

The crucial role of 18F-fluorodeoxyglucose positron emission tomography/computed tomography in diagnosing pulmonary valve endocarditis in patients after transcatheter pulmonary valve implantation: a case report

Kaat Rottiers ^{1*} and Liesbeth Rosseel²

¹Department of Cardiology, University Hospital, Corneel Heymanslaan 10, 9000 Ghent, Belgium; and ²Department of Cardiology, Azorg, Merestraat 80, 9300 Aalst, Belgium

Received 4 September 2024; revised 18 October 2024; accepted 11 December 2024; online publish-ahead-of-print 16 December 2024

Background

Patients after transcatheter pulmonary valve implantation (TPVI) are at increased risk for infective prosthetic valve endocarditis. Diagnosis of infective endocarditis (IE) following TPVI is particularly difficult due to impaired visualization of the transcatheter pulmonary valve (TPV) with echocardiography [Delgado V, Ajmone Marsan N, de Waha S, Bonaros N, Brida M, Burri H, et al. 2023 ESC guidelines for the management of endocarditis. *Eur Heart J* 2023;**44**:3948–4042]. The aim of this case report is to describe the significant role of 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) in diagnosing IE post-TPVI.

Case summary

A 22-year-old woman presented to the emergency department with fever and chest pain. Relevant past medical history included a left ventricular outflow membrane resection at infancy, a Ross procedure at the age of 4 with post-operative pacemaker implantation and Melody™ TPVI at the age of 16 because of pulmonary valve stenosis. Blood tests showed elevated inflammatory markers. Transthoracic echocardiography revealed elevated systolic pulmonary artery pressure of 53 mmHg. After 2 days, blood cultures appeared positive for *Streptococcus* species. Subsequently, transoesophageal echocardiography showed an elevated TPV peak gradient (25 mmHg). No clear valvular nor pacemaker lead vegetations were identified but could not be ruled out as inspection of the TPV was difficult. However, 18F-FDG PET/CT demonstrated heightened metabolism at the TPV, which confirmed the diagnosis of TPV IE. Intravenous antibiotic treatment was administered, which led to clinical improvement and normalization of the inflammatory markers.

Discussion

Transthoracic echocardiography and transoesophageal echocardiography often fail to provide adequate assessment, making 18F-FDG PET/CT crucial for diagnosing TPV IE in this case. Important to notice is the possibility of false-negative and false-positive diagnoses and the radiation exposure, particularly in this young population.

Keywords

Prosthetic valve endocarditis • Pulmonary valve • Congenital heart disease • 18F-FDG PET/CT • Transcatheter pulmonary valve implantation • Case report

ESC curriculum

2.5 Nuclear techniques • 4.10 Prosthetic valves • 4.11 Endocarditis • 9.7 Adult congenital heart disease

* Corresponding author. Tel: +32 488 608444, Email: kaatrottiers@proximus.be

Handling Editor: Christoph Sinning

Peer-reviewers: Ganesh Gajanan; Marie-Luise Dikou; Mohammed Shahbaaz Khan

Compliance Editor: Sheetal Vasundara Mathai

© The Author(s) 2024. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

Learning points

- The prevalence of infective endocarditis involving the native pulmonary valve is very low in the general population but increases in patients with congenital heart disease and right ventricle outflow dysfunction. Patients with previous transcatheter pulmonary valve implantation have a high risk, with an incidence rate of 1.6–4%/patient-year.
- Diagnosis of infective transcatheter pulmonary bioprosthetic valve endocarditis is specifically challenging due to difficult visualization of the prosthetic valve leaflets with echocardiography caused by stent frame artefacts.
- Incorporating 18F-fluorodeoxyglucose positron emission tomography/computed tomography into the diagnostic workup could improve the detection of pulmonary prosthetic valve endocarditis.

Introduction

Prevalence of infective endocarditis (IE) involving the native pulmonary valve is very low in the general population, accounting for <2% of all endocarditis cases, and increases in patients with congenital heart disease and right ventricle outflow dysfunction.¹ The risk for IE in patients following transcatheter pulmonary valve implantation (TPVI) is high, with a reported incidence rate of 1.6–4%/patient-year.^{2–7} Infective prosthetic valve endocarditis (PVE) appears to be more prevalent in patients with previous transcatheter as compared with surgical pulmonary valve replacement.^{2,5,6} The diagnosis of IE following TPVI is particularly challenging because of the difficult visualization of the transcatheter pulmonary valve (TPV) by both transthoracic (TTE) and transoesophageal echocardiography (TEE) due to the dense framework of this TPV.^{2–6,8,9} It is incorporated in the most recent 2023 European Society of Cardiology (ESC) guidelines that 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) is recommended for PVE; nevertheless, its application in pulmonary valve endocarditis after TPVI is less documented.^{2,5,9,10} The aim of this case report is to show the added value of 18-FDG PET/CT specifically in diagnosing TPV IE.

Summary figure

Case presentation

A 22-year-old Caucasian woman with a history of complex left ventricle outflow tract obstruction underwent surgical resection of the membrane at the age of 9 months. Four years later, a Ross procedure was performed for the treatment of recurrent subvalvular aortic stenosis. This procedure was complicated by complete atrioventricular block with implantation of an epicardial VVI pacemaker. After 5 years, the pacemaker was replaced with a transvenous single lead right ventricular pacemaker system due to malfunction. At the age of 16, TPVI with a Melody™ bioprosthesis was performed for the treatment of degenerative stenotic pulmonary homograft valve. The patient presented to the emergency department with a 3-day history of fever and stabbing chest pain, which worsened when lying down. The day before, she experienced generalized muscle pain and weakness. On physical examination at admission, the patient was febrile, the heart rate was 74 per minute, blood pressure was 124/67 mmHg, and oxygen saturation was 97% at room air. A systolic murmur was identified at the cardiac base. Inflammatory markers were elevated in the blood tests. Further infectious workup with chest X-ray and urine analysis did not reveal any signs of infection. Electrocardiogram showed sinus rhythm without any other abnormalities. Transthoracic echocardiography revealed pre-

Infancy	Surgical resection of the left ventricular outflow membrane for the treatment of left ventricle outflow tract obstruction.
2005	Recurrence of subvalvular aortic stenosis. Second sternotomy for a Ross procedure: surgical aortic valve replacement with the native pulmonary valve (autograft) and replacement of the pulmonary valve with a homograft. Post-operative complete atrioventricular block with implantation of an epicardial single lead pacemaker.
2010	Implantation of a transvenous single lead right ventricular pacemaker system due to malfunction of the epicardial pacemaker lead.
2017	Degenerative stenotic pulmonary homograft valve. Transcatheter pulmonary valve implantation with a Melody™ transcatheter pulmonary valve.
On admission (22 years old)	Hospital admission because of fever and chest pain. High inflammatory blood test markers. Transthoracic echocardiography showed preserved left ventricular ejection fraction, normal function of the aortic valve, and elevated systolic pulmonary arterial pressure of 53 mmHg. The bioprosthetic pulmonary valve could not be clearly visualized.
Day 2	Blood cultures isolated <i>Streptococcus</i> species (viridans). Transoesophageal echocardiography revealed an elevated transprosthetic pulmonary valve peak gradient of 25 mmHg and did not show any signs of vegetations at the heart valves or right ventricular pacemaker lead. Start intravenous antibiotic treatment with gentamicin and penicillin.
Day 5	18F-FDG PET/CT showed elevated metabolism at the transcatheter pulmonary valve, confirming the diagnosis of prosthetic valve infective endocarditis.
6 weeks after admission	Clinical improvement and normalization of the inflammatory markers. Stable transprosthetic pulmonary valve peak gradient of 26 mmHg with reduction of the systolic pulmonary artery pressure to 30 mmHg. Stop intravenous antibiotic treatment.
3 months after hospitalization	Clinical persistent asthenia and chest pain without recurrence of fever. Stable transprosthetic pulmonary valve peak gradient of 28 mmHg and systolic pulmonary artery pressure of 36 mmHg.

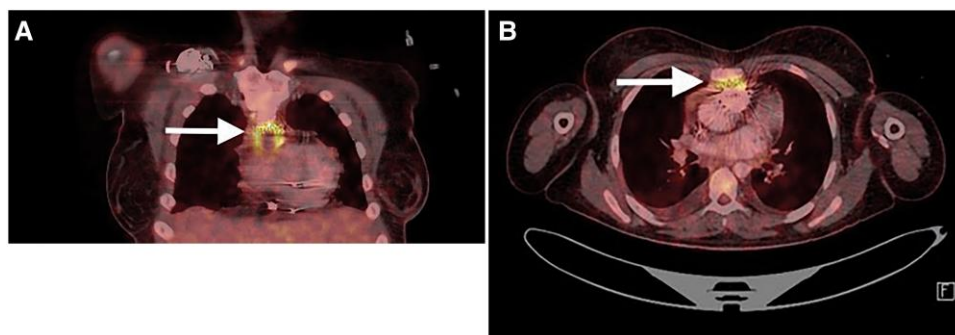


Figure 1 18F-fluorodeoxyglucose positron emission tomography/computed tomography on Day 5 showing enhanced glucose uptake on the Melody valve (indicated by arrows) in coronal view (A) and axial view (B).

served left ventricular ejection fraction, normal function of the aortic valve (autograft), and elevated systolic pulmonary artery pressure of 53 mmHg (previous value of 36 mmHg). The bioprosthetic pulmonary valve could not be clearly visualized. Blood cultures isolated omnisensitive *Streptococcus* species (viridans). Subsequently, a TEE was performed and showed an increased peak gradient of 25 mmHg (previous value of 15 mmHg) over the bioprosthetic pulmonary valve. No vegetations at the heart valves or at the right ventricular pacing lead could be identified. However, visualization and inspection of the pulmonary bioprosthesis were very difficult. Therefore, a correct diagnosis regarding potential IE could not be made based on echocardiography (TTE/TEE). A tailored antibiotic regimen with gentamicin for 2 weeks and penicillin for 6 weeks was started. Next, an 18F-FDG PET/CT was conducted and showed elevated metabolism at the level of the pulmonary valve prosthesis (Figure 1A and B), which confirmed the diagnosis of PVE of the pulmonary bioprosthesis. Fortunately, clinical improvement with normalization of the inflammatory markers, stable transprosthetic peak gradient (26 mmHg), and reduction of the systolic pulmonary artery pressure (30 mmHg) on echocardiography was seen after 6 weeks of antibiotic treatment. At follow-up consultation, 3 months after hospitalization, the patient reported persistent asthenia and chest pain without recurrence of fever. Transthoracic echocardiography revealed stable echocardiographic findings with a transprosthetic pulmonary valve peak gradient of 28 mmHg and a systolic pulmonary artery pressure of 36 mmHg.

Discussion

Patients post-TPVI are at increased risk for PVE with an incidence rate of 1.6–4%/patient-year and occurs in up to 32% of the cases within the first year after TPVI.^{2–7} Factors associated with a higher risk of TPV IE are younger age, a previous history of IE, and a higher transvalvular residual gradient after TPVI. In this case, the patient has a higher risk to develop IE because of her young age at implant and because of her higher immediate post-implant peak transvalvular gradient of 26 mmHg.^{2,7}

Elevated systolic pulmonary artery pressure was observed on TTE in this case, which can be attributed to inflammation on the TPV. Inflammation may cause tissue damage, thickening, or even minor obstructions that impair the valve's function. These changes impede blood flow from the right ventricle to the pulmonary artery, resulting in increased systolic pulmonary artery pressure. Due to inflammation on the TPV, a right heart catheterization could not be performed. After administering appropriate antibiotic treatment, we observed a reduction in systolic pulmonary artery pressure, returning to the level

recorded on her last consultation. Although the elevated systolic pulmonary artery pressure suggests the presence of inflammation or vegetations on the TPV, this is insufficient to definitively diagnose IE.

The modified Duke criteria are used as diagnostic criteria for IE and are based on major and minor criteria with an overall sensitivity of 80%. Major criteria include positive blood cultures and positive imaging (TTE/TEE), while predisposing conditions, fever, embolic vascular dissemination, and immunological phenomena are minor criteria.² Nevertheless, using the Duke criteria for the diagnosis of PVE has some important limitations. Echocardiography can be normal or inconclusive in up to 30% of the cases due to the presence of stent frame artefacts, which makes diagnosing PVE exceptionally challenging.^{2–6,8,9} In contrast to left-sided PVE, where TEE is superior to TTE for detecting vegetations, TEE does not always provide additional value in TPV endocarditis. The anterior position of the right ventricular outflow tract limits the echocardiographic detection of vegetations in right-sided IE.^{2,5,6,8} Therefore, additional imaging to confirm the diagnosis in patients with underlying congenital heart disease is necessary. The use of 18F-FDG PET/CT emerges as a crucial tool in diagnosing endocarditis of the TPV and, in this way, increasing the sensitivity of the Duke criteria.^{4,6,9,10} A multicentric study evaluated the detection rate of 18F-FDG PET/CT in pulmonary PVE and demonstrated a sensitivity and specificity of 79.1 and 72.7%, respectively, and a high positive predictive value of 91.9%.¹⁰ Another study that also included left-sided valve and electronic device endocarditis demonstrated an increase of the sensitivity of the Duke criteria from 39.1 to 87% by using 18F-FDG PET/CT.⁹

The 2023 ESC guidelines on endocarditis state that the use of 18F-FDG PET/CT in the diagnosis of endocarditis in patients after TPVI has been shown useful in cases with clinical suspicion and negative echocardiography (TTE/TEE). Therefore, the ESC diagnostic criteria introduced a multimodality imaging approach, acknowledging the significant contribution of 18F-FDG-PET/CT.² In this case by performing an 18F-FDG PET/CT, a definite diagnosis was made (two major criteria), which allowed for the continuation of appropriate antibiotic treatment, preventing the patient from receiving unnecessary therapy and avoiding the development of antibiotic resistance.

Nevertheless, it is important to consider some limitations when using 18F-FDG PET/CT. Notice that false-positive and false-negative diagnoses can occur when using 18F-FDG PET/CT. Low systemic inflammation or previous antibiotic therapy could favour false negatives. A false-positive diagnosis can be attributable to post-operative inflammation.^{9,10} The low negative predictive value indicates that a negative 18F-FDG PET/CT cannot rule out the diagnosis.¹⁰ Also, using 18F-FDG PET/CT implies an additional radiation exposure, which is important in patients with a congenital heart disease because of their young age.^{9,10}

This case highlights the challenges of diagnosing IE in a young patient with a complex cardiac history and emphasizes the pivotal role of 18F-FDG PET/CT in the diagnosis of TPV IE in patients after TPVI. This imaging modality should be considered as a useful diagnostic tool, especially in patients where echocardiography has negative or doubtful results. Therefore, it should be integrated in the diagnostic workup of pulmonary PVE.

Lead author biography



Dr Kaat Rottiers is a resident in cardiology. After completing medical school at the University of Ghent, she began her advanced training in internal medicine. Currently, Dr Rottiers has started her specialization in cardiology. During medical training, she developed a strong interest in the diagnosis and treatment of cardiovascular diseases, leading to her first article in this field.

Consent: The authors confirm that informed consent for submission and publication of this case report has been obtained from the patient in line with the COPE guidelines.

Conflict of interest: None declared.

Funding: None declared.

Data availability

The data underlying this article are available in the article and in its online Supplementary material.

References

1. Fusco F, Scognamiglio G, Correria A, Merola A, Colonna D, Palma M, et al. Pulmonary valve endocarditis in adults with congenital heart disease: the role of echocardiography in a case series. *Eur Heart J Case Rep* 2020;**4**:1–7.
2. Delgado V, Ajmone Marsan N, de Waha S, Bonaros N, Brida M, Burri H, et al. 2023 ESC guidelines for the management of endocarditis. *Eur Heart J* 2023;**44**:3948–4042.
3. Nordmeyer J, Ewert P, Gewillig M, Aljufan M, Carminati M, Kretschmar O, et al. Acute and midterm outcomes of the post-approval MELODY registry: a multicentre registry of transcatheter pulmonary valve implantation. *Eur Heart J* 2019;**40**:2255–2264.
4. Schmidt MR, Søndergaard L. Transcatheter pulmonary valve implantation: a melody to follow. *Eur Heart J* 2019;**40**:2265–2267.
5. Abdelghani M, Nassif M, Blom NA, Van Mourik MS, Straver B, Koolbergen DR, et al. Infective endocarditis after melody valve implantation in the pulmonary position: a systematic review. *J Am Heart Assoc* 2018;**7**:e008163.
6. Bos D, De Wolf D, Cools B, Eyskens B, Hubrechts J, Boshoff D, et al. Infective endocarditis in patients after percutaneous pulmonary valve implantation with the stent-mounted bovine jugular vein valve: clinical experience and evaluation of the modified Duke criteria. *Int J Cardiol* 2021;**323**:40–46.
7. McElhinney DB, Zhang Y, Aboulhosn JA, Morray BH, Biernacka EK, Qureshi AM, et al. Multicenter study of endocarditis after transcatheter pulmonary valve replacement. *J Am Coll Cardiol* 2021;**78**:575–589.
8. Cheung G, Vejlsstrup N, Ihlemann N, Arnous S, Franzen O, Bundgaard H, et al. Infective endocarditis following percutaneous pulmonary valve replacement: diagnostic challenges and application of intra-cardiac echocardiography. *Int J Cardiol* 2013;**169**:425–429.
9. Pizzi MN, Dos-Subirà L, Roque A, Fernández-Hidalgo N, Cuéllar-Calabria H, Pijuan Domènech A, et al. (18)F-FDG-PET/CT angiography in the diagnosis of infective endocarditis and cardiac device infection in adult patients with congenital heart disease and prosthetic material. *Int J Cardiol* 2017;**248**:396–402.
10. Venet M, Jalal Z, Ly R, Malekzadeh-Milani S, Hascoët S, Fournier E, et al. Diagnostic value of (18)F-fluorodeoxyglucose positron emission tomography computed tomography in prosthetic pulmonary valve infective endocarditis. *JACC Cardiovasc Imaging* 2022;**15**:299–308.