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 index (PMMI) as assessed by multidetector 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 PMMI 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±9.2 years) and older (72.6±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 cm²/m² (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 = sulfonylurea, 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 computed tomography angiography, psoas major muscle, stenosed coronary vessels.

1. Introduction
Coronary artery disease (CAD) is mainly caused by atherosclerosis. 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.[1-3] 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.[4] Calcification,[5] and plaque.[6] Aging is also a risk factor for CAD,[7] and the proportion of multi-vessel CAD has been reported to increase with aging.[8] In addition, aging has been reported to be associated with sarcopenia.[9] 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.[10] 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\textsuperscript{11,12} and liver cirrhosis.\textsuperscript{13} 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.\textsuperscript{14} The PMM is measured using image-viewing software by tracing the PMM at the lumbar L3 cross-section by CT.\textsuperscript{13} Although it has been reported that there is a relation between atherosclerosis and low muscle mass,\textsuperscript{15,16} 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.\textsuperscript{17} 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 mg/kg/s contrast medium (Iopamiron, 370 mg iodine/mL; Bayer Yakuhin. Ltd, Osaka, Japan) equivalent to the patient’s body weight × 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 0.4 s/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 ≥ 50% that could be identified in multplanar 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.\textsuperscript{18,19}

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),\textsuperscript{20} we measured PMM simultaneously at the umbilical level.\textsuperscript{21} 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)\textsuperscript{2}, VFA/height (m)\textsuperscript{2} or SFA/height (m)\textsuperscript{2}, 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)\textsuperscript{2}. 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 ≥ 140/90 mmHg or who were receiving antihypertensive therapy were considered to have HTN. Patients with LDL-C ≥ 140 mg/dl, TG ≥ 150 mg/dl, and/or HDL-C < 40 mg/dl or who were receiving lipid-lowering therapy were considered to have DL.\textsuperscript{22} DM was defined using the American Diabetes Association criteria\textsuperscript{23} 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 (PMM).
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 36%, respectively. The mean age was 66 ± 12 years and BMI was 23.8 ± 3.6 kg/m².

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, HbAlc, 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, HbAlc, 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 |
| Age, yr | 66 ± 12 | 62 ± 13 | 69 ± 10 | <.0001 |
| Gender (male), % | 48 | 41 | 45 | .0001 |
| Family history, % | 23 | 23 | 23 | .963 |
| Smoking, % | 34 | 31 | 38 | .029 |
| BMI, kg/m² | 23.8 ± 3.6 | 23.8 ± 3.5 | 23.8 ± 3.7 | .896 |
| HTN, % | 64 | 56 | 72 | <.0001 |
| SFB, 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, cm²/m² | 7.1 ± 2.1 | 7.1 ± 2.1 | 7.1 ± 2.0 | .847 |
| VFAI, cm²/m² | 45 ± 23 | 42 ± 22 | 47 ± 23 | .005 |
| SFAI, cm²/m² | 62 ± 33 | 64 ± 33 | 60 ± 33 | .077 |
| Gensini score | 11.2 ± 15.2 | 2.8 ± 3.8 | 19.4 ± 17.6 | <.0001 |

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 = diastolic blood pressure, 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 = percutaneous coronary intervention 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-G = 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
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 ± 9.2 years) and older (74.6 ± 5.3 years) groups. Next, the patients of each gender were divided into 2 groups according to age; relatively younger (53.4 ± 9.2 years) and older (72.6 ± 5.7 years) groups in males, and relatively younger (59.5 ± 8.7 years) and older (76.0 ± 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 ± 1.97 cm²/m²) tended to be lower than that in males without CAD (9.46 ± 1.78 cm²/m²) in the younger group ($P = .08$), but not the older group (7.70 ± 1.57 cm²/m² in patients with CAD vs 7.36 ± 1.63 cm²/m² 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
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 cm²/m².

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 cm²/m², 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.[16] Testosterone increases muscle mass by increasing muscle protein synthesis.[24] In addition, low testosterone levels in males have been associated with an increased atherosclerosis burden and increased risk of cardiovascular events.[25,26] Atherosclerosis induced by testosterone deficiency in male mice was T-cell-dependent.[27] 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.[28] 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.[29] 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.
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$^2$/m$^2$, 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$^2$/m$^2$. A clear standard range of PMMI has not been determined. Hamaguchi et al reported that the average PMMI was 8.85 ± 1.61 cm$^2$/m$^2$ for males and 5.77 ± 1.21 cm$^2$/m$^2$ for females in Japanese populations. Although the average values of PMMI in males without CAD (8.7 cm$^2$/m$^2$) and females with and without CAD (5.9 cm$^2$/m$^2$ and 5.8 cm$^2$/m$^2$) 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. A decrease in the levels of the miR-15a expression in basal conditions is observed in Type 1 DM patients. In addition, endothelial miR-16 is remarkably upregulated after vascular injury in the presence of peripheral muscle ischemia and exerts a negative effect on endothelial repair through the inhibition of RhoGDIs and nitric oxide production. 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.

| Predictors in the presence of CAD in males. | Predictors including BMI in addition to PMMI | Predictors including VFAI in addition to PMMI |
|--------------------------------------------|---------------------------------------------|---------------------------------------------|
| A. Males (all)                             | OR (95%CI)                                    | OR (95%CI)                                    |
| Age                                        | 1.063 (1.039–1.087)                           | 1.058 (1.034–1.082)                           |
| BMI                                        | 1.080 (0.995–1.171)                           | 1.009 (0.998–1.021)                           |
| HTN                                        | 1.026 (0.635–1.650)                           | 1.032 (0.636–1.675)                           |
| DL                                         | 1.409 (0.900–2.044)                           | 1.308 (0.633–2.559)                           |
| DM                                         | 1.145 (0.681–2.927)                           | 1.219 (0.723–2.567)                           |
| Smoking                                    | 1.458 (0.935–2.274)                           | 1.385 (0.887–2.162)                           |
| PMMI                                       | 0.924 (0.793–1.076)                           | 0.966 (0.839–1.113)                           |
| B. Males (Younger groups)                  | Predictors including BMI in addition to PMMI | Predictors in the presence of CAD in males. |
| Age                                        | 1.072 (1.026–1.120)                           | 1.063 (1.019–1.110)                           |
| BMI                                        | 1.116 (1.001–1.244)                           | 1.010 (0.993–1.028)                           |
| HTN                                        | 1.466 (0.742–2.897)                           | 1.507 (0.760–2.985)                           |
| DL                                         | 1.845 (0.867–3.118)                           | 1.456 (0.762–2.782)                           |
| DM                                         | 1.010 (0.469–2.176)                           | 1.216 (0.566–2.614)                           |
| Smoking                                    | 1.533 (0.808–2.905)                           | 1.403 (0.739–2.665)                           |
| PMMI                                       | 0.807 (0.657–1.032)                           | 0.870 (0.729–1.052)                           |
| C. Males (Older groups)                    | Predictors including BMI in addition to PMMI | Predictors in the presence of CAD in males. |
| Age                                        | 1.023 (0.965–1.083)                           | 1.022 (0.964–1.086)                           |
| BMI                                        | 1.009 (0.976–1.162)                           | 1.004 (0.989–1.023)                           |
| HTN                                        | 0.724 (0.344–1.525)                           | 0.698 (0.331–1.471)                           |
| DL                                         | 1.060 (0.551–2.039)                           | 1.060 (0.549–2.046)                           |
| DM                                         | 1.092 (0.527–2.260)                           | 1.095 (0.528–2.272)                           |
| Smoking                                    | 1.296 (0.682–2.446)                           | 1.360 (0.688–2.580)                           |
| PMMI                                       | 1.147 (0.875–1.504)                           | 1.141 (0.895–1.454)                           |

Table 4
Predictors in the presence of CAD in females.

| Predictors in the presence of CAD in females. | Predictors including BMI in addition to PMMI | Predictors including VFAI in addition to PMMI |
|----------------------------------------------|---------------------------------------------|---------------------------------------------|
| A. Females (all)                             | OR (95%CI)                                    | OR (95%CI)                                    |
| Age                                          | 1.061 (1.036–1.087)                           | 1.063 (1.034–1.087)                           |
| BMI                                          | 0.964 (0.904–1.027)                           | 0.997 (0.986–1.007)                           |
| HTN                                          | 1.997 (1.260–3.164)                           | 1.760 (1.098–2.822)                           |
| DL                                           | 1.185 (0.769–1.839)                           | 1.237 (0.790–1.938)                           |
| DM                                           | 2.353 (1.264–4.380)                           | 2.288 (1.211–4.321)                           |
| Smoking                                      | 1.190 (0.617–2.254)                           | 1.221 (0.623–2.398)                           |
| PMMI                                         | 1.008 (0.848–1.153)                           | 1.004 (0.852–1.154)                           |
| B. Females (Younger groups)                  | Predictors including BMI in addition to PMMI | Predictors in the presence of CAD in females. |
| Age                                          | 1.033 (0.986–1.082)                           | 1.042 (0.992–1.094)                           |
| BMI                                          | 0.942 (0.852–1.041)                           | 0.999 (0.963–1.019)                           |
| HTN                                          | 1.676 (0.847–3.316)                           | 1.365 (0.680–2.748)                           |
| DL                                           | 1.134 (0.591–2.178)                           | 1.160 (0.593–2.268)                           |
| DM                                           | 3.734 (1.462–9.537)                           | 3.082 (1.230–7.728)                           |
| Smoking                                      | 0.746 (0.313–1.781)                           | 0.775 (0.315–1.909)                           |
| PMMI                                         | 1.116 (0.877–1.419)                           | 1.094 (0.866–1.382)                           |
| C. Females (Older groups)                    | Predictors including BMI in addition to PMMI | Predictors in the presence of CAD in females. |
| Age                                          | 1.048 (0.986–1.113)                           | 1.056 (0.992–1.124)                           |
| BMI                                          | 0.972 (0.890–1.062)                           | 0.985 (0.981–1.009)                           |
| HTN                                          | 2.204 (1.152–4.217)                           | 2.061 (1.056–4.023)                           |
| DL                                           | 1.327 (0.729–2.414)                           | 1.373 (0.737–2.559)                           |
| DM                                           | 1.672 (0.718–3.895)                           | 1.757 (0.724–4.260)                           |
| Smoking                                      | 3.310 (0.854–12.532)                          | 3.228 (0.829–12.56)                           |
| PMMI                                         | 0.897 (0.696–1.156)                           | 0.914 (0.716–1.165)                           |
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,[33] we did not determine 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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References
[1] Fox CS, Massaro JM, Hoffmann U, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation 2007;116: 39–48.
[2] Rosito GA, Massaro JM, Hoffmann U, et al. Pericardial fat, visceral abdominal fat, cardiovascular disease risk factors, and vascular calcification in a community-based sample: the Framingham Heart Study. Circulation 2008;117:605–13.
[3] Kannel WB, Cupples LA, Ramaswamy R, et al. Regional obesity and risk of cardiovascular disease; the Framingham Study. J Clin Epidemiol 1991;44:183–90.
[4] Rumberger JA, Sheedy PF3rd, Breen JF, et al. Coronary calcium, as determined by electron beam computed tomography, and coronary disease on arteriogram. Effect of patient’s sex on diagnosis. Circulation 1995;91:1363–7.
[5] Nitta K, Akiba T, Suzuki K, et al. Assessment of coronary artery calcification in hemodialysis patients using multi-detector spiral CT scan. J Hypertens Res 2004;27:527–33.
[6] Achenbach S, Ropers D, Hoffmann U, et al. Assessment of coronary remodeling in stenotic and nonstenotic coronary atherosclerotic lesions by multidetector spiral computed tomography. J Am Coll Cardiol 2004;43:1842–7.
[7] Najar SS, Scuteri A, Lakatta EG. Arterial aging is it an immutable cardiovascular risk factor? Hypertension 2003;46:454–62.
[8] Ge J, Li J, Yu H, et al. Hypertension is an independent predictor of multivessel coronary artery disease in young adults with acute coronary syndrome. Int J Hypertens 2008;9Article ID 7623639.
[9] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis. Age Ageing 2010;39:412–23.
[10] Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16–31.
[11] Nattenmuller J, Wochner R, Muley T, et al. Prognostic impact of CT-quantified muscle and fat distribution before and after first-line chemotherapy in lung cancer patients. PLoS One 2017;12:e0169136.
[12] Choi MH, Kim KA, Hwang SS, et al. CT-quantified muscle and fat change in patients after surgery or endoscopic resection for early gastric cancer and its impact on long-term outcomes. Medicine 2018;97: e13878.
[13] Hiraoka A, Aibiki T, Okudaira T, et al. Muscle atrophy as presarcopenia in Japanese patients with chronic liver disease: computed tomography is useful for evaluation. J Gastroenterol 2015;50:1206–13.
[14] Hamaguchi Y, Kaido T, Okumura S, et al. Proposal for new diagnostic criteria for low skeletal muscle mass based on computed tomography imaging in Asian adults. Nutrition 2016;32:1200–5.
[15] Sampaio RA, Sewo-Sampaio PY, Yamada M, et al. Arterial stiffness is associated with low skeletal muscle mass in Japanese community-dwelling older adults. Geriatr Gerontol Int 2014;14(Suppl. 1):109–14.
[16] Ochi M, Kohara K, Tabara Y, et al. Arterial stiffness is associated with low thigh muscle mass in middle-aged to elderly men. Atherosclerosis 2010;212:327–32.
[17] Mitsutake R, Niumura H, Miura S, et al. Clinical significance of the coronary calcification score by multidetector row computed tomography for the evaluation of coronary stenosis in Japanese patients. Circ J 2006;70:1122–7.
[18] Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol 1983;51:606.
[19] Sayın MR, Çetiner MA, Karabag T, et al. The relationship between the Gensini score and complete blood count parameters in coronary artery disease. Kosuyolu Heart J 2012;15:51–4.
[20] Ueda Y, Shiga Y, Ikemoto Y, et al. Association between the presence or severity of coronary artery disease and pericardial fat, paracardial fat, epicardial fat, visceral fat, and subcutaneous fat as assessed by multidetector row computed tomography. Int Heart J 2018;59:693–704.
[21] Jaimovich SG, Guevara M, Pampin S, et al. Planificación Neuroquirúrgica con Software Osirix Neurosurgical planning using osirix software. Surg Neurol Int 2014;5(Suppl 5):S267–71.
[22] Japan Atherosclerosis Society Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases. Chapter 3: Goals of dyslipidemia management. J Atheroscler Thromb 2009;16(Suppl):15–25.
[23] American Diabetes Association. Screening for type 2 diabetes. Diabetes Care 2004;27(Suppl 1):S11–4.
[24] Griggs RC, Kingston W, Jozefowicz RF, et al. Effect of testosterone on muscle mass and muscle protein synthesis. J Appl Physiol 1989;66:498–503.
[25] Kelly DM, Jones TH. Testosterone: a vascular hormone in health and disease. J Endocrinol 2013;217:R47–71.
[26] Ohlsson C, Barrett-Connor E, Bhasin S, et al. High serum testosterone is associated with reduced risk of cardiovascular events in elderly men. The MrOS (Osteoporotic Fractures in Men) study in Sweden. J Am Coll Cardiol 2011;58:1674–81.
[27] Wilhelmson AS, Lantero-Rodriguez M, Svedlund-Eriksson E, et al. Testosterone protects against atherosclerosis in male mice by targeting thymic epithelial cells: brief report. Arterioscler Thromb Vasc Biol 2018;38:1519–27.
[28] Dudek P, Kozakowski J, Zglęczynski W. Late-onset hypogonadism. Menopause Rev 2017;16:66–9.
[29] Harada H, Koi H, Shibata R, et al. New diagnostic index for sarcopenia in patients with cardiovascular diseases. PLoS One 2017;12:e0178123.
[30] Schulte C, Karakas M, Zeller T. microRNAs in cardiovascular disease - clinical application. Clin Chem Lab Med 2017;55:687–704.
[31] García-Díaz DF, Camacho-Guillén P, Codner E, et al. miR15a and miR16 in Chilean type 1 diabetes patients: possible association with apoptosis, inflammatory, or autoimmune markers. J Endocrinol Invest 2018;41:1083–8.
[32] Sorrentino S, Iaconetti C, De Rosa S, et al. Hindlimb ischemia impairs endothelial recovery and increases neointimal proliferation in the carotid artery. Sci Rep 2018;8:761.
[33] Winzer EB, Wootek F, Linke A. Physical activity in the prevention and treatment of coronary artery disease. J Am Heart Assoc 2018;7:e007725.