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Role of Cardiac Imaging Tools

Stroke after Valve Intervention – How to Look For an Embolic Source

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Summary

Valve interventions in left sided valvular heart disease, mainly such as transcatheter aortic valve implantations (TAVI) and transcatheter edge-to-edge repairs (TEER) have emerged as alternative treatments in symptomatic severe aortic stenosis and severe mitral regurgitation. However, stroke remains a serious concern. The two main causes of embolisation after valve intervention are thrombosis and vegetations.

This review summarises the role of all the different tools of cardiac imaging including transthoracic echocardiography (TTE), transoesophageal echocardiography (TOE), cardiac computed tomography (CT) and 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) in the diagnosis and work-up of potential cardiac or aortal sources of embolism associated with valve interventions.

TTE provides a more comprehensive understanding of the implanted valve including its location and function. Contrast enhanced echocardiography offers additional value in order to detect left ventricular thrombus. Increased valve gradients can be attributed to patient-prosthesis mismatch, thrombus or pannus on the leaflets. Therefore, echocardiography performed immediately after the procedure, followed by follow-ups 4 weeks post-intervention and then annually is of major importance. In addition to echocardiography, cardiac CT can be highly beneficial for confirming or ruling out an abscess, pseudoaneurysm, fistulae and thrombosis. Nuclear molecular techniques, such as 18F-FDG-PET is another important advanced imaging technique, particularly in the management of infective endocarditis.

Keywords: Multimodality imaging; stroke after TAVI; cardiac CT; FDG-PET; thrombosis; infective endocarditis

Introduction

Valve interventions in left sided valvular heart disease as transcatheter aortic valve implantations (TAVI) and transcatheter edge-to-edge repairs (TEER) are increasingly used treatment methods in mainly symptomatic severe aortic stenosis and severe mitral regurgitation. The former has emerged as a valuable and alternative treatment to surgical aortic (SAVR) in high-/intermediate-risk patients and the latter to mitral valve repair (SMVR) in selected high-risk patients for primary mitral regurgitation or as a minimal-invasive treatment option in secondary mitral regurgitation. In experienced centres, TAVI may also be considered in aortic regurgitation in very high-risk patients, ineligible for a surgical approach. Percutaneous mitral commissurotomy (PMC) is recommended in symptomatic mitral stenosis without unfavourable characteristics for PMC or for symptomatic mitral stenosis with a contraindication or a high risk to surgery [1].

Post-procedural stroke, but also stroke in a long-term follow-up are one of the main concerns in valve interventions of left sided valvular heart disease. Cardioembolic stroke in general accounts up to 30% of ischaemic strokes. Approximately a third of ischaemic strokes remains an embolic stroke of undetermined source despite a detailed and rigorous work-up. A significant percentage of cardioembolic strokes in patients >75 years of age occur after valvular interventions [2]. Nevertheless, the most important cause of cardioembolic stroke is by far atrial fibrillation (AF). Cardioembolic strokes are serious conditions due to high-risk of stroke recurrence. In consequence, cardiac imaging has a central role to prevent further strokes and gives the hint to the further management and treatment of these patients. This mini review summarises all different important tools of cardiac imaging including transthoracic echocardiography (TTE), transoesophageal echocardiography (TOE), cardiac computed tomography (CT) and 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) in the diagnosis and work-up of potential cardiac or aortal sources of embolism associated with valve interventions. The two main causes of embolisation after valve intervention are thrombosis and vegetations.

Epidemiology

The incidence of stroke in TAVI trials are given between 0.7–4.7%. More than half of the ischemic attack (TIA) or stroke occurs within the first week after TAVI. The underlying reason is due to various intensity of follow-up with or without a neurologist and different population cohorts. Another explanation could be due to different valve types of the newer generation bioprosthetic valves [3, 4]. Interestingly, up to 80% patients after TAVI have clinically "silent" brain infarction shown in brain seen on magnetic resonance imaging (MRI). They are results of embolised debris during the procedure [5]. Another possible explanation of the mechanism of stroke are periprocedural hypotension or nonendothelialised valve stent struts being a thrombogenic surface [6]. However, randomized trial using transcatheter cerebral embolic protection did not show a significant neurocognitive function improvement or reduction of new lesions in protected territories [7]. Stroke is more seldom as a complication of endocarditis after valve intervention. Data from the Infectious Endocarditis after TAVR International Registry

demonstrated a stroke rate in 1 of 10 patients in this cohort [8].

In a larger systematic review and meta-analysis, the stroke incidence in TEER with MitraClip® device (Abbott Vascular, Santa Clara, CA, USA) is given 4.9% [9]. Compared to optimal medical treatment (OMT), there is no significantly different stroke rate. Hence, periprocedural stroke is very seldom and this elderly population depicts a high-risk profile with the underlying valvular heart disease as part of an advanced heart failure syndrome with mostly different comorbidities. In addition, data comparing TEER versus SMVR identified a trend towards lower stroke risk in TEER [9].

PMC is the first choice of treatment in rheumatic mitral valve and not suitable for degenerative mitral stenosis with mitral annular calcification. To keep the stroke rate low, there are unfavourable characteristics to be ruled out. Additionally, preprocedural transoesophageal echocardiography (TOE) eliminating patients with left atrial thrombi influenced favorably the stroke rate, given the rate between 2 and 3.8% [10, 11].

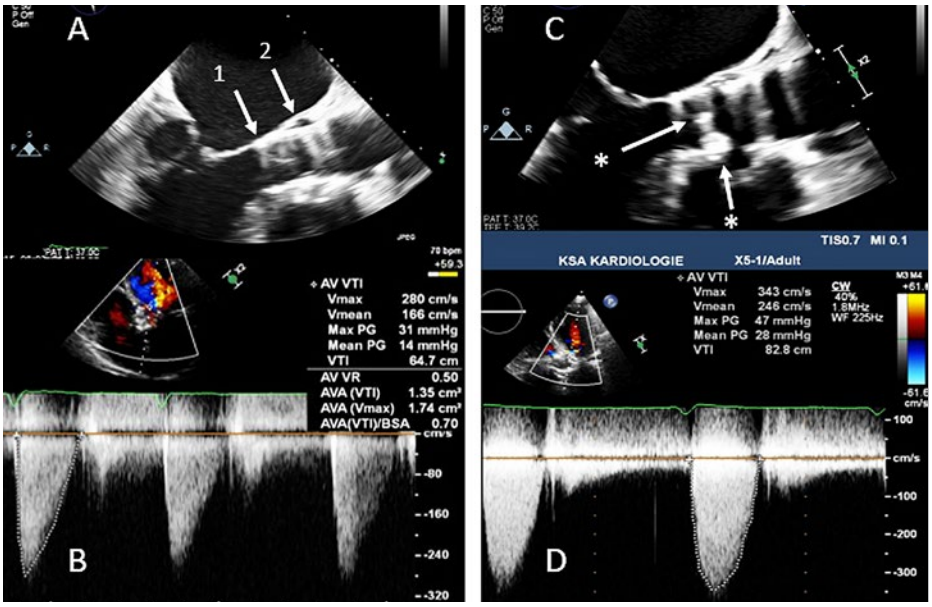

Figure 1: Illustrative case report with TTE and TOE images of a 82-year old man with previous implantation of double TAVI prosthesis and initial presentation of stroke and diagnosis of infective endocarditis of the aortic prosthesis. The functional, proximal TAVI prosthesis is an Edwards Sapien XT 26mm (see 1 in Panel A). A second prosthesis had to be implanted due to dislocation of the first Jena valve 25 mm (see 2 in Panel A) into the aorta ascendens in 2013. He presented with a stroke of unknown origin in 2021 showing a normal function of the proximal TAVI (normal neo-leaflets in end-diastole in Panel A and mean of 14 mmHg in Panel B). 6 months later, enterococcus faecalis growed in two separate blood cultures. New structures on the neo-leaflets of the Edwards Sapien XT prosthesis (* in Panel C) with significantly higher gradients than before (mean of 28 mmHg in panel D). Hence, giving these two major criteria according to the Duke criteria for infective endocarditis, an endocarditis of the aortic prosthesis was confirmed.

Thrombosis

Thrombosis is one of the primary sources of cerebral embolism. Very frequently, they lie in the left atrium (LA) and left atrial appendage (LAA). They are mostly, but not exclusively, seen in patients with AF. AF is a common comorbidity in patients undergoing an intervention. 40.7% in TAVI patients have preexisting AF and 6.8% have a new-onset AF [12]. In mitral regurgitation, presence of AF is independently associated with excess mortality long-term after diagnosis [13].

Therefore, first-line examination after a stroke in order to detect LAA thrombus favors a TTE and TOE. The latter sufficiently visualises the LAA anatomy and function and excludes any thrombus in the LA or LAA and provides a good tool for embolic risk stratification. LAA dysfunction can be measured by pulsed Doppler giving 20 cm/sec filling velocities. To exclude thrombi can be complicated by the presence of pectinate muscles. Contrast echo and three-dimensional echocardiography can be further tools to exclude or confirm thrombi. In difficult cases, multimodality imaging with adding cardiac CT can be helpful to improve the visualisation of the LAA. TOE also allows to investigate the aorta for any complex plaques with adjacent thrombi.

TTE is a harmless and widely accessible tool providing detailed information about the heart chambers and function. Contrast enhanced echocardiography offers additional value in order to detect left ventricular thrombus. Due to its excellent temporal resolution, TTE provides deeper understanding of the implanted valve with its location and function. Echocardiographic signs of obstructive prosthetic valve thrombosis are the following features: reduced valve mobility, presence of thrombus on the leaflet (preferably on TOE), abnormal transprosthetic flow, central abnormal prosthetic regurgitation, elevated transprosthetic gradients and reduced effective prosthetic area [12]. Normal values for the gradients and area for the different implanted valves are summarised at valveguide.ch. An easy link to the different valves at this page is provided in the "echocalc app" by the British Society of Echocardiography [15, 16, 17].

Higher valve gradients can be due to patient-prosthesis mismatch, thrombus or pannus on the leaflets. The latter two can be challenging to distinguish as a cause of bioprosthesis valve dysfunction. Therefore, it is crucial to perform an echocardiography immediately after intervention, 4 weeks after the intervention and then annually thereafter. The gradients always must be compared to baseline values. A sudden increase of the gradient comparing to the previous echocardiography rises the suspicion of a thrombosis formation. The American College of Cardiology recommendations on echocardiography provides several criteria for possible valve dysfunction (peak prosthetic aortic jet velocity 3 to 4 m/s, mean gradient 20 to 35 mm Hg, effective orifice area (EOA) between 0.8 and 1.2 cm^2/m^2). The European recommendations consider a stress echo increase of 10–19 mmHg for a possible obstruction and an increase of 20 mmHg or more for significant stenosis. The functional criteria for a significant stenosis by the American College of Cardiology are peak prosthetic aortic jet velocity >4 m/s, mean gradient >35 mm Hg and EOA <0.8 cm^2/m^2 [18, 19]. To facilitate everyday life and work, these criteria are summarised in the pocket guidelines Echocardiography/Doppler provided by the University Hospital of Zurich and Kantonsspital Aarau.

The most sensitive method to detect a valve leaflet thrombosis is a cardiac CT (Table 1) [20]. The criteria for a TAVI thrombosis are hypo-attenuated leaflet thickening with or without reduced leaflet motion of one or more leaflets, identifiable in two or more multiplanar curved reconstructions [21].

Infective Endocarditis

Infective endocarditis (IE) remains a severe disease. The incidence of IE is low with 1.4% [8] and is similar to patients with surgically implanted valve prosthesis, but is associated with high mortality (20–40%) and high complication rates with 10–30% to embolise. Imaging and particularly echocardiography is a key player in the diagnosis and management of IE

Table 1: Incidence of Transcatheter Aortic Valve Thrombosis (reproduced with permission from [17])

First Author (Year)	N	Prevalece of Thrombosis on MDCT (Time)	Prevalence of Thrombosis on Echo (Time)	Mean Gradient (mm Hg) – EOA (cm^2)
Latib et al. (2015)	4266	NA	0.61% (median, 181 days)	40.5 ± 14.0-NA
Pache et al. (2016)	156	10.6% (median, 5 days)	NA (median, 5 days)	8 ± 3.5-NA
Leetmaa et al. (2016)	140	4% (1–3 months)	NA (1–3 months)	19.2–1.44
Del Trigo et al. (2016)	1521	NA	4.5% (4 yrs)	26.1 ± 11-NA
Hansson et al. (2016)	405	7% (1–3 months)	NA (1–3 months)	10 ± 7–1.5 ± 0.5
Makkar et al (2016)	55	40% (median, 32 days)	NA (30 days)	9.2 ± 4.9-NA
Makkar et al (2016)	132	13% (median, 86 days)	NA (30 days)	8.4 ± 2.9-NA
Yanagisawa et al. (2017)	70	14.3% (1 yr)	NA (1 yr)	8.3 ± 0.8–1.03 ± 0.25
Chakravarty et al. (2017)	752	13% (median, 58 days)	6% (median, 58 days)	13.8 ± 10.0-NA
Vollema et al. (2017)	434	12% median, 35 days)	3% (3 yrs)	9.3 ± 4.7-1.99 ± 0.56
Jose et al. (2017)	642	9/10 (NA)	2.8% median, 181 days)	34 ± 14–1.06 ± 0.46
Sondergaard et al. (2017)	61	11% (140 ± 152 days)	NA	7.0 ± 3.2-NA

EOA = effective orifice area; MDCT = multi-detector row computed tomography; NA = not available.

as the imaging findings are major criteria in the diagnosis of IE. A major role is given to TOE. Beyond TTE and TOE however, cardiac CT and PET can be additive and of great value in certain circumstances [22].

As soon as infective endocarditis is suspected, TTE should be performed within 24 hours. If the echocardiography was negative, the TTE has suboptimal quality and there is high suspicion, a TOE must be performed. Another indication for TOE is a positive TTE to look for local complications (abscess, pseudoaneurysm, perforation, fistula, valve aneurysm and dehiscence of a prosthetic valve with paravalvular regurgitation with or without rocking motion of the implanted valve). Accordingly, this complication list emphasizes the role of TOE in managing and guiding the therapeutic strategy. If the TOE is also negative, the TOE must be repeated within 5–7 days.

In doubtful cases, cardiac CT can be very beneficial and useful to confirm or exclude an abscess, pseudoaneurysm and fistulae. It can also be performed to assess the entire aorta. CT can also be valuable to exclude further abscess in the heart or mediastinum, particularly in terms of preparation to surgical treatment.

Nuclear molecular techniques, such as 18F-FDG-PET is another important, supplementary advanced imaging technique in diagnostic difficulties. This imaging technique relies on the use of 18F-FDG that is actively incorporated by leucocyte, monocyte, macrophages and CD4+ T-lymphocytes. These cells are accumulated at the site of infection. The main value of 18F-FDG-PET is to avoid overtreatment of patients with possible IE by reassuring and excluding an IE. Limitations of the use of 18F-FDG PET/CT is given in the postinterventional period of 3 months due to inflammatory response to the implantation that results in non-specific 18F-FDG uptake. Moreover, following pathological conditions can also lead to higher 18F-FDG uptake and mimic an inflammation: active thrombi, soft atherosclerotic plaques, vasculitis, primary cardiac tumours, cardiac metastasis from a non-cardiac tumour and foreign body reactions [22].

It is emphasized that the diagnosis of IE is not only part of the cardiac imager, but clinical judgement of an endocarditis team. The team is mainly built up by cardiologist, cardiac surgeon and infectious disease specialist. Its cornerstones remain positive blood culture, vegetation in echocardiography and clinical features according to the Duke criteria. The sensitivity of the latter can be increased by additional modern cardiac imaging techniques.

In summary, echocardiography with TTE and TOE are the main tools in detecting any cardiac source after stroke in valve interventions. Modern multimodality imaging implementing cardiac CT and of 18F-FDG-PET can increase diagnostic sensitivity in certain circumstances.

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Keypoints

- Perform TTE within 24h with / without contrast.
- Perform comprehensive TOE within 48h including assessment of all valves' morphology and function, screening the LA, LAA and aorta for any thrombi.
- Higher diagnostic sensitivity given by multimodality imaging including cardiac CT and 18F-FDG-PET.
- CT depicts nicely any thrombosis formation in prothesis and any local complication.
- If endocarditis is possible, add 18F-FDG-PET (at the earliest 3 months after implantation).

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References
You will find the full list of references online at https://cardiovascmed.ch/article/doi/CVM.2023.02232.