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Short-Communication

Effect of curcumin on pulse wave velocity: a randomized double-blind placebo-controlled trial

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Abstract

Objective: Curcumin has anti-inflammatory and antioxidant activities. To date, no study has been conducted to assess the effect of curcumin on Pulse Wave Velocity (PWV) in individuals with increased arterial stiffness.

Materials and methods: The current study was a randomized double-blind trial conducted on a subset of the Persian Cohort study in Mashhad University of Medical Sciences, Mashhad, Iran. The individuals were restricted to subjects with PWV values in the highest quartile of the distribution. Volunteers were randomly assigned to either the curcumin (500 mg/day) treatment group or the placebo group. PWV was measured before and eight weeks after the intervention.

Results: There were no differences between the groups in PWV, aortic augmentation index, aortic pulse pressure, or aortic blood pressure after the intervention ($p>0.05$). Moreover, analysis of potential confounders showed no significant effects on changes in PWV ($p=0.958$).

Conclusion: The results revealed that eight weeks of curcumin supplementation did not exert significant improvements in arterial stiffness or central hemodynamics indices.

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Introduction

Cardiovascular diseases (CVD) are the main cause of death in many societies (Castellano et al. 2014). Several cardiovascular risk factors contribute to arterial stiffness and increased pulse wave velocity (PWV) (O'Rourke et al. 2016). Vascular stiffness is the primary indicator of structural and functional changes in the vessel wall (Mozos et al. 2017). It refers to decreased ability of an artery to expand and contract in response to changes in pressure (Cecelja and Chowienczyk 2012). Vascular aging is strongly associated with the reduction and fragmentation of elastin as well as the deposition of collagen, and the imbalance between these two leads to an increase in the stiffness of the vessel wall (Shirwany and Zou 2010).

The PWV is widely used index for assessing arterial damage and endothelial dysfunction (Vasan 2025). Owing to its low cost, high reproducibility and easy measurement, the PWV is considered the gold standard for non-invasive assessment of aortic stiffness (Van Bortel et al. 2012). Clinically, the PWV is used as a measure of arterial stiffness, which describes the flexibility, compliance, and elastic modulus of the arterial wall. Genetic factors, structural changes in the arterial wall and endothelial function can influence arterial stiffness, which is reflected as increased PWV (Pirro et al. 2007; Pirro et al. 2004). While gender does not affect the PWV, with each decade of life, the PWV value increases by 6-8%, and this trend becomes more obvious after the age of 50 (Díaz et al. 2014).

A meta-analysis in 2020 reported a carotid femoral PWV (cfPWV) cut-off point of 11.23 for predicting the risk of mortality from CVDs (Sequí-Domínguez et al. 2020). The cfPWV is a reliable predictor of mortality from CVDs and other causes of death. It provides a practical, non-invasive and reproducible method for estimating risk and can be used in high-risk populations (Vlachopoulos et al. 2010). Furthermore, the cfPWV cut-off values previously established by the scientific community are relevant for high-risk populations (Weisbrod et al. 2013).

Pre-clinical and clinical studies have shown that increased arterial stiffness can be mitigated by dietary modifications. Moreover, several lines of evidence have suggested the role of phytochemicals including polyphenols, in improving arterial stiffness. As a famous phytochemical, curcumin has been widely investigated for its biological activities (Mudgal et al. 2010). Curcumin has anti-lipidemic (Sahebkar 2013), anti-inflammatory (Karimian et al. 2017; Saberi-Karimian et al. 2020), antioxidant (Sahebkar et al. 2013), anti-tumor (Hamzehzadeh et al. 2018) and immunomodulatory (Shafabakhsh et al. 2019) activities. The use of curcumin in clinical trials has been reported to be safe at doses of 500 mg TID and 1 g/d for 4 weeks and makes it currently the focus of researchers for clinical use in the prevention and treatment of many inflammatory diseases (Panahi et al. 2015; Panahi et al. 2012). In a previous review, we evaluated the role of the natural curcumin as an inexpensive, tolerable and safe phytochemical for improving endothelial function (S. Karimian et al. 2017). Endothelial function plays an essential role in the development of vascular stiffness, arterial hypertension, heart failure, ischemia-reperfusion injury, Alzheimer's disease, and in the growth and proliferation of tumor cells. Curcumin has anti-inflammatory effects in endothelial cells. Furthermore, curcumin supplementation can increase antioxidant activity and improve endothelial function (S. Karimian et al. 2017).

Thus far, no study has been conducted on the effect of curcumin on improving PWV in subjects with increased arterial stiffness. Considering the pharmacological effects of curcumin, this study hypothesized that this phytochemical can effectively reduce arterial stiffness in individuals with increased PWV.

Materials and Methods

Study population

All subjects above 18 years of age, who were part of the Persian cohort at Imam Reza Hospital, were included in the study (Tohidinezhad et al. 2020). The study objectives were fully explained to the participants and they were given the choice to complete an informed consent form to participate. An information collection form was then prepared and completed for all participants. This form included demographic details (such as age, sex, address, national number, smoking status, weight, height, etc.), previous medical history, and history of drug use.

Inclusion criteria included the following: 1- Individual consent to participate in the study after the research team explained the objectives of the study, 2- Age over 18 years, and 3- Being in the highest quartile of the cohort distribution in terms of PWV. Moreover, the presence of gallstones and biliary obstruction were considered exclusion criteria.

According to the information of the study by Alidadi et al. (Alidadi et al. 2021), and considering the test power of 80% and the alpha error of 0.05, the sample size of 44 people in each group was estimated.

Study design

This study was a randomized double-blind clinical trial registered in the IRCT (IRCT20210413050958N3; Registration Date: 20-04-2022), after approval by the Research Vice-Chancellor of the Mashhad University of Medical Sciences (ID=4000802; IR.MUMS.MEDICAL.REC.1400.836).

The volunteers were randomly assigned to one of the following 2 treatment groups: one group was treated with 500 mg per day curcumin capsules (n=46), and the second group received placebo ones (n=47) for 56 days. The raw material of placebo and curcumin was obtained from Sami-Sabinsa Group Limited (India). Each 500 mg tablet of curcumin (which was in the form of C3 complex®) contained 5 mg of piperine (Bioperine®) to increase the bioavailability of curcumin (Heidari et al. 2023; Shoba et al. 1998).

Clinical Measurements

Fasting blood sugar was measured before and eight weeks after the intervention in all volunteers. Pulse wave speed indicators such as PWV and Pulse Wave Analysis (PWA) were also detected before and eight weeks after the intervention as follows: The PWV, Aortic Augmentation Index, Aortic Pulse Pressure and Aortic Blood Pressure measurement was done by device (SphygmoCor, version 8, Australia). SphygmoCor is a simple non-invasive method and the gold standard to evaluate the stiffness of the arteries in the clinic. Patients were instructed to fast prior to the clinical assessment. Each participant rested in a supine position for a minimum of 15 min to stabilize hemodynamic parameters. Subsequently, evaluation was performed by a physician who had been formally trained within the Persian cohort study framework.

Following completion of data collection, all validated data were extracted and entered into SPSS software for statistical processing.

Statistical analyses

Data analysis was done using SPSS Statistics 25.0 software and appropriate tests. Quantitative data is expressed as mean and standard deviation, and qualitative data as percentages and in the form of Tables and descriptive charts. For the comparison between the studied groups, quantitative variables were analyzed using the independent sample t-test, provided that data distribution was normal. If the data distribution was not normal, the non-parametric Mann-Whitney U test was employed. Within group comparisons were performed using the paired Student's t-test for normally distributed variables and the Wilcoxon signed-rank test for non-normally distributed variables. For qualitative data, the Chi square or Fisher's

exact test was used. Furthermore, a regression model was applied to adjust for the influence of confounding variables. The significance level was less than 0.05 and all tests were two-sided.

Results

A total of 113 subjects were initially assessed for eligibility in this study, out of whom, 20 patients were excluded, six because they did not meet the inclusion criteria and 14 declined to participate in the study. Ninety-three people were randomly divided into two groups for the study: one group was given a curcumin (500 mg/day)-piperine (5 mg/day) combination (Sami-Sabinsa Group Ltd., India), while the second group received a placebo.

During the follow-up period, five participants in the curcumin group withdrew from the study due to unwillingness to continue the treatment, undergoing surgery, or inability to receive the drug because of travel. In the placebo group, nine participants discontinued participation owing to unwillingness to continue and digestive problems (Figure 1).

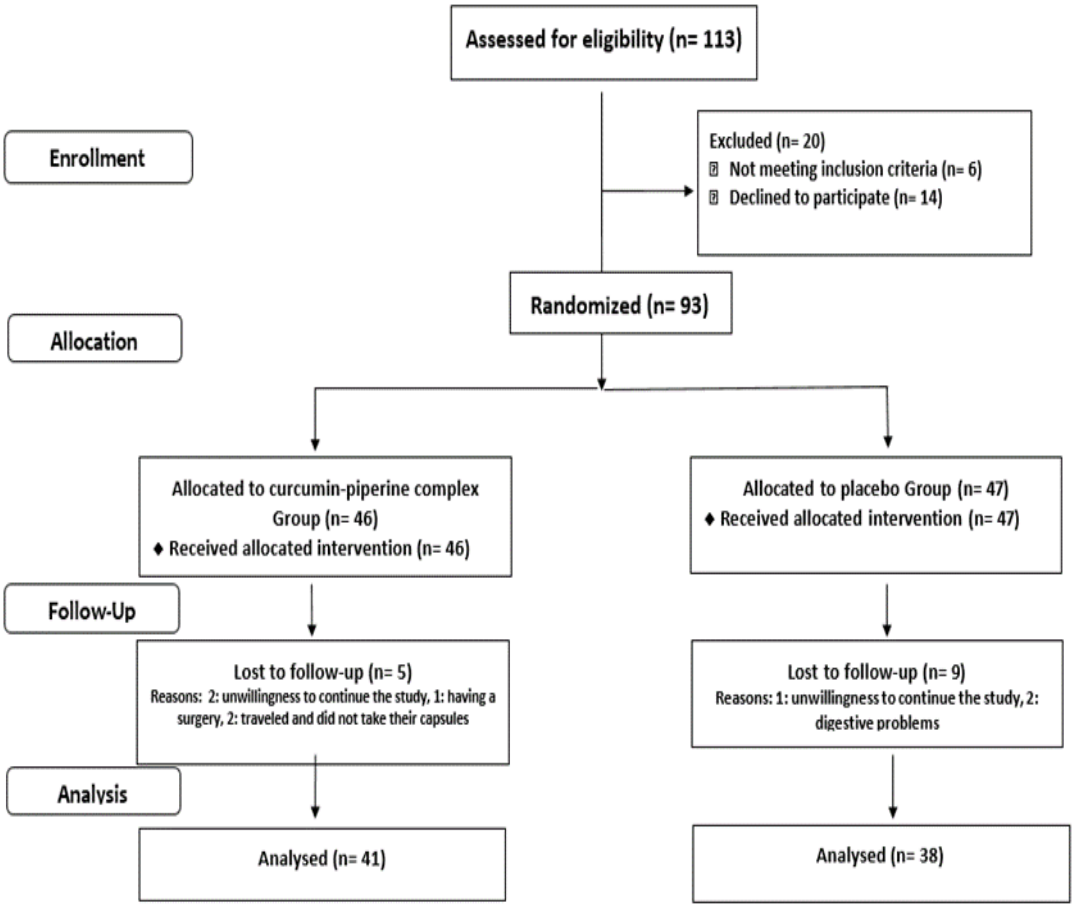

Figure 1. The flowchart of the study design

Baseline characteristics

Table 1 presents the baseline characteristics of the study population, stratified by treatment groups curcumin (n=46) and placebo (n=47). The data collectively showed that baseline features including demographic measures and clinical characteristics of participants were balanced between the study groups.

The average age across groups was comparable, with mean values ranging from 57.9 to 62.9 years, and no statistically significant differences were observed between the two groups (p =0.18). Weight

(p =0.51) and body mass index (BMI) (p =0.61) were also balanced at baseline, with the curcumin group showing a mean weight of 78.62±14.83 kg and BMI of 27.58 kg/m², while the placebo group reported 80.83±12.77 kg and 28.17 kg/m², respectively.

Table 2 summarizes the arterial stiffness indices and Fasting serum glucose (FSG) level in subjects at baseline and after 8 weeks of intervention. FSG levels were broadly similar between the groups prior to the intervention, averaging 124.88±33.83 mg/dl in the curcumin group and 140.90±47.62 mg/dl in placebo group (p=0.18), remaining consistent after the intervention across both groups (p=0.90).

Arterial stiffness indices also demonstrated close alignment between groups.

There was no significant difference in the PWV between the curcumin (9.16±1.54 m/s) and placebo (9.25±1.75 m/s) groups at baseline (p=0.85). Furthermore, the PWV did not show a significant difference between the curcumin (8.36±1.59 m/s) and placebo (8.22±1.45 m/s) groups after the intervention (p =0.68).

The results showed that aortic augmentation index was 23.91±11.66 and 27.00±11.09% in the curcumin and placebo groups at baseline, respectively, showing no significant difference (p=0.26). Moreover, there was no significant difference in aortic augmentation index between the study groups (25.57±11.66% in the curcumin and 25.93±11.91% in placebo group) after the intervention (p=0.91).

Aortic pulse pressure averaged 41.17±11.10 and 41.14±10.25 mmHg in the curcumin group before and after the intervention, respectively. As well, it averaged 43.29±10.88 and 45.38±10.44 mmHg in the placebo group, respectively, and showed non-significant difference between the two study groups before (p=0.43) and after (p=0.09) the intervention.

Moreover, there was no a significant difference in aortic blood pressure between the curcumin (124.83±16.10 mmHg) and placebo (124.15±13.00 mmHg) groups at baseline (p=0.79). Furthermore, the PWV did not have a significant difference between the two study groups (8.36±1.59 mmHg in the curcumin and 8.22±1.45 mmHg in placebo group) after the intervention (p=0.74).

Within group comparison showed a significant reduction in PWV after 8 weeks of intervention in both the curcumin (p<0.001) and placebo (p=0.001) groups. Meanwhile, other aortic hemodynamic parameters (including aortic pulse pressure, augmentation index, and blood pressure) did not change significantly in either group (p>0.05).

Changes after 8 weeks of intervention

Table 3 summarizes the changes in arterial stiffness indices and FSG level from baseline to the end of the 8-week intervention period in the curcumin and placebo groups. There were no significant difference in FSG changes between the two study groups (p>0.05).

In terms of vascular outcomes, the results showed that there was no comparable improvement in the PWV level between the two study groups, -0.89±1.52 in the curcumin group vs. -0.80±1.32 in the placebo group (p>0.05). Aortic pulse pressure demonstrated modest reductions overall, in the curcumin group showing a mean change of -0.32±11.43 compared to +1.69±9.04 in placebo group, although between-group comparisons showed non-significant differences (p=0.44). Moreover, differences in aortic blood pressure changes similarly remained non-significant between the two study groups (-2.89±15.66 mmHg in the curcumin group compared to -1.46±14.26 mmHg in the placebo group). No serious side effect was reported by participants during the study.

Table 1. Baseline characteristics of the study population

Variables	Curcumin (n=46)			Placebo (n=47)			p value		
	Total	Male	Female	Total	Male	Female	p^1 value	p^2 value	p^3 value
Age (years)	59.76 ±9.48	60.41 ±9.39	57.91±9.91	62.27±8.85	62.90 ±9.03	58.71±7.27	0.18	0.25	0.85
Weight (kg)	78.62 ±14.83	81.08±14.83	71.77±13.27	80.83±12.77	81.31±11.44	78.10±20.45	0.51	0.54	0.49
BMI (kg/m^2)	27.58±3.87	27.69±3.82	27.28±4.22	28.17±4.41	27.45±3.74	32.35±6.11	0.61	0.82	0.09
Drug Use, n (%)	25(51.0%)	19(48.7%)	6(60.0%)	24(49.0%)	20(51.3%)	4(40.0%)	0.75	0.61	1.00*
Diabetes Mellitus, n(%)	13(46.4%)	10(41.7%)	3(75.0%)	15(53.6%)	14(58.3%)	1(25.0%)	0.70	0.61	1.00*
Hypertension, n (%)	14(46.7%)	12(48.0%)	2(40.0%)	16(53.3%)	13(52.0%)	3(60.0%)	0.71	0.80	0.30*
Dyslipidemia, n (%)	7(58.3%)	6(60.0%)	1(50.0%)	5(41.7%)	4(40.0%)	1(50.0%)	0.51	0.50*	1.00*
Coronary Heart Disease, n (%)	2(40.0%)	2(50.0%)	0(0.0%)	3(60.0%)	2(50.0%)	1(100.0%)	1.00*	1.00*	0.37
Other Disorders, n (%)	7(70.0%)	4(66.7%)	3(75.0%)	3(30.0%)	2(33.3%)	1(25.0%)	0.18	0.41*	1.00*

Values are expressed as mean±SD. Between groups comparisons were assessed by parametric statistical analysis for normal distributed data and nonparametric test for non-normally distributed data. Abbreviations: BMI, body mass index. P1: Comparison between the curcumin and placebo groups in the total study population. P2: Comparison between the curcumin and placebo groups in the male subgroup. P3: Comparison between the curcumin and placebo groups in the female subgroup. * Fischer test was used.

Table 2. Arterial stiffness indices and FSG level in subjects at baseline and after 8 weeks of intervention

Variables		Curcumin (n=46)			Placebo(n=47)			p value		
		Total	Male	Female	Total	Male	Female	p^1 value	p^2 value	p^3 value
FSG(mg/dl)	Before	124.88±33.83	123.45 ± 33.52	132.75 ± 39.66	140.90±47.62	143.15 ± 49.21	119.50 ± 27.57	0.18	0.15	0.64
	After	115.93 ±35.57	114.78 ±40.26	119.40 ±17.84	119.31 ±20.97	120.58 ±23.22	115.50 ± 13.96	0.90	0.90	0.80
P^4 value		0.095	0.197	0.285	0.472	0.600	-			
Pulse wave velocity, (m/s)	Before	9.16 ±1.54	9.10 ±1.59	9.31±1.44	9.25 ±1.75	9.25 ±1.74	9.30±1.92	0.85	0.70	0.98
	After	8.36±1.59	8.28±1.64	8.59±1.47	8.22±1.44	8.30±1.52	7.78±0.89	0.68	0.95	0.24
P^4 value		<0.001	<0.001	0.091	0.001	0.003	0.092			
Aortic Augmentation Index, (%)	Before	23.91±11.66	23.37±12.29	25.75±9.67	27.00±11.09	26.32±11.10	34.00 ±9.84	0.26	0.34	0.24
	After	25.57±12.98	25.85±13.51	24.62±11.79	25.93±11.91	24.39±11.45	40.33±3.51	0.91	0.66	0.06
P^4 value		0.549	0.389	0.585	0.926	0.781	0.382			

Table 2. Continued

Aortic Pulse	Before	41.17±11.10	39.48±9.01	46.87±15.77	43.29 ±10.88	42.58±11.11	50.66±3.51	0.43	0.25	0.22
Pressure, (mmHg)	After	41.14±10.25	40.85±10.57	42.12± 9.672	45.38±10.44	44.54±10.72	52.66± 1.52	0.09	0.15	0.10
P[4] value		0.870*	0.666*	0.134*	0.323*	0.385*	0.225*			
Aortic Blood	Before	124.83±16.10	124.00±13.99	127.75±22.98	124.15±13.00	123.90±13.15	126.66±13.57	0.79	0.97	0.94
Pressure, (mmHg)	After	121.02±12.76	121.10±12.71	120.75±13.81	122.25±16.94	121.46±16.96	129.66±18.14	0.74	0.92	0.39
P[4] value		0.080	0.204	0.293*	0.650*	0.525	0.285			

Values are expressed as mean±SD. Between groups comparisons were assessed by parametric statistical analysis for normal distributed data and nonparametric test for non-normally distributed data. FSG, fasting serum glucose. P1: Comparison between the curcumin and placebo groups in the total study population. P2: Comparison between the curcumin and placebo groups in the male subgroup. P3: Comparison between the curcumin and placebo groups in the female subgroup. P4: Within group comparison. *: The paired Student's t-test was used.

Table 3. Changes in arterial stiffness indices and FSG level at baseline and after 8 weeks of intervention

Variables	**Curcumin (n=46)**			**Placebo (n=47)**			**p value**		
	Total	**Male**	**Female**	**Total**	**Male**	**Female**	**p[1] value**	**p[2] value**	**p[3] value**
FSG(mg/dl)	-17.16±35.64	-17.20±39.37	-17.00±22.60	-10.43±35.97	-10.16±39.40	-12.00	0.69	0.73	0.86
Pulse Wave Velocity, (m/s)	-.89±1.52	-.86±1.39	-.95±1.92	-.80±1.32	-.79±1.34	-.87±1.33	0.92	0.70	0.72
Aortic Augmentation Index, (%)	0.76±7.36	6.33±9.86	-1.12±5.57	0.16±9.53	-0.50±9.43	1.35±7.83	0.77	0.44	0.14
Aortic Pulse Pressure, (mmHg)	-0.32±11.43	1.03±12.11	-4.75±7.92	1.68±9.03	1.65±9.54	2.00±2.00	0.44	0.84	0.19
Aortic Blood Pressure, (mmHg)	-2.89±15.66	-2.89±15.66	-7.00±13.54	-1.46±14.26	-1.46 ±14.26	3.00±4.58	0.72	0.72	0.26

Values are expressed as mean±SD. between groups comparisons were made by parametric statistical analysis for normal distributed data and nonparametric test for non-normally distributed data. FSG, fasting serum glucose. P1: Comparison between the curcumin and placebo groups in the total study population. P2: Comparison between the curcumin and placebo groups in the male subgroup.P3: Comparison between the curcumin and placebo groups in the female subgroup.

Regression analysis

In the present analysis, none of the examined variables, including age, sex, drug use or disease history, nor their interactions, showed a statistically significant effect on the changes in the PWV, aortic blood pressure, aortic pulse pressure, or aortic augmentation index before and after the intervention. This suggests that these variables did not act as meaningful confounders for any of the assessed vascular outcomes.

Discussion

This study was a randomized, double-blind, placebo-controlled clinical trial conducted among subjects who were in the highest quartile (≥75th percentile) of the Persian cohort population in terms of the PWV. Recruited subjects received either curcumin (500 mg/day) or a placebo over an eight-week period. The PWV, aortic blood pressure, aortic augmentation index, and aortic pulse pressure were assessed.

In a mouse model of obesity, increased PWV induced by a high-fat/high-sucrose (HFHS) diet was reduced to normal levels after two months of returning to a standard chow diet (Weisbrod et al. 2013) . Furthermore, Fleenor et al. have reported that curcumin supplementation can improve oxidative stress by reducing superoxide level and NADPH oxidase expression, and increasing manganese-superoxide dismutase (Mn-SOD) in old male C57BL/6 N mice (Fleenor et al. 2013).

In contrast, the findings of the present clinical trial indicated that the intervention did not produce any statistically significant improvements in increased arterial stiffness or aortic hemodynamic indices. Curcumin supplementation did not demonstrate a beneficial effect on the PWV or aortic blood pressure over the eight-week intervention period. Although reductions in aortic augmentation index and aortic pulse pressure were observed in women receiving curcumin compared with the placebo group, these changes did not reach statistical significance. This inconsistency is likely due to curcumin low oral bioavailability and the chronic multifactorial nature of human arterial stiffness.

The obtained results confirm those of previous studies indicating that short-term curcumin supplementation may not significantly improve increased stiffness of large elastic arteries. For instance, Santos-Parker et al. reported that supplementation with 2000 mg/day of curcumin over 12 weeks improved microvascular and conduit endothelial function but had no effect on aortic PWV in healthy middle-aged and older adults (Santos-Parker et al. 2017). Similarly, Ghasemiadl et al. evaluated the effects of curcumin on the PWV in patients with diabetic hemodialysis over a 24 week period. They found no significant differences in the PWV between the study groups but there was a significant reduction within the treatment arm (Ghasemiadl et al. 2024). In contrast, a double-blind clinical trial conducted in 2021 among individuals with metabolic syndrome (MetS) reported that daily supplementation with 500 mg of curcumin for 12 weeks resulted in improvements in the PWV (Alidadi et al. 2021).

A recent meta-analysis showed that doses above 900 mg/day of curcumin can improve diastolic blood pressure, PWV, vascular cell adhesion molecule-1 (VCAM-1) and flow-mediated vasodilation in subjects with MetS, whereas low doses of curcumin had no effect on blood pressure (wen Tang et al. 2024). In this study, only a single dose was used, which was less than 900 mg/day. Mechanistically, curcumin is known to have anti-inflammatory and antioxidant effects, increase nitric oxide (NO) bioavailability, and modulate endothelial function through multiple signaling pathways such as Nrf2 and eNOS activation (Banez et al. 2020; Panahi et al. 2015). We previously reported the potential of curcumin, as an inexpensive, well-tolerated and safe phytochemical in improving endothelial function. The anti-

inflammatory effects of curcumin are exerted by reducing the transendothelial monocyte migration and downregulating of the mRNA expression of key adhesion molecules such as ICAM-1, VCAM-1 and P-selectin. Moreover, curcumin modulates multiple signaling pathways involved in endothelial inflammation, including NFκB, JNK, p38 and STAT-3 (Alidadi et al. 2021).

In the current study, a dose of 500 mg/day of curcumin over eight weeks did not lead to significant changes in the PWV or aortic hemodynamics in the relatively older adult population with a mean age of 61.03±9.21 years. Additionally, the non-significant trends observed in females warrant further investigation, possibly in studies with larger sample sizes, longer intervention durations, and higher doses of curcumin.

Some important limitations of the current study were that the subjects' diet and smoking history were not examined. Moreover, reversing arterial structural changes that affect the PWV may likely need longer intervention periods than those typically used in human trials. Finally, only a single dose of curcumin was used in this study which precludes the possibility of evaluation any dose-response relationship.

This study suggests that eight weeks of curcumin-piperine supplementation at a dose of 500 mg/day cannot significantly improve increased arterial stiffness in adults. However, subgroup trends may warrant further studies. Given that vascular structural changes might depend on longer treatment durations or higher doses of curcumin, future studies should explore these parameters.

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Conflicts of interest

The authors confirm no conflicts of interest.

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Ethical Considerations

The study protocol has been approved in Ethics Committee at Mashhad University of Medical Sciences, Mashhad, Iran.

Code of Ethics

IR.MUMS.MEDICAL.REC.1400.836

Authors' Contributions

Study Design, Maryam Alinezhad-Namaghi, Amirhosein Sahebkar, Maryam Saberi-Karimian; Data Collection, Fatemeh Shahabi, Parisa Sadinam, Saeed Eslami, Sina Vossoughinia; Statistical Analysis, Parisa Sadinam, Fatemeh Shahabi; Data Interpretation, Maryam Alinezhad-Namaghi, Amirhosein Sahebkar, Maryam Saberi-Karimian; Manuscript Preparation, Parisa Sadinam, Maryam Alinezhad-Namaghi, Amirhosein Sahebkar, Maryam Saberi-Karimian; Literature Search, Maryam Alinezhad-Namaghi, Amirhosein Sahebkar, Parisa Sadinam, Maryam Saberi-Karimian; Funds Collection, Maryam Saberi-Karimian.

Abbreviations

PWV: Pulse Wave Velocity; CVD: Cardiovascular diseases; cfPWV: carotid femoral PWV; BMI: body mass index; FSG: fasting serum glucose; HFHS: high-fat/high-sucrose; Mn-SOD: manganese- superoxide dismutase; MetS: metabolic syndrome; NO:

nitric oxide; ICAM-1: intercellular adhesion molecule-1; VCAM-1: vascular cell adhesion molecule-1; NFκB; Nuclear factor-kappa B; JNK: C-Jun-N-terminal-kinase, STAT-3: signal transducer and activator of transcription-3.

References

Alidadi M, Sahebkar A, Eslami S, et al. (2021) The effect of curcumin supplementation on pulse wave velocity in patients with metabolic syndrome: a randomized, double-blind, placebo-controlled trial Pharmacological properties of plant-derived natural products and implications for human health. Springer, p 1–11

Banez MJ, Geluz MI, Chandra A, et al. (2020) A systemic review on the antioxidant and anti-inflammatory effects of resveratrol, curcumin, and dietary nitric oxide supplementation on human cardiovascular health. Nutrition Research 78:11–26

Castellano JM, Narula J, Castillo J, Fuster V (2014) Promoting cardiovascular health worldwide: strategies, challenges, and opportunities. Rev Esp Cardiol (English Edition) 67(9):724–730

Cecelja M, Chowienczyk P (2012) Role of arterial stiffness in cardiovascular disease. JRSM Cardiovasc Dis 1(4):1–10

Díaz A, Galli C, Tringler M, Ramírez A, Cabrera Fischer EI (2014) Reference values of pulse wave velocity in healthy people from an urban and rural argentinean population. Int J Hypertens 2014(1):653239

Fleenor BS, Sindler AL, Marvi NK, Howell KL, Zigler ML, Yoshizava M (2013) Curcumin ameliorates arterial dysfunction and oxidative stress with aging. Exp Gerontol 48(2):269–276

Ghasemiadl M, Ghasemi S, Soleimani A, et al. (2024) The Effects of Curcumin Administration on Carotid Intima-Media Thickness and Pulse Wave Velocity in Diabetic Hemodialysis Patients: A Randomized, Double-Blinded, Placebo-Controlled Trial. Int J Prev Med 15:3

Hamzehzadeh L, Atkin SL, Majeed M, Butler AE, Sahebkar A (2018) The versatile role of curcumin in cancer prevention and treatment: A focus on PI3K/AKT pathway. J Cell Physiol 233(10):6530–6537

Heidari H, Bagherniya M, Majeed M, Sathyapalan T, Jamialahmadi T, Sahebkar A (2023) Curcumin-piperine co-supplementation and human health: A comprehensive review of preclinical and clinical studies. Phytother Res 37(4):1462–1487

Karimian MS, Pirro M, Majeed M, Sahebkar A (2017) Curcumin as a natural regulator of monocyte chemoattractant protein-1. Cytokine Growth Factor Rev 33:55–63

Mozos I, Malainer C, Horbańczuk J, et al. (2017) Inflammatory markers for arterial stiffness in cardiovascular diseases. Front Immunol 8:1058

Mudgal V, Madaan N, Mudgal A, Mishra S (2010) Dietary polyphenols and human health. Asian Journal of Biochemistry 5(3): 154-162.

O'Rourke MF, O'Brien C, Edelman ER (2016) Arterial stiffening in perspective: advances in physical and physiological science over centuries. Am J Hypertens 29(7):785–791

Panahi Y, Ghanei M, Bashiri S, Hajihashemi A, Sahebkar A (2015) Short-term curcuminoid supplementation for chronic pulmonary complications due to sulfur mustard intoxication: positive results of a randomized double-blind placebo-controlled trial. Drug research 65(11):567–573

Panahi Y, Sahebkar A, Parvin S, Saadat A (2012) A randomized controlled trial on the anti-inflammatory effects of curcumin in patients with chronic sulphur mustard-induced cutaneous complications. Ann Clin Biochem 49(6):580–588

Pirro M, Schillaci G, Mannarino MR, et al. (2007) Effects of rosuvastatin on 3-nitrotyrosine and aortic stiffness in hypercholesterolemia. Nutrition, Metabolism and Cardiovascular Diseases 17(6):436–441

Pirro M, Schillaci G, Savarese G, et al. (2004) Low-grade systemic inflammation impairs arterial stiffness in newly diagnosed hypercholesterolaemia. Eur J Clin Invest 34(5):335–341

S. Karimian M, Pirro M, P. Johnston T, Majeed M, Sahebkar A (2017) Curcumin and endothelial function: evidence and mechanisms of protective effects. Current pharmaceutical design 23(17):2462–2473

Saberi-Karimian M, Keshvari M, Ghayour-Mobarhan M, et al. (2020) Effects of

curcuminoids on inflammatory status in patients with non-alcoholic fatty liver disease: A randomized controlled trial. Complement Ther Med 49:102322 doi:10.1016/j.ctim.2020.102322

Sahebkar A (2013) Why it is necessary to translate curcumin into clinical practice for the prevention and treatment of metabolic syndrome? Biofactors 39(2):197–208

Sahebkar A, Mohammadi A, Atabati A, et al. (2013) Curcuminoids modulate pro-oxidant–antioxidant balance but not the immune response to heat shock protein 27 and oxidized LDL in obese individuals. Phytother Res 27(12):1883–1888

Santos-Parker JR, Strahler TR, Bassett CJ, Bispham NZ, Chonchol MB, Seals DR (2017) Curcumin supplementation improves vascular endothelial function in healthy middle-aged and older adults by increasing nitric oxide bioavailability and reducing oxidative stress. Aging (albany NY) 9(1):187

Sequi-Dominguez I, Cavero-Redondo I, Alvarez-Bueno C, Pozuelo-Carrascosa DP, Nunez de Arenas-Arroyo S, Martinez-Vizcaino V (2020) Accuracy of pulse wave velocity predicting cardiovascular and all-cause mortality. A systematic review and meta-analysis. J Clin Med 9(7):2080

Shafabakhsh R, Pourhanifeh MH, Mirzaei HR, Sahebkar A, Asemi Z, Mirzaei H (2019) Targeting regulatory T cells by curcumin: A potential for cancer immunotherapy. Pharmacol Res 147:104353

Shirwany NA, Zou M-h (2010) Arterial stiffness: a brief review. Acta Pharmacol Sin 31(10):1267–1276

Shoba G, Joy D, Joseph T, Majeed M, Rajendran R, Srinivas P (1998) Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. Planta Med 64(04):353–356

Tohidinezhad F, Khorsand A, Zakavi SR, et al. (2020) The burden and predisposing factors of non-communicable diseases in Mashhad University of Medical Sciences personnel: a prospective 15-year organizational cohort study protocol and baseline assessment. BMC Public Health 20(1):1637

Van Bortel LM, Laurent S, Boutouyrie P, et al. (2012) Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. Journal of hypertension 30(3):445–448

Vasan S (2025) Pulse Wave Velocity (PWV) and Endothelial Function Assessment: Principles and Pathophysiology Men's Health. Springer, p 303–306

Vlachopoulos C, Aznaouridis K, Stefanadis C (2010) Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol 55(13):1318–1327

Weisbrod RM, Shiang T, Al Sayah L, et al. (2013) Arterial stiffening precedes systolic hypertension in diet-induced obesity. Hypertension 62(6):1105–1110

wen Tang W, fei Huang F, Haedi AR, Shi QY (2024) The effect of curcumin supplementation on endothelial function and blood pressure in patients with metabolic disorders: A meta-analysis of meta-analyses. Prostaglandins Other Lipid Mediat 175:106900