Acute myocardial infarction associated with prosthetic valve leaflet thrombosis after transcatheter aortic valve implantation: a case report

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Background	Fatal thrombo-embolic events like cerebral stroke or myocardial infarction are rare complications of prosthetic heart valve leaflet thrombosis. Nevertheless, prevention and management of leaflet thrombosis is gaining increased attention, particularly with the widespread adoption of transcatheter heart valves.
Case summary	We herein present the case of a 79-year-old man who had undergone a transcatheter aortic valve implantation procedure. Seven months later, he presented with a non-ST-segment elevation myocardial infarction. Coronary angiography did not reveal obstructive lesions. A dedicated cardiac computed tomography scan showed thrombosis of both right- and non-coronary leaflets of the prosthetic aortic valve, while prosthetic valve function was normal on echocardiography. Transmural myocardial infarction lesions in the midventricular and apical inferior wall were detected by cardiac magnetic resonance imaging.
Discussion	Subclinical leaflet thrombosis of prosthetic aortic valves is a common finding. In this case report, we show that myocardial infarction presumably due to leaflet thrombosis was the first symptom in an otherwise asymptomatic patient. This finding raises the question of the validity in distinguishing between subclinical and clinical leaflet thrombosis based on prosthetic valve function.
Keywords	Valve thrombosis • Aortic stenosis • TAVI • MINOCA • Myocardial infarction • Case report

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Learning points

- Subclinical prosthetic valve leaflet thrombosis is a common finding.
- Diagnostic hallmarks of leaflet thrombosis range from hypoattenuated leaflet thickening to hypoattenuation affecting motion and finally elevated transvalvular gradients.
- The optimal antithrombotic regimen for prevention of leaflet thrombosis remains undetermined.
- Subclinical leaflet thrombosis may be the source of thromboembolic events including myocardial infarction.

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Introduction

Transcatheter aortic valve implantation (TAVI) has become an established treatment of severe symptomatic aortic valve stenosis in elderly patients across all surgical risk categories. In recent years, the phenomenon of subclinical leaflet thrombosis has gained cumulative interest. Although it is a frequent finding, its clinical significance is disputed and it is often considered a benign condition. The incidence of stroke or transient ischaemic attack because of subclinical leaflet thrombosis is low. Here, we report the case of a 79-year-old male patient suffering from acute myocardial infarction most likely caused by thrombo-embolic coronary occlusion, with subclinical leaflet thrombosis after TAVI being the suspected origin of coronary embolism.

Timeline

March 2018	Transcatheter aortic valve implantation
June 2018	3-month follow-up, clinically well, normal transvalvular gradients
October 2018	Non-ST-elevation acute coronary syndrome, transcatheter heart valve thrombosis
December 2018	Death from unknown cause

Case presentation

A 79-year-old man underwent TAVI with a self-expanding transcatheter heart valve (Acurate Neo, Size L, Boston Scientific, Ecublens, Switzerland) due to severe symptomatic aortic valve stenosis in March 2018. He was discharged on dual antiplatelet therapy (DAPT) including clopidogrel 75 mg/day for 6 months and aspirin 100 mg/day indefinitely. Before TAVI, coronary artery disease was excluded by invasive coronary angiography (Supplementary material online, *Videos S1* and *S2*). Seven months later, the patient woke up at night time because of sudden intense angina pectoris at rest ceasing spontaneously after approximately 2 h. The next morning, the patient called emergency medical services and he was admitted to the chest pain unit. The patient was asymptomatic at the time of presentation. On physical examination, his vital signs were stable and cardiac, pulmonary and abdominal examination was unremarkable. The 12-lead electrocardiogram (ECG) did not show any abnormalities. However, cardiac biomarkers were significantly elevated. His initial high-sensitivity cardiac troponin T was 386 ng/L and rose to 590 ng/L after 3 h (normal value < 14 ng/L). D-dimer levels were slightly increased to 1.42 mg/L (normal value < 1.28 mg/L, age-adjusted cut-off 0.79 mg/L). White blood cell count as well as C-reactive protein were within normal range. No left ventricular regional wall motion abnormalities were detected by transthoracic echocardiography.

Suspecting a non-ST-elevation acute coronary syndrome, initial treatment comprised intravenous administration of 5000 IU unfractionated heparin and 500 mg aspirin. Early invasive coronary angiography was performed, but no coronary occlusion could be detected (Supplementary material online, *Videos S3* and *S4*). Having excluded a
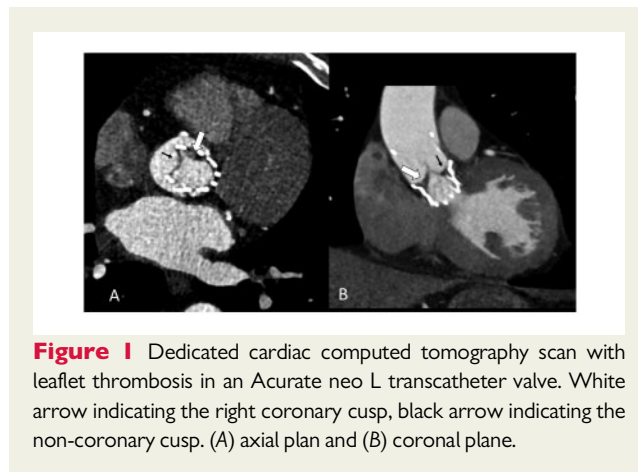

Figure 1 Dedicated cardiac computed tomography scan with leaflet thrombosis in an Acurate neo L transcatheter valve. White arrow indicating the right coronary cusp, black arrow indicating the non-coronary cusp. (*A*) axial plan and (*B*) coronal plane.

vessel occlusion as the reason for the acute chest pain, pulmonary embolism and aortic dissection were considered as differential diagnosis. Both were finally ruled out by multidetector computed tomography (CT). However, the CT scan indicated thrombosis of the prosthetic aortic valve. A dedicated cardiac CT scan confirmed thrombosis of both right and non-coronary leaflets (*Figure 1*). By means of cardiac magnetic resonance imaging (MRI), two acute transmural myocardial infarction lesions in the midventricular and apical inferior wall were detected (*Figure 2* and Supplementary material online, *Video S5*). Left ventricular ejection fraction measured by transthoracic echocardiography was normal and mean aortic pressure gradient had not changed significantly since the last routine control 3 months after prosthetic valve implantation (P_{mean} 9 mmHg).

A 24-h Holter ECG monitoring revealed no cardiac arrhythmias and intracardiac thrombi were excluded by transoesophageal echocardiography. Because of these findings, therapeutic anticoagulation with unfractionated heparin was started during the hospital stay. Finally, the patient was discharged in a good clinical condition on phenprocoumon [target international normalized ratio (INR) 2–3]. Antiplatelet therapy with aspirin was consequently stopped. A follow-up visit after 8 weeks with repetition of a CT scan was recommended. However, the patient did not attend planned follow-up. After contacting the patients' relatives, we found out that the patient had died from an unknown cause 2 months after the described clinical event. Further investigations including inquiry of the general practitioner did not contribute to any explanation for the cause of death.

Discussion

Prosthetic valve thrombosis has been reported in up to 40% of patients after TAVI.[1] The risk of leaflet thrombosis is highest in the first 3 months after the procedure due to incomplete device endothelialization.[2] Predisposing factors are a large aortic root in need of a large sized prosthetic device, a high body mass index, bicuspid aortic valves, male sex, and valve-in-valve procedures.[3,4] Moreover, device design may contribute to thrombogenicity (supra-annular vs. intra-annular).[5]

A pathophysiological continuum ranging from asymptomatic subclinical valve thrombosis to clinically apparent events has been suggested. In the first place, a hypoattenuated leaflet thickening may be
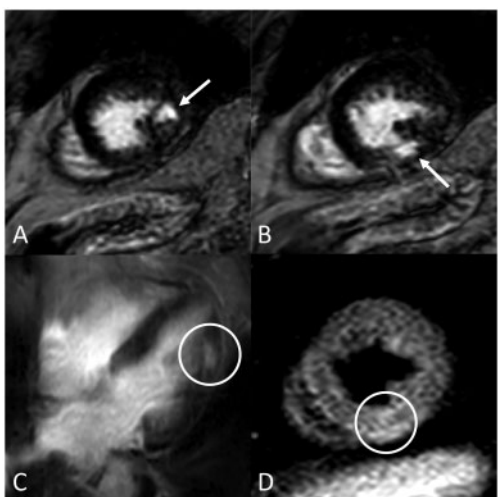
Figure 2 Cardiac magnetic resonance imaging with subendocardial to transmural late gadolinium enhancement. (*A*) and (*B*) Short-axis stack with late gadolinium enhancement of the mid-ventricular inferior wall and apex (white arrows). (*C*) Long-axis stack four chamber view and (*D*) STIR-sequence short-axis stack with oedema (white circle) of the mid-ventricular inferior wall.

seen on CT which may progress to hypoattenuation affecting motion when leaflet excursion is impaired by more than 50%. Once leaflet thrombosis and leaflet motion deteriorate further, elevated transvalvular gradients can be detected.[6] The transition from subclinical to overt clinical valve thrombosis is mainly marked by the occurrence of symptoms in terms of dyspnoea or impaired valve function.[7–9] Subclinical leaflet thrombosis is in most cases an incidental finding. The diagnostic reference standard in early stages is a dedicated cardiac CT.[6] Impaired leaflet excursion and elevated transvalvular gradients are proven by transoesophageal and transthoracic echocardiography, respectively.[10]

American and European evidence-based clinical practice guidelines recommend a DAPT for 3–6 months after TAVI.[11,12] Anyhow, DAPT does not seem to prevent leaflet thrombosis.[5] Consequently, the question arose if oral anticoagulation is favourable in this regard. The phase III GALILEO trial comparing rivaroxaban vs. DAPT after TAVI was stopped early after a preliminary analysis because of increased rates of all-cause mortality or a first thrombo-embolic and bleeding event in the rivaroxaban group. Yet in a substudy of this cohort, the oral anticoagulation group was more effective than the antiplatelet regime in preventing subclinical leaflet thrombosis.[13] In the absence of randomized studies, it remains unclear whether vitamin K antagonists (VKA) pose an alternative for the prevention of leaflet thrombosis. However, in a 2017 focused update on the management of valvular heart disease, the American Heart Association/American College of Cardiology states that oral anticoagulation with VKA (target INR 2.5) may be reasonable for at least 3 months after TAVI in patients at low risk of bleeding (Class IIb).[11]

Therapeutic strategies for patients with leaflet thrombosis after TAVI are derived from the experience gained in the treatment of surgical valve thrombosis.[14] According to current guidelines, anticoagulation with unfractionated heparin and/or VKA is the first-line therapy (Class IC).[12] The role of novel oral anticoagulants (NOACs) can only be deducted from observational studies and case reports, but the effectiveness of NOACs in successful thrombus regression has also been shown.[5,15] The use of NOACs may also be attempted when VKA fail.[16] In contrast to this, DAPT is not effective in resolving leaflet thrombosis.[17] Because of the lack of evidence for efficacy, and the increased risk for bleeding, the administration of a single or dual antiplatelet drug on top of oral anticoagulation (double or triple therapy) is currently discouraged.[18,19] Triple therapy may be considered in a minority of patients, for example in post-percutaneous coronary intervention patients with high risk of stent thrombosis and an indication for oral anticoagulation. To determine the duration of such a combined therapy, it is required to assess the risk of stent thrombosis as well as the risk of bleeding.[20]

In the herein presented case the patient was initially discharged on DAPT in accordance with guidelines. The large device size was the only factor predisposing for the development of valve thrombosis. Nevertheless, a myocardial infarction with non-obstructive coronary arteries supposedly due to valve thrombosis and coronary embolization occurred. This is particularly suggestive since the myocardial infarction areas detected by cardiac MRI corresponded to the supply territory of the right coronary artery with the detected thrombosis affecting the right coronary cusp. Interestingly, in this case, transvalvular gradients were not elevated at any time.

With only two other reported cases, myocardial infarction as a result of transcatheter valve leaflet thrombosis is a rare finding.[9,21] Nonetheless, our understanding of fatal thrombo-embolic events in the context of leaflet thrombosis should not only comprise transient ischaemic attacks or cerebral stroke but also acute myocardial infarction. Sudden onset of these embolic consequences in otherwise asymptomatic patients raises the question of the validity of distinguishing subclinical from clinical leaflet thrombosis.

Leaflet thrombosis following TAVI is a frequent finding. This is, to the best of our knowledge, one of the few case reports of a coronary thrombo-embolic event in a patient with normal transvalvular gradient and prosthetic valve thrombosis. If leaflet thrombosis is suspected, for example because of elevated transvalvular gradients, a diagnostic workup with a dedicated cardiac CT scan should be done. Although therapeutic anticoagulation seems to be the only non-invasive treatment for resolving valve thrombosis, it remains unclear which strategy and duration of therapy is effective and safe for the prevention of leaflet thrombosis.

Lead author biography

Johannes Rotta Detto Loria studied medicine at Lübeck University, Germany. He started his medical training at the University Heart Center Freiburg—Bad Krozingen. Currently, he is a doctor in residency in cardiology at the Heart Center Leipzig, Germany.

Supplementary material

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