

Modern Use of Echocardiography in Transcatheter Aortic Valve Replacement: an Up-Date

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ABSTRACT

Echocardiography is the cornerstone in the diagnosis of any valvular heart disease. The accurate diagnosis of aortic stenosis, the left ventricle function and the other heart valves evaluation are currently done by ultrasound alone.

Prosthetic valve choice and dimensions prior to implantation can be done solely by proper use of echocardiography. The emergence of new methods to cure aortic stenosis such as trans-catheter aortic valve replacement (TAVR) emphasized the diagnostic value of cardiac ultrasound. The usefulness of echocardiography in TAVR can be divided in the baseline assessment (common to patients treated by conventional surgery), intra-procedural guidance of valve deployment and post-procedural follow-up. In the baseline diagnostic work-up echocardiography should allow proper assessment of low-gradient severe aortic stenosis and especially of "low-flow, low-gradient" aortic stenosis, as far the benefit of any valve intervention in these cases may be overshadowed by persistent ventricular dysfunction.

"Classic" TAVR is performed with a trans-esophageal echocardiography probe in place, but recently intra-cardiac echocardiography (ICE) was advocated to reduce the need for general anesthesia. "Minimalist TAVR approach" recommends no echo-guidance and valve implantation by angiography alone. Post-TAVR echo assessment should allow prompt recognition of early complications and the severity of para-valvular leaks. Long term follow-up by echocardiography assesses prosthetic valve function, left ventricular functional recovery and the impact of the procedure on associated conditions (mitral regurgitation, pulmonary hypertension or tricuspid regurgitation).

This article emphasizes the role of the cardiologist with ultrasound skills in the assessment of patients addressed to TAVR.

INTRODUCTION

Aortic stenosis is the most common valvular heart disease in elderly patients, especially in developed countries where life expectancy increased considerably in the last three de-

cadecades. Surgical aortic valve replacement (SAVR) was the standard therapy for symptomatic severe aortic stenosis until 2002 when Alain Cribier reported the first trans-catheter aortic valve replacement (TAVR) in a living patient (1). Until then open surgery was the only treatment option for these patients. Modern statistics demonstrate

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however that between 30-60% of patients with severe aortic stenosis are denied surgery because of advanced age and/or significant comorbidities (2-4), making them more appropriate to a less invasive intervention such as TAVR. Nowadays this novel percutaneous technique is an alternative to open aortic valve surgery for selected high-risk or inoperable patients. Randomized trials proved that the self-expandable (SE) CoreValve (Medtronic Inc; Minneapolis, MN) and the balloon-expandable (BE) Sapien (Edwards Lifesciences, Irvine, CA) prostheses are equivalent to SAVR when looked at all-cause mortality rates at 1 year in high-risk patients with severe aortic stenosis treated by TAVR compared with SAVR (5,6). The same has been recently confirmed in intermediate risk patients (7). Depending on vascular anatomy (mainly of the ilio-femoral vessels and ascending aorta) there are several arterial access sites to the diseased valve: standard – trans-femoral or alternative access, trans-subclavian or trans-aortic for the CoreValve and trans-apical or trans-aortic for the SAPIEN valve (8).

The success of the procedure depends mainly on the appropriate selection of patients; according to actual guidelines for the management of valvular heart disease this assessment has to be performed by a local Heart Team, consisting of a Cardiologist skilled in echocardiography, an Interventional Cardiologist, a Cardiovascular Surgeon, an Anesthesiologist and a Radiologist (9,10).

Echocardiography plays a key role in patient selection, intra-procedural guidance, post-procedural assessment and long-term follow-up (11). □

ECHOCARDIOGRAPHY IN PATIENT SELECTION FOR TAVR

The first step in assessing a patient addressed for TAVR is to perform transthoracic echocardiography in order to confirm the diagnosis of severe aortic stenosis, the performance of the left and right ventricle and presence of other valvular heart disease. This echocardiography could be done by any general cardiologist. The assessment of the aortic valve complex has to be done by TAVR dedicated cardiologist.

According to European Guidelines, severe aortic stenosis is defined by a valve area $< 1\text{ cm}^2$ (indexed to body surface area $< 0.6\text{ cm}^2/\text{m}^2$), a mean trans-valvular gradient $> 40\text{ mmHg}$ or a maximum trans-valvular velocity $> 4\text{ m/s}$ (9).

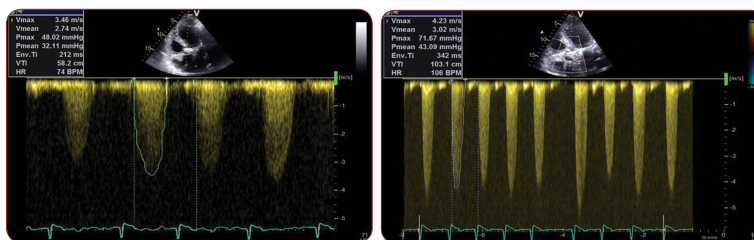


FIGURE 1. Echo example of contractility reserve in a patient with low gradient because of severe LV dysfunction with a LVEF of 30%. Mean baseline transvalvular gradient is 32 mmHg (Figure 1A); dobutamine infusion leads to an increase of transvalvular gradient to 43 mmHg

Apart from the majority of cases in which all the above mentioned criteria for severe aortic stenosis are met, there are also patients who have severe aortic stenosis but the trans-valvular gradient is reduced. One frequent situation, known as “low-flow, low-gradient” is the one that occurs in patients with aortic stenosis associated to severe systolic dysfunction (12). In these cases, a stress-test may be necessary to differentiate between severe aortic stenosis and a pseudo-severe disease, such as stress echocardiography using either exercise or dobutamine infusion (13,14) (Figure 1). Another particular situation is found in patients with severe aortic stenosis that have a low gradient and normal left ventricular systolic function, known as “paradoxical low-flow, low-gradient”. This occurs when ventricular volume is very low because of severe concentric left ventricular hypertrophy (15) (Figure 2). In all these particular situations echocardiography is essential in the diagnosis and quantification of disease severity.

Once the diagnosis of severe aortic stenosis is confirmed and the Heart Team considers the patient as being at high surgical risk or inoperable due to multiple comorbidities, morphological evaluation of the aortic valve complex is required in order to specify whether the patient is suitable for TAVR. The surgical risk is generally evaluated by well-known scores of European and American Cardiac Surgery Societies, Euroscore II respectively STS Score, that includes demographic, clinical, biological and a hemodynamic data with good assessment of the comorbidities, but poor evaluation of the frailty status. Both scores have good observed-to-expected mortality rate but they significantly underpredict the risk of TAVR patients (16).

Congenitally abnormal valves (single cusp or bicuspid) represent relative contraindications for TAVR, but some available data suggests that TAVR

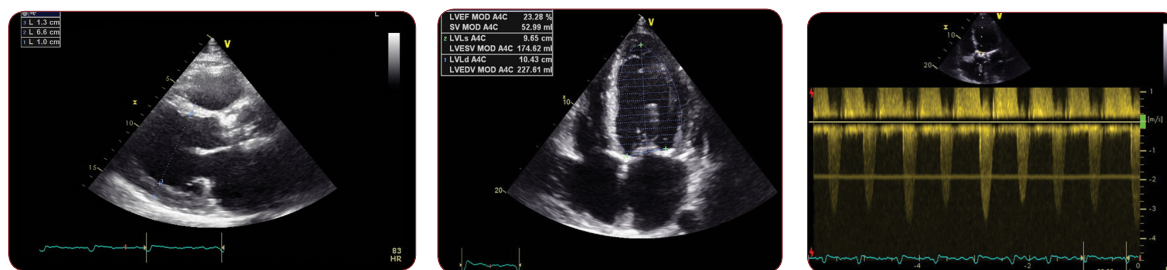


FIGURE 2. Echo example of “low-flow, low gradient” aortic stenosis. A dilated left ventricle (LVEDD of 66 mm), with a heavily calcified aortic valve (Figure 2A) is associated with a LVEF of 23% (Figure 2B) and a maximum mean transvalvular gradient of about 30 mmHg in atrial fibrillation (Figure 2C)

in bicuspid aortic valves is feasible with encouraging short and intermediate-term clinical outcomes (17,18) (Figure 3). Bicuspid aortic valve has been long considered a contraindication for TAVR for a number of reasons: aortic annular diameters too large and not suitable for current trans-catheter valves, asymmetric distribution of calcification precluding full expansion of the prosthesis with increased risk of para-valvular leak and annular rupture and also the dilatation of the ascending aorta (19). Because of the ability to adapt to various annular and root anatomies and because it is repositionable, SE valve is preferred in this kind of patients (20).

Calcium distribution across the aortic cusps is another important issue that can predict procedural success of a TAVR procedure. If there is symmetrical calcium distribution on the cusps para-valvular leaks generally do not occur (21). In the CHOICE trial the rate of para-valvular leaks more than mild was greater in SE CoreValve than in BE Sapien (22).

Otherwise, asymmetrical massive calcifications could represent a contraindication for TAVR predisposing both to para-valvular leaks and coronary ostia obstruction if these are located low (23). Occlusion of coronary artery ostia is rare and it was reported most often after BE valve implantation. (37)

It should be noted that a non-calcified aortic valve is a contraindication for TAVR because the stability of the prosthesis is reduced; this anatomical situation is seldom found in aortic stenosis. Patients with minimal aortic valve calcification and predominant regurgitation are also likely to benefit from SE valve prostheses (20).

Valve masses (fibro-elastoma, active endocarditis) represent contraindications for TAVR too, due to high risk of systemic embolism or recurrent endocarditis.

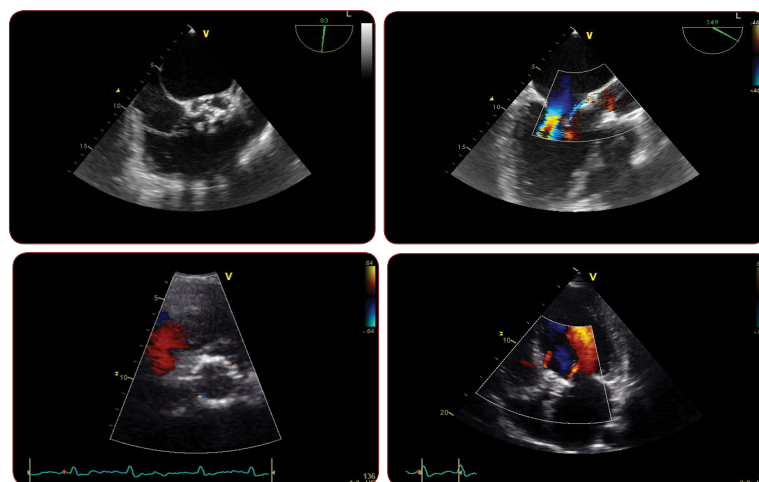


FIGURE 3. Echo example of contractility reserve in a patient with low gradient because of severe LV dysfunction with a LVEF of 30%. Mean baseline transvalvular gradient is 32 mmHg (Figure 1A); dobutamine infusion leads to an increase of transvalvular gradient to 43 mmHg

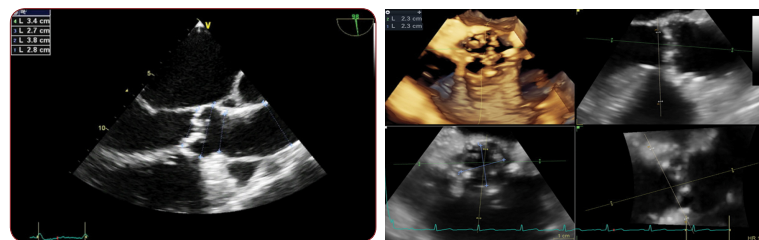


FIGURE 4. Echo measurements of the annulus, Valsalva sinuses, sino-tubular junction by trans-esophageal echocardiography (Figure 4A). Echo measurements of the aortic annulus can be significantly improved with the use of 3D echo (Figure 4B)

In determining the prosthesis size the most important is the dimension of the aortic ring. This can be most accurately measured by multi-slice CT of the aorta, but echocardiographic measurement is also useful (24). Valve oversizing may lead to risk of annulus rupture, while under-sizing may result in valve embolization or para-valvular regurgitation. The aortic ring dimensions may differ depending on the imaging method due to its elliptical shape. Usually annular measurements are

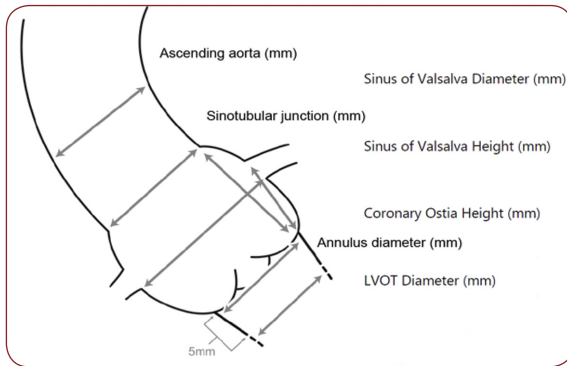


FIGURE 5. Measurements of aortic valve complex and of the ascending aorta necessary for pre-procedural assessment of a TAVR procedure.

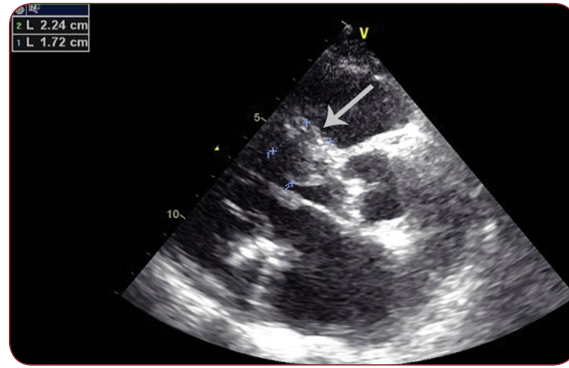


FIGURE 6. TTE from 4 chambers view or parasternal long axis view with major septal bulge in the LVOT under a calcified aortic valve.

performed on 2D echocardiographic long axis view where the ring is typically sub-evaluated (Figure 4A). 3D echocardiography seemed to fill this shortcoming (Figure 4B) but recently, a small prospective study showed that aortic annulus measurements by 3D TEE are significantly smaller than MS-CT. So, 3D-TEE should be used for TAVR sizing, only when MSCT is not available or contraindicated (25). Other studies comparing 3DTEE with MS-CT are in progress. Currently MS-CT is the gold standard for annular sizing (26).

There are four sizes for the Sapien Edwards valve available (20, 23, 26 and 29mm) which can be implanted in native valve rings of 16 to 27mm and four sizes for the CoreValve (23, 26, 29 and 31mm) which can be implanted in valves with native ring diameter ranging from 17mm to 29mm (27).

Cusp size and distance from the ring surface to coronary ostia are other parameters that must be assessed in order to predict coronary obstruction when the prosthesis is deployed. While AV annulus to right coronary ostium height can be measured in 2D trans-esophageal echocardiography (TEE), AV annulus to left coronary ostium length can only be measured using 3D techniques with reconstruction of the coronal plane (11).

Other aortic root measurements that need to be made are diameter and height of the sinuses of Valsalva, diameter of sino-tubular junction and diameters of the ascending aorta (Figure 5).

The aortic arch and descending aorta also need to be evaluated, because their ultrasound appearance could play an important role in choosing the therapeutic strategy. Thus, an unstable ulcerated plaque or heavy calcification of the

aortic arch suggests trans-femoral approach may be high risk. Porcelain ascending aorta is a contraindication for a trans-aortic approach; in these cases trans-apical access is recommended (28).

Also, another area of interest is the morphology of left ventricular outflow tract (LVOT). An important septal bulge protruding into the LVOT, mainly located under the aortic cusps, may impede correct valve expansion and presents a significant risk of prosthesis malposition (Figure 6). Angulation between LVOT and the ascending aorta depends partially on septal hypertrophy; in other cases horizontal distribution of the left ventricle in obese patients may be responsible for challenging valve implantation (29).

All of these measurements are made most accurately by MSCT but the presence of a high heart rate, arrhythmia and severe valve calcifications can substantially degrade image quality (30).

Left ventricular (LV) function influences the strategy of the procedure. Some patients considered for percutaneous valve implantations have severe left ventricular dysfunction, and if they have no contractile reserve, they have do not benefit from the valve intervention. A left ventricular ejection fraction (LVEF) of less than 30% in the absence of contractility reserve is a relative contraindication for TAVR (31). If any of these patients are however treated the number and duration of temporary pacing runs during valve implantation should be minimized to avoid hemodynamic compromise and asystole. In patients with very low LVEF<20%, but with inotropic reserve, the procedure may be performed. However trans-apical approach is contraindicated in these cases. Scarred, thin or aneurysmal left ventricular apex is

another contraindication for the trans-apical access.

There are also other hemodynamic abnormalities that need to be quantified. Patients with aortic valve disease with dominant aortic regurgitation may not be candidates for TAVR because the cusps are not calcified, which could lead to reduced prosthetic stability. It is important to define the baseline aortic regurgitation severity as it may be significantly increased by balloon pre-dilatation, potentially leading to hemodynamic instability and the necessity of prompt prosthesis implantation.

Mitral regurgitation is present in most patients with severe aortic stenosis prior to intervention (32) (Figure 7). Severe mitral regurgitation due to intrinsic mitral valve disease is another contraindication for TAVR. If MR is not severe and can be attributed to high systolic LV pressure, its proper quantification is important: during the TAVR procedure the mitral valve or its chords can be intercepted by the stiff guide wire, the balloon or prosthesis which could lead to acute hemodynamic compromise. Persistence of moderate or severe mitral regurgitation after TAVR is associated with increased mortality at one year (33,34).

Echocardiography should also exclude severe pulmonary hypertension and right ventricular dysfunction (35).

Pre-procedural echocardiographic assessment should end with the assessment of the pericardium. It is necessary to specify if there is a pericardial effusion and to quantify it. It also should be noted that a calcified pericardium contraindicates trans-apical approach.

ECHOCARDIOGRAPHY FOR INTRA-PROCEDURAL GUIDANCE DURING TAVR

If transthoracic echocardiography (TTE) plays an important role in the baseline assessment, intra-procedural assessment is based on trans-esophageal examination; TTE is limited to precisely establish the site of mini-thoracotomy for trans-apical approach (36). Intra-cardiac probes inserted by femoral vein access can be used to monitor valve implantation without the use of TEE, with conscious sedation (37). Recently a "minimalist TAVR approach" was described to avoid the use of TEE, while valve deployment is based on angiography alone (38). This allows a

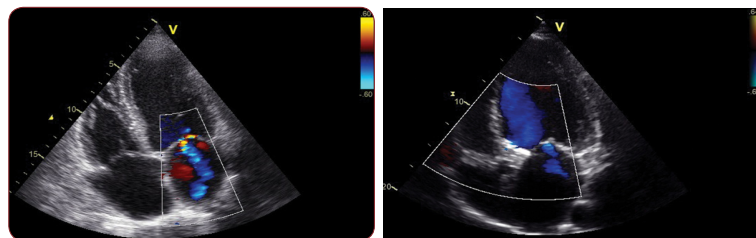


FIGURE 7. Moderate mitral regurgitation prior to TAVR (Figure 7A) that was reduced to grade I/IV after TAVR (Figure 7B)

shorter procedural time, lower bleeding risk, no Intensive Care Unit stay and significantly lowers hospital costs.

The standard TAVR procedure is generally performed under general anesthesia and in most cases with a TEE probe in place. The main role of TEE is assessment of LV function and of the complications that can occur immediately after the procedure (para-prosthetic leaks, mitral valve obstruction with secondary mitral regurgitation, prosthesis migration, pericardial effusion, LV function). It also provides information about balloon valvuloplasty, prosthesis deployment and functionality, all these in relation with fluoroscopy data.

Balloon valvuloplasty is usually but not always, performed prior both SE and BE valve implantation. After balloon valvuloplasty native cusp mobility, regional wall motion abnormalities (the cusps are pushed toward the coronary ostia) and aortic regurgitation severity should be reassessed. The latter may be responsible of hemodynamic instability with need of rapid valve implantation (11). Prosthesis deployment is made under rapid pacing for BE valve in order to minimize the cardiac output and to avoid prosthesis embolization. SE valve is implanted by slow deliverance with the possibility of repositioning before the final release.

After prosthesis deployment TEE is used for the assessment of valve position, function and also for detection of complications. Para-valvular leak (PVL) is the main limitation of TAVR and mild residual regurgitation is present at the majority of patients. In CHOICE trial the incidence of more than mild PVL was greater in SE CoreValve compared with BE Sapien (18.3% versus 4.1%) (22). It occurs more frequently in patients with asymmetric valve calcifications, bicuspid valves, undersized prosthesis or due to improper placement of the prosthesis, generally too low. Often PVLs are multiple and vena contracta is less useful to quantify the residual regurgitation. The ratio between the

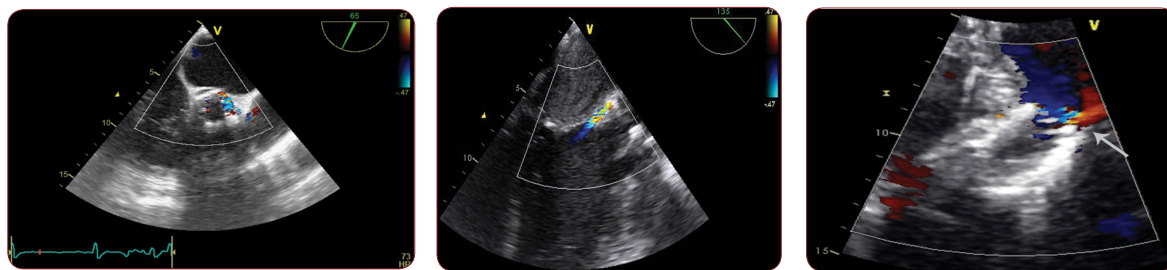


FIGURE 8. Examples of paravalvular leaks (PVL) post TAVR: severe PVL shown at intraoperative TEE in short axis (Figure 8A) and in long axis (Figure 8B). A mild PVL post TAVR is displayed in figure 8C at TTE

sum of diameters of all PVLs and prosthesis perimeter is the semiquantitative method used for PARTNER trial (39) and accepted by Valve Academic Research Consortium to quantify the significance of para-valvular regurgitation (40). The measurements are made in mid-esophageal aortic valve short axis view. If the diameter of all jets is less than 10% of the perimeter of the prosthesis regurgitation is considered as non-significant, while if the sum exceeds 20% of the prosthesis circumference para-valvular regurgitation is considered as severe (41) (Figure 8).

Spectral Doppler in trans-gastric views or quantification of the regurgitation flow in the thoracic descending aorta is also useful for PVL assessment. The presence of diastolic flow reversal in the descending aorta is indicative of a significant PVL. Jet extension beyond the tip of anterior mitral leaflet is another sign for significant PVL (11).

Balloon postdilatation of the valve can lead to the reduction or complete disappearance of the PVL. However postdilatation may induce aortic annular rupture and intra-prosthetic regurgitation due to an excessive dilatation or dislodgement of the prosthesis cusps. An immediate valve-in-valve procedure may become necessary in valves implanted too low (Figure 9). In case of self-expandable valves increased radial force of the second valve deployment may resolve the PVL (42). Intra-

prosthetic regurgitation is sometimes due to the presence of the stiff guidewire used for valve positioning and deployment; it completely disappears after guidewire removal.

Prosthesis embolization in the aorta or in the left ventricle is another significant complication of TAVR. In the case of aortic migration the prosthesis can be eventually recaptured and repositioned. Ventricular migration leads to surgical extraction. Prosthetic embolization is favored by high septal bulge, narrow sino-tubular junction or too short burst of rapid ventricular pacing prior to deployment.

It is known that the severe aortic stenosis is associated with different grades of mitral regurgitation. In PARTNER trial the patients with moderate to severe mitral regurgitation at baseline presented at 30 days after TAVR a significant improvement in the majority of cases (43).

TEE may detect new mitral regurgitation or worsening of preexisting regurgitation. This may occur as a result of anterior mitral leaflet damage, to subvalvular apparatus damage in transapical approach or by improper positioning of the stiff guidewire between the mitral chordate (44) and also, in patients with severe LV hypertrophy secondary to development of systolic anterior motion of the mitral leaflet (45).

Coronary ostia obstruction by displacement of a native cusp and coronary embolism are other

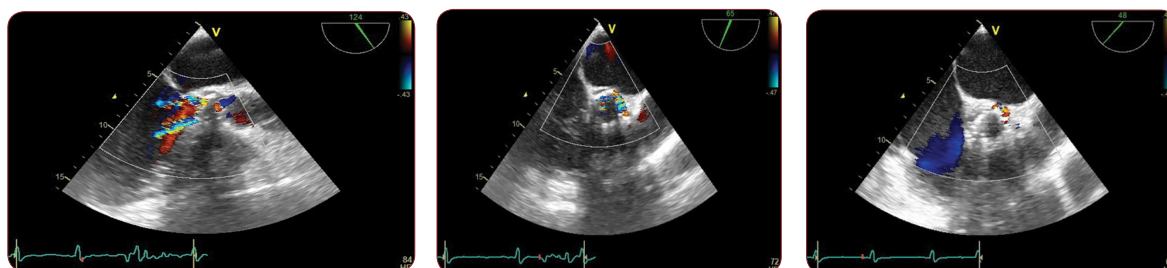


FIGURE 9. Severe PVL after a low positioning of a TAVR valve (Figure 9A and 9B) with significant decrease post valve-in-valve implantation (Figure 9C)

complications that can be recognized by echocardiography (46). Sudden appearance of pericardial effusion is due to annular rupture or ventricular perforation and needs appropriate emergency treatment.

POST-PROCEDURAL ASSESSMENT AND LONG-TERM FOLLOW-UP

In most of the cases patients should have transthoracic echocardiograms before discharge and at one month after intervention irrespective of access site. Transapical or transaortic valves should be examined after one month, because of the healing of the surgical wounds. Subsequent reassessments are performed at 6 months, 1 year and then annually. All measurements should be reported to the initial results.

Percutaneously implanted valves are evaluated in terms of hemodynamic performance and structural aspects (valve layout, position, the round shape of the stent, morphology and mobility of the cusps) and mainly about intra and para-prosthetic leak sites. Primary assessment is related to the reduction of trans-valvular pressure gradient and the effect on the left ventricular outflow tract.

Prosthesis evaluation consists mainly in measurements of maximum and mean pressure gradients and by calculating the effective area of the prosthesis (EOA) and Doppler velocity index (DVI). Both CoreValve and Sapien XT valves have an average gradient between 10-15 mmHg, with a slight increase in time, about 3.8% / year, although 5-year follow-up in the PARTNER Trials showed consistently good results when compared to the surgically implanted valves (6,7).

Measurement of EOA and DVI is challenging. There is general agreement that the Doppler sample should be positioned in the LVOT proximal to the stent; inside it acceleration of blood flow can lead to an overestimation of prosthesis EOA or DVI (Figure 10). A patient - prosthesis mismatch is declared as severe if EOA is $< 0.65 \text{ cm}^2/\text{m}^2$.

Another challenge is related to the measurement of LVOT diameter due to the presence of the stent. In the case of the Edwards valve LVOT diameter should be measured proximally to the ventricular end of the stent. The optimal site to measure LVOT diameter in patients with CoreValve has not yet been reported; by expert opinion it is stated that if the stent is implanted low in the LVOT, then diameter and velocity should be mea-

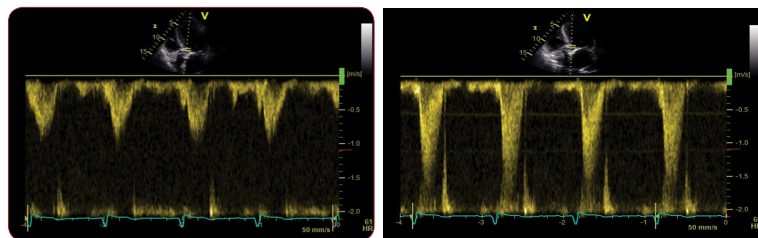


FIGURE 10. Post procedural measurements of transvalvular gradient after TAVR. It is widely accepted to take the measurements in the LVOT, immediately under the prosthetic valve (Figure 10A). Intravalvular measurements show falsely increased gradients in the same patient (Figure 10B)

sured in the proximal portion of the stent, irrespective of the depth of implantation.

Aortic regurgitation, either by para-valvular leak or intra-prosthetic should be carefully quantified, because it is correlated with short-and long-term mortality (47). Intra-prosthetic regurgitation is observed at the leaflets coaptation point, while para-prosthetic leaks are assessed immediately below the ventricular end of the stent. The most important view in evaluating the site and significance of para-valvular leaks is the parasternal short axis view. Para-valvular leak can be quantified at color Doppler by the ratio between the total leak lengths to the total circumference of the valve as explained above. The assessment of the total regurgitation volume can be done by making the difference between the stroke volume of a non-regurgitant valve and the stroke volume in the LVOT. Aortic regurgitation severity may be indirectly assessed by looking at the descending aorta backflow.

In patients with self-expandable valves it must be kept in mind the valve continues to expand for about 2 weeks after implantation. Some of the early para-valvular leaks may disappear, if they are initially mild, by continuous valve remodeling. Balloon-expandable valves do not share this property and para-valvular leaks tend to remain stable after implantation. The latest generation of Edwards's prostheses, the Sapien 3 valve has an outward skirt at the ventricular end, designed to reduce the chance of para-valvular leaks.

TAVR improves both systolic and diastolic function of the left ventricle, reduce mitral regurgitation (if mild or moderate) and diminish pulmonary hypertension. The lack of post-procedural improvement is due to improper patient selection (i.e. lack of contractility reserve, irreversible pulmonary hypertension, associated severe mitral re-

gurgitation) or incorrect valve selection or positioning (i.e. severe para-prosthetic leaks left untreated).

Echocardiographic follow-up is useful to identify possible complications of any valve replacement: infective endocarditis, valve thrombosis, migration of the prosthesis, secondary mitral regurgitation and highly situated ventricular septal defects due to annular calcium displacement in the ventricular septum. □

CONCLUSION

Echocardiography has an important role in all stages of TAVR for aortic stenosis. It is essential in selecting patients for TAVR by accurate assessment of ventricular function, including contractility reserve, and associated valve disease. It also contributes to measure annular size, the anat-

omy of the ascending aorta and to choose the adequate valve. Although ultrasound has a secondary role during valve deployment, it remains essential in estimating intra- and post procedural complications, such as mitral valve damage, annular rupture or pericardial effusion. Echocardiography is the method of choice for short and long term follow-up after TAVR because of widespread availability and its non-invasive nature.

In our experience the echocardiography is mandatory in the beginning of a TAVI program, when the interventionalists need rapid feedback of their maneuvers. When the learning curve tends to reach its end, the Heart Team has the option of a minimalist approach. Even in this setting a cardiologist with good echocardiography skills needs to be on place for emergent situations. □

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