

# Associations between the psoas major muscle index and the presence and severity of coronary artery disease

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## Abstract

The associations between the presence and severity of coronary artery disease (CAD) and measurements of the psoas major muscle (PMM) as assessed by multidetector row coronary computed tomography angiography (MDCT) are not known.

We enrolled 793 patients who were clinically suspected to have CAD or had at least one cardiac risk factor and had undergone MDCT. The number of significantly stenosed coronary vessels (VD) and measurements of the PMM index (PMMI) were determined using MDCT.

PMMI in the CAD group was significantly lower than that in the non-CAD group in males, but not females. In addition, the levels of PMMI tended to increase as the number of VD decreased in males. When male patients were divided into 2 groups according to median value of age, that is, relatively younger ( $53.4 \pm 9.2$  years) and older ( $72.6 \pm 5.7$  years) groups, the presence of CAD was independently associated with PMMI in the younger group by a multiple logistic regression analysis. The cut-off level of PMMI that gave the greatest sensitivity and specificity for the diagnosis of CAD in younger males was  $8.3 \text{ cm}^2/\text{m}^2$  (sensitivity 0.441, specificity 0.752).

In conclusion, PMMI may be an imaging marker for evaluating the presence and/or severity of CAD in males, and particularly in the non-elderly.

**Abbreviations:** ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin II receptor blocker, AUC = the area-under-the-curve, BMI = body mass index, CAD = coronary artery disease, CCB = calcium channel blocker, DBP = diastolic blood pressure, DL = dyslipidemia, DM = diabetes mellitus, DPP-4I = dipeptidyl peptidase-4 inhibitor, FBG = fasting blood glucose, HbA1c = hemoglobin A1c, HDL-C = high-density lipoprotein cholesterol, HTN = hypertension, LDL-C = low-density lipoprotein cholesterol, MDCT = multi-detector row computed tomography, MetS = metabolic syndrome, MI = myocardial infarction, PMMI = psoas major muscle index, ROC = a receiver-operating characteristic curve, SBP = systolic blood pressure, SFAI = subcutaneous fat area index, SU = sulfonyleurea, TC = total cholesterol, TG = triglyceride, UA = uric acid, VD = the number of significantly stenosed coronary vessels, VFAI = visceral fat area index.

**Keywords:** coronary artery disease, multidetector row coronary computed tomography angiography, psoas major muscle, stenosed coronary vessels

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TI and YS are equally to this manuscript.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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## 1. Introduction

Coronary artery disease (CAD) is mainly caused by arteriosclerosis. There are various risk factors for the onset and/or progression of CAD, such as hypertension (HTN), diabetes mellitus (DM), dyslipidemia (DL), and metabolic syndrome (MetS). Many studies have shown that visceral fat has a detrimental effect on metabolism and the risk of CAD.<sup>[1–3]</sup> The best tool for estimating visceral fat is multi-detector row computed tomography (MDCT). MDCT has become more widely available in many general hospitals and enables the accurate non-invasive assessment of coronary artery stenosis,<sup>[4]</sup> calcification,<sup>[5]</sup> and plaque.<sup>[6]</sup> Aging is also a risk factor for CAD,<sup>[7]</sup> and the proportion of multi-vessel CAD has been reported to increase with aging.<sup>[8]</sup> In addition, aging has been reported to be associated with sarcopenia.<sup>[9]</sup> Sarcopenia is a progressive and generalized skeletal muscle condition that is associated with an increased likelihood of adverse outcomes, including falls, fractures, physical disability and mortality. Diagnostic criteria for sarcopenia include low muscle strength, low muscle quantity or quality, and low physical performance.<sup>[10]</sup> Muscle mass can be measured by bioelectrical impedance analysis or dual-energy X-ray absorptiometry. Recently, a method for

measuring muscle mass by CT has been reported. The quantification of muscle mass by CT is associated with the prognosis of cancer<sup>[11,12]</sup> and liver cirrhosis.<sup>[13]</sup> It has also been considered that a psoas major muscle index (PMMI) may be useful for evaluating the skeletal muscle mass for the whole body.<sup>[14]</sup> The PMM is measured using image-viewing software by tracing the PMM at the lumbar L3 cross-section by CT.<sup>[13]</sup> Although it has been reported that there is a relation between atherosclerosis and low muscle mass,<sup>[15,16]</sup> the association between the presence and/or severity of CAD and PMMI is unclear.

Since the elderly patients have lower PMM associated with sarcopenia, and since aging is a risk factor for CAD, we hypothesized that PMM may be an imaging marker for evaluating the presence and/or severity of CAD. Therefore, we determined the levels of PMMI quantified using MDCT and image-viewing software, and investigated the association between PMMI and the presence and/or severity of CAD.

## 2. Methods

### 2.1. Study Subjects

Seven hundred ninety-three consecutive subjects who were clinically suspected of having CAD or who had at least one cardiac risk factor were enrolled in this cross-sectional study. All subjects underwent MDCT coronary angiography between April 2012 and August 2017. Patients with creatinine >2.0 mg/dl or contrast-induced allergy did not undergo MDCT. The protocol in this study was approved by the ethics committee of Fukuoka University Hospital, and all subjects gave their written informed consent to participate.

### 2.2. Evaluation of coronary stenosis using MDCT

We evaluated coronary stenosis using MDCT as previously described.<sup>[17]</sup> Two hundred sixty-nine patients who underwent MDCT were scanned by 64-MDCT on an Aquilion 64 (TOSHIBA, Tokyo, Japan), and 524 of these were scanned by 320-MDCT on an Aquilion ONE ViSION (TOSHIBA, Tokyo, Japan). The use of beta-blocker and nitroglycerin before scanning was left to the physician's discretion. In the first MDCT, a 70-mL bolus of contrast medium (Omnipaque, 350 mg iodine/mL; Daiichi Sankyo Co., Ltd., Tokyo, Japan) was injected at a flow rate of 3.6 mL/s, followed by 35 mL contrast agent and 30 mL saline solution, each at 1.8 mL/s, with a dual injector. In the second MDCT, 21.5 mgI/kg/s contrast medium (Iopamiron, 370 mg iodine/mL; Bayer Yakuhin. Ltd, Osaka, Japan) equivalent to the patient's body weight  $\times$  0.7 mL was injected over 10 seconds, followed by 35 mL contrast agent and 30 mL saline solution, each at 1.8 mL/s, with a dual injector.

The region of interest was placed within the ascending aorta, and the scan was started when the CT density reached 100 Hounsfield Units higher than the baseline CT density. The scan was performed between the tracheal bifurcation and diaphragm with the following parameters: 64-MDCT-collimation width 0.5 mm, rotation speed 0.4s/rotation, tube voltage 135 kV, and effective tube current 360 mA; 320-MDCT-collimation width 0.5 mm, rotation speed 0.275 sec/rotation, tube voltage 120 kV, and auto tube current.

Overall, 15 coronary artery segments were assessed in all patients. Narrowing of the normal contrast-enhanced lumen to  $\geq 50\%$  that could be identified in multiplanar reconstructions or cross-sectional

images was defined as significant stenosis in CAD. In addition, in all patients, the atherosclerotic severity of coronary artery disease was assessed in terms of the Gensini score.<sup>[18,19]</sup>

### 2.3. Measurement of psoas major muscle

CT scans were performed by MDCT and Ziostation workstation (Ziosoft Inc., Tokyo, Japan). When we performed CT imaging of the coronary artery and measured visceral fat area (VFA) and subcutaneous fat area (SFA) at the umbilical level (L4 to L5),<sup>[20]</sup> we measured PMM simultaneously at the umbilical level.<sup>[21]</sup> PMM was quantified using MDCT and image-viewing software (Osirix 9.0, Geneva, Switzerland) (Fig. 1). PMMI, VFA index (VFAI) and SFA index (SFAI) were calculated as PMM/height (m)<sup>2</sup>, VFA/height (m)<sup>2</sup> SFA/height (m)<sup>2</sup>, respectively.

### 2.4. Evaluation of risk factors for CAD

Body mass index (BMI), systolic blood pressure (SBP), diastolic BP (DBP), serum levels of total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C), uric acid (UA), fasting blood glucose (FBG), hemoglobin A1c (HbA1c), smoking status (current versus nonsmokers), family history [myocardial infarction (MI), angina pectoris or sudden death] and medication use were collected as risk factors in all patients.

BMI was calculated as weight (kg)/height (m)<sup>2</sup>. BP was determined as the mean of two measurements obtained in an office setting by the conventional cuff method using a mercury sphygmomanometer after at least 5 minutes of rest. All of the blood samples were drawn in the morning after the patients had fasted overnight. The characteristics of patients were obtained from medical records with regard to history of HTN, DL, DM and history of smoking. Patients who had a current SBP/DBP  $\geq 140/90$  mmHg or who were receiving antihypertensive therapy were considered to have HTN. Patients with LDL-C  $\geq 140$  mg/dl, TG  $\geq 150$  mg/dl, and/or HDL-C <40 mg/dl or who were receiving lipid-lowering therapy were considered to have DL.<sup>[22]</sup> DM was defined using the American Diabetes Association criteria<sup>[23]</sup> or the administration of a glucose-lowering drug.

### 2.5. Statistical analysis

A statistical analysis was performed using Excel 2016 (SSRI, Tokyo, Japan), the Stat View statistical software package (Stat



Figure 1. Measurement of the psoas major muscle index (PMMI).

View 5; SAS Institute Inc., Cary, NC) and EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan). Continuous variables are shown as the mean ± standard deviation. Categorical and continuous variables were compared between the groups by a chi-square analysis and *t* test, respectively. A multivariate analysis was performed by a logistic regression analysis for independent variables that were related to the presence or absence of CAD. A receiver-operating characteristic (ROC) curve analysis was used to determine the cut-off levels of PMMI to distinguish between the presence and absence of CAD at the highest possible sensitivity and specificity levels. A value of *P* < .05 was considered significant.

### 3. Results

#### 3.1. Patient characteristics in all patients and the non-CAD and CAD groups

Table 1 shows the characteristics of the 793 patients, who consisted of 379 (48%) males and 414 (52%) females. The frequencies of HTN, DM and DL in all patients were 64%, 20%, and 56%, respectively. The mean age was 66 ± 12 years and BMI was 23.8 ± 3.6 kg/m<sup>2</sup>.

There were several significant differences in patient characteristics between the non-CAD and CAD groups. The CAD group showed a significantly higher age, % males, % Smoking, % HTN, SBP, DBP, % DL, % DM, FBG, HbA1c, VFAI, and Gensini score, and significantly lower levels of HDL-C than the non-CAD group. The percentages of the use of angiotensin II receptor blocker (ARB)/angiotensin-converting enzyme inhibitor (ACEI), calcium channel blocker (CCB) and statin in all patients were 36%, 38%, and 32%, respectively. There were significant differences in medications between the non-CAD and CAD groups. The CAD group showed significantly higher percentages of the use of ARB/ACEI, CCB, β-blocker, statin, sulfonylurea (SU), and dipeptidyl peptidase-4 inhibitor (DPP-4I) than the non-CAD group.

#### 3.2. Patient characteristics in the non-CAD and CAD groups in males and females

Table 2 shows the differences in patient characteristics between the non-CAD and CAD groups in males and females. The CAD group showed a significantly higher age, % HTN, SBP, HbA1c, VFAI and Gensini score, and significantly lower levels of PMMI and HDL-C than the non-CAD group in males. The CAD group also showed significantly higher percentages of the use of statin than the non-CAD group in males. Among females, the CAD group showed a significantly higher age, % HTN, SBP, % DL, % DM, HbA1c, FBG and Gensini score and a significantly lower level of HDL-C than the non-CAD group. The CAD group also showed significantly higher percentages of the use of ARB/ACEI, CCB, β-blocker, statin, SU, and DPP-4I than the non-CAD group in females.

#### 3.3. Measurements of PMMI in the non-CAD and CAD groups

As shown in Tables 1 and 2, we analyzed whether there were differences in PMMI between the non-CAD and CAD groups in all patients, males and females. Although there was no difference in PMMI between the non-CAD and CAD groups in all patients, among males, PMMI in the CAD group was significantly lower than that in the non-CAD group.

**Table 1**  
Patient characteristics in all patients, non-CAD and CAD groups.

	All (n = 793)	non-CAD group (n = 391)	CAD group (n = 402)	non-CAD group vs CAD group P value
Age, yr	66 ± 12	62 ± 13	69 ± 10	<.0001
Gender (male), %	48	41	55	.0001
Family history, %	23	23	23	.963
Smoking, %	34	31	38	.029
BMI, kg/m <sup>2</sup>	23.8 ± 3.6	23.8 ± 3.5	23.8 ± 3.7	.896
HTN, %	64	56	72	<.0001
SBP, mmHg	136 ± 19	132 ± 17	139 ± 21	<.0001
DBP, mmHg	78 ± 13	77 ± 13	79 ± 13	.016
DL, %	56	51	60	.015
TG, mg/dl	137 ± 102	133 ± 108	141 ± 97	.254
HDL-C, mg/dl	57 ± 16	59 ± 17	54 ± 15	<.0001
LDL-C, mg/dl	115 ± 33	116 ± 34	113 ± 31	.194
DM, %	20	14	25	<.0001
HbA1c, %	6.1 ± 1.7	5.9 ± 0.8	6.3 ± 2.2	.002
FBG, mg/dl	107 ± 30	103 ± 29	112 ± 30	<.0001
PMMI, cm <sup>2</sup> /m <sup>2</sup>	7.1 ± 2.1	7.1 ± 2.1	7.1 ± 2.0	.847
VFAI, cm <sup>2</sup> /m <sup>2</sup>	45 ± 23	42 ± 22	47 ± 23	.005
SFAI, cm <sup>2</sup> /m <sup>2</sup>	62 ± 33	64 ± 33	60 ± 33	.077
Gensini score	11.2 ± 15.2	2.8 ± 3.8	19.4 ± 17.6	<.0001
Medications				
ARB/ACE-I, %	36	30	42	.0005
CCB, %	38	31	45	.0001
β-blocker, %	9.0	5.6	12	.001
DU, %	9.5	8.2	11	.227
Statin, %	32	25	38	.0001
Fibrate, %	1.0	1.0	1.0	.969
Ezetimib, %	1.9	2.8	1.0	.060
EPA, %	3.8	3.6	4.0	.769
SU, %	7.6	5.1	10	.014
α-GI, %	2.3	1.5	3.0	.171
Biguanide, %	6.3	4.9	7.7	.099
Thiazolidine, %	2.8	2.8	2.7	.948
DPP-4I, %	10	7.2	13	.005
Insulin, %	3.0	2.8	3.2	.730

Continuous variables are expressed as mean ± SD. CAD = coronary artery disease, BMI = body mass index, HTN = hypertension, SBP = systolic blood pressure, DBP = diastolic blood pressure, DL = dyslipidemia, TG = triglyceride, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, DM = diabetes mellitus; HbA1c = hemoglobin A1c, FBG = fasting blood glucose, PMMI = psoas major muscle index, VFAI = visceral fat area index, SFAI = subcutaneous fat area index, ARB = angiotensin II receptor blocker, ACE-I = angiotensin-converting enzyme inhibitor, CCB = calcium channel blocker, DU = diuretic, EPA = eicosapentaenoic acid, SU = sulfonylurea, α-GI = α-glucosidase inhibitor, DPP-4I = dipeptidyl peptidase-4 inhibitor.

#### 3.4. Association between PMMI and the number of significantly stenosed coronary vessels (VD)

The subjects were divided into 4 groups according to the number of significantly stenosed coronary vessels (0, 1, 2, and 3 VD groups) (Fig. 2). PMMI tended to increase as the number of VD increased in males (*P* for trend < .001), but not females. Males with multi-VD (2 and 3 VD) had significantly lower levels of PMMI than those with 0 VD.

#### 3.5. Associations between PMMI and age in all patients, males and females

PMMI was negatively associated with age in all patients, males and females (Fig. 3). The association between PMMI and age in

**Table 2**  
Patient characteristics in males and females with or without CAD.

	Males (n=379)			Females (n=414)		
	non-CAD group (n=160)	CAD group (n=219)	non-CAD vs CAD P value	non-CAD group (n=231)	CAD group (n=183)	non-CAD vs CAD P value
Age, yr	59 ± 14	66 ± 10	<.0001	65 ± 12	71 ± 9	<.0001
Family history, %	20	18.7	.756	26	28	.513
Smoking, %	53	60.3	.166	15	12	.279
BMI, kg/m <sup>2</sup>	24.4 ± 3.3	24.3 ± 3.7	.820	23.4 ± 3.7	23.3 ± 3.7	.727
HTN, %	59	70	.034	53	75	<.0001
SBP, mmHg	135 ± 16	140 ± 20	.007	130 ± 18	139 ± 21	<.0001
DBP, mmHg	81 ± 12	82 ± 13	.480	74 ± 13	76 ± 13	.158
DL, %	50	58	.123	52	62	.046
TG, mg/dl	156 ± 145	153 ± 118	.809	117 ± 68	127 ± 61	.102
HDL-C, mg/dl	55 ± 15	50 ± 12	.0008	63 ± 17	58 ± 17	.009
LDL-C, mg/dl	112 ± 34	111 ± 31	.848	119 ± 34	115 ± 32	.244
DM, %	21	29	.098	9.1	21	<.001
HbA1c, %	5.9 ± 1.0	6.4 ± 2.8	.038	5.9 ± 0.7	6.0 ± 0.7	.005
FBG, mg/dl	109 ± 33	113 ± 30	.237	99 ± 26	110 ± 29	<.0001
PMMI, cm <sup>2</sup> /m <sup>2</sup>	8.7 ± 2.0	8.2 ± 1.8	.006	5.9 ± 1.3	5.8 ± 1.3	.336
VFAI, cm <sup>2</sup> /m <sup>2</sup>	44 ± 22	49 ± 23	.034	41 ± 22	44 ± 24	.170
SFAI, cm <sup>2</sup> /m <sup>2</sup>	46 ± 20	47 ± 24	.840	77 ± 34	76 ± 36	.866
Gensini score	3.3 ± 4.2	22.5 ± 20.7	<.0001	2.3 ± 3.4	15.7 ± 11.9	<.0001
Medications						
ARB/ACE-I, %	33	42	.060	29	43	.004
CCB, %	30	37	.157	32	54	<.0001
β-blocker, %	6.3	12	.066	5.2	13	.007
DU, %	7.5	10	.393	8.7	12	.342
Statin, %	24	34	.048	26	43	<.001
Fibrate, %	1.3	1.4	.920	0.9	0.5	.744
Ezetimib, %	2.5	0.9	.223	3.0	1.1	.180
EPA, %	1.3	4.1	.102	5.2	3.8	.510
SU, %	8.1	12	.263	3.0	7.7	.043
α-GI, %	2.5	4.1	.397	0.9	1.6	.475
Biguanide, %	6.9	11	.133	3.5	3.3	.918
Thiazolidine, %	3.1	2.7	.826	2.6	2.7	.933
DPP-4I, %	10	15	.183	5.2	12	.019
Insulin, %	5.0	2.3	.152	1.3	4.4	.054

Continuous variables are expressed as mean ± SD.

CAD = coronary artery disease, BMI = body mass index, HTN = hypertension, SBP = systolic blood pressure, DBP = diastolic blood pressure, DL = dyslipidemia, TG = triglyceride, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, DM = diabetes mellitus, HbA1c = hemoglobin A1c, FBG = fasting blood glucose, PMMI = psoas major muscle index, VFAI = visceral fat area index, SFAI = subcutaneous fat area index, ARB = angiotensin II receptor blocker, ACE-I = angiotensin-converting enzyme inhibitor, CCB = calcium channel blocker, DU = diuretic, EPA = eicosapentaenoic acid, SU = sulfonylurea, α-GI = α-glucosidase inhibitor, DPP-4I = dipeptidyl peptidase-4 inhibitor.

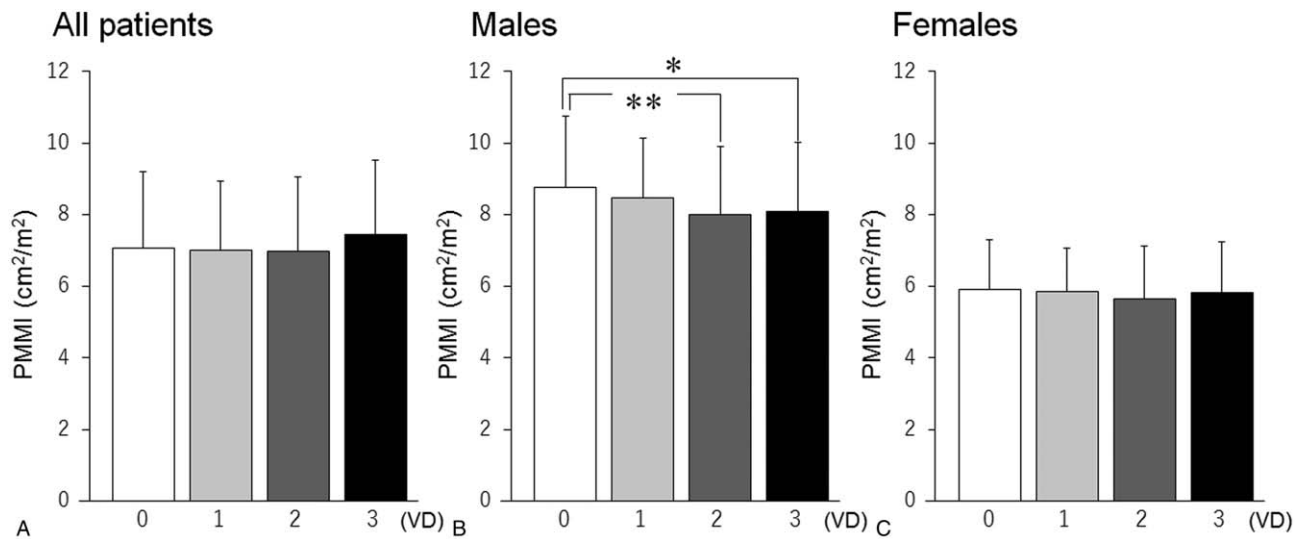
males was relatively high ( $r = -0.437$ ), whereas that in females was very low ( $r = -0.136$ ).

Further, all patients were divided into 2 groups according to median value of age; relatively younger ( $56.4 \pm 9.2$  years) and older ( $74.6 \pm 5.3$  years) groups. Next, the patients of each gender were divided into 2 groups according to age; relatively younger ( $53.4 \pm 9.2$  years) and older ( $72.6 \pm 5.7$  years) groups in males, and relatively younger ( $59.5 \pm 8.7$  years) and older ( $76.0 \pm 4.9$  years) groups in females. Associations between age and PMMI in the younger and older groups were determined. Among males, PMMI in the younger ( $r = -0.170$ ,  $P = .019$ ) and older ( $r = -0.209$ ,  $P = .004$ ) groups were significantly negatively associated with age, but the  $r$  values were relatively low.

### 3.6. Predictors of the presence of CAD in all patients, males and females

Since PMMI in the CAD group was significantly lower than that in the non-CAD group in males (Table 2), we sought to identify

predictors of the presence of CAD in males using independent variables by a logistic regression analysis in Table 3 (males) and 4 (females). We selected conventional coronary risk factors (age, BMI or VFAI, HTN, DL, DM and smoking) and PMMI (Table 3A–C). In all males, the presence of CAD was independently associated with age ( $P < .0001$ ) (Table 3A). We also sought to identify predictors of the presence of CAD in younger (Table 3B) and older (Table 3C) groups in males separately using independent variables, including conventional coronary risk factors and PMMI, by a logistic regression analysis. Because PMMI in male patients with CAD ( $8.98 \pm 1.97$  cm<sup>2</sup>/m<sup>2</sup>) tended to be lower than that in males without CAD ( $9.46 \pm 1.78$  cm<sup>2</sup>/m<sup>2</sup>) in the younger group ( $P = .08$ ), but not the older group ( $7.70 \pm 1.57$  cm<sup>2</sup>/m<sup>2</sup> in patients with CAD vs  $7.36 \pm 1.63$  cm<sup>2</sup>/m<sup>2</sup> in patients without CAD,  $P = .182$ ). The presence of CAD in younger males was associated with PMMI ( $P = .038$ ) in addition to age ( $P < .001$ ) and BMI ( $P = .042$ ), whereas there was no association between the presence of CAD and PMMI in older males. When we performed a logistic regression analysis using



**Figure 2.** Psoas major muscle index (PMMI) in all patients (A), males (B) and females (C) in the 0-VD, 1-VD, 2-VD, and 3-VD groups. VD = the number of significantly stenosed coronary vessels. \*\**P* < .01; \**P* < .05.

VFAI instead of BMI as an independent variable (Table 3D–F), the presence of CAD in younger males was not associated with VFAI and PMMI. There were differences in predictors of CAD in younger males between the results by a logistic regression analysis using BMI (Table 3B) and the results using VFAI (Table 3E) probably because VFAI was weakly associated with PMMI ( $r = 0.283, P < .0001$ ).

In all females, a logistic regression analysis using BMI as an independent variable indicated that the presence of CAD was associated with age ( $P < .001$ ), HTN ( $P = .003$ ) and DM ( $P = .007$ ) (Table 4A). The presence of CAD in younger and older females were associated with DM ( $P = .006$ ) and HTN ( $P = .017$ ), respectively (Table 4B and C), whereas there was no association between the presence of CAD and PMMI in all females, younger and older females Table 4A–C). When we performed a logistic regression analysis using VFAI instead of BMI as an independent variable (Table 4D), the presence of CAD was associated with age, HTN and DM. Predictors in the presence of CAD by a logistic regression analysis using VFAI as an independent variable were similar to those using BMI in all females, younger and older females (Table 4D–F).

**3.7. Cut-off values of PMMI and VFAI in younger males for the diagnosis of CAD**

We performed a ROC curve analysis to determine PMMI in younger males related to the presence of CAD (Fig. 4A). The ROC curve analysis showed that the area-under-the-curve (AUC) of PMMI was 0.582 (sensitivity 0.441, specificity 0.752). The cut-off level of PMMI that gave the greatest sensitivity and specificity for the diagnosis of CAD in younger males was  $8.3 \text{ cm}^2/\text{m}^2$ .

Since there was a significant difference in VFAI between non-CAD and CAD groups in males as shown in Table 2, we also performed a ROC curve analysis to determine VFAI in younger males related to the presence of CAD (Fig. 4B). The AUC and cut-off level of VFAI were 0.590 (sensitivity 0.566, specificity 0.608) and  $48.7 \text{ cm}^2/\text{m}^2$ , respectively. The AUC in VFAI was comparable to that in PMMI.

**4. Discussion**

In the present study, we investigated the associations between PMMI and the presence and severity of CAD as assessed by MDCT. PMMI in males, but not females, was associated with the presence and severity of CAD. Unexpectedly, in particular, the presence of CAD was independently associated with PMMI in non-elderly males, but not elderly males, by a multivariate logistic regression analysis.

The main finding in this study was that PMMI in males, but not females, was associated with the presence and severity of CAD. There may be some mechanisms why there was a gender difference. Although a reduction in muscle mass has been reported to be associated with atherosclerosis, this association was recognized only in males.<sup>[16]</sup> Testosterone increases muscle mass by increasing muscle protein synthesis.<sup>[24]</sup> In addition, low testosterone levels in males have been associated with an increased atherosclerosis burden and increased risk of cardiovascular events.<sup>[25,26]</sup> Atherosclerosis induced by testosterone deficiency in male mice was T-cell-dependent.<sup>[27]</sup> Testosterone may play a role in both muscle mass reduction and the mechanism of arteriosclerosis. Although we did not measure testosterone in this study, testosterone is known to decrease with age in males, but not females.<sup>[28]</sup> We found that the association between PMMI and age in males was relatively high ( $r = 0.437$ ), whereas that in females was very low ( $r = 0.136$ ). This suggests that testosterone might contribute to the association between muscle mass and CAD in males.

Next, the presence of CAD was independently associated with PMMI in younger males, but not older males, although the presence of CAD was most strongly associated with age by a multivariate logistic regression analysis in all males. This may be because the risk of CAD increased when patients in the younger group have a small muscle mass, probably due to less testosterone secretion. Aging generally exacerbates sarcopenia, that is, muscle mass decreases with aging.<sup>[29]</sup> The presence of CAD was not associated with PMMI in older males because this change occurs naturally in the elderly. Thus, loss of muscle mass in non-elderly people may be a risk related to the onset of CAD.

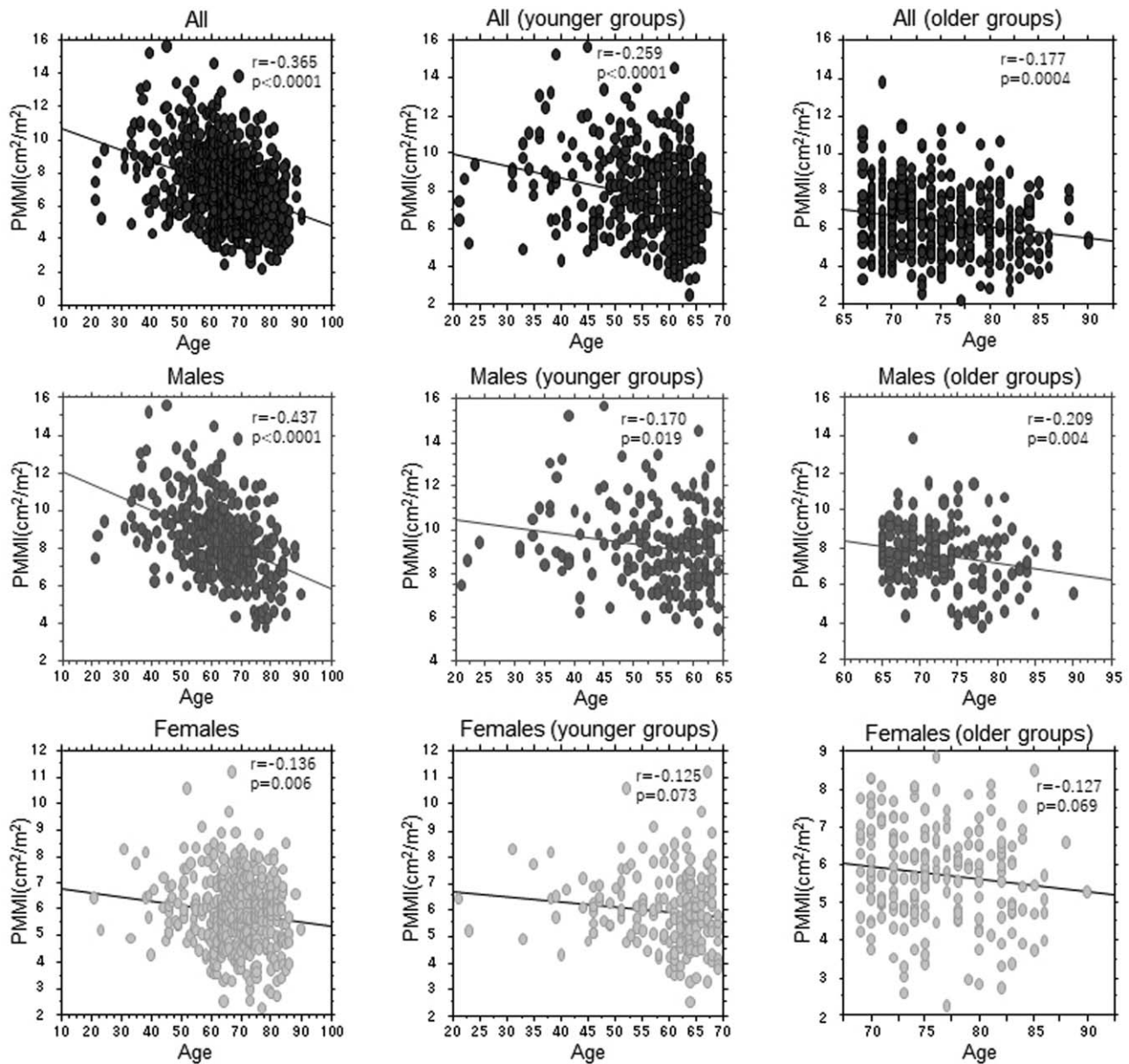


Figure 3. Association between the psoas major muscle index (PMMI) and age in all patients, males and females.

The ROC curve analysis showed that the AUC of PMMI was 0.582 (sensitivity 0.441, specificity 0.752). VFAI is also associated with the presence of CAD. Since there was a significant difference in VFAI between non-CAD and CAD groups in males as shown in Table 2, we also performed a ROC curve analysis to determine VFAI in younger males related to the presence of CAD. The AUC and cut-off level of VFAI were 0.590 (sensitivity 0.566, specificity 0.608) and 48.7 cm<sup>2</sup>/m<sup>2</sup>, respectively. The AUC in VFAI was comparable to that in PMMI.

The cut-off level of PMMI in younger males for the diagnosis of CAD was 8.3 cm<sup>2</sup>/m<sup>2</sup>. A clear standard range of PMMI has not been determined. Hamaguchi et al reported that the average PMMI was 8.85 ± 1.61 cm<sup>2</sup>/m<sup>2</sup> for males and 5.77 ± 1.21 cm<sup>2</sup>/m<sup>2</sup> for females in Japanese populations.<sup>14</sup> Although the average values of PMMI in males without CAD (8.7 cm<sup>2</sup>/m<sup>2</sup>) and females with and without CAD (5.9 cm<sup>2</sup>/m<sup>2</sup> and 5.8 cm<sup>2</sup>/m<sup>2</sup>) in this study

were similar to those in Japanese populations, most of the subjects in those populations were less than 65 years old, and thus much younger than our subjects (average age 65.5 years). In addition, we measured PMM at the umbilical level (L4 to L5), whereas they did it at L3 level. The standard range of PMM in large populations should be determined.

Many studies suggested microRNA (miR) as strong circulating biomarkers with high diagnostic as well as prognostic power in cardiovascular diseases.<sup>30</sup> A decrease in the levels of the miR-15a expression in basal conditions is observed in Type 1 DM patients.<sup>31</sup> In addition, endothelial miR-16 is remarkably upregulated after vascular injury in the presences of peripheral muscle ischemia and exerts a negative effect on endothelial repair through the inhibition of RhoGDIα and nitric oxide production.<sup>32</sup> Thus, the ischemia affects negative carotid remodeling increasing neointima formation after injury. We should analyze

**Table 3**

**Predictors in the presence of CAD in males.**

A. Males (all)	Predictors including BMI in addition to PMMI		D. Males (all)	Predictors including VFAI in addition to PMMI	
	OR (95%CI)	P value		OR (95%CI)	P value
Age	1.063 (1.039–1.087)	<.001	Age	1.058 (1.034–1.082)	<.001
BMI	1.080 (0.995–1.171)	.061	VFAI	1.009 (0.998–1.021)	.113
HTN	1.026 (0.635–1.658)	.917	HTN	1.032 (0.636–1.675)	.898
DL	1.409 (0.900–2.204)	.133	DL	1.308 (0.833–2.055)	.244
DM	1.145 (0.681–1.927)	.609	DM	1.219 (0.723–2.057)	.457
Smoking	1.458 (0.935–2.274)	.095	Smoking	1.385 (0.887–2.162)	.152
PMMI	0.924 (0.793–1.076)	.309	PMMI	0.966 (0.839–1.113)	.635

B. Males (Younger groups)	Predictors including BMI in addition to PMMI		E. Males (Younger groups)	Predictors including VFAI in addition to PMMI	
	OR (95%CI)	P value		OR (95%CI)	P value
Age	1.072 (1.026–1.120)	<.001	Age	1.063 (1.019–1.110)	.005
BMI	1.116 (1.001–1.244)	.042	VFAI	1.010 (0.993–1.028)	.245
HTN	1.466 (0.742–2.897)	.270	HTN	1.507 (0.760–2.985)	.240
DL	1.645 (0.867–3.119)	.126	DL	1.456 (0.762–2.782)	.256
DM	1.010 (0.469–2.176)	.980	DM	1.216 (0.566–2.614)	.616
Smoking	1.533 (0.808–2.905)	.189	Smoking	1.403 (0.739–2.665)	.300
PMMI	0.807 (0.657–0.992)	.038	PMMI	0.870 (0.720–1.052)	.151

C. Males (Older groups)	Predictors including BMI in addition to PMMI		F. Males (Older groups)	Predictors including VFAI in addition to PMMI	
	OR (95%CI)	P value		OR (95%CI)	P value
Age	1.023 (0.965–1.085)	.448	Age	1.022 (0.964–1.084)	.468
BMI	1.009 (0.876–1.162)	.905	VFAI	1.004 (0.989–1.020)	.590
HTN	0.724 (0.344–1.525)	.390	HTN	0.698 (0.331–1.471)	.344
DL	1.060 (0.551–2.039)	.861	DL	1.060 (0.549–2.046)	.863
DM	1.092 (0.527–2.260)	.813	DM	1.095 (0.528–2.272)	.808
Smoking	1.296 (0.682–2.464)	.429	Smoking	1.309 (0.688–2.490)	.412
PMMI	1.147 (0.875–1.504)	.319	PMMI	1.141 (0.895–1.454)	.288

Underlines are indicated *P* < .05.

PMMI = psoas major muscle index, BMI = body mass index, HTN = hypertension, DL = dyslipidemia, DM = diabetes mellitus, CAD = coronary artery disease.

**Table 4**

**Predictors in the presence of CAD in females.**

A. Females (all)	Predictors including BMI in addition to PMMI		D. Females (all)	Predictors including VFAI in addition to PMMI	
	OR (95%CI)	P value		OR (95%CI)	P value
Age	1.061 (1.036–1.087)	<.001	Age	1.069 (1.043–1.097)	<.001
BMI	0.964 (0.904–1.027)	.259	VFAI	0.997 (0.986–1.007)	.505
HTN	1.997 (1.260–3.164)	.003	HTN	1.760 (1.098–2.822)	.019
DL	1.185 (0.769–1.829)	.442	DL	1.237 (0.790–1.936)	.352
DM	2.353 (1.264–4.380)	.007	DM	2.288 (1.211–4.321)	.011
Smoking	1.190 (0.617–2.294)	.603	Smoking	1.221 (0.623–2.396)	.561
PMMI	1.006 (0.849–1.193)	.942	PMMI	1.004 (0.852–1.184)	.960

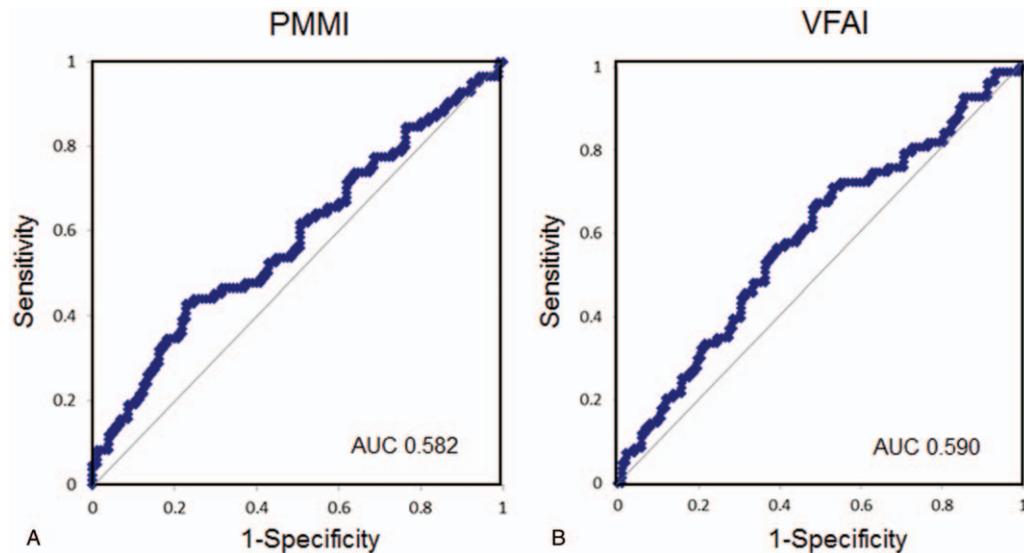
B. Females (Younger groups)	Predictors including BMI in addition to PMMI		E. Females (Younger groups)	Predictors including VFAI in addition to PMMI	
	OR (95%CI)	P value		OR (95%CI)	P value
Age	1.033 (0.986–1.082)	.171	Age	1.042 (0.992–1.094)	.099
BMI	0.942 (0.852–1.041)	.239	VFAI	0.999 (0.983–1.015)	.919
HTN	1.676 (0.847–3.316)	.138	HTN	1.365 (0.680–2.740)	.382
DL	1.134 (0.591–2.178)	.705	DL	1.160 (0.593–2.268)	.665
DM	3.734 (1.462–9.537)	.006	DM	3.082 (1.230–7.726)	.016
Smoking	0.746 (0.313–1.781)	.510	Smoking	0.775 (0.315–1.909)	.580
PMMI	1.116 (0.877–1.419)	.373	PMMI	1.094 (0.866–1.382)	.450

C. Females (Older groups)	Predictors including BMI in addition to PMMI		F. Females (Older groups)	Predictors including VFAI in addition to PMMI	
	OR (95%CI)	P value		OR (95%CI)	P value
Age	1.048 (0.986–1.113)	.135	Age	1.056 (0.992–1.124)	.085
BMI	0.972 (0.890–1.062)	.530	VFAI	0.995 (0.981–1.009)	.471
HTN	2.204 (1.152–4.217)	.017	HTN	2.061 (1.056–4.023)	.034
DL	1.327 (0.729–2.414)	.355	DL	1.373 (0.737–2.559)	.318
DM	1.672 (0.718–3.895)	.234	DM	1.757 (0.724–4.260)	.213
Smoking	3.310 (0.854–12.832)	.083	Smoking	3.228 (0.829–12.56)	.091
PMMI	0.897 (0.696–1.156)	.400	PMMI	0.914 (0.716–1.165)	.466

Underlines are indicated *P* < .05.

PMMI = psoas major muscle index, BMI = body mass index, HTN = hypertension, DL = dyslipidemia, DM = diabetes mellitus, CAD = Coronary artery disease.



**Figure 4.** Cut-off values of psoas major muscle index (PMMI) (A) and measured visceral fat area index (VFAI) (B) in younger males for the diagnosis of coronary artery disease. AUC = area-under-the-curve.

the association between the psoas muscle or miR and the presence and severity of CAD in near future.

**4.1. Study limitations**

This study has several important limitations. First, this study was cross-sectional and did not analyze clinical outcomes over the long term. Second, a considerable amount of time was needed to measure PMMI in each patient; the development of automated analytical software would be helpful. Third, PMM is involved in various physical activities of daily living like running, dancing, sitting, and walking. Although regular physical activity decreases the incidence of CAD,<sup>[33]</sup> we did not determined the activity in our study. Finally, a large-scale prospective study will be needed to address these issues.

**5. Conclusions**

PMMI may be an imaging marker for evaluating the presence and severity of CAD in males, and particularly in the non-elderly.

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**Writing – review & editing:** Takashi Kuwano, Atsushi Iwata, Shin-Ichiro Miura.

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