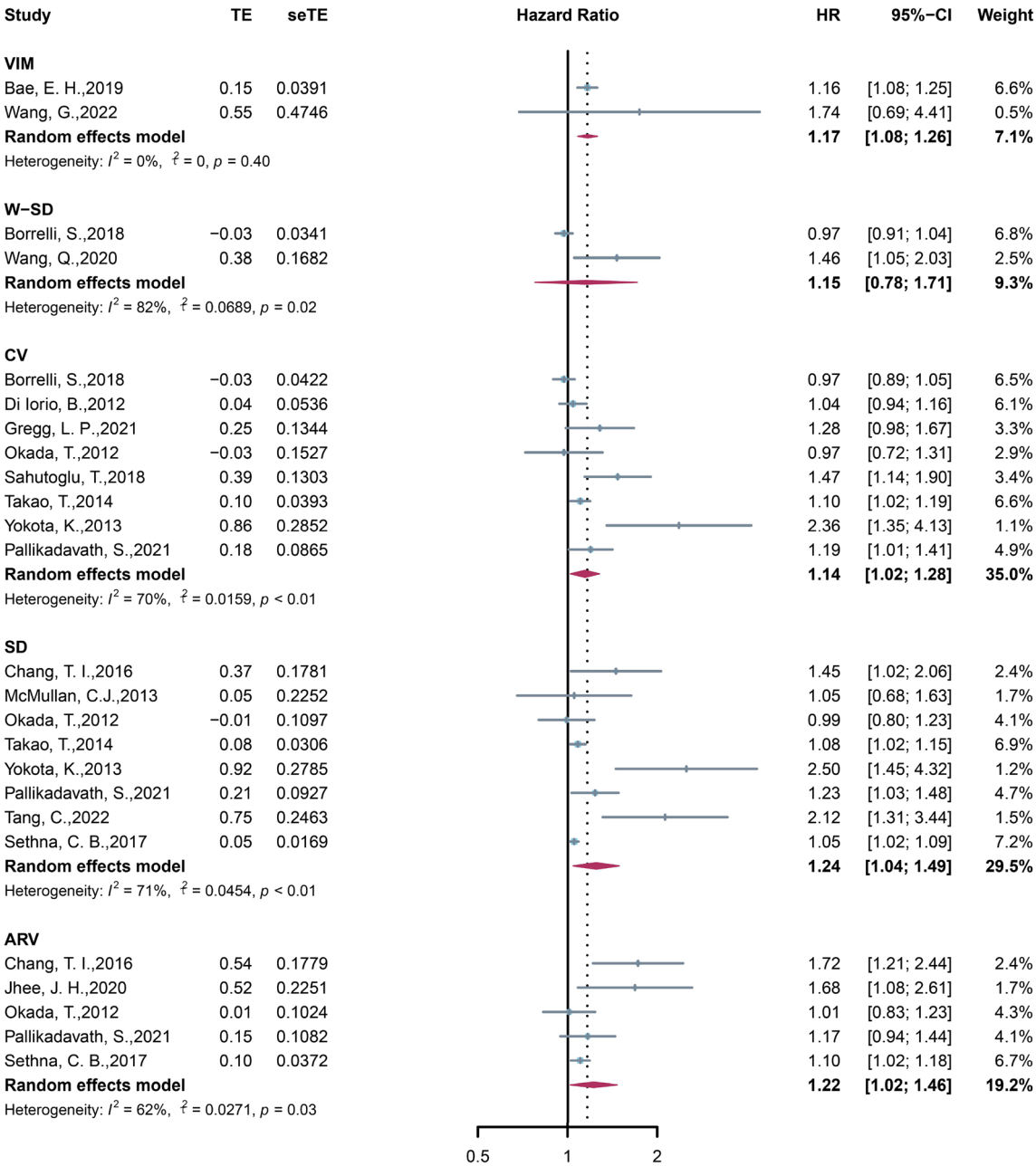

Figure 4 Meta-analysis of CKD progression by BPV metrics in a random-effects model. HR: hazard ratio. CI: confidence interval. VIM: variation independent of mean. W-SD: weighted standard deviation. CV: coefficient of variation. SD: standard deviation. ARV: average real variability.

1.22, 95% CI: 1.02–1.46, $P < 0.001$) were predictors of CKD progression, while W-SD (HR: 1.15, 95% CI: 0.78–1.71, $P = 0.667$) failed to show statistically significant associations with CKD progression.

Further subgroup analyses indicated that increased SBP was significantly related to CKD progression (HR: 1.18, 95% CI: 1.08–1.30, $P < 0.001$), while DBP failed to reach statistical significance (HR: 1.14, 95% CI: 1.01–1.27, $P < 0.001$) (Fig. 5). In addition, there was a significant association between both long-term and short-term BPV and CKD progression (HR: 1.18, 95% CI: 1.07–1.30, $P < 0.001$; HR: 1.33, 95% CI: 1.03–1.71, $P = 0.029$). In terms of race, BPV was a predictor of both CKD progression in East Asians (HR: 1.39, 95% CI: 1.11–1.73, $P < 0.001$) and Europeans or North Americans (HR: 1.12, 95% CI: 1.02–1.26, $P = 0.001$). Furthermore, the prognostic value of BPV was not affected by variable type (categorical variable vs. continuous variable), follow-up time (< 5 years vs. ≥ 5 years), or cohort size (< 10,000 vs. ≥ 10,000) (Supplementary Figure 1–5).

Sensitivity Analysis

In sensitivity analyses, we sequentially deleted a single study each time. Pooled HRs remained statistically significant after

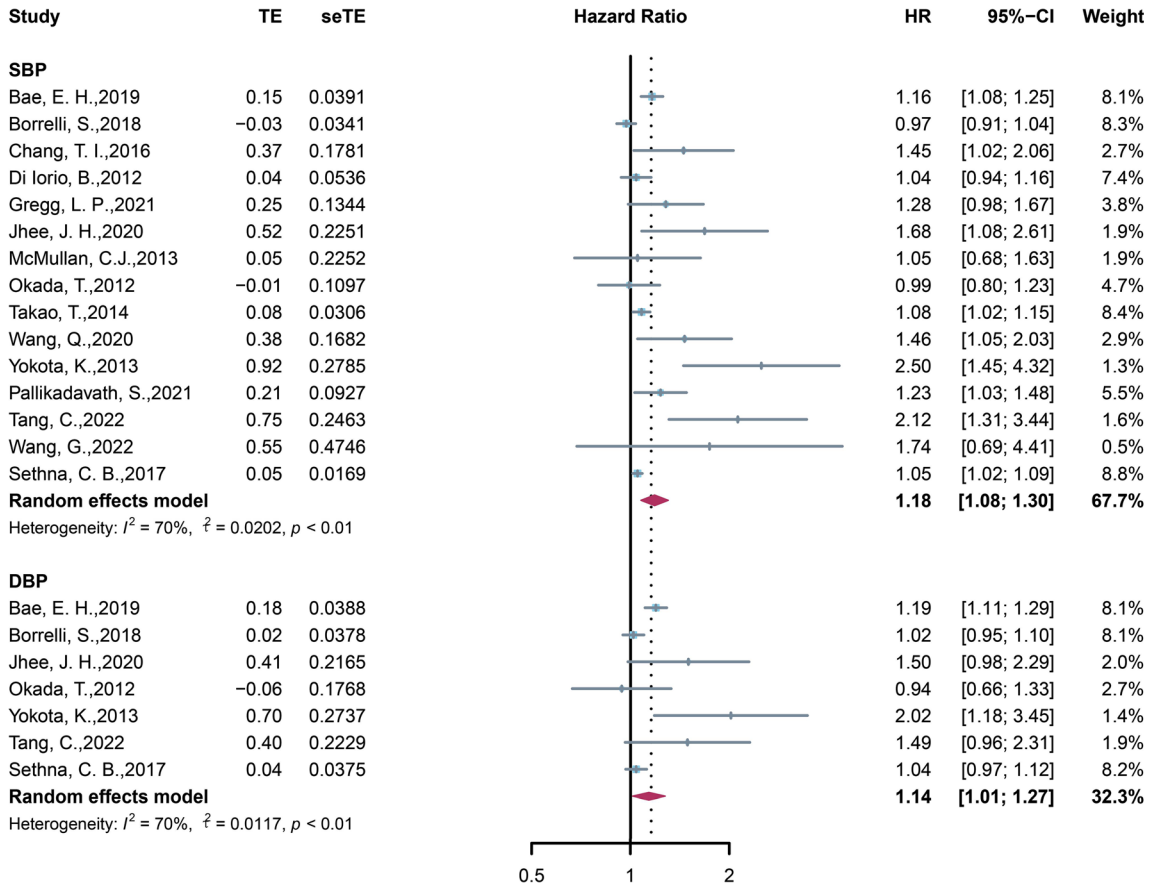

Figure 5 Meta analysis of CKD progression by BP type in a random-effects model. HR: hazard ratio. CI: confidence interval. DBP: diastolic blood pressure. SBP: systolic blood pressure.

individually omitting each study, indicating that the results of this meta-analysis were stable (Supplementary Figure 6).

DISCUSSION

This meta-analysis demonstrated that high BPV was significantly associated with poor renal outcomes, especially the incidence of ESRD, in the population with CKD. Both long-term and short-term BPV were risk factors for CKD progression. Secondary analyses showed that CV, SD, VIM, and ARV were the preferred BPV metrics to predict CKD progression. This is the first meta-analysis focusing on the association between BPV and CKD progression, approving the application value of BPV assessment in the population with CKD.

First, the prognostic relevance of BPV was studied by scholars specializing in cardiovascular research. There is mounting evidence indicating that both short-term and long-term BPV are independently associated with the development and progression of cardiovascular damage. Early studies mainly focused on the prognostic importance of short-term BPV assessed with 24-h ABPM.[2–4, 36] Frattola et al. conducted the first longitudinal trial, providing evidence that cardiovascular events of hypertension might depend on the degree of the 24-h BPV.[3] However, several recent clinical trials have shown that increased day-to-day and visit-to-visit BPV identified by HBPM were associated with cardiovascular outcomes to a far greater extent than short-term BPV.[37–40] A meta-analysis published in 2016 concluded that long-term BPV was a risk factor for death and cardiovascular events above the effect of mean BP.[41] Gradually, nephrologists have focused on the association between BPV and renal damage, investigating whether BPV could independently predict the development and progression of kidney disease. In 2006, an experimental study found that BPV was a more critical determinant than BP level for renal lesions in rats.[42] In 2010, Kilpatrick et al. analyzed data obtained from the Diabetes Control and Complications Trial (DCCT), indicating that visit-to-visit BPV independently predicted the risk of nephropathy in patients with type 1 diabetes.[43] Li et al. performed a meta-analytic study enrolling 14 cohort studies and showed that increased BPV could independently predict the incidence of CKD.[10]

In addition to CKD development, much effort has been devoted to exploring the risk factors for CKD progression. There are several known risk factors for CKD progression, such as male sex, diabetes, hypertension, and proteinuria.[44, 45] In the past 10 years, BPV management has appeared to be a new target for delaying CKD progression. The most likely

mechanisms of BPV are increased central sympathetic drive, increased arterial stiffness, reduced arterial/cardiopulmonary reflex, and humoral factors (such as the renin-angiotensin-aldosterone system [RAAS]).[1] Proposed mechanisms of BPV suggest a potential pathophysiologic association between BPV and renal damage. For example, several studies have shown that increased arterial neural activity was associated with CKD progression.[46–48] Overactivation of the RAAS and sympathetic neural activity are also known to be risk factors for CKD progression.[49–53]

Although the association between BPV and CKD progression has received widespread attention, the findings of clinical trials remain controversial. In this meta-analysis, we enrolled 21 cohort studies with different conclusions. Thirteen studies indicated that BPV was significantly associated with CKD progression, while the other 8 studies denied the prognostic value of BPV in patients with CKD. The current meta-analysis has added to evidence-based knowledge that high BPV could independently predict the progression of CKD.

In this meta-analysis, we investigated the association between BPV and different indicators of CKD progression, consisting of ESRD, a decline in eGFR, and an increase in serum creatinine. The prognostic value of BPV on the incidence of ESRD was validated. However, given the included studies, we were unable to conclude the predictive value of BPV on eGFR decline or serum creatinine increase among patients with CKD. Among eligible studies, only 1 small cohort reported the HR for BPV on serum creatinine increase. Two enrolled studies concluded that increased BPV was significantly associated with a higher risk of eGFR decline. However, the pooled effect was not significant. Notably, Jhee et al. defined the decline in eGFR > 3 ml/min/1.73 m^2 per year) as the endpoint, while Takao reported a decrease in eGFR to 45 ml/min/1.73 m^2. The obvious heterogeneity may have affected the results. Consequently, standardized endpoints are recommended in future studies, such as major adverse kidney events (MAKEs).[54, 55]

When focusing on different metrics of BPV, short-term BPV obtained from 24-h ABPM allowed calculation of the SD and CV. However, the discontinuous sampling of BP variations over 24 h limited their use. The application of W-SD and ARV could overcome this difficulty.[56] For long-term BPV obtained from OBPM or HBPM, the most commonly used metrics are SD and CV.[1] In this meta-analysis, we found that CV, SD, VIM, and ARV were significantly associated with CKD progression.

How does BPV compare with other risk factors for CKD progression? In this meta-analysis, the estimated standardized HR for BPV on CKD progression was 1.21. A cohort study published in 2018 showed that diabetes and proteinuria were risk factors for CKD progression (HR: 1.20 and 1.67, respectively).[57] A 5-year follow-up study showed that the urine albumin-to-creatinine ratio (UACR) was associated with a 1.33-fold risk of ESRD development.[58] Therefore, increased BPV has moderate prognostic value for CKD progression compared with classic risk factors.

Several limitations of our study should be noted. First, eligible studies varied in sample size (from 29 to 537,313). The majority of included studies were small cohort studies (n < 1000), while those with large sample sizes were either derived from the registry database or secondary analysis of clinical trials. Due to limited patient volume and quality in some of the studies, the results of certain pooled analyses (such as those of different BPV types and metrics of different geographical locations) must be interpreted with caution. Second, a variation in the methodological details (such as BP measurements, follow-up periods, and multivariate regression models) could have added to the heterogeneity. While we analyzed the source of heterogeneity through meta-regression and addressed protocol variability by stratified analysis, notable heterogeneity continued to exist in several subgroups. Third, the studies were conducted in East Asian, North American, and European countries. The applicability of our results to other regions remains to be determined. Nevertheless, we tried to minimize the bias throughout the process of study identification, quality evaluation, statistical analysis, and sensitivity assessment. These steps should strengthen the stability and accuracy of the meta-analysis.

CONCLUSION

This meta-analysis demonstrated that increased BPV was significantly associated with CKD progression. Among different BPV metrics, CV, SD, VIM, and ARV were identified to be risk factors for CKD progression. The prognostic value of BPV was not affected by BP type (SBP vs. DBP), BPV type (long-term BPV vs. short-term BPV), variable type (categorical variable vs. continuous variable), follow-up time (< 5 years vs. ≥ 5 years), or cohort size (< 10,000 vs. ≥ 10,000). Large-scale prospective studies are required to confirm our findings and to further understand whether BPV can be used as a therapeutic target in patients with CKD.

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Author Contribution *Letian Yang was responsible for study design, literature research, study selection, and manuscript drafting. Wei Wei was responsible for study design, statistical analysis, and manuscript drafting. Jian Li and Yajun Pu was responsible for data extraction. Bo Wang was responsible for manuscript revision. Ling Zhang and Yuliang Zhao were responsible for data verification and manuscript revision. Ping Fu and Tianlei Cui were responsible for the study design and manuscript revision.*

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Declarations:

Conflict of Interest: *The authors declare that they do not have a conflict of interest.*

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