Aortic root thrombus after left ventricular assist device implantation and aortic valve replacement

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Abstract

Data on the risk of aortic root thrombosis in patients with aortic valve replacement (AVR) and left ventricular assist device (LVAD) surgery are scarce. Two out of nine patients receiving AVR concomitant with LVAD surgery and two out of two patients receiving AVR on LVAD support, have an increased risk of aortic root thrombosis. Therefore, early anti-thrombotic therapy and vigilant diagnostic follow-up, using CT scans, are warranted to prevent thromboembolic events.

Keywords Left ventricular assist device; Aortic valve replacement; Aortic root thrombosis

Introduction

Currently, contemporary left ventricular assist devices (LVADs) utilize continuous flow, which are strongly associated with an increased risk for the development of aortic regurgitation (AR).¹ AR during LVAD support is associated with a negative impact on haemodynamics, hospitalization, and overall survival. Therefore, concomitant aortic valve (AV) replacement (AVR) is recommended in patients with moderate-to-severe AR.² Changes in the blood flow in the aortic root increase the risk of thromboembolic events. However, data on the risk of aortic root thrombosis and stroke after AVR concomitant with LVAD surgery are scarce. Therefore, we retrospectively reviewed all consecutive HeartMate II (HMII; n = 62) and HeartMate 3 (HM3; n = 42) implantations performed between December 2006 and December 2018 in our centre.

Case report

During this period, 11 (11%) patients received an AVR: nine concomitant during LVAD surgery, one trans-catheter AVR 337 days post-LVAD surgery, and one surgical AVR 520 days post-LVAD surgery (Table 1). In all patients, a computed tomography (CT) angiogram was performed to visualize the AVR position and function. After a median follow-up of 23.5 days (20.0–654.0) post-LVAD surgery, four patients (36%) were diagnosed with an aortic root thrombosis with CT angiogram (Figure 1). In three patients, the CT angiogram was performed during regular follow-up, while in one patient, transthoracic echocardiogram (TTE) results were suspicious for aortic root thrombosis, which was confirmed on CT angiogram. In contrast, none of the patients without an AVR were diagnosed with an aortic root thrombosis. Of the four patients diagnosed with an aortic root thrombosis, all appears to originated from the left coronary cusp but effected all the cusps and were between 3 and 5 mm in size, all preventing the AV to open. The aortic anatomy on the CT angiogram was compared between both patient groups, no differences in aortic root diameter were observed, and no aortic root pathology increasing the risk for aortic root thrombosis was identified.

No significant differences were observed in the platelet counts pre-LVAD (181.0 [157.0–211.0] vs. 167.5 [115.3–204.0], respectively, P = 0.788) and post-LVAD surgery (102.0...
### Table 1 | Clinical features of individual patients with aortic valve replacement

| Patient | 1  | 2  | 3  | 4  | 5  | 6  | 7  | 8  | 9  | 10 | 11 |
|---------|----|----|----|----|----|----|----|----|----|----|----|
| **Baseline** |    |    |    |    |    |    |    |    |    |    |    |
| Age | 55 | 52 | 61 | 52 | 39 | 24 | 63 | 65 | 53 | 56 | 59 |
| Gender | Male | Male | Male | Male | Male | Male | Male | Female | Male | Male | Female |
| HF aetiology | DC | IC | DC | DC | DC | IC | DC | DC | IC | IC |  |
| eGFR pre-LVAD, mL/min | 48 | 24 | 65 | 49 | 53 | 33 | 14 | 38 | 24 | 49 | 22 |
| ASAT pre-LVAD, U/L | 25 | 23 | 47 | 44 | 19 | 1071 | 84 | 43 | 73 | 38 | 39 |
| ALAT pre-LVAD, U/L | 18 | 48 | 38 | 24 | 16 | 996 | 26 | 44 | 140 | 54 | 30 |
| Gamma-GT pre-LVAD, U/L | 67 | 204 | 139 | 83 | 66 | 15 | 97 | 132 | 100 | 683 | 48 |
| Alkaline phosphatase pre-LVAD, U/L | 41 | 135 | 112 | 88 | 102 | 39 | 177 | 139 | 144 | 310 | 127 |
| Bilirubin pre-LVAD, μmol/L | 21 | 8 | 10 | 51 | 27 | 43 | 14 | 43 | 70 | 27 | 37 |
| MELD score pre-LVAD | 22 | 20 | 15 | 23 | 20 | 26 | 30 | 16 | 28 | 14 | 29 |
| Platelet count pre-LVAD, 10⁹/L | 157 | 182 | 221 | 170 | 211 | 93 | 104 | 149 | 181 | 186 | 210 |
| INR pre-LVAD | 1.9 | 1.2 | 1.8 | 1.9 | 2.0 | 2.0 | 1.6 | 1.6 | 1.8 | 1.2 | 2.9 |
| LVAD type | HMII | HMII | HMII | HMII | HMII | HMIII | HMIII | HMIII | HMIII | HMIII | HMIII |
| LVAD indication | BTT | BTT | BTT | BTT | BTT | BTT | BTT | DT | BTC | BTT | DT |
| Degree of AR (0–4) | 4 | 3 | 2 | 4 | 3 | 2 | 3 | 2 | 4 | 4 | 4 |
| **Post-LVAD** |    |    |    |    |    |    |    |    |    |    |    |
| Days until adequate heparin level | 2 | 6 | 4 | 2 | 4 | 4 | 7 | 1 | 3 | 2 | 4 |
| Days until introduction aspirin | 11 | 633^a | 5 | 13 | 5 | 39 | 32 | 12 | 9 | — | — |
| Platelets count post-LVAD, 10⁹/L | 97 | 113 | 160 | 102 | 156 | 52 | 75 | 62 | 95 | 119 | 105 |
| MAP (mmHg) | — | 92 | 88 | 84 | 88 | 87 | 83 | 86 | 88 | 84 | — |
| LVAD speed at last TTE | 9200 | 9000 | 8600 | 9000 | 9000 | 5300 | 5200 | 5100 | 5500 | 5300 | 5300 |
| Aortic valve opens at last TTE | No | No | No | No | Minimal opening | No | No | No | Yes | No | No |
| ART on TTE | No | No | No | No | No | No | No | Yes (22 days post-LVAD) | No | Yes (33 days post-TAVR) |  |
| ART on CT-a Outcome | No | No | No | No | No | No | No | Yes (27 days post-AVR) | No | Yes (30 days post-TAVR) |  |
| Days on LVAD support | 750 | 2163 | 939 | 1465 | 1359 | 622 | 564 | 398 | 167 | 599 (39 days with AVR) |  |

(Continues)
Additionally, none of the patients had a history of bleeding disorders or thromboembolic events, such as stroke or deep vein thrombosis. Directly post-operatively, from Day 1 post-surgery, heparin was introduced with gradual increasing doses in both patients diagnosed with an aortic root thrombosis and those free of aortic root thrombosis. No difference was seen in the time-to-therapeutic heparin dosage between the groups: the median time of 3.5 (1.0–5.0) and 4.0 (2.0–7.0) days, respectively. In both patient groups, some patients reached a therapeutic heparin dosage owing to post-operative bleeding events leading to the temporary lowering of the heparin dosages. When patients were discharged from the intensive care unit and had no bleeding events, the intravenous heparin was switched for an oral vitamin K antagonist. Aspirin was introduced later post-LVAD surgery in patients diagnosed with an aortic root thrombosis as compared with patients free of aortic root thrombosis [median time-to-introduction of aspirin 22.0 (12.0–32.0) vs. 10.0 days (5.0–39.0), respectively]. The delayed introduction of aspirin in both groups was mainly caused by a high bleeding risk or actual bleeding events.

One patient diagnosed with an aortic root thrombosis suffered from an ischaemic stroke 24 days post-AVR. Unfortunately, this patient suffered from extensive neurological damage and passed away 39 days post-AVR. The follow-up in the other patients was without any thromboembolic events.
Discussion

The material of bioprosthetic valves is thrombogenic and activates the coagulation cascade, increasing the risk for thrombus formation in patients with an AVR. Aortic root thrombosis can increase the risk of thromboembolic events, such as ischaemic stroke. Additionally, patients with an aortic root thrombosis are at risk for occlusion of the ostium of the left main coronary, especially if the thrombosis is formed in the left coronary cusp. Early introduction of antiplatelet and anticoagulation therapy is very important, because thrombi might start forming in the first 24 h after implantation and remained elevated in the first 3 months. The importance of the early introduction of, especially, antiplatelet (Day 1 post-implantation) along with the anticoagulation therapy is also shown in our patients, because three out of four patients developed an aortic root thrombosis shortly after AVR procedure. Additionally, minimal or lack of AV opening, owing to excessive LV unloading by the LVAD, causes a blind pouch in the aortic root, increasing the risk of thrombus formation, especially in patients who are longer on LVAD support. Ideally, LVAD speed settings are optimized, resulting in optimal LV unloading and an intermittent opening AV. However, this can be challenging, as demonstrated in our patients: optimal LVAD speed settings were determined based on clinical and TTE parameters. However, hardly any patient had an intermittent opening AV.

Three out of four patients who were diagnosed with an aortic root thrombosis had ischaemic heart disease as the underlying cause of their heart failure. It is known that patients with ischaemic heart disease have an increased risk for thrombus formation. However, whether these patients with LVAD implantation and AVR have an increased risk for aortic root thrombosis is unknown.

TTE examination is commonly used in the follow-up of LVAD patients. However, diagnosing an aortic root thrombosis on the basis of TTE images can be difficult, leading to the underdiagnosis of aortic root thrombosis. In non-LVAD patients, trans-oesophageal echocardiography and CT angiogram have shown to be superior in detecting aortic root thrombosis. Similarly, the diagnosis of AV thrombosis was only made based on CT angiogram results in our patients, indicating that CT angiogram might be superior over TTE in LVAD patients with an AVR as well.

The use of anticoagulation therapy after AVR has shown to be effective in patients without an LVAD, and the International Society for Heart & Lung Transplantation recommends starting aspirin and adequate heparin therapy within 1 day post-LVAD implantation. However, studies investigating the optimal timing of anticoagulation and antiplatelet therapy initiation after an AVR in LVAD patients are lacking. The current European Society of Cardiology/European Association for Cardio-Thoracic Surgery Guidelines advice for the prompt introduction of aspirin, that is, on Day 1 post-operative AVR.

Conclusions

In conclusion, LVAD patients with an AVR had an increased risk of aortic root thrombosis and probably increased risk for ischaemic stroke. To prevent these thromboembolic events, early introduction of anti-thrombotic therapy should carefully been balanced against the bleeding risk. Furthermore, vigilant diagnostic follow-up is needed for the timely diagnosis of aortic root thrombosis, potentially using CT scans, although this might increase the risk of radiation exposure. Our results are hypothesis generating and are limited by the small sample size and lack of a randomized controlled comparison between patients with and without aortic AVR. Therefore, prospective, multicentre studies are urgently needed to elucidate aortic root thrombosis after AVR and LVAD implantation and the possible risk of thromboembolic events.

Conflict of interest

None declared.

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References

1. Deo SV, Sharma V, Cho YH, Shah IK, Park SJ. De novo aortic insufficiency during long-term support on a left ventricular assist device: a systematic review and meta-analysis. ASAIO J 2014; 60: 183–188.
2. Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA, Morgan JA, Arabia F, Bauman ME, Buchholz HW, Deng M, Dickstein ML, el-Banayosy A, Elliot T, Goldstein DJ, Grady KL, Jones K, Hryniewicz K, John R, Kaaan A, Kusne S, Loewe M, Massicotte MP, Moazami N, Mohacsi P, Mooney M, Nelson T, Pagani F, Perry W, Potapov EV, Eduardo Rame J, Russell SD, Sorensen EN, Sun B, Strueber M, Mangi AA, Petty MG, Rogers J. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. J Heart Lung Transplant 2013; 32: 157–187.
3. Lim WY, Lloyd G, Bhattacharyya S. Mechanical and surgical bioprosthetic valve thrombosis. Heart 2017; 103: 1934–1941.
4. Falk V, Baumgartner H, Bax JJ, De Bonis M, Hamm C, Holm PJ, Jung B, Lancellotti P, Lansac E, Muñoz DR, Rosenhek R. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur J Cardio-Thorac Surg* 2017; 52:616–664.

5. Jilaihawi H, Asch FM, Manasse E, Ruiz CE, Jelnin V, Kashif M, Kawamori H, Maeno Y, Kazuno Y, Takahashi N, Olson R, Alkhatib J, Berman D, Friedman J, Gellada N, Chakravarty T, Makkar RR. Systematic CT methodology for the evaluation of subclinical leaflet thrombosis. *JACC Cardiovasc Imaging* 2017; 10:461–470.