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Central arterial and peripheral arterial blood pressure in patients with chronic kidney disease undergoing versus not undergoing hemodialysis

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Abstract

Objective: We assessed the consistency of noninvasive and invasive measurements of central arterial pressure (CAP) and the difference between peripheral brachial artery pressure and CAP in patients with chronic kidney disease (CKD) undergoing versus not undergoing hemodialysis.

Methods: This single-center cross-sectional study was performed from May to December 2018. The patients were divided into a control group (n = 50), CKD group (stages 3–5, n = 50), and dialysis group (n = 20), and all underwent measurement of peripheral humeral arterial pressure and noninvasive and invasive measurement of CAP. Group differences and correlations between CAP and peripheral arterial pressure were assessed.

Results: The consistency between noninvasive and invasive CAP was better in the control and CKD groups than in the dialysis group. In the dialysis group, the noninvasive equipment underestimated the actual CAP. The CAP was close to the peripheral brachial artery pressure in the dialysis group, while the CAP was significantly lower than the peripheral brachial artery pressure in the control and CKD groups.

Conclusion: Noninvasive equipment underestimates the actual CAP in patients undergoing dialysis and should be used with caution. The difference between the peripheral arterial pressure and CAP was smaller in patients undergoing dialysis than in patients with CKD and controls.

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Introduction

The increasing incidence and prevalence of chronic kidney disease (CKD) has become an important public health problem.[1,2] Hypertension is found in as much as 90% of patients undergoing renal dialysis and is often inadequately controlled.[3–5] Cardiovascular disease is the most important cause of death and morbidity in patients with end-stage renal disease,[5] and effective antihypertensive treatment can alter the risk factors for cardiovascular disease and reduce cardiovascular disease-induced morbidity and mortality. Hypertension in patients with end-stage renal disease undergoing dialysis is elevated in young individuals of both sexes across all ethnic groups compared with the general population.[6] Although brachial blood pressure (BP) can be well controlled, morbidity and mortality associated with cardiovascular disease in many patients do not automatically lead to parallel disease alleviation, suggesting that the measured brachial BP may not be an ideal therapeutic target.[7–10] Indeed, systolic BP varies across the arterial tree, and counterintuitively, central or aortic systolic BP is lower than the corresponding brachial values.

Central arterial pressure (CAP) refers to the BP at the aortic root. The CAP is different from the peripheral brachial artery pressure.[7] CAP is a result of a complex wave formed by forward and reflected pressure waves; in the presence of physiological or pathological conditions that affect arterial elasticity, such as age, hypertension, and sex, the reflected waves vary in size according to the time required to travel from the distal reflex point to the ascending aorta, resulting in variations in the peripheral brachial artery pressure and central motility.[11–13] Notably, however, because CAP is close to the heart, it represents the pressure in the systemic hemodynamics in proximity to the starting point. Therefore, it theoretically reflects BP and cardiovascular and cerebrovascular events with greater accuracy, providing predictive value for renal function progression and peripheral vascular complications.[7]

Central systolic BP places a direct burden on the left ventricle. Abundant evidence now shows that central hemodynamic parameters are independent predictors of cardiovascular morbidity and mortality and are more closely correlated with cardiovascular risk than is brachial BP.[14,15]

BP measurements are often highly inaccurate and poorly reflect the true BP load because of numerous factors, such as the white-coat effect and the patient's eagerness to start dialysis and leave the unit quickly.[16] Weir et al.[17] measured the central systolic and central diastolic BP in 2144 patients with CKD from the Chronic Renal Insufficiency Cohort study and found that the mean central systolic BP was 10 mmHg lower while the diastolic BP was similar. Before and after patients begin dialysis, the BP values display a J- or U-shaped association with cardiovascular events and survival, which most likely reflects the low accuracy of relevant measurements.[4]

Although reduced peripheral BP, ambulatory BP, and renal outcomes in patients with CKD have been reported, whether CAP and peripheral arterial BP are correlated in patients undergoing dialysis remains unexplored. A paucity of relevant data exists in the literature. Therefore, in this single-center cross-sectional study, we assessed whether noninvasive and invasive measurements of CAP are consistent and analyzed the difference between peripheral brachial artery pressure and CAP in patients with CKD undergoing versus not undergoing hemodialysis.

Patients and methods

Study design and patients

This single-center cross-sectional study was performed from 1 May to 30 December 2018 and included patients who were scheduled for needle coronary angiography examination or treatment in the cardiology catheter room of Shenzhen People's Hospital. Patients who met the inclusion and exclusion criteria (see below) underwent measurement of peripheral humeral arterial pressure and noninvasive and invasive measurements of CAP. The selected patients were divided into a control group, CKD group (stages 3–5), and dialysis group (hemodialysis/continuous ambulatory peritoneal dialysis).

The inclusion criteria were as follows. Patients in the CKD group met the 2018 diagnostic criteria for chronic renal disease, including proteinuria, abnormal urinary sediment, renal tubule dysfunction, imaging renal abnormalities, histopathological abnormalities, and a persistently low estimated glomerular filtration rate (eGFR) of $<60\,mL/min/1.73\,m^2$ for more than 3 months.[18] These patients required coronary angiography examination or treatment. Patients in the dialysis group met the criteria for end-stage renal disease, including an eGFR of $<15\,mL/min/1.73\,m^2$ with the need for abdominal or blood-penetrating renal replacement therapy.[19] The dialysis time was more than 3 months, and the patients required coronary angiography examination or treatment. The control group included patients without CKD (i.e., those with an eGFR of $>75\,mL/min/1.73\,m^2$), no signs of structural kidney disease, and no history of chronic renal insufficiency. These patients' sex and age distributions were matched with those in the CKD and dialysis groups. Patients in all groups were at least 18 years of age. The exclusion criteria were severe arrhythmia (such as atrial fibrillation), severe acute left heart failure and other diseases causing systemic circulatory hemodynamic instability, a >10-mmHg difference in BP, artery occlusion or absence of a pulse, recent injuries or deformities in the arm or wrist, and unwillingness to participate in the study.

This study followed the Helsinki Declaration of the World Medical Association and the ethical principles formulated by the Medical Ethics Committee of Shenzhen People's Hospital. All participants provided written informed consent for complete clinical data collection and publication.

Relevant clinical data were collected using the Shenzhen People's Hospital Electronic Medical Record System and Clinical Data Inspection System.

Clinicodemographic information collection

During the same clinical visit, the patient's age, height, weight, body mass index, waist circumference, dialysis course, sex, current medications, and current medical conditions (peripheral artery disease, diabetes mellitus, coronary heart disease, and cerebrovascular disease) were recorded.

Laboratory measures

Blood was collected from all participants within 1 month prior to the renal denervation procedure to assess the following parameters: hemoglobin, serum albumin, parathyroid hormone, serum calcium, serum phosphorus, cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, inflammation index, high-sensitivity C-reactive protein, and other laboratory parameters. The laboratory results were obtained within 3 days before and after coronary angiography.

BP measurements

Peripheral brachial artery BP. The patients were placed in the sitting position in a quiet room for 10 minutes before brachial BP measurement. Two consecutive measurements were performed with an electronic sphygmomanometer (OMRON, Kyoto, Japan) on the left upper arm. We ensured that both measurements were accurate, and they were then averaged to obtain the peripheral brachial artery pressure.

CAP. Estimated (noninvasive) CAP was determined using the A-PULSE CASPro noninvasive CAP measuring device (Healthstats, Singapore), and the recording time was 10 seconds. The wrist sensor was placed in the strongest pulsatile region of the radial artery in the left wrist; the cuff band was worn on the same side of the arm, and the position and tightness of the sensor were adjusted to obtain a qualified waveform. Noninvasive CAP was measured, and the mean BP at the brachial artery was used for calibration. The CAP was automatically measured after age and sex inputs. The CAP reading was obtained by converting the mapping function of the equipment's software; only high-quality data with a minimum operator index of 80 were accepted (the median operator index was 98). The mean value was considered the noninvasive systolic CAP reading, and measurements were repeated twice.

For invasive CAP measurement before coronary angiography, when the lead wire reached the root of the ascending aorta, the pressure curve was recorded at the end of the catheter through the transducer's external polyconductive physiological recorder. Calibration was then performed to ensure a tight connection of the pipes during the measurement. With no leakage and a stable pressure curve, a continuous invasive CAP value (at least 10 seconds) was recorded, and the measurement was performed six consecutive times. The first measurement was excluded, and the remaining five were averaged and recorded.

Statistical analysis

SPSS Version 17.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. MedCalc (MedCalc Software, Ostend, Belgium) was employed for graph production. Baseline data were summarized descriptively. Measurement data are presented as mean $\pm$ standard deviation, and count data are expressed as percentage. Data normality was assessed using histograms or QQ graphs. A one-sided paired-sample t test was used for normally distributed data, and an independent-sample t-test was used for data with a skewed distribution. The consistency of noninvasive and invasive CAP measurements was compared by a two-sample t test, Pearson correlation analysis, and Bland–Altman map analysis. Pearson correlation analysis was performed to identify associations among various parameters. A P value of <0.05 was considered statistically significant.

Results

Baseline patient characteristics

From 1 May to 30 December 2018, 134 patients undergoing coronary angiography

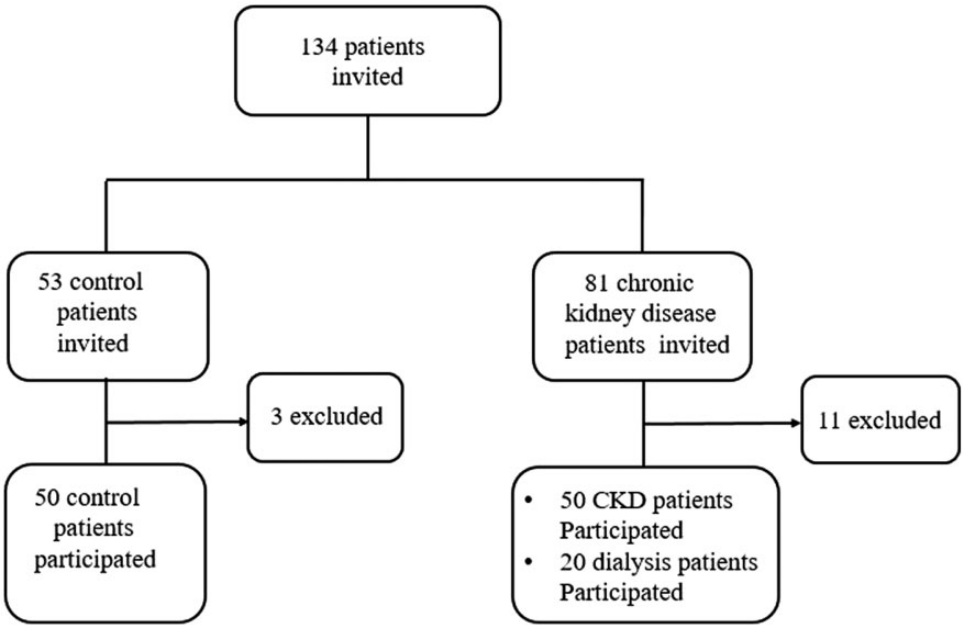

Figure 1. Flow chart showing the inclusion process of the 134 patients invited to participate in the study. CKD, chronic kidney disease.

were enrolled in this study (Figure 1). Fourteen patients were excluded (four patients undergoing dialysis and two patients with CKD were administered nitroglycerin during coronary angiography, which affected the actual CAP values; insufficient time was available during the coronary angiography procedure to perform the CAP measurements in five patients; and three patients were excluded for technical reasons). Therefore, 120 patients were included in the final analysis (CKD group, $n = 50$; dialysis group, $n = 20$; and control group, $n = 50$). The demographic characteristics of all patients are presented in Table 1. Overall, the control, CKD, and dialysis groups were similar in their age distribution, sex distribution, smoking status, and body mass index. The three groups mainly included middle-aged and older men. The patients in the dialysis group were younger, had a lower prevalence of diabetes, and had a lower body mass index than patients in the CKD group (all $P < 0.05$). Hypertension was found in 70% and 80% of patients in the CKD and dialysis groups, respectively, and these proportions were significantly higher than the control value (52%) (both $P < 0.05$). The left ventricular ejection fraction was >50% in all three groups but was slightly lower in the dialysis group than in the control and CKD groups. Patients in the CKD and dialysis groups received more antihypertensive drugs than patients in the control group. The incidence rates of coronary heart disease in the dialysis and CKD groups were 60.5% and 42.9%, respectively, and were higher than that in the control group (31.6%) ($P = 0.04$); there was no significant difference between the CKD and dialysis groups.

BP measurements in the three groups

Analysis of variance showed no significant difference in brachial artery pressure

Table 1. Baseline characteristics in the control, CKD, and dialysis groups.

Characteristics	Control	CKD	Dialysis	P
Patient number	50	50	20	–
Age, years	69.3 ± 10.1	69.6 ± 10.5	64.0 ± 10.6	0.13
BMI, kg/m^2	25.16 ± 4.16	23.96 ± 3.42	22.52 ± 2.97	0.07
Female sex	14 (28)	16 (32)	8 (40)	0.62
Smoking	16 (32)	14 (28)	6 (30)	0.91
Diabetes	9 (18)	12 (24)	8 (40)	0.15
History of hypertension	26 (52)	35 (70)	16 (80)	<0.001
eGFR, mL/min/1.73 m^2	86.42 ± 13.93	51.35 ± 8.01[a]	5.12 ± 1.9[b,c]	<0.001
Ejection fraction, %	65.1 ± 4.9	58.6 ± 10.9	49.0 ± 10.5	0.09
Antihypertensive treatment	15 (30)	20 (40)[a]	14 (70)[b]	0.009
ACE inhibitor/ARB	7 (14)	7 (14)	9 (45)[b,c]	0.006
Beta-blocker	8 (16)	12 (24)	11 (55)[c]	0.003
Calcium channel blocker	12 (24)	19 (38)	6 (30)	0.32
Diuretics	6 (12)	6 (12)	0 (0)[b,c]	0.03
Combined medication	10 (20)	12 (24)	12 (60)[c]	0.02
Coronary angiography results	13 (26%)	24 (48)[a]	10 (50)[b]	0.04

CKD, chronic kidney disease; BMI, body mass index; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate. Data are presented as mean ± standard deviation or n (%). Continuous data were compared by analysis of variance, with the multiple-sample Student–Newman–Keuls test. Comparisons between groups were performed by the chi-square test. [a]$P < 0.05$ compared with the control group; [b]$P < 0.05$ compared with the control group; [c]$P < 0.05$ compared with the CKD group. $P < 0.05$ indicated a statistically significant difference.

Table 2. Blood pressure levels in the control, CKD, and dialysis groups.

Blood pressure	Control	CKD	Dialysis	P
Patients, n	50	50	20	–
BSBP	149.1 ± 20.1	152.3 ± 20.8	160.1 ± 19.9[a]	0.129
BDBP	85.1 ± 11.3	85.3 ± 10.2	85.6 ± 9.4	0.978
CSBP	137.4 ± 19.0	143.1 ± 20.2	157.1 ± 21.0[a,b]	0.001
CDBP	73.3 ± 11.8	72.3 ± 13.1	80.5 ± 8.4[a,b]	0.031
NCSBP	143.3 ± 20.2	148.2 ± 19.9	148.0 ± 19.3	0.433
BPP	64.1 ± 18.4	66.9 ± 16.8	74.5 ± 14.9	0.062
CPP	64.1 ± 16.9	70.8 ± 19.5	76.7 ± 18.2[a,b]	0.031

CKD, chronic kidney disease; BSBP, brachial systolic blood pressure; BDBP, brachial diastolic blood pressure; CSBP, central systolic blood pressure; CDBP, central diastolic blood pressure; NSBP, noninvasive central systolic blood pressure; BPP, brachial artery pulse pressure; CPP, central artery pulse pressure. P values were obtained by analysis of variance, with the multiple-sample Student–Newman–Keuls test among the three groups. [a]$P < 0.05$ compared with the control group; [b]$P < 0.05$ compared with the CKD group. $P < 0.05$ was statistically significant. Values are mmHg.

among the three groups. The CAP was 137.4 ± 19.0, 143.1 ± 20.2, and 157.1 ± 21.0 mmHg in the control, CKD, and dialysis groups, respectively. The CAP in the dialysis group was higher than that in the control and CKD groups (both $P < 0.05$). There was no significant difference in CAP between the control and CKD groups. Detailed data are provided in Table 2.

Table 3. Comparison of noninvasive and invasive central arterial pressure in the three groups.

Groups	Mean difference	SD	t-value	95% CI	P
Control	5.9	6.0	7.0	4.2–7.6	<0.001
CKD	5.1	6.8	5.2	3.1–7.0	<0.001
Dialysis	−9.2	7.4	−5.5	−12.6 to −5.7	<0.001

Mean difference is the mean of the difference between noninvasive and invasive central arterial blood pressure values. CKD, chronic kidney disease; SD, standard deviation; CI, confidence interval. A paired t-test was used for assessments. Values are mmHg.

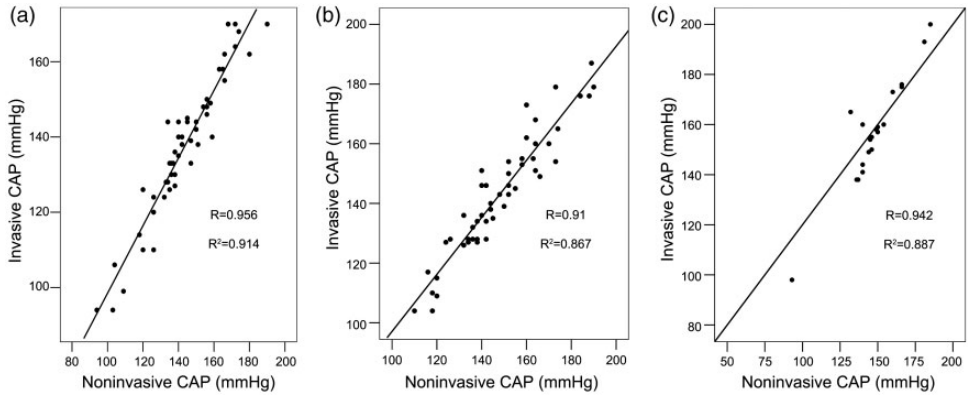

Figure 2. Scatter plots of noninvasive and invasive CAP in the various groups. (a) Control group (n = 50). (b) Chronic kidney disease group (n = 50). (c) Dialysis group (n = 20). CAP, central arterial pressure.

Differences between estimated systolic CAP or systolic brachial BP and invasive aortic systolic BP in the CKD and dialysis groups

Differences between invasive aortic systolic BP and estimated systolic CAP and brachial BP, respectively, in the CKD and dialysis groups are shown in Table 3. The estimated (noninvasive) CAP was about 5.9 (4.2–7.6) mmHg ($P < 0.001$) higher than the invasive aortic BP in the control group, and it was 5.1 (3.1–7.0) mmHg higher in the CKD group ($P < 0.001$). Meanwhile, the estimated CAP was 9.2 (5.7–12.6) mmHg ($P < 0.001$) lower than the invasive aortic BP in the dialysis group.

Correlation and consistency between estimated CAP and invasive aortic systolic BP in the three patient groups

The correlation between the estimated CAP and invasive aortic systolic BP in the three groups is shown in Figure 2. The correlation coefficients (R values) obtained by Pearson correlation analysis were 0.956 ($P < 0.001$), 0.91 ($P < 0.001$), and 0.942 ($P < 0.001$) in the control, CKD, and dialysis groups, respectively, indicating significant correlations (Figure 2(a)–(c)). Associations of differences between the estimated CAP and invasive aortic systolic BP in the control, CKD, and dialysis groups were assessed by linear regression analysis,

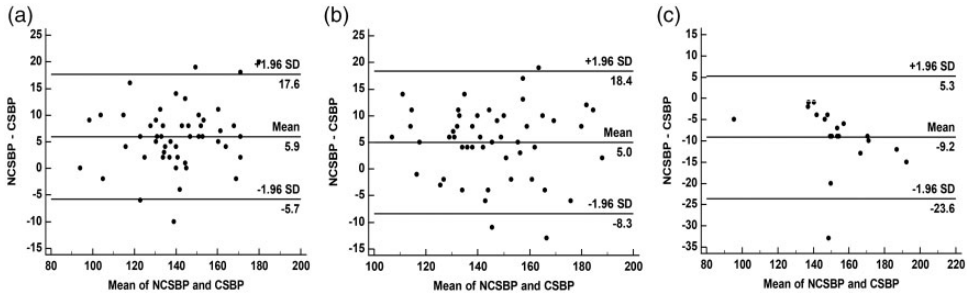

Figure 3. Bland–Altman plots of noninvasive central and central arterial blood pressure in various groups. (a) Control group (n=50). (b) Chronic kidney disease group (n=50). (c) Dialysis group (n=20). Values are mmHg. CSBP, central systolic blood pressure; NCSBP, noninvasive central systolic blood pressure; SD, standard deviation.

Table 4. Comparisons of peripheral arterial and central arterial blood pressure in the three patient groups.

Groups	Mean difference	SD	t-value	95% CI	P
Control	11.7	5.3	15.8	10.3–13.2	<0.001
CKD	9.1	7.8	8.2	6.9–11.4	<0.001
Dialysis	3.0	7.5	1.8	−0.5 to 6.5	0.088

Mean difference is the mean of the difference between peripheral brachial artery and central arterial blood pressure values. CKD, chronic kidney disease; SD, standard deviation; CI, confidence interval. Values are mmHg.

and the R^2 values were 0.914, 0.867, and 0.887, respectively. We further used Bland–Altman plots to assess the consistency between the estimated CAP and invasive CAP in the control (Figure 3(a)), CKD (Figure 3(b)), and dialysis (Figure 3(c)) groups. The mean difference in the control group was 5.9 (−5.7 to 17.6) mmHg ($P < 0.001$), that in the CKD group was 5.1 (−8.3 to 18.4) mmHg ($P < 0.001$), and that in the dialysis group was −9.2 (−23.6 to 5.3) mmHg ($P < 0.001$).

Peripheral arterial BP and CAP differences in the three patient groups

Differences in the brachial BP and CAP in the control, CKD, and dialysis groups are shown in Table 4. The mean brachial artery pressure in the control and CKD groups was significantly higher than the invasive CAP; the differences were 11.7 ± 5.3 mmHg ($P < 0.001$) and 9.1 ± 7.8 mmHg ($P < 0.001$), respectively. However, the mean difference between the peripheral brachial artery BP and CAP in the dialysis group was 3.0 ± 7.5 mmHg, with no significant difference. The peripheral brachial BP and CAP differences were further compared by variance analysis. The results showed that the BP difference in the control and CKD groups was greater than that in the dialysis group ($F = 11.8$, $P < 0.001$). However, there was no significant difference between the control and CKD groups.

Discussion

In this study, we explored the magnitude of the differences between peripheral BP and CAP in CKD, dialysis, and control populations to provide insights into the objective

assessment of CAP in patients with CKD and patients undergoing dialysis. Brachial systolic BP seemed to be a more accurate estimate of the actual systolic CAP than the A-PULSE CASPro-derived estimate in the dialysis group, indicating that noninvasive assessment of aortic BP should be performed with caution in patients with CKD and those undergoing dialysis.

In this study, we selected the A-PULSE CASPro device as a noninvasive assessment tool for CAP because of its proven good correlation and consistency with invasive CAP measurements in the general population, in addition to its simplicity of operation and portability. As shown above, CAP assessed by the A-PULSE was 4.2 to 7.6 mmHg higher in the control group than the measured invasive CAP, was overestimated by 3.1 to 7.0 mmHg in the CKD group, and was underestimated by 5.7 to 12.6 mmHg in the dialysis group. The comparative standard for the consistency of arterial BP measurements by the Association for the Advancement of Medical Instrumentation[20] is a mean of <5 mmHg with a standard deviation of <8 mmHg. Next, we assessed the noninvasive device from the perspective of differences and correlations. The results revealed some differences between the noninvasive CAP obtained with the device and the actual CAP. Especially in the dialysis group, noninvasive CAP measurement often underestimated the actual CAP. Therefore, noninvasive devices should be carefully evaluated when measuring CAP in patients undergoing dialysis.

The pulse wave amplification effect of the vein to the peripheral artery can be regarded as the difference between systolic CAP and systolic peripheral arterial BP. The peripheral brachial artery BP is reportedly higher than the CAP (40 mmHg).[21,22] Notably, pulse wave amplification is affected by many factors, such as age, sex, height, and others, and shows great individual differences.[23]

As shown above, the peripheral brachial artery BP was close to the CAP in the dialysis group, while the CAP was significantly lower than the peripheral brachial artery BP in the control and CKD groups. In addition, there was no significant difference in the peripheral brachial artery BP among the three patient groups. The CAP was higher in the dialysis group than in the control and CKD groups, which suggests that only using the peripheral brachial artery BP to assess the actual BP in different patients might miss hidden information.

The following parameters might explain the above results in patients with CKD and those undergoing dialysis: oxidative stress, inflammatory factors, blood lipid and urinary toxins, and activation of the renin-angiotensin-aldosterone system in the CKD population, especially in patients with end-stage renal disease undergoing dialysis. Under the influence of many factors, such as calcium and phosphorus metabolism disorders, two pathological changes occur: arteriosclerosis and atherosclerosis. These pathological changes are more prominent in the end-stage dialysis population.[24] This increases the stiffness of the blood vessels and pulse wave conduction. In the dialysis group, we observed a higher CAP that was close to the peripheral brachial artery BP. In addition, there was no significant difference between the peripheral brachial BP and CAP in the control and CKD groups. Because the control group included prospective coronary angiography patients, some had hypertension, a smoking history, obesity, and other high-risk factors for coronary artery disease, and they therefore had a greater risk of coronary atherosclerosis; the blood vessel hardness in these patients was also greater than that in the normal population. In the CKD group, however, most patients with renal insufficiency had early-stage disease,

and arteriosclerosis associated with chronic renal insufficiency was not serious. Meanwhile, age was matched for the control patients based on the other groups. The slight differences in the sex distribution, smoking history, and diabetes history may explain why there were no significant differences between the CAP and brachial arterial BP in the control and CKD groups.

We measured CAP directly in an invasive way and compared the CAP and peripheral BP in the CKD and dialysis groups. We found that the differences between the peripheral BP and CAP in the dialysis group differed from those in the control and CKD groups. Because of the inextensibility of invasive BP, we assessed whether the current noninvasive CAP equipment in the CKD and dialysis groups accurately reflects the actual value and can thus be used in the CKD and dialysis groups. However, BP assessed by the noninvasive device was significantly different from that obtained by the invasive method in the dialysis group; thus, it should be used with caution in such patients. Further improvement in the accuracy of noninvasive devices is needed for future assessment of CAP in patients with CKD and those undergoing dialysis.

This study had several limitations. First, the patients in the CKD group did not show a balanced distribution of the number of individuals at each disease stage. Therefore, the difference between peripheral brachial artery BP and CAP, which may be correlated with the change in the GFR, was not further analyzed in the CKD group. This should be assessed in future studies. Second, invasive CAP was selected instead of noninvasive CAP as an observation indicator. In addition, there is an inevitable ethical constraint on the need for patients to have clinical indications for coronary angiography; therefore, the CKD and dialysis groups were relatively small in size, which might have affected the statistical power of this study. Furthermore, because of the small sample size, an adjusted regression analysis model was lacking when comparing the peripheral BP and CAP. This should be further explored in future research. Finally, this was a cross-sectional study; a prospective study with a large sample size is required to confirm the current findings.

Conclusion

This study demonstrated that noninvasive BP measurements significantly differ from invasive BP measurements in patients undergoing dialysis. The difference between the peripheral arterial pressure and CAP was smaller in patients undergoing dialysis than in patients with CKD and controls. Therefore, ambulatory measurement of BP by noninvasive methods should be used with caution, and novel noninvasive techniques should be developed to address this issue.

Authors' contributions

LP S and R Z carried out the studies, participated in collecting the data, and drafted the manuscript. LP S and XZ Z performed the statistical analysis and participated in its design. All authors read and approved the final manuscript.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Ethics statement

This study followed the Helsinki Declaration of the World Medical Association and the ethical principles formulated by the Medical Ethics Committee of Shenzhen People's Hospital. All participants provided written informed consent for complete clinical data collection and publication.

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