ORIGINAL RESEARCH

Optical Coherence Tomography to Evaluate Plaque Burden and Morphology in Patients With Takotsubo Syndrome

Ingo Eitel, MD;* Thomas Stiermaier, MD;* Tobias Graf, MD; Christian Möller, MD; Karl-Philipp Rommel, MD; Charlotte Eitel, MD; Gerhard Schuler, MD; Holger Thiele, MD;† Steffen Desch, MD†

***Background*—**Disrupted atherosclerotic plaques in the left anterior descending coronary artery are discussed controversially as a potential pathophysiological mechanism in Takotsubo syndrome (TTS). Therefore, the aim of the present study was to assess plaque burden and morphology by using optical coherence tomography in patients with TTS.

***Methods and Results*—**A total of 23 consecutive TTS patients were included in this single-center study and underwent optical coherence tomography imaging of the left main coronary artery and the left anterior descending coronary artery at acute presentation. All patients fulfilled the established diagnostic criteria for TTS and the diagnosis was confirmed with a multimodality imaging approach including cardiac magnetic resonance in 16 patients (69.6%). Atherosclerotic plaques located in the left anterior descending coronary artery or both the left anterior descending coronary artery and the left main coronary artery were detected in 16 TTS patients (69.6%), with 6 patients exhibiting multiple plaque types. In addition to the predominant fibrocalcific (52.2%) and lipid-rich plaques (30.4%), thin-cap fibroatheromas were also found in 6 patients (26.1%). However, ruptured plaques or intracoronary thrombi were not observed. Vessel stenosis >50% was found in 3 patients (13.0%) by analyzing cross-sectional areas. Clinical characteristics and cardiac magnetic resonance findings did not differ significantly between TTS patients with and without atherosclerotic plaques.

***Conclusions*—**Using optical coherence tomography, the present study revealed a high prevalence of atherosclerotic plaques in patients with TTS, including a considerable number of highly vulnerable thin-cap fibroatheromas. However, ruptured plaques or intracoronary thrombi were not observed and are therefore most likely not the underlying mechanism of TTS. **(*J Am Heart Assoc.* 2016;5:e004474 doi: 10.1161/JAHA.116.004474)**

Key Words: OCT • pathophysiology • plaque • stress-induced cardiomyopathy • Takotsubo syndrome

The first case of Takotsubo syndrome (TTS) was reported in Japan more than 25 years ago.[1] Since then, TTS has emerged as an important form of acute heart failure and a major differential diagnosis in patients with symptoms suggestive of acute coronary syndrome. An increasing number of cases worldwide and intensive research efforts have expanded the experience with TTS.[2] Therefore, the epidemiology, clinical features, and most recently prognostic implications of the disease have been well characterized.[2–5] However, the causative mechanisms of TTS have not been fully elucidated yet. Increasing evidence suggests that catecholamine excess leading to enhanced sympathetic activity and impaired coronary microcirculation might play a major role.[6–8] Nevertheless, this theory is not entirely conclusive since not all TTS patients exhibit stressful triggers and elevated catecholamine levels.[9] Several alternative pathophysiological mechanisms have been proposed including disrupted atherosclerotic plaques in the left anterior descending coronary artery (LAD) causing myocardial infarction with spontaneous lysis of thrombus. This concept is primarily based on a small study that reported ruptured plaques in the middle portion of the LAD in 5 TTS patients using intravascular ultrasound (IVUS).[10] Furthermore, insights from cardiac magnetic resonance (CMR) imaging have proven that extensive anterior myocardial infarction can mimic the typical

From the Medical Clinic II (Cardiology/Angiology/Intensive Care Medicine), University Heart Center Lübeck, University Hospital Schleswig-Holstein, Lübeck, Germany (I.E., T.S., T.G., C.M., C.E., H.T., S.D.); German Center for Cardiovascular Research (DZHK), partner site Hamburg/Kiel/Lübeck, Lübeck, Germany (I.E., T.S., T.G., C.M., C.E., H.T., S.D.); Department of Internal Medicine–Cardiology, University of Leipzig–Heart Center, Leipzig, Germany (K.-P.R., G.S.).

*Dr Eitel and Dr Stiermaier are co-first authors.

†Dr Thiele and Dr Desch are co-senior authors.

Correspondence to: Ingo Eitel, MD, Medical Clinic II, University Heart Center Lübeck, University Hospital Schleswig-Holstein, Ratzeburger Allee 160, 23538 Lübeck, Germany. E-mail: ingo.eitel@uksh.de

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contraction pattern of TTS patients with typical apical ballooning.[11] However, another IVUS study in 10 TTS patients could not confirm the pathogenic role of plaque rupture.[12] Optical coherence tomography (OCT) is a novel, light-based intravascular imaging modality with an ≈10 times higher resolution than that of IVUS. Therefore, OCT has emerged as the preferred approach to evaluate structural characteristics of the coronary artery wall as well as atherosclerotic plaque morphology.[13]

In view of the inconclusive data in previous investigations using IVUS, the aim of the present study was to assess plaque burden and morphology by using OCT in patients with TTS in order to determine a potential causality between acute plaque rupture and the occurrence of TTS.

Methods

Study Population

This prospective study was conducted at the University of Leipzig—Heart Center and included consecutive patients diagnosed with TTS between January 2012 and December 2013. All patients presented with acute chest pain and/or dyspnea and fulfilled the Mayo Clinic criteria: (1) transient hypokinesis, akinesis, or dyskinesis of the left ventricular apical and/or midventricular or basal segments extending beyond a single epicardial vascular distribution; (2) absence of significant obstructive coronary artery disease or angiographic evidence of acute plaque rupture; (3) new electrocardiographic abnormalities (ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin levels; and (4) absence of pheochromocytoma and myocarditis.[14] However, coexisting coronary artery disease that did not sufficiently explain the extent of wall motion abnormalities was not considered as an exclusion criterion. Clinical outcome and complete recovery of left ventricular dysfunction were evaluated during an outpatient visit 6 months after initial presentation. Main exclusion criteria for study participation were age <18 years, cardiogenic shock, acute myocardial infarction, thrombotic occlusion of a coronary artery, severe comorbidity limiting life expectancy to <6 months, inappropriate coronary anatomy to perform OCT, pregnancy, or participation in another trial.

The study was approved by the local Institutional Review Board and conducted according to the Declaration of Helsinki. All patients provided written informed consent.

Optical Coherence Tomography Image Acquisition and Analysis

Coronary angiography was performed in all patients because of suspected acute coronary syndrome. Patients with typical wall motion abnormalities in left ventriculography suggestive of TTS were considered eligible for the study. OCT images were acquired with the C7-XR™ Imaging System (St. Jude Medical/LightLab Imaging) and a 2.7-F OCT catheter (Dragonfly™; St. Jude Medical). Under fluoroscopic guidance, the flushed and calibrated catheter was advanced over a guidewire to the distal part of the LAD. Image acquisition was performed with automatic pullback (speed set at 20 mm/s) during continuous flushing of the vessel with contrast medium (rate of 2–5 mL/s) using a power injector. Complete visualization of the LAD and the left main coronary artery was assured by repeated pullbacks.

OCT images were evaluated regarding the presence of plaques in the left main coronary artery or in the LAD. Plaque morphology was determined according to previously validated criteria for plaque characterization.[15] Homogeneous, signal-rich lesions were identified as fibrous plaques. Lipid-containing plaques were defined as diffusely bordered, signal-poor regions with overlying signal-rich bands, corresponding to fibrous caps. The lipid content of a plaque was semiquantified according to the number of involved quadrants on the cross-sectional image. If lipid was present in ≥2 quadrants, a plaque was considered lipid-rich. The thinnest part of the fibrous cap was measured repeatedly and an average value was calculated. Lesions with a fibrous cap thickness of <65 μm were diagnosed as thin-cap fibroatheromas (TCFA). OCT images of fibrocalcific plaques reveal signal-poor regions with sharply delineated borders. Exemplary illustrations of various atherosclerotic plaque morphologies are provided in Figures 1 and 2. Plaque rupture was defined as a discontinuity in the fibrous cap and a cavity formation in the plaque. Intracoronary thrombus was identified as a mass protruding from the surface of the vessel wall into the vessel lumen. The minimum lumen cross-sectional area within the plaque was determined and compared with a reference cross-sectional area proximal to the plaque to identify stenoses >50%.

All OCT images were analyzed independently by 2 investigators using a dedicated OCT Review Workstation (Ilumien™; St. Jude Medical). Any disagreements were resolved by consensus.

Cardiac Magnetic Resonance Imaging

Diagnosis confirmation via CMR imaging was performed in patients without contraindications with a 1.5-T whole-body scanner (Intera CV, Philips Medical Systems) within 1 week after admission. The standard protocol included the following: (1) steady state–free precession images for assessment of left ventricular and right ventricular function and regional wall motion abnormalities as well as the presence of pericardial effusion, pleural effusion, or thrombi; (2) T2-weighted images

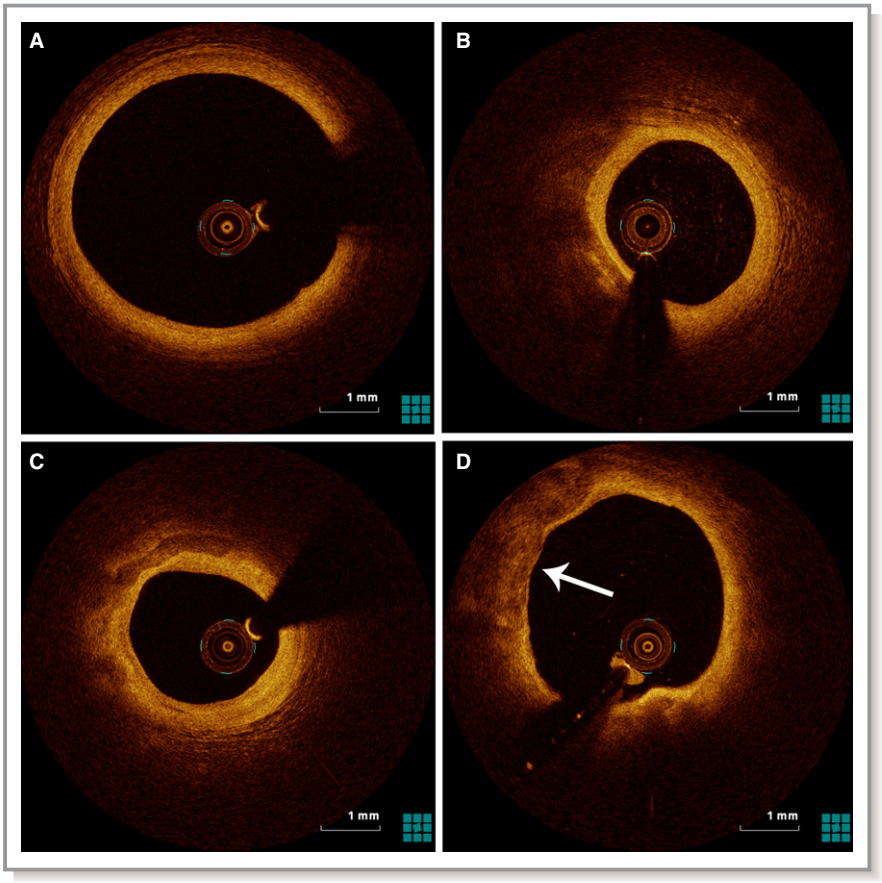

Figure 1. Optical coherence tomography examples of different plaque morphologies. A, Coronary artery wall without evidence of plaques. B, Lipid-rich plaque (signal poor, diffusely bordered). C, Fibrocalcific plaque (signal-poor, sharply delineated borders). D, Thin-cap fibroatheroma (thinnest part of the cap <65 μm; arrow).

for assessment of myocardial edema and the T2-ratio; (3) T1-weighted turbo spin echo imaging performed prior to and during the first 3 minutes after an intravenous bolus of gadolinium-based contrast agent (0.1 mmol/kg) for the assessment of early gadolinium enhancement ratio; and (4) late gadolinium enhancement imaging covering the entire left ventricle ≈10 to 15 minutes after intravenous administration of a second bolus of gadolinium-based contrast agent (0.1 mmol/kg).[3,16]

Images were analyzed offline with certified CMR evaluation software (cmr42, Circle Cardiovascular Imaging Inc) by blinded, experienced investigators. The core laboratory has proven low inter- and intraobserver variability and excellent reproducibility.[17] Standard methods of left ventricular functional analysis, edema analysis, calculation of the early gadolinium enhancement ratio, and late gadolinium enhancement images for the assessment of myocardial fibrosis/necrosis were used as previously described.[3,16] A T2 signal intensity ratio ≥1.9 and an early gadolinium enhancement ratio ≥4 were the predefined thresholds to identify myocardial inflammation. Significant late gadolinium enhancement was defined as >5 SD above normal myocardium.

Statistical Analysis

Categorical variables are reported as frequencies and percentages and were compared with the χ^2 test or the Fisher's exact test in case of small event rates. Normally distributed continuous variables are presented as mean±SD. Comparisons were performed with the Student *t* test. Non-normally distributed continuous variables are reported as median with interquartile range and were compared with the Mann–Whitney *U* test. The Shapiro–Wilk test was used to test for normal distribution.

Baseline clinical characteristics and CMR data were compared between patients with evidence of plaques in OCT images and patients without plaques.

Statistical analyses were performed with SPSS (version 17.0; SPSS Inc, Chicago, IL). A 2-sided probability ≤0.05 was considered statistically significant.

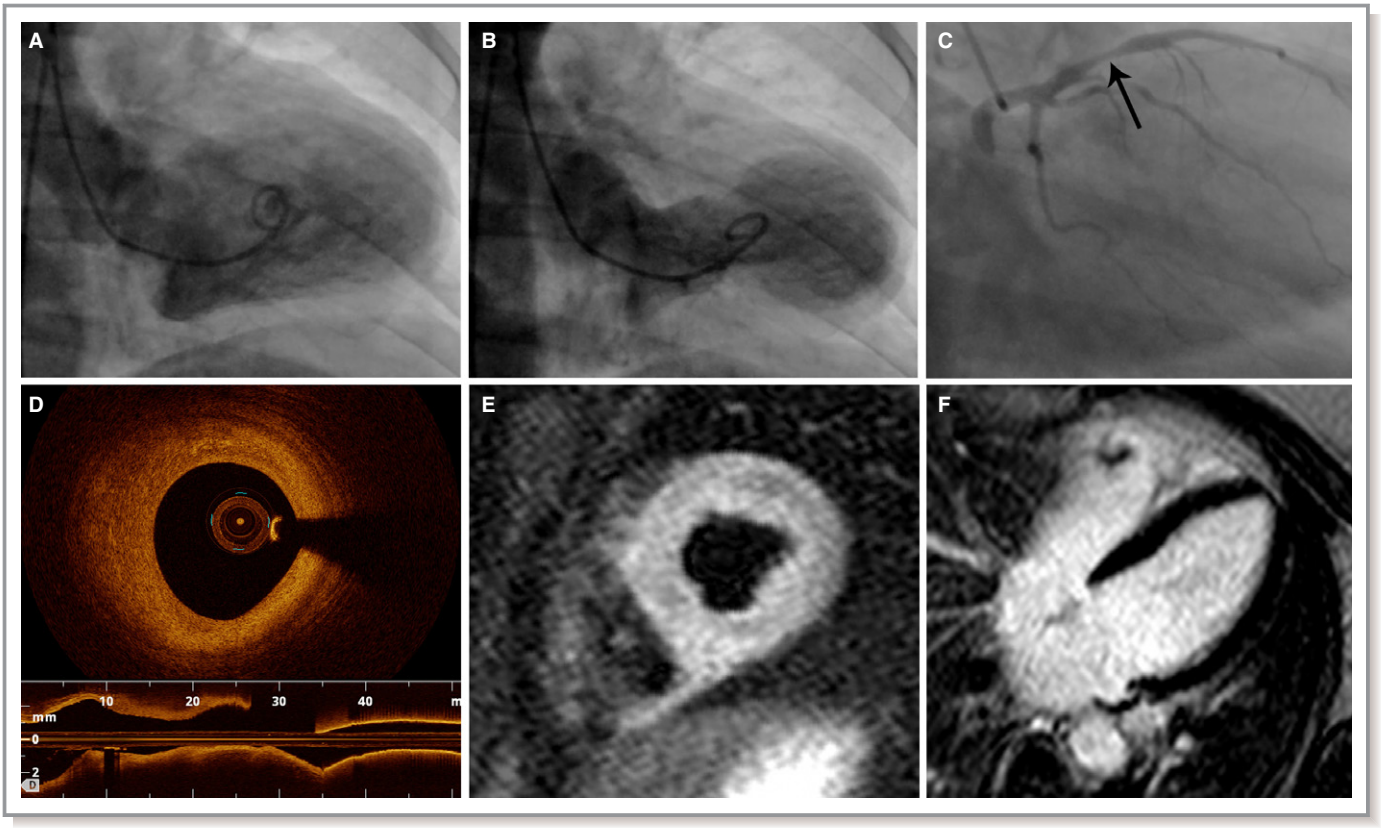

Figure 2. Patient with Takotsubo syndrome and a fibrous plaque in the proximal left anterior descending coronary artery. A 46-year-old woman presenting with chest pain and ST-segment elevations in the precordial leads demonstrated typical apical ballooning, which is illustrated in the end-diastolic (A) and end-systolic (B) images from left ventriculography. Coronary angiography revealed a moderate stenosis of the proximal LAD (C, arrow), which did not resolve after intracoronary administration of nitroglycerin. A fibrous plaque (homogeneous, signal-rich) was identified in OCT imaging (D) with a minimum lumen cross-sectional area of 6.4 mm^2 and a calculated area stenosis of 60%. The interventionalist decided to perform stent implantation because of ongoing symptoms and ECG abnormalities. CMR imaging confirmed the diagnosis of TTS by demonstrating circumferential myocardial edema in the area of left ventricular dysfunction (E, midventricular short-axis slice) without any evidence of late gadolinium enhancement (F, 4-chamber view). CMR indicates cardiac magnetic resonance; OCT, optical coherence tomography; TTS, Takotsubo syndrome.

Results

Left ventriculography revealed a typical contraction pattern suggestive of TTS in 30 consecutive patients (Figure 3). Of these, 26 patients were eligible for study participation in the absence of exclusion criteria and underwent OCT imaging. Three patients were excluded subsequently because of CMR evidence of myocardial infarction with spontaneous lysis of thrombus (n=2) or myocarditis (n=1). Consequently, the final study population comprised 23 patients with the confirmed diagnosis of TTS and OCT imaging data. Diagnosis verification via CMR was performed in 16 of these patients (69.6%) in median 2 days (interquartile range 2–3) after initial presentation. The reasons for not pursuing CMR were the following: permanent pacemaker (n=3), claustrophobia/no informed consent (n=3), and organizational error (n=1).

Clinical Characteristics and Cardiac Magnetic Resonance Results

The main patient characteristics are summarized in Table 1. The majority of patients were postmenopausal females with a preceding stressful trigger. Apical ballooning was the predominant contraction pattern and resulted in a moderately reduced left ventricular ejection fraction at acute presentation with complete recovery during follow-up. Compared to patients without plaques, TTS patients with evidence of plaques in OCT imaging were numerically older (P=0.14) and had a higher prevalence of hypertension (P=0.08) without reaching statistical significance (Table 1). All-cause mortality after 6 months was 8.7% with 1 death occurring in each group. The causes of death were septic shock in the patient without plaques and severe heart failure resulting in cardiogenic shock in the patient with plaques. Recurrence of TTS

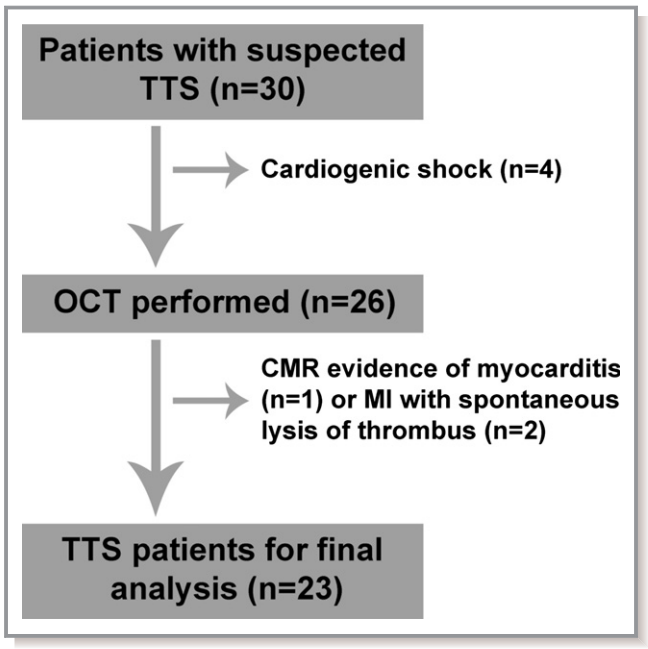

Figure 3. Study flow chart. CMR indicates cardiac magnetic resonance; MI, myocardial infarction; OCT, optical coherence tomography; TTS, Takotsubo syndrome.

after complete recovery of left ventricular function was not observed.

CMR imaging results are provided in Table 2. Circumferential myocardial edema matching the distribution of left ventricular dysfunction was visible in all patients. However, none of the patients had evidence of significant late gadolinium enhancement. CMR findings did not differ according to the presence of atherosclerotic plaques.

Optical Coherence Tomography Results

A total of 75 pullbacks were performed in the 23 TTS patients. Atherosclerotic plaques were detected in 16 patients (69.6%) and were located in the LAD or both the LAD and the left main coronary artery (Table 3). Six patients exhibited multiple plaque types whereby fibrocalcific and lipid-rich plaques were the predominant types. TCFA were diagnosed in 6 patients (26.1%). However, ruptured plaques or intracoronary thrombi were not observed in the study population (Table 3). By analyzing cross-sectional areas, >50% lumen stenosis was detected in 3 patients. In 1 of these patients, the interventionalist decided to implant a drug-eluting stent because of ongoing chest pain and persistent ST-segment elevations in the ECG (Figure 2). The lesions in the other 2 patients were treated conservatively in the absence of typical angina pectoris. Atherosclerotic plaques in a long wrap-around LAD (defined as any part of the vessel outreaching the apex) were observed in 9 patients, of whom 8 exhibited apical ballooning and 1 patient showed a midventricular ballooning type.

Discussion

The present study is the first comprehensive assessment of plaque burden and morphology in consecutive patients with TTS by using OCT, the reference standard for intracoronary imaging. The results illustrate that atherosclerotic plaques including unstable TCFA with a high vulnerability to rupture are a frequent finding in patients with TTS. However, disrupted plaques or intracoronary thrombi were not observed in our cohort of patients presenting with acute TTS. Therefore, acute plaque rupture is most likely not the underlying mechanism causing TTS.

Pathophysiological Role of Plaque Rupture in Takotsubo Syndrome

Based on the detection of disrupted atherosclerotic plaques in 5 TTS patients by using IVUS, plaque rupture and transient coronary artery occlusion with spontaneous lysis of thrombus was suggested as a potential causative mechanism of TTS.[10] The peculiar distribution of left ventricular wall motion abnormalities was interpreted in the presence of a long wrap-around LAD supplying a large part of the inferior myocardial wall.[10,18] However, another IVUS study did not find any evidence of ruptured plaques or intracoronary thrombi in 10 TTS patients and wrap-around LAD was not a consistent finding in TTS either.[12,19,20] Furthermore, atypical ballooning patterns and right ventricular involvement are not attributable to a single lesion in the LAD. In the present study, high-resolution OCT, the reference standard for plaque characterization, was performed immediately at acute presentation in a large series of consecutive TTS patients. Although more than two thirds of TTS patients exhibited various types of atherosclerotic plaques including unstable TCFA, plaque rupture or intracoronary thrombi were not observed in our cohort. Of note, also in the 8 patients with apical ballooning in the presence of plaques in a long wrap-around LAD, the occurrence of TTS cannot be attributed to this constellation in the absence of plaque rupture in OCT imaging. Therefore, these results confirm and expand the evidence against a causative role of plaque rupture in TTS and emphasize that TTS and myocardial infarction with spontaneous lysis of thrombus are different entities. However, acute myocardial infarction can both trigger TTS as well as mimic the typical TTS contraction pattern in case of a culprit lesion in the LAD.[11,21,22] In this clinical scenario, contrast-enhanced CMR imaging is very helpful for diagnosis confirmation and differential diagnosis as it enables myocardial tissue characterization. Our study is unique as it combines both state of the art intracoronary imaging with CMR imaging. In TTS usually no late gadolinium enhancement can be seen in correlation with the complete recovery of left

Table 1. Clinical Characteristics

Variable	All Patients (n=23)	With Plaques (n=16)	Without Plaques (n=7)	*P* Value
Age, y	73.0±10.7	75.2±9.9	68.0±11.5	0.14
Male sex	3 (13.0)	2 (12.5)	1 (14.3)	1.00
Cardiovascular risk factors				
Current smoking	3 (13.0)	3 (18.8)	0 (0)	0.53
Hypertension	21 (91.3)	16 (100)	5 (71.4)	0.08
Hypercholesterolemia	4 (17.4)	2 (12.5)	2 (28.6)	0.56
Diabetes mellitus	8 (34.8)	7 (43.8)	1 (14.3)	0.35
Days of hospitalization	6 (4–7)	6 (5–7)	4 (3–8)	0.26
Wrap-around LAD*	14 (61)	9 (56)	5 (71)	0.49
Ballooning pattern				
Apical	19 (82.6)	14 (87.5)	5 (71.4)	0.56
Midventricular	4 (17.4)	2 (12.5)	2 (28.6)	0.56
Stressful event	16 (69.6)	12 (75.0)	4 (57.1)	0.63
Emotional	7 (30.4)	4 (25.0)	3 (42.9)	0.63
Physical	9 (39.1)	8 (50.0)	1 (14.3)	0.18
CK at admission, μmol/L×s	2.2 (1.5–3.9)	2.1 (1.5–4.3)	2.3 (1.7–3.9)	0.82
Troponin T at admission, ng/L	321.4±222.5	347.3±249.2	252.3±117.3	0.24
Initial LV ejection fraction, %	41.7±7.9	42.5±8.7	39.9±5.9	0.47
Follow-up LV ejection fraction, %	59.0±6.5	59.2±6.6	58.5±7.4	0.87
6-month mortality	2 (8.7)	1 (6.3)	1 (14.3)	0.53

Data are presented as number (%), mean±SD, or median (interquartile range). *P* values were calculated for the comparison between patients with and without plaques in optical coherence tomography imaging. CK indicates creatine kinase; LAD, left anterior descending; LV, left ventricular.
*Defined as any part of the vessel outreaching the apex.

ventricular dysfunction, whereas in acute myocardial infarction causing such distinct wall motion abnormalities, a classical ischemic subendocardial or transmural scar can be detected (Figure 4). Therefore, our data underline that in the acute setting TTS cannot be diagnosed based solely on coronary angiography and left ventriculography, but requires a multimodality imaging approach also including echocardiography, CMR, and/or single photon emission computed tomography/positron emission tomography. Nevertheless, the discrimination between TTS and true aborted myocardial infarction without any irreversible myocardial damage remains challenging despite recent advances in imaging techniques.[22,23]

Alternative Pathophysiological Concepts in Takotsubo Syndrome

Several hypotheses regarding the causative mechanisms of TTS are discussed in current literature, which partly explain single aspects of the disease but do not fully capture the etiology of TTS. Coronary artery vasospasm or myocardial bridging as well as obstruction of the left ventricular outflow tract seem rather unlikely major pathophysiological factors since they are not mandatory in TTS patients and fail to account for atypical variants and right ventricular ballooning.[20,24–26] Catecholamine excess leading to sympathetic overstimulation is the most popular pathophysiological concept in TTS.[6–8] Apart from the association of the disease with stressful triggers, further evidence is provided by studies demonstrating elevated plasma catecholamine levels and histological findings in myocardial biopsies that were similar to the known cardiotoxic effects of catecholamines.[8,27] Furthermore, several investigations confirmed impaired coronary microcirculation during the acute phase of TTS using different detection methods.[28,29] Therefore, catecholamine excess and microvascular dysfunction seem to contribute to some extent to the occurrence of TTS, albeit both concepts are not entirely conclusive. Stressful triggers and elevated catecholamine levels are not a consistent finding in all TTS patients and microvascular dysfunction might as well be secondary due to left ventricular dysfunction or catecholamine excess.[9] Moreover, the reason for the local

Table 2. Cardiac Magnetic Resonance Results

Variable	All Patients (n=16)	With Plaques (n=12)	Without Plaques (n=4)	*P* Value
LV ejection fraction, %	42.7±8.3	42.7±9.7	42.5±3.0	0.95
LV end-diastolic volume, mL	141.7±50.6	131.2±53.2	170.8±31.6	0.19
LV end-systolic volume, mL	78.8±40.4	71.7±44.5	98.3±17.5	0.28
Right ventricular involvement	3/16 (18.8)	1/12 (8.3)	2/4 (50.0)	0.14
Pericardial effusion	4/16 (25.0)	3/12 (25.0)	1/4 (25.0)	1.00
Pleural effusion	9/16 (56.3)	6/12 (50.0)	3/4 (75.0)	0.59
Thrombi	0/16 (0)	0/12 (0)	0/4 (0)	—
Focal edema*	14/14 (100)	10/10 (100)	4/4 (100)	—
Elevated T2 SI ratio*	14/14 (100)	10/10 (100)	4/4 (100)	—
T2 SI ratio (cutoff ≥1.9)	2.3 (2.1–2.5)	2.3 (2.1–2.4)	2.5 (2.3–3.2)	0.15
Elevated EGE ratio†	9/13 (69.2)	5/9 (55.6)	4/4 (100)	0.23
EGE ratio (cutoff ≥4)	4.7±1.4	4.4±1.4	5.6±1.2	0.19
Elevated EGE ratio and T2 SI ratio†	9/13 (69.2)	5/9 (55.6)	4/4 (100)	0.23
LGE	0/16 (0)	0/12 (0)	0/4 (0)	—

Data are presented as n/N (%), mean±SD, or median (interquartile range). *P* values were calculated for the comparison between patients with and without plaques in OCT imaging. EGE indicates early gadolinium enhancement; LGE, late gadolinium enhancement; LV, left ventricular; OCT, optical coherence tomography; SI, signal intensity.
*Not assessed in 2 patients due to poor image quality.
†Not assessed in 3 patients due to poor image quality.

distribution of abnormal contraction while sparing other surrounding segments as well as the role of sex and female hormone status considering the predominance of postmenopausal women have not been elucidated and deserve further research efforts.

Table 3. Optical Coherence Tomography Results

Variable	TTS Patients (n=23)
Atherosclerotic plaques	16 (69.6)
Location of plaques	
LMCA only	0 (0)
LAD only	10 (43.5)
LMCA+LAD	6 (26.1)
Types of plaques*	
Fibrocalcific plaque	12 (52.2)
Lipid-rich plaque	7 (30.4)
Fibrous plaque	1 (4.3)
Thin-cap fibroatheroma	6 (26.1)
Plaque rupture	0 (0)
Thrombus	0 (0)
Cross-sectional area stenosis >50%	3 (13.0)

Data are presented as number (%). LAD indicates left anterior descending; LMCA, left main coronary artery; TTS, Takotsubo syndrome.
*In case of several plaques of the same type, patients contributed only once to each category. Four patients exhibited 3 different plaque types and 2 patients had 2 types of plaques.

Frequency and Clinical Implications of Plaques in Takotsubo Syndrome Patients

Our study revealed a notably high prevalence of atherosclerotic plaques in patients with TTS, albeit a pathophysiological role could not be established. The detection of plaques is not entirely surprising, considering the advanced age and the cardiovascular risk profile of TTS patients. Meanwhile, the coexistence of coronary artery disease and TTS is generally accepted and also reflected in current guidelines.[14,30] However, the frequency of coronary artery disease in previous investigations using coronary angiography varied considerably between 10% and 60%.[5,31,32] These rates were clearly outperformed in the present study because of the unique sensitivity of OCT to also detect nonobstructive plaques. Of note, about one quarter of TTS patients revealed highly vulnerable TCFA prone to rupture and thrombosis. Although the rate of nonfatal myocardial infarction among TTS patients was low in a previous investigation (0.3% per patient year), several recent trials reported substantial long-term mortality rates including a considerable number of patients with undetermined or unknown causes of death.[4,5] Coronary artery occlusion attributable to ruptured plaques causing fatal myocardial infarction cannot be excluded in these

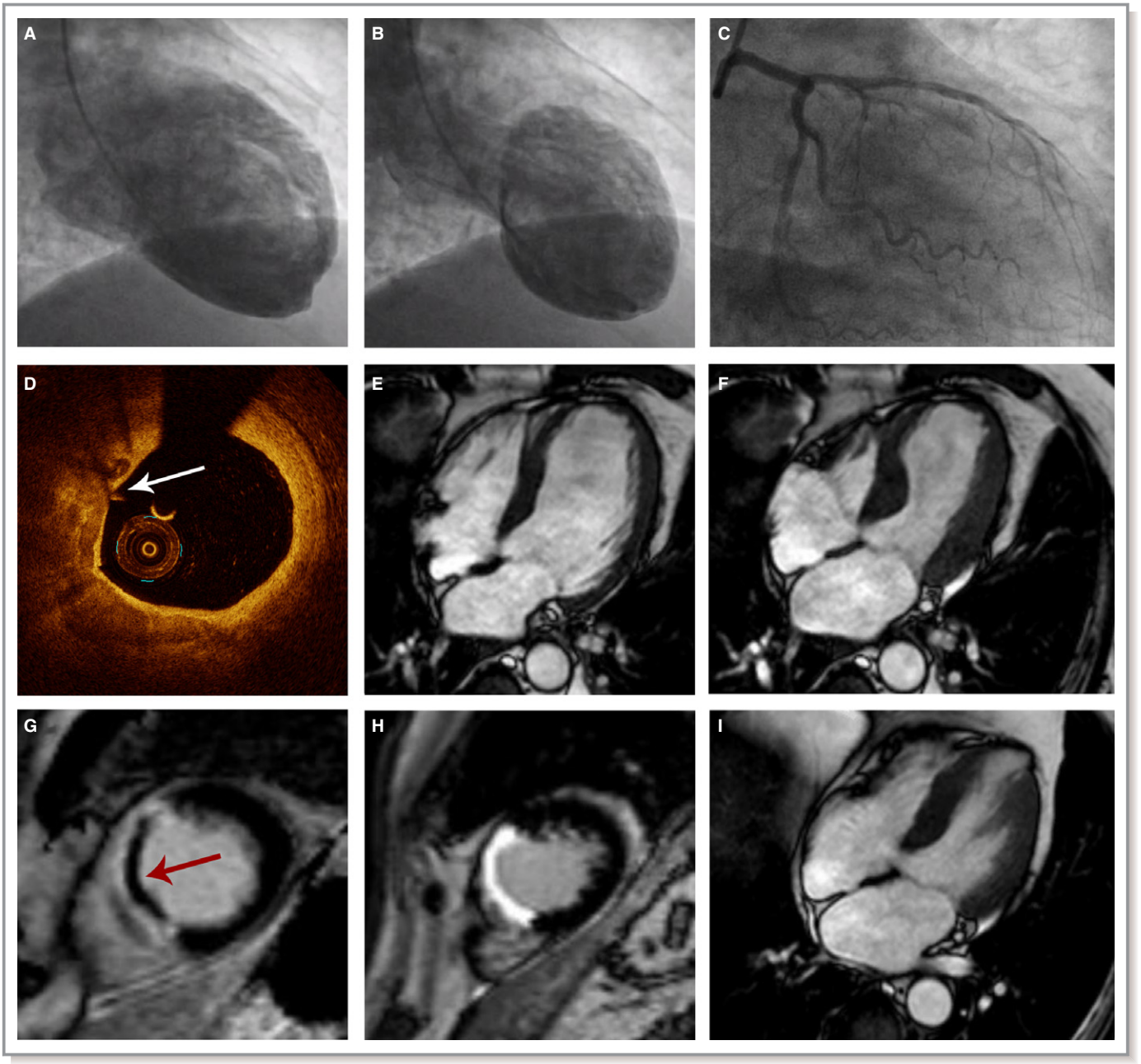

Figure 4. Myocardial infarction mimicking Takotsubo syndrome. A 67-year-old male patient presented with intermittent chest pain of varying intensity for several days. The ECG revealed significant ST-segment elevations in leads V_2 to V_5 and the high-sensitivity troponin T at admission was 1462 ng/L. End-diastolic (A) and end-systolic (B) images from left ventriculography demonstrated circumferential apical and midventricular hypokinesis/akinesis with preserved basal contraction in the absence of significant obstructive coronary artery disease (C), suggestive of typical TTS. OCT imaging showed several TCFA with a presumably ruptured plaque in the proximal LAD (D, arrow) without evidence of intracoronary thrombi. End-diastolic (E) and end-systolic (F) steady state–free precession CMR images in 4-chamber view confirmed the TTS-like contraction pattern, albeit the contractility of the lateral wall seems to be largely preserved. Contrast-enhanced CMR imaging demonstrated late gadolinium enhancement of the anterior/anteroseptal midventricular and apical segments (G, midventricular short-axis slice) with substantial microvascular obstruction (arrow). Follow-up CMR imaging 3 months after acute presentation confirmed transmural infarction in late gadolinium enhancement imaging (H, midventricular short-axis slice) with persistent apical hypokinesis/akinesis (I, end-systolic 4-chamber view). Therefore, this patient was diagnosed with subacute anterior myocardial infarction with spontaneous lysis of thrombus. CMR indicates cardiac magnetic resonance; LAD, left anterior descending coronary artery; OCT, optical coherence tomography; TCFA, thin-cap fibroatheromas; TTS, Takotsubo syndrome.

patients. Therefore, the question regarding the optimal therapeutic approach in patients with TTS arises. In particular, cholesterol-lowering therapy contributes to plaque stabilization and has most recently proven beneficial even in intermediate-risk patients without cardiovascular disease.[33,34] Furthermore, antihypertensive and antiplatelet therapies

might reduce progression of atherosclerotic plaques and reduce the complications of plaque rupture.[33] However, medical therapy in TTS patients has not been investigated systematically, and any potential benefit remains speculative in the absence of randomized controlled trials.

Limitations

The present study was a single-center OCT evaluation of consecutive TTS patients presenting within a 2-year period. Nevertheless, the study population was relatively small. Therefore, the results should be viewed as preliminary and require confirmation in large-scale trials, ideally with a multicenter approach. The prognostic implications of atherosclerotic plaques in TTS patients could not be determined because of the small sample size with a low number of events. Furthermore, the results may not be exactly applicable to TTS patients with cardiogenic shock since these patients were excluded from the study. Plaque burden in the right and left circumflex coronary artery were not evaluated. Finally, the lack of a control population hampers the comparison of the observed frequency of atherosclerotic plaques with age- and sex-matched patients without TTS.

Conclusions

The present study in a well-characterized population of consecutive patients with TTS revealed a high prevalence of atherosclerotic plaques by using OCT, including a considerable number of TCFA prone to rupture and thrombosis. However, ruptured plaques or intracoronary thrombi were not observed in this cohort of patients with acute TTS and are therefore most likely not the key factors in the pathophysiology of TTS.

Disclosures

None.

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