Reduced tongue pressure and platelet count in relation to hypertension among community dwelling elderly Japanese subjects

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Background: Age-related disruption of the microvascular endothelium exacerbates hypertension and sarcopenia. Reduced maximum voluntary tongue pressure against the palate (MTP) is known to be associated with sarcopenia. On the other hand, elevated platelet count acts as an indicator of active endothelial repair. However, no studies have reported the association between reduced MTP and platelet count in the context of hypertension status. To evaluate the association between reduced MTP and platelet count, we conducted a cross-sectional study of 1,607 elderly Japanese who had undergone an annual health check from 2015 to 2016.

Methods: Since hypertension should mask the beneficial effects of endothelial repair, subjects were stratified by hypertension status. Among the present study population, 876 subjects had hypertension. Reduced tongue pressure was defined as an MTP at or under the 20th percentile of the study population (<23.9kPa for men and <21.8kPa for women).

Results: Independent of known cardiovascular risk factors, a significant inverse association between platelets and reduced tongue pressure was seen among non-hypertensive, but not hypertensive, subjects. The fully adjusted odds ratios (OR) and 95% confidence intervals (CI) of 1 standard deviation (SD) increment of platelet count (5.4×10^4/μL for men and 5.2×10^4 /μL for women) were 0.73 (0.60, 0.90) and 1.13 (0.94, 1.35) for non-hypertensive subjects and hypertensive subjects, respectively.

Conclusions: Independent of known cardiovascular risk factors, platelet count is significantly inversely associated with reduced tongue pressure among elderly non-hypertensive Japanese subjects. This finding could be an efficient tool to clarify a part of mechanism underlying reduced tongue pressure.

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Key words: endothelium, hypertension, platelet, sarcopenia, tongue pressure.

Background

Reduced maximum voluntary tongue pressure against the palate (MTP) is reported to be a sensitive indicator for predicting pneumonia occurrence in acute stroke patients [1], and is also related to sarcopenia or sarcopenic dysphagia [2]. Since dysphagia is a fundamental cause of aspiration pneumonia, measurement of MTP should be an efficient tool for estimating the risk of pneumonia in elderly subjects.

On the other hand, sarcopenia is associated with impairment

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of capillary function [3]. Moreover, platelet-derived angiogenesis regulators promote angiogenesis during wound healing, tumor growth, and response to ischemia [4]; and platelet rich plasma also promotes angiogenesis [5]. Therefore, platelet count might be inversely associated with reduced MTP by indicating capillary repair activity. Previously we reported a significant inverse association between atherosclerosis and MTP among hypertensive subjects with low platelet levels but not among those with high platelet levels [6]. The present study indicates to some extent that vascular maintenance activity, as evaluated in terms of platelet levels, could influence the maintenance of MTP.

However, no studies have clarified the association between platelet count and reduced MTP in the context of hypertension status. In addition, although elevated platelet count acts as an indicator of active endothelial repair, this beneficial effect is limited to non-hypertensive subjects [7].

Therefore, the association between platelet count and reduced MTP should account for hypertension status. To test this, we conducted a cross-sectional study of 1,607 elderly Japanese subjects aged ≥60 years who had undergone an annual health check-up from 2015 to 2016.

Methods

Subjects and methods

The study population comprised 1,712 elderly Japanese residents aged ≥60 years from the western rural communities of the Goto Islands, who underwent an annual health check-up from 2015 to 2016 as recommended by the Japanese government. Among all subjects, those without MTP data (n=14) or without platelet data (n=8) were excluded.

To avoid the influence of stroke aftereffects, subjects with a history of stroke (n=83) were also excluded. The remaining patients, comprising 1,607 subjects (mean age of 72.8 years (standard deviation (SD): 7.4; range: 60-95) were enrolled in the study.

This study was approved by the Ethics Committee for Use of Humans of Nagasaki University (project registration number 0501120073).

Data collection and laboratory measurements

Trained interviewers obtained information on clinical characteristics. Body weight and height were measured with an automatic body composition analyzer (BF-220; Tanita, Tokyo, Japan), and body mass index (BMI;kg/m^2) was calculated. Systolic and diastolic blood pressure were recorded at rest. Blood samples were collected in an EDTA-2K tube and a siliconized tube. The number of platelets and white blood cells in samples from the EDTA-2K tube were measured at SRL, Inc. (Tokyo, Japan) using an automated procedure.

Triglycerides (TG) and serum creatinine were measured enzymatically. HDL-cholesterol (HDL) was measured using a direct method, and hemoglobin A1c (HbA1c) was measured using the latex coagulation method. Glomerular filtration rate (GFR) was estimated by using an established method recently proposed by a working group of the Japanese Chronic Kidney Disease Initiative [8]. According to this adaptation, GFR (ml/min/1.73m^2) = 194 × (serum creatinine (enzyme method))$^{-1.094}$ × (age)$^{-0.287}$ × (0.739 for women). MTP was evaluated by the method proposed by Tsuga et al. using the JMS tongue pressure measurement device, Orarize (JMS Co., Ltd. Hiroshima, Japan) [9]. Reduced MTP was defined as a tongue pressure at or under the 20th percentile of the study population (<23.9kPa for men and <21.8kPa for women) as like our previous study [10]. Diabetes was diagnosed as an HbA1c≥6.5% and/or taking glucose-lowering medication.

Statistical analysis

Characteristics of the study population stratified by platelet levels were expressed as mean ± standard deviation. A trend test was performed with a regression model for mean values, and a logistic regression model was used for proportion.

Logistic regression models were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) to determine the influence of platelet levels on reduced MTP.

Adjustments for confounding factors were made using three models. In the first model (Model 1), adjustment was made only for age and sex. The second model (Model 2) included other possible confounding factors, namely, BMI (kg/m^2), smoking status (never-smoker, former smoker, current smoker), alcohol consumption [never-drinker, former drinker, current drinker (23-45g/week, 46-68g/week, ≥69g/week, respectively)], systolic blood pressure (mmHg), anti-hypertensive medication use (yes, no), serum HDL-cholesterol (mg/dL), serum triglycerides (mg/dL), HbA1C (%) and GFR (ml/min/1.73 m^2). Since white blood cells may be associated with platelet levels and indicate inflammation, which might act as a confounding factor for the association between platelet levels and MTP, a further analysis additionally adjusted for white blood cells (Model 3) was carried out, as the simple correlation coefficient (r) for platelets and white blood cells was r = 0.29 (p<0.001).

We also calculated the association stratified by hypertension status, since platelet levels are positively associated with endothelial repair in non-hypertensive subjects and positively associated with atherosclerosis in hypertensive subjects [7].

To confirm the validity of using a sex-combined model for the present analysis, we also performed a sex-specific analysis.

Since insulin resistance may contribute to the development of sarcopenia [11], and platelets from subjects with diabetes exhibit increased reactivity [12], diabetes might act as a confounding factor on the association between platelet levels and reduced MTP. We therefore conducted a further analysis limited to subjects without diabetes.

All statistical analyses were performed with the SAS system for Windows (version 9.4; SAS Inc., Cary, NC), with values of <0.05 regarded as being statistically significant.

Results

Characteristics of the present study population are shown in Table 1. Platelet levels were positively associated with systolic blood pressure, current smoker status, TG, GFR, WBC, and MTP; and inversely associated with age. Figure 1 shows sex-specific distribution of MTP by age class. For the younger age class (age<90), even the median values of MTP for men are slightly higher than those for women. For the elderly class (age≥90), however, those for men are slightly lower.

Although no significant association between platelet count and reduced MTP was found for total subjects (Table 2),

Table 1. Characteristics of the study population in relation to platelet levels.

	Platelet levels			P for trend
	Low (T1)	T2	High (T3)	
No. of participants	535	533	539	
Gender (men), %	40.7	40.2	40.3	0.978
Age, years	74.0 ± 7.3	72.9 ± 7.3	71.4 ± 7.4	<0.001
Body mass index (BMI), kg/m^2	23.5 ± 3.5	23.5 ± 3.5	23.5 ± 3.2	0.955
Systolic blood pressure, mmHg	141 ± 20	140 ± 19	143 ± 19	0.047
Diastolic blood pressure, mmHg	80 ± 12	81 ± 11	81 ± 12	0.079
Anti-hypertensive medication use, %	53.8	48.8	51.9	0.249
Current drinker, %	26.4	25.9	26.7	0.954
Current smoker, %	6.0	6.9	11.1	0.004
Serum triglycerides (TG), mg/dL	97 ± 56	105 ± 53	112 ± 66	<0.001
Serum HDL-cholesterol (HDL), mg/dL	58 ± 14	59 ± 15	60 ± 14	0.092
Hemoglobin A1c (HbA1c), %	5.8 ± 0.6	5.8 ± 0.7	5.9 ± 0.6	0.071
Serum creatinine, mg/dL	0.77 ± 0.24	0.74 ± 0.23	0.74 ± 0.35	0.144
Glomerular filtration rate (GFR), mL/min/1.73m^2	67.5 ± 15.2	70.4 ± 15.2	71.1 ± 15.4	<0.001
White blood cells (WBC), /μL	5245 ± 1407	5768 ± 1348	6240 ± 1568	<0.001
Maximum voluntary tongue pressure against the palate (MTP), kPa	29.8 ± 10.1	30.0 ± 9.8	31.7 ± 10.2	0.004

Values: mean ± standard deviation. Platelet counts among men are < 18.9 × $10^4/\mu$L for T1, 18.9-22.9 × $10^4/\mu$L for T2, and ≥ 23.0 × $10^4/\mu$L for T3, and among women are < 20.5 × $10^4/\mu$L for T1, 20.5-25.0 × $10^4/\mu$L for T2, and ≥ 25.1 × $10^4/\mu$L for T3

Table 2. Odds ratios (OR) and 95% confidence intervals (CI) for reduced maximum voluntary tongue pressure against the palate (MTP) in relation to platelet count.

	Platelet count			P for trend	1 SD increment of platelet count
	Low (T1)	T2	High (T3)		
Total subjects					
No. at risk	535	533	539		
No. of cases	124	112	85		
(percentage)	(23.2)	(21.0)	(15.8)		
Model.1	1.00	0.96 (0.71, 1.30)	0.75 (0.54, 1.03)	0.079	0.91 (0.80, 1.04)
Model.2	1.00	0.99 (0.73, 1.35)	0.78 (0.57, 1.08)	0.148	0.93 (0.82, 1.06)
Model.3	1.00	0.99 (0.73, 1.35)	0.78 (0.56, 1.09)	0.156	0.93 (0.81, 1.06)

Model.1: adjusted only for sex and age. Model.2: further adjusted for body mass index, systolic blood pressure, anti-hypertensive medication use (yes, no), alcohol consumption (never-drinker, former-drinker, current-drinker [23-45g/week, 46-68g/week, ≥ 69g/week, respectively]), smoking status (never-smoker, former-smoker, current-smoker), HDL-cholesterol, triglycerides, HbA1C, and GFR. Model.3: Model.2 + further adjusted for white blood cell count. Reduced maximum voluntary tongue pressure against the palate (MTP) is defined as a tongue pressure that is at or under the 20%th percentile of tongue pressure among the study population (<23.9kPa for men and < 21.8kPa for women). SD: standard deviation. Platelet counts among men are < 18.9 × $10^4/\mu$L for T1, 18.9-22.9 × $10^4/\mu$L for T2, and ≥ 23.0 × $10^4/\mu$L for T3, and among women are < 20.5 × $10^4/\mu$L for T1, 20.5-24.9 × $10^4/\mu$L for T2, and ≥ 25.0 × $10^4/\mu$L for T3. A 1 SD increment in platelet count is 5.4 × $10^4/\mu$L for men and 5.2 × $10^4/\mu$L for women.

when the analysis was limited to non-hypertensive subjects, a significant inverse association was observed (Table 3).

Since the study population was comprised of both non-hypertensive subjects (n=731) and hypertensive subjects (n=876), to avoid the influence of sample size bias on the correlation between platelet count and reduced MTP, we evaluated the

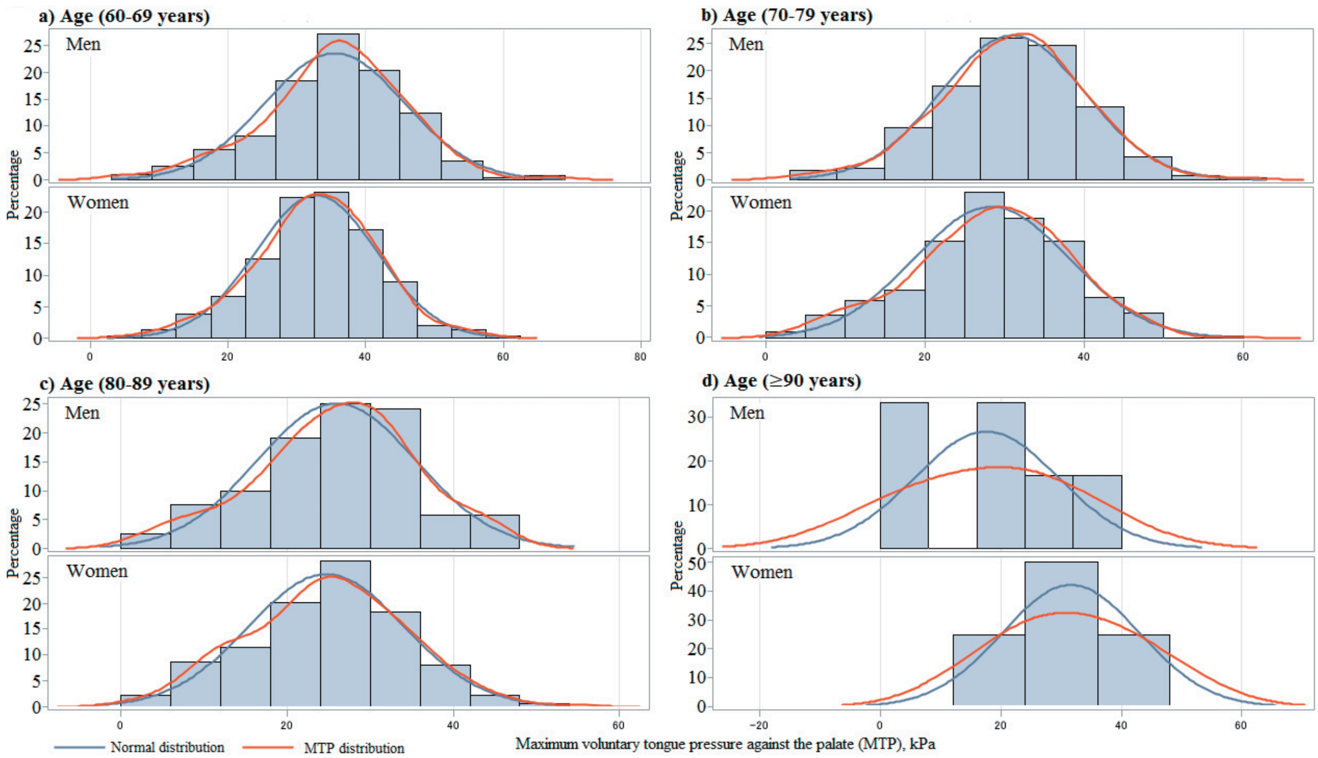

Figure 1. Sex-specific distribution of MTP by age classes

Table 3. Odds ratios (OR) and 95% confidence intervals (CI) for reduced maximum voluntary tongue pressure against the palate (MTP) in relation to platelet count by hypertension status.

	Platelet count			P for trend	1 SD increment of platelet count
	T1 (Low)	T2	T3 (High)		
Non-hypertension					
No. at risk	251	246	234		
No. of cases	73	52	28		
(percentage)	(29.1)	(21.1)	(12.0)		
Model.1	1.00	0.77 (0.50, 1.18)	0.41 (0.25, 0.68)	<0.001	0.74 (0.61, 0.91)
Model.2	1.00	0.78 (0.51, 1.21)	0.44 (0.26, 0.72)	0.001	0.75 (0.62, 0.92)
Model.3	1.00	0.76 (0.49, 1.18)	0.41 (0.24, 0.69)	<0.001	0.73 (0.60, 0.90)
Hypertension					
No. at risk	284	287	305		
No. of cases	51	60	57		
(percentage)	(18.0)	(20.9)	(18.7)		
Model.1	1.00	1.25 (0.81, 1.91)	1.23 (0.80, 1.89)	0.353	1.09 (0.92, 1.29)
Model.2	1.00	1.29 (0.84, 2.01)	1.25 (0.80, 1.94)	0.333	1.10 (0.92, 1.31)
Model.3	1.00	1.34 (0.86, 2.09)	1.31 (0.83, 2.08)	0.253	1.13 (0.94, 1.35)

Model.1: adjusted only for sex and age. Model.2: further adjusted for body mass index, systolic blood pressure, anti-hypertensive medication use (yes, no), alcohol consumption (never-drinker, former-drinker, current-drinker [23-45g/week, 46-68g/week, ≥ 69g/week, respectively]), smoking status (never-smoker, former-smoker, current-smoker), HDL-cholesterol, triglycerides, HbA1C, and GFR. Model.3: Model.2 + further adjusted for white blood cell count. Reduced maximum voluntary tongue pressure against the palate (MTP) is defined as a tongue pressure that is at and under the 20%th percentile of tongue pressure among the study population (<23.9kPa for men and <21.8kPa for women). SD: standard deviation. Platelet counts among men are < $18.9 \times 10^4/\mu L$ for T1, $18.9\text{-}22.9 \times 10^4/\mu L$ for T2, and $\geq 23.0 \times 10^4/\mu L$ for T3, and among women are < $20.5 \times 10^4/\mu L$ for T1, $20.5\text{-}24.9 \times 10^4/\mu L$ for T2, and $\geq 25.0 \times 10^4/\mu L$ for T3. A 1 SD increment in platelet count is $5.4 \times 10^4/\mu L$ for men and $5.2 \times 10^4/\mu L$ for women.

interaction between platelet count and hypertension state (non-hypertension and hypertension) on reduced tongue pressure. Significant interaction between platelet count and hypertension status was observed, with a p value for the effect of this fully adjusted interaction on reduced tongue pressure of p=0.002.

Sex-specific associations between platelets and reduced MTP by hypertension status (Table 4) show essentially the same associations for men and women.

Since diabetes might act as a confounding factor for the association between platelets and reduced MTP, we conducted a further analysis limited to subjects without diabetes, and found essentially the same associations (Table 5).

Table 4. Sex specific odds ratios (OR) and 95% confidence intervals (CI) for reduced maximum isometric tongue pressure in relation to platelet count by hypertension status.

	Platelet count			P for trend	1 SD increment of platelet count
	Low (T1)	T2	High (T3)		
Men					
Non-hypertension					
No. at risk	104	102	88		
No. of cases	25	22	10		
(percentage)	(24.0)	(21.6)	(11.4)		
Model.1	1.00	1.28 (0.63, 2.61)	0.59 (0.25, 1.37)	0.291	0.83 (0.60, 1.15)
Model.2	1.00	1.34 (0.63, 2.85)	0.63 (0.26, 1.51)	0.385	0.80 (0.57, 1.14)
Model.3	1.00	1.30 (0.61, 2.77)	0.58 (0.24, 1.44)	0.311	0.77 (0.53, 1.10)
Hypertension					
No. at risk	114	112	129		
No. of cases	20	26	27		
(percentage)	(17.5)	(23.2)	(20.9)		
Model.1	1.00	1.49 (0.76, 2.93)	1.81 (0.91, 3.59)	0.091	1.24 (0.96, 1.59)
Model.2	1.00	1.38 (0.69, 2.77)	1.57 (0.77, 3.20)	0.215	1.17 (0.90, 1.52)
Model.3	1.00	1.48 (0.73, 3.00)	1.76 (0.84, 3.70)	0.133	1.23 (0.93, 1.62)
Women					
Non-hypertension					
No. at risk	147	144	146		
No. of cases	48	30	18		
(percentage)	(32.7)	(20.8)	(12.3)		
Model.1	1.00	0.59 (0.34, 1.01)	0.34 (0.19, 0.64)	<0.001	0.70 (0.55, 0.90)
Model.2	1.00	0.60 (0.34, 1.09)	0.36 (0.19, 0.67)	0.001	0.72 (0.56, 0.92)
Model.3	1.00	0.58 (0.33, 1.02)	0.34 (0.18, 0.65)	0.008	0.70 (0.54, 0.91)
Hypertension					
No. at risk	170	175	176		
No. of cases	31	34	30		
(percentage)	(18.2)	(19.4)	(17.0)		
Model.1	1.00	1.10 (0.64, 1.91)	0.95 (0.54, 1.67)	0.856	0.98 (0.77, 1.23)
Model.2	1.00	1.27 (0.71, 2.27)	1.09 (0.61, 1.97)	0.763	1.05 (0.83, 1.34)
Model.3	1.00	1.26 (0.70, 2.27)	1.08 (0.58, 1.99)	0.743	1.04 (0.81, 1.34)

Model.1: adjusted only for age. Model.2: further adjusted for body mass index, systolic blood pressure, anti-hypertensive medication use (yes, no), alcohol consumption (never-drinker, former-drinker, current-drinker [23-45g/week, 46-68g/week, ≥ 69g/week, respectively]), smoking status (never-smoker, former-smoker, current-smoker), HDL-cholesterol, triglycerides, HbA1C, and GFR. Model.3: Model.2 + further adjusted for white blood cell count. Reduced maximum isometric tongue pressure is defined as a tongue pressure that is at and under the 20%th percentile of tongue pressure among the study population (< 23.9kPa for men and < 21.8kPa for women). SD:standard deviation. Platelet counts among men are $< 18.9 \times 10^4/\mu L$ for T1, $18.9\text{-}22.9 \times 10^4/\mu L$ for T2, and $\geq 23.0 \times 10^4/\mu L$ for T3, and among women are $< 20.5 \times 10^4/\mu L$ for T1, $20.5\text{-}24.9 \times 10^4/\mu L$ for T2, and $\geq 25.0 \times 10^4/\mu L$ for T3. A 1 SD increment in platelet count is $5.4 \times 10^4/\mu L$ for men and $5.2 \times 10^4/\mu L$ for women.

Table 5. Odds ratios (OR) and 95% confidence intervals (CI) for reduced maximum voluntary tongue pressure against the palate (MTP) in relation to platelet count by hypertension status among subjects without diabetes.

	Platelet count			P for trend	1 SD increment of platelet count
	T1 (Low)	T2	T3 (High)		
Non-hypertension					
No. at risk	218	220	210		
No. of cases	63	48	24		
(percentage)	(28.9)	(21.8)	(11.4)		
Model.1	1.00	0.80 (0.51, 1.26)	0.38 (0.22, 0.65)	<0.001	0.73 (0.59, 0.91)
Model.2	1.00	0.85 (0.54, 1.35)	0.42 (0.25, 0.73)	0.003	0.76 (0.61, 0.95)
Model.3	1.00	0.81 (0.51, 1.29)	0.38 (0.22, 0.67)	0.011	0.73 (0.58, 0.92)
Hypertension					
No. at risk	241	248	259		
No. of cases	46	55	49		
(percentage)	(19.1)	(22.2)	(18.9)		
Model.1	1.00	1.32 (0.84, 2.08)	1.21 (0.76, 1.92)	0.431	1.09 (0.91, 1.30)
Model.2	1.00	1.35 (0.85, 2.16)	1.25 (0.77, 2.03)	0.362	1.11 (0.92, 1.34)
Model.3	1.00	1.42 (0.88, 2.28)	1.33 (0.81, 2.20)	0.272	1.14 (0.94, 1.39)

Model.1: adjusted only for sex and age. Model.2: further adjusted for body mass index, systolic blood pressure, anti-hypertensive medication use (yes, no), alcohol consumption (never-drinker, former-drinker, current-drinker [23-45g/week, 46-68g/week, ≥ 69g/week, respectively]), smoking status (never-smoker, former-smoker, current-smoker), HDL-cholesterol, triglycerides, HbA1C, and GFR. Model.3: Model.2 + further adjusted for white blood cell count. Reduced maximum voluntary tongue pressure against the palate (MTP) is defined as a tongue pressure that is at and under the 20%th percentile of tongue pressure among the study population (< 23.9kPa for men and < 21.8kPa for women). SD: standard deviation. Platelet counts among men are < 18.9/μL for T1, 18.9-22.9 /μL for T2, and ≥ 23.0 /μL for T3, and among women are < 20.5/μL for T1, 20.5-24.9 /μL for T2, and ≥ 25.0 /μL for T3. A 1 SD increment in platelet count is 5.4 /μL for men and 5.2 /μL for women.

Discussion

The major finding of the present study of community dwelling elderly Japanese subjects demonstrates that independent of known cardiovascular risk factors, platelets are significantly inversely associated with reduced MTP among non-hypertensive, but not hypertensive, subjects.

Sarcopenia is associated with impairment of capillary function [3]. Low skeletal muscle capillarization may contribute to sarcopenia and reduced exercise capacity in older adults by limiting the diffusion of substrates, oxygen, hormones, and nutrients [13]. And aging has a deleterious impact on the endothelium via peripheral microcirculation [14,15].

On the other hand, platelets have been functionally implicated in a range of angiogenesis-dependent processes, including physiological roles in wound healing, vascular development and blood/lymphatic vessel separation, while facilitating aberrant angiogenesis in a range of diseases such as cancer and atherosclerosis [16]. In recent years, platelets have been revealed to play an important role in vascular endothelial repair in conjunction with circulating CD34-positive cells [16-21]. And from our previous study, platelet count acts as an indicator of vascular repair, with hypertension seen to mask the beneficial effects of increased platelet and CD34-positive cell count [7].

Age-related increases in inflammatory agents such as cytokines, advanced glycation products (AGEs) and matrix metalloproteinases (MMPs) can disrupt the microvascular endothelium, resulting in blood flow impairment [22]. Therefore, platelet count may indicate endothelial repair activity that is stimulated by aging-related endothelial injury, with hypertension acting as a strong confounding factor. Furthermore, even though platelet is significantly positively associated with arterial stiffness [7] and hypertension [23], in our previous study a significant inverse association between MTP and atherosclerosis was observed for hypertensive subjects with lower platelet (<$21.4\times10^4/\mu$L), but not for hypertensive subjects with higher platelet counts (≥$21.4\times10^4/\mu$L) [6]. Therefore, even hypertensive subjects with high platelet levels could receive a beneficial influence on the maintenance of muscle mass, although the degree of endothelial injury, which can be assessed in terms of atherosclerosis, might act as a confounding factor on the analysis in the present study for hypertensive subjects.

Since sarcopenic obesity is reported to be associated with an independent risk of hypertension [24], our present findings not only represent an efficient tool to clarify the background mechanism behind reduced MTP, but also to clarify the background mechanism underlying the association between sarcopenia and hypertension.

Potential limitations of this study warrant consideration. Although, age-related increases in inflammatory agents may influence the association between platelet count and reduced MTP, no data regarding inflammatory agents was available for this study. Further analyses that include age related inflammatory agents such as cytokines, advanced glycation products (AGEs) and matrix metalloproteinases (MMPs) will be necessary. Finally, because this was a cross-sectional study, causal relationships were not able to be established.

Conclusions

In conclusion, independent of known cardiovascular risk factors, platelets are significantly inversely associated with reduced MTP among non-hypertensive, but not hypertensive, subjects. This finding represents an efficient tool to clarify a part of background mechanism governing reduced tongue pressure.

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Disclosure statement

The authors declare no conflict of interest

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