ORIGINAL ARTICLE

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Relationship of myocardial hibernation, scar, and angiographic collateral flow in ischemic cardiomyopathy with coronary chronic total occlusion

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Background. The relationship between myocardial viability and angiographic collateral flow is not fully elucidated in ischemic cardiomyopathy (ICM) with coronary artery chronic total occlusion (CTO). We aimed to clarify the relationship between myocardial hibernation, myocardial scar, and angiographic collateral flow in these patients.

Methods and Results. Seventy-one consecutive ICM patients with 122 CTOs and 652 dysfunctional segments within CTO territories were retrospectively analyzed. Myocardial hibernation (perfusion-metabolism mismatch) and the extent of ^{18}F-fluorodeoxyglucose (FDG) abnormalities were assessed using ^{99m}Tc-sestamibi and ^{18}F–FDG imaging. Myocardial scar was evaluated by late gadolinium enhancement (LGE) cardiac magnetic resonance (CMR) imaging. Collateral flow observed on coronary angiography was assessed using Rentrop classification. In

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these patients, neither the extent nor frequency of myocardial hibernation or scar was related to the status of collateral flow. Moreover, the matching rate in determining myocardial viability was poor between any 2 imaging indices. The extent of ^{18}F-FDG abnormalities was linearly related to the extent of LGE rather than myocardial hibernation. Of note, nearly one-third (30.4%) of segments with transmural scar still had hibernating tissue. Hibernation and non-transmural scar had higher sensitivity (63.0% and 66.7%) than collateral flow (37.0%) in predicting global functional improvement.

Conclusions. Angiographic collateral cannot accurately predict myocardial viability, and has lower sensitivity in prediction of functional improvement in CTO territories in ICM patients. Hence, assessment of myocardial viability with non-invasive imaging modalities is of importance. Moreover, due to the lack of correlation between myocardial hibernation and scar, these two indices are complementary but not interchangeable. (J Nucl Cardiol 2019;26:1720–30.)

Key Words: Ischemic cardiomyopathy · chronic total occlusion · collateral · myocardial viability

Abbreviations

CTO	Chronic total occlusion
CAD	Coronary artery disease
CMR	Cardiac magnetic resonance
LGE	Late gadolinium enhancement
ICM	Ischemic cardiomyopathy
FDG	Fluorodeoxyglucose
PET/CT	Positron emission tomography/computed tomography
SPECT	Single photon emission computed tomography
LV	Left ventricular
EF	Ejection fraction

INTRODUCTION

Coronary artery chronic total occlusion (CTO) is common finding on coronary angiography in patients with coronary artery disease (CAD).[1] Assessment of myocardial ischemia and viability in CTO-subtended territories is essential for determining appropriate therapies.[2–4] Radionuclide perfusion-metabolism imaging and contrast-enhanced cardiac magnetic resonance (CMR) imaging are important non-invasive modalities in the evaluation of myocardial viability.[5,6] Moreover, epicardial collateral flow is the prerequisite for maintaining myocardial viability because there are no microvascular connections across myocardial zones and each vascular distribution is independent.[7] Coronary angiography is a conventional tool to visualize epicardial collaterals; nevertheless, the relationship between angiographic collateral flow and myocardial viability is not fully elucidated. Several studies have investigated the relationship between collateral flow and non-invasive imaging indices, but the results were controversial.[8–11] The late gadolinium enhancement (LGE) on CMR, a direct index of myocardial scar and indirectly reflecting

myocardial viability, has been demonstrated to be lower in segments with well-developed collaterals.[9,10] Of note, these studies involved patients with a wide spectrum of cardiac function and did not specialize in patients with ischemic cardiomyopathy (ICM). Contrarily, radionuclide perfusion-metabolism mismatch, a distinct and direct index of myocardial hibernation, was proved to be independent of collateral status in ICM patients.[11] The discrepancies among these studies resulted in difficulties in clinical decision-making.

Thus, we analyzed myocardial hibernation, scar, and angiographic collateral flow simultaneously in a cohort of ICM patients with CTO, and aimed to clarify the relationship between myocardial viability and angiographic collateral flow.

METHODS

Study Population

This is a retrospective study that was approved by the Ethics Committee of Hospital; the requirement to obtain informed consent was waived. From September 2009 to October 2012, 251 consecutive patients with CAD underwent both myocardial radionuclide imaging [^{99m}Tc-sestamibi single-photon emission computed tomography (SPECT) for perfusion evaluation, and ^{18}F–fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) imaging for metabolism evaluation] and contrast-enhanced CMR imaging within 1 week of each other. Of them, 147 patients had a CTO in at least 1 major epicardial coronary artery. Patients with 1 or more of the following conditions were further excluded: left ventricular (LV) ejection fraction (EF) > 50% ($n = 14$), > 50% stenosis in the left main artery ($n = 10$), acute coronary syndrome within 90 days prior to myocardial radionuclide/CMR imaging ($n = 19$), previous coronary revascularization ($n = 17$), complicated valvular cardiomyopathy ($n = 5$), the time interval between coronary angiography and radionuclide/CMR imaging was more than 3 months ($n = 6$), or poor radionuclide and/or CMR images

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($n = 5$). Thus, the remaining 71 ICM patients with CTO made up the study cohort.

Coronary Angiography

Coronary angiography was performed by the use of standard techniques. Two experienced observers who were unaware of the other imaging data assessed the angiograms retrospectively and independently. Discrepancies were resolved by consensus. CTO was defined by the presence of a coronary artery stenosis causing complete interruption of antegrade flow in a major epicardial coronary artery or minimal contrast penetration through the lesion without distal vessel opacification (thrombolysis in myocardial infarction grade 0-1 flow).[1] Because patients with acute coronary syndromes within 90 days of angiography were excluded, the presence of a total occlusion on coronary angiography was assumed to be chronic. The presence of collateral to CTO was determined by the degree of opacification of the native vessel distal to its occlusion, and was graded using the Rentrop classification (class 0 = no visible filling of collaterals, class 1 = filling of side branches, class 2 = partial filling of epicardial segment of the occluded vessel, and class 3 = total filling of epicardial segment).[12] Rentrop score = 0 or 1 was defined as poorly developed collaterals, Rentrop score = 2 as moderately developed collaterals, and Rentrop score = 3 as well-developed collaterals.

Myocardial Perfusion-^{18}F-FDG Imaging

Myocardial perfusion imaging with ^{99m}Tc-sestamibi was performed at rest, using a dual-head gamma camera (e.cam, Siemens Medical Solution, Inc.).[13] Sixty-ninety min after injection of ^{99m}Tc-sestamibi (740-925 MBq), perfusion images were acquired with 64 views, at 25 seconds per view, using a zoom factor of 1.23. Images were reconstructed by standard filtered back projection with a Butterworth filter (cut-off frequency, 0.4 cycles/cm; order, 5.0) and displayed as short-axis and horizontal and vertical long-axis slices.

Myocardial ^{18}F-FDG imaging was performed within 2 days of ^{99m}Tc-sestamibi imaging. After an overnight fast for at least 12 hours, an oral glucose of 25-50 g was given to the patients according to their serum glucose level. In diabetes patients, acipimox was administrated (500 mg, oral dose) before glucose loading. Insulin was intravenously administrated if the blood glucose level > 9 mmol/l at 45 min after oral glucose administration with close monitoring of blood glucose.[14] When the blood glucose level was appropriate, ^{18}F-FDG (3 MBq/kg) was administered intravenously. Images were acquired 1-2 hours after tracer injection using a Biograph 64 PET/CT scanner (Siemens Medical Solutions, Knoxville, TN) equipped with high-performance LSO PET crystals and a 64-slice CT. After a scout CT acquisition (120 kV, 10 mA) used for proper patients positioning, CT transmission scanning (140 kV, 35 mA) was performed for attenuation correction and anatomical localization. Images were reconstructed using attenuation weighted-OSEM iterative reconstruction (8 subsets, 4 iterations).

^{99m}Tc-sestamibi and ^{18}F-FDG image analysis were both performed using an automated program (QPS: version 3.1, Cedars-Sinai Medical Center, Los Angeles, CA, USA). A polar map was derived and displayed using the American Heart Association 17-segment model. Myocardial perfusion and ^{18}F-FDG uptake were separately scored by consensus visual analysis of 2 observers blinded to the rest of the patient data. Segmental tracer activity was categorized on a 5-point scale to indicate segmental ^{99m}Tc-sestamibi and ^{18}F-FDG uptake: 0 = normal tracer activity; 1 = mildly reduced tracer activity; 2 = moderately reduced tracer activity; 3 = severely reduced tracer activity; and 4 = absence of tracer activity.[15] Reduced blood flow (score 1-4) associated with preserved or enhanced FDG uptake (perfusion-metabolism mismatch) signified myocardial hibernation. Dysfunctional myocardium with normal perfusion irrespective metabolism (match or reverse mismatch) was considered as viable. The FDG score in reverse mismatch was reverted to 0. Myocardial segments were assigned to three vascular territories, with seven segments for the left anterior descending artery (LAD), five for the left circumflex artery (LCx), and five for the right coronary artery (RCA).[15] If the LCx was dominant, two inferior segments were reassigned from the RCA to the LCx.[15]

Two indices were derived from perfusion-FDG imaging to indicate myocardial viability. First, the extent of hibernating myocardium within a CTO territory was expressed using a hibernation index, which was computed as follows: summed segmental positive difference of perfusion and ^{18}F-FDG scores/(the number of dysfunctional segments within the territory × 4). Second, the extent of ^{18}F-FDG abnormalities within a CTO territory was also calculated, which was computed as follows: summed segmental ^{18}F-FDG scores/(the number of dysfunctional segments within the territory × 4).

CMR

CMR was performed using a 1.5-T Siemens Magnetom Avanto scanner (Siemens AG, Erlangen, Germany) equipped with fast gradients (45 m T/m amplitude, 200 m T/m/ms slew rate) and an 8-element phased-array cardiac coil. Scout images acquired by using half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequence were used to analyze the morphology and structure of the heart. Continuous slices encompassing the entire left ventricle from apex to base were obtained during breath-hold using the following parameters: slice thickness, 8 mm; matrix, 256 × 256; 25 phases per cardiac cycle; and a field of view of 350–400 mm. Each slice was acquired in a separate breath-hold cycle after expiration. Delayed enhancement T1-weighted images were acquired 10 min after bolus injection of gadolinium diethylenetriamine penta-acetic acid (Magnevist, Schering AG, Berlin, Germany; 0.2 mmol/kg) with a phase-sensitive inversion recovery sequence (repetition time 700 ms/echo time 4.2 ms; section thickness, 8 mm; matrix, 156 mm × 256 mm; flip angle, 251; bandwidth, 130 kHz/PX).[16] Retrospective electrocardiographic-gating cine images were acquired using a true fast imaging with steady-state precession (TrueFisp) sequence.

CMR images were analyzed by two investigators blinded to the other imaging and angiographic information. Endocardial and epicardial borders were manually drawn on all LV short-axis images. LV functional parameters were derived from cine CMR images and included the LV end-diastolic volume (EDV), end-systolic volume (ESV), and EF. LV aneurysm was also suggested by findings on CMR. The segmental wall motion abnormality was assessed using a 17-segment model and 4-point scale: 0 = normal, 1 = mildly hypokinetic, 2 = severely hypokinetic, 3 = akinetic or dyskinetic. A segment with a score ≥ 1 was considered dysfunctional. The transmurality of LGE was visually assessed using the same 17-segment model but on a 5-point scale: 0 = absence of hyperenhancement, 1 = hyperenhancement of 1% to 25% LV wall thickness, 2 = hyperenhancement extending from 26% to 50%, 3 = hyperenhancement extending from 51% to 75%, and 4 = hyperenhancement extending from 76% to 100%.

The extent of myocardial scar within a CTO territory was expressed using a scar index, which was computed as follows: summed segmental LGE scores/(the number of dysfunctional segments within the territory × 4).

Comparison Among Imaging Modalities

To facilitate the comparison among different imaging modalities on a per-vessel level, the following definitions were made: (1) a CTO territory with one or more segments showing hibernation was defined as having hibernating myocardium; (2) a CTO territory with a scar index less than 0.5 was defined as having non-transmural scar; (3) a CTO territory supplied by angiographic collateral with Rentrop class of 3 was defined as having sufficient collateral.

Follow-Up

To assess the ability of variable imaging indices in predicting functional improvement after revascularization, echocardiographic results before and after coronary revascularization were compared. A 5% or more increase of LVEF value after revascularization was defined as having functional improvement.

Statistical Analysis

Statistical analysis was performed with SPSS 19.0 software (SPSS Inc., Chicago, IL). Continuous variables were described as means and standard deviations (SD), or medians and interquartile ranges, depending on the normality of distribution assessed using the Kolmogorov-Smirnoff test. Kruskal–Wallis one-way analysis of variance was used to compare indices of myocardial hibernation and myocardial scar in the three groups of angiographic collateral grades. Differences between two groups were analyzed using Fisher's exact test for categorical variables. Comparisons between groups with continuous data were made by the unpaired Student t test. Spearman's correlation was applied to evaluate the correlation of hibernation and scar indices that were not distributed normally. The inter- and intra-observer agreement for analyzing myocardial perfusion, ^{18}F-FDG uptake, CMR, and angiographic collateral scores were assessed from 20 randomly selected cases. The Cohen κ was 0.80 and 0.87 for the perfusion score, 0.83 and 0.90 for the ^{18}F-FDG score, 0.84 and 0.88 for LGE transmurality, 0.76 and 0.81 for wall motion, and 0.75 and 0.83 for Rentrop classification. Differences were considered statistically significant with a 2-tailed P value of < .05.

RESULTS

Patients' Characteristics

Table 1 shows the characteristics of the enrolled 71 ICM patients. The median age of this study population was 59 years (interquartile range 52-63), and 87% were male. The majority of patients (87.3%) had a history of old myocardial infarction, and 42.3% had decompensated heart failure. All patients had LGE on CMR. Pathological Q waves on electrocardiogram (ECG) were found in 51.6% of CTO territories. Notably, most of the patients (95.8%) had multiple-vessel disease on coronary angiography. There were 122 CTOs, of which, 35 (28.7%) had poorly collaterals (Rentrop class 0 = 8 and class 1 = 27), 50 (41.0%) had moderately developed collaterals (Rentrop class 2), and 37 (30.3%) had well-developed collaterals (Rentrop class 3). Most CTO lesions (86.1%) were located in the proximal and middle of coronary vessels. Of 703 segments within CTO territories, 652 (92.7%) were dysfunctional, most of them (89.6%) had perfusion abnormalities (perfusion-metabolism match or mismatch), whereas 68 (10.4%) have normal perfusion but decreased FDG uptake (perfusion-metabolism reverse mismatch).

Myocardial Viability and Angiographic Collateral Flow

There was no significant difference of the myocardial hibernation index among CTOs with different collateral flow classifications (Figure 1A). Similarly, no significant difference of myocardial scar index was observed (Figure 1B). The frequencies of hibernating and non-transmural scar were also not significantly different among Rentrop grades (Figure 2). Thus, both the extents and frequencies of myocardial hibernating and scar were independent of the status of collateral flow (Figures 3, 4). Moreover, the matching rate in determining myocardial viability within a CTO territory was poor between any 2 imaging indices (Table 2).

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Table 1. Patients' characteristics

Demographics	Results (%)
Age, range (years)	59, 52–63
Male gender	62 (87.3)
Hypertension	43 (60.6)
Diabetes mellitus	36 (50.7)
Hyperlipidemia	50 (70.4)
Smoking	41 (57.5)
Previous history of myocardial infarction	
Yes	62 (87.3)
No	9 (12.7)
Angina	
No	47 (66.2)
Stable angina	13 (18.3)
Unstable angina	11 (15.5)
NYHA functional class	
I	2 (2.8)
II	39 (54.9)
III	22 (31.0)
IV	8 (11.3)
Coronary angiography	
1-vessel disease	3 (4.2)
2-vessel disease	7 (9.9)
3-vessel disease	61 (85.9)
1-vessel CTO	34 (47.9)
2-vessel CTO	28 (39.4)
3-vessel CTO	9 (12.7)
LAD-CTO	50 (41.0)
LCx-CTO	28 (23.0)
RCA-CTO	44 (36.1)
Functional parameters of CMR	
EDV (ml)	225 ± 74
ESV (ml)	161 ± 68
EF (%)	28 ± 9
Ventricular aneurysm	36 (50.7)

Results are shown as median (1st quartile to 3rd quartile), n (frequency %) or mean ± SD
CTO, chronic total occlusion; *LAD*, left anterior descending artery; *LCx*, left circumflex artery; *RCA*, right coronary artery; *EDV*, end diastolic volume; *ESV*, end systolic volume; *EF*, ejection fraction

Myocardial Hibernation and Scar

On a per-vessel level, the hibernation index was not linearly correlated with the myocardial scar index (Figure 5A). Contrarily, the extent of ^{18}F-FDG abnormalities was linearly correlated with the scar index (Pearson $r = 0.76$, 95% confidence interval 0.67-0.82, $P < .0001$) (Figure 5B). On a per-segment level,

segments with subendocardial scar (LGE score 1 or 2) had more hibernating tissue than those with transmural scar (LGE score 3 or 4) and those without scar (LGE score 0) (Figure 6); the latter 2 had similar frequencies. Of note, 30.4% of segments with transmural scar still had hibernating tissue.

Functional Improvement and Myocardial Viability

Of the 71 studied patients, 46 received coronary revascularization (coronary artery bypass grafting, 44; percutaneous coronary angioplasty, 2). The median functional follow-up was 84 days (range 8 to 353 days). Twenty-seven patients (58.7%) showed functional improvement. Myocardial hibernation and non-transmural LGE had higher sensitivity (63.0% and 66.7%) than sufficient collateral (37.0%) in predicting global functional improvement, whereas the specificity was not significantly different among the 3 indices (Table 3).

DISCUSSION

The main finding of this study was that, in ICM patients with CTOs, the extents and frequencies of myocardial hibernation and scar are not related to the status of angiographic collateral flow. In addition, although segments with subendocardial scar had greater probability of having hibernating tissue, nearly one-third of segments with transmural scar still showed myocardial hibernation. Moreover, myocardial hibernation and scar had higher sensitivity in predicting LV functional recovery than collateral flow.

Relationship between Myocardial Viability and Angiographic Collateral Flow in CTO

CTOs are common findings on coronary angiography in patients with CAD.[1] Myocardium supplied by a CTO may have variable pathophysiological characteristics, ranging from normal perfusion to impaired coronary flow reserve, stress-induced ischemia, resting ischemia, hibernation, and eventually necrosis.[17,18] A prerequisite for revascularizing CTOs is that the myocardium in the subtended zone be viable.[2] On one hand, in patients with normal/mildly decreased wall motion, evaluation of ischemia burden is indicated, which is helpful for guiding percutaneous coronary intervention.[19] On the other hand, in ICM patients who show severe motion abnormality and depressed contractile function, viability assessment should be recommended for coronary artery bypass grafting selection.[20] Overall, coronary revascularization was tended to be beneficial only in ICM patients with viable myocardium, although
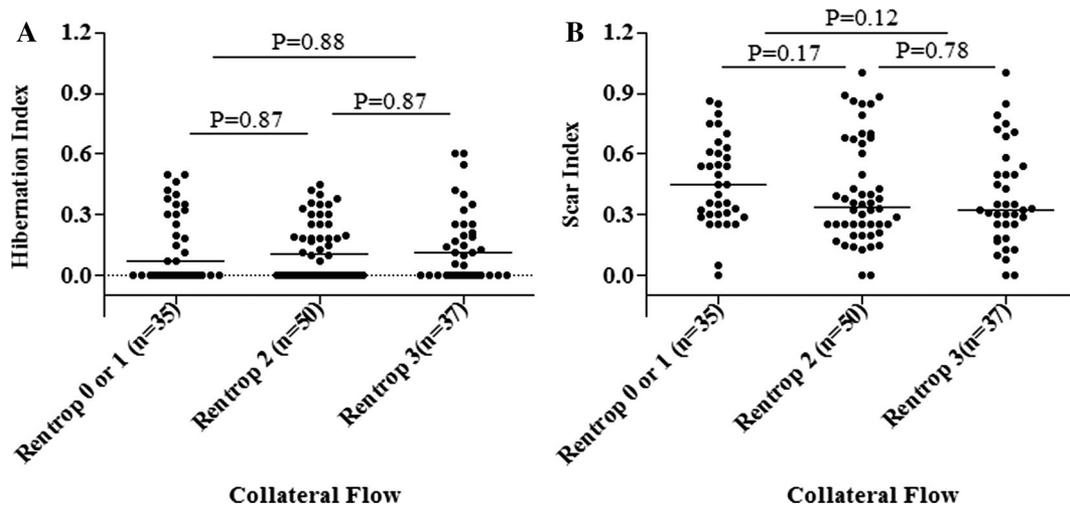
Figure 1. Relationship between angiographic collateral flow and myocardial hibernation (**A**) and scar (**B**). Both the extent of myocardial hibernation and scar are independent of angiographic collateral flow.
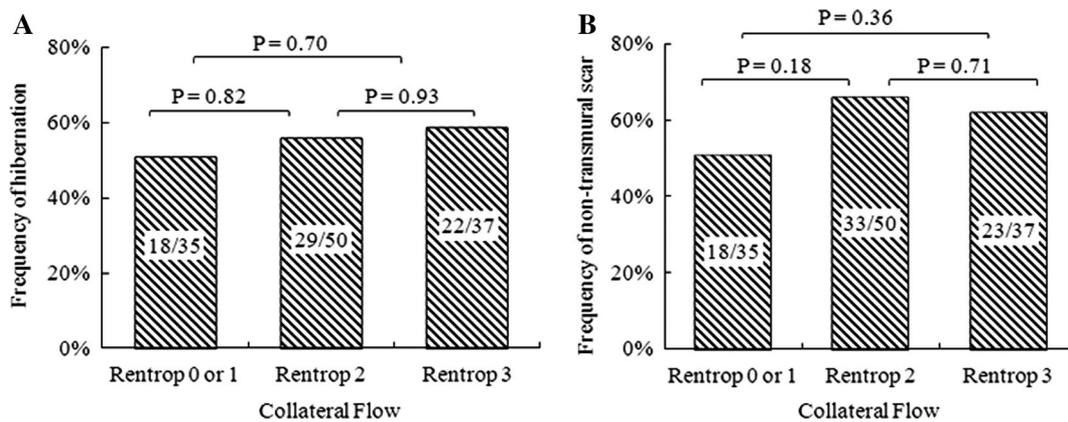

Figure 2. Relationship between angiographic collateral flow and the frequency of myocardial hibernation (**A**) and scar (**B**). Both the frequencies of myocardial hibernation and non-transmural scar were not significantly different among Rentrop grades.

recent prospective trials had challenging results.[21–24] Similarly, several observational studies have demonstrated the prognostic value of myocardial viability evaluation in patients with CTO, and more prospective trials are anticipated to provide stronger evidence.[3]

Non-invasive imaging modalities have long been employed to evaluate myocardial viability, including radionuclide perfusion and metabolism imaging, low-dose dobutamine stress echocardiography, and CMR with LGE.[6,25] The status of collateral flow on angiography, a distinct index for patients with CTO, is also presumably related to viability. Since there are no microvascular connections across myocardial zones and each vascular distribution is independent, epicardial angiographic collateral is the prerequisite for

maintaining myocardial viability.[7] Several studies have investigated the relationship between collateral flow and LGE on CMR.[9,10] Choi et al. found that increased angiographic collateral flow was associated with a lower frequency of LGE volume (%) and lower degree of LGE transmurality.[9] Similarly, Ripley et al. also observed that a good collateral circulation was more likely to supply viable myocardium using LGE CMR.[10] Contrary to the above two studies, we did not find a relation between collateral flow grades and the extent and frequency of myocardial LGE. Several differences exist between those previous studies and the present study. Our patients had more prevalence of decompensated heart failure (42.3%), more severely depressed EF (28±9%), more prevalence of old myocardial infarction (87.3%),
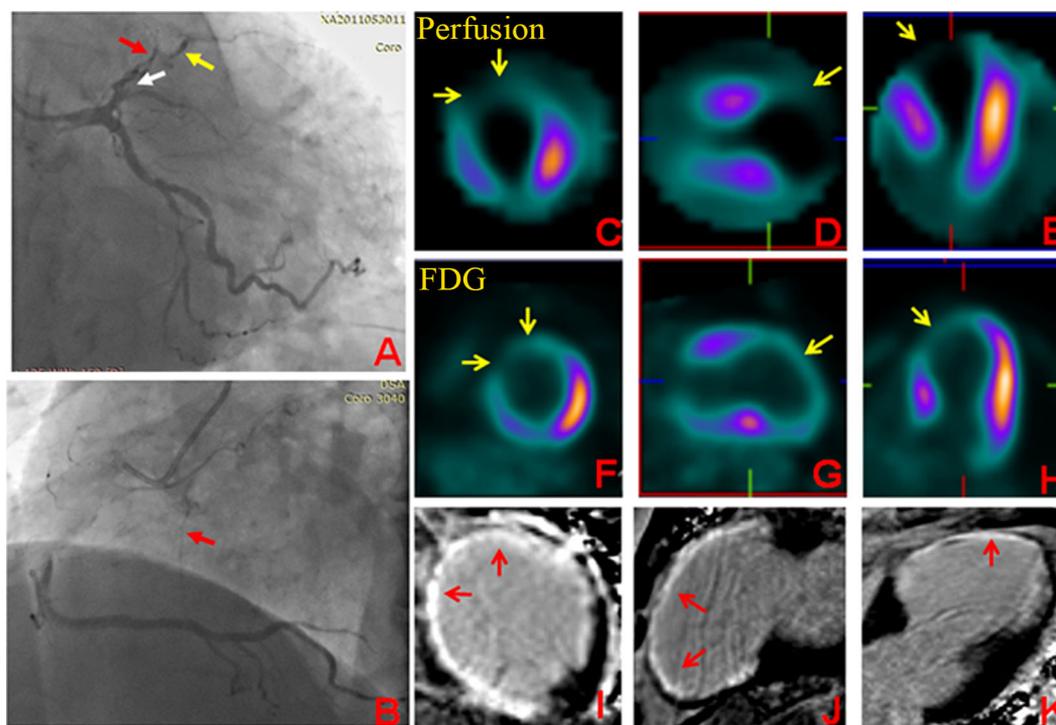
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Figure 3. An example of good collateral flow but no viable myocardium identified. This patient had occluded LAD (white arrow, panel **A**) with well-developed collaterals from the septal branch (red arrow, panel **A**) and collateral from right coronary artery (red arrow, panel **B**). The mid-distal LAD was filled by collateral flow (yellow arrow). Myocardial perfusion (panels **C**, **D**, **E**) and ^{18}F-FDG imaging (panels **F**, **G**, **H**) showed a match pattern in the anterior and septal walls (yellow arrows) signified the lack of myocardial hibernation (panels **C** through **H**). CMR demonstrated transmural scar in the corresponding LAD territory (red arrows, panels **I** through **K**).

more frequency of multiple-vessel disease (95.8%), multiple CTOs (52.1%), and less well-developed collaterals on coronary angiography (30.3%). In brief, our patient population was a cohort of ICM, whereas the aforementioned studies involved patients with a wide spectrum of cardiac function and did not specialize in ICM patients.[26] As to the relationship between collateral flow and hibernation, Di Carli et al. conducted a landmark study 2 decades ago.[11] They found that the extent of myocardial hibernation was unrelated to the presence or magnitude of collateral vessels. To our best knowledge, the present study was the first to simultaneously investigate the relationship of myocardial hibernation, scar, and angiographic collateral flow. On one hand, our study again confirmed that hibernation is independent of angiographic collateral flow in ICM patients. On the other hand, the relationship between collateral flow and myocardial scar may be different in ICM patients compared to those with preserved or mildly decreased contractile function.

The lack of correlation between collateral flow and myocardial viability may have several explanations.[11] First, coronary collaterals cannot be accurately assessed by conventional angiography. Due to the limitation of spatial resolution, angiographic assessment of collateral flow was limited to detecting anastomotic vessels ranging between 40 and 200 μm. Moreover, conventional angiography may fail to visualize collateral circulation due to the existence of extracardiac anastomosis and the low pressure gradient between the supplying artery and the recipient artery.[11] Second, a recent study demonstrated that the microvascular integrity rather than the development of coronary collaterals was of relevance for myocardial viability and functional recovery.[27] Third, although epicardial angiographic collateral is the prerequisite for maintaining myocardial viability, good collaterals cannot prevent the occurrence of myocardial ischemia and infarction.[28] Insufficient collaterals can result in ischemia, but may be enough to maintain myocardial viability.

Relationship between Myocardial Hibernation and Scar in CTO

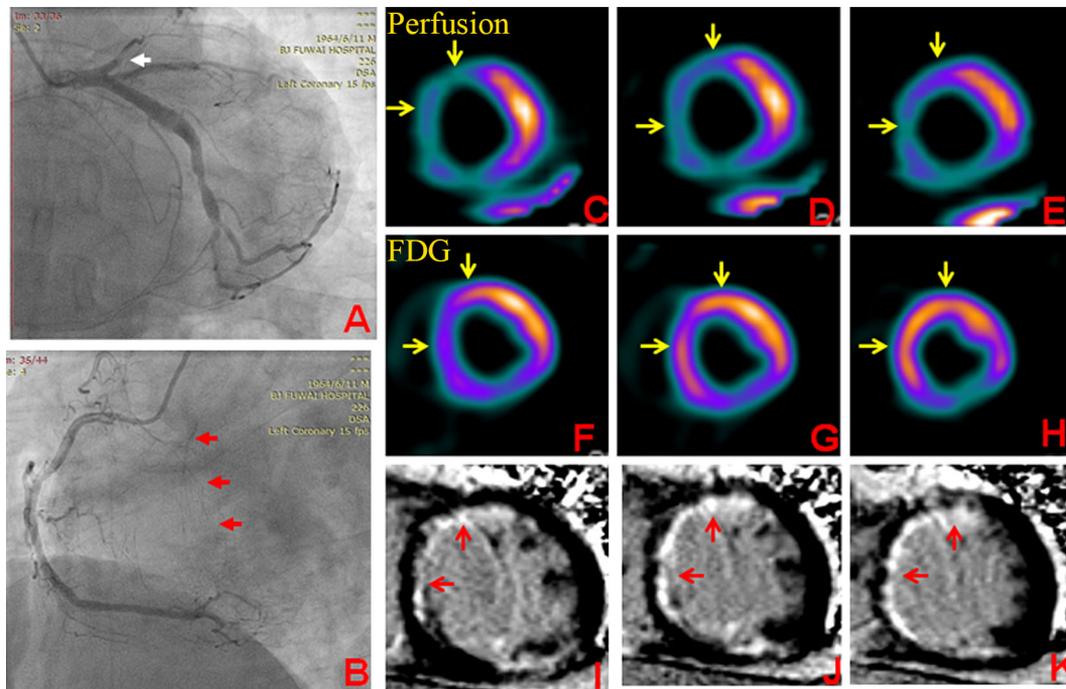The relationship between hibernation and scar has been previously investigated.[16,29,30] Roes et al.

Figure 4. An example of poor collateral flow but preserved myocardial viability. This patient had occluded LAD (white arrow, panel **A**) with poor-developed collaterals from the right coronary artery (red arrows, panel **B**). Myocardial perfusion (panels **C**, **D**, **E**) and ^{18}F-FDG imaging (panels **F**, **G**, **H**) showed a mismatch pattern in the anterior and septal walls (yellow arrows) signified myocardial hibernation (panels **C** through **H**). CMR demonstrates the subendocardial scar in the corresponding LAD territory (red arrows, panels **I** through **K**).

Table 2. Comparison of the three indices in determining myocardial viability

	Kappa coefficient	Matching rate (%)
Collateral flow vs. myocardial hibernation	0.033	49.2
Collateral flow vs. LGE	0.047	48.4
Hibernation vs. LGE	0.005	51.6

Matching rate indicated each pair of indices had consistent results in judging myocardial status within a CTO territory
LGE, late gadolinium enhancement; *CMR*, cardiac magnetic resonance

demonstrated the presence of hibernation in segments with variable extents of LGE.[29] Our study was the first to compare hibernation and LGE in patients with CTOs. We found that the occurrence of perfusion-metabolism mismatch was independent of scar, which was in concordance with that of Roes's study.[29] The absence of linear correlation was partly attributed to the fact that LGE delineates the scar tissue of the endocardium but cannot detect the pathophysiology of the epicardial rim. Theoretically, the epicardium may be normal, or ischemic but viable. Contrary to perfusion-metabolism mismatch, the epicardial FDG activity contained different features of myocardium including hibernation, stunning and normal myocardium. As a result, the extent of ^{18}F-FDG abnormalities rather than hibernation was linearly correlated with the LGE score, which was
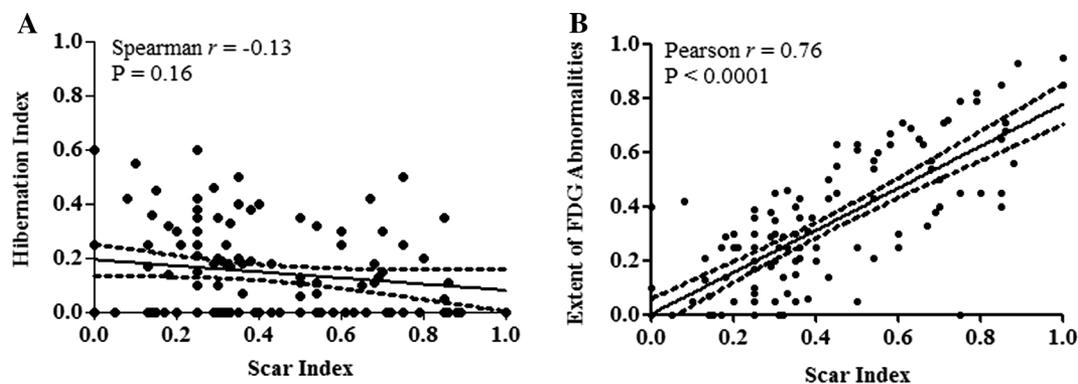
Figure 5. On a per-vessel level, the hibernation index was not correlated to the scar index (**A**), whereas the extent of FDG abnormalities was linearly correlated with the scar index (**B**).

proved by both a prior and the present study.[29] Notably, although hibernation and LGE score were lack of correlation, they had similar ability in predicting global functional improvement.
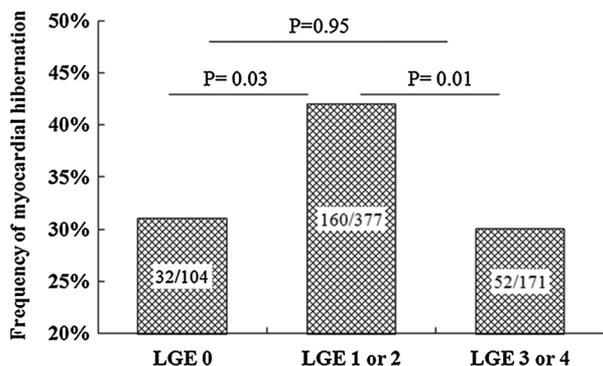

Figure 6. Myocardial hibernation is more prevalent in segments with subendocardial scar (LGE 1 or 2) than those with transmural scar (LGE 3 or 4) and without scar (LGE 0).

Limitations

The results of the present study came from a specific cohort of ICM. Therefore, it would not be applicable to CAD patients with preserved LV function. Also, these results may not be appropriate for patients with single coronary CTO, since 52.1% of our patients had multi-vessel CTOs; multi-vessel CTOs would have complicated the relationship between collaterals and the occluded coronaries. The pathophysiological validation of the relationship among myocardial hibernation, scar, and collaterals was out of reach of this study, since it was only a retrospective clinical observation. Furthermore, subjectivity and diversity on scoring of myocardial perfusion, metabolism, and LGE could not be avoided; however, excellent reproducibility of scoring of myocardial perfusion, ^{18}F-FDG, CMR, and collateral grades on coronary angiography was shown. Additionally, empirical assignment of myocardial segments to specific coronary arteries may be incorrect in some patients. The echocardiographic results of follow-up were from different hospitals; bias was unavoidable. Even more serious, quantitative assessment of regional

Table 3. Comparison of imaging indices in predicting functional improvement

	Hibernation (%)	Non-transmural LGE (%)	Sufficient collateral (%)
Sensitivity	63.0	66.7	37.0[a]
Specificity	42.1	42.1	42.1

Hibernation indicated patients had ≥ 1 CTO territory with myocardial hibernation. Non-transmural LGE indicated patients had ≥ 1 CTO territory with a scar index < 0.5. Sufficient collateral indicated patients had ≥ 1 CTO territory supplied by collateral of Rentrop class 3

[a]$P < .05$ compared with hibernation and non-transmural LGE

wall motion was absent. The present study mainly investigated the relationship and discrepancy among myocardial hibernation, scar, and angiographic collateral flow. Thus, which index is most efficient in guiding treatment and prognostic evaluation remains unknown. Finally, this was a retrospective study with a small sample size, and therefore a large-scale prospective study is warranted.

CONCLUSIONS

Angiographic collateral cannot accurately predict myocardial viability and global functional improvement in ICM with CTO. Hence, assessment of myocardial viability with non-invasive modalities is necessary. Moreover, due to the non-linear correlation between myocardial hibernation and scar, these 2 indices are rather complementary than interchangeable.

NEW KNOWLEDGE GAINED

Myocardial hibernation and scar are independent of angiographic collateral flow; thereby the latter one is not a reliable index to predict myocardial viability in ICM with CTO. Furthermore, myocardial metabolism, rather than perfusion-metabolism mismatch, is closely related to myocardial scar.

Disclosure

None declared.

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