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A Slightly Low Hemoglobin Level Is Beneficially Associated with Arterial Stiffness in Japanese Community-Dwelling Women

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Abstract

Pulse wave velocity (PWV) is a simple and noninvasive method of measuring arterial stiffness for the assessment of cardiovascular disease (CVD) in high-risk populations. This association may be further confounded by hemoglobin status, which is involved in the development of atherosclerosis. We randomly recruited 120 men and 223 women aged 69 ± 9 and 68 ± 7 years, respectively, during their annual health examination in a single community. Arterial stiffness was evaluated by brachial – ankle PWV (baPWV). The value of baPWV was different from men and women. In men, baPWV was not related to hemoglobin levels ($r = 0.013$, $P = .886$), but in women baPWV increased significantly and progressively with increased hemoglobin levels ($r = 0.276$, $P < .001$). Stepwise multiple regression analysis using the baPWV as objective variables, adjusted for confounding factors as explanatory variables, showed that only in women, hemoglobin levels ($\beta = 0.165$, $P = .001$) as well as age ($\beta = 0.268$, $P < .001$), body mass index (BMI; $\beta = -0.165$, $P < .001$), systolic blood pressure (SBP; $\beta = 0.429$, $P < .001$), prevalence of antihypertensive ($\beta = 0.154$, $P = .002$), heart rate (HR; $\beta = 0.108$, $P = .017$), and antilipidemic medication ($\beta = 0.094$, $P = .036$), and estimated glomerular filtration rate (eGFR; $\beta = -0.147$, $P = .003$) were significantly and independently associated with baPWV. Multivariate-adjusted baPWV was significantly higher in hemoglobin groups of ≥12.7 g/dL (Group-2, Group-4) than in the lowest hemoglobin group (10.0–12.6 g/dL; $P = .032$). A slightly low hemoglobin level was beneficially associated with arterial stiffness in community-dwelling women but not men.

Keywords: hemoglobin, pulse wave velocity, arterial stiffness, atherosclerosis, risk factor, woman

INTRODUCTION

Pulse wave velocity (PWV) is a simple and noninvasive method of measuring arterial stiffness (1) and a surrogate marker for and an independent predictor of mortality and morbidity in some cardiovascular diseases (CVD) such as ischemic heart disease and stroke (2–5). A new method for measuring brachial–ankle PWV (baPWV) has been proposed in Japan (6), and its method is also considered a marker of CVD and atherosclerotic risk factors (7).

Increased hemoglobin values often accompany insulin resistance and compensatory hyperinsulinemia in humans (8–10). Conversely, anemia has also been suggested to be responsible for insulin resistance (11). Paradoxically, baPWV is elevated in patients with chronic kidney disease (CKD) (12,13) and type 2 diabetes (14), which leads to severe anemia and insulin resistance. To our knowledge, studies that demonstrate a relationship between hematological parameters such as hemoglobin and baPWV are very few. This study aimed to investigate whether hemoglobin was independently associated with baPWV.

First, we investigated the relationship between hematological parameters and risk factors such as hypertension, hyperglycemia, and dyslipidemia. Next, we investigated whether increased hemoglobin was independently associated with arterial stiffness using baPWV. For this, we used cross-sectional data from community-dwelling subjects.

MATERIALS AND METHODS

Subjects

Participants were recruited at the time of their annual health examination in a single community. Information on medical history, present conditions, and drugs

Table 2. Relationship between various confounding factors including hemoglobin and baPWV of subjects categorized by gender

	Men, $N = 120$				Women, $N = 223$			
	Age-adjusted Pearson's correlation coefficient		Stepwise multiple linear regression analysis		Age-adjusted Pearson's correlation coefficient		Stepwise multiple linear regression analysis	
Characteristic	*R*	*P* value	B	*P* value	*R*	*P* value	B	*P* value
Age (years)	—	—	0.363	<.001	—	—	0.268	<.001
BMI (kg/m^2)	0.025	.791	—	—	−0.002	.974	−0.165	<.001
Current alcohol consumption (%)	0.076	.411	—	—	−0.047	.485	—	—
Current smoking (%)	−0.050	.585	—	—	−0.057	.394	—	—
MBP (mmHg)	0.445	<.001	0.328	<.001	0.588	<.001	0.426	<.001
Antihypertensive medication (Yes = 1, No = 0)	0.312	.001	0.177	.023	0.319	<.001	0.154	.002
HR (beat/min)	0.301	.001	0.186	.013	0.237	<.001	0.108	.017
TG (mg/dL)	0.120	.194	—	—	0.131	.051	—	—
HDL-C (mg/dL)	0.084	.361	—	—	−0.030	.655	—	—
LDL-C (mg/dL)	−0.058	.529	—	—	−0.061	.548	—	—
Antilipidemic medication (Yes = 1, No = 0)	0.067	.470	—	—	0.143	.033	0.094	.036
FPG (mg/dL)	0.097	.295	—	—	0.155	.021	—	—
Antidiabetic medication (Yes = 1, No = 0)	0.129	.161	—	—	0.066	.329	—	—
eGFR (mL/min/1.73 m^2)	−0.093	.316	—	—	−0.238	<.001	−0.147	.003
CVD (Yes = 1, No = 0)	−0.043	.639	—	—	0.066	.329	—	—
Red blood cell count (×10^4/mm^3)	0.213	.020	—	—	0.359	<.001	—	—
Hemoglobin (g/dL)	0.221	.016	—	—	0.380	<.001	0.165	.001
Hematocrit (%)	0.238	.009	—	—	0.318	<.001	—	—
R^2	—	—	0.584	<.001	—	—	0.578	<.001

Abbreviation: baPWV – brachial–ankle pulse wave velocity; BMI, body mass index; MBP, mean blood pressure; HR, heart rate; TG, triglycerides; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; eGFR – estimated glomerular filtration rate; FPG, fasting plasma glucose; CVD, cardio vascular disease.

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Table 1. Characteristics of subjects categorized by gender and hemoglobin status

	Hemoglobin (g/dL)				
Men	Group-1	Group-2	Group-3	Group-4	*P* for trend*
Characteristics	10.0–14.0	14.1–14.9	15.0–15.9	≥16.0 g/dL	
Number	31	29	36	24	
Age (y)	73 ± 8	71 ± 6	67 ± 8	63 ± 11	<.001
BMI (kg/m^2)	21.2 ± 2.5	23.0 ± 2.9	23.9 ± 3.4	24.5 ± 2.7	<.001
Current alcohol consumption (%)	61.3	82.8	77.8	87.5	.098
Current smoking (%)	16.1	20.7	30.6	37.5	.256
CVD (%)	16.1	13.8	5.6	8.3	.502
SBP (mmHg)	136 ± 24	145 ± 17	144 ± 22	143 ± 21	.319
DBP (mmHg)	76 ± 10	82 ± 9	86 ± 10	85 ± 10	<.001
MBP (mmHg)	96 ± 14	103 ± 10	105 ± 13	104 ± 12	.011
HR (beat/min)	60 ± 8	59 ± 9	61 ± 8	63 ± 10	.437
Antihypertensive medication (%)	32.3	34.5	19.4	29.2	.535
TG (mg/dL)	82 (62–104)	76 (65–99)	94 (66–120)	128 (76–176)	.001
HDL-C (mg/dL)	60 ± 15	60 ± 14	60 ± 15	53 ± 18	.303
LDL-C (mg/dL)	108 ± 24	110 ± 31	119 ± 29	112 ± 31	.379
Antilipidemic medication (%)	3.2	0	2.8	4.2	.778
FPG (mg/dL)	95 (90–104)	94 (88–98)	95 (89–102)	100 (96–118)	.013
Antidiabetic medication (%)	0	0	5.6	12.5	.073
eGFR (mL/min/1.73 m^2)	74.0 ± 19.0	76.4 ± 14.2	76.8 ± 15.0	76.3 ± 15.0	.894
Red blood cell count (×10^4 /mm^3)	418 ± 38	454 ± 23	481 ± 25	512 ± 34	<.001
Hematocrit (%)	39.3 ± 3.2	43.7 ± 1.5	45.9 ± 1.2	49.5 ± 2.7	<.001
	Hemoglobin (g/dL)				
Women	Group-1	Group-2	Group-3	Group-4	*P* for trend*
Characteristics	10.0–12.6	12.7–13.2	13.3–13.9	≥14.0 g/dL	
Number	57	56	55	55	
Age (y)	69 ± 7	68 ± 7	66 ± 8	68 ± 6	.188
BMI (kg/m^2)	23.3 ± 2.7	23.1 ± 3.3	24.2 ± 3.4	24.4 ± 3.3	.074
Current alcohol consumption (%)	24.6	26.8	21.8	27.3	.909
Current smoking (%)	1.8	0	1.8	0	.572
CVD (%)	7.0	10.7	10.9	9.1	.886
SBP (mmHg)	137 ± 22	139 ± 25	145 ± 21	151 ± 23	.007
DBP (mmHg)	77 ± 12	79 ± 13	83 ± 11	86 ± 10	<.001
MBP (mmHg)	97 ± 14	99 ± 16	104 ± 13	108 ± 14	<.001
HR (beat/min)	63 ± 8	67 ± 9	69 ± 11	65 ± 10	.015
Antihypertensive medication (%)	24.6	33.9	36.4	34.5	.538
TG (mg/dL)	94 (71–124)	109 (72–156)	114 (86–136)	97 (73–157)	.332
HDL-C (mg/dL)	65 ± 18	61 ± 15	61 ± 13	60 ± 14	.244
LDL-C (mg/dL)	124 ± 24	127 ± 28	130 ± 30	134 ± 28	.291
Antilipidemic medication (%)	8.8	8.9	12.7	9.1	.879
FPG (mg/dL)	91 (87–98)	95 (91–103)	93 (88–100)	98 (92–103)	.008
Antidiabetic medication (%)	5.3	7.1	1.8	5.5	.622
eGFR (mL/min/1.73 m^2)	76.7 ± 18.4	75.6 ± 15.3	77.9 ± 14.9	75.6 ± 16.1	.862
Red blood cell count (×10^4/mm^3)	394 ± 25	420 ± 17	444 ± 19	466 ± 22	<.001
Hematocrit (%)	36.8 ± 2.2	39.4 ± 1.4	41.3 ± 1.5	43.2 ± 1.8	<.001

Abbreviations: BMI – body mass index; CVD – cardio vascular disease; SBP – syatolic blood pressure; DBP – diastolic blood pressure; MBP – mean blood pressure; HR – heart rate; TG – triglycerides; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; FPG – fasting plasma glucose; eGFR – estimated glomerular filtration rate
Data presented are mean ± SD. Data for triglycerides and fasting plasma glucose were skewed and are presented as median (interquartile range). Data for triglycerides and fasting plasma glucose were skewed and log-transformed for analysis.
*One-way ANOVA test or χ^2 test.

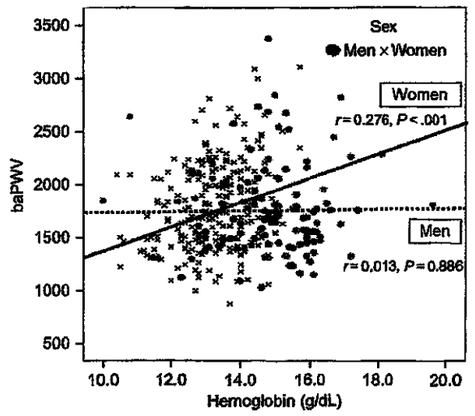

Figure 1. Relationship between hemoglobin and baPWV of subjects categorized by gender. Abbreviation: baPWV – brachial to ankle pulse wave velocity.

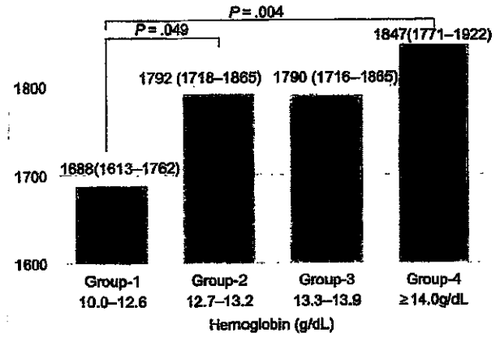

Figure 2. Multivariate-adjusted baPWV of women categorized by hemoglobin status. Data presented are the mean (95% confidence interval) values. Multivariate-adjusted for significantly confounding factors (i.e., age, BMI, MBP, HR, antihypertensive medication, antilipidemic medication, eGFR) in multiple linear regression analysis of Table 2. Abbreviations: baPWV – brachial to ankle pulse wave velocity; BMI – body mass index; MBP – mean blood pressure; HR – heart rate; eGFR – estimated glomerular