Pulmonary function assessment post-left ventricular assist device implantation

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Abstract

Aim The lungs—and particularly the alveolar-capillary membrane—may be sensitive to continuous flow (CF) and pulmonary pressure alterations in heart failure (HF). We aimed to investigate long-term effects of CF pumps on respiratory function.

Methods and results We conducted a retrospective study of patients with end-stage HF at our institution. We analysed pulmonary function tests [e.g. forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1)] and diffusing capacity of the lung for carbon monoxide ($D_{LCO}$) from before and after left ventricular assist device (LVAD) implantation and compared them with invasive haemodynamic studies. Of the 274 patients screened, final study analysis involved 44 patients with end-stage HF who had CF LVAD implantation between 1 February 2007 and 31 December 2015 at our institution. These patients (mean [standard deviation, SD] age, 50 (9) years; male sex, n = 33, 75%) received either the HeartMate II (Thoratec Corp.) pump (77%) or the HeartWare (HeartWare International Inc.) pump. The mean (SD) left ventricular ejection fraction was 21% (13%). At a median of 237 days post-LVAD implantation, we observed significant $D_{LCO}$ decrease (−23%) since pre-implantation ($P < 0.001$). $\Delta D_{LCO}$ had an inverse relationship with changes in pulmonary capillary wedge pressure (PCWP) and right atrial pressure (RAP) from pre-LVAD to post-LVAD implantation: $\Delta D_{LCO}$ to $\Delta PCWP$ ($r = 0.50, P < 0.01$) and $\Delta D_{LCO}$ to $\Delta RAP$ ($r = 0.39, P < 0.05$). We observed other reductions in FEV1, FVC, and FEV1/FVC between pre-LVAD and post-LVAD implantation. In mean (SD) values, FEV1 changed from 2.3 (0.7) to 2.1 (0.7) ($P = 0.005$); FVC decreased from 3.2 (0.8) to 2.9 (0.9) ($P = 0.01$); and FEV1/FVC went from 0.72 (0.1) to 0.72 (0.1) ($P = 0.50$). Landmark survival analysis revealed that $\Delta D_{LCO}$ from 6 months after LVAD implantation was predictive of death for HF patients [hazard ratio (95% confidence interval), 0.60 (0.28–0.98); $P = 0.03$].

Conclusions Pulmonary function did not improve after LVAD implantation. The degree of $D_{LCO}$ deterioration is related to haemodynamic status post-LVAD implantation. The $\Delta D_{LCO}$ within 6 months post-operative was associated with survival.

Keywords Continuous flow pumps; $D_{LCO}$; Pulmonary circulation

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Introduction

In the past decade, left ventricular assist devices (LVADs) have become an integrated component of treatment algorithms for patients with end-stage heart failure (HF) in the clinical setting of lifelong destination therapy. Use of LVADs generating continuous flow (CF) has increased exponentially as survival rates have increased up to 80% at year 1 and ~70% at year 2 post-implantation.$^{1,2}$ Despite the evidence of beneficial effect of LVAD therapy on gross pulmonary haemodynamics,$^3$ respiratory failure occurs in 2.73 events per 100 patient-months in the first 12 months post-LVAD implantation, exceeding the rate of renal dysfunction or stroke or the incidence of right ventricle failure.$^4$ Furthermore, respiratory failure incidence in the LVAD population increased from the 2008–11 period to the 2012–14 period.$^4$ However, it is not clearly understood how LVADs influence the lungs.
The heart and lungs serve as an integrated organ system. They are linked neurohumorally and hemodynamically (e.g. atrial natriuretic peptide, brain-type natriuretic peptide, and angiotensin II). Structural and functional alterations of the lungs in HF are well described\(^6\) and correlate to HF severity and patient survival.\(^7\)

Therefore, it is hypothesized that the alteration in CF LVAD influences pulmonary function (PF) and is related to survival rate. However, knowledge is still lacking about the long-term effect of CF pumps on the lungs.\(^2,8,9\) Accordingly, the present retrospective study was to investigate changes in PF post-LVAD placement in relation to the haemodynamic changes and their association with survival.

### Methods

**Patients**

From the 274 patients screened, final study analysis involved 44 patients with end-stage HF who had CF LVAD implantation between 1 February 2007 and 31 December 2015 at Mayo Clinic in Rochester, Minnesota. Study participants included only the patients originally indicated as a bridge to transplant with pulmonary function tests (PFTs) and invasive haemodynamic studies available pre-LVAD and post-LVAD implantation as part of follow-up evaluation on waiting list. Patients with PFTs provided in non-hemodynamically stable conditions or with comments of not ‘adequate’ or poor effort were excluded, as were those who underwent cardiac transplant. In addition, patients with implanted pulsatile pumps were excluded; patients were excluded if they had received concomitant right ventricle mechanical support, had received extracorporeal membrane oxygenation perioperatively, or had missed post-LVAD PFT or invasive haemodynamic study follow-up. Patient demographic characteristics were evaluated for functional and haemodynamic qualities. Maximal exercise capacity test before LVAD implantation was available for 34 patients (77%) and showed a mean (SD) peak oxygen consumption at 11.8 (4.1) mL/kg/min.

**Statistical analysis**

Variables were summarized as mean (SD) for continuous measurements and frequency (percentage) for categorical measurements. Pre-implantation and post-implantation values were compared with the use of matched-pair \(t\)-test or Wilcoxon signed rank test. Pearson product moment correlation was conducted to test the relationship between pre-implantation and post-implantation values. For sub-analysis of PF and diffusion capacity, we grouped patients as within 6 months (6MG) and 12 months (12MG) post-LVAD on the basis of time when they had PFTs and \(D_{LCO}\) assessments. The groups were analysed separately. This approach allowed for analysis of changes in PFT data in earlier vs. later post-implantation periods. Cox proportional hazards model was used to assess survival experience of the two groups, and log-rank \(P\)-value and hazard ratio (HR) were reported. \(P < 0.05\) was considered statistically significant. Data were analysed through statistical software (JMP Pro 10; SAS Institute Inc.).

**Results**

Patient demographic characteristics, including medical history, cardiac risk factors, and related blood marker levels, were analysed for functional and haemodynamic qualities (Table 1).
**Table 1** Characteristics of the 44 study participants

| Characteristic | Valuea |
|----------------|--------|
| Baseline       |        |
| Age, year      | 59 (9) |
| Male sex       | 33 (75)|
| Weight, kg     | 87.4 (14.6) |
| Height, m      | 1.75 (0.08) |
| Body mass index, kg/m² | 28.7 (4.7) |
| Cardiomyopathy |        |
| Non-ischaemic dilated | 23 (52) |
| Ischaemic      | 17 (39) |
| Hypertrophic   | 4 (9)  |
| Diabetes mellitus | 15 (34) |
| Hypertension   | 21 (13) |
| COPD           | 8 (18) |
| Obstructive sleep apnoea | 16 (36) |
| Chronic kidney disease | 30 (68) |
| Hyperlipidaemia| 19 (43) |
| Atrial fibrillation | 25 (56) |
| Smoking        | 10 (22) |
| Functional class NYHA   |        |
| I              | 4 (10) |
| III+           | 40 (90) |
| Treatment      |        |
| β-Blocker      | 41 (93) |
| ACE-I/ARB      | 24 (54) |
| Amiodarone     | 26 (59) |
| Loop diuretic, >80 mg/day | 26 (59) |
| HeartMate II LVADb | 34 (77) |
| HeartWare LVADC | 10 (23) |
| LVEF, %        | 21 (13) |
| LVEDD, mm      | 67.3 (12.2) |
| Haemoglobin, g/dL | 11.5 (1.7) |
| Leucocytes, ×10⁹/L | 7.5 (2.6) |
| Platelets, ×10¹¹/L | 179 (59) |
| Creatinine, mg/dL | 1.4 (0.5) |
| Serum urea nitrogen, mg/dL | 27.1 (16.9) |
| Potassium, mmol/L | 4.1 (0.4) |
| Total bilirubin, mg/dL | 21.4 (12.5) |
| AST, U/L       | 62.5 (143.8) |
| ALT, U/L       | 62.4 (188.2) |
| NT-proBNP, pg/mL | 5744 (5868) |

**Functional and haemodynamic**

| INTERMACS class | I | II | III | IV | V | VI |
|-----------------|---|----|-----|----|---|----|
| RAP, mm Hg      | 13.9 (6.3) | 14.0 (3.2) |
| PAP, mm Hg      | 53.8 (14.8) | 25.8 (8.2) |
| PADP, mm Hg     | 38.0 (11.4) | 22.9 (7.2) |
| CO, L/min/m²    | 4.0 (1.4) | 20.0 (6.6) |
| CIx, L/min/m²   | 3.9 (2.6) | 7.9 (5.3) |

**Pulmonary function tests after left ventricular assist device implantation**

| Character | Value |
|-----------|-------|
| FVC, %    | 66.3% (17.3%) |
| FEV₁, %   | 60.6% (19.6%) |
| FEF₂⁵, %  | 61% (15%) |
| FEF₂⁰, %  | 48% (17%) |
| FEV₁/FVC  | 71% (14%) |

**Pulmonary function and diffusing capacity of the lung for carbon monoxide post-left ventricular assist device implantation**

Pre-LVAD implantation, impaired age-predicted %FVC, %FEV₁, and %D_LCO were observed and were further impaired post-LVAD (median, 237 days post-LVAD) (Figure 1). Table 2 illustrates the alteration in PF pre-LVAD and post-LVAD implantation. Significant relationships were found in FVC, FEV₁, and D_LCO between pre-LVAD and post-LVAD (r = 0.59, P = 0.001; r = 0.70, P < 0.001; and r = 0.74, P < 0.001; respectively).

**Subanalysis of pulmonary function based on time since left ventricular assist device implantation**

In subsequent analysis, the 6MG (n = 14; median, 103 days post-LVAD) showed significant decreases in mean (SD) D_LCO [16.8 (4.5) to 13.2 (6.0) mL/mm Hg/min, P = 0.05], %D_LCO [61% (15%) to 48% (17%), P = 0.002], and D_LCO to alveolar volume (Vₐ) [3.6 (0.8) to 3.0 (1.0), P = 0.01] after LVAD. However, no significant changes in %FEV₁ [64% (19%) to 59% (21%), P = 0.27] and %FVC [71% (17%) to 63% (18%), P = 0.07] were observed. In contrast, the 12MG (n = 28; median, 370 days post-LVAD) showed significant declines in mean (SD) D_LCO [18.27 (5.2) to 14.24 (4.8) mL/mm Hg/min, P < 0.001], %D_LCO [67% (20%) to 52% (16%), P < 0.001], D_LCO to Vₐ ratio [3.8 (0.9) to 3.2 (0.8), P < 0.001], %FEV₁ [2.3 (0.7) vs. 2.0 (0.6), P = 0.04], %FVC [66.3% (17.3%) vs. 60.6% (19.6%), P = 0.04], and %FVC [71% (14%) vs. 64% (16%), P = 0.01].

**Pulmonary vascular hemodynamic post-left ventricular assist device implantation**

In analysis of haemodynamics (n = 28; median, 370 days post-implantation), mean (SD) PCWP was reduced by 10.1 (1.6) mm Hg from pre-LVAD to post-LVAD (P < 0.01), indicating a decrease in left ventricular (LV) filling pressure (Table 3). Similarly, reductions were found in mean (SD) mPAP by 15.1 (2.2) mm Hg (P < 0.01) and PVR by 1.4 (0.3) mm Hg (P < 0.01) from pre-LVAD implantation. These results suggest that LV filling pressure and PVR were improved following LVAD implantation. In addition, the data revealed a significant inverse relationship between ΔD_LCO and ΔPWP, pulmonary artery pressure (PAWP), and pulmonary capillary wedge pressure (PCWP). Furthermore, ΔD_LCO was inversely related to ΔPWP (r = 0.39, P < 0.05). However, trends noticed in other variables, including ΔD_PAP, ΔPWP, and ΔPVR, were not related to ΔD_LCO (P > 0.05) in the available data. Figure 2 illustrates the relationship between changes in PCWP and D_LCO.
Survival analysis

Survival analysis from a landmark point of 6 months showed that $\Delta D_{LCO}$ can be a significant predictor of death for LVAD patients [HR (95% confidence interval, CI), 0.60 (0.28–0.98); $P = 0.03$]. However, this predictive effect was attenuated when analysed within 12 months [HR (95% CI), 0.88 (0.72–1.06); $P = 0.22$]. No patient had transplant within 6 months; however, five patients underwent transplant within 12 months. After adjustment for transplant within 12 months, the effect of $\Delta D_{LCO}$ on death was not altered [HR (95% CI), 0.88 (0.70–1.07); $P = 0.20$]. Kaplan–Meier survival curve is carried from the first year on the basis of $\Delta D_{LCO}$ stratification (Figure 3). Furthermore, $D_{LCO}$ also appeared to be a significant predictor of death at 6 months [HR (95% CI), 0.58 (0.28–0.85); $P = 0.03$] and 12 months [HR (95% CI), 0.83 (0.70–0.96); $P = 0.02$] post-LVAD implantation (Figure 4).

Table 2 Pulmonary function change before to after left ventricular assist device implantation

| Variable                  | LVAD implantation, Mean (SD) | p-value |
|---------------------------|------------------------------|---------|
| $D_{LCO}$, mL/mm Hg/min   | 18.3 (5.2)                   | <0.01   |
| $%D_{LCO}$                | 69 (18)                      | <0.01   |
| $D_{LCO}$ to $V_A$ ratio  | 3.8 (0.8)                    | <0.01   |
| $FEV_1$, L                | 2.3 (0.7)                    | <0.01   |
| $%FEV_1$                  | 68 (17)                      | 0.01    |
| $FVC$, L                  | 3.2 (0.8)                    | 0.01    |
| $%FVC$                    | 73 (14)                      | <0.01   |
| $FEV_1$ to $FVC$ ratio    | 0.72 (0.1)                   | 0.50    |

$D_{LCO}$ indicates diffusing capacity of the lung for carbon monoxide; $D_{LCO}/V_A$, diffusing capacity of the lung for carbon monoxide to alveolar volume; LVAD, left ventricular assist device; $%D_{LCO}$, age % predicted diffusing capacity of the lung for carbon monoxide corrected for haemoglobin; $%FEV_1$, age % predicted forced expiratory volume in 1 s; $%FVC$, age % predicted forced vital capacity.

Table 3 Change in pulmonary vascular haemodynamics before to after left ventricular assist device implantation

| Variable                  | LVAD implantation, Mean (SD) | p-value |
|---------------------------|------------------------------|---------|
| RAP, mm Hg                | 14.7 (6.0)                   | 0.03    |
| PASP, mm Hg               | 55.8 (13.0)                  | <0.01   |
| PAPD, mm Hg               | 26.7 (8.1)                   | <0.01   |
| mPAP, mm Hg               | 39.7 (11.4)                  | <0.01   |
| PCWP, mm Hg               | 23.4 (5.9)                   | <0.01   |
| CO, L/min                 | 4.3 (1.5)                    | 0.96    |
| Clx, L/m³                 | 2.1 (0.7)                    | 0.55    |
| PVR, Woods U              | 3.8 (1.7)                    | <0.01   |
| PVRi, Woods U/m²          | 7.7 (3.3)                    | <0.01   |

Clx, cardiac index; CO, cardiac output; LVAD, left ventricular assist device; mPAP, mean pulmonary artery pressure; PAPD, pulmonary artery diastolic pressure; PASP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; PVRi, pulmonary vascular resistance index; RAP, right atrial pressure; SD, standard deviation.

Discussion

In the present study, we observed significant reductions in $D_{LCO}$ and PF post-LVAD implantation, with decreases in pulmonary arterial resistance, mPAP, and PCWP compared with pre-LVAD implantation. However, degree of $D_{LCO}$ deterioration post-LVAD was relative to the successful intravascular volume management post-LVAD.

A remarkable $D_{LCO}$ decrease in the 6MG without significant changes in $%FEV_1$ and $%FVC$ may suggest early alteration in $D_{LCO}$ post-LVAD implantation compared with changes in $%FEV_1$ and $%FVC$, which may develop later. Furthermore, the degree of reduction in $D_{LCO}$ within 6 months post-LVAD implantation was significantly associated with survival.
Forced vital capacity

With a shared intrathoracic space, an LVAD patient has to accommodate an alien object (pump) with a gross volume from ~50 mL (HeartWare) to ~63 mL (HeartMate II), excluding inflow and outflow conduits, which anatomically has a constant role in certain limitations of maximal inspiration volumes. Cardiothoracic surgery can transiently decrease spirometric measurements.\(^1\)–\(^3\) In addition, respiratory muscle weakness and consequent reduction in PF have been found in patients with chronic HF.\(^1\) The acute post-surgical PF changes likely have a minor effect on the observed reduction in FVC due to a longer follow-up. Nevertheless, FVC reduction occurs by ~300 mL in nearly 9 months post-surgery, likely due to a combination of aetiological factors.

Forced expiratory volume in 1 s

Data also showed a reduction in %FEV\(_1\) from pre-LVAD to post-LVAD implantation [mean (SD), 68% (17%) to 62% (19%), \(P = 0.01\)] with no significant change in FEV\(_2\) to FVC ratio and no significant difference between the 6MG and 12MG. Obstructive PF abnormalities are traditionally associated with congestive HF, mainly as effects of post-capillary pulmonary hypertension.\(^5\)\(^,\)\(^6\) Both devices in the present study provide a similar level of circulatory support, allowing improved control of fluid congestion because of increased renal perfusion and a positive effect on LV unloading.\(^1\)\(^7\)

In concordance with previous literature, the haemodynamic follow-up data showed significant reductions in RAP and PCWP (Table 3). Despite the haemodynamic and volume optimization post-LVAD implantation documented in approximately two-thirds of the studied population, the data did not show an improvement in %FEV\(_1\) that could have been speculated. Therefore, we hypothesized that the mechanism of airflow obstruction post-LVAD might be different from a conventional HF model. The bronchial circulation surrounding the bronchial tree is the only portion of lung vasculature directly exposed to CF conditions. This exposure could lead to potential engorgement of the bronchial vascular network.

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during LVAD support, thereby contributing to bronchial obstruction. The currently available data do not provide information to confirm the proposed hypothesis, and thus, this continues to be speculation.

Diffusing capacity of the lung for carbon monoxide

Remarkably, the study data showed a profound decrease in pulmonary $D_{\text{LCO}}$ post-LVAD implantation consistent with findings of Mohamedali et al.\textsuperscript{18} This decline remained significant when corrected for $V_c$ (Figure 2) and was clearly evident in subsequent analyses of the 6MG and 12MG.

Because of the retrospective nature of our study, it lacks early post-implantation haemodynamic data, but we can anticipate a decrease of pulmonary pressures in ~3 to 6 months post-LVAD implantation.\textsuperscript{19,20} Therefore, we suggest that the early decrease in $D_{\text{LCO}}$ is likely related to changes in pulmonary vascular pressures post-LVAD implantation. However, data supported the relationship between optimal haemodynamic unloading and change in diffusing capacity post-LVAD implantation (Figure 3). Presented data did not show any other significant relationship between pulmonary vascular pressures and diffusing capacity, probably because of an inability to timely match $D_{\text{LCO}}$ data with invasive haemodynamic studies.

The inverse relationship between improved haemodynamics and $D_{\text{LCO}}$ is of particular interest. Despite the fact that the study design does not allow for direct understanding, the literature provides several possible concepts, which may support current findings.

The complex relationship between $D_{\text{LCO}}$ and the pulmonary vascular pressures and PVR has been described in a chronic HF model.\textsuperscript{5} In particular, diffusion capacity is a point of heart and lung concurrence through its two components: membrane conductance, a term describing rate of reaction of the gas with haemoglobin, and capillary blood volume ($V_c$). Decreased membrane conductance, observed in severe chronic HF\textsuperscript{21} and inversely correlating with PVR,\textsuperscript{22} could represent thickening of the alveolar-capillary barrier from fluid accumulation or fibrosis. According to Gehlbach and Geppert,\textsuperscript{5} this phenomenon has been thought to be a protective mechanism against pulmonary oedema in patients with chronic pulmonary venous hypertension.

First, after the heart transplant, fibrotic transformation of the alveolar-capillary membrane may not be fully reversed.\textsuperscript{23} In addition, $V_c$ initially decreases, but it eventually increases over time. These fibrotic formations may contribute to a decrease in lung diffusion.\textsuperscript{23} A study by Ewert et al.\textsuperscript{24} reported that lung diffusion did not improve after orthotopic heart transplant and could be the effect of cyclosporine. It is possible that long-term elevation of neurohumoral drive potentiated by CF may contribute to some of the observed changes post-LVAD implantation.\textsuperscript{5,25} However, further studies are needed to determine this mechanism.

Second, in healthy condition, the alveolar type II cell transport of sodium ion provides the major force for excessive water removal from the alveolar space (Starling forces).\textsuperscript{26} This mechanism of sodium/water conductance system is important for optimal gas transfer and is altered in HF with increased PCWP.\textsuperscript{27} Interestingly, the optimization of the pulmonary pressures may not improve the transport mechanisms in chronic HF.\textsuperscript{28} In addition, low pulse pressure of CF LVAD negatively affects nitric oxide production, inflammatory biomarker levels (e.g. tumour necrosis factor-$\alpha$ and C-reactive protein),\textsuperscript{29} and endothelial function.\textsuperscript{8,29,30} Chronic inflammation may possibly contribute to alteration of sodium/alveolar fluid balance post-LVAD implantation. Alterations of endothelial and alveolar cells are thought to be primarily responsible for lung diffusion decrease in patients with HF. Nevertheless, experimental observations are also consistent with an involvement of alveolar water mechanism.\textsuperscript{26}

Third, Permutt and Caldini\textsuperscript{31} showed that it is the static recoil pressure relative to the left atrial pressure (and not a total vascular resistance) that provides the driving pressure back to the heart.\textsuperscript{32,33} The magnitude of the static pressure is determined by the blood volume and the elastic properties of the blood vessels. An increase in $V_c$ is associated with an increase in the upstream end of the driving pressure returning blood to the heart.\textsuperscript{34} The blood volume distribution is also affected by the influence of one ventricle on the other through ventricular interdependence.\textsuperscript{35}

For a specified increase in $V_c$, the increase in static recoil is proportional to the reciprocal of the compliance of the pulmonary circulation.\textsuperscript{34,36} Therefore, variable functional uncoupling of right ventricular and LV performance, described by Uriel et al.,\textsuperscript{37} post-LVAD implantation might also contribute to a potential ventilation-perfusion mismatch and consequently affect the diffusing capacity through a decrease in the capillary recruitment. This occurrence may be related to a relative rigidity of the current pumps, which do not respond to different physiological demands and body positions because of a fixed revolutions per minute setting. Our data showed a significant inverse relationship between $\Delta D_{\text{LCO}}$ and change in pump flow from discharge to 6 months post-LVAD implantation ($r = -0.35$, $P = 0.04$) for patients with HeartMate II pumps. Because no other relationship reached significance, further prospective evaluation is necessary for profound understanding of $D_{\text{LCO}}$ changes post-LVAD implantation.

Lastly, although the CF pumps provide better durability over the pumps providing pulsatile flow,\textsuperscript{3} pulsatile flow has been shown to be beneficial for pulmonary capillary recruitment and the rate of oxygen uptake.\textsuperscript{38,39} New-generation pumps implementing artificial pulsatility will be of interest for future research of lung diffusion in the LVAD population.\textsuperscript{40}
Prospective studies using appropriate techniques (re-breath $D_{LCO}$ assessment) are needed to evaluate the dynamic changes in membrane conductance and Vc post-implantation. Nevertheless, we have hypothesized that the Vc component has a dominant role within the first 6 months to 1 year post-LVAD implantation. Remodelling of the alveolar-capillary membrane with long-standing changes in membrane conductance may occur in the long term (~12 months) after implantation.

The association between $D_{LCO}$ and survival in the HF population has been previously described, with more recent data also from HF patients with preserved ejection fraction. In correspondence with a recently published study by Bedzra et al., our data do not support association between $D_{LCO}$ pre-LVAD implantation and patient survival. Nevertheless, the degree of change between pre-LVAD implantation to 6 months post-implantation does carry predictive value, as well as the $D_{LCO}$ value itself at 6 and 12 month landmark points. The mortality risk associated with $D_{LCO}$ may reflect more complex pathophysiological pathways, in which studying the LVAD model may be of great help for further understanding.

Limitations

The present retrospective study addressed some limitations. Small sample size limits multivariate HR analyses. The study involved eight patients (18%) with chronic obstructive pulmonary, and 10 patients (22%) were smokers. Potential bias could have been introduced in selection of only those patients with available post-LVAD PFT data, who in the present study were patients considered for consequent heart transplant, likely at a younger age and with a greater clinical perspective. However, the post-LVAD PFT data were indicated electively as a part of follow-up evaluation for those on the heart transplant waiting list. To the contrary, this high selection in retrospective design may be of some benefit allowing to more closely elucidate hypothesized mechanisms. Certain time variation between PFTs and absence of serial follow-up data restrict the ability to comment on the development of PFT changes over time post-LVAD implantation. Single-breath $D_{LCO}$ technique does not allow calculation of membrane conductance and Vc components, and the clinical data lack reproducibility. The retrospective nature of the study does not allow for physiological explanation of observed PF changes.

Conclusions

Our findings suggest that PF may not improve following LVAD implantation. However, lung diffusing capacity appears to be a significant predictor of survival in patients with LVADs. Information is lacking for determining alterations in PF and pressure in HF following LVAD implantation. Therefore, these important findings are hypothesis generating for further prospective physiological studies.

The alveolar-capillary interface and bronchial circulation are particularly susceptible to the alterations in blood flow and pressure characteristics of the LVAD population. The described functional changes may be associated with complex pulmonary vascular and cardiac changes, including right ventricular function after LVAD implantation and potential alterations of the alveolar-capillary membrane. We believe these data are important for generation of hypotheses for prospective studies, because studies have not been performed on alterations in breathing mechanics, the gas exchange after LVAD placement, and the association with right ventricular and LV function after LVAD implantation. As a result, a profound understanding of relationships between pulmonary vascular circulation and lung function changes in the LVAD setting could contribute to protection of function in the lung exposed to CF and potentially add to optimization of this therapy in the future. Clinical interpretations of PFTs in the LVAD population must be interpreted with caution until more studies provide solid evidence for clinical outcomes.

Conflict of interest

None declared.

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