CLINICAL RESEARCH

Multimodality imaging guidance for percutaneous paravalvular leak closure: Insights from the multi-centre FFPP register

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Abbreviations: CT, Computed Tomography; FFPP, Fermeture de Fuite Paraprothétique; IQR, Interquartile Range; MRI, Magnetic Resonance Imaging; PVL, Paravalvular Leak; SD, Standard Deviation; TOE, Transoesophageal Echocardiography.

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Introduction.

Summary

Background. — Percutaneous paravalvular leak (PVL) closure has emerged as a palliative alternative to surgical management in selected high-risk patients. Percutaneous procedures are challenging, especially for mitral PVL. Accurate imaging of the morphologies of the defects is mandatory, together with precise guidance in the catheterization laboratory to enhance success rates.

Aims. — To describe imaging modalities used in clinical practice to guide percutaneous PVL closure and assess the potential of new imaging tools.

Methods. — Data from the ‘Fermeture de Fuite paraprothétique’ (FFPP) register were used. The FFPP register is an international multi-institutional collaborative register started in 2017 with a retrospective and a prospective part. A descriptive analysis of multimodality imaging used to guide PVL closure in clinical practice was performed.

Results. — Data from 173 procedures performed in 19 centres from three countries (France, Belgium and Poland) were collected, which included eight cases of PVL following transcatheter valve replacement. Transoesophageal echocardiography was used in 167 cases (96.5%) and 3D echocardiography in 87.4% of cases. In one case, 3D-echocardiography was fused with fluoroscopy images in real time using echonavigator software. Details about multimodality imaging were available from a sample of 31 patients. Cardiac computed tomography (CT) was performed before 10 of the procedures. In one case, fusion between preprocedural cardiac CT angiography data and fluoroscopy data was used. In two cases, a 3D model of the valve with PVL was printed.

Conclusion. — Echocardiography, particularly the 3D mode, is the cornerstone of PVL imaging. Other imaging modalities, such as cardiac CT and cardiac magnetic resonance imaging, may be of complementary interest. New techniques such as imaging fusion and printing may further facilitate the percutaneous approach of PVLs.

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Valve cardiaque ;
Echocardiographie
3D ;
IRM 4D flow

nécessaire pour décrire la morphologie des défauts, guider la procédure percutanée et augmenter le taux de succès.

Objectifs. — L’objectif de cette étude est de décrire les différents examens d’imagerie utilisés en pratique courante et leur intérêt respectifs ainsi que l’éventuel apport des nouvelles techniques.


Résultats. — L’étude a inclus 173 procédures réalisées dans 19 centres de trois pays, incluant huit procédures sur des FPP sur valves implantées par voie percutanée. L’échographie transeosphagienne a été utilisée dans 167 cas (96,5 %) dont 87,4 % avec le mode 3D. Dans un cas, l’échocardiographie 3D a été fusionnée avec la fluoroscopie en temps réel. Au sein d’un échantillon de 31 patients dont les données des différents examens d’imagerie étaient disponibles, 10 scanners cardiaques ont été réalisés. Dans un cas, ce scanner a été fusionné avec la fluoroscopie durant la procédure. Deux modèles 3D de valves avec FPP ont été imprimés.

Conclusion. — L’échocardiographie et en particulier le mode 3D est la pierre angulaire de l’imagerie des FPP. Les autres techniques d’imagerie incluant le scanner et l’IRM sont complémentaires. Les nouvelles techniques incluant la fusion et l’impression 3D contribueront possiblement à mieux appréhender les FPP et leur traitement percutané.

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Background

Paravalvular leak (PVL) is a common complication following surgical or percutaneous valve replacement. PVL is reported in 7–17% of patients following surgical mitral valve replacement and in 5–10% following aortic valve replacement [1,2]. PVL has also been reported after percutaneous valve replacement [3]. In approximately 3% of patients, PVL leads to heart failure, haemolysis or a combination of both — requiring intervention [4–6]. PVL is mainly observed in polyvalvar multi-operated patients. Symptomatic patients with PVL are usually managed surgically [7]. Surgical closure of a PVL or valve replacement has been associated with improved event-free survival compared with conservative management [8]. However, valve replacement is challenging in high-risk patients and is associated with a high rate of morbidity, mortality or recurrent PVL [1,8,9]. Given the suboptimal results from surgical repair of PVL, a less invasive approach may be beneficial. Percutaneous PVL closure has emerged as a palliative alternative to surgical management in selected patients [10]. Since the first report of percutaneous PVL closure in 1992, small series and then multi-centre retrospective studies have been published [10–14]. However, PVL closure is one of the most challenging structural heart interventions, particularly for the mitral valve. Technical challenges include assessment of the shape and size of the defects, PVL localization and crossing, device choice and positioning. PVL closure failure — either secondary to failure to implant a device or related to residual PVL — remains high, even in experienced centres, ranging from 10 to 40% [15,16]. Echocardiography is the cornerstone of imaging of PVL, for diagnosis and for guidance of percutaneous PVL closure [2,17]. In particular, 3D echocardiography has become a valuable tool [18]. We therefore aimed to describe imaging modalities used in clinical practice to guide percutaneous PVL closure, and to assess the potential benefits of new imaging tools.

Methods

All French centres where percutaneous PVL is performed were contacted to participate in this study. Volunteers from international centres were also welcomed. Data from the ‘Fermeture de Fuite paraprothétique’ (FFPP) register – an international multi-institutional collaborative register that was started in 2017 — were used. This register has two parts – retrospective and prospective. The retrospective part included all intended PVL procedures performed in participating centres until the end of 2016. The prospective part started on 1 January 2017 and included all consecutive attempts of PVL closure in participating centres. Inclusions are ongoing until 31 December 2018. Anonymized data were acquired through an online electronic case report form (©2018 easy-crfr.com) by each centre investigator. Patient demographics, clinical features, pre-procedural clinical condition, echocardiographic features, procedural characteristics, procedural complications, in-hospital outcomes, adverse events during follow-up and vital status were collected. For the retrospective part, vital status was checked in 2017. Data from a previous retrospective study [12] were included and the vital status of these 14 patients was updated. For the prospective part, follow-up data are ongoing and are collected at 1 month, 1 year and 2 years after the procedure. These data are.

The study design conformed to the French medical Jardé law. The study was submitted to the Commission nationale de l’informatique et des libertés (CNIL n° 2008713 v 0) on 18 November 2016. The study design was approved by an ethics committee (Comité Consultatif sur le traitement de l’information en matière de recherche dans le domaine de la santé) on 23 November 2016. Patient informed consent was obtained. An exemption for patient consent was granted by the ethics committee for patients included in the retrospective arm who died during follow-up.
For this study, which focused on imaging, procedural data regarding technical details and imaging were extracted. We also analysed multimodality imaging in a sample of 31 procedures performed in three centres.

Statistical analysis

Statistical analyses were performed using Stata 11.2 software (StataCorp, College Station, Texas). Continuous data are described as medians (interquartile ranges [IQRs]) and categorical variables as numbers and percentages.

Results

Data from 173 procedures performed in 19 centres from three countries (France, Belgium and Poland) were collected. The retrospective part of the study included 99 procedures; the prospective part included 74 procedures. The first included procedures were performed in 2009; the number of procedures performed each year is shown in Fig. 1.

Procedures

Procedures were attempted to close aortic PVL (n = 37), mitral PVL (n = 133) and tricuspid PVL (n = 3). These attempts were performed on valves implanted percutaneously in eight cases (Melody and Sapien prosthesis in the tricuspid position, n = 2; Sapien and Corevalve in the aortic position, n = 5; and Sapien in the mitral position, n = 1). The median (IQR) fluoroscopy duration was shorter in aortic versus mitral PVL closures: 14.5 (9–33) vs 50 (26–71) minutes (P < 0.0001).

Echocardiography

Transoesophageal echocardiography (TOE), which was used in 167 cases (96.5%), was used in all three cases of tricuspid PVL closure. When TOE was performed, 3D echocardiography was used in 87.4% of cases. During mitral PVL closure, 2D TOE (with or without 3D TOE) was used in almost all cases (n = 131, 98.5%); significantly more so than during aortic PVL closure, where it was used in 33/37 cases (89.2%) (P < 0.01).

When 3D-TOE guidance was used, various different modes were applied. The biplane 2D view was used to guide interatrial septum puncture. PVL diameter was measured on 2D views. The extension and severity of the regurgitant jet were assessed in 2D and 3D colour views. PVL shapes were assessed on 3D en-face views of the valves. Colour Doppler 3D en-face views were used to accurately localize the defect position. The same view was used to guide crossing of the PVL with a wire and to control the position of the wire through the PVL rather than inside the prosthesis. Device deployment and positioning were often performed on 2D views. The 3D views were useful to check the relationship of the plugs or occluders with the prosthesis. A step-by-step description of a 3D-TOE-guided procedure is shown in Fig. 2.

In one case, 3D-TOE images were combined and fused in real time with fluoroscopy images using echonavigator software (Philips Healthcare, Best, The Netherlands) (Fig. 3). The Echonavigator™ enables real-time image synchronisation and fusion of 2D or 3D-TOE images with fluoroscopy images. The system places the two imaging modalities within the same coordinate system, then localizes and tracks the TOE probe. It is also feasible to place markers, in real-time, on specific points of interest on the echocardiography images that are automatically displayed on the fluoroscopy images. This tool was applied to depict the position of the PVL on the fluoroscopy view and facilitate the PVL crossing (Video 1).

Details about multimodality imaging were available in 31 patients. Cardiac computed tomography (CT) was performed before 10 procedures. CT allowed us to localize and measure the PVL using multiplanar reformating mode (Supplementary material 1). Moreover, in one case of a small aortic PVL closure, fusion between pre-procedural cardiac CT angiography data and fluoroscopy data was used. Aortic valve, sternum, rachis and tracheal tree were segmented in 3D (EP Xpress, General Electric, Boston, USA). A landmark was positioned on the PVL. The landmark and 3D volumes were recorded and fused with live fluoroscopy imaging during the procedure (HeartVision 2, General Electric). The tracheal tree, spine and sternum were used to adjust the imaging fusion and were then withdrawn from the screen. The landmark on the PVL was in a good position and was used to guide the wire across the small defect. In a few cases, from the cardiac CT angiography data, a 3D volume-rendering analysis together with a multi-planar reformattion tool was used to delineate the prosthesis valve as well as the PVL with an off-label use of 3Mensio structural heart module (Pie Medical imaging, Bilthoven, the Netherlands). This software allowed us to simulate the fluoroscopy view and the position of the PVL on the fluoroscopy view, facilitating the choice of working fluoroscopy angulation and localization of the PVL (Fig. 4).

In two cases, 3D models of valve prostheses with PVL were printed. In a case of a mitral PVL, the 3D volume dataset from a TOE examination were used (Fig. 5). In a case of residual PVL after percutaneous PVL closure, cardiac CT angiography data were used (Fig. 6).

In one case of mitral PVL, cardiac magnetic resonance imaging (MRI) with 4D blood flow sequence was performed (Fig. 7). The data were useful for assessing the severity of
Figure 2. Mitral PVL closure in an 88-year-old patient with heart failure. The procedure was performed through a transapical approach under 3D-TOE guidance. A. 2D colour-doppler view of the mitral PVL regurgitant jet. B. 3D colour en-face view of the mitral bioprosthesis from the left atrium. The PVL is localized near the LAA. C. 3D en-face view of the mitral bioprosthesis from the left atrium. D. A wire was inserted in the PVL. The 3D en-face view allowed us to check the positioning of the wire in real time. E. 2D-TOE view. A first Amplatzer Duct Occluder 1 was deployed from the left atrium. F. 3D en-face view of the mitral bioprosthesis from the left atrium. The device was deployed in a good position without overhang of the bioprosthesis. G. A residual PVL was crossed by a wire. H. A second device (muscular ventricular septal defect occluder) was deployed in a good position. LAA: left atrial appendage; LV: left ventricle; PVL: paravalvular leak; TOE: transoesophageal echocardiography.
the regurgitant jet together with an anatomical measure of the jet at the vena contracta.

**Discussion**

Percutaneous PVL closure is a useful alternative to conventional surgical management. However, such procedures remain challenging, and multi-modality imaging plays a pivotal role. In our study, echocardiography was the first-line imaging tool during the management of PVL. Comprehensive PVL imaging is a key element for the success of transcatheter closure and is mostly performed by echocardiography. PVL regurgitant jet severity can be assessed by echocardiography, and device choice and size remain largely based on echocardiography derived measurements in the catheterization laboratory. During the procedure, PVL crossing is guided by echocardiography, as is device positioning. The relationship with surrounding structures can be assessed, as can prosthetic valve function. Device position and residual PVL are investigated before device release. En-face 3D views of the prosthetic valves allowed a comprehensive assessment of the various shapes of PVL. PVL morphologies ranged from pinpoint to large crescent defects.

Echocardiography, however, still has limitations for the accurate assessment of the severity of leakages. Skill and experience of the interventionist and the echocardiographer are crucial for PVL closure success. A common understanding and language between such personnel is important. In particular, discrepancies have been reported in the naming of PVL location. Following previous reports and an expert consensus before this study, the mitral valve was likened to a clock-face from an atrial view. Noon was positioned relative to the aortic root. Nine o’clock was relative to the left atrial appendage [19]. The aortic annulus was also analysed in a clockwise format with a slight modification from a previous report [20]. Noon was set to the commissure between the left coronary sinus and the right coronary.
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Figure 4. Cardiac CT angiography derived 3D analysis using 3Mensio structural heart module software (Pie Medical imaging, Bilthoven, the Netherlands). The PVL (yellow circle) was delineated on multiplane analysis and displayed on a simulation of a fluoroscopy view (bottom left). CT: computed tomography; PVL: paravalvular leak.

Figure 5. From a 3D volume acquisition obtained by 3D TOE using 3D zoom mode, data were exported in a Cartesian DICOM format using QLab software (Philips Healthcare, USA). Cartesian DICOM files were then imported into dedicated software (Mimics 19, Materialise, Leuven, Belgium) for segmentation and to generate a 3D model (blue model) after isolation of the zone of interest. The 3D model was delivered in a 3D pdf format, which permits virtual cropping and navigation within the 3D volume, and was exported in STL format, which is the printable format. Model printing (red model) was realized using Stream 3D pro printer (France volumic, France) with thermo-plastic filaments and layer-by-layer technique, with layer thickness of 0.1 mm. DICOM: digital imaging and communications in medicine; LAA: left atrial appendage; PVL: paravalvular leak; STL: standard tessellation language; TOE: transoesophageal echocardiography.
sinus, 4 o’clock to the commissure between the right coronary sinus and the non-coronary sinus, and 8 o’clock to the commissure between the non-coronary sinus and the left coronary sinus.

Intraoperative TOE was considered essential for mitral and tricuspid PVL in our study, and this was used in nearly all cases despite requiring general anaesthesia. Moreover, one of our cases illustrated that a new imaging modality with real-time fusion of 3D-echocardiography and fluoroscopy could be of interest in these complex procedures. On the other hand, for aortic PVL closures (which are technically easier to close, with a higher success rate), detailed pre- and per-procedural transesophageal echocardiography was considered sufficient in some cases, obviating the need for general anaesthesia. Nonetheless, acoustic shadowing from valve prostheses can pose significant challenges for the diagnosis and morphological description of PVL when relying on echocardiography alone [21]. Other imaging modalities, such as cardiac CT angiography, may be useful [16,22].

Cardiac CT angiography can be used to assess anatomical characteristics such as size, location and path. However, assessment of PVL on cardiac CT angiography is challenging and requires technical considerations, which may explain why this examination was not routinely used in our cohort. The challenge involves locating a path of contrast, which is often irregular and in the order of millimetres, in a mobile area with very contrasting tissue characteristics (metal struts and myocardium) and exposure to beam-hardening artefacts and cardiac movements. The realization of such an examination hence requires thoughtful preparation and efficient equipment. We follow the Society of Cardiovascular Computed Tomography’s guidelines for patient preparation and image acquisition [23]. Image acquisition requires optimization of different parameters including heart rate, cardiac phase, windowing and slice thickness. Moreover, patients with PVL tend to have a long medical history, often with multiple surgeries on one or several valves. As a result, large areas of scarring fibrosis, myocardial sheath rearrangements, suture line, pledges and myocardial resections could influence PVL assessments. A first gated non-contrast scan may be useful to help analyse areas of contrast continuity. Based on our experience, there is no evidence for using a retrospective electrocardiogram-gated (two cases) rather than a prospective electrocardiogram-triggered scan (seven cases) [23,24].

Many patients with PVL present with heart failure, limiting the use of beta-blockers. Some authors have found it harder to evaluate PVL for aortic valve prostheses at ventricular systole, and for mitral valve prosthesis at end-diastole (likely related to atrial systole). They estimated that the optimum valve evaluation for both aortic and mitral prosthetic valves was at mid-diastole [25]. Our experience is somewhat different. It seems to us that an optimal evaluation of mitral leaks is obtained during the ventricular systole and seems logically little influenced by heart rate, whereas the evaluation of aortic leaks is better at mid-diastole and benefits from optimized temporal resolution by a low heart rate. However, a full R-R interval study is helpful for the assessment of mechanical valve leaflet motion, and to minimize the possibility of an inaccurate assessment of a potential PVL tract. Windowing is an essential element of prosthetic valve assessment on CT, but despite seeming obvious, it can be problematic [26]. A very soft window with considerable windowing adjustments is needed to minimize beam hardening. Based on published data, almost all valve types can be assessed, although very little is known about ball and cage models because of extreme beam hardening artefact from the thicker metal struts. Spatial resolution must be optimized to fit with the millimetric sizes of PVL. A reconstructed slice thickness of 0.5 or 0.6 mm can be recommended. Data from the CT scan can be segmented in 3D and merged with fluoroscopy using dedicated software. This offers the ability to delineate the PVL and superimpose it as a target on the fluoroscopy view for the interventionist. However, this fusion is not in real time and does not follow cardiac cavity motion [27]. Nevertheless, this tool was somewhat useful in one case in this study. In successful technical conditions, cardiac CT angiography offers a useful anatomic image, but does not provide functional evaluation. It can also help to describe the morphology of a PVL, but is less sensitive for the assessment of its severity.

MRI may also be useful for a functional assessment of PVL. MRI is particularly useful for providing anatomical and functional evaluations of leaks using cine-cardiac imaging, while it is also useful for planimetry measurements [28,29]. As a result, morphological gradient echo analysis is relevant for surface estimation, but is no longer relevant for millimetric defects. For PVL, the limitations of this technique are the small size of some PVL and metal artefacts. In clinical practice, MRI can be useful for functional analysis of PVL, which is difficult to appreciate by cardiac ultrasound. MRI has also been used for the functional evaluation of PVL after transaortic valve implantation [3,30]. More recently, 4D flow
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imaging has been developed from MRI data. This innovative modality of blood-flow imaging with 3D time-resolved, phase-contrast cardiac MRI allows qualitative and quantitative analyses. This tool seems potentially interesting for PVL analysis. In one case in this study, MRI was easy and fast and allowed anatomical study (size, location and trajectory) and functional analysis of a mitral PVL without being impacted by metallic artefacts.

Finally, our study illustrates the potential interest of 3D cardiac modelling and printing. One of the challenges of percutaneous PVL closure is choosing which device will best suit the complexity of the PVL shape without interfering with the prosthetic valve function. Testing a device before the procedure using an ex-vivo 3D printed model could be of interest. Moreover, these models could be used to develop new-dedicated devices adjusted to the various morphologies and thus limiting the rate of post-procedural residual PVL. Printing is also used in other complex cases, such as congenital heart diseases, to plan the therapeutically strategy [31]. Printing from a 3D-echocardiography dataset is particularly useful for displaying valves and sub-valvular apparatus. Printing from CT scans benefits from its high spatial resolution and displays cardiac chambers and the interventricular septum clearly. Multimodal imaging and 3D cardiac computational modelling further offer a new way to better understand the complexity and shape of PVL [32].

Limitations

Only echocardiography data were available for the whole study population. Multimodality imaging data were only available in a sample of procedures performed by a small group of investigators. Thus, comments about the new imaging techniques mainly reflect the opinions of experts and are based on a small number of cases. Moreover, given the lack of a gold standard method to measure PVL, it remains hard to compare the accuracy of the different available techniques. However, this study offers an overview of the different imaging tools that are currently available for heart teams facing these challenging situations.

Conclusion

Our study highlights the pivotal role of 2D and 3D echocardiography for guiding percutaneous PVL closure. Improved technical methods of CT scans and MRI increase the complementary role of these imaging modalities. Combining the
strengths of these techniques with fluoroscopy by image fusion seems of potential interest to facilitate the procedures. Modelling and printing offer new possibilities of pre-procedural planning and simulation of the procedures. Increased use of multi-modality imaging is associated with continuous improvement in the percutaneous management of PVL.

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Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://10.1016/j.acvd.2018.05.001.

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