

# Clinical Impact of Hemorheology on Subclinical Myocardial Injury in Patients with Hypertension

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## Abstract

**Background:** The blood concentration of high-sensitivity cardiac troponin T (hs-cTnT) is a useful biomarker for myocardial injury or the pathogenesis of hypertension. Little is known about the relationship between hemorheology and myocardial injury in patients with hypertension. This cross-sectional study aimed to clarify the clinical impact of hemorheology on subclinical myocardial injury assessed with a microchannel array flow analyzer (MC-FAN) and its impact on hs-cTnT in patients with hypertension.

**Methods:** A total of 447 outpatients (men: 181; women: 266; mean age:  $65 \pm 13$  years), with no history of cardiovascular disease, including admission for heart failure, who were undergoing treatment for hypertension, were enrolled. Whole blood passage time (WBPT) as a marker of hemorheology was measured with a MC-FAN, and the relationship between hs-cTnT levels and various clinical parameters, including WBPT, was examined.

**Results:** hs-cTnT levels were detected in 400 patients (89.5%). WBPT was significantly higher in patients with detectable hs-cTnT levels than in those with undetectable hs-cTnT levels ( $60.5 \pm 16.8$  s versus  $50.2 \pm 14.2$  s,  $P < 0.001$ ). In patients with detectable hs-cTnT levels, there was a significant positive correlation between WBPT and hs-cTnT level ( $r = 0.33$ ;  $P < 0.001$ ). Multiple regression analysis revealed that WBPT was an independent variable when hs-cTnT was a subordinate factor ( $\beta = 0.15$ ;  $P < 0.01$ ). Receiver-operating characteristic curve analysis indicated that a cutoff value for WBPT of 55.6 s yielded the largest area under the curve (0.744;  $P < 0.001$ ) for discriminating high hs-cTnT levels as  $\geq 0.014$  ng/mL.

**Conclusion:** The results indicate that WBPT is independently associated with hs-cTnT in hypertensive patients with no history of cardiovascular events, suggesting that impairment of hemorheology in small cardiac vessels causes subclinical myocardial injury. In addition, the study suggests that progression of myocardial injury can be prevented by maintaining WBPT at approximately  $\leq 55$  s.

**Keywords:** Hemorheology; Microchannel array flow analyzer; High-sensitivity troponin T; Advanced glycation end products; Cardio-ankle vascular index; Oxidative stress; Hypertension

## Introduction

Recent clinical studies have demonstrated that the blood concentration of cardiac troponin T (high-sensitivity cardiac troponin T (hs-cTnT)) can be measured by a highly sensitive assay. The blood concentration of hs-cTnT is a useful biomarker to evaluate myocardial injury or to predict cardiovascular events at the clinical stage [1]. In addition, several studies have reported the clinical significance of hs-cTnT in patients with hypertension [2-5].

Impairment of hemorheology is an important risk factor for cardiovascular disease as well as atherosclerosis [6, 7]. In recent years, the microchannel array flow analyzer (MC-FAN), which is a commercial device that assesses hemorheology using microscopic images, has been introduced in clinical settings [8]. MC-FAN has a simple methodology and is superior to other methods in the accuracy of channel dimensions and high reproducibility. Clinical studies have demonstrated relationships between increased whole blood passage time (WBPT), measured with MC-FAN, and cardiovascular risk factors or cardiovascular events [9-12].

Little is known about the relationships between hemorheology and myocardial injury in patients with hypertension. This study aimed to elucidate the association of WBPT with hs-cTnT in patients with hypertension and without apparent cardiovascular disease, including heart failure.

## Patients and Methods

### Study population

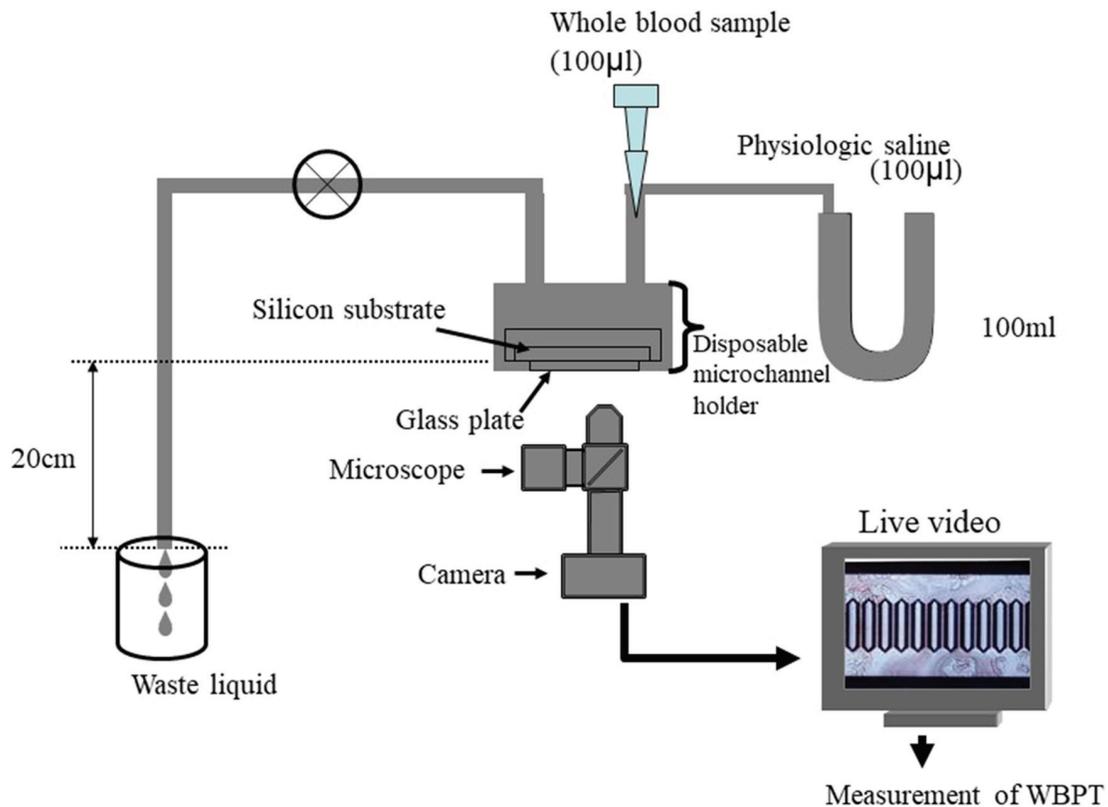
This study was conducted at the Hitsumoto Medical Clinic in Shimonoseki City, Japan, between March 2016 and February 2018. The study population comprised 447 outpatients (males: 181 (40.5%) and females: 266 (59.5%); mean age:  $65 \pm 13$  years) undergoing treatment for hypertension. No patient had a history of cardiovascular events, such as coronary artery, cerebrovascular, or peripheral vascular disease or admission for heart

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**Figure 1.** System of microchannel array flow analyzer. The microchannel passage time of 100  $\mu\text{L}$  of physiological saline was measured as a control, and then that of venous whole blood obtained from the subjects with 5% heparinization was determined. The WBPT of the subjects was expressed after correction for the passage time of physiological saline. Inter- and intra-assay coefficients of variation for WBPT were 8% and 5%, respectively. WBPT: whole blood passage time.

failure. All patients provided informed consent, and the study protocol was approved by the Local Ethics Committee of the Hitsumoto Medical Clinic (approval number: 2016-02).

### Evaluation of hemorheology by MC-FAN

The evaluation of hemorheology was performed by measuring WBPT with an MC-FAN HR300 rheometer (MC Healthcare, Tokyo, Japan), as previously reported (Fig. 1) [8, 10]. Briefly, the microchannel passage time for 100  $\mu\text{L}$  of physiological saline as a control was measured, followed by the microchannel passage time for 100  $\mu\text{L}$  of a heparinized whole blood sample obtained from a patient. The WBPT for patients was corrected for the passage time of physiological saline. The microchannel formation was 7- $\mu\text{m}$  wide, 30- $\mu\text{m}$  long and 4.5- $\mu\text{m}$  deep. WBPT was measured within 60 min of blood sampling. The inter- and intra-assay coefficients of variation for WBPT were 8% and 5%, respectively.

### Estimation of clinical parameters

Various clinical parameters, classic coronary risk factors, exercise habits, glucose-related parameters, blood cell count,

kidney function, left ventricular hypertrophy estimated by electrocardiography, brain natriuretic peptide (BNP), oxidative stress, arterial function and hs-cTnT levels were evaluated. The degree of obesity was evaluated by the body mass index, calculated as the weight in kilograms divided by the height in square meters. Exercise habits were considered positive for those who performed aerobic exercise for more than 30 min three times a week. Current smoking was defined as smoking at least one cigarette per day during the previous 28 days. Treatment with antihypertensive drugs was stopped 24 h or more before measurement, and right brachial blood pressure was measured twice with a mercurial sphygmomanometer with the patient in a sitting position. The average of two readings was used to determine systolic and diastolic blood pressure. Dyslipidemia was defined as low-density lipoprotein cholesterol level  $\geq 140$  mg/dL, high-density lipoprotein cholesterol level  $\leq 40$  mg/dL, triglyceride level  $\geq 150$  mg/dL or the use of antidyslipidemic medication. Skin autofluorescence (AF) as a marker of advanced glycation end products (AGEs) in the tissues was measured with a commercial instrument (AGE Reader<sup>TM</sup>, DiagnOptics, Groningen, The Netherlands), as described previously [13]. Briefly, AF was defined as the average light intensity per nanometer in the range between 300 and 420 nm. AF levels were expressed in arbitrary units. All measurements were taken at the volar side of the lower

arm, approximately 10 - 15 cm below the elbow fold, with the patient in a seated position. The severity of left ventricular hypertrophy was evaluated using Cornell (R wave in aVL + S wave in V3) electrocardiographic voltage calculations [14]. Arterial function was evaluated by the cardio-ankle vascular index (CAVI) using a VaSera CAVI instrument (Fukuda Den-shi, Tokyo, Japan) according to previously described methods [15]. Briefly, brachial and ankle pulse waves were determined with inflatable cuffs by maintaining the pressure between 30 and 50 mm Hg to ensure a minimal effect on systemic hemodynamics from the pressure of the cuffs. Blood pressure and pulse pressure were simultaneously measured with the patient in the supine position. CAVI was measured after the patient rested for 10 min in a quiet room. CAVI was calculated by the formula  $CAVI = a((2\rho/\Delta P) \times \ln(Ps/Pd)PWV^2) + b$ , where a and b are constants,  $\rho$  is blood density,  $\Delta P$  is Ps - Pd, Ps is systolic blood pressure, Pd is diastolic blood pressure and PWV is pulse wave velocity.

### Evaluation of blood parameters

Blood samples were collected from the antecubital vein in the morning after 12 h of fasting. Total cholesterol and triglyceride concentrations were measured by standard enzymatic methods. Serum high-density lipoprotein cholesterol concentrations were measured by selective inhibition, and serum low-density lipoprotein cholesterol concentrations were measured by the Friedewald equation [16]. Patients with a serum triglyceride concentration  $\geq 400$  mg/dL were excluded, considering the accuracy of this method. Glucose and insulin concentrations were measured by the glucose oxidase method and enzyme immunoassay, respectively. To measure insulin resistance, homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as follows [17]:  $HOMA-IR = \text{fasting glucose concentration (mg/dL)} \times \text{fasting insulin concentration } (\mu\text{g/mL})/405$ . Estimated glomerular filtration rate (eGFR) was calculated by the adjusted Modification of Diet in Renal Disease Study equation, which was proposed by the working group of the Japanese Chronic Kidney Disease Initiative [18]. The blood concentration of BNP was measured with a commercial kit (SHIONOSPOT Reader; Shionogi & Co., Osaka, Japan). The derivatives of reactive oxygen metabolites (d-ROMs) test as a marker of oxidative stress *in vivo* was conducted with a commercial kit (Diacron, Grosseto, Italy) [19]. hs-cTnT levels were also measured with a commercial kit (Roche Diagnostics, Basel, Switzerland) [20]. In the hs-cTnT assay, the lower limit of detection was 0.003 ng/mL.

### Statistical analysis

The data were analyzed by Stat View-J 5.0 (HULINKS, Tokyo, Japan) and MedCalc for Windows version 14.8.1 (MedCalc Software, Ostend, Belgium). The data are expressed as means  $\pm$  SD. Between-group comparisons were performed by Student's *t*-test or the Mann-Whitney *U* test, and the correlation coefficient was estimated by Spearman rank-order correla-

tion analysis. Multivariate analysis was conducted by multiple regression analysis. Receiver-operating characteristic (ROC) curves were constructed, and the Youden index was used to determine the optimal cutoff for WBPT for determining high hs-cTnT levels. A *P* value  $< 0.05$  was considered to indicate statistical significance.

### Results

Table 1 presents the patients' characteristics. hs-cTnT levels were detected in 400 patients (89.5%). Age, systolic blood pressure, presence of diabetes mellitus, fasting blood glucose level, HOMA-IR, skin AF, Cornell voltage, BNP, d-ROMs test, CAVI and frequency of antidiabetic medication were significantly higher and eGFR was significantly lower in patients with detectable hs-cTnT levels. WBPT was significantly higher in patients with detectable hs-cTnT levels. Correlations among hs-cTnT level, WBPT and various clinical parameters in patients with detectable hs-cTnT levels are presented in Table 2. Gender, age, presence of diabetes mellitus, fasting blood glucose level, skin AF, eGFR, Cornell voltage, BNP, d-ROMs test and CAVI were significantly correlated with hs-cTnT levels. Body mass index, exercise habits, current smoking status, presence of diabetes mellitus, skin AF, white blood cell count, hematocrit, eGFR, d-ROMs test and CAVI were significantly correlated with WBPT. The correlations between hs-cTnT level and WBPT are shown in Figure 2. Significantly positive correlations were observed between the two parameters. Table 3 shows the results of multiple regression analysis for hs-cTnT levels or WBPT as a subordinate factor. Explanatory factors were selected either by checking multicollinearity among variables or by the stepwise method. Skin AF, CAVI, WBPT, age, d-ROMs test, eGFR and BNP level were selected as independent variables when hs-cTnT level was used as a subordinate factor; CAVI, hs-cTnT level, d-ROMs test, skin AF, hematocrit, exercise habits and current smoking status were selected as independent variables when WBPT was used as a subordinate factor. Figure 3 shows the ROC curve analysis for detection of high hs-cTnT levels as  $\geq 0.014$  ng/mL based on WBPT. A WBPT cutoff of 55.6 s yielded the largest area under the curve, 0.744 (95% confidence interval: 0.699 - 0.784; *P*  $< 0.001$ ), indicating a sensitivity of 85.7% and a specificity of 57.0% for discriminating hs-cTnT levels as  $\geq 0.014$  ng/mL.

### Discussion

Yagi et al reported that the mean WBPT in healthy controls with no history of traditional cardiovascular risk factors, such as hypertension, hypercholesterolemia and diabetes mellitus, was 37.1 s [21], whereas the mean WBPT in the present study was 59.4 s. Thus, these results indicate that the impairment of hemorheology in hypertensive patients was progressive compared with that in healthy controls. Furthermore, independent associations between WBPT and hs-cTnT levels in this study suggest that the impairment of hemorheology affects the pro-

**Table 1.** Patient Characteristics

	Overall	hs-cTnT non-detection	hs-cTnT detection	P value
n (male/female)	447 (181/266)	47 (21/26)	400 (160/240)	0.535
Age (years)	65 ± 13	58 ± 12	66 ± 12	< 0.001
Body mass index (kg/m <sup>2</sup> )	23 ± 4	23 ± 3	23 ± 4	0.541
Exercise habits, n (%)	150 (34)	16 (34)	134 (34)	0.941
Current smoker, n (%)	118 (26)	11 (23)	107 (27)	0.624
Systolic BP (mm Hg)	161 ± 8	157 ± 10	162 ± 8	< 0.01
Diastolic BP (mm Hg)	96 ± 9	94 ± 10	96 ± 9	0.176
Dyslipidemia (%)	281 (63)	28 (60)	253 (63)	0.713
Total cholesterol (mg/dL)	212 ± 40	218 ± 38	211 ± 40	0.173
LDL cholesterol (mg/dL)	135 ± 36	137 ± 33	135 ± 36	0.553
Triglyceride (mg/dL)	128 ± 64	131 ± 66	128 ± 64	0.750
HDL cholesterol (mg/dL)	52 ± 15	55 ± 15	51 ± 14	0.063
Diabetes mellitus (%)	174 (39)	6 (13)	168 (42)	< 0.001
FBG (mg/dL)	116 ± 24	104 ± 20	118 ± 24	< 0.001
HOMA-IR	2.1 ± 1.4	1.5 ± 1.0	2.1 ± 1.4	< 0.01
SkinAF (AU)	2.6 ± 0.6	2.2 ± 0.6	2.6 ± 0.5	< 0.001
White blood cell (/μL)	5,610 ± 1,585	5,630 ± 1,364	5,608 ± 1,611	0.929
Hematocrit (%)	39.1 ± 5.5	39.2 ± 2.3	39.1 ± 5.8	0.943
Plate (10 <sup>4</sup> /μL)	23.8 ± 5.9	24.2 ± 8.0	23.8 ± 5.6	0.636
eGFR (mL/min/1.73 m <sup>2</sup> )	66 ± 21	73 ± 17	65 ± 22	< 0.05
Cornell voltage (mm)	15 ± 6	12 ± 7	15 ± 5	< 0.001
Log-BNP (pg/mL)	1.8 ± 0.4	1.6 ± 0.4	1.8 ± 0.3	< 0.01
d-ROMs test (U. Carr)	335 ± 101	299 ± 103	339 ± 101	< 0.01
CAVI	9.0 ± 1.4	8.5 ± 1.2	9.0 ± 1.4	< 0.01
WBPT (s)	59.4 ± 16.8	50.2 ± 14.2	60.5 ± 16.8	< 0.001
log-hs-cTnT (ng/mL)	-1.9 ± 0.3	-	-1.9 ± 0.3	-
<b>Medication</b>				
CCB, n (%)	349 (78)	40 (85)	309 (77)	0.219
RAS inhibitor, n (%)	186 (42)	22 (47)	164 (41)	0.446
β-blocker, n (%)	67 (15)	6 (13)	61 (15)	0.653
Statin, n (%)	147 (33)	14 (30)	133 (33)	0.634
Anti-diabetic drugs, n (%)	133 (30)	6 (13)	127 (32)	< 0.01

Data are expressed as mean ± SD. hs-cTnT: high-sensitivity cardiac troponin T; BP: blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; FBG: fasting blood glucose; HOMA-IR: homeostatic model assessment of insulin resistance; AF: autofluorescence; eGFR: estimated glomerular filtration rate; BNP: brain natriuretic peptide; d-ROMs: derivatives of reactive oxygen metabolites; CAVI: cardio-ankle vascular index; WBPT: whole blood passage time; CCB: calcium channel blocker; RAS: renin-angiotensin system.

gression of subclinical myocardial injury in patients with hypertension. Skin AF, CAVI and d-ROMs test were selected as independent variables for both hs-cTnT and WBPT as subordinate factors.

Hemorheology assessed by MC-FAN is an *in vitro* measurement that uses artificial blood vessels, with a 7-μm wide, 30-μm long and 4.5-μm deep vessel lumen. Thus, assessment of hemorheology by MC-FAN is assumed to correspond to values obtained for small vessels. Small vessels are consid-

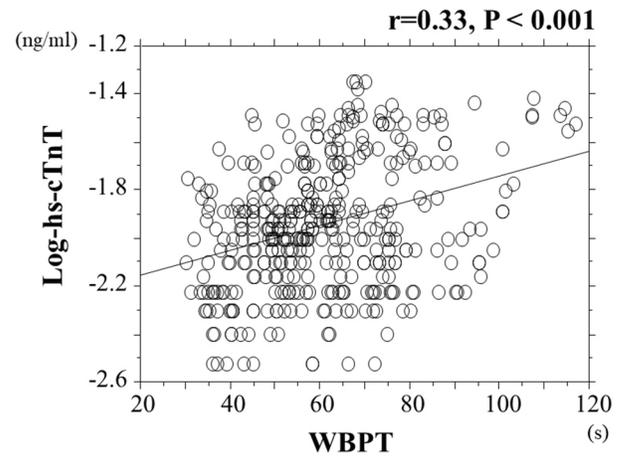
ered to be present in a portion of skin biopsies along with systemic vessels, including heart vessels. On the contrary, the results of this study indicated that skin AF as a marker of AGEs in tissues was selected as an independent variable when hs-cTnT was a subordinate factor. In addition, skin AF had an independent association with WBPT. Skin AF is reported to reflect pentosidine levels, which are major components of AGEs on the volar side of the lower arm according to the results of skin biopsy [22]. Therefore, impairment of hemor-

**Table 2.** Correlation Between hs-cTnT, WBPT and Clinical Parameters in hs-cTnT Detectable Patients

	log-hs-cTnT/r	WBPT/r
Sex (female = 0, male = 1)	-0.11*	0.05
Age	0.27***	0.08
Body mass index	0.02	0.11*
Exercise habits (No = 0, Yes = 1)	0.08	-0.16**
Current smoker (No = 0, Yes = 1)	0.10	0.17**
Systolic BP	0.09	0.06
Diastolic BP	0.07	0.03
Dyslipidemia (No = 0, Yes = 1)	0.02	0.01
Total cholesterol	0.09	0.03
LDL cholesterol	0.06	0.04
Triglyceride	0.09	0.07
HDL cholesterol	-0.03	-0.02
Diabetes mellitus (No = 0, Yes = 1)	0.16**	0.11*
FBG	0.11*	0.10
HOMA-IR	0.09	0.09
Skin AF	0.41***	0.21***
White blood cell	0.08	0.11*
Hematocrit	0.09	0.18***
Plate	0.08	0.07
eGFR	-0.19***	-0.14**
Cornell voltage	0.15**	0.09
log-BNP	0.26***	0.08
d-ROMs test	0.29***	0.29***
CAVI	0.39***	0.37***
CCB (No = 0, Yes = 1)	-0.05	-0.04
RAS inhibitor (No = 0, Yes = 1)	-0.09	-0.08
β-blocker (No = 0, Yes = 1)	-0.04	0.03
Statin (No = 0, Yes = 1)	-0.07	-0.09
Anti-diabetic drugs (No = 0, Yes = 1)	-0.09	-0.06

r: expressed correlation coefficient. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001. hs-cTnT: high-sensitivity cardiac troponin T; WBPT: whole blood passage time; BP: blood pressure; LDL: low-density lipoprotein; HDL: high-density lipoprotein; FBG: fasting blood glucose; HOMA-IR: homeostatic model assessment of insulin resistance; AF: autofluorescence; eGFR: estimated glomerular filtration rate; BNP: brain natriuretic peptide; d-ROMs: derivatives of reactive oxygen metabolites; CAVI: cardio-ankle vascular index; CCB: calcium channel blocker; RAS: renin-angiotensin system.

heology is a possible cause of the accumulation of AGEs in systemic tissues, including the heart. In addition, Hofmann et al have clarified a significant relationship between AGE-modified cardiac tissue collagen and skin AF [23]. Several pathways by which AGEs or their receptors influence myocardial injury have been reported [24-26]. Furthermore, basic studies have indicated that AGEs influence hemorheology by mechanisms such as platelet aggregation, leukocyte-endothelial in-



**Figure 2.** Relationship between hs-cTnT and WBPT. There is significantly positive correlation between log-hs-cTnT and WBPT (r = 0.33, P < 0.001). hs-cTnT: high-sensitivity troponin T; WBPT: whole blood passage time.

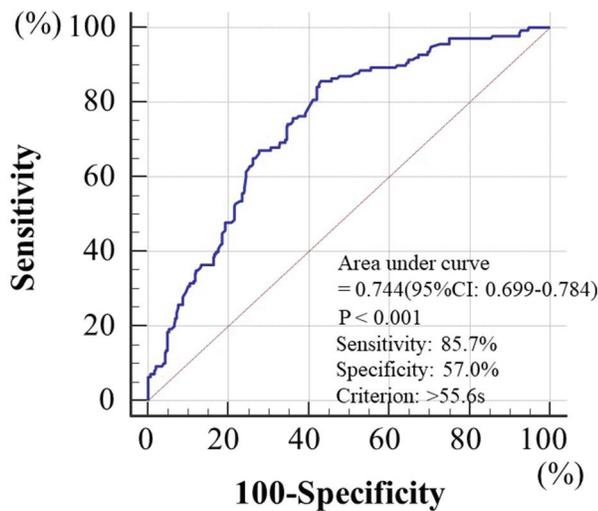
teraction and morphological changes in the erythrocyte membrane [27-29]. Thus, the results of this and previous studies indicate that hemorheology and AGEs are associated not only on the volar side of the lower arm but also in small cardiac vessels, consequently leading to myocardial injury in patients with hypertension.

CAVI is explored as a marker of arterial stiffness, which

**Table 3.** Multiple Regression Analysis

Explanatory factor	β	P value
(A)Skin AF	0.27	< 0.001
CAVI	0.16	< 0.01
WBPT	0.15	< 0.01
Age	0.13	< 0.01
d-ROMs test	0.12	< 0.01
eGFR	-0.11	< 0.01
log-BNP	0.10	< 0.05
Cornell voltage	0.09	0.068
(B)CAVI	0.26	< 0.001
log-hs-cTnT	0.18	< 0.01
d-ROMs test	0.17	< 0.01
Skin AF	0.15	< 0.01
Hematocrit	0.13	< 0.01
Exercise habits	-0.12	< 0.01
Current smoker	0.11	< 0.05
eGFR	-0.09	0.057

(A) Subordinate factor is log-hs-cTnT, R<sup>2</sup> = 0.35; (B) subordinate factor is WBPT, R<sup>2</sup> = 0.30. AF: autofluorescence; CAVI: cardio-ankle vascular index; WBPT: whole blood passage time; d-ROMs: derivatives of reactive oxygen metabolites; eGFR: estimated glomerular filtration rate; BNP: brain natriuretic peptide; hs-cTnT: high-sensitivity cardiac troponin T.



**Figure 3.** Cutoff value of WBPT for discriminating hs-cTnT levels as  $\geq 0.014$  ng/mL. Receiver-operating characteristic indicated that a WBPT cutoff of 55.6 s yielded the largest area under the curve, 0.744 (95% confidence interval: 0.699 - 0.784;  $P < 0.001$ ), indicating a sensitivity of 85.7% and a specificity of 57.0% for discriminating hs-cTnT levels as  $\geq 0.014$  ng/mL. WBPT: whole blood passage time; hs-cTnT: high-sensitivity troponin T.

is independently associated with blood pressure [15]. Several recent studies have reported the significance of left ventricular dysfunction in the progression of myocardial injury. Furthermore, increases in aortic artery stiffness or arterial reflection wave are known to be caused by left ventricular dysfunction [30, 31]. Therefore, the independent relationship between CAVI and hs-cTnT identified in this study is thought to reflect subclinical myocardial injury via left ventricular dysfunction resulting from an increase in afterload or arterial reflection wave. In addition, some researchers have reported that CAVI reflects endothelial function [32, 33]. Endothelial dysfunction has also been known to cause left ventricular dysfunction and myocardial injury [34, 35]. Thus, the results of this study indicate the importance of arterial dysfunction in subclinical myocardial injury in patients with hypertension. CAVI was also selected as an independent variable for WBPT as a subordinate factor in multivariate analysis. Some studies have reported relationships between WBPT and arterial function, such as arterial stiffness, endothelial function and vascular resistance [9, 21, 36, 37]. Therefore, increased WBPT due to increased hs-cTnT levels may be partly explained by arterial dysfunction.

A number of studies indicate that oxidative stress has a crucial role in the pathogenesis of hypertension [38, 39]. The results of the present study also indicate that the d-ROMs test, as a marker of oxidative stress, is associated with both myocardial injury and hemorheology in patients with hypertension. Several pathways have been identified by which oxidative stress causes myocardial injury, such as dysfunction of the mitochondrial electron transport complex, activity of nicotinamide adenine dinucleotide phosphate oxidase, apoptosis of myocardial cells and nitric oxide synthase uncoupling [40-42]. In addition, several mechanisms are also reported by which oxidative stress causes impairment of hemorheology, such as

platelet aggregation and elevation of plasma viscosity [43, 44]. Thus, oxidative stress is an important target factor for the prevention of both the progression of myocardial injury and impairment of hemorheology in patients with hypertension.

It is useful to have target cutoff levels of WBPT for predicting abnormal hs-cTnT levels in clinical settings. This study clarifies the clinical usefulness of assessing WBPT to detect hs-cTnT levels as high as  $\geq 0.014$  ng/mL, which is shown to be discriminatory of increased hs-cTnT levels [45]. ROC curve analysis for hs-cTnT levels as high as  $\geq 0.014$  ng/mL indicated that a cutoff value for WBPT of 55.6 s yielded the largest area under the curve (0.744) for discriminating high hs-cTnT levels. Although this was a cross-sectional study, we believe that it is possible to evaluate the risk of the progression of myocardial injury in patients with hypertension by measuring WBPT. Some clinical studies have indicated that medication, exercise habits and smoking cessation improve hemorheology [46-51]. In this cross-sectional study, exercise habits and current smoking status were independently associated with WBPT, although no significant association was observed between medication and WBPT. We suggest that progression of myocardial injury can be prevented by interventions, such as lifestyle modification or aggressive use of medication, which is effective to improve hemorheology in hypertensive patients to maintain WBPT at approximately  $\leq 55$  s.

This study has several limitations. First, the contents of medical treatment may have influenced the study results. Second, angiography, computed tomography, magnetic resonance imaging and echocardiography were not performed; thus, asymptomatic cardiovascular diseases may have remained undetected. Third, assessment of hemorheology by MC-FAN is an *in vitro* method that uses artificial blood vessels; therefore, the hemorheological data obtained might differ from those obtained *in vivo* because of the influence of vascular factors, such as endothelial or smooth muscle cells. However, the results of this study indicate that WBPT is a considerable risk factor for the progression of subclinical myocardial injury in patients with hypertension. Finally, this study was cross-sectional and conducted in a single unit with a relatively small sample size. Future multicenter prospective studies, including intervention therapies, will be required to confirm the results of this study.

## Conclusions

WBPT is independently associated with hs-cTnT in hypertensive patients with no history of cardiovascular events, suggesting that impairment of hemorheology in small cardiac vessels causes subclinical myocardial injury. In addition, this study suggests that the progression of myocardial injury can be prevented by maintaining WBPT at approximately  $\leq 55$  s. Additional prospective studies, including intervention therapies, will be required to confirm the results of this study.

## Conflict of Interest

The author has no competing interests.

## Grant Support

None.

## Financial Disclosure

The author has reported no conflicts of interest.

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