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Correlation of Angina Pectoris and Perfusion Decrease by Collateral Circulation in Single-Vessel Coronary Chronic Total Occlusion Using Myocardial Perfusion Single-Photon Emission Computed Tomography

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Abstract
Purpose To evaluate the perfusion decrease in donor myocardium by collateral circulation and its correlation with angina pectoris in patients with chronic total occlusion (CTO) using myocardial perfusion single-photon emission computed tomography (MPS).
Materials and Methods Thirty-six patients with single-vessel CTO without any other stenosis were included. All patients underwent MPS and coronary angiography (CAG) within 2 months. Total 72 donor arteries were evaluated for the grades of collaterals to the CTO artery using the Rentrop grading system on CAG. Perfusion defects and perfusion scores in donor and CTO territories were analyzed on MPS. Myocardial perfusion of donor and CTO territories were evaluated according to the presence of angina pectoris and the grades of collateral circulation.
Results When the CTO territory was ischemic, symptomatic patients showed higher summed difference scores in the CTO territory compared to asymptomatic patients (3.5±2.4 vs. 1.5 ±0.8 for symptomatic and asymptomatic groups respectively; p=0.034). However, when the CTO territory was nonischemic, symptomatic patients showed higher summed stress scores (SSS, 4.3±2.9 vs. 1.6±1.2; p=0.032) and summed rest scores (SRS, 4.2±2.5 vs. 1.5±1.1; p=0.003) in the donor territories. On the per-vessel analysis, perfusion defects in donor territories were more frequent (0 % vs. 53 % vs. 86 % for Rentrop 0, Rentrop 1–2 and Rentrop 3, respectively; p<0.001) and showed higher SSS (0.0±0.0, 1.3 ±1.6 and 2.1±1.1 for Rentrop 0, Rentrop 1–2 and Rentrop 3, respectively; p=0.001) and SRS (0.0±0.0, 1.0±1.4 and 1.7± 1.2; p=0.003) at higher Rentrop grades, but their patterns were variable.
Conclusion Angina pectoris was related to either ischemia of the myocardium beyond CTO or a perfusion decrease in the donor myocardium. The perfusion decrease in donor myocardium positively correlated with the collateral grades.

Keywords Coronary occlusion · Collateral circulation · Angina pectoris · Myocardial perfusion imaging

Introduction

Chronic total occlusion (CTO) is a complete or near complete occlusion of the vessel by a heavy atherosclerotic plaque burden [1]. It is a relatively common finding in patients indicated for invasive coronary angiography (CAG), with a reported incidence of up to 15–52 % [2–4].

Vascular resistance decreases beyond the occlusion site as a response to decreased luminal pressure within the arteriolar bed primarily supplied by the occluded artery. It causes a pressure gradient across the native collateral bed and increases

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the flow velocity toward the occluded artery. Such hemodynamic changes induce maturation of the native collateral channels along with the formation of de novo collateral channels as a result of biochemical changes involving various endothelial and inflammatory cells and induced cytokines [5, 6]. Collateral circulation protects the jeopardized myocardium beyond the stenotic or occlusive lesions and consequently improves the prognosis of patients with coronary heart diseases [7–10].

Although the degree of functional restoration of blood flow capacity is usually around 40 % of the original artery [11], redirected blood flow to the occluded artery can lead to a significant perfusion deprivation from the donor myocardium because two myocardial territories must be fed by a single donor artery [12]. Several recent studies evaluated this phenomenon using invasive CAG and fractional flow reserve (FFR) [13–16]. They showed significantly decreased FFR< 0.8 despite the mild degree of stenotic lesions in the donor arteries. In addition, FFR of donor arteries was recovered only by recanalization of the recipient artery. Significant perfusion deprivation from the donor artery was likely due to collateral circulation.

Myocardial perfusion single-photon emission computed tomography (MPS) is a widely used tool that provides relative information on perfusion at a myocardial dimension [17]. Myocardial viability or ischemia of the collateral-dependent myocardium can be provided by MPS, which is of extreme importance to the decision concerning percutaneous coronary intervention (PCI) or bypass surgery in patients with CTO. Consistent with the reports above, several studies showed a perfusion decrease by collateral circulation even in the absence of any stenotic lesion in donor arteries using MPS [12, 18, 19]. However, the clinical implication of a perfusion decrease in the donor myocardium remains unclear, and no relevance to the therapeutic strategy in patients with CTO has been suggested. Therefore, we analyzed the perfusion decrease in donor myocardium by collateral circulation in patients with single-vessel CTO using MPS and its relation to angina pectoris.

Materials and Methods

Patients

We enrolled a total of 36 patients who were diagnosed with single-vessel CTO defined as an estimated luminal narrowing of≥99 % in one of the three main coronary arteries or a major branch [20]. In all patients, CAG and MPS were performed within 2 months, and there was no angiographic stenosis>50 % in the other coronary branches (donor arteries). CAG was performed after MPS for further evaluation of abnormal findings on MPS in 22 patients, while MPS was performed to evaluate myocardial perfusion after CTO was documented on CAG in the other 14. Exclusion criteria included a previous revascularization, change in clinical symptoms between CAG and MPS, other structural diseases such as valvular heart diseases, coronary anatomical variation, stenosis or occlusion of the left main stem and bronchial asthma for which the use of adenosine was contraindicated. Cases with bridging collateral circulation from other normal segments of the same artery with CTO were not included in our study. Acquisition of clinical characteristics and image analysis data were based on retrospective medical charts and image reviews as ethically approved by our Institutional Review Board.

Patients were classified into two groups according to the presence of angina pectoris, where angina pectoris was defined as having typical (substernal location, precipitation by exertion/emotional stress, and relief by rest and/or nitrates) or atypical chest pain (substernal location+either precipitation by exertion/emotional stress or relief by rest and/or nitrates) [21] regardless of other related clinical symptoms such as dyspnea, palpitation or fatigue.

Grading of Collateral Circulation

Two experienced interventional cardiologists unaware of the results of MPS performed the grading of collaterals. According to CAG findings, collaterals from each of the two donor arteries toward the CTO artery were classified on a per-vessel basis as follows: Rentrop 0=none, Rentrop 1=filling of side branches only, Rentrop 2=partial filling of the epicardial segment and Rentrop 3=complete filling of the epicardial segment [22].

Myocardial Perfusion Single-Photon Emission Computed Tomography

A 1-day rest/stress, single-isotope protocol was performed in all enrolled patients. They were instructed to stop intake of medications or foods that could affect vasodilator stress (nitrate, beta-blocker, calcium channel blocker and methylxanthine derivatives such as caffeine). In addition, all patients were required to fast for at least 4 h before image acquisition. For acquisition of the rest image, 370 MBq (10 mCi) of either Tc-99 m methoxyisobutyl isonitrile (MIBI) or Tc-99 m tetrofosmin was injected intravenously. Thirty minutes after injection, the image was acquired. Immediately after rest image acquisition, adenosine was intravenously infused at a 0.14 mg/kg/min infusion rate, and 3 min later, 1110 MBq (30 mCi) of Tc-99 m MIBI or Tc-99 m tetrofosmin was injected. The stress image was acquired 30 min later. Images were acquired every 3 degrees over a 180-degree semicircular orbit, which was initiated from 45 degrees right anterior oblique. Patients were maintained in supine position with their arms placed over the head. Two types of dual-head gamma

cameras (DST-XLi and NM-CT 670, GE Healthcare) were used for image acquisition.

Image Analyses on MPS

Two experienced nuclear medicine physicians blinded to the results of CAG participated in the MPS analyses. Acquired images were reconstructed to the polar plot for segmentation analysis using dedicated QGS/QPS® software (GE Healthcare). The left ventricle was divided into 17 segments and grouped respectively by three vessel territories—the left anterior descending artery (LAD), left circumflex (LCx) and right coronary artery (RCA) territories—using the standard 17-segment model according to the 2002 recommendation of the American Heart Association [23]. The territory supplied by the CTO artery was defined as the CTO territory, while the other two supplied by donor arteries were defined as donor territories.

The presence of perfusion defects (PD) in each of the donor territories was determined by consensual visual analysis by the two observers. When present, they were further classified into reversible, fixed or reverse patterns. For semiquantitative analysis, 0 to 4 points were consensually scored for each segment on both stress and rest images using a 5-point scoring system (0=normal, 1=equivocal, 2=moderate, 3=severe reduction of radioisotope uptake, 4=absence of detectable tracer uptake). The summed stress score (SSS) and summed rest score (SRS) were calculated by summing the stress and rest scores of individual segments throughout the whole myocardium, respectively. The summed difference score (SDS) was calculated by summing the differences between stress and rest scores (stress score – rest score). Perfusion scores were calculated for every single donor (SSS_{donor}, SRS_{donor} and SDS_{donor}) and CTO territory (SSS_{CTO}, SRS_{CTO} and SDS_{CTO}) on a per-vessel basis. SSS_{donor}, SRS_{donor} and SDS_{donor} of the two donor territories were summed for each patient (SSS_{DONOR}, SRS_{DONOR} and SDS_{DONOR}). When there was no visual reversibility with the $SDS_{CTO}<1$, the CTO territory was regarded as nonischemic, and otherwise ischemic [24].

Statistical Analyses

Clinical characteristics and MPS results were compared between symptomatic and asymptomatic groups. For further evaluation according to ischemia of the CTO territory, comparison was again performed within patients with ischemic and nonischemic CTOs. The correlation between perfusion scores and angina severity according to the Canadian Cardiovascular Society (CCS) classification was also evaluated.

For per-vessel analysis of donor arteries, the presence and patterns of PD in donor territories, and their perfusion scores were compared among different Rentrop grades.

Mann-Whitney U-test and Kruskal-Wallis test were used for continuous variables and Fisher's exact test and chi-square test for categorical variables. Spearman's rank correlation test was used for correlation analysis. Statistical significance was defined as $p<0.05$, and SPSS 21.0 (SPSS, Chicago, IL, USA) was used for statistical calculation.

Results

Correlation of Angina Pectoris and Perfusion of Donor and Recipient Myocardium

The clinical characteristics of the enrolled patients are listed in Table 1. The symptomatic group included 16 patients (CCS class I in 2, II in 2, III in 6 and IV in 6), and the remaining 20 were asymptomatic. The symptomatic group did not show any significant difference in clinical characteristics or MPS results as compared to asymptomatic group, except for a higher prevalence of diabetes (50 % vs. 15 % for symptomatic and asymptomatic groups, respectively; $p=0.034$) (Table 2).

Ischemic CTO was observed in 18 of 36 patients. Within those with ischemic CTO, the symptomatic group (n=10) showed significantly higher SDS_{CTO} (3.5±2.4 vs. 1.5±0.8; $p=0.034$) compared to the asymptomatic group (n=8). A positive but only borderline correlation was found between SDS_{CTO} and CCS class (Spearman's rho=0.465, $p=0.052$). There was no significant difference in SSS_{CTO}, SRS_{CTO} or perfusion scores of donor territories. However, within the patients with nonischemic CTO, the symptomatic group (n=6) showed significantly higher SSS_{DONOR} (4.3±2.9 vs. 1.6±1.2 for symptomatic and asymptomatic groups, respectively; $p=0.032$) and SRS_{DONOR} (4.2±2.5 vs. 1.5±1.1; $p=0.003$) compared to the asymptomatic group (n=12). A significant, positive correlation was found between perfusion scores of the donor myocardium and CCS class of angina pectoris (Spearman's rho=0.600, $p=0.008$ and Spearman's rho=0.700, $p=0.001$ for SSS_{DONOR} and SRS_{DONOR}, respectively). However, there was no significant difference in SDS_{DONOR} or perfusion scores of the CTO territory (Figs. 1, 2 and 3).

No significant differences of clinical characteristics or LV functional parameters were found between symptomatic and asymptomatic groups, regardless of nonischemic or ischemic CTOs.

Per-Vessel Analyses for Donor Arteries

Among the 72 included donor arteries, collateral grades were Rentrop 0 in 6 (8 %), Rentrop 1–2 in 45 (63 %) and Rentrop 3 in 21 (29 %) arteries. On MPS, PD was observed in 42 (58 %) donor territories. No significant difference in Rentrop grades, presence or patterns of PD, or perfusion scores of donor

Table 1 Clinical characteristics of the enrolled patients (n=36)

Age (years)		68.3±9.4
Male sex		26 (72)
Angina pectoris		16 (44)
CCS class I		2
CCS class II		2
CCS class III		6
CCS class IV		6
MPS-CAG interval (days)		6.1±13.2
Smoking	Non-smoker	21 (59)
	Ex-smoker	3 (8)
	Current smoker	12 (33)
Hypertension		22 (61)
Diabetes		11 (31)
Dyslipidemia		11 (31)
Obesity (BMI≥25 kg/m^2)		11 (31)
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker		11 (31)
Beta blocker		7 (19)
Calcium channel blocker		5 (14)
Statin		11 (31)
Antiplatelet agent		11 (31)
Nitrates		6 (17)
Arteries with CTO		
LAD		17 (47)
LCx		3 (8)
RCA		16 (45)
SPECT results		
SSS		10.2±7.4
SRS		8.8±6.8
SDS		1.4±2.8
LVEDV (ml)		109.9±49.9
LVESV (ml)		57.0±39.1
LVEF (%)		51.8±12.6
TID ratio		0.99±0.14
Ischemic CTOs		18 (50)
Radiopharmaceuticals for MPS		
Tc-99 m tetrofosmin		29 (81)
Tc-99 m MIBI		7 (19)

Data are mean ± SD, or n followed by percentage in parentheses

NYHA, New York Heart Association; MPS, myocardial perfusion single-photon emission computed tomography; CAG, coronary angiography; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; SSS_{WHOLE}, summed stress score of whole myocardium; SRS_{WHOLE}, summed rest score of whole myocardium; SDS_{WHOLE}, summed difference score of whole myocardium; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; TID, transient ischemic dilation; CTO, chronic total occlusion; MIBI, methoxyisobutyl isonitrile

territories were observed among three different branches, except for SRS_{donor}, which showed the lowest value in the LCx territory (1.84±1.21 vs. 0.76±1.12 vs. 1.10±1.55 for LAD, LCx and RCA territories, respectively; p=0.016).

PD in the donor territory was significantly more frequently observed with richer collaterals (0 % vs. 53 % vs. 86 % for Rentrop 0, Rentrop 1-2 and Rentrop 3, respectively; p< 0.001). But once the PDs were present, their patterns were similar between Rentrop 1–2 and Rentrop 3: 8 (33 %), 12 (50 %) and 4 (17 %) for reversible, fixed and reverse PDs, respectively, for Rentrop 1–2 and 6 (33 %), 11 (61 %) and 1 (6 %) PDs for Rentrop 3 (p=0.522).

We found a significant stepwise increase in SSS_{donor} (0.0± 0.0, 1.3±1.6 and 2.1±1.1 for Rentrop 0, Rentrop 1–2 and Rentrop 3, respectively; p=0.001) and SRS_{donor} (0.0±0.0, 1.0±1.4 and 1.7±1.2; p=0.003) as Rentrop grades escalated, but no difference in SDS_{donor} (0.0±0.0, 0.3±0.8 and 0.4±1.0; p=0.527) (Fig. 4).

Discussion

The present study demonstrated that angina pectoris in patients with CTO might result from not only ischemic myocardium beyond occlusion, but also from a perfusion decrease in donor myocardium. When the CTO territory showed ischemia, angina pectoris was related to its severity. But without ischemia in the CTO territory, angina pectoris was related to the perfusion status of donor myocardium. Although there was no angiographical stenosis in donor arteries, a perfusion decrease indicated by visible PD, and an increase in perfusion scores on MPS was observed in more than half of the included donor arteries' territories. It was even more prominent with richer collaterals.

From the aspect of the diagnosis of coronary artery disease, all the perfusion defects observed in the donor territories in our study were "false positives," leading to a misdiagnosis of multivessel disease even though the enrolled patients did not have corresponding stenosis in the donor arteries (single-vessel CTO). The possibility of a single-vessel CTO with collateral circulation can easily be neglected in the setting of the initial evaluation of coronary artery disease without given CAG findings. However, it should be considered, although MPS results are indicative of multivessel disease, regarding the high prevalence (58 %) of unexpected perfusion defects in the donor territories by collateral circulation rich enough to induce significant perfusion defects, as demonstrated in our study.

Considering the aspect of the therapeutic strategy after CTO has been documented on CAG, however, the perfusion defects in donor territories should not be considered simply as false positives confusing the MPS interpretation, but informative findings showing hemodynamic changes via the collateral circulation. They were related to the collateral grades and even anginal symptoms in patients with single-vessel CTO. Current

Table 2 Comparison of clinical characteristics and MPS results between the symptomatic and asymptomatic patients

		Symptomatic (n=16)	Asymptomatic (n=20)	p-value
Age (years)		68.1±8.9	68.5±9.9	1.000
Male sex		10 (63)	16 (80)	0.285
MPS-CAG intervals (days)		2.8±10	8.7±14.9	0.095
Smoking	Non-smoker	9 (56)	12 (60)	0.852
	Ex-smoker	1 (6)	2 (10)	
	Current smoker	6 (38)	6 (30)	
Hypertension		12 (75)	10 (50)	0.176
Diabetes		8 (50)	3 (15)	0.034*
Dyslipidemia		5 (31)	6 (30)	1.000
Obesity		7 (44)	4 (20)	0.159
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker		5 (31)	6 (30)	1.000
Beta blocker		3 (19)	4 (20)	1.000
Calcium channel blocker		0 (0)	5 (25)	0.053
Statin		3 (19)	8 (40)	0.277
Antiplatelet agent		4 (25)	7 (35)	0.718
Nitrates		2 (13)	4 (20)	0.672
Arteries with CTO	LAD	8 (50)	9 (45)	0.905
	LCx	1 (6)	2 (10)	
	RCA	7 (44)	9 (45)	
Ischemic CTOs		10 (63)	8 (40)	0.315
MPS results	SSS	11.0±8.8	9.4±6.2	1.000
	SRS	9.3±8.6	8.3±5.3	0.498
	SDS	1.8±3.4	1.2±2.2	0.109
	SSS_{DONOR}	3.2±2.9	2.0±1.6	0.249
	SRS_{DONOR}	3.0±2.7	1.6±1.2	0.124
	SDS_{DONOR}	0.2±1.2	0.4±1.1	0.718
	SSS_{CTO}	7.8±6.9	7.6±5.1	0.912
	SRS_{CTO}	5.7±6.6	7.6±5.1	0.158
	SDS_{CTO}	2.1±2.6	0.4±1.5	0.146
	LVEF (%)	52.6±16.1	51.1±9.2	0.211
	LVEDV (ml)	113.6±53.1	106.9±48.3	0.765
	LVESV (ml)	59.6±47.1	55.0±32.4	0.863

SSS_{DONOR}, sum of summed stress scores of the two donor territories; SRS_{DONOR}, sum of summed rest scores of the two donor territories; SDS_{DONOR}, sum of summed difference scores of the two donor territories; SSS_{CTO}, summed stress score of the CTO territory; SRS_{CTO}, summed rest score of the CTO territory; SDS_{CTO}, summed difference score of the CTO territory

guidelines for PCI or bypass surgery in coronary artery disease include ischemia or viability in the CTO territory or symptoms for the decision of revascularization, but no specific recommendations of a perfusion decrease in donor myocardium and its evaluation [21, 25–27]. A perfusion decrease in the donor territory shown by MPS, without signs of ischemia in the CTO territory, would not be taken into consideration for revascularization of the CTO in routine management flow. Accordingly, 14 subjects in our study were referred for MPS after CTO had been documented on CAG, and elective PCI was performed at the clinicians' discretion mainly regarding the ischemia or viability in the CTO territory or severity of angina pectoris, but regardless of the perfusion decrease in the donor territories. However, in our data, the perfusion decrease in the donor territories was more significantly associated with angina pectoris in patients with nonischemic CTOs compared to that of the CTO territory. The ischemic severity of the CTO territory was important only when it was ischemic. So, it is assumable that there can be some additional patients who do not show ischemia in the CTO territory, but may benefit from PCI in terms of symptom relief by decreasing the perfusion deprivation via collateral circulation. Further studies are

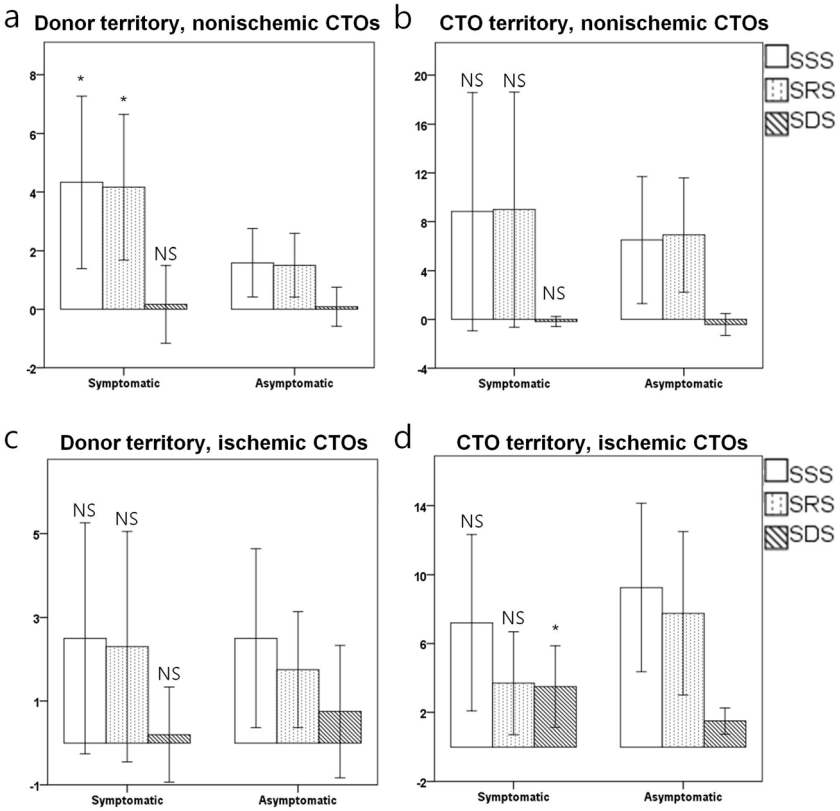

Fig. 1 Comparison of perfusion scores of donor and CTO territories between the symptomatic and asymptomatic groups. In nonischemic CTOs (**a**, **b**), higher SSS and SRS of the donor territories were associated with angina pectoris, while higher SDS_{CTO} of the CTO territory was in ischemic CTOs (**c**, **d**). *p<0.05 against the asymptomatic group; NS, not significant; CTO, chronic total occlusion; SSS, summed stress score; SRS, summed rest score; SDS, summed difference score

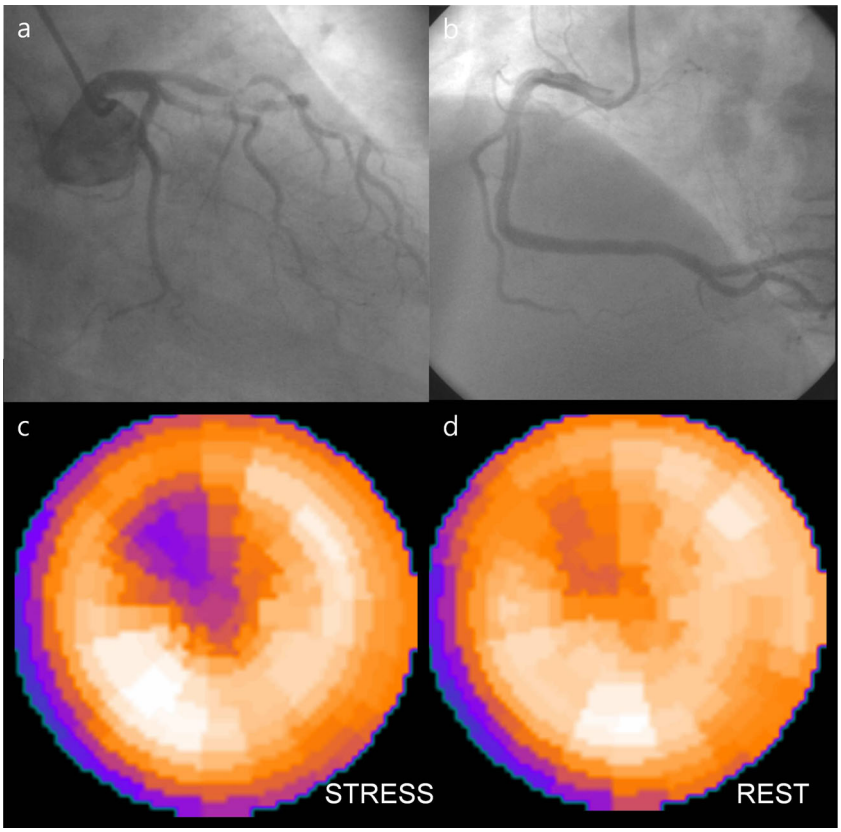

Fig. 2 CAG (**a**, **b**) and MPS (**c**, **d**) of a 74-year-old male patient with CCS class II angina pectoris with CTO in LAD (**a**). No definite collateral circulation is noted (Rentrop 0) on CAG (**a**, **b**). A reversible perfusion defect is noted in the LAD territory (ischemic CTO), without significant perfusion defects in the donor (LCx/RCA) territories (**c**, **d**). CAG, coronary angiography; MPS, myocardial perfusion single-photon emission computed tomography; CCS, Canadian Cardiovascular Society; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery

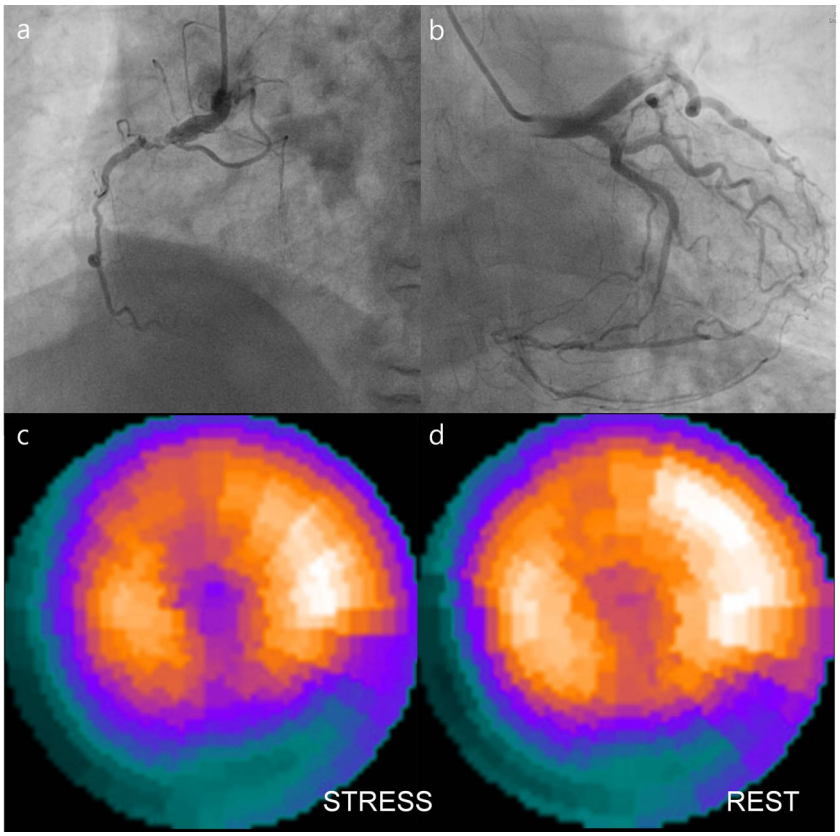

Fig. 3 CAG (**a**, **b**) and MPS (**c**, **d**) of a 73-year-old male patient with CCS class III angina pectoris with CTO in RCA (**a**), with no sign of ischemia in its territory. Rich collateral branches (Rentrop 3) originating from the LAD and LCx are noted on CAG (**b**). A large, fixed perfusion defect is noted in the RCA territory without definite reversibility. Reversible perfusion defects are noted in the donor (LAD/LCx) territories

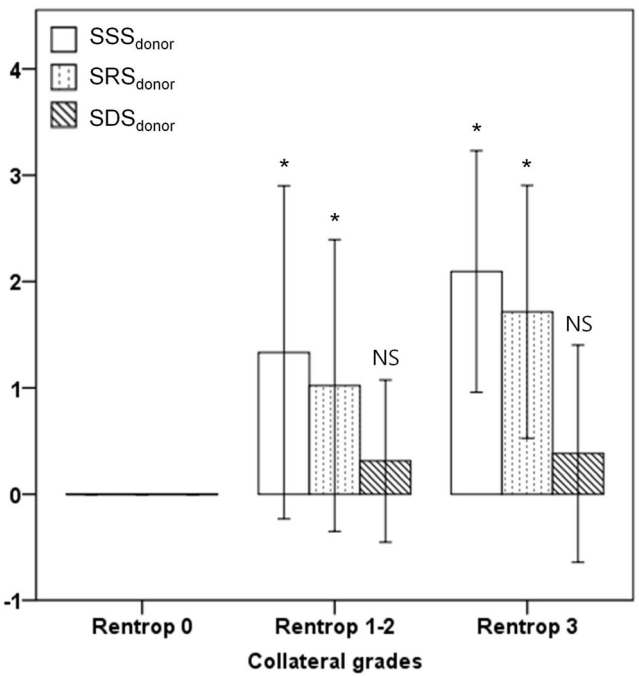

Fig. 4 Comparison of perfusion scores of donor territories among different Rentrop grades. SSS and SRS increased in a stepwise manner as the Rentrop grades escalated, while SDS was similar among different Rentrop grades. *$p<0.05$ against the other Rentrop grades

required regarding the symptom relief by revascularization of CTO and the role of a perfusion decrease in the donor myocardium, and MPS will be an excellent tool in such investigations.

Noninvasive evaluation of a perfusion decrease in the donor myocardium using MPS has been conducted in several previous studies [12, 18, 19]. Koga et al. [12] reported that Tl-201 MPS of 47 patients with severe (≥95 %) to total occlusion with or without collaterals showed 8 out of 52 PDs located in the sectors of nonstenotic arteries, and 6 of them were related to well-developed collateral vessels on CAG. They also found that the extent of PDs in the donor myocardium was significantly greater in patients with collaterals compared to those without in LAD and RCA lesions. They found no definite correlation between collateral grades and PD severity, probably due to separate analysis of the extent and severity of PD in donor myocardium. A combined assessment of the severity and extent of PD in donor myocardium using perfusion scores revealed a positive relationship between coronary steal and collateral grades in our study.

Recent reports described significant ischemia of the donor artery with only mild stenosis, probably induced by collateral circulation [13–16]. Consistent with our results, a positive relationship between collateral grades and ischemic severity in the donor artery was also observed in a report of eight patients who underwent recanalization of CTO [13], where

the increase in the FFR of the donor artery after recanalization was significantly higher in the patients with Rentrop-2 to Rentrop–3 collaterals while the FFR of the donor artery remained stable in those with Rentrop-0 or Rentrop-1 collaterals.

Interestingly, however, despite the significant increase of perfusion severity by escalating collateral grades, the patterns of PDs in donor territories were variable—reversible, fixed or reverse—and independent of collateral grades. The variability of perfusion change might reflect the variable changes in myocardial perfusion by a vasodilatory stimulus with intravenous adenosine infusion and its complex relation to symptom. Reversible or fixed PD is considered to be associated with an insufficient perfusion reserve or resting perfusion due to the increased myocardial volume to feed. Reverse PD can attribute to the collateral flow drawn back to the donor during vasodilatory stress because of the limited flow reserve capacity in the CTO territory. Such a paradoxical improvement of perfusion is often called "collateral steal" [28]. Which kind of hemodynamic change will be induced by vasodilatory stress cannot be determined via our data, but our observation of various perfusion changes by collateral circulation will help understand the complex hemodynamic aspect in patients with collateralized CTO.

This study had several limitations. First, the retrospective design could have resulted in a considerable level of selection bias and heterogeneity of study subjects. Second, we simply correlated the presence of symptoms and myocardial perfusion without further investigation of the complex hemodynamic changes through collateral channels and various patterns of chest pain because of the small sample size. Another limitation was that we did not fully prove that the perfusion decrease in the donor territory was induced by collateral circulation because of the lack of follow-up MPS studies. It was clear that there was no other stenosis except CTO; however, perfusion can be decreased even by diffuse atherosclerosis without definite focal angiographic stenosis [29].

Conclusions

Angina pectoris may occur without definite signs of ischemia in the CTO territory by a perfusion decrease in the donor myocardium. A perfusion decrease in the donor myocardium by collateral circulation in single-vessel CTO was more prominent with richer collaterals.

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Conflict of Interest Sang-Geon Cho, Ki Seong Park, Sae-Ryung Kang, Jahae Kim, Haeng Man Jun, Jae Yeong Cho, Hae Chang Jeong, Ju Han Kim, Geum-Cheol Jeong, Hee Jeong Park, Seong Young Kwon, Jung-Joon Min and Henry Hee-Seung Bom declare that they have no conflict of interest.

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*The manuscript has not been published before, is not under consideration for publication anywhere else and has been approved by all co-authors.

Ethical Statement The study was approved by the Chonnam National University Hospital Institutional Review Board (IRB no. CNUH-2014-153) and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The institutional review board waived the need to obtain informed consent.

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