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Original Article

# High serum leptin levels are associated with central arterial stiffness in geriatric patients on hemodialysis

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## Abstract

**Objective:** Central arterial stiffness predicts cardiovascular (CV) mortality in hemodialysis (HD) patients. The aging process transforms lipid distribution and thus alters adipokine secretion. The harmful effects of leptin on CV events may change in the elderly. The purpose of this study was to investigate the relationship between leptin and central arterial stiffness markers through carotid–femoral pulse wave velocity (cfPWV) in geriatric HD patients. **Materials and Methods:** Patients over 65 years old on chronic HD were recruited. Blood samples were collected, and the cfPWV was measured with the SphygmoCor system. The patients with cfPWV values >10 m/s were defined as the high arterial stiffness group. **Results:** In total, 30 (51.7%) of the 58 geriatric patients on chronic HD in this study were in the high arterial stiffness group. The high arterial stiffness group had higher rates of diabetes mellitus ($P$ = 0.019), hypertension ($P$ = 0.019), and higher systolic blood pressure ($P$ = 0.018), pulse pressure ($P$ = 0.019), body mass index ($P$ = 0.018), serum leptin levels ($P$ = 0.008), and hemoglobin levels ($P$ = 0.040) than those in the low arterial stiffness group. Multivariable forward stepwise linear regression analysis showed logarithmically transformed leptin (log-leptin, β =0.408, adjusted $R^2$ change = 0.164; $P$ = 0.001) and diabetes (β =0.312, adjusted $R^2$ change = 0.085; $P$ = 0.009) were associated with cfPWV values in geriatric HD patients. Moreover, an increased serum leptin level (odds ratio: 1.053; 95% confidence interval: 1.007–1.100; $P$ = 0.023) was an independent factor for central arterial stiffness among geriatric HD patients after multivariate logistic regression analysis. **Conclusion:** In this study, a higher serum leptin level was correlated with central arterial stiffness in geriatric HD patients.

**Keywords:** *Carotid–femoral pulse wave velocity, Geriatric, Hemodialysis, Leptin*

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## Introduction

Patients over 65 years old are a growing group worldwide in the chronic dialysis population [1]. The number of patients with prevalent end-stage renal disease (ESRD) continues to increase in all age groups, with the relative magnitude of increase greater in older age groups [2]. Older dialysis patients usually have numerous cardiovascular (CV) risks including diabetes, hypertension, and dyslipidemia, and atypical risks such as hyperhomocysteinemia and chronic inflammation [3]. Therefore, measurement of arterial elastic properties is becoming a method of risk stratification.

Central arterial stiffness is recognized as a surrogate end point for CV diseases and is the functional consequence of artery wall calcification. In the ESRD population, this disorder is closely linked to disturbances of calcium and phosphate homeostasis and to bone metabolism irregularities. Carotid–femoral pulse wave velocity (cfPWV) is a valid, noninvasive, and inexpensive technique for measuring central arterial stiffness [4]. Independent of the classic CV risk factors, a higher cfPWV level represents a strong predictor of the future CV events and all-cause mortality, and the predictive ability is superior in people with a higher baseline CV risk [5,6].

Leptin is secreted by adipose tissue and the level is proportional to the body fat mass. It has a well-documented function in glucose homeostasis, insulin sensitivity, and energy expenditure [7]. An association of leptin and CV disease has been reported in conditions including hypertension, the atherosclerotic process, and endothelial cell dysfunction through direct sympathetic system stimulation, dysregulated vascular smooth

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muscle, and increased oxidative stress [8-10]. In the aging process, alterations in adipose cell size, number, and proliferation lead to adipokine dysregulation [11,12]. However, the association between leptin and central arterial stiffness in geriatric hemodialysis (HD) patients remains to be explored. The aim of the present study was to assess the association between serum leptin levels and central arterial stiffness measured by cfPWV in geriatric HD patients.

## Materials and methods

### Patients

The study participants were recruited in the HD department at Buddhist Tzu Chi General Hospital, Hualien, Taiwan, in mid-2015. The study was approved by the Protection of Human Subjects Institutional Review Board of Tzu Chi University and Hospital (IRB103-136-B). A total of 158 HD participants were enrolled and signed informed consents. Of these, 100 were excluded because of an HD duration <6 months ($n$ = 2), each HD session >4 h ($n$ = 10), each HD session <4-h ($n$ = 22), HD 2 times per week ($n$ = 2), acute infection ($n$ = 1), acute myocardial infarction ($n$ = 1), pulmonary edema ($n$ = 1), missing clinical data ($n$ = 7), and age under 65 years ($n$ = 54). Finally, a total of 58 HD patients older than 65 years were included in the study. All patients in the study used the same high-flux polysulfone disposable artificial kidney (FX class dialyzer, Fresenius Medical Care, Bad Homburg, Germany), received standard 4-h dialysis 3 times/week using standard bicarbonate dialysate and had been on HD for more than half year. There were 27 men, and 31 women, with ages ranging from 66 to 92 years old. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were taken at the points of appearance and disappearance of the Korotkoff sounds before the start of the HD session. Pulse pressure was calculated by subtracting the DBP from the SBP.

### Anthropometric analysis

All anthropometric analyses were performed at the midweek dialysis. Body height was measured to the nearest half centimeter, and body weight was measured to the nearest half-kilogram with the patient in light clothing and no shoes before and after the HD session. Waist circumference was measured to the nearest half centimeter at the shortest point below the lower rib margin and the iliac crest. Body mass index (BMI) was calculated as the weight (kilograms) divided by the height squared (meters) [13-16].

### Biochemical investigations

All blood samplings were performed at the midweek dialysis. Blood samples of approximately 5 mL were collected just before the start of the HD session; about 0.5 mL was used to check hemoglobin levels and white blood cell counts (Sysmex K-1000, Sysmex American, Mundelein, IL, USA); the rest were immediately centrifuged at 3000 ×$g$ for 10 min. Serum samples were stored at 4°C and used for biochemical analyses within 1 h after collection. Serum levels of creatinine, blood urea nitrogen (predialysis urea), glucose, total cholesterol, triglycerides (TG), iron, total iron-binding capacity, ferritin, total calcium, and phosphorus were measured through autoanalyzer (COBAS Integra 800, Roche Diagnostics, Basel, Switzerland). Serum leptin (SPI-BIO, Montigny le Bretonneux, France) concentrations were determined using a commercially available enzyme immunoassay [13-16]. Serum intact parathyroid hormone levels (iPTH) were measured using enzyme-linked immunosorbent assays (Diagnostic Systems Laboratories, Webster, Texas, USA) [13-16]. At the end of the HD session, ultrafiltration was stopped, blood flow was slowed to 100 mL/min for 20 s, and blood samples were drawn from the arterial blood line sampling port for postdialysis serum urea measurements. The urea reduction rate was calculated as ([predialysis urea − postdialysis urea] ×100)/[predialysis urea]). The adequacy of dialysis was estimated by the measurement of the single-pool fractional clearance index for urea (Kt/Vurea) using Gotch's formula.

### Carotid–femoral pulse wave velocity measurements

The cfPWV was measured transcutaneously with a pressure tonometer (SphygmoCor system, AtCor Medical, West Ryde, Australia) on the carotid and femoral sites, and the pressure pulse waveform was recorded, as previously described [14,15]. These measurements were performed in all patients in the supine position after a minimum 10 min rest in a quiet, temperature-controlled room before the start of the midweek HD session. Recordings were made simultaneously with an electrocardiographic (ECG) signal, which provided an R-timing reference. Pulse wave recordings were performed consecutively at the carotid and femoral segments. The integrated software (SphygmoCor system, AtCor Medical, West Ryde, Australia) was used to process each set of pulse wave and ECG data, to calculate the mean time difference between the R-wave and the pulse wave on a beat-to-beat basis, among an average of 10 consecutive cardiac cycles. The cfPWV was calculated using the distance and the mean time difference between the two recorded points (carotid–femoral segment). In this study, patients with cfPWV values above 10 m/s were defined as the high arterial stiffness group, while those with values below 10 m/s were regarded as the low arterial stiffness group. The cut-off value was determined according to the European Society of Hypertension and European Society of Cardiology guidelines in 2013 [17].

### Statistical analysis

Data were tested with the Kolmogorov–Smirnov test for normal distribution. Data were expressed as means ± standard deviation for normally distributed results and as medians and interquartile ranges for nonnormally distributed data. Comparisons between patients were performed using Student's independent $t$-test (two-tailed) for normally distributed data, or the Mann–Whitney U-test for parameters with a nonnormal distribution. The glucose, ferritin, TG, iPTH, leptin, and HD duration datasets showed skewed nonnormal distributions, and therefore were recalculated by logarithm transformation to base 10; after this transformation, the log-glucose, log-ferritin, log-TG, log-iPTH, log-leptin, and log-HD duration were normally distributed. Data expressed as the number of patients were analyzed by the Chi-square test. Clinical variables that correlated with cfPWV values in geriatric HD patients were first evaluated by univariable linear regression analysis. Variables that were significantly associated with cfPWV values in geriatric HD patients were tested for independence

by multivariate forward stepwise regression analysis (adopted factors: diabetes, age, waist circumference, BMI, body fat mass, post-HD body weight, SBP, pulse pressure, hemoglobin, log-TG, and log-leptin). Variables that were significantly associated with central arterial stiffness in HD patients were tested for independence by multivariate logistic regression analysis (adopted factors: Diabetes, hypertension, waist circumference, BMI, pulse pressure, hemoglobin, and leptin). All statistical analyses employed SPSS for Windows (version 19.0; SPSS Inc., Chicago, IL, USA). The $P < 0.05$ was considered statistically significant.

## Results

Demographic, biochemical, and clinical characteristics of the 58 geriatric HD patients are shown in Table 1. The mean age of participants was 75.14 years with a median HD duration of 4.14 years. Men accounted for 46.5% of participants. A total of 34 patients (58.6%) had diabetes mellitus and 33 (56.9%) had hypertension. Thirty patients (51.7%) were defined as having high arterial stiffness and 28 patients (48.3%) were defined as having low arterial stiffness. The high arterial stiffness group had higher BMI ($P = 0.018$), SBP ($P = 0.018$), and pulse pressure ($P = 0.019$) than the low arterial stiffness group. Serum leptin ($P = 0.008$) and hemoglobin ($P = 0.040$) levels were also significantly higher in the high arterial stiffness group.

Comorbidity and the use of antihypertensives and anti-lipid drugs are presented in Table 2. There were higher percentages of participants with diabetes ($P = 0.019$) and hypertension ($P = 0.019$) in the high than the low arterial stiffness group. The effects of the use of β-blockers, calcium channel blockers (CCB), angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), statins and fibrates on blood pressure, atherosclerosis, and lipid burden were also recorded. No statistically significant differences were recorded between groups in subgroup analysis for sex, use of ACEi, ARB, β-blockers, CCB, statins, or fibrates.

Table 3 shows the correlation between cfPWV values and clinical variables in these 58 geriatric HD patients. Univariate linear regression analyses revealed positive correlations between pre-HD body weight ($r = 0.293$; $P = 0.026$), post-HD body weight ($r = 0.300$; $P = 0.022$), BMI ($r = 0.313$; $P = 0.017$), pulse pressure ($r = 0.275$; $P = 0.036$), hemoglobin level ($r = 0.270$; $P = 0.040$), and log-leptin level ($r = 0.422$; $P = 0.001$). Table 4 shows the multivariate, forward stepwise linear regression analysis of the variables significantly associated with cfPWV value (diabetes, hypertension, post-HD body weight, BMI and hemoglobin, and log-leptin). Log-leptin (β = 0.408, adjusted $R^2$ change = 0.164, $P = 0.001$) and diabetes (β = 0.312, adjusted $R^2$ change = 0.085, $P = 0.009$) were independent factors of the cfPWV value in geriatric HD patients.

**Table 1: Clinical variables of the 58 geriatric hemodialysis patients with high or low central arterial stiffness**

| Characteristics | All patients ($n$=58) | Low central arterial stiffness group ($n$=30) | High central arterial stiffness group ($n$=28) | $P$ |
|---|---|---|---|---|
| Age (years) | 75.14±6.03 | 74.93±6.39 | 75.36±5.73 | 0.792 |
| HD duration (years) | 4.14 (1.88-8.47) | 4.35 (1.76-10.44) | 4.09 (2.04-6.41) | 0.565 |
| Pre-HD body weight (kg) | 57.38±15.93 | 55.08±12.69 | 60.98±11.03 | 0.065 |
| Post-HD body weight (kg) | 56.04±12.00 | 53.24±12.46 | 59.03±10.92 | 0.066 |
| Waist circumference (cm) | 90.24±11.17 | 87.93±11.74 | 92.71±10.16 | 0.104 |
| BMI (kg/m$^2$) | 22.64±4.09 | 21.43±3.63 | 23.94±4.23 | 0.018* |
| cfPWV (m/s) | 9.79±4.17 | 6.58±2.30 | 13.23±2.70 | <0.001* |
| SBP (mmHg) | 136.97±24.52 | 129.67±24.76 | 144.79±22.09 | 0.018* |
| DBP (mmHg) | 69.66±13.78 | 68.07±12.95 | 71.36±14.67 | 0.368 |
| Pulse pressure (mmHg) | 67.31±19.35 | 61.60±18.06 | 73.43±19.11 | 0.019* |
| White blood count (×1000/uL) | 5.77±1.76 | 5.75±1.96 | 5.79±1.57 | 0.934 |
| Hemoglobin (g/dL) | 10.34±1.02 | 10.02±1.23 | 10.68±0.76 | 0.013* |
| Iron (μg/dL) | 74.24±26.64 | 78.83±28.83 | 69.32±23.60 | 0.176 |
| Total iron-binding capacity (μg/dL) | 252.93±35.83 | 257.33±40.30 | 248.21±30.35 | 0.337 |
| Ferritin (ng/mL) | 203.90 (102.58-422.70) | 245.10 (56.45-494.23) | 190.95 (123.18-320.03) | 0.950 |
| Total cholesterol (mg/dL) | 140.64±28.48 | 135.97±28.03 | 145.64±28.62 | 0.199 |
| Triglycerides (mg/dL) | 131.21±77.92 | 121.37±63.33 | 141.75±91.04 | 0.324 |
| Glucose (mg/dL) | 132.50 (114.00-179.00) | 128.50 (109.00-163.50) | 141.50 (120.75-210.00) | 0.104 |
| Blood urea nitrogen (mg/dL) | 57.38±15.93 | 56.43±16.22 | 58.39±15.85 | 0.644 |
| Creatinine (mg/dL) | 8.48±1.72 | 8.53±1.58 | 8.42±1.89 | 0.807 |
| Total calcium (mg/dL) | 8.93±0.76 | 8.81±0.71 | 9.06±0.79 | 0.200 |
| Phosphorus (mg/dL) | 4.39±1.24 | 4.29±1.29 | 4.50±1.21 | 0.519 |
| Intact parathyroid hormone (pg/mL) | 240.97±210.83 | 248.65±194.66 | 232.74±230.22 | 0.777 |
| Leptin (ng/mL) | 12.49 (4.13-52.58) | 7.90 (2.60-26.68) | 21.87 (6.24-74.22) | 0.008* |
| Urea reduction rate | 0.75±0.04 | 0.75±0.05 | 0.74±0.03 | 0.805 |
| Kt/V (Gotch) | 1.38±0.16 | 1.39±0.19 | 1.37±0.13 | 0.643 |

*$P$<0.05 is considered statistically significant. Values for continuous variables are given as means±SD and were tested by Student's $t$-test; variables not normally distributed are given as medians and interquartile range and were tested by Mann-Whitney U-test. HD: Hemodialysis, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, Kt/V: Fractional clearance index for urea, SD: Standard deviation, cfPWV: Carotid-femoral pulse wave velocity, BMI: Body mass index

**Table 2: Distribution of hemodialysis patients with high and low central arterial stiffness in subgroup analysis**

| Characteristics | Low central arterial stiffness group (%) | High central arterial stiffness group (%) | *P* |
|---|---|---|---|
| Gender | | | |
| Male | 14 (46.7) | 13 (46.4) | 0.986 |
| Female | 16 (53.3) | 15 (53.6) | |
| Diabetes | | | |
| No | 22 (73.3) | 12 (42.9) | 0.019* |
| Yes | 8 (26.7) | 16 (57.1) | |
| Hypertension | | | |
| No | 21 (70.0) | 11 (39.3) | 0.019* |
| Yes | 9 (30.0) | 17 (60.7) | |
| Hepatitis B carrier | | | |
| No | 27 (90.0) | 27 (96.4) | 0.334 |
| Yes | 3 (10.0) | 1 (3.6) | |
| Hepatitis C carrier | | | |
| No | 24 (80.0) | 24 (85.7) | 0.565 |
| Yes | 6 (20.0) | 4 (14.3) | |
| ARB use | | | |
| No | 24 (80.0) | 17 (60.7) | 0.107 |
| Yes | 6 (20.0) | 11 (39.3) | |
| β-blocker use | | | |
| No | 24 (80.0) | 16 (57.1) | 0.060 |
| Yes | 6 (20.0) | 12 (42.9) | |
| CCB use | | | |
| No | 19 (63.3) | 15 (53.6) | 0.451 |
| Yes | 11 (36.7) | 13 (46.4) | |
| Statin use | | | |
| No | 27 (90.0) | 23 (82.1) | 0.386 |
| Yes | 3 (10.0) | 5 (17.9) | |
| Fibrate use | | | |
| No | 28 (93.3) | 24 (85.7) | 0.341 |
| Yes | 2 (6.7) | 4 (14.3) | |

*$P$<0.05 is considered statistically significant. Data are expressed as *n* (%) of patients and analysis was done using the Chi-square test.
ARB: Angiotensin receptor blockers, CCB: Calcium channel blockers

**Table 3: Correlation of carotid-femoral pulse wave velocity levels and clinical variables in univariate linear regression analysis among the 58 geriatric hemodialysis patients**

| Variable | *r* | *P* |
|---|---|---|
| Age (years) | 0.084 | 0.532 |
| Log-HD duration (years) | 0.024 | 0.859 |
| Pre-HD body weight (kg) | 0.293 | 0.026* |
| Post-HD body weight (kg) | 0.300 | 0.022* |
| Waist circumference (cm) | 0.202 | 0.128 |
| BMI (kg/m$^2$) | 0.313 | 0.017* |
| SBP (mmHg) | 0.230 | 0.082 |
| DBP (mmHg) | 0.023 | 0.866 |
| Pulse pressure (mmHg) | 0.275 | 0.036* |
| White blood count (×1000/uL) | 0.077 | 0.568 |
| Hemoglobin (g/dL) | 0.270 | 0.040* |
| Iron (μg/dL) | −0.181 | 0.173 |
| Total iron-binding capacity (μg/dL) | −0.204 | 0.124 |
| Total cholesterol (mg/dL) | 0.024 | 0.857 |
| Triglycerides (mg/dL) | 0.126 | 0.345 |
| Blood urea nitrogen (mg/dL) | −0.098 | 0.464 |
| Creatinine (mg/dL) | 0.098 | 0.467 |
| Total calcium (mg/dL) | 0.180 | 0.175 |
| Phosphorus (mg/dL) | −0.045 | 0.739 |
| Intact parathyroid hormone (pg/mL) | −0.131 | 0.327 |
| Log-leptin (ng/mL) | 0.422 | 0.001* |
| Urea reduction rate | −0.019 | 0.885 |
| Kt/V (Gotch) | −0.030 | 0.823 |

*$P$<0.05 was considered statistically significant. Data for ferritin, glucose, and leptin levels showed skewed distributions, and therefore were log-transformed before analysis. HD: Hemodialysis, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, Kt/V: Fractional clearance index for urea, BMI: Body mass index

Adjustment of the factors significantly associated with central arterial stiffness (adopted factors: diabetes, hypertension, waist circumference, BMI, pulse pressure, hemoglobin, and leptin) in multivariate logistic regression analysis revealed that increased serum leptin levels (odds ratio [OR]: 1.053; 95% confidence interval [CI]: 1.007–1.100; $P$ = 0.023), hemoglobin level (OR: 2.869; 95% CI: 1.176–6.999; $P$ = 0.021), and pulse pressure (OR: 1.078; 95% CI: 1.003–1.159; $P$ = 0.041) were independent factors of central arterial stiffness among geriatric HD patients [Table 5].

## Discussion

This study reported that the serum leptin level was positively associated with central arterial stiffness in geriatric HD patients and was an independent factor of the cfPWV value in geriatric HD patients.

The aging process is associated with fat redistribution, including peripheral subcutaneous fat loss and central fat accumulation [12,18]. Older people are susceptible to adipokine dysregulation caused by visceral obesity [12,19]. Several mechanisms have been proposed to explain the correlation of hyperleptinemia with arterial stiffness. One possible mechanism is that hyperleptinemia enhances sympathetic tone and decreases kidney natriuresis, causing hypertension. Another possible mechanism is that hyperleptinemia stimulates intimal monocyte recruitment, macrophage cell transformation, and vascular smooth muscle cell proliferation, causing atherosclerotic changes; induces endothelial nitric oxide imbalance-mediated endothelial dysfunction, and finally prompts induction of platelet aggregation-related thrombosis induction [17]. Many cross-sectional studies have also proved a relationship between arterial stiffness and hyperleptinemia among healthy individuals, obese, diabetic, hypertensive, and elderly patients, kidney transplantation recipients, and coronary artery disease patients [14,15,20]. The results of the present study also showed that hyperleptinemia was positively associated with central arterial stiffness and was an independent factor for the cfPWV value in geriatric HD patients.

Our results revealed a positive association between central arterial stiffness and diabetes in geriatric HD patients. Diabetes is a traditional risk factor for arterial stiffness in elderly diabetic people [21]. Diabetes accelerates arterial aging, resulting in stiffer arteries and a steeper increase in pulse pressure in elderly participants [22]. Hyperinsulinemia accentuates renin–angiotensin–aldosterone axis activity, leads to vascular wall hypertrophy and alters vessels elasticity. In addition, advanced glycation end products further induce endothelium injury. These effects promote

**Table 4: Multivariate forward stepwise regression analysis of the factors correlated with carotid-femoral pulse wave velocity levels among 58 geriatric hemodialysis patients**

| Items | Beta | Adjusted $R^2$ | Adjusted $R^2$ change | *P* |
|---|---|---|---|---|
| Log-leptin (ng/mL) | 0.408 | 0.164 | 0.164 | 0.001* |
| Diabetes mellitus | 0.312 | 0.249 | 0.085 | 0.009* |

*$P$<0.05 was considered statistically significant. Analysis was done using multivariate logistic regression analysis (adopted factors: Diabetes mellitus, hypertension, SBP, pulse pressure, post-HD body weight, BMI, hemoglobin, and log-leptin). HD: Hemodialysis, SBP: Systolic blood pressure, BMI: Body mass index

**Table 5: Multivariate logistic regression analysis of the factors correlated with central arterial stiffness among 58 geriatric hemodialysis patients**

| Variable | OR | 95% CI | *P* |
|---|---|---|---|
| Leptin (ng/mL) (each increase of 1 ng/mL) | 1.053 | 1.007-1.100 | 0.023* |
| Hemoglobin (g/dL) (each increase of 1 g/dL) | 2.869 | 1.176-6.999 | 0.021* |
| Pulse pressure (mmHg) (each increase of 1 mmHg) | 1.078 | 1.003-1.159 | 0.041* |

*$P$<0.05 was considered statistically significant. Analysis was done using multivariate logistic regression analysis (adopted factors: Diabetes, hypertension, waist circumference, BMI, pulse pressure, hemoglobin, and leptin). OR: Odds ratio, CI: Confidence interval, BMI: Body mass index

atherosclerosis [23]. Our study revealed that diabetes mellitus was positively correlated with cfPWV values. After multiple regression analysis, diabetes was also an independent factor for the cfPWV value in geriatric HD patients.

BMI and waist circumference are commonly used to assess general and abdominal adiposity, and the increase in central arterial stiffness in patients with metabolic syndrome is strongly related to the amount of visceral adipose tissue [24,25]. Our results also noted BMI and waist circumference were positively associated with the cfPWV value in geriatric HD patients. Gender differences have been reported in the traditional vascular risk factors for hypertension [25]. Mean arterial pressure contributed independently to variations in cfPWV values in community participants in South Africa [26]. The prevalence of systolic hypertension for those over 60 years old is twice that of those between 40 and 59 years [27]. The SBP is elevated in both age groups, whereas a normal or low DBP in the elderly is due to aortic stiffening and increased pulse pressure [27]. Our results noted higher prevalence of hypertension, elevated SBP, and elevated pulse pressure in the high arterial stiffness group and pulse pressure was positively associated with the cfPWV value. Moreover, this difference in pulse pressure between central arterial stiffness groups remained after multivariate adjustment. The cfPWV value was significantly higher in men with type 2 diabetes mellitus in one study [28]. However, the BMI in women was associated with a higher cfPWV value in 1517 participants in the Nijmegen Biomedical Study, and age 50–70 years and female sex were associated with higher cfPWV values in community participants in South Africa [25,26]. Our results did not find statistically significant gender differences in central arterial stiffness among geriatric HD patients. The reasons for the sex differences in hypertension are multifactorial, implying different roles of sex hormones, the renin–angiotensin system, sympathetic activity, and arterial stiffness [29]. Further larger prospective studies are needed to establish these relationships.

The current study also revealed a correlation between hemoglobin levels and high central arterial stiffness. There were similar findings in a large Japanese study in a healthy population with BMI <25 kg/m$^2$ [30]. Another study in which the brachial-ankle PWV was measured found a lower hemoglobin level was independently beneficial for peripheral arterial stiffness in a healthy community population, but only in women [31]. Possible mechanisms accounting for this correlation include activation of nuclear factor-kappa B transcription, decreased nitric oxide to mediate vascular homeostasis by hemoglobin, and plaque instability and atherosclerosis progression caused by hemoglobin membranes [32-34]. Another study proposed a conflicting opinion that only the density score, composed of hemoglobin and total protein, would alter PWV instead of hemoglobin alone [35]. This relationship between the hemoglobin level and the severity of arterial stiffness is not conclusive.

There are a few limitations in our study. First, since our study participants were elderly HD participants from a single center at East Taiwan, and further assessment is needed to determine whether the results are applicable to other populations. Second, the current data lack comprehensive assessment and in-depth nutritional evaluation, such as the subjective global assessment score, to further analyze the relationship between nutrition and leptin in the geriatric dialysis population. Third, the study had a small sample size and a cross-sectional design, which may affect the statistical significance. Only 58 geriatric HD participants were enrolled in this study, and the power to predict central arterial stiffness was only 0.73. Further long-term prospective studies are needed to confirm the relationship between central arterial stiffness and hyperleptinemia in geriatric HD patients.

## Conclusion

A higher serum leptin level was associated with central arterial stiffness in geriatric HD patients. Moreover, diabetes was also positively associated with the cfPWV value in these geriatric HD patients.

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### Conflict of interest

There are no conflicts of interest.

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