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Circulation: Cardiovascular Interventions

ORIGINAL ARTICLE

Quantification of Myocardial Mass Subtended by a Coronary Stenosis Using Intracoronary Physiology

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BACKGROUND: In patients with stable coronary artery disease, the amount of myocardium subtended by coronary stenoses constitutes a major determinant of prognosis, as well as of the benefit of coronary revascularization. We devised a novel method to estimate partial myocardial mass (PMM; ie, the amount of myocardium subtended by a stenosis) during physiological stenosis interrogation. Subsequently, we validated the index against equivalent PMM values derived from applying the Voronoi algorithm on coronary computed tomography angiography.

METHODS: Based on the myocardial metabolic demand and blood supply, PMM was calculated as follows: PMM (g)=APV×D^2×π/(1.24×10^{-3}×HR×sBP+1.6), where APV indicates average peak blood flow velocity; D, vessel diameter; HR, heart rate; and sBP, systolic blood pressure. We calculated PMM to 43 coronary vessels (32 patients) interrogated with pressure and Doppler guidewires, and compared it with computed tomography–based PMM.

RESULTS: Median PMM was 15.8 g (Q1, Q3: 11.7, 28.4 g) for physiology-based PMM, and 17.0 g (Q1, Q3: 12.5, 25.9 g) for computed tomography–based PMM (*P*=0.84). Spearman rank correlation coefficient was 0.916 (*P*<0.001), and Passing-Bablok analysis revealed absence of both constant and proportional differences (coefficient A: –0.9; 95% CI, –4.5 to 0.9; and coefficient B, 1.00; 95% CI, 0.91 to 1.25]. Bland-Altman analysis documented a mean bias of 0.5 g (limit of agreement: –9.1 to 10.2 g).

CONCLUSIONS: Physiology-based calculation of PMM in the catheterization laboratory is feasible and can be accurately performed as part of functional stenosis assessment.

VISUAL OVERVIEW: A visual overview is available for this article.

Key Words: blood flow velocity ■ computed tomography angiography ■ coronary circulation ■ coronary stenosis ■ myocardium

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WHAT IS KNOWN

- The amount of myocardium subtended by coronary stenoses constitutes a major determinant of prognosis as well as of the benefit of coronary revascularization.
- The simple assessment of myocardial mass at the catheterization would provide the great benefit on the decision-making for treatment of coronary artery disease as well as the physiological understanding.

WHAT THE STUDY ADDS

- We devised the novel method to estimate the amount of partial myocardial mass subtended by a stenosis during physiological stenosis interrogation based on the blood flow continuity principle between myocardial metabolic demand and blood supply.
- Our novel method would be feasible to assess partial myocardial mass at the regions without the history of myocardial infarction in the patients with the preserved left ventricular function.

The prognosis of obstructive coronary artery disease (CAD) is largely determined by the amount of ischemic myocardium.[1–3] In agreement with this, the benefit of coronary revascularization in the setting of stable CAD, compared with medical therapy, is influenced by the amount of myocardial mass subtended by target stenoses.[2,4] The fact that it is not the presence of ischemia per se, but the ischemic burden which drives prognosis, explains the apparent discordance between functional stenosis severity measured with fractional flow reserve (FFR) and clinical outcomes found in trials, with surprisingly low rates of major adverse cardiac events in patients with physiologically significant stenoses treated by medical therapy alone.[5] Of note, subtended myocardial mass does influence intracoronary physiological measurements like FFR, instantaneous wave-free ratio, and the index of microvascular resistance.[6–10]

All the above would justify the calculation of myocardial mass as part of patient risk assessment in CAD, setting the indication and planning PCI, and interpreting the results of intracoronary physiological tests. Although noninvasive ischemia testing before invasive coronary angiography does allow to estimate the extent of ischemic myocardium, it is not routinely performed in clinical practice. Moreover, the amount of subtended myocardial mass distal to a stenosis is particularly difficult to measure noninvasively in contemporary practice. Applying Voronoi algorithm on coronary computed tomography angiography (CCTA) can be used to calculate partial myocardial mass (PMM) subtended by a specific coronary location anatomically (Figure 1).[11,12] However, CCTA-based PMM is not widely used, and certainly it is not applicable to perform ad-hoc decision-making in the catheterization laboratory. On the contrary, methods available in the catheterization laboratory based on the coronary angiogram require labor-intensive measurements of the vascular distribution distal to a stenosis, which only provide assessments of relative myocardial mass, and are not feasible during a procedure.[13,14]

From all the above, it is therefore fair to state that the assessment of subtended myocardial mass in the catheterization laboratory is an urgent unmet need in the management of CAD patients. Because of this, we designed a novel method to estimate subtended PMM in the catheterization laboratory using available tools of intracoronary physiology. As part of our research, we performed a validation of the method using comparison of physiology-based PMM measurement with anatomy-based estimation on CCTA which, as discussed above, constitutes the contemporary standard of reference for PMM calculation.[11,12]

METHODS

Study Population

Using the pooled dataset of the Amsterdam UMC and Tsuchiura Kyodo General Hospital, patients who underwent both CCTA and invasive coronary physiological assessment for suspected stable angina or non-ST segment elevation acute coronary syndrome (NSTE-ACS) were included in this study. We excluded patients with a history of coronary artery bypass surgery, prior myocardial infarction in the perfusion territory of the investigated coronary artery, unstable heart failure, significant valvular disease, persistent arrhythmia, chronic renal failure requiring hemodialysis, and extremely tortuous vessels. We also excluded vessels with severe stenosis (visual estimation ≥85%), non-ST-segment elevation myocardial infarction culprit vessels, vessels with visible collaterals, as well as

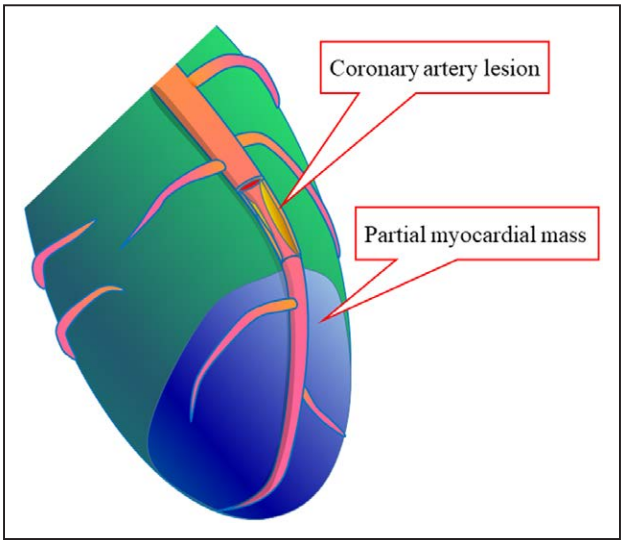

Figure 1. Schema of partial myocardial mass at the concerned region. The blue region indicates the partial myocardial mass at the area of risk.

patients with significantly reduced systolic left ventricular (LV) function (ejection fraction <50%). The study was approved by the human research ethics committee of the respective institutions, and all the patients gave written informed consent. The authors declare that all supporting data are available within the article.

Calculation of Partial Myocardial Mass

The cornerstone of this method to estimate PMM is the proportional relationship between coronary blood flow in an epicardial vessel and the myocardial oxygen demand of the subtended myocardium (Figure 2).[15] According to the flow continuity principle, coronary blood flow volume at the Doppler flow sensing position (Q_{inflow}) equals total myocardial blood flow volume required for the metabolic demand of the subtended myocardial bed (Q_{myo}).

$$Q_{inflow(ml/min)} = Q_{myo(ml/min)}$$

Q_{inflow} can be estimated as:

$$Q_{inflow(ml/min)} = V_{(cm/min)} \times CSA_{(cm2)}$$

where V is the average blood flow velocity and CSA is the cross-sectional area of the coronary artery. CSA can be estimated from the vessel diameter (D, mm) at the Doppler flow sensing position and V can be approximated as 0.5×average peak coronary blood flow velocity (APV, cm/s), which can be directly measured with a Doppler sensor–equipped guidewire during cardiac catheterization.[16] Thus, Q_{inflow} is calculated as follow:

$$Q_{inflow(ml/min)} = APV \times 0.5_{(cm/sec)} \times 60 \times \left(D \times 0.5_{[mm]}\right)^2 \times \pi \times 10^{-2}$$

On the other hand, Q_{myo} can be estimated by

$$Q_{myo(ml/min)} = q_{(ml/min/g)} \times PMM_{(g)}$$

where q is the average myocardial blood flow at the distal bed in milliliters per minute per gram of myocardium and PMM is the amount of perfused myocardial mass in gram. Resting q per gram of (functional) myocardial tissue is determined by the myocardial demand. As documented by Czernin et al[17] using positron emission tomography, q in resting conditions can be estimated from resting heart rate (HR) (beats per minute [bpm]) and systolic blood pressure (sBP) (mmHg) using the equation:

$$q_{(ml/min/g)} = 9.3 \times 10^{-5} \times HR_{rest(bpm)} \times sBP_{rest\ (mmHg)} + 0.12$$

Since coronary blood flow volume at the Doppler flow sensing position (Q_{inflow}) equals total myocardial blood flow volume required for the metabolic demand of the subtended myocardial bed (Q_{myo}), the equation between Q_{inflow} and Q_{myo} can be rewritten as:

$$APV_{rest} \times 0.5 \times 60 \times \left(D \times 0.5\right)^2 \times \pi \times 10^{-2} = \left(9.3 \times 10^{-5} \times HR_{rest} \times sBP_{rest} + 0.12\right) \times PMM$$

From this equation, PMM can be calculated as follows:

$$PMM = \frac{APV_{rest} \times D^2 \times \pi}{1.24 \times 10^{-3} \times HR_{rest} \times sBP_{rest} + 1.6}$$

Coronary Angiographic and Physiological Assessments

Each patient underwent standard selective coronary angiography to assess the coronary anatomy through a 5- or 6-F system. An intracoronary bolus injection of nitroglycerin (0.2 mg) was administered before the physiological assessment. In NSTE-ACS patients, the culprit lesion was treated before the physiological assessment. All the physiological measurements were performed by using a 0.014-inch dual sensor–equipped

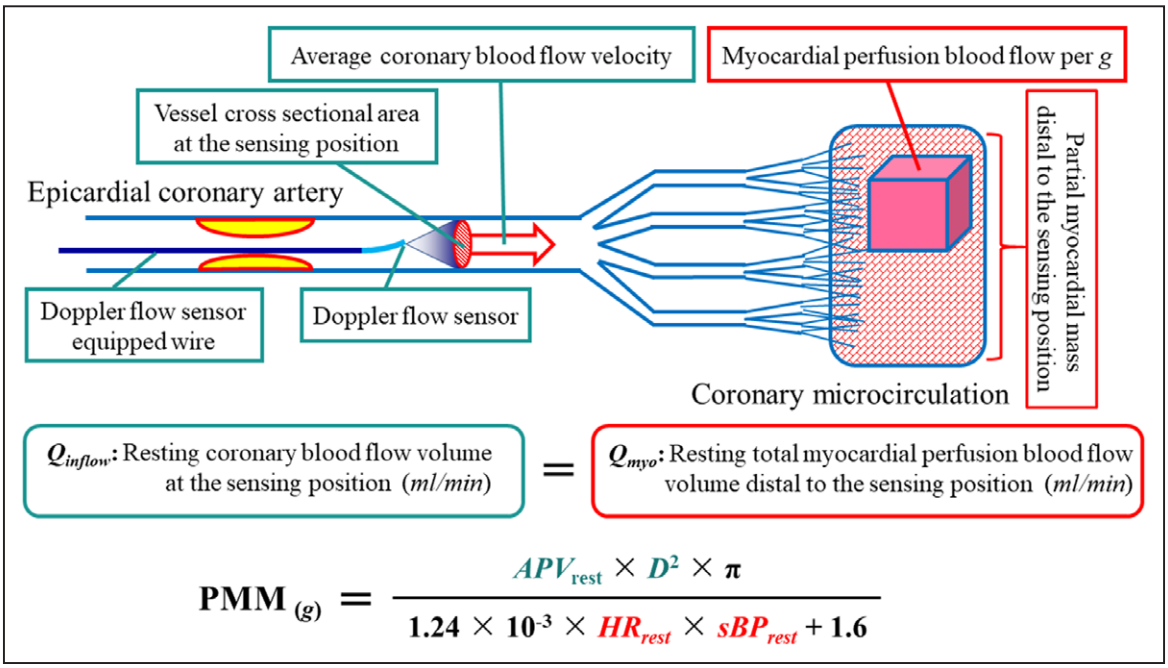

Figure 2. Flow continuity principle between myocardial metabolic demand and blood supply.
This principle is based on the assumption that the coronary blood flow volume at the Doppler flow sensing position (Q_{inflow}) equals the total myocardial perfusion blood flow volume required for the metabolic demand of the subtended myocardial bed (Q_{myo}). Based on this equation, partial myocardial mass (PMM) at the concerned left ventricular region can be calculated using measurable parameters at coronary catheterization. APV indicates average peak blood flow velocity; D, vessel diameter at the Doppler flow sensing position; HR, heart rate, and sBP, systolic blood pressure.

guidewire (Combowire; Philips-Volcano, San Diego, CA) to obtain the coronary pressure and flow velocity data simultaneously. The corresponding Doppler flow sensing positions were recorded on cine angiograms. Offline quantitative coronary angiography analyses were performed to measure the vessel diameter at the Doppler flow sensing position (5 mm distal to the sensor position), as well as the angiographic lesion severity by using a validated software (QCA-CMS version 7.3, MEDIS medical, Leiden, the Netherlands). The vessel diameters were assessed by 2 different directional angiograms at the end diastolic phase, and their mean value was calculated and used for further calculations.

Physiological data were extracted from the digital archive (ComboMap, Philips-Volcano, San Diego, CA). The APV and the HR during stable conditions at rest were assessed by using a custom software package written by Imperial College London, United Kingdom, in MatLab (Mathworks, Inc, Natick, MA), and the corresponding sBP was obtained from raw digitized data. We used an average of these values over 3 consecutive heartbeats for all calculations. Two experienced analysts, who were fully blinded to all the relevant clinical data, analyzed all the hemodynamic signals and the angiographic assessments independently. Each analyst calculated PMM values according to the aforementioned formula, and the mean value of these 2 measurements was used for comparisons with CCTA-based PMM. One of these analysists (Dr Murai) repeated the analysis of all hemodynamic signals and angiographic data and repeated the calculation of physiology-based PMM. These measurements were used to calculate the intraobserver variability of physiology-based PMM.

Coronary Computed Tomographic Image Analysis

The CT image data were obtained by usual CCTA protocol of each institution. The details of CT acquisition were described in the Data Supplement. The CT DICOM image data were transferred to an offline workstation (Aquarius iNtuition, TERARECON, Inc, Tokyo, Japan). This work station contains dedicated software to assess the PMM perfused at an arbitrary point of coronary artery on the basis of the Voronoi algorithm, which specifies the region of the LV myocardium according to the distance to the closest coronary artery. After detecting all the visible coronary branches and confirming whole LV myocardial region, the software integrates the coronary vessel trees and the LV myocardium 3 dimensionally in an automatic manner. Coregistration of the coronary flow sensing position between the angiography and the CCTA was performed, and the myocardial mass distal to the specified sensing position on the CCTA was quantified (Figure 3). Finally, the CCTA-based PMM was calculated as the product of the estimated myocardial mass at the concerned LV region and the specific gravity of the myocardium (1.05 g/cm^3). CCTA-based PMM values were assessed by 2 different analysts, and the mean value of these measurements was used in the comparisons with physiology-based PMM.

Statistical Analysis

Data were analyzed on a per-patient basis for clinical characteristics and on a per region basis for all other calculations. Normality of the distribution of the values was assessed by Shapiro-Wilk statistics, and the homogeneity of variances was assessed by Levene test. Continuous variables are expressed as the mean±SD for the normally distributed variables and as the median values with first and third quartile (Q1, Q3) for the non-normally distributed variables. Categorical variables are presented as counts and percentages. The intra- and interobserver variability of the physiology-based PMM values were assessed by using Spearman rank correlation test and Bland-Altman plot. Intracluster correlation was calculated to evaluate the reproducibility of physiology- and CCTA-based PMM

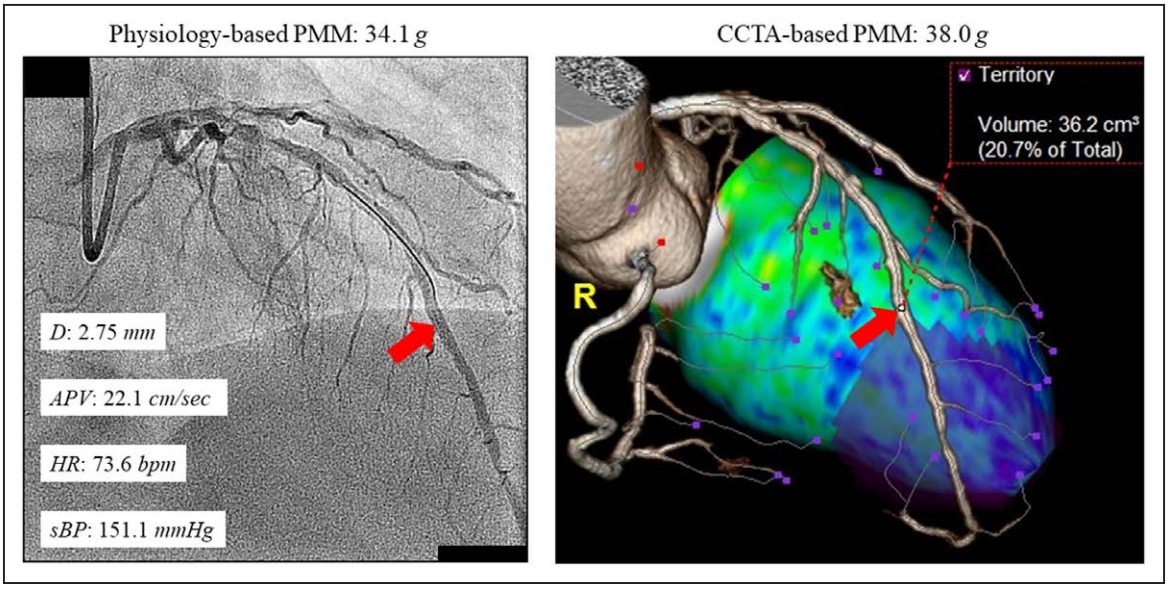

Figure 3. The assessment of physiology- and coronary computed tomography angiography (CCTA)-based partial myocardial mass (PMM). The Doppler flow sensing position was located at the mid left anterior descending coronary artery (red arrow) and mean vessel diameter, systolic blood pressure (sBP), heart rate (HR), and average peak blood flow velocity (APV) at the position were 2.75 mm, 151.1 mm Hg, 73.6 bpm, and 22.1 cm/s. As the result, physiology-based PMM was calculated as 34.1 g. On the contrary, CCTA-based PMM at the same position was 38.0 g. D indicates mean vessel diameter at the Doppler flow sensing position.

measurements. The correlation and the difference between the physiology- and CCTA-based PMM measurements were analyzed with the Spearman rank correlation, Passing-Bablok analysis, Wilcoxon test, and Bland-Altman plot with 95% limits of agreement. The statistical analysis was performed by using SPSS version 22.0 (SPSS, Inc, Chicago, IL), except for Passing-Bablok analysis, which was conducted by using the STATA 14.1 statistical software package (StataCorp, College Station, TX). A *P* of <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

The initial study population was made of 36 patients with CAD who underwent both invasive physiological assessment and CCTA on clinical grounds. In these patients, a total of 51 myocardial regions, outlined by the coronary distribution pattern beyond the index stenosis, were identified. After careful assessment of each myocardial region, 8 were excluded from analysis because of inadequate data quality (Data Supplement). The remaining 43 myocardial regions (32 patients) were entered in the analysis of our study. All 32 patients showed well-preserved ejection fraction (>50%), and 8 patients (25.0%) presented with multivessel disease. The study population consisted of patients with angiographic intermediate coronary lesions, and median diameter stenosis was 50.4% (Q1, Q3: 41.4%, 56.6%). The complete baseline characteristics are listed in Table 1. Table 2 shows the parameters for physiology- and CCTA-based PMM calculation.

Table 1. Baseline Characteristics

Clinical Characteristics	n=32 Patients
Patients characteristics	
Age, y	63.9±9.1
Male, n (%)	28 (87.5)
NSTE-ACS, n (%)	5 (15.6)
Height, cm	169.1±9.3
Weight, kg	74.8±14.5
BMI, kg/m^2	26.1±4.0
Multi vessel disease (≥2)	8 (25.0)
Coronary risk factors	
Hypertension, n (%)	15 (46.9)
Hyperlipidemia, n (%)	17 (53.1)
Diabetes mellitus, n (%)	6 (18.8)
Current smoker, n (%)	8 (25.0)
Prior myocardial infarction, n (%)	5 (15.6)
Prior PCI, n (%)	12 (37.5)
Prior stroke, n (%)	1 (3.1)
Medication, n (%)	
Aspirin	22 (68.8)
ACE inhibitors or ARB	10 (31.3)
β-Blocker	11 (34.4)
CCB	12 (37.5)
Statin	20 (62.5)
Laboratory data	
Hemoglobin, g/dL	14.1±1.3
Creatinine, mg/dL	0.87±0.16
eGFR, mL/min per 1.73 m^2	68.5 (59.4–73.7)
Angiographic characteristics	**n=43 vessels**
Target regions	
LAD, n (%)	34 (79.1)
LAD proximal; mid; distal; diagonal branch	4 (9.3); 20 (46.5); 7 (16.3); 3 (7.0)
LCX, n (%)	4 (9.3)
RCA, n (%)	5 (11.6)
QCA lesion assessments	
Minimal lumen diameter, mm	1.51±0.44
Reference vessel diameter, mm	2.73±0.51
% stenosis diameter, %	50.4 (41.4–56.6)
Lesion length, mm	10.8±4.9

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BMI, body mass index; CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate; LAD, left anterior descending coronary artery; LCX, left circumflex artery; NSTE-ACS, non-ST segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; QCA, quantitative coronary angiography; and RCA, right coronary artery.

Reproducibility of Physiology-Based PMM Estimation

The median values of the physiology-based PMM assessed by the 2 different analysts were 15.0 g (Q1, Q3: 11.6, 26.8 g) and 16.0 g (Q1, Q3: 11.8, 28.7 g). Spearman rank correlation showed good interobserver variability in the physiology-based PMM values (ρ=0.97; *P*<0.001), and Bland-Altman analysis documented a mean bias of –0.1 g and a range of –4.5 to 4.3 g for the limit of agreement. (Figure 4A and 4B). The interobserver intracluster correlation was 0.990.

The intraobserver reproducibility is shown in Figure I in the Data Supplement. Spearman rank correlation was 0.97, and its mean bias and the limit of agreement were –0.3 g and –4.4 to 3.7 g. Intraobserver intracluster correlation was 0.991.

Relationship Between Physiology- and CCTA-Based PMM Values

Median values of physiology- and CCTA-based PMM were 15.8 g (Q1, Q3: 11.7, 28.4 g; range, 3.9 to 67.9 g) and 17.0 g (Q1, Q3: 12.5, 25.9 g; range, 4.6 to 73.7 g), respectively (*P*=0.84; Table 2). Spearman rank correlation showed a good correlation between the 2 methods (ρ=0.92; *P*<0.001). Passing-Bablok

Table 2. Physiology-Based and CCTA-Based Assessments

Physiological and Angiographic Parameters	
APV, cm/s	18.4 (13.3–23.5)
HR, bpm	65.4±8.9
sBP, mm Hg	138.8±17.7
D, mm	1.93 (1.63–2.40)
Physiology-based PMM, g	15.8 (11.7–28.4)
CCTA parameters	
Whole LVM, g	140.3 (112.2–170.7)
Ratio of PMM to whole LVM, %	12.6 (8.1–20.2)
CCTA-based PMM, g	17.0 (12.5–25.9)

APV indicates average peak coronary flow velocity; CCTA, coronary computed tomography angiography; D, mean vessel diameter at the Doppler flow sensing position; HR, heart rate; LVM, left ventricular myocardial mass; PMM, partial myocardial mass, and sBP, systolic blood pressure.

analysis revealed absence of both constant and proportional differences (coefficient A: –0.9, 95% CI, –4.5 to 0.9; and coefficient B: 1.00, 95% CI, 0.91 to 1.25; Figure 5A). Bland-Altman analysis documented a mean bias of 0.5 g and a range of –9.1 to 10.2 g for the limit of agreement (Figure 5B). Figure 6 shows a representative case for the study. This patient, who had mild LV hypertrophy and an intermediate coronary stenosis at the left main trunk, underwent 3 physiological assessments at different locations in the left anterior descending coronary artery as indicated in the figure. The calculations of myocardial mass, obtained from separate and blinded expert analysts, were very similar between the 2 methods.

DISCUSSION

The main finding of our study is that calculation of the myocardial mass subtended by a coronary stenosis is feasible and can be performed in the catheterization laboratory with currently available tools. Physiology-based PMM, calculated from rate pressure product, angiography-based vessel diameter, and invasive coronary flow velocity, provides similar estimates of myocardial mass as CCTA-based PMM, with the distinct advantage of ad-hoc performance in the catheterization laboratory.

Observational studies have shown that, in stable CAD patients, an amount of ischemic myocardium equivalent to 10% to 15% of total LV mass effectively predicts a benefit of coronary revascularization over medical treatment.[18] While identifying ischemia-generating stenoses in the catheterization laboratory is feasible using pressure-derived indices like FFR or instantaneous wave-free ratio, quantification of the myocardial mass in jeopardy was an unmet need. The proposed method to measure PMM can be combined with pressure-derived indices to obtain functional and prognostic information on epicardial coronary stenoses.[1–4,6–10] PMM is derived from resting myocardial oxygen consumption and does not require administration of coronary vasodilators. Therefore, it is fully compatible with iFR and other non-hyperaemic indices of stenosis severity. This would facilitate its clinical use.

Physiology- Versus Computed Tomography-Based Myocardial Mass Calculation

One important aspect of our method was the assumption that because coronary autoregulation ensures preservation of resting coronary flow over a wide range of epicardial stenosis severity,[19] the presence of the index epicardial stenosis should not interfere with PMM estimation. In that regard, the stenosis interrogated in our study had intermediate severity (median % diameter stenosis, 50.4%). This may not be valid for very tight stenoses that are causing ischemia at rest.

Another relevant topic was the choice of a standard of reference for the validation of physiology-based PMM. We chose CCTA-based PMM, which is the current most accurate method to estimate absolute myocardial mass.[11,12] In this study, CCTA-based

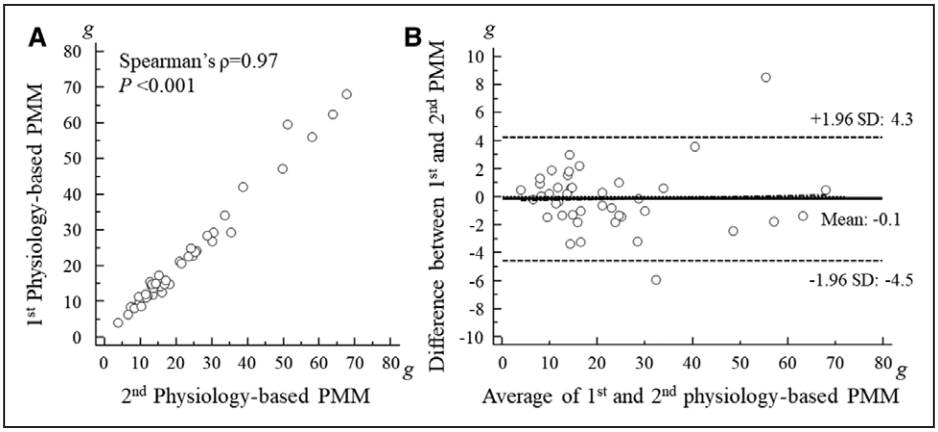

Figure 4. Spearman rank correlation and Bland-Altman analysis for interobserver variability for physiology-based partial myocardial mass (PMM). **A**, Spearman rank correlation and (**B**) Bland-Altman plot. SD indicates the differences between first and second PMM values.

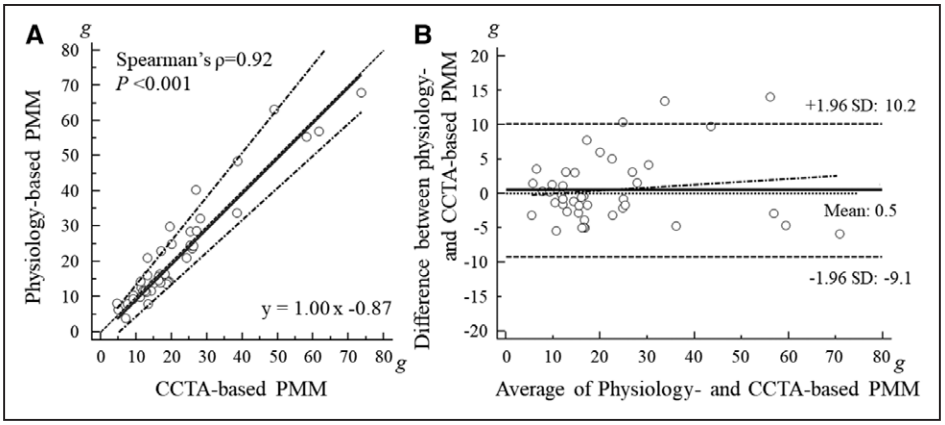

Figure 5. Passing-Bablok regression and Bland-Altman analyses of agreement between the 2 methods.
A, Passing-Bablok fit and Spearman ρ and (**B**) Bland-Altman analysis of agreement. CCTA indicates coronary computed tomography angiography; and PMM, partial myocardial mass.

PMM showed an excellent interobserver reproducibility (intracluster correlation=0.994; *P*<0.001). A strong linear relationship between physiology- and CCTA-based myocardial mass estimations was documented (Figure 5) where even serial assessments in the same coronary artery could identify the subtended myocardial mass at each measurement location with high accuracy (Figure 6). It could be argued that CCTA-based myocardial mass is a pure anatomic measurement, whereas the proposed physiology-based method represents the functional myocardial mass. But, on the other hand, the existence of such a close correspondence of PMM values obtained with fundamentally different approaches supports the validity of our findings. In interpreting the diagnostic power of our approach, it should be kept in mind that we were cautious in not including in our study patients with myocardial infarction in the analyzed regions because in that case anatomic myocardial mass might be larger than the functional myocardial mass estimated by coronary physiology. As functional myocardial mass is derived from the relationship between resting myocardial metabolism and coronary blood flow, it remains plausible that physiology-based PMM might be more adequate than anatomy-based PMM in appraising the prognostic implications and expected benefit of revascularization. On the contrary, systemic conditions that might alter baseline myocardial metabolism (like thyrotoxicosis, anemia, hypoxia, etc) may interfere with physiology-based estimation of PMM. Yet, many of these conditions also constitute contraindications for coronary pressure measurements in contemporary clinical practice.

Clinical Implications of Physiology-Based Myocardial Mass Estimation

Both invasive and noninvasive techniques are nowadays routinely used to identify whether or not a coronary stenosis induces myocardial ischemia.[20] Ischemia-inducing coronary stenoses are subsequently considered eligible for coronary revascularization. However, 2 important issues remain.

First, previous studies have documented that the amount of ischemic myocardium importantly drives the prognostic benefit of revascularization over medical

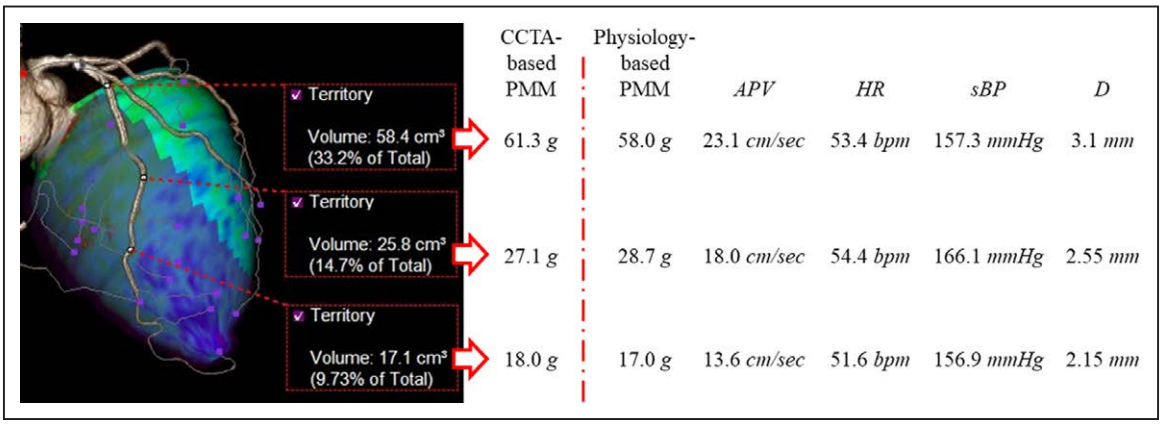

Figure 6. The representative case for the comparison between physiology- and coronary computed tomography angiography (CCTA)-based partial myocardial mass (PMM) values.
APV indicates average peak blood flow velocity; D, mean vessel diameter at the Doppler flow sensing position; HR, heart rate; and sBP, systolic blood pressure.

therapy.[2,4] This is supported by the recent FAME II trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation), which documented that 73% of patients with abnormal FFR values do not suffer from major adverse cardiac events.[5] Since abnormal FFR values are considered a surrogate for myocardial ischemia, this indicates that solely the presence of myocardial ischemia itself does not optimally identify stenoses that benefit from revascularization in terms of hard clinical end points. Hence, it seems of distinct relevance to be able to identify both the presence and extent of myocardial ischemia ad-hoc in the individual patient. Our novel assessment of the salvageable PMM by PCI would provide a unique approach to assess the ischemic burden of the coronary artery lesions.

Second, it has been suggested that subtended myocardial mass importantly impacts coronary physiology techniques such as FFR, instantaneous wave-free ratio, and index of microvascular resistance.[6–10] It has been hypothesized that differences in myocardial mass may explain differences in these indices, for example, between adjacent perfusion regions and between men and women. The ad-hoc availability of myocardial mass estimation would allow to further study these suggested phenomena, and if confirmed that such interaction is indeed present, would allow to interpret the obtained physiology values in relation to the subtended myocardial mass.

Finally, this novel method can be estimated simply without additional drugs, new devices, or special techniques, so that it can be adopted immediately into the general clinical practice.

Limitations

In this present validation study, all patients had well-preserved cardiac function, and presented without any history of transmural myocardial infarction in the studied vessel. Moreover, the vessels supplying collateral flow to other vessels, as well as the vessels with very severe stenosis were not included in the study. Hence, although this has provided the optimal population for validation purposes, it limits the external validity of our findings. Therefore, evaluation of this concept in other conditions and comorbidities should be subject of subsequent study. This study included NSTE-ACS nonculprit vessels (6 assessments in 5 patients). The impact of NSTE-ACS on nonculprit vessel microvascular function remains debated, although evidence is accumulating that such impact may be minimal in stable NSTE-ACS patients.[21] The NSTE-ACS patients in this study indeed presented stable hemodynamic conditions, no heart failure, and no ST-segment elevation after PCI. Figure IIA in the Data Supplement shows that their estimated PMM values were very similar to those of CCTA-based PMM. Nonetheless, further study is required before extrapolation of these study results to the full spectrum of NSTE-ACS patients. Furthermore, the majority of PMM assessments were performed in the left anterior descending coronary artery (31 assessments, 72.1%). However, when limited to non-left anterior descending coronary artery vessels and diagonal branches, physiological PMM estimation provided similar results (Figure IIB in the Data Supplement).

Moreover, the physiological assessment of PMM requires the invasive assessment of coronary flow velocity. Flow velocity measurements are currently technically challenging and require operator experience with this specific armamentarium. These data were acquired in centers with experience in Doppler velocity assessment, and no inadequate flow tracings were documented. Moreover, technological advancements are ongoing and are expected to lead to more feasible flow measurement technology in the near future, improving the feasibility of routine myocardial mass calculation in clinical practice.

Conclusions

Physiology-based calculation of subtended myocardial mass (PMM) in the catheterization laboratory is feasible and can be accurately performed as part of functional stenosis assessment with intracoronary pressure and Doppler guidewires.

ARTICLE INFORMATION

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Disclosures

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