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Original article

## Prediction of functional recovery after percutaneous coronary revascularization for chronic total occlusion using late gadolinium enhanced magnetic resonance imaging

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### ABSTRACT

**Background:** Limited data are available regarding the prediction for functional recovery using late gadolinium enhanced magnetic resonance imaging (LGE MRI) after coronary revascularization for chronic total occlusion (CTO PCI).

**Methods:** We studied 59 patients (mean age,  $66 \pm 11$  years) who underwent successful CTO PCI. Two-dimensional echocardiography and strain measurements were performed before and  $8 \pm 2$  months after CTO PCI. The findings of segmental assessment were compared with the extent of LGE MRI using a 16-segment model.

**Results:** From baseline to follow-up, ejection fraction ( $54.2 \pm 12.1\%$  to  $56.1 \pm 10.6\%$ ,  $p = 0.010$ ), global longitudinal strain (LS) ( $-15.1 \pm 5.1$  to  $-16.7 \pm 5.1$ ,  $p < 0.001$ ), global circumferential strain (CS) ( $-14.0 \pm 4.9$  to  $-15.9 \pm 4.9$ ,  $p < 0.001$ ), and wall motion score (WMS) index ( $1.45 \pm 0.53$  to  $1.33 \pm 0.39$ ,  $p = 0.014$ ) significantly improved. In the territory of the CTO vessel, LS and CS significantly improved in segments of LGE  $\leq 50\%$ , but not in segments of LGE  $> 50\%$ . However, WMS improved only in segments of LGE 1–25%. At baseline and at follow-up, CS allowed better discrimination of segments of LGE  $> 50\%$  than WMS [at baseline; area under the curve (AUC) 0.79 vs. 0.68, respectively,  $p = 0.001$ ; at follow-up; AUC 0.84 vs. 0.69, respectively,  $p < 0.001$ ]. Discriminatory ability of LS for segments of LGE  $> 50\%$  significantly improved from baseline to follow-up (AUC 0.73 vs. 0.83,  $p < 0.001$ ).

**Conclusions:** The cut-off value of the extent of LGE MRI is 50% to detect segments that will functionally recover after CTO PCI. Change in LS was more sensitive for removal of ischemia by CTO PCI, indicating the utility of LS to monitor the therapeutic effects of CTO recanalization.

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### Introduction

Chronic total occlusion (CTO) is not uncommon in patients with coronary artery disease. The catheterization-documented incidence of CTO has been reported as 20–30% [1]. CTO revascularization is associated with an improvement in cardiac function and long-term clinical outcome [2]. Assessment of myocardial viability

before revascularization is crucial, as the benefit of CTO revascularization depends on the presence or absence of myocardial viability of CTO territory. The opening of an occluded coronary artery that supplies a viable but dysfunctional myocardium could recover systolic dysfunction, relieve patients' symptoms, and improve their outcomes [2]. The initial success rates of percutaneous coronary intervention (PCI) of CTO have markedly improved due to the development of new techniques and devices [3]. Furthermore, the restenosis rate has dramatically decreased with the elaboration of drug-eluting stents [4]. Therefore, the clinical importance of CTO PCI has increased, and the use of CTO PCI is gaining wider acceptance as a therapeutic option for patients with coronary artery disease.

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Among non-invasive cardiac imaging modalities, late gadolinium enhanced (LGE) magnetic resonance imaging (MRI) is known as the most accurate method to evaluate myocardial viability in patients with coronary artery disease. LGE MRI can accurately assess the transmural extent of infarction [5] and predict functional recovery after revascularization in chronic and acute myocardial infarction [5,6]. Generally, a transmural extent of 50% is considered to be a cut-off value to predict contractile functional recovery for patients who undergo coronary revascularization. However, no data are available regarding the optimal cut-off value of the transmural extent of LGE MRI to detect myocardial segments that will functionally recover after CTO revascularization.

Two-dimensional (2D) speckle-tracking echocardiography (STE) is widely used for the assessment of myocardial systolic function [7,8]. 2D STE can provide a quantitative evaluation of three-directional myocardial fibers, longitudinal strain (LS), circumferential strain (CS) and radial strain. The quantitative assessment of systolic function using 2D STE is more objective than visual wall motion assessment [9].

The aim of this study was to explore the optimal cut-off value of the transmural extent of LGE MRI for the functional recovery after CTO revascularization using 2D STE.

## Methods

### Study population

We retrospectively screened 70 consecutive CTO patients for possible inclusion in the study. All patients underwent successful CTO PCI for occluded coronary artery and angiographic follow-up at  $9 \pm 2$  months. CTO was defined as a coronary obstruction with thrombolysis in myocardial infarction (TIMI) flow grade 0 with an estimated duration of  $>3$  months. Revascularization had to be achieved in all perfusion beds. Exclusion criteria included atrial fibrillation, general contraindications to MRI examination (e.g. device implantation, severe renal dysfunction, claustrophobia, etc.), insufficient echocardiographic image quality, significant valvular heart disease, periprocedural myocardial infarction, acute coronary syndrome during the follow-up period, and reocclusion of the CTO vessel at the angiographic follow-up. Reocclusion was defined as a TIMI flow grade 0–1 in the target vessel. Finally, 59 patients (mean age,  $66 \pm 11$  years) were enrolled as the study group. This study was approved by the institutional review board of Kanagawa Cardiovascular and Respiratory Center. All patients gave written informed consent to participate in this study.

### Angioplasty procedure

All study participants had a native vessel occlusion estimated to be of at least 3 months in duration based on a history of sudden chest pain, a previous myocardial infarction in the same target vessel territory, or the time between diagnosis made on coronary angiography and PCI. All of the patients had symptomatic angina and/or a positive ischemia study. PCI and stent implantation were performed in a standard manner. Second-generation drug-eluting stents were used in all of the angioplasty procedures. Heparin was administered to maintain an activated clotting time  $>250$  s. A CTO PCI was performed with modern techniques, such as bilateral injections; specialized hydrophilic, tapered tip, and stiff wires; parallel wire techniques; intravascular ultrasonography-guided techniques; and a retrograde approach when possible. After the PCI, all patients were prescribed lifelong aspirin. Clopidogrel was prescribed for at least 12 months in all patients. Procedural success was defined as successful recanalization and dilation of at least one CTO per patient with or without stent implantation, a residual stenosis of  $<50\%$ , and TIMI flow  $>2$ . Periprocedural myocardial

infarction was defined as a creatine kinase-myocardial band elevation  $\geq 2$  times the upper limit of normal after the procedure. Creatine kinase-myocardial band level was routinely assessed 18 h after PCI in all patients or at least 3 times every 6 h in patients with symptoms suggesting ischemia. If creatine kinase-myocardial band level was elevated, additional measurements were made every 6 h until peak value was reached and the values decreased to normal.

### Laboratory data

Blood samples for the measurement of serum brain natriuretic peptide, creatinine, high-sensitivity C-reactive protein, and white blood cell count were taken prior to and  $8 \pm 2$  months after CTO PCI. The estimated glomerular filtration rate was calculated using the Modification of Diet in Renal Disease equation for creatinine, as modified by the Japanese Society of Nephrology: estimated glomerular filtration rate ( $\text{mL}/\text{min}/1.73 \text{ m}^2$ ) =  $194 \times (\text{serum creatinine})^{-1.094} \times (\text{age})^{-0.287} (\times 0.739 \text{ if female})$  [10].

### Echocardiography

Echocardiography was performed using a Vivid E9 system (GE Vingmed Ultrasound AS, Horten, Norway) equipped with a 2.5-MHz transducer. Parasternal long-axis, short-axis views (basal, midventricular, and apical levels) and three standard apical views (four chamber, two chamber, and long axis) were acquired by a frame rate of 56–92 frames/s. Left ventricular (LV) ejection fraction was determined by manual tracing of end-systolic and end-diastolic endocardial borders using the biplane Simpson's method. For the assessment of regional systolic function, the 16-segment model of the American Society of Echocardiography was used to divide the left ventricle. Wall motion score (WMS) was calculated using the following score as previously described [11] (1 = normokinesis or hyperkinesis; 2 = hypokinesis; 3 = akinesis; 4 = dyskinesis; 5 = aneurysm). Left atrial volume, peak early diastolic velocity, deceleration time from the peak of the early diastolic wave to baseline, peak atrial systolic velocity, peak early diastolic velocity/peak atrial systolic velocity ratio, peak early diastolic motion velocity, and peak early diastolic velocity/peak early diastolic motion velocity ratio were obtained and measured according to the American Society of Echocardiography guidelines [12].

### Myocardial strain assessment

The echocardiographic strain measurements were repeated in pre- and  $8 \pm 2$  months after CTO PCI. For CS analysis, three short-axis views (basal, midventricular, and apical levels) were analyzed. For LS analysis, three standard apical views (two-chamber, three-chamber, four-chamber views) were analyzed according to the 16-segment model. Strain analysis was performed using an offline dedicated software package (EchoPAC version 113; GE Vingmed Ultrasound AS). This system allows analysis of peak systolic segmental CS from short-axis views and analysis of peak global and segmental systolic LS from apical views. These markers are acoustic speckles that are equally distributed within the myocardium and that can be identified as well as followed frame-to-frame during several consecutive images. The natural acoustic markers are expected to change their position from frame-to-frame in accordance with the surrounding tissue motion. The system calculates mean strain values for whole predefined LV segments. For global strain analysis, peak strain values from each of the 16 segments were averaged. Strain analysis was performed by the consensus of two observers. The analysis system automatically determines tracking quality. In this analysis, only segments with optimal tracking quality were included. Segments with suboptimal

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