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Changes in pulmonary artery pressure before and after left ventricular assist device implantation in patients utilizing remote haemodynamic monitoring

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Abstract

Aims The time course of changes in pulmonary artery (PA) pressure due to left ventricular assist devices (LVADs) is not well understood. Here, we describe longitudinal haemodynamic trends during the peri-LVAD implantation period in patients previously implanted with a remote monitoring PA pressure sensor.

Methods and results We retrospectively studied PA pressure trends in patients implanted with CardioMEMS™ PA pressure sensor between October 2007 and March 2017 who subsequently had an LVAD procedure. Data are presented as mean ± standard deviation, and P-values are calculated using standard t-test with equal variance. Among 436 patients in cohort, 108 (age 58 ± 11 years, 82% male) received an LVAD and 328 (age 60 ± 13 years, 70% male) did not. The mean PA pressure at sensor implant was higher by 29% (P < 0.001) among patients who later received LVAD. Mean PA pressure 6 months prior to LVAD implant was 35.5 ± 8.5 mmHg, increasing to 39.4 ± 9.9 mmHg (P = 0.04) at 4 weeks before LVAD, and then decreasing 27% to 28.8 ± 8.4 mmHg (P < 0.001) at 3 months post-implant and stabilizing at 31.0 ± 9.4 mmHg at 1 year.

Conclusions Patients who later receive LVADs have higher PA pressures at sensor implant and show a further increase leading up to LVAD implantation. There is a significant reduction of PA pressures post-LVAD implantation that persists long term. PA pressure monitoring may aid in the clinical decision making of timing for LVAD implantation and in management of LVAD patients.

Keywords Left ventricular assist device; Pulmonary artery pressure monitoring; Implantable haemodynamic monitoring; CardioMEMS

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Introduction

Heart failure (HF) affects 5.7 million people annually, accounting for the principal diagnosis in one out of every eight discharges, with direct and indirect costs of >$30 billion annually.1,2 In conjunction with a better understanding of physiology and an expanding armamentarium of diagnostic tools and medications, remote monitoring of pulmonary artery (PA) pressures and implantation of mechanical circulatory support devices have proven instrumental in the management of advanced HF. Specifically, frequent monitoring of PA pressures has been shown to significantly reduce long-term HF hospitalization rates as shown in both the CHAMPION [CardioMEMSTM Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in New York Heart Association Functional Class III Heart Failure Patients] clinical trial and in real-world experience.3–5
Despite maximal guideline-directed medical therapies and haemodynamic-guided care, clinical disease progression occurs in HF patients, in many cases requiring left ventricular assist devices (LVADs) or heart transplant. LVADs have been an increasingly utilized therapy for those with advanced HF and have resulted in improvements in patient functional status and quality of life, in addition to improved clinical outcomes relative to medical therapy. While it is known that PA pressures decrease after both pulsatile and continuous flow LVAD implants, the magnitude, time course, and long-term sustainability of PA pressure changes is not well understood. Implantation of LVAD in patients previously implanted with a PA pressure sensor gives us an opportunity to describe longitudinal haemodynamic trends in LVAD patients. Therefore, in this manuscript, we set out to characterize haemodynamic changes in the period leading up to LVAD implant and long-term follow-up thereafter.

Methods

We conducted a retrospective cohort analysis of patients who received a PA sensor implant (CardioMEMS™, Abbott, Sylmar, CA) with remote monitoring between October 2007 and March 2017 with a known LVAD implantation status. The group that did not receive an LVAD served as the control group, and we excluded patients who either received a heart transplant or died without receiving an LVAD. In addition, patients who did not have a valid transmission or had the sensor implanted after the LVAD were excluded. We searched for LVAD implants using the Abbott patient device tracking system from October 2010 to March 2017 and the CHAMPION clinical trial from October 2007 to September 2010.

The CHAMPION cohort that did not have an LVAD, heart transplant, or death was deemed as the comparator for this analysis (non-LVAD group, Figure 1).

Baseline remote monitoring data

For all patients who met the inclusion criteria, de-identified baseline demographic information (age, sex, ejection fraction) was retrieved from the Abbott Merlin.net™ database. The date and time of each PA pressure transmission along with the derived metrics (mean, systolic, and diastolic PA pressures) were also retrieved. For each individual patient, a time series of PA pressure was generated wherein linear interpolation was used to fill in missing data. The PA pressure trend data were censored at known pressure sensor inactivation or end of follow-up—whichever came first. Seven day causal running averages were calculated using the time series in order to reduce noise.

As LVAD implant was expected to change PA pressures non-linearly, the linear interpolation was not performed...
across LVAD implant. Rather, in such cases, two time series were calculated: one from sensor implant to last PA pressure transmission before LVAD implant and a second from first PA pressure transmission after LVAD implant to end of follow-up or last transmission.

**Trends in pulmonary artery pressure and statistical analysis**

PA pressure trends were studied in the LVAD and non-LVAD groups over specific time frames described later. Haemodynamics were reported as the mean and standard deviation of 7 day averaged pressures, plotted as mean and standard error, and compared using standard t-test unless stated otherwise.

First, we studied PA pressure trends in the LVAD and non-LVAD groups immediately after sensor implant through 6 months. We also studied the long-term PA pressure trends among the LVAD recipients by quartiles at three time points: sensor implant, LVAD baseline (4 weeks prior to LVAD implant), and 3 months post-LVAD. The quartiles were based on the mean PA pressures at sensor implant. The relative change in PA pressure at different time points was assessed as a percentage change and compared using a paired t-test with equal variance.

Second, we present the PA pressure trend from 6 months prior to LVAD implant to 1 year post-LVAD implant among all patients in LVAD group. We utilized a pre-LVAD baseline of 4 weeks instead of 1 week, owing to fewer transmissions near the implant time period perhaps because PA pressure data were not routinely transmitted or collected in hospital in the immediacy of the LVAD implant. For the same reason, data in the first 2 weeks post-VAD implant were omitted. The percentage change at 1 year relative to the LVAD baseline (4 weeks prior to LVAD implant) was determined and compared using a t-test with equal variance. The longitudinal data for mean PA pressure were further reported as mean, standard deviation, and median, 75th, and 95th percentiles.

Not all patients are expected to respond to an LVAD implant in the same manner; hence, in order to characterize the changes in PA pressure post-LVAD implant, we utilized the LVAD baseline mean PA pressure to generate quartiles and compared their baseline vs. 3 months’ LVAD haemodynamic outcomes using a paired t-test with equal variance.

**Results**

A total of 632 patients were identified who had received a PA pressure sensor implant with remote monitoring between October 2007 and March 2017 and had a known LVAD implantation status (either implanted or not implanted). Of these patients, 172 either received a heart transplant or died without receiving an LVAD and were excluded. Another 24 patients had no valid transmission or had the sensor implanted after the LVAD and hence were also excluded. The remaining 436 patients met the inclusion criteria, of which 108 patients received an LVAD after their sensor implant (LVAD group) and 328 did not (non-LVAD group).

**Baseline remote monitoring data**

The baseline patient characteristics of the two groups are shown in Table 1. The LVAD group was aged 58.1 ± 11.3 years, and the non-LVAD group had a similar age at 60.3 ± 13 years (P = 0.117). Gender distribution was statistically different between the groups with 82% male in the LVAD group and 70% in the non-LVAD group (P = 0.009). The ejection fraction was lower in the LVAD group at 21.3 ± 9.2% than in the non-LVAD group where it was 30.3 ± 14.2% (P < 0.002). The mean PA pressures at sensor implant were 29% higher (P < 0.001) in the LVAD group compared with the non-LVAD group (Figure 2). The pulse pressure was 23.9 ± 6.9 and 20.3 ± 6.6 mmHg in the two groups, respectively, without any statistically significant difference.

Among the excluded patients who received a heart transplant or died without receiving an LVAD, the average age was 65.0 ± 12.2, and 76% were male. These patients had mean PA pressure of 35.4 ± 10.0 mmHg at sensor implant and 34.7 ± 9.7 mmHg at the 6 month time point post-sensor implant, which were no different than patients who received LVAD at any time point (P > 0.05).

**Trends in pulmonary artery pressure**

Among patients who eventually received an LVAD, the average time between sensor and LVAD implant was 0.9 ± 0.9 years. The patients in the lowest quartile of mean PAP, pulmonary artery pressures.

### Table 1 Baseline characteristics of patients in left ventricular assist device and non-left ventricular assist device group

| Characteristics                  | LVAD group | Non-LVAD group | P-values |
|----------------------------------|------------|----------------|----------|
| Patients (n)                     | 108        | 328            |          |
| Age (years)                      | 58.1 ± 11.3| 60.3 ± 13      | 0.117    |
| Age ≥ 65 years                   | 34 (31%)   | 134 (41%)      | 0.083    |
| Gender (male)                    | 89 (82%)   | 228 (70%)      | 0.009    |
| Ejection fraction (%)            | 21.3 ± 9.2 | 30.3 ± 14.2    | <0.001   |
| Pulmonary artery pressures at sensor implant |          |                |          |
| Systolic PAP (mmHg)              | 52.6 ± 13.4| 42.9 ± 13.7    | <0.001   |
| Diastolic PAP (mmHg)             | 28.7 ± 8.5 | 22.6 ± 9.0     | <0.001   |
| Mean PAP (mmHg)                  | 37.4 ± 10.4| 29.1 ± 10.2    | <0.001   |
| Pulse PAP (mmHg)                 | 23.9 ± 6.9 | 20.3 ± 6.6     | <0.001   |

PAP, pulmonary artery pressures.
PA pressures at sensor implant showed the highest increase (12.8 ± 7.7 mmHg) in mean PA pressures, compared with changes of 2.1 ± 6.7, −1.9 ± 7.1, and −2.2 ± 5.3 mmHg in the other three quartiles, respectively (Figure 3). These patients also showed the longest duration (541 ± 448 days) between sensor implant and LVAD implant compared with 318 ± 331, 210 ± 201, and 210 ± 240 days in other quartiles, respectively. The trends in PA pressure for the 6 months pre-LVAD and 1 year post-LVAD implantation are illustrated in Figure 4. There was a steady increase in mean PA pressures from 35.5 ± 8.5 mmHg at 6 months before LVAD to 39.4 ± 9.9 mmHg 4 weeks prior to LVAD implantation and was decreasing sharply after receiving LVAD to 30.1 ± 8.0 mmHg at 2 weeks and 28.8 ± 8.4 mmHg (27% decrease, P < 0.001) at 3 months after LVAD. The PA pressures in the surviving patients at 1 year had a mean PA pressure of 31.0 ± 9.4 mmHg. The trends in mean, systolic, diastolic, and pulse PA pressures were similar except for pulse pressure, which did not change after the 3 month time point (Figure 4). The heart rate in the post-LVAD time period was higher than that in the pre-implant period.

The distribution of PA pressure values over time for the patients who received an LVAD implant are plotted in Figure 5. The 25th to 75th percentiles as well as the 5th to 95th percentile illustrate the ranges in PA pressures at each time point in the analysis cohort. Although PA pressures had reduced from pre-LVAD, 75% of patients continued to have high mean PA pressures (>25 mmHg) at 6 months post-LVAD.

**Discussion**

We present in-depth, dynamic, and temporal trends in ambulatory PA pressure using an implantable PA pressure sensor. Results show that patients who later received an LVAD had high pressures at the PA pressure sensor implant and that these high pressures were sustained for the period before LVAD placement. Among patients who had lower PA pressures at time of their remote PA pressure sensor implant, who then went on to receive an LVAD, there was a marked increase in PA pressures immediately prior to LVAD implantation. In contrast, patients who already had high PA pressures at time of sensor implantation remained with high PA pressures before receiving an LVAD.

There was an immediate reduction in PA pressures following LVAD that was haemodynamically significant and persisted over the 12 months following implantation. Importantly, those patients with the highest mean PA pressures had the greatest reduction in their mean PA pressures post-LVAD implant. These results are the first characterization of long-term haemodynamic trends in patients who receive LVADs and suggest the following:

1. long-term poor haemodynamics before receiving LVAD,
2. acute increase in PA pressures during 3 months immediately before receiving LVAD,
3. immediate improvement in haemodynamics after receiving LVAD,
4. sustenance of the improvement up to at least 1 year, and
sub-optimal magnitude of improvement in haemodynamics after receiving LVAD.

These observations underscore a potentially important clinical role for remote haemodynamic monitoring in clinical decision making and patient management before and after LVAD implantation. Specifically, in patients who have multiple devices—in this case PA pressure sensor and LVAD—there is an opportunity to gain diagnostic information that may benefit clinical management.

Previous literature with Swan–Ganz catheterization (SGC) has shown significant reduction in PA pressures following LVAD implantation.\textsuperscript{13–15} The advantage of utilizing remote monitoring is the avoidance of the invasive nature of the SGC and catheter-related complications (PA rupture, propensity for arrhythmias, inadvertent ventricular rupture, etc.) and longitudinal collection of ambulatory haemodynamic data. The ability to remotely monitor PA pressures in a non-invasive way is certainly attractive especially in a population of HF patients who are not only on anticoagulation but also supported by mechanical circulatory support with a propensity for bleeding.

That being said, there is a paucity of data from patients implanted with a haemodynamic monitoring sensor who ultimately require mechanical circulatory support. A sub-analysis from the CHAMPION trial did suggest utility in using these devices to improve the timing of LVAD implantation.\textsuperscript{12} Patients in the arm being actively treated based on PA pressure had non-statistically significant but shorter time to LVAD implantation than had the control group. In addition, there was little to no change in PA pressures in these patients, suggesting some degree of fixed pulmonary pressures. Our study suggests that patients who receive LVAD had high PA pressures even at the time of sensor implantation. These patients who are not yet sick enough to warrant an LVAD but have an elevated PA pressure may require more frequent monitoring and medical adjustments in order to prevent decompensation and/or earlier LVAD implantation.

Another theoretical advantage for remote monitoring is the ability to distinguish a subset of patients who may have reversible pulmonary hypertension from those who have a fixed component that cannot be altered by pharmacologic or mechanical methods. Thus, an important clinical application of a remote monitoring PA pressure sensor technology...
Figure 4  Temporal changes in mean PA pressures between 6 months pre-LVAD implantation and 1 year post-LVAD implantation. LVAD, left ventricular assist device; PA, pulmonary artery.

Figure 5  Distribution of mean PA pressure over time, showing median, 25th, and 75th percentiles between 6 months pre-LVAD implantation and 1 year post-LVAD implantation. LVAD, left ventricular assist device; PA, pulmonary artery.
may be establishing heart transplant eligibility for patients with post-LVAD pulmonary hypertension.

There are several limitations that must be considered when interpreting these results. First, we cannot postulate whether PA pressures directly led to the decision to implant an LVAD or affected the timing of LVAD placement given the retrospective nature of the study design. Furthermore, confounding cannot be excluded. The use of multiple databases with limited granular data such as re-hospitalization rates limits the scope of our analyses as well as our understanding of the impact of remote monitoring PA pressure sensor on the care of LVAD patients. Another limitation is that there are no immediate sensor PA pressure data while in hospital post-LVAD implantation, as most patients had invasive haemodynamic monitoring or other methods of clinical assessment during the recovery phase from LVAD implantation. As a result, the immediate effect of LVAD implantation on PA pressures could not be determined.

Given the aforementioned limitations, these results are hypothesis generating only; however, they may serve as a foundation for future studies. It is possible that remote haemodynamic monitoring may be used to tailor therapy in the LVAD patient in order to optimize right and left ventricular function over time. Additionally, haemodynamic monitoring may also help to improve patient functional capacity and quality of life. This monitoring may even have the potential to diagnose and address complications of mechanical support, including arrhythmia and pump malfunction. The recently launched Intellect 2-HF (Investigation to optimize haemodynamic management of LVADs using the CardioMEMSTM; ClinicalTrials.gov NCT03247829) study should shed additional light on these concepts.

Conclusions

Our findings demonstrate that the PA pressures are elevated at the time of PA pressure sensor implantation in patients who later received LVAD. Following LVAD implantation, PA pressures are significantly reduced, and the reduction is maintained at least up to a year. PA pressure monitoring may provide insight into optimal timing for LVAD implantation and assist in the clinical management of patients with mechanical circulatory support.

Conflict of interest

A.K., S.J., N.U., and B.L. received consulting fees from Abbott. R.A., R.B., and D.F. are employees and stockholder of Abbott. M.B.-B., J.N.K., and S.L. have no disclosures.

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