



# The Effect of Wrist Circumference on Vascular Stiffening Due to Body Mass Index, Weight, Body Surface Area, and Waist Circumference as Mediators

Noor Mohammad Noori <sup>1</sup>, Maryam Nakhaee Moghadam <sup>1</sup>, Alireza Teimouri <sup>1,\*</sup>

<sup>1</sup> Children and Adolescents Health Research Center, Research Institute of Cellular and Molecular Science in Infectious Diseases, Zahedan University of Medical Science, Zahedan, Iran

\*Corresponding Author: Children and Adolescents Health Research Center, Research Institute of Cellular and Molecular Science in Infectious Diseases, Zahedan University of Medical Science, Zahedan, Iran. Email: [alirezateimouri260@gmail.com](mailto:alirezateimouri260@gmail.com)

Received: 25 February, 2025; Accepted: 26 February, 2025

## Abstract

**Background:** Wrist circumference is emerging as a potential indicator of vascular health, but its relationship with vascular stiffening remains under explored.

**Objectives:** This study investigates the mediating roles of Body Mass Index (BMI), weight, body surface area (BSA), and waist circumference (WC) in the association between Wrist circumference and vascular stiffness.

**Methods:** This cross-sectional study was conducted to examine the mediating effects of BMI, weight, BSA, and WC on the association between wrist circumference and vascular stiffness in children and adolescents aged 5 - 18 years who referred to the pediatric clinics affiliated with Zahedan University of Medical Sciences (ZaUMS) in the years 2022 and 2023. Physical examinations and standardized measurements of wrist circumference, BMI, weight, BSA, and WC were conducted, with vascular stiffness parameters including arterial distensibility, Aortic Stiffness Beta Index, and pressure strain elastic modulus evaluated.

**Results:** The analysis revealed that BMI, weight, BSA, and WC significantly mediated the relationship between wrist circumference and specific vascular stiffness measures, notably for Aortic Stiffness Beta Index and pressure strain elastic modulus. Sobel test results indicated significant mediation effects for BMI, BSA, and WC in both right and left wrist circumferences, though mediation was not significant for arterial strain.

**Conclusions:** The findings underscore the importance of body composition variables in cardiovascular health assessments, suggesting that indirect effects (IDE) of wrist circumference on vascular stiffness can vary by the type of body composition metric and vascular parameter. These insights offer potential pathways for identifying at-risk populations and tailoring cardiovascular interventions based on anthropometric assessments.

**Keywords:** Mediators, Wrist Circumference, Vascular Stiffening, Children

## 1. Background

Cardiovascular disease (CVD) remains a major health burden worldwide, and understanding the factors involved in its development is important for prevention and effective treatment (1). Atherosclerosis, which is a characteristic of CVD, reflects the loss of elasticity of arterial walls and efficiency and is also a predictor of adverse cardiovascular outcomes (2). Among these, waist circumference (WC), an easily measurable human parameter, has received increasing attention as a

potential marker (3-5). However, the mechanism by which WC influences arterial stiffness remains unclear.

Body composition plays an important role in cardiovascular health. The most widely used measure of obesity is Body Mass Index (BMI). However, BMI does not fully capture differences in body composition because it cannot differentiate between muscle mass and fat mass (6). A higher BMI usually reflects increased body fat, which is associated with increased atherosclerosis. Excess adipose tissue can cause systemic inflammation, oxidative stress, and changes in fat metabolism, all of which contribute to arterial stiffness. Therefore, BMI

may mediate the relationship between WC and arterial stiffness, reflecting the distribution of fat in the body and its effect on arterial health (7).

Although weight is a simple measurement, it can also be affected by factors other than body fat, such as muscle mass and bone density (8). Body weight, which is directly linked to the body's total mass and composition, is one of the factors that affect cardiovascular health. Excessive body weight due to fat is a common factor to be considered when checking whether the load applied to the vascular system is excessively high, leading to arterial stiffness. This is not only about the wrist, but it does mean that weight can act as a mediator on the wrist-to-vascular pathway; people with a dystrophic body suffer greater vascular oppression (7).

Body size, as reflected in body surface area (BSA), which takes both height and weight into account, provides a more accurate picture of one's dimensions (9). Body surface area has recently been shown to be a more representative metric of body size by measuring the total BSA rather than just height and weight. It gives an index of body size, which is a function of height and weight. Although BSA is not the main element of fat distribution in comparison to BMI, it can still affect vascular stiffness by the size and metabolic demands of the body. It may be that larger BSA in this population is associated with higher cardiovascular load and therefore, greater vascular stiffening, thus playing an intermediary role (10).

Waist circumference, which is used specifically for abdominal obesity, is said to have the most potent connection with vascular stiffness (11). Waist circumference is a central adiposity index, describing the amount of fat that has accumulated around the abdomen. Central obesity, which is one of the components of metabolic syndrome, the cluster of conditions that increase cardiovascular risk, is closely related to it. The most dangerous part of abdominal fat is the time of accompanying higher levels of excretory products (cytokines) and insulin resistance, which, in turn, make blood vascular stiffening. Therefore, WC could mediate the activity of wrist circumference in regard to vascular stiffening through its degree of central obesity and its associated risks (12).

Wrist circumference, which is a simple, cost-effective, and non-invasive measurement, has recently emerged as a new indicator of heart disease risk (3).

## 2. Objectives

Researchers have revealed that WC, a newly recognized anthropometric parameter, is not an

accurate measure of anxiety, stress, and CVDs such as heart disease and stroke (13). Based on the evidence, we state that BMI, weight, BSA, and WC may be the intermediaries of the wrist circumference and vascular stiffness relationship.

## 3. Methods

### 3.1. Study Design and Participants

This cross-sectional study sought to evaluate the mediating roles of BMI, weight, BSA, and WC on the association between wrist circumference (both right and left) and vascular stiffness. Study participants included children and adolescents from 5 through 18 years of age who referred to the pediatric clinics affiliated with Zahedan University of Medical Sciences (ZAUMS) in the years 2022 and 2023. According to the protocol requirements, subjects to be admitted must be free from any cardiac diseases, diabetes, or other chronic disorders that could directly impact vascular health. Participants on corticosteroids or medications that could theoretically alter vascular stiffness were excluded from the analysis.

### 3.2. Data Collection

Trained health professionals carried out the physical examination and questionnaire surveys for the purpose of data collection. The circumference of the wrist was measured at its thinnest part, using a flexible measuring tape, while the participant had their arms relaxed with their palms facing towards the ceiling. Key anthropometric data were also collected, including BMI, calculated as weight in kilograms divided by height in meters squared ( $\text{kg}/\text{m}^2$ ). Weight was measured using a calibrated digital scale, and BSA was determined using the DuBois formula:  $\text{BSA} = 0.007184 \times (\text{height in cm})^{0.725} \times (\text{weight in kg})^{0.425}$ . Waist circumference was measured at the midpoint between the lowest rib and the top of the iliac crest.

### 3.3. Ethical Considerations

The study was approved by the ethical committee of the Research Deputy, Zahedan University of Medical Sciences, Iran ([IR.ZAUMS.REC.1400.095](https://doi.org/10.21859/IR.ZAUMS.REC.1400.095)).

### 3.4. Statistical Analysis

Statistical analyses were conducted using SPSS software to aid mediation analysis such as Pearson correlation.

### 3.5. Formulas and Measures

Mediation analysis is a statistical method that helps us understand how an independent variable (IV) impacts a dependent variable (DV) through a mediator variable (MV). The MV clarifies the process by which the IV influences the DV. The analysis generally follows these steps and formulas:

(1) Defining the relationships: In a mediation model, the aim is to determine how the MV accounts for the relationship between the IV and the DV. The relationships can be outlined in the following paths:

- Path a: The effect of the IV on the MV.
- Path b: The effect of the MV on the DV, while accounting for the IV.
- Path c: The total effect (TE) of the IV on the DV.
- Path c': The direct effect (DE) of the IV on the DV, while controlling for the MV.

(2) Formulas and calculation:

- Total effect (c): The TE represents the overall impact of the IV on the DV, without considering the mediator.  $c = \text{Effect of IV on DV}$

- Direct effect (c'): The DE is the effect of the IV on the DV when accounting for the mediator.  $c' = \text{Effect of IV on DV (controlling for MV)}$

- Indirect effect ( $a \times b$ ): The indirect effect (IDE) represents the portion of the IV-DV relationship that is explained by the mediator. It is the product of the effect of the IV on the MV (path a) and the effect of the MV on the DV (path b).  $\text{IDE} = a \times b$

- Mediation effect: Mediation effect is quantified as the difference between the TE and the DE.  $\text{Mediation effect} = c - c'$

(3) Statistical testing: To determine whether the mediation effect is statistically significant, several methods can be used:

- Sobel test: This test assesses whether the IDE ( $a \times b$ ) is significantly different from zero. The Sobel test formula is:  $Z = \frac{a \times b}{\sqrt{(b^2 \times \sigma a^2) + (a^2 \times \sigma b^2)}}$

- Correlation analysis: Pearson correlation coefficients were computed to explore the bivariate relationships between wrist circumference, vascular stiffness, and mediating variables. This preliminary analysis helped establish the associations necessary for subsequent mediation analysis.

- Mediation analysis: Mediation analysis was employed to explore how BMI, weight, BSA, and WC mediate the relationship between wrist circumference and vascular stiffness. The analysis was conducted using

the Sobel test to assess the significance of the IDEs. The following steps were performed:

- Step 1: Regressed vascular stiffness on wrist circumference to determine the TE.
- Step 2: Regressed each mediator (BMI, weight, BSA, WC) on wrist circumference to assess the effect of wrist circumference on the mediator (path a).
- Step 3: Regressed vascular stiffness on the mediators while controlling for wrist circumference to estimate the DE and the effect of the mediators on vascular stiffness (path b).
- Step 4: Calculated the IDE as the product of paths a and b ( $a \times b$ ). The significance of the IDEs was evaluated using the Sobel test and bootstrapping to provide confidence intervals (14).

## 4. Results

This section presents the findings from the mediation analyses exploring the relationships between wrist circumference and vascular stiffness parameters, specifically examining the roles of BMI, Weight, BSA, and WC. The results highlight significant mediation effects across various vascular stiffness metrics for both left and right wrist circumferences.

**Table 1** summarizes the findings from the mediation analysis involving BMI. For the left WC, significant results include: Arterial Distensibility, with a TE of 0.00038, yielding a Sobel value of -2.564 and a P-value of 0.010, which indicates a notable IDE. The Aortic Stiffness Beta Index showed an IDE of 0.855, with a Sobel value of 2.205 and a P-value of 0.027, suggesting significant mediation. Additionally, the pressure strain elastic modulus had a TE of -11.407, a Sobel value of 2.252, and a P-value of 0.024, highlighting a significant mediation effect. In the right WC analysis, arterial distensibility demonstrated a TE of -0.00004, with a significant Sobel value of -2.896 and a P-value of 0.004, indicating strong mediation. The Aortic Stiffness Beta Index exhibited an IDE of 1.14, accompanied by a Sobel value of 2.388 and a P-value of 0.017, suggesting significant mediation. Lastly, the pressure strain elastic modulus reflected an IDE of 10.7199, with a Sobel value of 2.396 and a P-value of 0.017, confirming significant mediation.

**Table 2** presents the findings from the mediation analysis involving Weight. For the Left WC, significant results include: Arterial distensibility, with a TE of 0.00038, yielding a Sobel value of -2.726 and a P-value of 0.006, indicating a notable mediation effect. The Aortic Stiffness Beta Index showed an IDE of 0.898, with a Sobel value of 2.153 and a P-value of 0.031, suggesting significant mediation. Additionally, the pressure strain

**Table 1.** Body Mass Index Mediation on the Relationship Between Left and Right Wrist Circumference on Vascular Stiffness Parameters

Dependent and IVs	TE	DE	IDE	$\alpha$	$\sigma_{\alpha}$	$\beta$	$\sigma_{\beta}$	Sobel Value	P-Value
<b>Left WC</b>									
Arterial strain	0.415	0.599	-0.184	1.221	0.339	-0.151	-0.147	-0.987823	0.3232394
Arterial distensibility	0.00038	-0.00023	0.00061	1.221	0.339	-0.000157	0.000043	-2.564121	0.0103438
Aortic Stiffness Beta Index	-1.308	-2.163	0.855	1.221	0.339	0.7	0.251	2.2050937	0.0274475
Pressure strain elastic modulus	-11.407	-19.664	8.257	1.221	0.339	6.764333	2.343369	2.2524663	0.0242928
<b>Right WC</b>									
Arterial strain	0.282	0.531	-0.249	1.595	0.333	-0.156355	0.090203	-1.62992	0.1031182
Arterial distensibility	-0.00004	0.000216	-0.00026	1.595	0.333	-0.00016	0.000044	-2.89626	0.0037763
Aortic Stiffness Beta Index	-0.7294	-1.8694	1.14	1.595	0.333	0.714912	0.259375	2.3889775	0.0168953
Pressure strain elastic modulus	-4.1791	-14.899	10.7199	1.595	0.333	6.722983	2.429738	2.39592	0.0165789

Abbreviations: WC, waist circumference; IV, independent variable, TE, total effect; DE, indirect effects; IDE, indirect effects.

elastic modulus exhibited a TE of -11.407, a Sobel value of 2.310, and a P-value of 0.021, highlighting a significant mediation effect. In the right WC analysis, arterial distensibility demonstrated a TE of -0.00004, with a significant Sobel value of -2.958 and a P-value of 0.003, indicating strong mediation. The Aortic Stiffness Beta Index exhibited an IDE of 1.09, accompanied by a Sobel value of 2.207 and a P-value of 0.027, suggesting significant mediation. Lastly, the pressure strain elastic modulus reflected an IDE of 10.879, with a Sobel value of 2.326 and a P-value of 0.020, confirming significant mediation.

Table 3 highlights the key findings from the mediation analysis involving BSA. For the Left WC, significant results include: Arterial distensibility, with a TE of 0.00038, resulting in a Sobel value of -2.249 and a P-value of 0.025, indicating a notable mediation effect. The Aortic Stiffness Beta Index showed an IDE of 0.8645, with a Sobel value of 2.158 and a P-value of 0.031, suggesting significant mediation. Additionally, the pressure strain elastic modulus had a TE of -11.407, a Sobel value of 2.305, and a P-value of 0.021, highlighting a significant mediation effect. In the right WC analysis, arterial distensibility demonstrated a TE of -0.00004, with a significant Sobel value of -2.392 and a P-value of 0.017, indicating strong mediation. The Aortic Stiffness Beta Index exhibited an IDE of 1.05418, accompanied by a Sobel value of 2.215 and a P-value of 0.027, suggesting significant mediation. Finally, the pressure strain elastic modulus reflected an IDE of 10.5875, with a Sobel value of 2.343 and a P-value of 0.019, confirming significant mediation.

Table 4 presents the key findings from the mediation analysis involving WC. For the Left WC, significant results include the Aortic Stiffness Beta Index, which exhibited an IDE of 0.984, accompanied by a Sobel value

of 2.396 and a P-value of 0.017, indicating a notable mediation effect. Additionally, the pressure strain elastic modulus showed a TE of -11.407, with a Sobel value of 2.419 and a P-value of 0.016, highlighting a significant mediation effect. In the Right WC analysis, arterial distensibility demonstrated a TE of -0.00004, with a significant Sobel value of -2.697 and a P-value of 0.007, indicating strong mediation. The Aortic Stiffness Beta Index exhibited an IDE of 1.2816, with a Sobel value of 2.609 and a P-value of 0.009, suggesting significant mediation. Finally, the pressure strain elastic modulus reflected an IDE of 11.8669, with a Sobel value of 2.594 and a P-value of 0.009, confirming significant mediation.

## 5. Discussion

Vascular stiffness, commonly assessed by pulse wave velocity (PWV), refers to increased systemic membrane rigidity, which is also known as the indices of arterial strain, arterial distensibility, Aortic Stiffness Beta Index, and pressure strain elasticity modulus (15). It is highly predictive of heart attack and stroke (1, 16, 17). The primary purpose of the present study was to find the useful mediators in the connection between wrist circumference and vascular stiffness. Body Mass Index, BSA, weight, and WC were the parameters that showed a mediating effect in this association, although there were only slight differences in their effects, as the results showed. Recently, the anthropometric features of vascular stiffness have been proposed as a phenotype to vascular stiffness in the latest studies (15, 18). Nevertheless, this relationship is only probably intervened by other anthropometric methods that need to be cogitated to grasp the rooted mechanisms correctly.

**Table 2.** Weight Mediation on the Relationship Between Left and Right Wrist Circumference on Vascular Stiffness Parameters

Dependent and IVs	TE	DE	IDE	$\alpha$	$\sigma_\alpha$	$\beta$	$\sigma_\beta$	Sobel Value	P-Value
<b>Left WC</b>									
Arterial strain	0.415	0.577	-0.162	4.63	1.116	-0.035	0.027	-1.2373047	0.215974
Arterial distensibility	0.00038	0.000251	0.000129	4.63	1.116	-0.000047	0.000013	-2.7256568	0.0064174
Aortic Stiffness Beta Index	-1.308	-2.206	0.898	4.63	1.116	0.194	0.077	2.1534825	0.0312808
Pressure strain elastic modulus	-11.407	-20.604	9.197	4.63	1.116	1.986	0.714	2.3103199	0.0208705
<b>Right WC</b>									
Arterial strain	0.282	0.479	-0.197	5.646	1.098	-0.035	0.027	-1.2569698	0.2087646
Arterial distensibility	-0.00004	0.000226	-0.00027	5.646	1.098	-0.000047	0.000013	-2.9575274	0.0031012
Aortic Stiffness Beta Index	-0.7294	-1.82	1.09	5.646	1.098	0.193	0.079	2.2066495	0.0273386
Pressure strain elastic modulus	-4.1791	-15.058	10.879	5.646	1.098	1.927	0.739	2.3256406	0.0200377

Abbreviations: WC, waist circumference; IV, independent variable, TE, total effect; DE, indirect effects; IDE, indirect effects.

**Table 3.** Body Surface Area Mediation on the Relationship Between Left and Right Wrist Circumference on Vascular Stiffness Parameters

Dependent and IVs	TE	DE	IDE	$\alpha$	$\sigma_\alpha$	$\beta$	$\sigma_\beta$	Sobel Value	P-Value
<b>Left WC</b>									
Arterial strain	0.415	0.564	-0.149	0.074	0.019	-2.025591	1.581	-1.21704901	0.22358557
Arterial distensibility	0.00038	0.000238	0.000142	0.074	0.019	-0.002755	0.001	-2.24917441	0.0245014
Aortic Stiffness Beta Index	-1.308	-2.1725	0.8645	0.074	0.019	11.745536	4.531655	2.15775671	0.03094675
Pressure strain elastic modulus	-11.407	-20.296	8.889	0.074	0.019	120.82388	42.246351	2.30521992	0.02115426
<b>Right WC</b>									
Arterial strain	0.282	0.463329	-0.181329	0.09	0.019	-2.014798	1.624504	-1.19980907	0.2302135
Arterial distensibility	-0.00004	0.00021	-0.00025	0.09	0.019	-0.002772	0.001	-2.39244908	0.01673635
Aortic Stiffness Beta Index	-0.7294	-1.78358	1.05418	0.09	0.019	11.699928	4.668196	2.21532026	0.02673809
Pressure strain elastic modulus	-4.1791	-14.7666	10.5875	0.09	0.019	117.512	43.5988	2.34261705	0.01914903

Abbreviations: WC, waist circumference; IV, independent variable, TE, total effect; DE, indirect effects; IDE, indirect effects.

The measurement of wrist circumference becomes a promising rough proxy in cardiovascular studies because this feature is correlated with the variability of both lean mass and fat mass. It is a lot easier to be measured and less susceptible to short-term weight changes than new techniques, such as WC (19). On the other hand, the pure connection between the wrist circumference and vascular stiffness is not an easy case; hence it is plausible that wrist circumference would be more of a marker than a direct cause of vascular stiffness increment (4).

The cutoff point was that the BMI factor was a mediator in the relationship between wrist circumference and various vascular stiffness parameters. The significant mediation effects were found for arterial distensibility, Aortic Stiffness Beta Index, and pressure-strain elastic modulus for both left and right wrist circumference. In particular, these results indicated the importance of BMI in the

explanations of how wrist circumference influenced these vascular parameters, thus emphasizing the role of body composition in the cardiovascular evaluation. Increased BMI appears to be a cardiovascular risk factor, including hypertension, dyslipidemia, and diabetes, driving the active center (15) effect resulting in vascular stiffness. Several studies have demonstrated that people who have larger wrist circumference also have a higher BMI, which hints that the BMI might be the factor that links the wrist circumference to vascular stiffness. The reason for all of these observations would be, of course, the fact that having a thicker wrist would be associated with increased obesity (20), and, further, inflammation and fat build-up, which are both mechanisms leading to vascular stiffness (15). Thus, BMI could be a link between obesity and vascular stiffness, as obesity allows the endothelium to be damaged, a major player that has been oftentimes defined as the key to vascular stiffness. Higher BMI is associated with more fatty tissue, which

**Table 4.** Waist Circumference Mediation on the Relationship Between Left and Right Wrist Circumference on Vascular Stiffness Parameters

Dependent and IVs	TE	DE	IDE	$\alpha$	$\sigma_{\alpha}$	$\beta$	$\sigma_{\beta}$	Sobel Value	P-Value
<b>Left WC</b>									
Arterial strain	0.415	0.535	-0.12	3.65	0.995	-0.033	0.03	-1.05364863	0.29204382
Arterial distensibility	0.00038	0.000213	0.000167	3.65	0.995	0.0000048	0.000015	0.31878937	0.74988624
Aortic Stiffness Beta Index	-1.308	-2.292	0.984	3.65	0.995	0.269	0.085	2.39622292	0.01656501
Pressure strain elastic modulus	-11.407	-20.737	9.33	3.65	0.995	2.554	0.794	2.41852527	0.01558356
<b>Right WC</b>									
Arterial strain	0.282	0.438	-0.156	4.674	0.978	-0.0334	0.031	-1.05104124	0.29323965
Arterial distensibility	-0.00004	0.000189	-0.000229	4.674	0.978	-0.000049	0.000015	-2.69686391	0.00699959
Aortic Stiffness Beta Index	-0.7294	-2.011	1.2816	4.674	0.978	0.274	0.088	2.60881249	0.0090857
Pressure strain elastic modulus	-4.1791	-16.046	11.8669	4.674	0.978	2.539	0.822	2.5941562	0.00948234

Abbreviations: WC, waist circumference; IV, independent variable; TE, total effect; DE, indirect effects; IDE, indirect effects.

may result in inflammation that is recurrent in a human's body and endothelial dysfunction, which is the second main area of exercise. Adipose tissue is the richest deposit of one of the key inflammatory cytokines, namely, TNF-alpha and IL-6, which are capable of destroying the elastic fibers in the arterial wall, thereby causing stiffness (21, 22). Besides, the accumulation of visceral fat, that is measured in BMI, has been particularly associated with the stiffening of the blood vessels, and it is implicitly BMI that takes on the role of a mediator in this association (23).

The analysis focused on the weight indicated that it was a factor that mediated the relationship between the wrist circumference and the parameters of the vascular stiffness. Significant mediation effects were shown for arterial distensibility, Aortic Stiffness Beta Index, and pressure-strain elastic modulus for left and right wrist circumference. Thus, the results confirmed the hypothesis that weight is a major determining factor in mediating wrist circumference and vascular stiffness, which emphasizes the importance of body weight as part of the cardiovascular health evaluation. Body weight is a fundamental measure closely related to BMI but provides additional insights when it is considered independently. While BMI provides a normalized weight for height, the actual body weight might additionally contribute to the vascular stiffness through the hemodynamic factors (24). Increased body weight might bring about higher blood pressure, which in turn subjects the arteries to a greater level of tension, thus making them stiffer. Hence, the wrist circumference may, through its effect on the body weight, influence the vascular stiffness. Larger wrist circumference is related to higher body weight, which is one of the factors that may account for increased vascular stiffness in that respect (25, 26). The relationship between body weight (weight gain) and body shape (vascular stiffness) can be

both direct and indirect. The direct way is that undesirable weight down the cardiovascular system, thus increasing blood pressure and higher vascular stiffness. Among other mediators, the weight might indirectly impact the results of the BMI and WC, which are themselves the variables that are associated with vascular stiffness. Therefore, when scrutinizing the mediating role of weight, it is mandatory to take weight's main effect on stiffness and its interaction with other offsets into account (26, 27).

The analysis during mediation showed that BSA played a role in mediating the connection between wrist size and various measures of stiffness like arterial distensibility and Aortic Stiffness Beta Index along with pressure strain elastic modulus. The impact of BSA on stiffness was evident in relation to both left and right wrist sizes; however, it did not show an effect on arterial strain in either wrist size. This discovery highlights the significance of taking BSA into account during health assessments as it plays a role in moderating the impact of wrist circumference on vascular stiffness levels. Body surface area is a metric used to estimate the surface area of the body and is commonly utilized in medical contexts for determining medication dosages and evaluating heart function. It differs from BMI in that it factors in height and weight to offer an evaluation of body size with a focus on cardiovascular results. The connection between BSA and vascular rigidity could be influenced by factors like blood volume and heart output, both of which are impacted by BSA itself. Wider wrist size might be associated with a larger BSA, consequently impacting vascular stiffness indirectly. Body surface area could play a role in how wrist size affects stiffness through its impact on these factors. A higher BSA is linked to increased blood volume, which could raise blood pressure levels and contribute to increased rigidity.

In addition to this, BSA is connected with the overall size of the body and thus variable metabolic activity, which might affect vascular health. Body surface area could act as the medium for the proportion of wrist circumference to vascular stiffness by capturing information on body size and functioning, which BMI and weight alone do not associate with.

Mediation analysis confirmed the role of WC as a powerful mediator between wrist circumference and several indices of vascular stiffness, including the Aortic Stiffness beta index, arterial distensibility, and pressure-strain elastic modulus. Both aortic stiffness and pressure-strain elastic modulus showed evidence for significant mediation. Interestingly, there was no sufficient effect of WC on arterial strain and arterial distensibility with respect to either left or right wrist circumference, suggesting that WC's effects could be limited to these vascular parameters. This emphasizes the necessity to incorporate WC in the evaluation of cardiovascular health due to its effect on certain measures of vascular stiffness. Waist circumference is a well-established measure of central obesity, which is closely linked to cardiovascular risk factors and outcomes. Unlike BMI, which provides a general estimate of body fat, WC specifically reflects abdominal fat, which is metabolically active and strongly associated with vascular stiffness (19). Larger wrist circumference could indicate a larger WC that might give rise to vascular stiffness via its effect on central obesity (28). Central obesity, as measured by WC, is more significantly negative concerning vascular health, as visceral fat stimulates inflammation, insulin resistance, and dyslipidemia. These processes, in turn, advance stiffening of the arterial walls (29). The central obesity measure could act as an intermediate factor between wrist circumference and vascular stiffness through its representation of central fat amount that affects vascular function. This mediation pathway underlines the need to study fat distribution along with body size when vascular stiffness is being examined (30).

We expect that BMI, weight, BSA, and WC will mediate the relationship between wrist circumference and vascular stiffness. We conjecture that a smaller circumference of the wrist is associated with more body fat within the torso region, which in turn stiffens the arterial wall (28).

### 5.1. Novelty and Contribution

The most important new insight that this study offers is a more advanced understanding of how different body composition metrics mediate the association between wrist circumference and vascular

stiffness in children. Through mediation analysis, using various statistical methods, it provides an analysis of how body composition influences vascular health. These insights can be integrated into the establishment of solid cardiovascular risk factors and more targeted and effective interventions to prevent and manage vascular stiffness. This approach may warrant improved clinical practices and public health strategies for the prevention of cardiovascular risk through personalized body composition management.

### 5.2. Limitations and Considerations

The aforementioned BMI, BSA, Weight, and WC were all separately included with other confounding factors that may still influence the relationship between wrist circumference and vascular stiffness. The sample size used in the analysis may serve to highlight the point that as sample size increases, the generalizability of the findings increases too. The mediation analysis does not establish causation; it shows the interactions that BMI and other body composition metrics have within the relationship between wrist circumference and vascular stiffness.

### 5.3. Conclusions

This study concluded that BMI, weight, BSA, and WC mediate the relationship between wrist circumference and vascular stiffness parameters (arterial distensibility, Aortic Stiffness Beta Index, pressure strain, and elastic modulus). These findings underscore the importance of comprehensive cardiovascular assessment, which includes BMI, WC, and BSA. Longitudinal studies are essential for understanding causal relations and mediation dynamics over time. Effect mediators may change according to age, gender, and ethnicity, which would further justify formulating interventions for each specific population.

## Acknowledgements

We would like to extend our deepest gratitude to all individuals and institutions who supported this research. Special thanks are owed to our colleagues and collaborators who contributed their valuable insights and feedback throughout the study.

## Footnotes

**Authors' Contribution:** N. M. N., M. N. M., and A. T. were jointly responsible for conceptualizing the research project and designing the study methodology.

N. M. N. conducted the primary data collection and analysis, while A. T. contributed to the statistical analysis and interpretation of the results. M. N. M. was responsible for reviewing the literature and data collection. All authors played a significant role in drafting the manuscript and provided critical revisions for intellectual content. All authors have reviewed and approved the final version of the manuscript for submission.

**Conflict of Interests Statement:** The authors declare that there are no conflicts of interest regarding the publication of this study. All authors affirm that they have no affiliations, financial interests, or competing personal relationships that could influence the outcome or interpretation of the research.

**Data Availability:** The dataset presented in the study is available on request from the corresponding author during submission or after publication. The data are not publicly available due to being part of a larger database.

**Ethical Approval:** The study was approved by the ethical committee of the Research Deputy, Zahedan University of Medical Sciences, Iran (IR.ZAUMS.REC.1400.095).

**Funding/Support:** This research was not supported by any grant, academic institution, or research council.

**Informed Consent:** Written informed consent was obtained from all participants.

## References

- Noori NM, Mahjoubifard M, Shahramian I, Teimouri A, Jahangirifard A. Comparison between procalcitonin, brain natriuretic peptide, and uric acid in children with cardiomyopathy and controls. *Biomed Res Int.* 2015;2015:510450. [PubMed ID: 26495299]. [PubMed Central ID: PMC4606136]. <https://doi.org/10.1155/2015/510450>.
- Kim HL, Ahn DW, Kim SH, Lee DS, Yoon SH, Zo JH, et al. Association between body fat parameters and arterial stiffness. *Sci Rep.* 2021;11(1):20536. [PubMed ID: 34654852]. [PubMed Central ID: PMC8519992]. <https://doi.org/10.1038/s41598-021-00175-z>.
- Namazi N, Djalalinia S, Mahdavi-Gorabi A, Asayesh H, Mansourian M, Noroozi M, et al. Association of wrist circumference with cardio-metabolic risk factors: a systematic review and meta-analysis. *Eat Weight Disord.* 2020;25(1):151-61. [PubMed ID: 29971623]. <https://doi.org/10.1007/s40519-018-0534-x>.
- Mohebi R, Mohebi A, Sheikholeslami F, Azizi F, Hadaegh F. Wrist circumference as a novel predictor of hypertension and cardiovascular disease: results of a decade follow up in a West Asian cohort. *J Am Soc Hypertens.* 2014;8(11):800-7. [PubMed ID: 25455005]. <https://doi.org/10.1016/j.jash.2014.08.010>.
- Amini A, Soltanian N, Iraj B, Askari G, Ebneyamin S, Ghias M, et al. Association of wrist circumference with cardio metabolic risk factors. *J Pak Med Assoc.* 2012;62(3 Suppl 2):S34-6. [PubMed ID: 22768455].
- Neeland IJ, Yokoo T, Leinhard OD, Lavie CJ. 21st Century Advances in Multimodality Imaging of Obesity for Care of the Cardiovascular Patient. *JACC Cardiovasc Imaging.* 2021;14(2):482-94. [PubMed ID: 32305476]. [PubMed Central ID: PMC7554055]. <https://doi.org/10.1016/j.jcmg.2020.02.031>.
- Piko N, Bevc S, Hojs R, Petreski T, Ekart R. Higher Body Mass Index is associated with increased arterial stiffness prior to target organ damage: a cross-sectional cohort study. *BMC Cardiovasc Disord.* 2023;23(1):460. [PubMed ID: 37710152]. [PubMed Central ID: PMC10503091]. <https://doi.org/10.1186/s12872-023-03503-5>.
- Carson JS, Khosrozadeh H, Norbury WB, Herndon DN. Nutritional Needs and Support for the Burned Patient. In: Herndon D, Sood R, editors. *Total Burn Care.* Amsterdam, Netherlands: Elsevier Health Sciences; 2018. p. 287-300.e2. <https://doi.org/10.1016/b978-0-323-47661-4.00028-9>.
- Palmu S, Kuneinen S, Kautiainen H, Eriksson JG, Korhonen PE. Body surface area may explain sex differences in findings from the oral glucose tolerance test among subjects with normal glucose tolerance. *Nutr Metab Cardiovasc Dis.* 2021;31(9):2678-84. [PubMed ID: 34218989]. <https://doi.org/10.1016/j.numecd.2021.05.018>.
- Looney DP, Potter AW, Arcidiacono DM, Santee WR, Friedl KE. Body surface area equations for physically active men and women. *Am J Hum Biol.* 2023;35(2). e23823. [PubMed ID: 36285812]. <https://doi.org/10.1002/ajhb.23823>.
- Bojanic D, Ljubojevic M, Krivokapic D, Gontarev S. Waist circumference, waist-to-hip ratio, and waist-to-height ratio reference percentiles for abdominal obesity among Macedonian adolescents. *Nutr Hosp.* 2020;37(4):786-93. [PubMed ID: 32686451]. <https://doi.org/10.20960/nh.03006>.
- Ross R, Neeland IJ, Yamashita S, Shai I, Seidell J, Magni P, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. *Nat Rev Endocrinol.* 2020;16(3):177-89. [PubMed ID: 32020062]. [PubMed Central ID: PMC7027970]. <https://doi.org/10.1038/s41574-019-0310-7>.
- Hajsadeghi S, Firouzi A, Bahadoran P, Hassanzadeh M. The value of wrist circumference for predicting the presence of coronary artery disease and metabolic syndrome. *Indian Heart J.* 2016;68 Suppl 3(Suppl 3):S5-9. [PubMed ID: 28038723]. [PubMed Central ID: PMC5198876]. <https://doi.org/10.1016/j.ihj.2016.10.011>.
- Kumar A, Yadav US, Mandal M, Yadav SK. Impact of Corporate Innovation, Technological Innovation and ESG on Environmental Performance: Moderation Test of Entrepreneurial Orientation and Technological Innovation as Mediator Using Sobel Test. *Int J Sustainable Dev Plann.* 2024;19(7):2635-50. <https://doi.org/10.18280/ijdsdp.190720>.
- Noori NM, Nakhaei-Moghadam M, Teimouri A. Assessment of aortic elasticity parameters in obese and overweight children. *Turk J Pediatr.* 2023;65(1):46-53. [PubMed ID: 36866984]. <https://doi.org/10.24953/turkjped.2020.3365>.
- Noori NM, Teimouri A, Keshavarz K, Moradi M. Assessment of Aortic Elasticity and the Doppler Tissue Echocardiography in Thalassemia Major Children. *J Child Sci.* 2020;10(1):e63-73. <https://doi.org/10.1055/s-0040-1713595>.
- Bonarjee VVS. Arterial Stiffness: A Prognostic Marker in Coronary Heart Disease. Available Methods and Clinical Application. *Front Cardiovasc Med.* 2018;5:64. [PubMed ID: 29951487]. [PubMed Central ID: PMC6008540]. <https://doi.org/10.3389/fcvm.2018.00064>.
- Sobhani S, Vakili S, Javid Jam D, Aryan R, Khadem-Rezaian M, Eslami S, et al. Relationship between anthropometric indices and arterial stiffness: Insights from an epidemiologic study. *Obes Sci Pract.* 2022;8(4):494-9. [PubMed ID: 35949287]. [PubMed Central ID: PMC9358735]. <https://doi.org/10.1002/osp4.582>.



19. Suwala S, Junik R. Body Mass Index and Waist Circumference as Predictors of Above-Average Increased Cardiovascular Risk Assessed by the SCORE2 and SCORE2-OP Calculators and the Proposition of New Optimal Cut-Off Values: Cross-Sectional Single-Center Study. *J Clin Med*. 2024;**13**(7). [PubMed ID: 38610696]. [PubMed Central ID: PMC11012561]. <https://doi.org/10.3390/jcm13071931>.
20. Pereira LMC, Souza MFC, Aida F, Getirana-Mota M, Santos-Junior AMD, Filho M, et al. Wrist Circumference Cutoff Points for Determining Excess Weight Levels and Predicting Cardiometabolic Risk in Adults. *Int J Environ Res Public Health*. 2024;**21**(5). [PubMed ID: 38791764]. [PubMed Central ID: PMC1120788]. <https://doi.org/10.3390/ijerph21050549>.
21. Kwaifa IK, Bahari H, Yong YK, Noor SM. Endothelial Dysfunction in Obesity-Induced Inflammation: Molecular Mechanisms and Clinical Implications. *Biomolecules*. 2020;**10**(2). [PubMed ID: 32069832]. [PubMed Central ID: PMC7072669]. <https://doi.org/10.3390/biom10020291>.
22. Aroor AR, Jia G, Sowers JR. Cellular mechanisms underlying obesity-induced arterial stiffness. *Am J Physiol Regul Integr Comp Physiol*. 2018;**314**(3):R387-98. [PubMed ID: 29167167]. [PubMed Central ID: PMC5899249]. <https://doi.org/10.1152/ajpregu.00235.2016>.
23. Mao J, Gan S, Gong S, Zhou Q, Yu F, Zhou H, et al. Visceral fat area is more strongly associated with arterial stiffness than abdominal subcutaneous fat area in Chinese patients with type 2 diabetes. *Diabetol Metab Syndr*. 2024;**16**(1):123. [PubMed ID: 38840161]. [PubMed Central ID: PMC1151495]. <https://doi.org/10.1186/s13098-024-01356-2>.
24. Cooper JN, Buchanich JM, Youk A, Brooks MM, Barinas-Mitchell E, Conroy MB, et al. Reductions in arterial stiffness with weight loss in overweight and obese young adults: potential mechanisms. *Atherosclerosis*. 2012;**223**(2):485-90. [PubMed ID: 22703865]. [PubMed Central ID: PMC3411893]. <https://doi.org/10.1016/j.atherosclerosis.2012.05.022>.
25. Orr JS, Gentile CL, Davy BM, Davy KP. Large artery stiffening with weight gain in humans: role of visceral fat accumulation. *Hypertension*. 2008;**51**(6):1519-24. [PubMed ID: 18458161]. [PubMed Central ID: PMC2614391]. <https://doi.org/10.1161/HYPERTENSIONAHA.108.112946>.
26. Stanek A, Grygiel-Gorniak B, Brozyna-Tkaczyk K, Myslinski W, Cholewka A, Zolghadri S. The Influence of Dietary Interventions on Arterial Stiffness in Overweight and Obese Subjects. *Nutrients*. 2023;**15**(6). [PubMed ID: 36986170]. [PubMed Central ID: PMC10058695]. <https://doi.org/10.3390/nu15061440>.
27. Fernandes-Silva MM, Shah AM, Claggett B, Cheng S, Tanaka H, Silvestre OM, et al. Adiposity, body composition and ventricular-arterial stiffness in the elderly: the Atherosclerosis Risk in Communities Study. *Eur J Heart Fail*. 2018;**20**(8):1191-201. [PubMed ID: 29663586]. [PubMed Central ID: PMC6685543]. <https://doi.org/10.1002/ehf.1188>.
28. Mousapour P, Barzin M, Valizadeh M, Mahdavi M, Hadaegh F, Azizi F, et al. Wrist circumference as a novel predictor of transition from metabolically healthy to unhealthy phenotype in overweight/obese adults: a gender-stratified 15.5-year follow-up. *BMC Public Health*. 2021;**21**(1):2276. [PubMed ID: 34903195]. [PubMed Central ID: PMC8670068]. <https://doi.org/10.1186/s12889-021-12371-7>.
29. Dhawan D, Sharma S. Abdominal Obesity, Adipokines and Non-communicable Diseases. *J Steroid Biochem Mol Biol*. 2020;**203**:105737. [PubMed ID: 32818561]. [PubMed Central ID: PMC7431389]. <https://doi.org/10.1016/j.jsbmb.2020.105737>.
30. Guimaraes Filho GC, Silva LT, Silva R. Correlation among Waist Circumference and Central Measures of Blood Pressure. *Arq Bras Cardiol*. 2022;**119**(2):257-64. [PubMed ID: 35674568]. [PubMed Central ID: PMC9363063]. <https://doi.org/10.36660/abc.20210432>.