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Research Article

The Multiscale Dynamics of Beat-to-Beat Blood Pressure Fluctuation Mediated the Relationship Between Frailty and Arterial Stiffness in Older Adults

Xin Jiang, MD,[1,2,3,*] Yurun Cai, PhD,[4,5,] Xiaoyan Wu, MS,[1,2] Baofeng Huang, MS,[1,2,3] Yurong Chen, BS,[1] Lilian Zhong, BS,[1,2,3] Xia Gao, MS,[1,2,3] Yi Guo, MD,[2,3,6,7] and Junhong Zhou, PhD[8,9,10,]

[1]Department of Geriatrics, Shenzhen People's Hospital, Shenzhen, Guangdong, People's Republic of China. [2]The Second Clinical Medical College, Jinan University, Shenzhen, Guangdong, People's Republic of China. [3]The First Affiliated Hospital, Southern University of Science and Technology, Shenzhen, Guangdong, People's Republic of China. [4]Department of Health and Community Systems, University of Pittsburgh School of Nursing, Pittsburgh, PA, USA. [5]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA. [6]Department of Neurology, Shenzhen People's Hospital, Shenzhen, Guangdong, People's Republic of China. [7]Shenzhen Bay Laboratory, Shenzhen, Guangdong, People's Republic of China. [8]Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife, Roslindale, Maryland, USA. [9]Division of Gerontology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA. [10]Harvard Medical School, Boston, Massachusetts, USA.

*Address correspondence to: Yi Guo, MD, Department of Neurology, Shenzhen People's Hospital, 1017 Dongmen Rd N, Luohu District, Shenzhen, Guangdong 518020, People's Republic of China. E-mail: xuanyi_guo@163.com

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Abstract

Background: Beat-to-beat blood pressure (BP) is an important cardiovascular output and regulated by neurophysiological elements over multiple temporal scales. The multiscale dynamics of beat-to-beat BP fluctuation can be characterized by "BP complexity" and has been linked to age-related adverse health outcomes. We here aimed to examine whether BP complexity mediates the association between arterial stiffness and frailty.

Method: This cross-sectional study was completed between January and October 2021. A total of 350 older adults completed assessments for frailty, arterial stiffness (ie, average brachial–ankle pulse wave velocity), and beat-to-beat finger BP. The complexity of beat-to-beat systolic blood pressure (SBP) and diastolic blood pressure (DBP) BP series was measured using multiscale entropy. The relationships between frailty, BP complexity, and arterial stiffness were examined using analysis of variance and linear regression models. The effects of BP complexity on the association between arterial stiffness and frailty were examined using mediation analyses.

Results: Compared with non-frail, prefrail, and frail groups had significantly elevated lower SBP and DBP complexity ($F > 11$, $p < .001$) and greater arterial stiffness ($F = 16$, $p < .001$). Greater arterial stiffness was associated with lower BP complexity ($\beta < -0.42$, $p < .001$). Beat-to-beat SBP and DBP complexity mediated the association between arterial stiffness and frailty (indirect effects >0.28), accounting for at least 47% of its total effects on frailty (mediated proportion: SBP: 50%, DBP: 47%).

Conclusion: This study demonstrates the association between BP complexity and frailty in older adults, and BP complexity mediates the association between arterial stiffness and frailty, suggesting that this metric would serve as a marker to help characterize important functions in the older adults.

Keywords: Arterial stiffness, Beat-to-beat blood pressure, Frailty, Multiscale entropy

Maintaining cardiovascular health is critical for everyday activities. The age-related deterioration within the cardiovascular system, such as increased arterial stiffness, is highly prevalent in the older adult population (1). The increase in arterial stiffness has been linked to frailty syndrome, a common age-related syndrome that is associated with poor health outcomes in older adults (2–5). Orkaby et al. observed that, for example, compared with non-frail older adults, those with prefrailty and/or frailty had significantly greater arterial stiffness (5). However, less is known about the underlying elements that contribute to the association between arterial stiffness and frailty in older adults.

The blood pressure (BP) fluctuation is one important cardiovascular output and has been used to help characterize the cardiovascular system for years. Studies have linked altered BP fluctuation (eg, increased BP variability) to aging and frailty (6). BP is determined by multiple elements, such as the cardiac output and systemic vascular resistance, and is regulated continuously by neural and hormonal feedback procedures in neurovascular systems, including baroreceptors, resistance vessels, and sympathetic and parasympathetic nervous systems, over *multiple, not single,* temporospatial scales (7,8). The multiscale dynamics of continuous beat-to-beat BP fluctuation are thus "complex," containing rich physiologically meaningful patterns pertaining to those underlying elements and their interactions (9,10). The traditional measures (ie, mean BP level, BP variability) based upon a single temporal scale may thus not fully capture such physiological complexity within BP regulation.

Recently, studies have emerged to quantitatively measure such physiological complexity in beat-to-beat BP fluctuations by using techniques derived from theories of nonlinear dynamics, such as multiscale entropy (MSE) (11). It has been observed that the complexity of beat-to-beat BP fluctuations (ie, BP complexity) is associated with the health of vascular systems (9,10,12) and frail status in the preoperative period (13), and predicts the risk of dementia or Alzheimer's disease (12). This suggests that BP complexity may be a marker for the pathology in those age-related diseases and functional decline. However, the relationship between BP complexity and frailty syndrome in older adults, and if BP complexity is one mediator on the relationship between arterial stiffness and frailty has not been fully understood. By knowing this, it will ultimately help optimize the management of frailty syndrome and cardiovascular health in older adults.

In this study, we assessed the level of frailty in a group of older adults, measured their BP complexity and other BP characteristics (eg, BP level), and assessed the brachial–ankle arterial stiffness by measuring the pulse wave velocity in these older adults. We hypothesized that (i) older adults with more severe frailty status would have lower BP complexity; (ii) lower BP complexity would be associated with greater arterial stiffness; and (iii) BP complexity would mediate the association between arterial stiffness and frailty.

Methods

Participants

This study was initiated in January 2021 and completed in October 2021. The participants were recruited via the search of an electronic clinical data repository in Department of Gerontology, Shenzhen People's Hospital, Shenzhen, China. This repository was initiated on January 1, 2020, consisting of information of older adults who had clinical visits for annual physical examination or primary care, without any emergent or severe clinical conditions. The cutoff date of the search was set on January 1, 2021. Therefore, in these data repositories, older adults who had a clinical visit within the previous 12 months (ie, between January 1, 2020, and January 1, 2021) and expressed interests in participating in future studies were contacted. The inclusion criteria were: (i) age greater than 60 years at the visits of this study and (ii) with the ability to walk for at least 1 minute without physical assistance. The exclusion criteria were (i) diagnosis of terminal disease (eg, cancer), (ii) diagnosis of dementia or other overt neurological diseases (eg, Parkinson's disease or stroke), (iii) history of brain trauma or injury, (iv) hospitalization within the past 6 months, (v) uncontrolled hypertension, (vi) chronic kidney disease, dyslipidemia, (vii) other cardiovascular diseases (CVDs) (eg, heart failure, coronary artery disease), and (viii) inability to understand the study protocol. All experimental methods and protocols were approved by the Institutional Review Board of Shenzhen People's Hospital and carried out in accordance with the guidelines in the Declaration of Helsinki. All the participants provided written consent to participate in this study.

Study Protocol

After screening, each eligible participant completed 2 study visits separated by 1 day. On the first visit, they completed a series of questionnaires to assess the demographics (eg, age, sex, body mass index [BMI]), health behaviors (eg, smoking), and the assessment of frailty. One study personnel monitored all the procedures to ensure the safety of participants. On the second study visit, they completed a continuous beat-to-beat finger BP assessment, and the assessment of arterial stiffness in the same laboratory under the administration of study personnel.

Assessment of frailty

Frailty was assessed using Fried Frailty Phenotype Criteria (14), including unintentional weight loss, low energy or self-reported exhaustion, low physical activity, slowness as assessed by slowed walking speed, and weakness as measured by low grip strength. On the basis of the report and results of the assessment, the severity of frailty was categorized into three stages: non-frail (no criterion was presented), prefrail (1 or 2 criteria were presented), and frail (3 or more criteria were presented).

Characteristics related to hypertension

Hypertension is a significant and highly prevalent cardiovascular condition in older adults. We thus included hypertensive characteristics as assessed in the previous clinical visits for each participant. Specifically, hypertension was characterized as systolic BP (SBP) ≥140 mmHg and/or diastolic BP (DBP) ≥90 mmHg by measuring the brachial artery of the right arm using a sphygmomanometer. Within hypertensive participants, hypertension had been controlled using antihypertension medication. The antihypertension medication was categorized as calcium–channel blockers (CCB), angiotensin–converting enzyme inhibitors (ACEI), angiotensin-II receptor blockers (ARB), β-blockers (BB), and diuretics. The number of antihypertensive medications each participant used at the same time and the duration of hypertension (ie, history of hypertension) were also recorded.

Blood pressure recordings

After resting, each participant then completed a BP assessment when sitting in a quiet assessment room with 1 study staff. During the assessment, the participant was instructed not to talk and to keep motionless (eg, not moving the arms). The objects which may interfere with testing, such as mobile phones, were stored in a box outside the room. The continuous SBP and DBP series were recorded using the Finometer PRO system (Finapres Medical Systems B.V., Enschede,

The Netherlands) at the middle finger of the left hand in the supine position for at least 10 min (10 to 15 min) with a sampling frequency of 100 Hz (15). All the BP recordings consisted of at least 700 continuous beats. The BeatScope software package (Finapres Medical Systems B.V.) was then used to calculate the BP values of each beat. For the preprocessing of the BP series, we followed the widely used procedure that has been validated in our previous studies (9,10,12). Specifically, outliers in the BP series of which the value was greater or lower than the mean ±2 standard deviations (*SD*) of the series were interpolated by the mean of this series (7,8,12). The preprocessed BP series of 700 sampling points were then used to obtain BP complexity.

Blood pressure complexity

The *complexity* of SBP and DBP series was quantified using MSE, a well-developed and widely used technique that quantifies the entropy or recurrence in physiological series over different temporal or spatial scales. Specifically, the continuous BP series was first "coarse-grained" for scales from 1 to 5, that is, the original series was divided into nonoverlapping windows of length equaling a scale factor from 1 to 5 sampling points. Thus, in the coarse-graining process, the series at Scale 1 was the raw series consisting of 700 data points, that at Scale 2 was constructed by averaging every 2 non-overlapped points, consisting of 350 points (ie, 700 points/2). The sample entropies of each "coarse-grained" series were then calculated by using the negative natural logarithm of the conditional probability that a time series, having repeated itself within a tolerance r for m points (pattern length), will also repeat itself for $m + 1$ points without self-matches (11,16,17). We followed the same procedure of MSE calculation in the previous studies of ours and others (9,10,16,17) by choosing the parameter of tolerance $r = 0.15$ and the number of matching points $m = 2$. Blood pressure complexity was then defined as the averaged entropy across 5 scales. Lower MSE reflects lower complexity.

Additionally, the mean level of SBP and DBP was used in the following analyses.

Assessment of arterial stiffness

Following the standard testing procedures as suggested in previous studies (18,19), arterial stiffness was assessed by measuring the left- and right-side brachial–ankle pulse wave velocity (baPWV; Omron, Kyoto, Japan) when participants were in a resting state. The average baPWV of the left and the right side was used in the following analysis.

Statistical Analysis

Statistical analyses were performed with JMP Pro. 15 software (SAS Institute, Cary, NC) and Mplus 8.4 (Muthén & Muthén, Los Angeles, CA). Data distribution and missing values were checked for all variables.

The relationship of frailty to BP complexity (ie, SBP and DBP complexity) was examined by 2-way analysis of variance (ANOVA) models. The model factor was frailty status (ie, non-frail, prefrail, and frail) and the dependent variable was SBP and DBP complexity in separate models. Tukey's post hoc analysis was used to examine the location of significance when a significant difference was observed in ANOVA models. Similar models were used to examine the relationship between frailty and demographics, arterial stiffness (ie, average baPWV), and mean BP level. All these models were adjusted for age (here participants with older age had significantly lower SBP [$\beta = -0.5$, $p = .007$] and/or DBP [$\beta = -0.58$, $p = .001$] complexity), sex, BMI, the status of regular alcohol use (ie, yes or no) and smoking (ie, smoker or nonsmoker), hypertensive status (ie, hypertensive or normotensive), use of antihypertension medication and the duration of hypertension, which were believed to contribute to frailty, arterial stiffness, and BP complexity.

Then the relationship between BP complexity and arterial stiffness was examined using linear regression models. These models were adjusted for age, sex, BMI, the severity of frailty, regular alcohol use, smoking, hypertensive status (ie, hypertensive and normotensive), use of antihypertension medication, and the duration of hypertension.

To test the hypothesis that BP complexity would mediate the relationship between arterial stiffness and frailty, we utilized mediation analyses. The complexity of SBP and DBP was used as a mediator in separate models. The independent variable was arterial stiffness (ie, average baPWV), and the dependent variable was frailty level. We calculated the total effects of arterial stiffness on frailty (ie, total effect, path c), and the association between arterial stiffness and BP complexity (path a). Then we examined the association between BP complexity and frailty (path b), which provided the estimates for direct effects (path c′). The percentage of mediation (ie, P_M) was determined by dividing indirect effect (path a × path b) by total effect (path c). A bootstrapping method with 5000 bootstrap samples was used to calculate the 95% bias corrected and accelerated confidence interval (95% BCa CIs) around the mediated and direct effects. All these models were adjusted for age, sex, BMI, regular alcohol use, smoking, hypertensive status, use of antihypertension medication, and the duration of hypertension. The significance level was set at $p < .05$.

Results

A total of 350 participants completed the tests of this study; of whom, 142 were identified as non-frail, 170 were prefrail, and 38 were frail. Table 1 shows the demographics and clinical and functional characteristics of the entire population and within each group of frailty.

The relationship between frailty and BP complexity and arterial stiffness

The ANOVA models demonstrated significant relationships between frailty and BP complexity (SBP: $F = 11$, $p < .001$; DBP: $F = 13$, $p < .001$). The Tukey post hoc analyses revealed elevated significant differences in SBP and DBP complexity between groups of frailty. Specifically, SBP and/or DBP complexity were the highest in the non-frail group, lower in the prefrail group, and the lowest in the frail group (Table 1). No significant difference in mean SBP ($F = 0.7$, $p = .44$) or DBP ($F = 2.1$, $p = .22$) level was observed between groups.

Similarly, a significant elevated difference in arterial stiffness as assessed by average baPWV between groups of frailty was also observed ($F = 16$, $p < .001$). The frail group had the greatest arterial stiffness (ie, highest baPWV) when compared with the non-frail group (Table 1). In addition, compared with non-frail and prefrail groups, the frail group had a significantly greater number of hypertensive older adults ($p = .01$) and a longer history of hypertension ($p = .01$) (Table 1).

The relationship between BP complexity and arterial stiffness

Linear regression analyses revealed that, across all the participants, arterial stiffness as assessed by average baPWV was significantly associated with SBP ($\beta = -0.45$, $p < .001$) and DBP ($\beta = -0.42$, $p < .001$) complexity (Figure 1). Participants with greater baPWV (ie, worse arterial stiffness) had lower SBP and/or DBP complexity. All these relationships were independent from age, sex, BMI, frailty

Table 1. Demographics and Clinical Information, Characteristics of Blood Pressure, Blood Composition and Vessel Function in Participants

Mean ± *SD*	Total (*n* = 350)	Nonfrail (*n* = 142)	Prefrail (*n* = 170)	Frail (*n* = 38)	*p* Value
Age (years)	71.2 ± 8.2	68.3 ± 6.1[A]	71.5 ± 7.7[B]	80 ± 7.9[C]	<.001
Sex(*n* = female)	179	68	92	19	.11
BMI	24.2 ± 3.6	24 ± 3.9[A]	24.8 ± 3.8[A]	23.2 ± 3.2[B]	.04
Smoking (*n* = smokers)	48	27	16	5	.87
Regular alcohol use (*n* = yes)	6 (1.7%)	4 (2.8%)	1 (0.5%)	1 (2.6%)	.19
Hypertension (*n* = yes)	226 (64%)	84 (59%)[A]	107 (63%)[A]	35 (92%)[B]	.01
Hypertension history (years)	11.4 ± 8.3	10.1 ± 8.3[A]	9.9 ± 6.9[A]	15.6 ± 10.5[B]	.01
Antihypertension medication (*n*)					
CCB	100 (28%)	32 (22%)	56 (33%)	12 (31%)	
ACEI	11 (3.1%)	2 (28%)	5 (2.9%)	4 (11%)	
ARB	58 (16%)	20 (1.4%)	29 (17%)	9 (24%)	
BB	48 (14%)	18 (13%)	22 (13%)	8 (21%)	
Diuretics	18 (5.1%)	6 (4.2%)	8 (4.7%)	4 (11%)	
Use of antihypertension medication (*n*)					
None	126 (36%)	58 (41%)	63 (37%)	3 (8%)	
1	154 (44%)	58 (41%)	71 (42%)	25 (66%)	
2	47 (13%)	16 (11%)	24 (14%)	7 (18%)	
>2	25 (7%)	10 (7%)	12 (7%)	3 (8%)	
Average baPWV (m/s)	17.6 ± 4.1	16.2 ± 3.2[A]	18.1 ± 4.1[B]	20.6 ± 5[C]	<.001
Mean BP level					
SBP	133.6 ± 15.7	133 ± 14.5	134.9 ± 15.8	135.3 ± 25.8	.44
DBP	77.7 ± 9.9	78.6 ± 9.7	77.1 ± 9.6	76.6 ± 10.9	.22
BP complexity					
SBP	1.45 ± 0.28	1.51 ± 0.23[A]	1.41 ± 0.25[B]	1.31 ± 0.19[C]	<.001
DBP	1.37 ± 0.32	1.39 ± 0.29[A]	1.26 ± 0.28[B]	1.16 ± 0.29[C]	<.001

Notes: Different superscript letters (A, B, and C) within each row indicate the mean that was significantly different from one another as determined by Tukey's post hoc testing of ANOVA models with a significant effect of frailty level on BP complexity.

ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin-II receptor blockers; baPWV = brachial–ankle pulse wave velocity; BB = β-blockers; BMI = body mass index; CCB = calcium–channel blockers; DBP = diastolic blood pressure; SBP = systolic blood pressure.

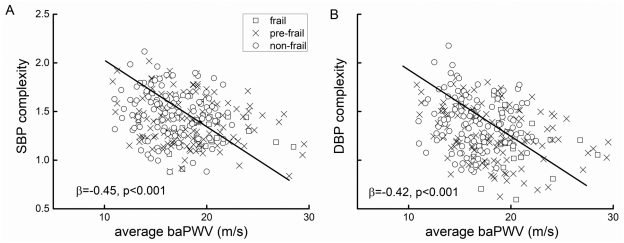

Figure 1. The association between arterial stiffness and systolic blood pressure (SBP) (A) and diastolic blood pressure (DBP) (B) complexity. The arterial stiffness was measured by average brachial–ankle pulse wave velocity (baPWV) and greater baPWV reflected higher arterial stiffness. Linear regression models adjusted for age, sex, BMI, frailty, regular alcohol use, smoking status, hypertension, the use of antihypertension medication, and the duration of hypertension showed that older adults with lower SBP ($\beta = -0.45$, $p < .001$) and/or DBP ($\beta = -0.42$, $p < .001$) complexity had greater arterial stiffness. Different markers on the figure presented different frailty severity.

status, hypertensive status, use of antihypertension medication, duration of hypertension, regular alcohol use, and smoking.

Mediation effects of BP complexity on the relationship between arterial stiffness and frailty

No significant effects of interaction between arterial stiffness and BP complexity on frailty were observed ($p > .12$). The mediation procedures revealed that the association between arterial stiffness and frailty was mediated by both SBP and DBP complexity (Figure 2). Specifically, separate mediation models showed that arterial stiffness as quantified by the average baPWV was associated with SBP (path a: $\beta = -0.51$, $p < .001$) and DBP (path a: $\beta = -0.50$, $p < .001$) complexity. Although the total effects of arterial stiffness on frailty status were statistically significant (path c; $\beta = 0.59$, $p = .003$), the direct effects of arterial stiffness on frailty were no longer significant after introducing BP complexity as mediator (path c′: SBP complexity: $\beta = 0.29$, $p = .17$; DBP complexity: $\beta = 0.29$, $p = .21$). Systolic BP complexity accounted for 50% of the total effects on arterial stiffness (indirect effects [ie, path a × path b] = 0.29, mediated proportion [P_M] = 50%, 95% Bca CI = 0.14~0.52), and DBP complexity accounted for 47% of such total effects (indirect effects = 0.28, P_M = 47%, 95% Bca CI = 0.13~0.50).

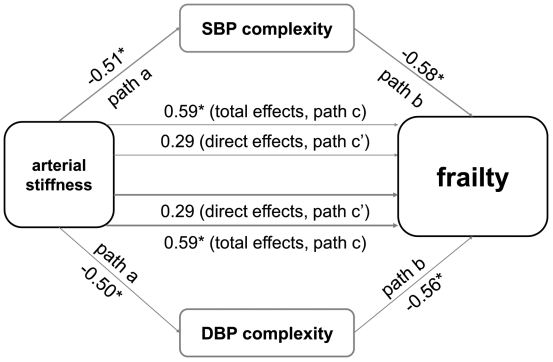

Figure 2. BP complexity mediated the relationship between arterial stiffness and frailty. We performed 2 mediation analyses to separately examine the mediation effects of systolic blood pressure (SBP) (top of the figure) and diastolic blood pressure (DBP) (bottom of the figure) complexity. The separate mediation analyses showed that: (i) Arterial stiffness was negatively associated with SBP and DBP complexity (path a; $\beta < -0.50$, $p < .001$); (ii) BP complexity was associated with the degree of frailty (path b: $\beta < -0.56$, $p < .001$); and (iii) significant total effect of arterial stiffness on frailty was observed (path c; $\beta = 0.59$, $p = .003$), while the direct effects (path c′) of arterial stiffness on frailty were not significant after using SBP or DBP complexity as the mediator (SBP complexity: $\beta = 0.29$, $p = .17$; DBP complexity: $\beta = 0.3$, $p = .21$). *$p < .01$.

Discussion

This study provides novel evidence that the multiscale dynamics of short-term (about 10 minutes) continuous beat-to-beat SBP and DBP fluctuations, as quantified by "complexity," is associated with frailty status and arterial stiffness in older adults; and such BP complexity mediated the association between arterial stiffness and frailty. These findings provide novel insights into the regulation of BP that is pertaining to the important functional characteristics and health status in older adults.

Fried et al. recently proposed a new conceptual model for frailty that the physical frailty may be a state that emerges when aging or age-related conditions disrupt the regulation of multiple interconnected biophysiological systems, "severely compromising homeostasis" and the complex dynamics of those systems (20). This conceptual model is in line with the theory of complexity in aging, that is, aging and age-related conditions often alter the quantity and/or quality of elements in a given physiological system and their multi-scale interactions, leading to the disrupted multiscale dynamics (ie, loss of complexity) in spontaneous signals of this system (21). Therefore, by measuring the complexity from physiological signals, it gives us a new scope beyond the traditional single–scale measures (eg, mean or variability) to understand how physiological systems are regulated; and complexity metrics may ultimately help the characterization of physical frailty and provides novel insights into its underlying physiological pathway.

Numerous studies have shown that "complexity" is a marker that is linked to important functional performance and can capture age- and disease-related subtle changes in physiological systems (9,10,17,22–26). For example, we previously observed that lower BP complexity is associated with hypertension and is a mediator on the effects of hypertension on WMLs and walking speed in older adults (9,10). In another study, Rangasamy et al. characterized the complexity of BP signals as measured invasively during the preoperative period and the frailty status based upon preoperative patient characteristics. They observed that this BP complexity was closely associated with the frailty status in people during the preoperative period (13). Inconsistent with these previous observations, we here observed that the lower complexity of the beat-to-beat continuous BP fluctuation is associated with greater functional decline, as assessed by frailty status. Taken together, these findings may suggest that BP complexity captures the subtle changes in the regulation of the cardiovascular system pertaining to the level of important functions in older adults. It should also be noted that unlike the traditional measures of BP that may have to be assessed over a long term of time (eg, over days, months, or years), BP complexity, based upon short–term BP recordings (ie, about 10 min), may serve as a novel and convenient marker to help the management of functions in older adults in future's clinical and rehabilitative practice.

The mediation effect of BP complexity on the relationship between arterial stiffness and frailty was examined, and we observed that SBP and DBP complexity contributed over 47% to this association. Numerous studies have well established the relationship between frailty and CVDs, and suggested that the frailty and CVD

shared some physiological pathways including the pathological changes in hematological, endocrine, and immunological systems (2,27) with each other. Arterial stiffness is a central phenomenon in the aging of the cardiovascular system and has been closely linked to the risk of cardiovascular events (eg, atherosclerosis, heart failure) (28–30). Ohkuma et al., for example, observed that the baseline baPWV in older adults without CVD is associated with the risk of development of CVD in the follow-up 6 years and a half. The hazard ratio for CVD was 3.5 times more in those in the highest quintile of baPWV when compared with those in the lowest quintile (30). Recently studies also observed that increased arterial stiffness was a risk factor to the elements of frailty, including sarcopenia and age-related muscle loss (31,32). Zhang et al., for example, observed in a group of community-dwelling older adults that the increased arterial stiffness as assessed by greater baPWV was associated with the loss of skeletal muscle mass and function, one important contributor to frailty (31). Our findings of mediation analysis may provide novel insights into such association, that is, in older adults even without major CVD or target organ damage, the changes in arterial stiffness may alter BP fluctuation, disrupting its complex pattern; such disruption (as captured by lower BP complexity), even subtle, diminishes the capacity of the vascular circulation system to efficiently and effectively regulate the blood supply for important functional performance (eg, mobility, cognitive function), leading to an elevated grade of frailty syndrome in older adults. The observed association between BP complexity and arterial stiffness may also, in turn, indicate that BP complexity would also potentially be linked to the risk of those cardiovascular events, which needs to be explored in future studies with a longitudinal design.

One important limitation is that this study only examined the cross-sectional relationship between BP complexity and other characteristics in older adults with relatively healthy cardiovascular function. Therefore, the generalizability of the observations in this study needs more cautiousness. Future longitudinal studies are highly demanded to examine the causal relationship between BP complexity, arterial stiffness, and the progress of frailty in diverse populations, such as those with CVD or targeted organ damage. We carefully assessed the characteristics related to hypertension, but due to the uneven number of use of antihypertension medication (see Table 1), we did not explicitly examine whether the use of medication (eg, using only 1 type of medication vs using 5 types of medications) would affect the relationship between BP complexity and frailty, which is worthwhile to be explored in future studies to provide insights into the pharmaceutical effects on BP regulation in older adults. The BP series was measured only in a short term at resting state in this study. While this suggests that a novel BP complexity metric can be obtained conveniently, previous studies, on the other hand, showed that the ambulatory BP across hours or days was also associated with important functional status (eg, cognitive function) in the older adults (33,34). It is thus worthwhile to characterize the BP complexity of ambulatory BP recordings over larger scales.

In conclusion, the findings of this study suggest that BP complexity as quantified using short-term continuous BP recordings may capture subtle changes within cardiovascular systems that are pertaining to frailty in the older adult population, holding great promise to help the assessment and management of cardiovascular health, and other important functions in older adults. Future studies with a more diverse population and a longitudinal design are warranted to confirm and expand the findings in this study.

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Conflict of Interest

None declared.

Acknowledgments

X.J., Y.G., and J.Z. designed the study; X.J., X.W., B.H., Y.C., L.Z., and X.G. collected the data; X.J., Y.C., Y.G., and J.Z. analyzed the data and performed statistical analyses; X.J., Y.C., Y.G., and J.Z. interpreted the results and drafted the manuscript; and all authors contributed to and approved the final version.

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