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Relationships between arterial stiffness and the cluster of cardiovascular disease risk factors

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KEYWORDS
Cardiovascular disease risk factor; Arterial stiffness; Pulse wave velocity; Cluster.

ABSTRACT

Evidence indicated that individuals with more than one cardiovascular disease (CVD) risk factor were more likely to develop CVD events, compared with those with a single risk factor. Arterial stiffness is known as an independent risk factor for CVD. This study aimed to explore the association of clustering of CVD risk factors and arterial stiffness. Arterial stiffness was measured in both male and female adults aged 49.04 ± 15.79 years who visited the vascular screening clinic at the Physical Therapy Center, Mahidol University. Participants with two or more risk factors were assigned to the cluster of CVD risk factors group. This study was part of a routine-to-research (R2R) project; therefore, all participants who were willing to receive the service from September 2021 to April 2023 were recruited into the study with their permission. The results showed that the brachial-ankle pulse wave velocity (baPWV), an arterial stiffness indicator, was highest in the clustering of CVD risk factors group (1594 cm/sec^2), higher in the single CVD risk factor group (1263cm/sec^2) than in none of CVD risk factors participant (1148 cm/sec^2). The overall mean resting mean arterial blood pressure level was 90 mmHg. In conclusion, clustering of CVD risk factors significantly correlated with arterial stiffness. Lifestyle modification should be strongly encouraged for individuals with more than one CVD risk factor to reduce the burden of CVD.

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Introduction

Cardiovascular disease (CVD) is the leading cause of mortality and morbidity globally, affecting over 523 million people[1]. To combat this burden of CVD, it is crucial to focus on primary cardiovascular prevention. Addressing CVD risk factors is one of the fundamental strategies to identify high-risk patients so that management with counselling and medicine can begin as early as possible. Hypertension, type 2 diabetes, dyslipidemia, and overweight are four major risk factors of cardiovascular disease[2,3]. Previous studies have revealed that CVD risk factors tend to be clustered in specific individuals[4,5]. A survey of suburban residents in Beijing, China, demonstrated that the prevalence of ≥1, ≥2, and ≥3 major CVD risk factors was 83.5%, 47.2%, and 17.5%, respectively[6].

Arterial stiffness is well-recognized as an emerging risk factor for CVD [7,8]. The brachial-ankle pulse wave velocity (baPWV) is a simple, accurate, and reproducible method for assessing the stiffness of medium- to large-sized arteries[9]. Based on the current meta-analysis study, Japanese participants who had higher baPWV values also had a higher risk of CVD. These results suggest that the baPWV may predict the future risk of CVD development in clinical practice, independent of traditional risk factors[10]. Moreover, evidence showed that major CVD risk factors, including hypertension[11], type 2 diabetes[12], dyslipidemia[13], and overweight and obesity[14], were associated with an accelerated increase in the brachial-ankle PWV. In the Baltimore Longitudinal Study of Aging (BLSA), it was found that arterial stiffness can predict the onset of hypertension[15]. Another critical CVD risk factor is hyperglycemia, which affects the properties and function of the arterial wall. In pre-diabetes, diabetes, or subjects with metabolic syndrome, these structural changes in the arterial wall can be observed[16]. Findings from a longitudinal study indicated that central obesity is a predictor of arterial stiffness over a 16-year period[17].

Increased arterial stiffness has been documented as an independent risk factor for future cardiovascular events and total mortality[18]. The Faculty of Physical Therapy, Mahidol University, has launched a vascular health screening program for adults to examine arterial stiffness levels as a CVD risk factor. Lifestyle modification strategies have been suggested to all participants, especially individuals with clustered CVD risk factors and high levels of arterial stiffness. Previous studies have been focused on the association of arterial stiffness level and individual risk factors. However, the CVD patients commonly have many comorbid diseases, such as hypertension, diabetes, and dyslipidemia together. To our current understanding, the relationship between arterial stiffness and the aggregation of CVD risk factors remains inadequately explored. Consequently, we conducted a cross-sectional study as part of a routine-to-research (R2R) initiative. This study aimed to compare arterial stiffness, as measured by baPWV, among individuals with clustering, single, and no cardiovascular disease risk factors.

Materials and methods

Participants

Adults who visited the vascular screening clinic at the Physical Therapy Center, Mahidol University, were enrolled in the study. The inclusion criteria were: 1) sedentary participants aged ≥ 18 years; 2) no cardiovascular disease, pulmonary disease, kidney disease, or infection; 3) not pregnant. Sedentary behavior is defined as individuals who engage in less than 60 minutes of moderate-intensity physical activity per week, as determined by a history-taking assessment. The participant who are smoking were excluded from data analyses. The final data analysis includes a total of 148 individuals. The investigation was conducted from September 2021 to April 2023 after approval from the Ethics Committee of the Mahidol University Institutional Review Board (MU-CIRB 2021/324.2806). All participants provided written informed consent prior to data collection.

Participant classifying criteria

We defined the four major traditional CVD risk factors as follows: 1) hypertension, 2) type 2 diabetes, 3) dyslipidemia, and 4) overweight and obesity. Participants with two or more risk factors were assigned to the cluster of CVD risk factors group. All risk factors are based on physician diagnosis, except overweight and obesity. A body mass index (BMI) greater than 25 kg/m^2 was defined as overweight or obesity.

Outcome measurements

Before the testing session, participants abstained from food, alcohol, and caffeine for at least four hours. Premenopausal women were tested during the early follicular phase of the menstrual cycle. All testing was performed 24 to 48 hours after the last exercise bout.

During the on-site screenings, the physical therapist reviewed the medical history, lifestyle behavior (e.g., alcohol use, smoking), and blood biochemistry laboratory. Weight and height were measured using an electronic scale. BMI was calculated as weight in kilograms divided by height in square meters.

An automated vascular testing system (VP-1000 plus, Omron Healthcare, Bannockburn, Illinois) was used to assess the participants' heart rate, brachial and ankle blood pressure, and baPWV after they had been resting quietly in a supine position for at least 15 minutes. Brachial and ankle artery pulse waves were recorded by arterial applanation tonometry in the blood pressure cuff wrapping around four extremities. Time delay was measured automatically with the foot-to-foot method, and pulse wave velocity was subsequently calculated. Ankle–brachial pressure index (ABI) was calculated as ankle systolic blood pressure divided by brachial systolic blood pressure.

Statistical analysis

All variables were expressed as mean ± SD. The significance of differences among groups was determined using one-way ANOVA or Kruskal-Wallis H test, as appropriate. Pearson correlation coefficients were used to examine the association between baPWV, BMI, and mean arterial pressure. A significance level of p-value < 0.05 was used to determine statistical significance.

Results

Table 1 presents participant characteristics based on a number of CVD risk factors. Out of the 95 individuals in the study, 33.1% had clustering of CVD risk factors, and 45.3% were free of any defined CVD risk factors. The participants in the single and clustering of CVD risk factors group were older and had a higher BMI than those in the free of CVD risk factors group. In addition, the participants in the cluster group had significantly higher arterial blood pressure than those in the single and none of the CVD risk groups.

The brachial-ankle pulse wave velocity (baPWV) was significantly highest in the group with a clustering of cardiovascular disease (CVD) risk factors (1594 cm/sec^2). This was followed by the group with a single CVD risk factor (1263 cm/sec^2). Participants with no CVD risk factors had the lowest measurement at 1148 cm/sec^2, as shown in figure 1.

Body mass index (Figure 2) and mean arterial pressure (Figure 3) were positively associated with baPWV in the pooled population (r = 0.26, p-value < 0.05 and r = 0.74, p-value < 0.05, respectively).

Table 1 Selected participant characteristics

Variable	Total (n=148)	None (n=67)	Single (n=32)	Cluster (n=49)
Age, years	49.04 ± 15.79 (52)	43.29 ± 15.89 (37)	50.97 ± 17.80* (56)	65.31 ± 6.66* (64)
Body weight, kg	61.04 ± 12.95 (57)	56.36 ± 9.82 (51)	64.56 ± 15.80* (60)	68.12 ± 12.22* (62)
Height, cm	159.69 ± 7.81 (155)	161.26 ± 8.05 (158)	158.78 ± 7.43 (155)	158.37 ± 6.55 (155)
BMI, kg/m^2	23.84 ± 4.22 (22.45)	21.57 ± 2.66 (21.25)	25.68 ± 4.48* (25.23)	25.85 ± 4.33* (24.2)
Heart rate (beats/min)	65 ± 2 (63)	63 ± 2 (61)	65±3 (63)	68 ± 2 (65)
Systolic BP, mmHg	123.84 ± 17.89 (117)	116.57 ± 16.28 (114)	120.03 ± 12.27 (120)	145.38 ±16.90*† (145)
Diastolic BP, mmHg	74.08 ± 9.59 (73)	70.07 ± 9.32 (69)	73.30 ± 7.64 (75)	81.46 ± 6.79*† (80)
Mean BP, mmHg	93.65 ± 13.74 (90)	88.54 ± 12.89 (86)	91.37 ± 9.46 (91)	110.54 ±12.94*† (109)
Pulse pressure, mmHg	49.23 ± 11.66 (45)	45.98 ± 9.58 (44)	46.73 ± 10.15 (44)	63.92 ± 15.98*† (61)
Ankle-brachial index	1.11 ± 0.08 (1.11)	1.10 ± 0.08 (1.11)	1.14 ± 0.07 (1.15)	1.12 ± 0.08 (1.12)
Hypertension, n (%)	35 (21.25)	-	8 (1.56)	27 (19.57)
Diabetes, n (%)	47 (25.19)	-	12 (4.95)	35 (21.29)
Overweight, n (%)	24 (17.39)	-	11 (9.42)	13 (7.97)
Dyslipidemia, n (%)	47 (34.06)	-	14 (8.70)	28 (25.36)

Note: Values are mean ± SD (median). * *p*-value < 0.05 vs. none, † *p*-value < 0.05 vs. single.

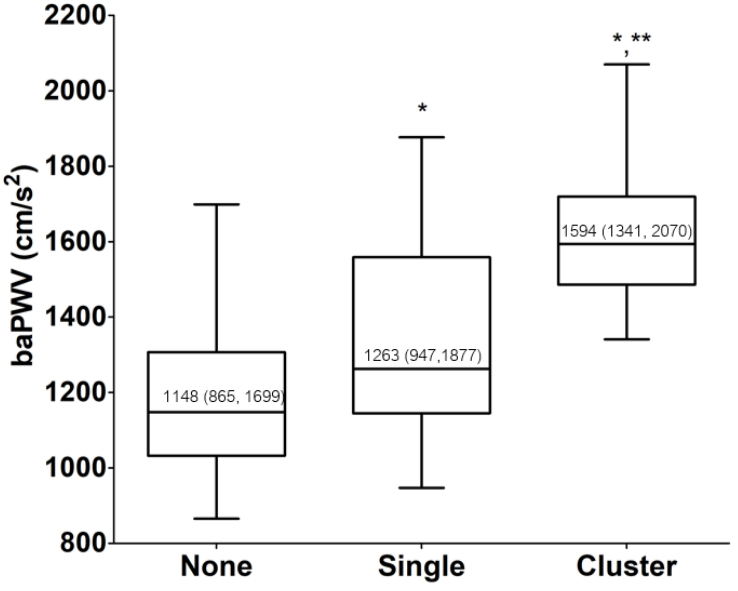

Figure 1 Brachial-ankle pulse wave velocity among none-, single-, and cluster CVD risk factors.
Note: Values are presented using median and interquartile range. * *p*-value < 0.05 vs. none, ***p*-value < 0.05 vs. single

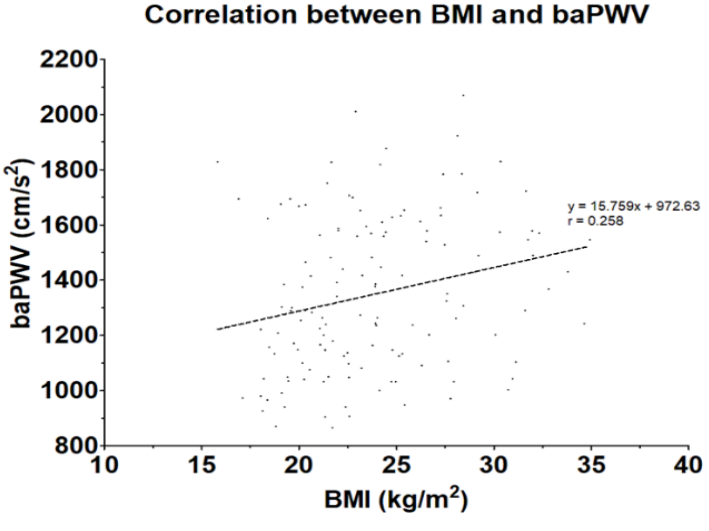

Figure 2 Association between body mass index (BMI) and brachial ankle pulse wave velocity (baPWV).

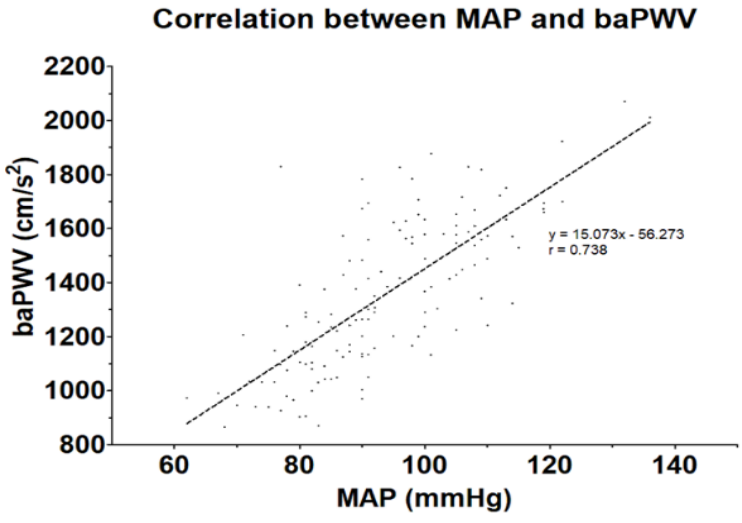

Figure 3 Association between mean arterial pressure (MAP) and brachial ankle pulse wave velocity (baPWV).

Discussion

Our study indicated that the adult population characterized by a cluster of CVD risk factors has the highest arterial stiffness level compared to those with single or no CVD risk factors. The possible mechanisms underlying the relationship between the clustering of CVD risk factors and arterial stiffness remain unclear. Previous studies have reported that diabetes and hypertension contribute additively to increased pulsatility, systolic blood pressure, and aortic pulse wave velocity (PWV)[19,20]. In our study, the leading risk factors in the cluster group were hypertension and diabetes. The explanation may be that high blood pressure and insulin resistance lead to endothelial dysfunction to a greater severity than a single risk factor. Endothelial dysfunction induces structural and functional changes in the arterial wall, resulting in increased arterial stiffness[21].

The cluster risk factor group was older than the single and no-risk factor groups. With advancing age, individuals are more likely to develop multiple health conditions, commonly referred to as multimorbidity[22]. Numerous studies have demonstrated that arterial stiffness increases progressively with age even in healthy individuals. This relationship remains even after adjusting for blood pressure, indicating that aging itself contributes independently to arterial stiffness[23]. This finding was consistent with the results of this study, which showed that baPWV was highest in the group with cluster risk factors.

In addition, the results of this study demonstrated the positive relationship between baPWV and BMI and MAP. This finding aligns with a previous systematic review and meta-analysis study. Overweight and obese adults exhibit significantly greater arterial stiffness compared to healthy-weight controls, even without prevalent cardiovascular disease[24]. Arterial stiffness is associated with hypertension. Baseline blood pressure is associated with a clinically significant progression of arterial stiffness, regardless of age[25].

Arterial stiffness is recognized as a predictor of cardiovascular events and all-cause mortality[26]. Evidence of meta-analysis shows that measuring arterial stiffness provides valuable predictive information for CVD risk, beyond what is indicated by the traditional Framingham Heart Study risk score[10,26]. Aortic PWV and carotid femoral PWV (cfPWV) are considered as the gold standard indices of arterial stiffness[27]. However, it might

be challenging to incorporate measurement of the aortic PWV or cfPWV in routine clinical settings because of the technical difficulties involved in its measurement, special training requirements, and exposure of the inguinal region.

Brachial ankle pulse wave velocity (baPWV) is automatically measured using a separate cuff for each of the four limbs by an oscillometric method[28]. Because of its simplicity and ease of measurement, baPWV may be more easily applied in clinical practice than aortic PWV or cfPWV. A previous study reported that baPWV had closely correlated with the directly measured aortic PWV and cfPWV[29]. The meta-analysis study from 14,673 Japanese participants without a history of CVD reported that measurement of the baPWV could enhance the efficacy of predicting the risk of development of CVD over that of the Framingham risk score, which is based on the traditional cardiovascular risk factors[10]. This study indicated the relationship between baPWV and a cluster of CVD risk factors. This finding highlights the role of arterial stiffness in mediating CVD risk factors, while also providing a valuable reference for informing the design of clinical trials. Thus, the measurement of the baPWV should be encouraged to be applied more broadly in general clinical settings as a tool for CVD risk prediction.

The Physical Therapy Center at Mahidol University has launched a service, focusing on screening for CVD risk using baPWV. We encourage exercise as a lifestyle modification in the population with a high level of baPWV and who have other CVD risks. Aerobic exercise has been proven to be an effective lifestyle modification strategy to improve arterial stiffness and endothelial function[30]. We educate our clients on how to exercise effectively and lifestyle modification strategies to control CVD risk factors and reduce the burden of CVD.

Our study has some limitations that must be monitored. This study used a convenience sample, which could introduce bias. It is a routine-to-research study (R2R) launched between September 2021 and April 2023. All clients who met the inclusion criteria were recruited into the study. We had not calculated the sample size. We were unable to collect the medication information that the participant received. Some medications may affect arterial stiffness. Finally, our study employed a cross-sectional design, which cannot provide insight into the mechanisms underlying the observed association.

Conclusion

The clustering of CVD risk factors, including high blood pressure, elevated cholesterol levels, obesity, and diabetes, has been significantly correlated with increased arterial stiffness.

Take home messages

The arterial stiffness is associated with adverse cardiovascular outcomes, highlighting the importance of effectively addressing these risk factors. Consequently, lifestyle modifications are crucial in mitigating this risk. Individuals exhibiting multiple CVD risk factors should be strongly encouraged to adopt healthier lifestyle changes.

Conflicts of interest

The authors declare no conflict of interest.

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Author contribution

Sarinda Sataman: Conceptualization, Project administration Data Collection, Writing.

Pornsiri Pipatkasira: Conceptualization, Project administration, Data Collection.

Pornpiroon Phuegsilp: Data Collection, Resources.

Benjawan Saelao: Data Collection, Resources.

Thanwalai Pisalayon: Formal analysis.

Nantinee Nualnim: Conceptualization, Formal analysis, Writing – Review & Editing.

Data availability

Data available on request due to privacy/ ethical restrictions

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