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CASE REPORT

Monitoring pulmonary pressures during long-term continuous-flow left ventricular assist device and fixed pulmonary hypertension: redefining alleged pathophysiological mechanisms?

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Abstract

Pulmonary hypertension (PH) type II (classified by the World Health Organization) is a common complication in chronic left-sided heart failure. In advanced heart failure therapy, fixed PH is an absolute contraindication for heart transplantation after which a left ventricular assist device (LVAD) is the only remaining option. With remote monitoring, we can now continuously evaluate the pulmonary artery pressures during long-term LV unloading by the LVAD. In this case, we demonstrate that fixed PH can be reversed with LVAD implantation, whereby previous thoughts of this concept should be redefined in the era of assist devices.

Keywords Heart failure; Pulmonary hypertension; CardioMEMS; LVAD; HeartMate 3

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Introduction

In patients with chronic left-sided heart failure (HF), pulmonary hypertension (PH) (classified by the World Health Organization as group 2) is a common complication.[1] PH occurs in up to 60% of the patients with severe left ventricular systolic dysfunction, and up to 70% in patients with HF with preserved ejection fraction.[2] HF causes chronic pulmonary congestion, resulting in elevated pulmonary capillary wedge pressure (PCWP). The right ventricle (RV) adapts slowly over time in order to overcome the increasing PCWP, leading to increasing pulmonary artery pressures (PAPs). Over time, this process results in pulmonary capillary and arterial remodelling. The vascular wall stiffens and loses its elasticity and ability to compensate for the higher pressures, resulting in elevated pulmonary vascular resistance (PVR). Additionally, several pulmonary diseases affect the PVR and cause PH. At screening for candidacy for heart transplantation (HTx), the standard procedure is to perform a right heart catheterization (RHC) to study these aspects in detail. If at the Swan–Ganz measurement the patient has PH, we perform a vasodilator test to evaluate the reversibility of PH and PVR. Reversibility is crucial in potential HTx candidates. Because the RV of the donor heart will not be capable to build up PAPs to overcome the fixed high PVR, after a period of stunning by ischemia, the RV is most likely to fail immediately. Left ventricular assist device (LVAD) therapy can be successful in lowering PAPs by unloading the left ventricle, which will aid in the treatment of PH caused by left-sided heart disease.[3] However, limited data are available on the topic whether fixed PH can be reversed as well. The acute and chronic effects of LVAD therapy on PH have not been clearly investigated. The recently introduced CardioMEMS sensor offers the possibility to study this concept, because it allows for remote daily monitoring of PAPs, even in LVAD patients,[4] as we have shown in our case.

Case report

A 53-year-old man with a history of severe dilated cardiomyopathy was admitted with progressive HF, despite maximal tolerated medical therapy. During the admission, the patient was screened for both HTx and LVAD implantation. The RHC revealed a cardiac output of 3.8 L/min, PAP 61/31 mmHg (mean 43), PCWP 28 mmHg, and PVR 316 dynes/s/cm^5 (3.9 Woods). During the vasodilator test of reversibility, intravenous nitroglycerin was up-titrated to maximum tolerated dosage (100 μg/min) without inducing systemic hypotension; PAP [47/23 mmHg (34)], PCWP (20 mmHg), and the PVR (295 dynes/s/cm^5, 3.7 Woods) remained elevated, confirming the diagnosis of fixed PH. In the multidisciplinary heart team, the patient was rejected as candidate for HTx owing to irreversible PH and was accepted for LVAD (HeartMate 3, Abbott Inc, Atlanta, GA, USA) as bridge to transplant or destination therapy. A CardioMEMS device was implanted, followed by LVAD implantation 2 weeks later. Post-operatively, the LVAD support provided additional room for further up-titration of the medical therapy. Echocardiography and PAPs were used to up-titrate renin–angiotensin system inhibition, mineralocorticoid receptor antagonist, and diuretics and the LVAD speed settings. The patient recovered well with an uncomplicated course and was discharged home.

In the outpatient setting, haemodynamic feedback provided by the CardioMEMS was used for further treatment optimization. A combination of hydralazine/isosorbide dinitrate was started and slowly up-titrated resulting in a small decline in PAP. However, this was limited owing to complaints of dizziness.

Approximately 160 days after LVAD implantation, the patient was admitted owing to dehydration and hypotension due to insufficient intake, which was identified by the sudden drop in PAPs. During admission, antihypertensive medication and diuretics had to be lowered or stopped, allowing the renal function to recover. After discharge, medication was up-titrated again to maximum tolerated dosage, limited once more by complaints of dizziness. Even though further up-titration of medication was not possible, the mean PAP (mPAP) continued to decline gradually and then finally normalized. Approximately 290 days post-LVAD implantation, a consistent mPAP $<$ 25 mmHg was reached. During follow-up, the patient regularly underwent echocardiography, demonstrating a stable RV function and only a minor tricuspid valve regurgitation, suggesting that the decline in mPAP was caused by reversibility of the 'fixed' PH and was not due to a decline in RV function. Currently, the candidacy for HTx is re-evaluated, and likely no cardiac issues will be raised for acceptance on the waiting list.

Discussion

This case report demonstrates for the first time the continuous follow-up of PAP data in a LVAD patient with fixed PH, for up to 300 days post-LVAD implantation. This case demonstrates that LVAD therapy is a successful treatment for lowering PAP in patients with fixed PH, additional to optimal medical treatment. The reversibility of PH and candidacy for HTx thereby become a more dynamic state, which changes views on these programmes in light of expanding LVAD programmes.

The increase of left ventricular filling pressure leads to an increase in post-capillary pressure and elevated PCWP in the pulmonary circulation. This leads to endothelial dysfunction, making the vascular walls less flexible owing to smooth muscle cell hypertrophy and hyperplasia, increasing the PVR. Thereby, PH arises, followed by remodelling of the arterial wall. This is characterized by medial hypertrophy and intimal fibrosis. Longstanding PH can grow to a state of fixed PH. Current data are conflicting about the reversibility of severe or fixed PH, with some data suggesting that LVAD therapy can reverse fixed PH. However, it remains unclear whether this is caused by remodelling of the pulmonary vascular wall or LV unloading and remodelling. Furthermore, the cut-off between fixed and reversible PH is unclear, and there is no agreement on the time needed to reach irreversibility.[5]

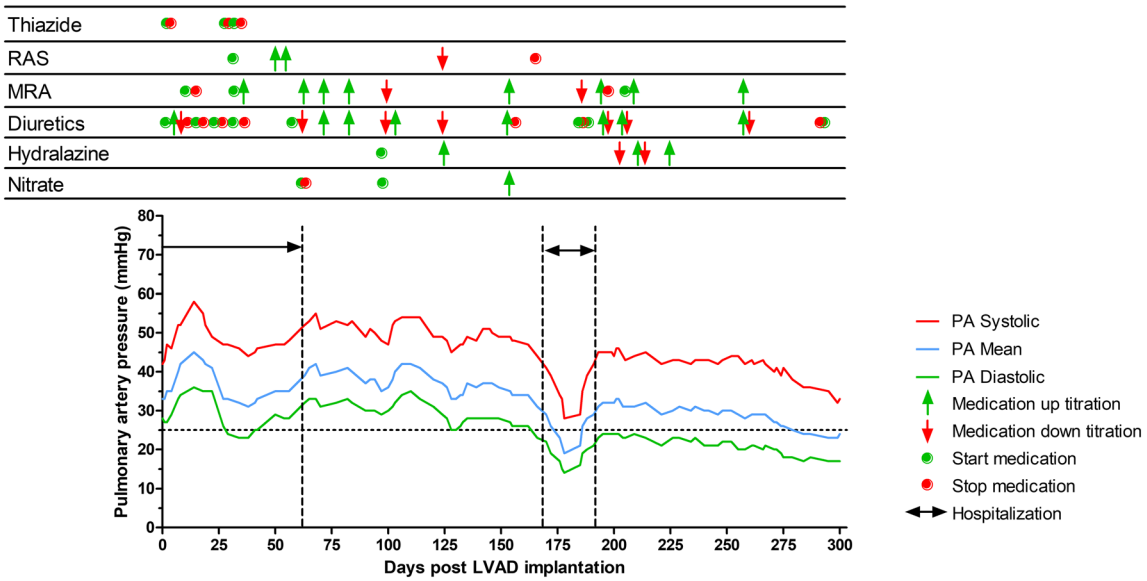
Continuous-flow LVADs unload the left ventricle and lower the cardiac filling pressures. As has been shown previously, LVAD therapy is more effective in treating 'fixed' PH than is maximal medical therapy.[3,5] The CardioMEMS device allows for daily PAP readings (*Figure 1*) and was used to observe the haemodynamic changes after medication changes. As shown in this case, up-titrating the medical therapy to maximal tolerated dosage did not lead to a normalization of the PAPs. However, as shown, during the longer-term follow-up, the PAPs slowly declined, and after 0.5 to 1 year of LVAD support, the PAPs normalized with an mPAP $<$ 25 mmHg. These results show the natural decline of PAP while on LVAD support besides the haemodynamic effects of maximal tolerated medical therapy.

Previous studies investigating the reversibility of fixed PH were limited to repeated invasively measured PAP readings, instead of continuous PAP readings. So the timing of reversibility of fixed PH is still unclear.

Mikus *et al*. investigated the reversibility of PH during LVAD support at 6, 12, and 18 months of follow-up and concluded that the biggest reduction in PAP will occur within the first 6 months post-LVAD implantation.[5] In contrast, our case shows a slow decline in PAP over time in which the PAP of our patient normalized only after 300 days on LVAD support. This result suggests that the decline of PAP can occur past the 6 months suggested in the previous study.

Reversibility of fixed PH is very important because fixed PH is a contraindication for HTx. When HTx is performed in a patient with fixed PH, the stunned RV of the donor could not overcome the high afterload and fails owing to elevated

Figure 1 Daily pulmonary artery pressure readings and medication changes. LVAD, left ventricular assist device; MRA, mineralocorticoid receptor antagonist; PA, pulmonary artery; RAS, renin–angiotensin system.



PVR. RV failure is a major cause of both mortality and morbidity after LVAD implantation as well (20–50% of patients).[6] By lowering PAP, there is more potential to improve or maintain RV function at long-term LVAD support, which is essential, especially in destination therapy. This could help in the long-term survival of LVAD patients who depend on a good working RV for a proper functioning LVAD. This case demonstrates that the haemodynamic feedback, provided by the CardioMEMS, can be used to optimize medical therapy also in LVAD patients. And this provides feedback on haemodynamic changes, which could help to detect problems such as dehydration or decompensation in earlier stages.

Conclusions

Continuous-flow LVAD can reverse fixed PH, even after a period of 6 months on LVAD support. The CardioMEMS sensor enables to monitor and guide the treatment of PH in patients with an LVAD and severe PH.

Conflict of Interest

None declared.

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