



# Clinical and imaging predictors of impaired myocardial perfusion in symptomatic patients after percutaneous coronary intervention: insights from dynamic CT myocardial perfusion imaging

Haiyan Ma<sup>1,2#</sup>, Xu Dai<sup>1#</sup>, Xiaojun Yang<sup>3</sup>, Xihui Zhao<sup>2</sup>, Rongpin Wang<sup>2</sup>, Jiayin Zhang<sup>4</sup>

<sup>1</sup>Institute of Diagnostic and Interventional Radiology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China;

<sup>2</sup>Department of Radiology, Guizhou Provincial People's Hospital, Guiyang, China; <sup>3</sup>Department of Radiology, People's Hospital of Quzhou, Quzhou, China; <sup>4</sup>Department of Radiology, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

#These authors contributed equally to this work.

*Correspondence to:* Jiayin Zhang. Department of Radiology, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, 85 Wujin Rd., Shanghai 200080, China. Email: andrewssmu@msn.com; Rongpin Wang. Department of Radiology, Guizhou Provincial People's Hospital, 83 East Zhongshan Rd., Guiyang 550002, China. Email: wangrongpin@126.com.

**Background:** We aimed to investigate the relationship between baseline clinical characteristics and postprocedural myocardial perfusion as determined by dynamic computed tomography myocardial perfusion imaging (CT-MPI).

**Methods:** We retrospectively included consecutive symptomatic post percutaneous coronary intervention (PCI) patients, who underwent dynamic CT-MPI + coronary CT angiography (CCTA) and who were revealed to have patent stents on previously revascularized lesions. Myocardial blood flow (MBF) was measured for stented territories and reference territories. Various baseline clinical and angiographic parameters were tested for the association with reduced MBF of stented territories.

**Results:** A total of 81 patients with 96 stented vessels were included in the analysis. The mean effective doses of radiation for the whole integrated CT protocol (calcium score + dynamic CT-MPI + CCTA) was  $4.89 \pm 1.14$  (2.58–6.93) mSv. Overall, 49 stented vessels had reduced MBF ( $75.3 \pm 17.2$  mL/100 mL/min) within related territories, whereas 47 stented vessels had normal MBF ( $138.6 \pm 20.5$  mL/100 mL/min). Peak levels of high-sensitivity cardiac troponin I (hs-cTnI), N-terminal pro-B-type natriuretic peptide (NT-pro-BNP), high-sensitivity C-reactive protein (hs-CRP), and glucose were significantly higher, while preprocedural thrombolysis in myocardial infarction (TIMI) flow grade was lower in participants with reduced MBF of stented territories. Acute myocardial infarction (AMI) also predominantly presented in participants with decreased MBF after revascularization. According to multivariate analysis, peak hs-cTnI level was the strongest predictor [adjusted hazard ratio (HR): 4.548,  $P=0.003$ ] for decreased myocardial perfusion, followed by TIMI flow grade, AMI, stenotic extent, and NT-pro-BNP.

**Conclusions:** The baseline hs-cTnI peak level was the strongest predictor for decreased myocardial perfusion after revascularization, followed by AMI, stenotic extent, and NT-pro-BNP.

**Keywords:** Coronary artery disease (CAD); computed tomography (CT); percutaneous coronary intervention (PCI); myocardial perfusion imaging (MPI); myocardial blood flow (MBF)

Submitted Aug 16, 2020. Accepted for publication Mar 12, 2021.

doi: 10.21037/qims-20-977

View this article at: <http://dx.doi.org/10.21037/qims-20-977>

## Introduction

Percutaneous coronary intervention (PCI) is a common procedure in treating obstructive coronary artery disease (CAD) (1,2). The main treatment aim of this invasive procedure is to restore the myocardial perfusion of the ischemic myocardium, which is subtended by coronary stenosis. According to a previous largescale observational study, patients with ischemic but viable myocardia were more likely to benefit from early revascularization (3). However, complete recovery of blood flow to the ischemic myocardium cannot be achieved in all patients and reduced myocardial perfusion with patent stents has been previously reported (4,5). To date, the clinical factors, which are associated with postprocedural myocardial perfusion recovery, remain unknown.

Dynamic computed tomography myocardial perfusion imaging (CT-MPI) is an emerging technique that allows full quantification of myocardial blood flow (MBF) and incorporates both functional and anatomical evaluation of CAD (6,7). The accuracy of dynamic CT-MPI derived parameters for diagnosing ischemic coronary stenosis or acute myocardial injury has been validated on the latest platform of dual source CT (8-10). However, only one previous study has employed this novel technique to detect reduced MBF after PCI without correlating this perfusion abnormality to preprocedural clinical and imaging characteristics (4). We hypothesized that different baseline clinical characteristics may contribute to the myocardial perfusion recovery after PCI and that this blood flow improvement can be quantified by dynamic CT-MPI. Therefore, the purpose of the current study was to investigate the relationship between baseline clinical characteristics and postprocedural myocardial perfusion as determined by dynamic CT-MPI.

## Methods

### Participant population

We reviewed the database in our institute between January 2017 and December 2019 for consecutive symptomatic post-PCI patients who underwent dynamic CT-MPI and coronary CT angiography (CCTA) for evaluation of suspected in-stent restenosis (ISR) or unrevascularized native lesions before staged PCI. Patients were retrospectively included if dynamic CT-MPI + CCTA revealed patent stents on previously revascularized lesions. The exclusion criteria were as follows: (I) dynamic CT-MPI

+ CCTA revealing the presence of ISR; or (II) patients with unassessable stents; or (III) patients with *de novo* obstructive lesions (defined as stenotic extent  $\geq 50\%$ ) on stented vessels; (IV) patients with concomitant cardiomyopathy; (V) incomplete baseline clinical data; or (VI) a significantly impaired image quality on dynamic CT-MPI (*Figure 1*). The hospital ethics committee approved this study, and the need for written informed consent was waived due to its retrospective nature.

### Scan protocol of dynamic CT-MPI + CCTA

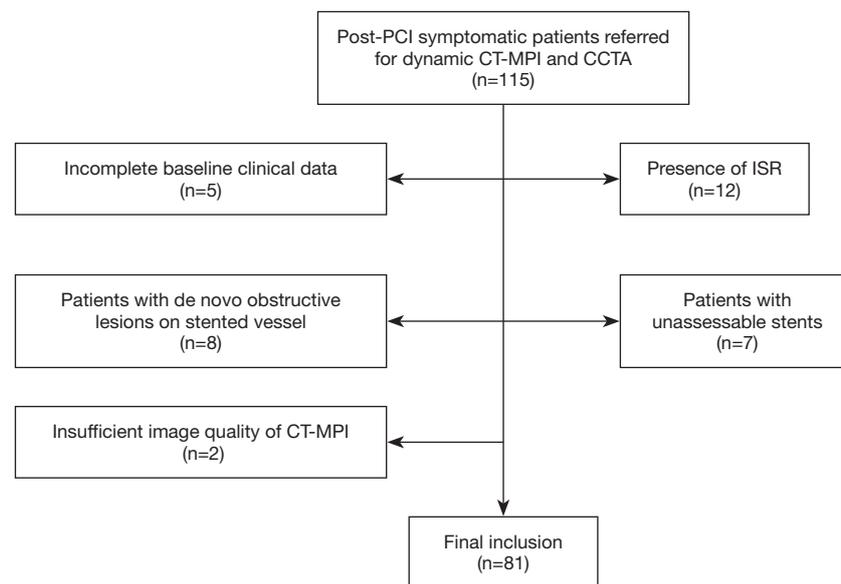
A third-generation dual source CT (SOMATOM Force, Siemens Healthineers, Forchheim, Germany) was employed for all image acquisition. We used an integrated protocol which incorporated calcium score imaging, dynamic CT-MPI, and CCTA as previously reported (8). In brief, the calcium score was performed first to measure the calcification burden of epicardial vessels. A dynamic CT-MPI acquisition shuttle mode technique was triggered after 3 minutes of intravenous infusion of adenosine triphosphate (ATP) at 160  $\mu\text{g}/\text{kg}/\text{min}$ . Nitroglycerin was given sublingually to all participants 5 minutes after dynamic CT-MPI, prior to the acquisition of CCTA which was performed using a prospective electrocardiogram (ECG)-triggered sequential technique. The details of scan parameters are given in the [Appendix 1](#).

### Image analysis of dynamic CT-MPI

The CT-MPI data were reconstructed using a dedicated kernel for reduction of iodine beam-hardening artifacts (Qr36) and analyzed using a commercially available CT-MPI software package (Myocardial perfusion analysis, VPCT body, Siemens Healthineers, Forchheim, Germany). Motion correction was applied for necessary CT studies to correct breathing-related misregistration of the left ventricle. Quantification of MBF was performed using a hybrid deconvolution algorithm (11,12).

For quantitative analysis, region of interest (ROI) was manually placed to sample the MBF on a segment base according to 17-segment model with exclusion of apical segments (13). The ROI was drawn to cover the whole area of suspected perfusion defect within the segment or to cover the whole segment when the perfusion defect was absent. The short axis view of the myocardial color-coded map was used for quantification of all segments.

The stented territories (supplied by stented vessel) and



**Figure 1** Flow chart of inclusion and exclusion. PCI, percutaneous coronary intervention; CT, computed tomography; MPI, myocardial perfusion imaging; CCTA, coronary computed tomography angiography; ISR, in-stent restenosis.

reference territories (supplied by native vessels without diameter stenosis  $\geq 30\%$ ) were each determined according to the fusion images of coronary vasculature and perfusion map. The mean value of MBF was measured for each segment of both stented territories and reference territories. An MBF  $< 100$  mL/min/100 mL was used as the cutoff value to differentiate ischemic from nonischemic segments (8).

A pair of cardiovascular radiologists (with 10 and 6 years of experience in cardiac CT imaging) who were blinded to clinical histories independently analyzed all CT-MPI data. The mean values of MBF measured by the two observers were used for analysis.

### Image analysis of CCTA

Axial images were reconstructed with smooth kernel (Bv 40, for evaluation of native coronary arteries) and sharp kernel (Bv 44, for evaluation of stents). Third-generation iterative reconstruction with different strength factors (strength 3 for smooth kernel data and strength 4 for sharp kernel data) was applied to all image datasets. The cardiac phase with the best image quality was manually determined and transferred to an offline workstation (SyngoVia, Siemens Healthineers, Forchheim, Germany) for further analyses.

Stent patency was assessed using sharp kernel image data and on reconstructed cross-sectional images. Binary ISR was considered as an in-stent neointimal proliferation

with diameter stenosis  $\geq 50\%$  (14). Native coronary arteries with diameter  $\geq 1.5$  mm were also evaluated and obstructive lesions were defined as diameter stenosis  $\geq 50\%$ . The same two cardiovascular radiologists who were blinded to clinical histories independently analyzed all CCTA data. The presence of obstructive CAD or ISR was determined by consensus reading.

### Baseline clinical characteristics

Baseline individual clinical characteristics were collected from the electronic medical record system by study investigators. Characteristics included patients' symptoms [stable angina, unstable angina, and acute myocardial infarction (AMI)], conventional high-risk factors of CAD (hypertension, diabetes mellitus, hyperlipidemia, and smoking), and blood biochemical parameters, such as peak level of high-sensitivity cardiac troponin I (hs-cTnI), N-terminal pro-B-type natriuretic peptide (NT-pro-BNP), and high-sensitivity C-reactive protein (hs-CRP). The angiographic features of target lesion, including stenotic extent, thrombolysis in myocardial infarction (TIMI) flow grade, and lesion length, were also recorded.

### Statistical analysis

Statistical analysis was performed with commercially

**Table 1** Demographic data

Characteristics	Data
Number of participants	81
Age (years)	65.6±9.7
Male	64 (79.0)
Risk factors	
Hypertension	51 (63.0)
Diabetes mellitus	30 (37.0)
Dyslipidemia	29 (35.8)
Current smoker	38 (46.9)
Current symptoms	
Atypical chest pain	42 (51.9)
Stable angina	39 (48.1)
Previous history of AMI	50 (61.7)

Values are mean ± SD, n (%). AMI, acute myocardial infarction; SD, standard deviation.

available statistical software (MedCalc Statistical Software version 15.2.2, MedCalc Software BVBA, Ostend, Belgium). Qualitative or quantitative variables are expressed as mean ± standard deviation (SD), percentages, or median and interquartile range. Differences between normally distributed data [age, body mass index (BMI), apolipoprotein A to apolipoprotein B ratio (APOA/APOB ratio), total cholesterol, lesion length, and preprocedural TIMI flow grade] were compared using the Student's *t*-test, whereas differences between data that were not normally distributed (hs-cTnI, NT-pro-BNP, NLR ratio, triglyceride, stenotic extent, systolic blood pressure, and diastolic blood pressure) were analyzed by the Mann-Whitney U test. The differences between categorical baseline variables (AMI and stent location) were analyzed by either chi-square test or Fisher's exact test. Interobserver agreement of MBF measurement was assessed by intraclass correlation coefficient (ICC). We investigated the effects of different variables on post-PCI myocardial perfusion by univariate and multivariate logistic regression analyses. The variables that were predictors for reduced post-PCI myocardial perfusion were included in the multivariate logistic regression model. Receiver operating characteristic (ROC) curve analysis was performed by the DeLong method on baseline clinical and angiographic characteristics for identifying patients with reduced myocardial perfusion after revascularization. The area under curve (AUC) of each

parameter was calculated. A two-tailed P value <0.05 was considered statistically significant.

## Results

### *Clinical characteristics*

A total of 115 post-PCI patients with dynamic CT-MPI and CCTA between 1 January 2017 and 31 December 2019 were retrospectively reviewed. A total of 12 patients were excluded due to the presence of ISR, and 5 patients were excluded because of incomplete preprocedural clinical data. A further 8 patients were excluded because of the presence of *de novo* obstructive lesions on stented vessels. In addition, 7 patients with unassessable stents and 2 patients with insufficient image quality of CT-MPI were also excluded (Figure 1). Finally, 81 participants with 96 stented vessels were included in the analysis. The mean effective doses of radiation for the whole integrated CT protocol (calcium score + dynamic CT-MPI + CCTA) was 4.89±1.14 (2.58–6.93) mSv when using 0.014 as the conversion factor. The mean interval between CT examinations and previous PCI was 11.2±7.4 months [6–30]. Clinical demographic details are displayed in Table 1.

### *MBF of stented segments and reference segments*

The interobserver agreement for measurement of MBF was good, as evidenced by the ICC of 0.987 (P<0.001). The mean MBF of all stented segments was 112.3±40.6 mL/100 mL/min, of which 187 segments were revealed to be ischemic (75.3±17.2 mL/100 mL/min) and 367 to be nonischemic (138.6±20.5 mL/100 mL/min). The mean MBF of all reference segments was 140.7±19.8 mL/100 mL/min. Overall, 49 stented vessels had reduced MBF within related territories, whereas 47 stented vessels had normal MBF.

### *Baseline clinical and invasive angiographic characteristics between stented territories with normal and reduced perfusion*

Various baseline clinical characteristics were compared between participants with normal and reduced MBF of stented territories. According to the current results, peak levels of hs-cTnI, NT-Pro-BNP, hs-CRP, and glucose were significantly higher in participants with reduced MBF of stented territories (Table 2). Representative cases

**Table 2** Baseline clinical characteristics between participants with normal and reduced post-PCI myocardial perfusion

Baseline clinical characteristics	Patients with reduced post-PCI myocardial perfusion of stented territory (n=48)	Patients with normal post-PCI myocardial perfusion of stented territory (n=33)	P value
Age (years)	65±10	66±9	0.897
BMI (kg/m <sup>2</sup> )	24.99±3.10	24.50±2.62	0.970
Hs-cTnI (ng/L)*	212.00 (15.50, 5,533.75)	5.00 (2.00, 93.50)	<0.001
NT-pro-BNP (ng/L)*	310.10 (91.06, 1,085.93)	96.69 (37.59, 154.10)	<0.001
Hs-CRP (mg/L)*	2.50 (1.12, 8.48)	0.92 (0.48, 2.66)	0.009
NLR ratio	3.32 (2.13, 6.64)	2.47 (1.69, 4.86)	0.080
APOA/APOB	1.35±0.43	1.33±0.34	0.883
Total cholesterol (mmol/L)	4.75±1.16	4.57±1.05	0.485
Triglyceride (mmol/L)	1.36 (0.96, 2.05)	1.40 (1.06, 1.73)	0.920
Glucose (mmol/L)	6.51 (5.27, 8.90)	5.62 (4.98, 7.49)	0.023
SBP (mmHg)	144.00 (131.25, 160)	170.00 (121.50, 180.00)	0.190
DBP (mmHg)	89.00 (80.00, 92.75)	90.00 (70.00, 110.00)	0.772
AMI	37 (37/48, 77%)	13 (13/33, 39%)	0.001

Values are mean ± SD, n (%), or median (interquartile range). \*, Refers to peak level of those parameters during hospitalization if multiple measurements were recorded. PCI, percutaneous coronary intervention; BMI, body mass index; hs-cTnI, high-sensitivity cardiac troponin I; NT-pro-BNP, N-terminal pro-B-type natriuretic peptide; hs-CRP, high-sensitivity C-reactive protein; NLR, neutrophil to lymphocyte ratio; APOA/APOB, apolipoprotein A to apolipoprotein B ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; AMI, acute myocardial infarction; SD, standard deviation.

are displayed in *Figures 2,3*. The presence of AMI was also predominant in patients with decreased MBF after revascularization (77% vs. 39%, P=0.001). Other clinical parameters were not significantly different between the two subgroups (*Table 2*).

As for invasive angiographic characteristics, baseline stenotic extent was markedly higher in lesions with decreased post-PCI MBF while preprocedural TIMI flow grade was significantly lower. The lesion location and length were similarly distributed between two subgroups (*Table 3*).

#### *Univariate and multivariate analysis of predictors for decreased myocardial perfusion*

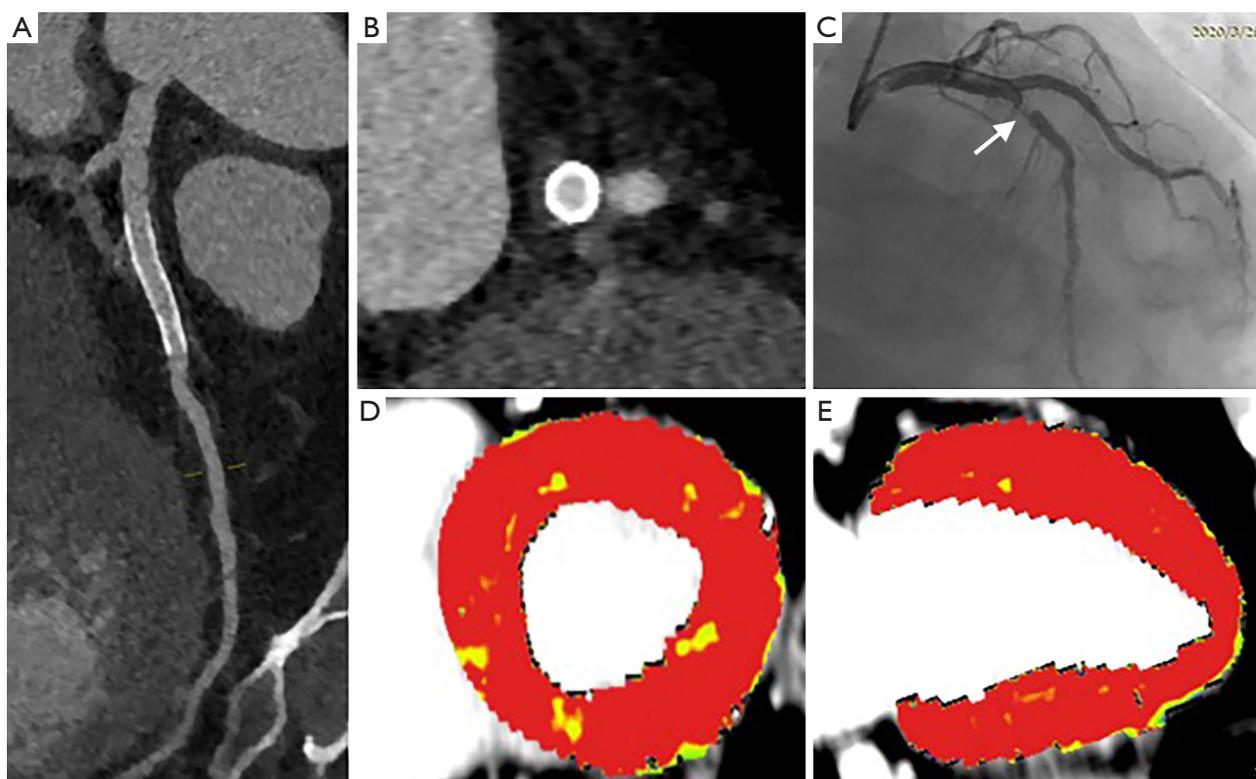
Multiple clinical and angiographic parameters were included in the univariate analysis. As revealed by the current study, hs-cTnI, diabetes, NT-pro-BNP, hs-CRP, AMI, stenotic extent, and preprocedural TIMI flow grade were all associated with decreased myocardial perfusion after PCI in univariate analysis (*Table 4*). When these parameters were input into multivariate analysis, peak hs-

cTnI level was the strongest predictor [adjusted hazard ratio (HR): 4.548, P=0.003] for decreased myocardial perfusion, followed by TIMI flow grade, AMI, stenotic extent, and NT-pro-BNP (*Table 4*). According to ROC curve analysis, stenotic extent and peak hs-cTnI level were the two best parameters for identifying patients with reduced myocardial perfusion after revascularization (*Figure 4*). When using the best cutoff values derived from ROC curve analysis, hs-cTnI, preprocedural stenotic extent, and TIMI flow grade were found to have high diagnostic accuracy for identifying patients with reduced MBF (*Table 5*).

#### **Discussion**

The current study revealed that the baseline hs-cTnI peak level was the strongest predictor for decreased myocardial perfusion after revascularization, followed by preprocedural TIMI flow grade. In addition, a large proportion of patients with AMI did not have normal MBF even after successful revascularization.

Dynamic CT-MPI combined with CCTA is a novel noninvasive imaging modality for detection of reduced



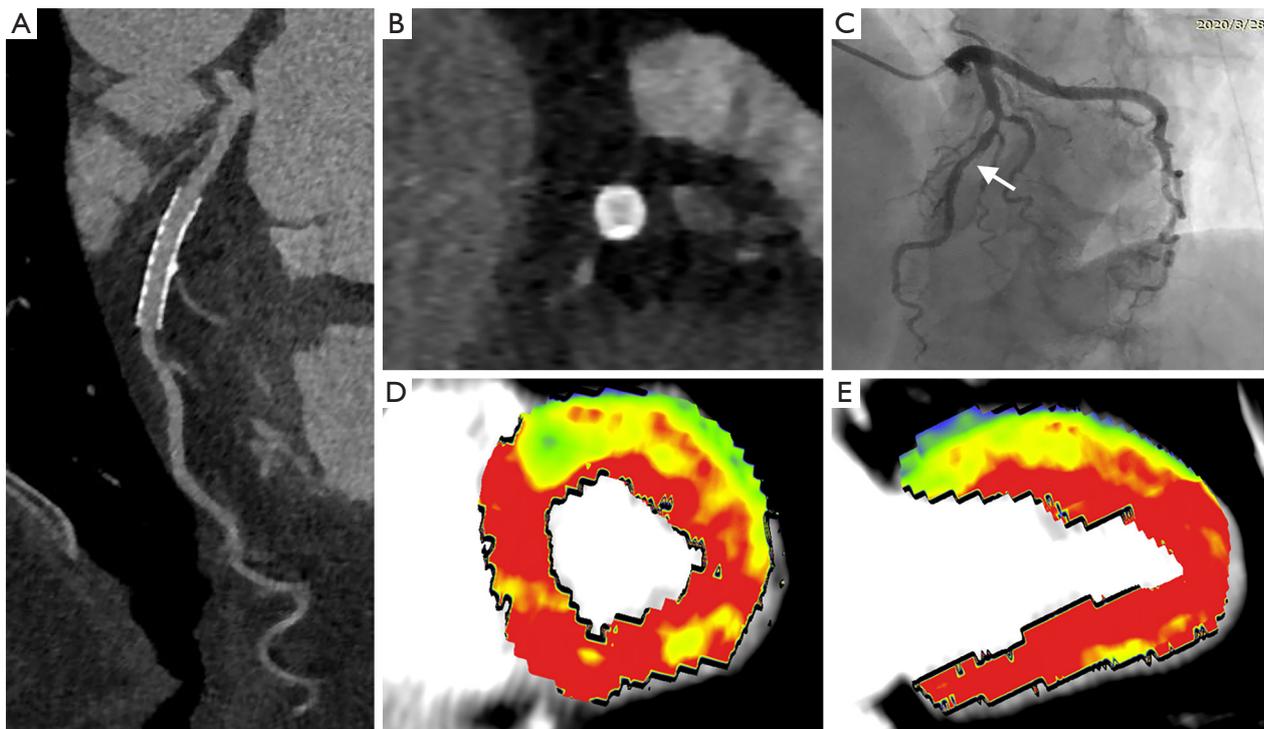
**Figure 2** A 44-year-old male with normal myocardial perfusion 13 months after PCI. (A,B) CPR and cross-sectional images of follow-up CCTA revealed patent stent at the middle LAD. (C) The baseline ICA showed focal severe stenosis at the middle LAD (white arrow). The baseline peak hs-cTnI level was 0.04 ng/L. (D,E) Follow-up dynamic CT-MPI revealed normal myocardial perfusion of the anterior wall (MBF: mL/100 mL/min). PCI, percutaneous coronary intervention; CPR, curved planar reformation; CCTA, coronary computed tomography angiography; LAD, left anterior descending; ICA, invasive coronary angiography; hs-cTnI, high-sensitivity cardiac troponin I; ISR, in-stent restenosis; CT, computed tomography; MPI, myocardial perfusion imaging; MBF, myocardial blood flow.

myocardial perfusion after revascularization. So far, only 1 previous study with 37 participants had investigated the prevalence of impaired perfusion in symptomatic patients with patent stents (4). Compared to that study, the current study focused more on the relationship between baseline characteristics and reduced MBF after revascularization. Our study confirmed a previous finding in which the incidence of myocardial ischemia with patent stents was relatively high in symptomatic patients. Using a significantly larger sample size, we further identified several baseline clinical and imaging characteristics which were able to predict impaired myocardial perfusion after PCI.

hs-cTnI is a routinely used laboratory biomarker which is highly associated with myocardial injury following AMI (15,16). In addition to AMI, the peak level of hs-cTnI also rises after PCI in patients without myocardial infarction if periprocedural myocardial injury occurs. This is not

uncommon and typically caused by distal embolization during procedures (17). In these circumstances, despite the patent coronary stents, microvascular perfusion may be reduced in a substantial portion of the perfusion territory of the treated coronary artery because distal embolization could cause abnormalities at the level of the microvasculature (18). Therefore, it is conceivable that among all baseline clinical characteristics, the peak level of hs-cTnI was the strongest predictor for decreased myocardial perfusion after revascularization.

As for angiographic features, the stenotic extent and preprocedural TIMI flow grade were also two independent predictors for decreased MBF of the stented territory after revascularization. This is in line with the finding of a previous  $^{15}\text{O}$ -water positron emission tomography study that indicated lower lesion complexity and lesser stenotic extent were significantly associated with better regional MBF



**Figure 3** A 72-year-old female with reduced myocardial perfusion 10 months after PCI. (A,B) CPR and cross-sectional images of follow-up CCTA revealed patent stent at middle LAD. (C) The baseline ICA showed focal severe stenosis at middle LAD (white arrow). The baseline peak hs-cTnI level was 52.8 ng/L. (D,E) Follow-up dynamic CT-MPI revealed reduced myocardial perfusion of the anterior wall (MBF = mL/100 mL/min). PCI, percutaneous coronary intervention; CPR, curved planar reformation; CCTA, coronary computed tomography angiography; LAD, left anterior descending; ICA, invasive coronary angiography; hs-cTnI, high-sensitivity cardiac troponin I; ISR, in-stent restenosis; CT, computed tomography; MPI, myocardial perfusion imaging; MBF, myocardial blood flow.

**Table 3** Baseline angiographic characteristics between stented territories with normal and reduced perfusion

Baseline angiographic characteristics	Stented vessels with reduced post-PCI myocardial perfusion (n=49)	Stented vessels with normal post-PCI myocardial perfusion (n=47)	P value
Stenotic extent (%)	90 [80, 100]	85 [80, 90]	0.01
Lesion length (mm)	22.2±9.2	22.4±8.4	0.754
Preprocedural TIMI flow grade	1.64±1.37	2.70±0.64	0.001
Stent location, n (%)			
LAD	26 (53.1)	17 (36.2)	
RCA	13 (26.5)	18 (38.3)	
LCx	10 (20.4)	12 (25.5)	

Values are mean ± SD, n (%); or median (interquartile range). PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction; LAD, left anterior descending; RCA, right coronary artery; LCx, left circumflex; SD, standard deviation.

**Table 4** Univariate and multivariate analysis of predictors for decreased myocardial perfusion after PCI

Baseline clinical characteristics and invasive coronary angiography parameters	Univariate		Multivariate	
	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Age	2.136 (0.862–6.924)	0.795	–	–
Hs-cTnI	2.092 (0.763–5.441)	0.002	4.548 (1.669–12.392)	0.003
NLR ratio	1.146 (0.506–1.374)	0.138	–	–
APOA/APOB	1.263 (0.924–1.367)	0.924	–	–
BMI	1.071 (0.645–2.182)	0.385	–	–
Diabetes mellitus	1.863 (0.615–4.162)	0.049	2.186 (0.773–6.181)	0.14
Total cholesterol	3.361 (2.715–6.325)	0.560	–	–
Triglyceride	1.554 (0.815–5.144)	0.998	–	–
Systolic blood pressure	2.165 (0.892–4.177)	0.420	–	–
Diastolic blood pressure	1.865 (0.935–3.215)	0.693	–	–
NT-pro-BNP	1.103 (0.746–1.002)	<0.001	1.001 (1.000–1.003)	0.039
Hs-CRP	0.301 (0.127–0.614)	0.039	0.234 (0.069–0.793)	0.16
AMI	1.300 (1.032–1.281)	0.002	1.104 (1.103–1.328)	0.027
Stenotic extent	1.042 (1.063–1.121)	0.005	1.073 (1.025–1.123)	0.002
Lesion length	1.023 (0.875–1.253)	0.785	–	–
TIMI flow grade	2.114 (1.025–1.168)	0.008	2.316 (1.054–1.241)	0.003

PCI, percutaneous coronary intervention; HR, hazard ratio; CI, confidence interval; hs-cTnI, high-sensitivity cardiac troponin I; NLR, neutrophil to lymphocyte ratio; APOA/APOB, apolipoprotein A to apolipoprotein B ratio; BMI, body mass index; NT-pro-BNP, N-terminal pro-B-type natriuretic peptide; hs-CRP, high-sensitivity C-reactive protein; AMI, acute myocardial infarction; TIMI, thrombolysis in myocardial infarction.

recovery after revascularization (19). Moreover, pre-PCI TIMI flow grade has been proven to be inversely associated with myocardial injury and microvascular obstruction. It is therefore within expectations that TIMI flow grade was an independent predictor for reduced myocardial perfusion after revascularization.

The current study also demonstrated the potential clinical value of dynamic CT-MPI + CCTA as a “one-stop shop” imaging modality for the comprehensive evaluation of symptomatic post-PCI patients. Anatomical assessment of stent patency by either CCTA or invasive coronary angiography (ICA) is currently the standard method in post-PCI patients with recurrent symptoms (20). However, as revealed by the present study, more than half of the cohort with patent stents had reduced MBF within stented territory. This finding indicates that lumen evaluation might be inadequate for accurate diagnosis in symptomatic patients after revascularization. In contrast to CCTA, dynamic CT-MPI + CCTA is able to detect

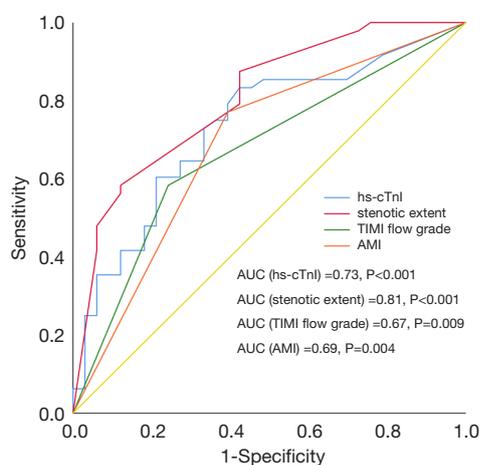
both anatomical and functional abnormality in one examination at a relatively low radiation dose (4.89 mSv), which makes it suitable in the current clinical scenario. Moreover, the baseline hs-cTnI peak level was found to be the strongest predictor for decreased myocardial perfusion after PCI. Thus, in clinical practice, patients with high baseline hs-cTnI peak level might be considered a high-risk population of impaired microvascular dysfunction after revascularization. Follow-up CT-MPI + CCTA is therefore preferred as the first-tier imaging modality for such patients with recurrent symptoms.

In spite of the above findings, the current study also had several limitations. First, only symptomatic post-PCI patients with patent stents were included due to the retrospective design. Asymptomatic post-PCI patients were not referred for dynamic CT-MPI + CCTA in our institute because of improper indications. Thus, it remains unclear whether similar findings can be revealed in the cohort of asymptomatic post-PCI patients. Also, the retrospective

design of the current study led to heterogeneity of the population (patients with and without a history of AMI) and a limited sample size. Future prospective studies with larger sample sizes are warranted to eliminate the impact of confounding factors. In addition, the period range between PCI and follow-up CT scan was relatively wide in our study. This nonuniform time interval was another confounding factor that might have influenced the recovery of blood

flow after PCI. Finally, cardiac MRI with late gadolinium enhancement was not available after PCI. Hence, it is not feasible to differentiate myocardial ischemia from scarring secondary to myocardial infarction. Finally, the baseline plaque features of target lesions were not evaluated, as preprocedural CCTA was not available in all participants. The CCTA has been recognized as a useful tool for high-risk plaque analysis (21). It may bear valuable information regarding the association between plaque characteristics and post-PCI myocardial perfusion.

In conclusion, the baseline hs-cTnI peak level was the strongest predictor for decreased myocardial perfusion after revascularization, followed by preprocedural TIMI flow grade. In addition, a large proportion of patients with AMI did not have fully recovered MBF even after successful revascularization.



**Figure 4** A 72-year-old female with reduced myocardial perfusion 10 months after PCI. (A,B) CPR and cross-sectional images of follow-up CCTA revealed patent stent at middle LAD. (C) The baseline ICA showed focal severe stenosis at middle LAD (white arrow). The baseline peak hs-cTnI level was 52.8 ng/L. (D,E) Follow-up dynamic CT-MPI revealed reduced myocardial perfusion of the anterior wall (MBF = mL/100 mL/min). PCI, percutaneous coronary intervention; CPR, curved planar reformation; CCTA, coronary computed tomography angiography; LAD, left anterior descending; ICA, invasive coronary angiography; hs-cTnI, high-sensitivity cardiac troponin I; ISR, in-stent restenosis; CT, computed tomography; MPI, myocardial perfusion imaging; MBF, myocardial blood flow.

**Acknowledgments**

*Funding:* This study was supported by the Science and Technology Foundation of the Health Commission of Guizhou province (gzwjkj 2020-1-176), International Exemplary Cooperation Base of Precision Imaging for Diagnosis and Treatment {QKHPTRC[2019]5803}, Medical Guidance Scientific Research Support Project of Shanghai Science and Technology Commission (19411965100) and Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant Support (20161428).

**Footnote**

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/qims-20-977>). Dr. HM received grant from Science and Technology Foundation of the Health Commission of Guizhou province (gzwjkj 2020-1-176).

**Table 5** Different baseline parameters for identifying patients with decreased myocardial perfusion after PCI

Parameter	AUC	Cutoff value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Hs-cTnI (ng/L)	0.73	>1.5	89.6 (43/48)	81.8 (27/33)	91.5 (43/47)	79.4 (27/34)	86.4 (70/81)
Stenotic extent (%)	0.8	≥77.5	87.5 (42/48)	87.9 (29/33)	91.3 (42/46)	82.9 (29/35)	87.7 (71/81)
Preprocedural TIMI flow grade	0.67	≤2	81.3 (39/48)	87.9 (29/33)	84.8 (39/46)	82.9 (29/35)	84 (68/81)

PCI, percutaneous coronary intervention; AUC, area under curve; PPV, positive predictive value; NPV, negative predictive value; hs-cTnI, high-sensitivity cardiac troponin I; TIMI, thrombolysis in myocardial infarction.

Dr. RW received grant from International Exemplary Cooperation Base of Precision Imaging for Diagnosis and Treatment {QKHPTRC[2019]5803}. Dr. JZ received grants from Medical Guidance Scientific Research Support Project of Shanghai Science and Technology Commission (Grant No. 19411965100) and Shanghai Municipal Education Commission-Gaofeng Clinical Medicine Grant Support (Grant No. 20161428). The other authors have no conflicts of interest to declare.

*Ethical Statement:* The hospital ethics committee approved this study, and the need for written informed consent was waived due to its retrospective nature.

*Open Access Statement:* This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

## References

1. Sousa JE, Serruys PW, Costa MA. New frontiers in cardiology: drug-eluting stents: Part I. *Circulation* 2003;107:2274-9.
2. Sousa JE, Serruys PW, Costa MA. New frontiers in cardiology: drug-eluting stents: Part II. *Circulation* 2003;107:2383-9.
3. Hachamovitch R, Rozanski A, Shaw LJ, Stone GW, Thomson LE, Friedman JD, Hayes SW, Cohen I, Germano G, Berman DS. Impact of ischaemia and scar on the therapeutic benefit derived from myocardial revascularization vs. medical therapy among patients undergoing stress-rest myocardial perfusion scintigraphy. *Eur Heart J* 2011;32:1012-24.
4. Li Y, Yuan M, Yu M, Lu Z, Shen C, Wang Y, Lu B, Zhang J. Prevalence of decreased myocardial blood flow in symptomatic patients with patent coronary stents: insights from low-dose dynamic CT myocardial perfusion imaging. *Korean J Radiol* 2019;20:621-30.
5. Schumacher SP, Stuijzand WJ, Driessen RS, van Diemen PA, Bom MJ, Everaars H, Kockx M, Raijmakers PG, Boellaard R, van de Ven PM, van Rossum AC, Opolski MP, Nap A, Knaapen P. Impact of specific crossing techniques in chronic total occlusion percutaneous coronary intervention on recovery of absolute myocardial perfusion. *Circ Cardiovasc Interv* 2019;12:e008064.
6. Alessio AM, Bindschadler M, Busey JM, Shuman WP, Caldwell JH, Branch KR. Accuracy of myocardial blood flow estimation from dynamic contrast-enhanced cardiac CT compared with PET. *Circ Cardiovasc Imaging* 2019;12:e008323.
7. Yu M, Shen C, Dai X, Lu Z, Wang Y, Lu B, Zhang J. Clinical outcomes of dynamic computed tomography myocardial perfusion imaging combined with coronary computed tomography angiography versus coronary computed tomography angiography-guided strategy. *Circ Cardiovasc Imaging* 2020;13:e009775.
8. Li Y, Yu M, Dai X, Lu Z, Shen C, Wang Y, Lu B, Zhang J. Detection of hemodynamically significant coronary stenosis: CT myocardial perfusion versus machine learning CT fractional flow reserve. *Radiology* 2019;293:305-14.
9. Yu M, Chen X, Dai X, Pan J, Wang Y, Lu B, Zhang J. The value of low-dose dynamic myocardial perfusion CT for accurate evaluation of microvascular obstruction in patients with acute myocardial infarction. *AJR Am J Roentgenol* 2019;213:798-806.
10. Pan J, Yuan M, Yu M, Gao Y, Shen C, Wang Y, Lu B, Zhang J. Myocardial blood flow quantified by low-dose dynamic CT myocardial perfusion imaging is associated with peak troponin level and impaired left ventricle function in patients with ST-elevated myocardial infarction. *Korean J Radiol* 2019;20:709-18.
11. Bamberg F, Klotz E, Flohr T, Becker A, Becker CR, Schmidt B, Wintersperger BJ, Reiser MF, Nikolaou K. Dynamic myocardial stress perfusion imaging using fast dual-source CT with alternating table positions: initial experience. *Eur Radiol* 2010;20:1168-73.
12. Rossi A, Merkus D, Klotz E, Mollet N, de Feyter PJ, Krestin GP. Stress myocardial perfusion: imaging with multidetector CT. *Radiology* 2014;270:25-46.
13. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, Pennell DJ, Rumberger JA, Ryan T, Verani MS; American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation* 2002;105:539-42.
14. Li Y, Yu M, Li W, Lu Z, Wei M, Zhang J. Third

- generation dual-source CT enables accurate diagnosis of coronary restenosis in all size stents with low radiation dose and preserved image quality. *Eur Radiol* 2018;28:2647-54.
15. Chia S, Senatore F, Raffel OC, Lee H, Wackers FJ, Jang IK. Utility of cardiac biomarkers in predicting infarct size, left ventricular function, and clinical outcome after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. *JACC Cardiovasc Interv* 2008;1:415-23.
  16. Hassan AK, Bergheanu SC, Hasan-Ali H, Liem SS, van der Laarse A, Wolterbeek R, Atsma DE, Schaliq MJ, Jukema JW. Usefulness of peak troponin-T to predict infarct size and long-term outcome in patients with first acute myocardial infarction after primary percutaneous coronary intervention. *Am J Cardiol* 2009;103:779-84.
  17. Balian V, Galli M, Marcassa C, Cecchin G, Child M, Barlocco F, Petrucci E, Filippini G, Michi R, Onofri M. Intracoronary ST-segment shift soon after elective percutaneous coronary intervention accurately predicts periprocedural myocardial injury. *Circulation* 2006;114:1948-54.
  18. Jaffe R, Dick A, Strauss BH. Prevention and treatment of microvascular obstruction-related myocardial injury and coronary no-reflow following percutaneous coronary intervention: a systematic approach. *JACC Cardiovasc Interv* 2010;3:695-704.
  19. Aikawa T, Naya M, Koyanagawa K, Manabe O, Obara M, Magota K, Oyama-Manabe N, Tamaki N, Anzai T. Improved regional myocardial blood flow and flow reserve after coronary revascularization as assessed by serial 15O-water positron emission tomography/computed tomography. *Eur Heart J Cardiovasc Imaging* 2020;21:36-46.
  20. Hickethier T, Wenning J, Bratke G, Maintz D, Michels G, Bunck AC. Evaluation of soft-plaque stenoses in coronary artery stents using conventional and monoenergetic images: first in-vitro experience and comparison of two different dual-energy techniques. *Quant Imaging Med Surg* 2020;10:612-23.
  21. Yuan M, Wu H, Li R, Yu M, Dai X, Zhang J. The value of quantified plaque analysis by dual-source coronary CT angiography to detect vulnerable plaques: a comparison study with intravascular ultrasound. *Quant Imaging Med Surg* 2020;10:668-77.

**Cite this article as:** Ma H, Dai X, Yang X, Zhao X, Wang R, Zhang J. Clinical and imaging predictors of impaired myocardial perfusion in symptomatic patients after percutaneous coronary intervention: insights from dynamic CT myocardial perfusion imaging. *Quant Imaging Med Surg* 2021;11(7):3327-3337. doi: 10.21037/qims-20-977

**Dynamic CT-MPI + coronary CT angiography protocol**

Calcium score was firstly performed to calculate the calcification burden of each pericardial vessels. The scan range of dynamic CT-MPI was determined based on the calcium score images to cover the whole left ventricle as well as all coronary arteries. Adenosine triphosphate was intra-venously infused over 3 min at 160  $\mu\text{g}/\text{kg}/\text{min}$  before triggering the MPI acquisition. A fixed volume of contrast media (50 mL, Ultravist, 370 mg iodine/mL, Bayer, Berlin, Germany) was given in a bolus injection at the rate of 6 mL/s in all participants, followed by a 40 mL saline flush by using dual-barrel power injector (Tyco, Cincinnati, OH, USA). Dynamic CT-MPI acquisition was started 4 s after the begin of contrast injection. The end-systolic phase (triggered at 250 ms after the R wave in all participants) was set for the dynamic acquisition by using a shuttle mode technique with a coverage of 10.5 cm for complete imaging of the whole left ventricle. Scans were launched every second or third heart cycle according to participants' heart rate, resulting in a series of 10 to 15 phases acquired over a fixed period of 32 s. The acquisition parameters of dynamic CT-MPI is listed as follow: collimation =  $96\times 0.6$  mm,

CARE kV was used and the reference tube voltage =80 kVp, rotation time =250 ms, CARE dose 4D was used and the effective current =300 mAs, reconstructed slice thickness =3 mm and reconstructed slice interval =2 mm.

Nitroglycerin was given sublingually in all participants 5 minutes after dynamic CT-MPI, prior to the acquisition of coronary CT angiography. Coronary CT angiography was performed by using a bolus tracking technique, with regions of interest placed in the ascending aorta. A bolus of contrast media was injected into antecubital vein at the rate of 4–5 mL/s, followed by a 40 mL saline flush by using dual-barrel power injector. The amount of the contrast media was determined according to the patient's body weight and scan time. Prospective ECG-triggered sequential acquisition was performed in all participants for coronary CT angiography, with the center of the triggering window set at diastole or systole depending on the heart rate, with collimation = $96\times 0.6$  mm, reconstructed slice thickness =0.75 mm, reconstructed slice interval =0.5 mm, rotation time =250 ms and application of automated tube voltage and current modulation (CAREKv, CARE Dose 4D, Siemens Healthineers, Germany). The reference tube current was set as 320 mAs and the reference tube voltage was set as 100 kVp.