

the disease-free segment adjacent to the intramural hematoma in patients with SCAD and the middle segment of the left anterior descending artery in those with nonobstructive CAD. Plaque volume (PV) was defined as intimal volume plus medial volume. Volume was divided by lesion length to correct for the different lesion length in each patient and described as adjusted volume (cubic millimeters/millimeter). Differences between the groups were tested using the Mann-Whitney *U* test. The study protocol was approved by the institutional review board of the Mayo Clinic, and written consent was obtained from all study subjects.

OCT was performed at median 44 days (interquartile range [IQR]: 14.5 to 446 days) after the first presentation of SCAD. Imaging segment length was comparable in both groups (12.9 mm [IQR: 9.7 to 17.1] vs. 12.2 mm [IQR: 7.7 to 14.0], $p = 0.16$). Patients with SCAD had lower PV (1.18 mm³/mm [IQR: 0.91 to 1.78] vs. 2.51 mm³/mm [IQR: 1.76 to 2.97], $p = 0.008$) and higher vasa vasorum volume (VVV) (0.47 mm³/mm [IQR: 0.32 to 0.56] vs. 0.19 mm³/mm [IQR: 0.10 to 0.24], $p < 0.001$) than those with nonobstructive CAD. VVV/% PV, VVV/PV, and VVV/vessel volume were higher in patients with SCAD than those with nonobstructive CAD (1.85 [IQR: 1.41 to 3.22] vs. 0.66 [IQR: 0.38 to 1.03], $p < 0.001$; 0.37 [IQR: 0.24 to 0.45] vs. 0.08 [IQR: 0.04 to 0.11], $p < 0.001$; 0.07 [IQR: 0.06 to 0.09] vs. 0.02 [IQR: 0.01 to 0.03], $p < 0.001$, respectively) (Figures 1D to 1F).

The present study shows that patients with a history of SCAD have a higher density of coronary adventitial VV in nonculprit segments adjacent to the SCAD region. A previous study found that neoangiogenesis of capillary vessels branching from the VV in the adventitia and leakage of neoangiogenetic capillaries is one mechanism of spontaneous cervical artery dissection (3). In the present study, we made a similar observation of extensive proliferation of adventitial VV in patients with SCAD. This finding supports a common intramural hematoma/atypical dissection predisposition in adventitial VV that extends to patients with SCAD. Extravasation of blood from proliferative adventitial VV may lead to the formation of microhematoma between media and adventitia that could result in coronary dissection. However, the present study does not provide a causal relationship between SCAD and increased VV density, which may be reactive.

In conclusion, the present study demonstrated that the adventitial VV is increased in patients with SCAD and suggested that proliferation of adventitial VV may be linked to development of SCAD in humans. Further studies are needed to determine the causal relationship between VV and SCAD.

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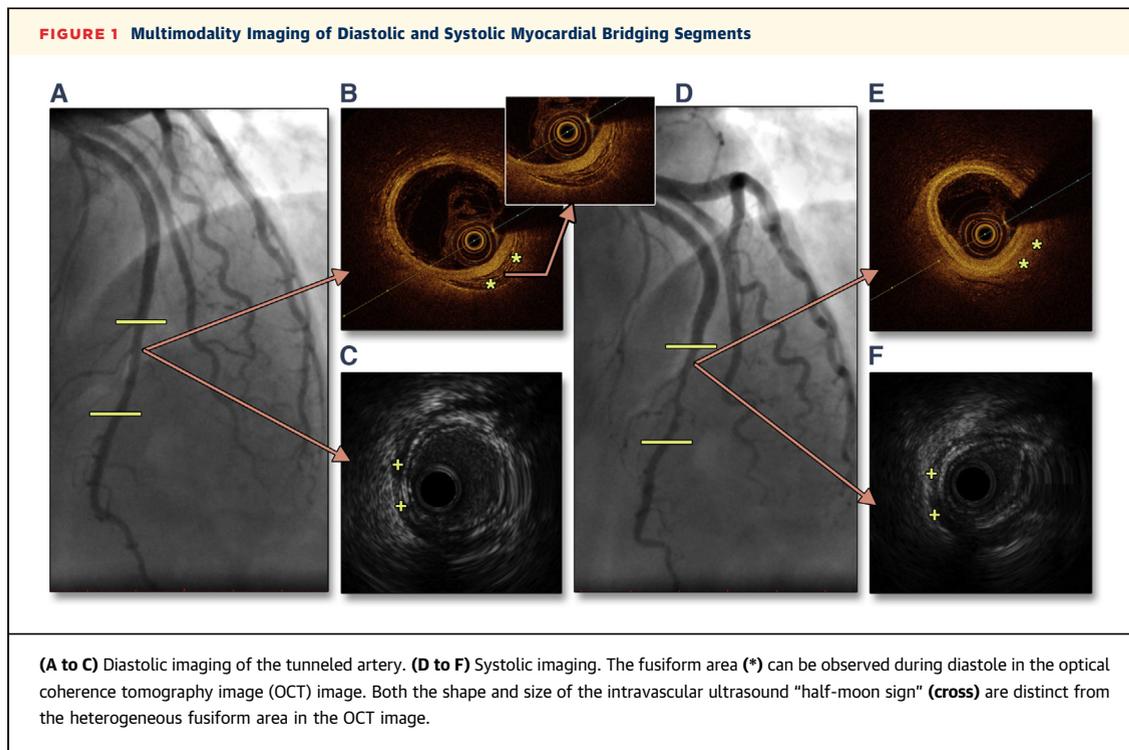
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Fusiform Appearance of Myocardial Bridging Detected by OCT



Myocardial bridging (MB) is characterized by epicardial coronary artery tunneling through the myocardium, with angiographic “milking” and an intravascular ultrasound (IVUS) “half-moon” echolucent (1). Optical coherence tomography (OCT), a light-based technique, can provide unprecedented in vivo imaging of coronary vessel wall structure, especially of intima and plaque composition, with a high resolution of 10 μm. So far, there are no data on visualization of MB using OCT.

From November 2013 to July 2014, we prospectively identified 36 patients with angiographically “milking” of the left anterior descending artery (LAD) consistent with the diagnosis of MB. Both OCT and IVUS imaging were performed after patients gave informed consent. OCT was also performed at the most compressed site manually after automatic pullback. In all patients and in all MB segments corresponding to OCT and IVUS imaging, a heterogeneous, generally signal-poor



fusiform area with a sharply delineated border closely surrounding the adventitia of the tunneled artery was detected with no gap between the fusiform area and the adventitia (Figure 1). In all patients, the fusiform area in the MB segment was continuous in the longitudinal OCT view, but the morphology changed depending on lumen compression. Most (33 of 36, 92%) MB segments showed a single fusiform area, whereas 3 showed 2 fusiform areas.

MB length, compression ratio (calculated as: $[(1 - \text{systolic external elastic membrane-cross-sectional area (CSA)} \div \text{diastolic external elastic membrane (EEM)-CSA}] \times 100\%$), remodeling index (calculated as $[\text{diastolic external elastic membrane-CSA} \div \text{the reference EEM-CSA}]$), and the thickness of "half-moon" echolucent area in the IVUS images and the thickness, length, and arc of the fusiform area in the OCT images were measured and calculated. The fusiform length was 15.6 ± 6.5 mm (range 10 to 18 mm) and appeared to depend on the MB length and heart rate. The thickness and arc of the fusiform zone (during diastole) measured 0.42 ± 0.11 mm (range 0.25 to 0.69 mm) and $176.3 \pm 53.1^\circ$ (range 106° to 287.5°), respectively. In addition, OCT detected atherosclerosis proximal to the MB segment in all patients, but only once in an MB segment in a patient with intimal thickening. The following data are normally distributed, and we used Pearson

correlation in the correlation analysis. The fusiform thickness had no correlation with that of the IVUS-detectable echolucent band ($R = -0.029$; $p = 0.934$). Notably, the correlation between the compression ratio and the arc of the heterogeneous fusiform area at the most compressed tunneled artery was significant ($R = -0.49$; $p = 0.003$).

Histological examination using a pig heart model confirmed that the fusiform, heterogeneous signal-poor area was mainly composed of connective tissue and was located at the junction of the MB myocardium and epicardium.

The main findings of the present OCT study were as follows. 1) OCT detected a heterogeneous signal-poor fusiform area with well-delineated borders indicating the existence of the tunneled artery through the myocardium, but this was not the same as the echolucent band found by IVUS ("half-moon phenomenon") that directly represented the myocardium surrounding the artery. 2) The fusiform area identified by OCT was more easily seen during cardiac diastole. 3) The severity of systolic MB compression was attenuated with an increase in the size of the fusiform arc. We documented these features as well as the histological correlations in a porcine model. According to previous histological evidence, the OCT fusiform area mainly consisted of loose connective tissue in the periarterial space beneath the MB.

Despite its higher resolution, OCT may not be the optimal imaging modality to detect a MB, mainly because of its limited penetration and rapid OCT fiber pullback and image acquisition (20 mm/s vs. 0.5 mm/s in IVUS). For this reason, we also performed OCT manually with the lens stationary at the MB segment.

In conclusion, in patients with MB documented angiographically and by IVUS, OCT detected a sharp border and heterogeneous, signal-poor fusiform area indicative of arterial tunneling through the myocardium that was distinct from the echolucent muscle band found on IVUS.

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Independent Impact of RV Involvement on In-Hospital Outcome of Patients With Takotsubo Syndrome



Takotsubo syndrome (TTS) is an acute clinical condition characterized by transient left ventricular dysfunction and reversible heart failure, the pathogenetic mechanism of which remains unclear. Although left ventricular apical ballooning is the most frequent morphological pattern, other variant forms have been described (1). In addition, right ventricular involvement (RVi), characterized by the presence of right ventricular (RV) apical dysfunction (biventricular ballooning), has been documented using echocardiography or cardiac magnetic resonance imaging. However, the prevalence, clinical profile, and

in-hospital course of TTS patients with RVi are still not well defined. To date, although RVi has been associated with a higher complication rate (2), no correlation with short-term cardiac morbidity or mortality has been reported. The aim of this study was to describe the prevalence and prognostic impact of RVi in TTS.

TTS patients with typical left ventricular apical ballooning enrolled in the Tako-tsubo Italian Network from January 2002 to June 2014 were included. Eleven hospitals contributed by providing data from a minimum of 11 to a maximum of 32 patients for each center. Patients presenting more than 24 h after symptom onset were excluded. The structure and methods of the Tako-tsubo Italian Network have been previously published (2). Data were prospectively recorded on a standardized form including information on patient demographics, pre-existing comorbidities, signs and symptoms at presentation, medical history, trigger events (emotional or physical), ST-segment elevation changes on admission, and clinical observations during hospitalization. The Charlson comorbidity index was calculated. Blood samples were collected every 6 h to measure peak troponin I concentrations in the acute phase. Brain natriuretic peptide (BNP) levels were also recorded daily during the acute phase. Standard transthoracic 2-dimensional echocardiography was performed within 6 h of hospital admission. The echocardiography transducer was adjusted to the level of the RV chamber to achieve optimal visualization of RV size and endocardial borders. To define RVi, the RV wall motion was evaluated qualitatively by visual assessment, in the parasternal long axis, apical, and subcostal 4-chamber views. All patients underwent coronary angiography and left ventriculography within 24 h of symptom onset to confirm the TTS diagnosis. Acute heart failure, cardiogenic shock, and in-hospital mortality were considered major adverse events. The study was approved by the local ethics committee, and all patients gave consent for the use of their medical records for research purposes.

The study population included 339 patients (mean age 69.7 ± 11.2 years; 91.7% female patients). RVi was observed in 56 patients (16.5% of the overall population). Demographic, clinical, electrocardiographic, and echocardiographic features of the overall population and a comparison at univariate analysis of the same variables in patients with and without RVi are reported in Table 1. In the overall population, acute heart failure was the most frequent major adverse event ($n = 57$, 16.8%). Cardiogenic shock and in-hospital death occurred in 23 (6.8%) and 6 (1.8%) patients, respectively.

On multivariate analysis, RVi (hazard ratio [HR]: 2.561; 95% confidence interval [CI]: 1.227 to 5.346;