CASE REPORT

When echo gets in the way: physiological factors affecting Doppler data

J Jose BSc BSE[1], K Randall BSc BSE[2], J Baron BMBS MD FRCP FESC[2] and **J Khoo MB BChir DPhil FRCP FESC[3]**

[1]School of Medicine, University of Nottingham, Nottingham, UK
[2]University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UK
[3]University Hospitals of Leicester NHS Trust, Leicester, UK

Correspondence should be addressed to J Jose: mzyjj2@nottingham.ac.uk

Summary

Transthoracic echocardiography (TTE) is widely used as a pre-operative screening tool. It can provide extensive information about cardiac function and underlying pathology, which could influence decisions regarding surgery. This patient was referred for TTE as part of pre-op screening, as he had a biological prosthetic aortic valve. This was a rare case where misleading TTE measurements inadvertently led to the patient being referred for transcatheter aortic valve implantation (TAVI), which delayed non-cardiac surgery.

Key Words

- ▶ anaemia
- ▶ transcatheter aortic valve replacement
- ▶ prosthetic valve
- ▶ Doppler echocardiography
- ▶ cardiac physiology

Learning points:

- Echocardiographers and referrers should be familiar with physiological and haemodynamic conditions that can affect measurements.
- Echocardiographic results should be interpreted in wider clinical context, particularly when it changes management.
- Lack of clinical information on the referral form limits echocardiographer's ability to interpret results in clinical context.
- Referring non-cardiologists may not be aware of haemodynamic factors that could affect echocardiographic measurements.

Background

This report describes the case of a patient who went as far as the table for a TAVI based on misleading TTE measurements. This case highlights pitfalls in failing to interpret findings on echocardiography in the clinical context of patient presentation. It aims to refresh clinical reasoning and knowledge of echocardiographers and clinicians alike.

This case highlights the role of TTE in clinical decision making; the importance of communicating relevant clinical information on TTE referral forms, especially when care is being carried out across several centres, and interpreting TTE results in context of haemodynamic factors which might affect measurements.

Case presentation

A 77-year-old male was admitted with breathlessness, chest pain and gastrointestinal (GI) bleeding to his local teaching hospital. The breathlessness had been

increasing for 2 weeks and was occurring even at rest on admission. The admitting ward arranged TTE as he had a bioprosthetic 23 mm mosaic aortic valve replacement (AVR) with single saphenous vein graft, and a murmur was noted. The results were also important due to pending prostate biopsy for suspected prostate cancer and because a duodenal polyp (possibly malignant) was found on endoscopy and surgery was being contemplated.

TTE showed a significant increase in gradient compared to previous year. Based on this, the patient was referred to a tertiary centre for valve-in-valve TAVI. His GI surgery and prostate biopsy were deferred until TAVI could be carried out. The case was discussed in the MDT at the regional TAVI centre where the TTE, coronary angiogram and CT were reviewed and he was accepted for valve-in-valve TAVI, to be carried out with transoesophageal echocardiography (TOE) guidance.

Investigation

TTE at the district general hospital showed well-seated 23 mm mosaic aortic valve prosthesis with a peak gradient of 103 mmHg, mean gradient of 67 mmHg and estimated orifice area (EOA) of 0.9 cm² (Fig. 1) and EOA indexed for body surface area (BSA) of 0.5 cm²/m² with a left ventricular tract outflow tract (LVOT) of 1.9 cm. The velocity ratio (DVI) was 0.26. The leaflets were not clearly visualised and there was no regurgitation.

The left ventricle was normal size with mild concentric left ventricular hypertrophy and dynamic function with estimated ejection fraction >65%. The gradients were significantly elevated from previous scan. Previous TTE from under a year ago showed a well-seated prosthetic valve with a peak gradient of 48 mmHg, mean of 23 mmHg and an EOA of 1.3 cm² (Fig. 2). On table TTE showed a peak gradient of 54 mmHg and mean gradient of 30 mmHg (Fig. 3), EOA 1.3 cm², and EOA/BSA 0.7 cm²/m². Perioperative TOE was performed with nine sprays of local Lignocaine spray and 2 mg Midazolam i.v. sedation. This showed a well-seated AVR with 3D area of 1.32 cm² (Fig. 4). DVI was 0.35. LVOT was measured at 1.9 cm and there was no significant difference in LVOT area between TTE and TOE. There was no regurgitation and his left ventricular function was normal. At this time, the patients' blood pressure (BP) was 115/56 mmHg with a heart rate (HR) of 70 bpm. BP and HR were not measured during the pre-op TTE for direct comparison. CT scan was arranged as part of assessment. The report concentrated on measurements and did not comment on the valve morphology.

Treatment and outcome

The patient was referred to tertiary centre for TAVI based on significant increase in valve gradients and decrease in calculated orifice area on TTE. The values obtained during perioperative TOE were within the recommended parameters for a 23 mm mosaic valve (1). Based on this,
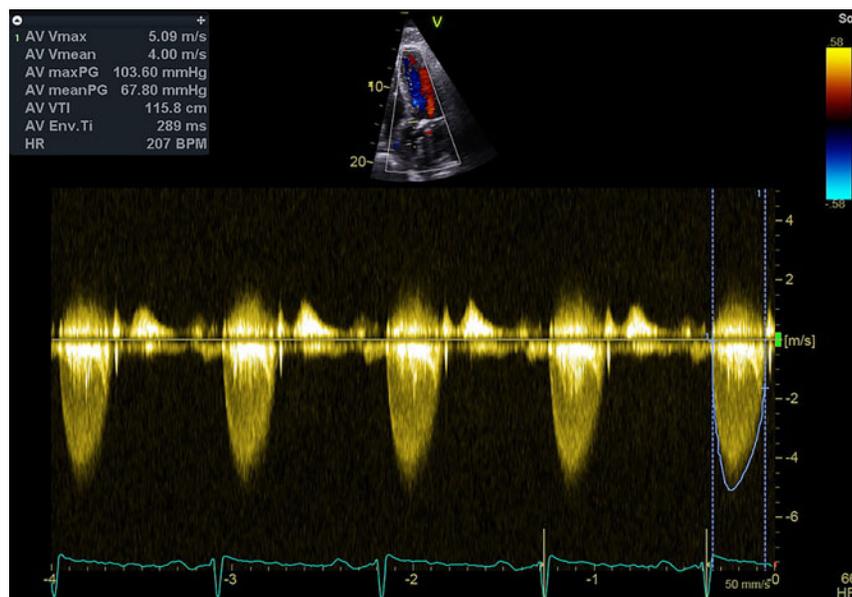
Figure 1
Increased aortic gradients. TTE at the district general hospital showed well-seated 23 mm mosaic aortic valve prosthesis with a peak gradient of 103 mmHg and mean gradient of 67 mmHg.
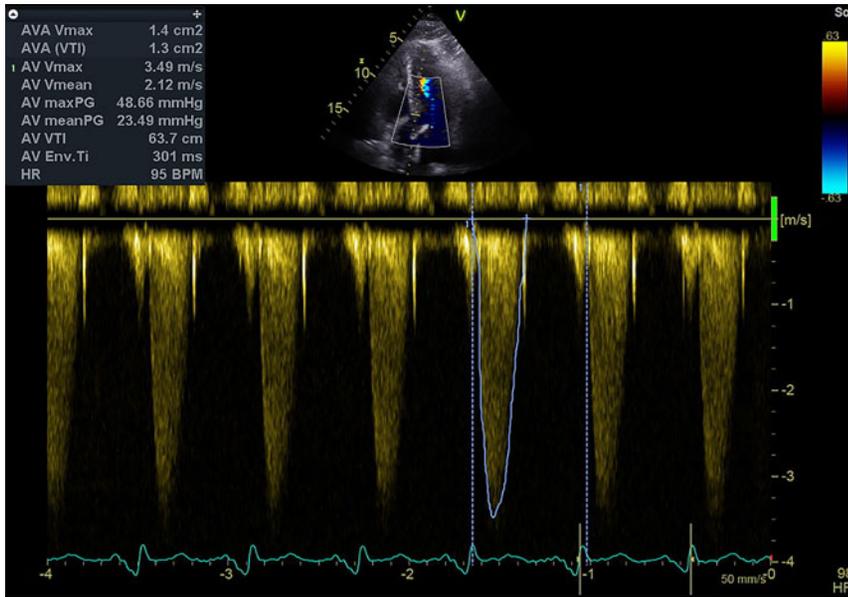
Figure 2
Previous aortic gradients. Previous TTE from under a year ago showed a well-seated prosthetic valve with a peak gradient of 48 mmHg, mean of 23 mmHg and an EOA of 1.3 cm².

his TAVI procedure was cancelled. It was advised that his pending surgeries could proceed as there was no evidence of prosthetic valve dysfunction.

Discussion

This is a case where misleading TTE measurements took a patient as far as the TAVI table, delaying other surgery and procedures until problems (non-existent) with his aortic valve could be resolved. There are many learning points and clinical reasoning problems that need to be addressed:

- Why was there a significant change in aortic valve gradients from one TTE to the other?
- Do we disproportionately rely on Doppler gradients when visibility of prosthetic valve leaflets is poor due to imaging limitations?
- Did the referring physician make all relevant clinical details available on the referral form? If so, could the delay have been avoided?
- Was the interpreting professional familiar with physiological factors that could affect echocardiographic measurements?
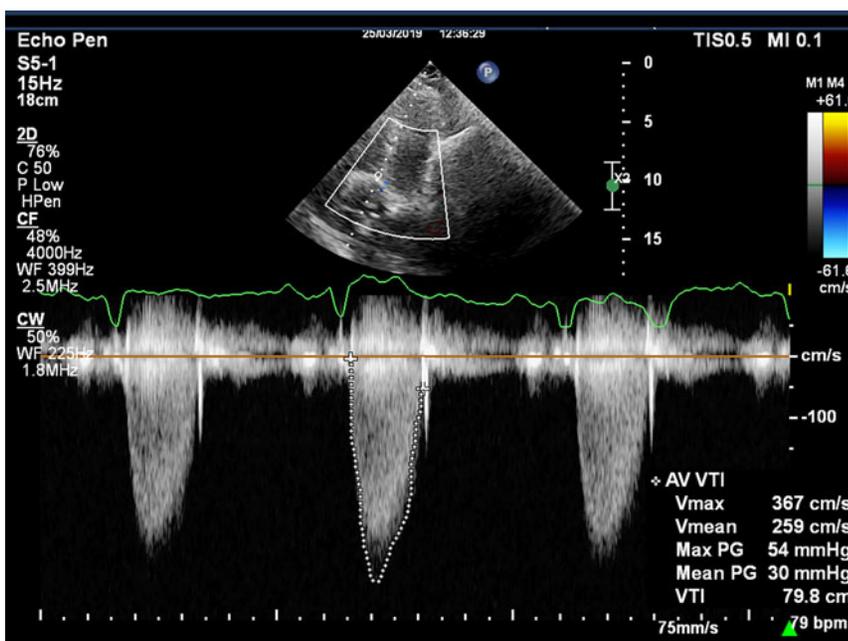
Figure 3
Perioperative gradients. This showed a well seated bioprosthetic aortic valve with peak gradient of 54 mmHg and mean gradient of 30 mmHg.
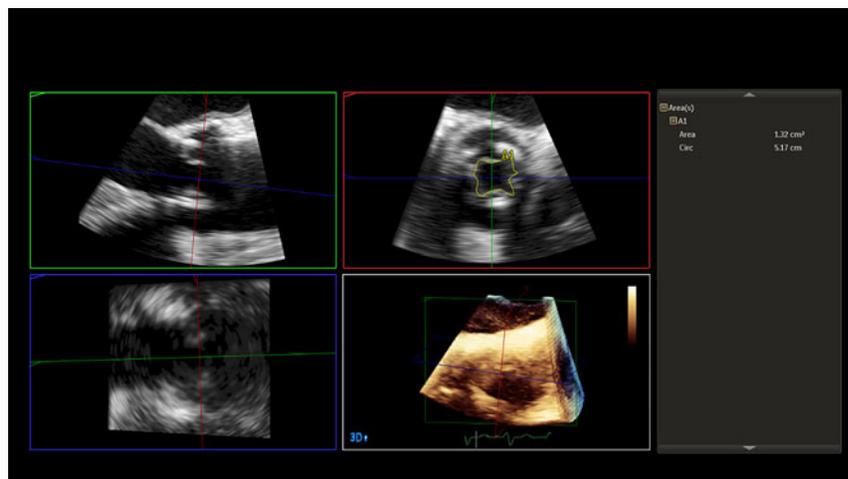
Figure 4
Perioperative TOE 3D area. 3D aortic valve area estimated at 1.32 cm^2.

- What can be done to avoid pitfalls in interpreting data and mitigate changes in measurements due to physiological factors?

On the TTE the year before, there was nothing to suggest prosthetic valve dysfunction. When the pre-op screening TTE was performed, the valve leaflet visibility was poor. However, there was considerable increase in gradients, and this combined with the patients' recent symptoms of breathlessness led to the conclusion of valve failure with severely reduced aortic valve area. Based on this a decision was made to refer the patient for valve-in-valve TAVI.

Structural dysfunction is the major cause of failure of bioprosthetic heart valves (flexible-stent-mounted, glutaraldehyde-preserved porcine aortic valves and bovine pericardial valves). Within 15 years following implantation, approximately 50% of porcine aortic valves suffer the major prosthesis-related complication with this type of valve – tissue failure. The principal underlying pathologic process is cuspal calcification; secondary tears frequently precipitate regurgitation.

Calcification can also cause pure stenosis owing to cuspal stiffening. Calcific deposits are usually localized to cuspal tissue (intrinsic calcification), but calcific deposits extrinsic to the cusps may develop in thrombi or endocarditic vegetations (extrinsic calcification). Progressive collagen deterioration, independent of calcification, is also a likely important contributor to the limited durability of bioprosthetic valves (2, 3). Bovine pericardial valves also calcify but design-related tearing has been prominent (4, 5). When the peri-operative TOE was performed, the valve was found to be functioning within acceptable parameters.

The cause of high gradients at the time of pre-op screening TTE was retrospectively attributed to profound anaemia present at the time. His haemoglobin was 56 g/L (Fig. 5) and subsequently required 8 units of blood transfusion. The cause was possibly a polyp in the duodenum, which was awaiting surgical removal. The presenting symptoms, which were presumed to be due to the valve degeneration, were also compatible with his anaemia. He remained anaemic for few months due to recurrent bleeds. Anaemia caused increased cardiac output and increased forward flow through his valve. Increased cardiac output is the main haemodynamic factor, mediated by lower afterload, increased preload, and positive inotropic and chronotropic effects (6). Decreased afterload is due to vasodilatation and reduced vascular resistance as a consequence of lower
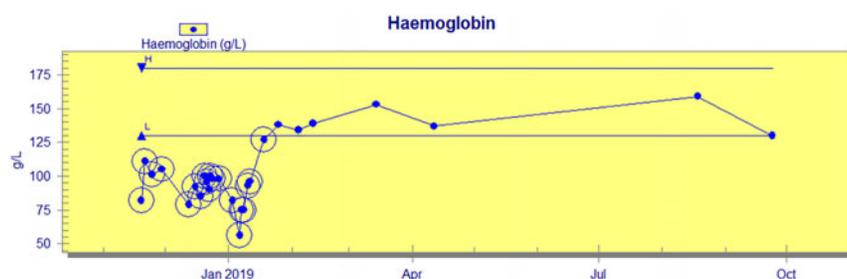
Figure 5
Haemoglobin graph. This figure shows the patients' haemoglobin levels during serial blood tests done from November 2018 to October 2019. In January 2019, there was profound anaemia with haemoglobin at 56 g/L.

blood viscosity, hypoxia-induced vasodilatation, and enhanced nitric oxide activity (6). Vasodilatation also involves recruitment of microvessels and, in the case of chronic anaemia, stimulation of angiogenesis. With decreased afterload, the venous return (preload) and left ventricular (LV) filling increase, leading to increased LV end-diastolic volume and maintenance of a high stroke volume and high stroke work.

High stroke work is also due to enhanced LV contractility attributed to increased concentrations of catecholamines and non-catecholamine inotropic factors. In addition, heart rate is increased in anaemia, due to hypoxia-stimulated chemoreceptors and increased sympathetic activity (6).

Correcting anemia reduces cardiac output and improves echocardiographic parameters of peak velocity and mean gradient (7), hence the reduction in gradients in this patient. Since there was no evidence of valve dysfunction, it was advised that his GI surgery could proceed without further delay.

Echocardiographers should be familiar with haemodynamic factors that could affect the validity of Doppler measurements that use Bernoulli's equation and the continuity principle. This case underlines the role of anaemia causing high output and higher gradients. Other high output states to keep in mind include pregnancy, morbid obesity, liver disease, lung disease, arteriovenous shunts including cardiac shunts, haemodialysis fistulas and arterio-venous malformations (8).

So, what can be done to avoid pitfalls in interpreting data? One of the major failings in comparing aortic valve measurements is the use of different LVOT dimensions. This can be mitigated by quoting the velocity ratio, using either Vmax or VTI which is independent of the LVOT dimension. When assessing prosthetic valve replacements, particularly when comparing across modality from TTE and TOE, we suggest that it is important to include the heart rate and blood pressure each time a scan is done. The minimum requirements for assessment of an AVR are: Vmax, Mean gradient, DVI, EOA and indexed EOA. One could also think of 3D volumes to compare stroke volume and change in EF. This will help to interpret the results in clinical context and query whether changes in velocity (as in this case) could be due to non-valvular factors. If the echocardiographer and interpreting physicians are familiar with these factors and ensure they are communicated in the referral and the report, situations like this could be avoided to a good extent.

In conclusion, this is a case where echocardiographic measurements misled clinicians to refer a patient for an unwarranted procedure. It highlights the importance of identifying profound anemia as a cause for increased gradients across prosthetic valves in some patients, especially when TTE is limited at visualising prosthetic leaflets. Operators should follow the steps suggested previously to mitigate the effects of non-valvular factors. It is also suggested that clinicians include anemia in clinical details when referring for TTE and refer for TOE if there is any uncertainty about valve degeneration.

Patient consent
Written informed consent has been obtained from the patient.

Author contribution statement
Justin Jose collected the clinical details, performed the literature search and prepared the manuscript. Kirsty Randall contributed to the collection of data and preparation. Dr Julia Baron was the cardiologist in charge of the patient and gave academic cardiological advice and edited the article. Dr Jeffrey Khoo critically revised the manuscript and provided advice.

References

1 Pibarot P & Dumesnil JG. Prosthetic heart valves: selection of the optimal prosthesis and long-term management. *Circulation* 2009 **119** 1034–1048. (https://doi.org/10.1161/CIRCULATIONAHA.108.778886)

2 Vesely I, Barber JE & Ratliff NB. Tissue damage and calcification may be independent mechanisms of bioprosthetic heart valve failure. *Journal of Heart Valve Disease* 2001 **10** 471–477.

3 Sacks MS & Schoen FJ. Collagen fiber disruption occurs independent of calcification in clinically explanted bioprosthetic heart valves. *Journal of Biomedical Materials Research* 2002 **62** 359–371. (https://doi.org/10.1002/jbm.10293)

4 Schoen FJ, Fernandez J, Gonzalez-Lavin L & Cernaianu A. Causes of failure and pathologic findings in surgically removed Ionescu-Shiley standard bovine pericardial heart valve bioprostheses (emphasis on progressive structural deterioration). *Circulation* 1987 **76** 618–627. (https://doi.org/10.1161/01.cir.76.3.618)

5 Walley VM & Keon WJ. Patterns of failure in Ionescu-Shiley bovine pericardial bioprosthetic valves. *Journal of Thoracic and Cardiovascular Surgery* 1987 **93** 925–933. (https://doi.org/10.1016/S0022-5223(19)37054-0)

6 Metivier F, Marchais SJ, Guerin AP, Pannier B & Gérard M. Pathophysiology of anaemia: focus on the heart and blood vessels. *Nephrology Dialysis Transplantation* 2000 **15** (Supplement_3) 14–18. (https://doi.org/10.1093/oxfordjournals.ndt.a027970)

7 Gómez M, Ble M, Cladellas M, Molina L, Comín-Colet J, Enjuanes C, Roqueta C, Soler C & Bruguera J. Effect of correction of anemia on echocardiographic and clinical parameters in patients with aortic stenosis involving a three-cuspid aortic valve and normal left ventricular ejection fraction. *American Journal of Cardiology* 2015 **116** 270–274. (https://doi.org/10.1016/j.amjcard.2015.04.020)

8 Reddy YNV, Melenovsky V, Redfield MM, Nishimura RA & Borlaug BA. High-output heart failure: a 15-year experience. *Journal of the American College of Cardiology* 2016 **68** 473–482. (https://doi.org/10.1016/j.jacc.2016.05.043)