Direct Left Atrial Pressure Monitoring in Ambulatory Heart Failure Patients
Initial Experience With a New Permanent Implantable Device

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Background—We describe the first human experience with a permanently implantable, direct left atrial pressure (LAP) monitoring system in ambulatory patients with chronic heart failure.

Methods and Results—Eight patients with established heart failure and at least 1 heart failure hospitalization or unplanned visit for parenteral therapy in the last year underwent device implantation under fluoroscopic guidance. All subjects received aspirin 150 mg and clopidogrel 75 mg daily. Subjects measured LAP twice daily and attended a clinic regularly for data upload and device calibration. Right heart catheterization was performed at the time of device implantation and at 12 weeks. The device was implanted in all subjects with no procedural complications. At the 12-week follow-up, 87% of device LAP measurements were within ±5 mm Hg of simultaneous pulmonary capillary wedge pressure readings over a wide range of pressures (1.6 to 71 mm Hg). Net drift corrected by calibration was -0.2 ± 1.9 mm Hg/mo. During short-term follow-up, there were no device-related complications or systemic emboli. There were no deaths, no unplanned heart failure clinic visits, and no admissions for heart failure.

Conclusions—Ambulatory monitoring of direct LAP with a new implantable device was well tolerated, feasible, and accurate at a short-term follow-up. Further follow-up and investigation are warranted to evaluate the clinical utility of LAP monitoring in patients with heart failure. (Circulation. 2007;116:2952-2959.)

Key Words: heart failure ■ hemodynamics ■ atrium

Despite major advances in drug and device therapy and more intensive clinical monitoring, mortality and admission rates for heart failure (HF) remain high.1–5 The growing cost of health care for HF is well documented.2 New management strategies are needed to improve outcomes and to lower overall treatment costs.2,4

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HF decompensation is characterized by increased left atrial pressure (LAP) causing symptomatic pulmonary congestion and frank edema.2 The possible precipitants for acute HF are numerous, but they share the common pathway of elevated LAP. The rise in LAP usually is gradual and precedes symptom onset.6 Hence, accurate monitoring of LAP could allow earlier identification of incipient decompensation and guide adjustment of vasodilator and diuretic dosing.6 No direct measurement of LAP in ambulatory HF patients is available yet, and there is no reliable, objective guide to optimal diuretic and vasodilator dosing. Current management strategies for ambulatory patients remain empirical, relying on clinical symptoms and signs to detect decompensation despite documented poor correlation of these indicators with LAP.7 Hemodynamic monitoring has the potential to detect increases in LAP before clinical deterioration. Recent studies in which LAP estimates derived from right ventricular hemodynamics or thoracic impedance monitoring were used to guide treatment suggest that there may be an important role for hemodynamic monitoring of HF in selected outpatients.6,8

We report here the first human experience with a permanently implantable direct LAP monitoring device in a series of 8 ambulatory HF patients.

Methods

Subjects from a single center were enrolled in a prospective, multicenter, nonrandomized, open-label feasibility clinical trial called Hemodynamically Guided Home Self-Therapy in Severe Heart Failure Patients (HOMEOSTASIS I), which was designed to...
evaluate the preliminary safety, reliability, and functionality of the permanently implantable LAP monitoring system (HeartPOD, Sava-
cor, Inc, a subsidiary of St Jude Medical, Inc, Minneapolis, Minn) in ambulatory patients with HF. Local institutional review boards and ethics committees approved the study. All patients gave written informed consent.

Patients
We enrolled 8 patients with a history of New York Heart Association functional class III to IV HF and at least 1 hospital admission or presentation to an emergency department or clinic for acute decompensated HF requiring parenteral diuretic, vasodilator, or positive inotrope during the previous 12 months. Exclusion criteria included prior atrial septal surgery; patent foramen ovale ≥2 mm stroke or systemic thromboembolism within 6 months; chronic atrial fibrilla-
tion; atrial or ventricular thrombus; gastrointestinal bleeding in the last 6 months; requirement for chronic anticoagulation; or intolerance to aspirin, clopidogrel, or ticlopidine. Chronic atrial fibrillation was an exclusion criterion because of the increased potential for thromboembolic complications. An additional 10 subjects with chronic atrial fibrillation will be studied when 20 subjects in sinus rhythm have been enrolled. Enrollment began immediately after intracardiac echocardiography or transesophageal echocardiography determination of left atrial anatomy and just before transseptal puncture.

Device
The device (Figure 1) consists of an implantable sensor lead coupled with a subcutaneous antenna coil, a patient advisory module (PAM), and the clinician’s personal computer software. The sensor system, implanted into the atrial septum oriented to the left atrium (LA), comprises a 3×7-mm hermetically sealed sensor module with a titanium pressure sensing membrane and circuitry for measuring and communicating LAP, temperature, and intracardiac electrogram. LAP is calculated by subtracting the absolute pressure obtained by the implant from an atmospheric reference measured by a pressure sensor located in the PAM. Folding nitinol anchors affix the sensor module in the interatrial septum, accommodating any septal thickness. The implant is powered and interrogated through the skin by 125-kHz radiofrequency wireless transmissions from the PAM. During interrogation, high-fidelity physiological waveforms (LAP and intracardiac electrogram) captured for periods of up to 20 seconds are stored in the memory of the PAM. The PAM has the capacity (13 Mb of memory) to store ~3 months of data if 6 waveforms are acquired each day (540×15-second waveforms).

Implantation
Using a Seldinger technique, one sheath was placed in the right femoral vein below the inguinal ligament and a second sheath was placed 1 cm above the inguinal ligament using a wire in the lower sheath to guide the puncture. Transseptal puncture was performed via the sheath above the inguinal ligament so that the subcutaneous antenna coil could be secured in a pocket created in the lower right rectus abdominus sheath after sensor lead positioning. After closed femoral transseptal puncture with a Brockenbrough needle passed through an 8F Brockenbrough dilator, heparin 5000 IU was admin-
istered, and an 11F delivery sheath was placed in the LA. The sensor system was implanted under fluoroscopic guidance by advancing the sensor lead until the distal anchor unfolded and contacted the left side of the atrial septum. The sheath was withdrawn so that the sensor module spanned the atrial septum with its pressure sensing membrane positioned 1 to 2 mm into the LA (Figure 2). The antenna coil was connected to the proximal end of the sensor lead and placed in a subcutaneous pocket just above the lower rectus abdominus sheath. Transesophageal echocardiography or intracardiac echo-
cardiography was available during all of the procedures. After implantation, patients received at least 150 mg/d aspirin and, for a minimum of 6 months, clopidogrel 75 mg daily to reduce the likelihood of thromboembolic events.

Study Protocol
Before implantation, a complete history, physical examination, ECG, echocardiogram, chest x-ray, exercise testing for V˙O2, and modified Valsalva maneuver (to ascertain ability to achieve airway pressure >40 mm Hg with an open glottis for >10 seconds) were conducted in each patient.

After device implantation, subjects were seen at 2, 6, and 12 weeks for clinical review, data upload, and noninvasive device calibration. Subjects were instructed to measure LAP twice daily with additional measurements in the event of symptoms. LAP measurements were acquired in a semirecumbent position after 5 minutes of rest. In addition, subjects were asked to record symptoms on the PAM. These data were uploaded for offline analysis of trends and LAP waveforms by docking the PAM with a personal computer running the clinician’s personal computer software. In the first 12 weeks, patients were managed primarily on the basis of clinical status by physicians who were aware of LAP trends.

Follow-Up Studies
Patients were followed up at 2, 6, and 12 weeks. With a validated modified Valsalva technique to raise intrathoracic pressure, noninvasive device calibration was performed at each time point by measuring simultaneous airway pressure and LAP during 8-second forced expiration (sustained pressure with an open glottis) through a mouthpiece connected to the PAM atmospheric reference pressure transducer after administration of sublingual glycyl trinitrate. When intrathoracic pressure is raised such as during Valsalva, cardiac filling pressures, including LAP, equalize with intrathoracic pressure as estimated by the airway pressure (Figure 3), and criteria for accepting valid modified Valsalva attempts have previously been described. Right heart catheter studies were performed with a fluid-filled Swan-Ganz catheter and compared with simultaneous...
LAP measurements from the device at implantation and at 12 weeks to assess accuracy and stability of the device. Fluoroscopy was used to guide pulmonary artery catheter flotation and balloon occlusion and to position and zero the external transducer at the level of the LAP device. Appropriate pulmonary capillary wedge pressure (PCWP) waveforms were confirmed by typical appearance and, if necessary, by oxygen saturation. Simultaneous LAP and PCWP tracings were obtained from a 15-second acquisition during normal respiration. Waveforms were recorded at 25 mm/s over a range 0 to 50 mm Hg. After baseline PCWP and LAP measurements, further simultaneous values were obtained during a series of physiological and pharmacological maneuvers designed to test device accuracy across a range of physiologically relevant pressures. These included the standard Valsalva maneuver (sustained pressure with a closed glottis), sustained handgrip, intravenous fluid bolus, and sublingual glyceryl trinitrate administration.

Statistics
When appropriate, the data are described as mean±SD. The pooled intrapatient correlation coefficient between LAP values from the device and PCWP measurements was calculated from a mixed-model ANOVA. Bland-Altman plots were used to compare the difference between the 2 measurement techniques.

Results
Patients
Eight male patients were enrolled at a single center. Patient demographics are shown in Table 1. Most patients had systolic dysfunction and ischemic cardiomyopathy and were in New York Heart Association functional class II at the time of enrollment. Three patients had previously received a biventricular pacemaker or implantable cardiac defibrillator. The use of loop diuretics, β-blockers, and angiotensin-converting enzyme inhibitors was consistent with current HF management guidelines. There were no withdrawals during follow-up, and complete data were available for all subjects.

Implantation
Devices were successfully implanted in all subjects, and there were no procedural complications. The mean implantation
Table 1. Patient Demographics

| Age, y | 72 ± 7 (65–83) |
| NYHA class II/III/IV, n | 6/2/0 |
| Ischemic/idiopathic/hypertensive origin, n | 5/2/1 |
| Prior myocardial infarction, n | 4 |
| Prior CABG, n | 3 |
| Hypertension, n | 3 |
| Medications at baseline, n |
| Aspirin/β-blocker/loop diuretic/ACEI/digoxin/aldosterone antagonist, n | 8/8/8/1/2 |
| Median HF-related events over past 12 mo,* n | 1 (1–2) |
| LV ejection fraction, % | 27 ± 13 (15–57) |
| LA dimension, mm | 51 ± 6 (46–60) |
| CRT or ICD, n | 3 |
| Peak VO₂, mL · kg⁻¹ · min⁻¹ | 14.3 ± 2.1 (12.6–17.7) |
| Plasma creatinine, mg/dL | 1.2 ± 0.3 (0.8–1.5) |

*Indicates simultaneous values.

Table 2. Comparison Between Mean Hemodynamic Indices, Including Direct Catheter-Derived LAPS and Device LAPS at Implantation and 3-Month Follow-Up

<table>
<thead>
<tr>
<th>Baseline (n = 8)</th>
<th>At 3 Months (n = 8)</th>
<th>Change During 3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, bpm</td>
<td>63.7 ± 11.9</td>
<td>60.3 ± 9.8</td>
</tr>
<tr>
<td>Systolic arterial pressure, mm Hg</td>
<td>116.8 ± 9.5</td>
<td>131.6 ± 18.2</td>
</tr>
<tr>
<td>Diastolic arterial pressure, mm Hg</td>
<td>61.6 ± 3.7</td>
<td>68.0 ± 9.7</td>
</tr>
<tr>
<td>Systolic PAP, mm Hg</td>
<td>39.3 ± 8.4</td>
<td>32.4 ± 8.9</td>
</tr>
<tr>
<td>Diastolic PAP, mm Hg</td>
<td>17.4 ± 4.5</td>
<td>13.3 ± 4.8</td>
</tr>
<tr>
<td>Cl, L · min⁻¹ · m⁻¹</td>
<td>2.27 ± 0.60</td>
<td>2.32 ± 0.39</td>
</tr>
<tr>
<td>Mean PCWP, mm Hg*</td>
<td>15.8 ± 8.2</td>
<td>12.4 ± 5.7</td>
</tr>
<tr>
<td>Mean device LAP, mm Hg*</td>
<td>17.1 ± 8.3</td>
<td>13.4 ± 4.8</td>
</tr>
</tbody>
</table>

PAP indicates pulmonary artery pressure; CI, cardiac index. Values are mean ± SD.

All cases to determine septal anatomy and the absence of LA thrombus and to document device placement.

Baseline hemodynamic indices demonstrated compensated cardiac index and filling pressures (Table 2). There was excellent concordance between device- and catheter-derived LA waveforms (Figure 4) and between PCWP and direct LAP measured by a fluid-filled catheter (15.8 ± 8.0 versus 13.9 ± 6.4 mm Hg, respectively).

At follow-up right heart catheterization (Table 2), there was a tight intrapatient correlation coefficient (r = 0.95, P < 0.001) between mean device LAP and catheter-derived mean PCWP (Figure 5). Bland–Altman analysis demonstrated excellent agreement, with 87% of device LAP measurements being within ± 5 mm Hg and 96% within ± 10 mm Hg of PCWP measurements from right heart catheterization across a wide range of LAPS (1.6 to 71 mm Hg).

Abnormalities in waveform, primarily affecting V-wave morphology, were identified in 2 patients. In 1 patient, an artifically exaggerated v wave occurred with filling pressures > 20 mm Hg from 8 weeks after implantation. In a second patient, prominent x descents and reductions in v-wave amplitude that were more pronounced with inspiration developed from week 4 after implantation. Transesophageal echocardiography in the latter demonstrated that the device was deployed in a patent foramen ovale tunnel. A weaker correlation was found between device LAP and PCWP (r = 0.84, P < 0.001) for the 2 subjects with distorted waveforms. Conversely, in the 6 patients with normal waveforms, there was a very close correlation (r = 0.99, P < 0.001; Figure 5).

Noninvasive calibration was performed successfully by all patients, and waveforms were acceptable for analysis in 94% of attempts. The mean net device offset drift for patients 2 through 8 was 1.2 ± 1.3 mm Hg/mo (Figure 6). In the first patient, greater drift (5.8 mm Hg/mo) developed 4 weeks after implantation as a result of a manufacturing fault that was repeatedly corrected accurately by noninvasive calibration.

Development of a correction constant subsequently allowed reliable clinical use of the device in this patient. This fault was not seen in any other devices.

At the 3-month follow-up, there were no deaths or device-related complications. No devices needed to be repositioned or replaced. Two patients were hospitalized. One subject was...
admitted with a pulmonary embolus; a calf vein thrombus of indeterminate age was found on the contralateral side of the device. A second patient was admitted for elective percutaneous coronary intervention to treat stable but limiting angina. No strokes, transient ischemic attacks, or systemic embolism occurred during follow-up. There was no requirement for device extraction during follow-up. There were no unplanned emergency department or clinic visits for decompensated HF during short-term follow-up.

Subjects took 92%±8% of all scheduled twice-daily readings. All patients initially exhibited daily variation in LAP, although the amount of variation differed between individuals. High-fidelity waveforms demonstrated significant variation in morphology (Figure 7), with large c-V waves frequently present when LAP was high (Figure 7A). After right heart catheterization at 3 months, treatment was adjusted on the basis of daily LAP readings. In 5 of the 8 subjects, more optimal LAP profiles were seen after treatment changes. One subject had large daily variation in LAP (Figure 8A) and developed class IV symptoms when 

Figure 4. ECG and direct LAP from the left atrial sheath (LAP-sheath, A) and intracardiac electrogram and LAP from LAP-sensing device (B) in 1 patient at the time of device implantation showing concordance of high-fidelity waveforms.

Discussion

We describe the first use of a permanent implantable device that directly measures LAP. The device was safely implanted in 8 patients in 1 center and accurately recorded high-fidelity LAP waveforms that were stable at a 12-week follow-up. There were no complications during implantation, nor were there any adjudicated to be device related during follow-up. However, the pulmonary embolus in 1 subject may have been related to the implantation procedure. Implantation from a superior approach as either a standalone device or a combined cardiac resynchronization–defibrillator device in the future may reduce the risk of lower-limb deep vein thrombosis. In preclinical studies using the same antiplatelet regimen,10 there was no evidence of cardiac or systemic thromboembolism in any of the animal models. Significantly, while patients were on aspirin and clopidogrel, there was no systemic embolization, a potential hazard of left atrial devices, especially in HF when there may be atrial dilatation, fibrillation, and stasis. The absence of adverse events related to left atrial instrumentation and device implantation is consistent with recent experience from transseptal puncture during atrial fibrillation ablation procedures and with implantation of atrial septal closure devices, for which rates of systemic embolization are low.11 Subjects received long-term aspirin and 6 months of clopidogrel to provide dual antiplatelet therapy until after complete neoendothelialization. Data from closure devices suggest that this occurs at 12 weeks.12,13 In animal studies that will be reported elsewhere, neointimal tissue of varying thickness had developed over the sensor diaphragm and anchors 4 to 8 weeks after device implantation.

Across the group, mean device drift was small and readily corrected by noninvasive calibration. The offset drift encountered in 1 patient has now been documented in further bench and animal studies, and corrective actions have been implemented. The v-wave artifact has been observed in 2 animals in which the device was not orthogonal to the septum. The mechanism for this may reflect the specific pattern of tissue overgrowth over the sensor tip. Asymmetrical tissue coverage of the sensor tip. Asymmetrical tissue coverage in this setting may produce traction on the sensor membrane during ventricular systole, leading to distortion of v-wave morphology. Careful attention to ensure that device deployment is orthogonal to the atrial septum appears to prevent this effect. Despite these waveform abnormalities in 2 patients, both devices remain clinically usable, providing reliable estimates of LAP.
LAP is a key hemodynamic index in chronic HF. Current HF management strategies lack an accurate indicator of LAP that can be assessed frequently in either the clinic or the community. Symptoms, physical signs, and weight are insensitive in detecting alterations in filling pressures, as are biochemical markers of end-organ dysfunction. B-type natriuretic peptides are powerful independent prognostic markers, but their role in monitoring HF is still under investigation.

Echocardiography can estimate LAP, but its frequent use in the community is limited by availability.

Therapeutic devices such as implantable cardiac defibrillators and cardiac resynchronization therapy play an increasingly important role in the management of HF, and this has rekindled interest in ambulatory hemodynamic monitoring. Some cardiac resynchronization therapy devices now monitor heart rate variability or intrathoracic impedance as indicators of volume status. Trends in these variables may allow the early detection of HF decompensation. Transcutaneous thoracic impedance and blood volume analysis can assess instantaneous volume status in chronic HF. These methods can be time-consuming and require a healthcare visit. Standalone implantable devices have been developed, including 1 device that estimates LAP by deriving pulmonary artery diastolic pressure from right ventricular pressure at the pulmonary valve opening. Although routine use of a pulmonary artery catheter did not improve outcomes compared with standard care in patients admitted with acute decompensation of advanced HF, the recently reported Chronicle Offers Management to Patients with Advanced Signs and...
Symptoms of Heart Failure (COMPASS HF) trial suggests that continuous hemodynamic monitoring may reduce HF events in ambulatory patients.22,23

Outpatient monitoring of direct LAP offers potential advantages over devices sited in the right ventricle or pulmonary artery, including more accurate assessment of left ventricular filling without confounding from pulmonary vascular abnormalities. Accurate waveform data may provide mechanistic information about perturbations in LAP such as underlying mitral regurgitation, dynamic ischemia,24 or pericardial abnormalities. In addition to providing an early warning for impending decompensation by monitoring trends in LAP, this device can be used to dynamically adjust medical therapy to avert hospitalization for HF decompensation. The integrated intracardiac electrogram may detect atrial or other arrhythmias that are prevalent in HF. In addition, the device potentially could provide information on the hemodynamic impact of rhythm changes and could guide the optimization of atrioventricular and ventricular-ventricular pacing intervals. In this small cohort of high-risk patients, more optimal LAP profiles were obtained in 5 of 8 subjects, and there were no HF hospitalizations during follow-up. In addition, LAP monitoring provided specific mechanistic information about dynamic ischemia and guided specific changes in pharmacotherapy and coronary revascularization. In the future, remote transmission of data could allow more frequent or rapid review of LAP trends, which could allow earlier optimization of dynamically adjusted medical therapy.

Study Limitations
This study assessed only short-term device accuracy and safety in 1 center. Longer-term stability, reliability, and safety are currently under investigation as part of a multicenter trial. Although we altered treatment according to symptoms and observed subsequent falls in LAP in 2 subjects, the effect on outcomes from the use of this device remains to be established. Although widely used in clinical practice as an estimate of LAP, PCWP measured by a fluid-filled catheter by its nature may not be an ideal standard for estimating left ventricular filling pressures in all patients, particularly if there are coexistent pulmonary vascular or mitral or aortic valvular abnormalities. However, for all patients in the present study, there was good concordance between simultaneous direct LAP and PCWP measured by a fluid-filled catheter at the time of implantation. For logistical and safety reasons, directly measured LAP (via a fluid-filled catheter) was measured only at implantation and not at follow-up. In this study, devices were implanted via the right femoral vein because equipment to perform transseptal puncture from a superior approach was still in the developmental stage. New techniques could allow implantation from a supraclavicular approach that could facilitate combination with cardiac resynchronization therapy or cardiac resynchronization therapy–implantable cardiac defibrillator devices.

Conclusions
A new implantable direct LAP monitoring system was safely implanted and accurately measured LAP during short-term follow-up. Further studies are required to test whether this device has the potential to improve outcomes in HF by optimization of treatment based on LAP measurement.

Acknowledgments
We thank Catherine Cruickshank and Joy Le Lievre for help in coordinating the study and Karen Harvey and Jackie Sutherland for technical help.

Sources of Funding
The study was sponsored by a grant from Savacor, Inc, a subsidiary of St Jude Medical, Inc (Minneapolis, Minn). This study was supported in part by an award from the National Heart Foundation of New Zealand.

Disclosures
Drs Whiting, Kar, and Eigler report a financial interest in the manufacture of the study device. The other authors report no conflicts.

References


CLINICAL PERSPECTIVE
The mortality and morbidity rates associated with heart failure remain high despite major advances in drug and device therapy and the implementation of intensive clinical monitoring programs. Currently, there is no dependable, objective guide to optimize medical therapy that might be directed against congestive symptoms. Elevated left atrial pressure (LAP) is one of the principal hemodynamic abnormalities in left ventricular failure. Monitoring LAP in ambulatory subjects with chronic heart failure could allow earlier identification of impending decompensation and guide adjustment of medication dosing. This study reports the first human experience with a novel, permanently implantable, direct LAP monitoring system in ambulatory patients with New York Heart Association class II to III heart failure. The device was implanted in 8 patients with a recent history of acute decompensation and accurately recorded high-fidelity left atrial waveforms that were stable at 12-week follow-up. At short-term follow-up, there were no deaths, embolic events, or complications adjudicated to be device related. Eighty-seven percent of device LAP measurements were within ±5 mm Hg of simultaneous pulmonary capillary wedge pressure measurements from right heart catheterization across a wide range of LAPs. In 5 of the 8 subjects, LAP profiles were optimized after treatment changes, and no subjects experienced acute decompensation of their heart failure during the follow-up period. At short-term follow-up, we found that monitoring of direct LAP with the study device was well tolerated, feasible, and accurate. Extended follow-up is required to evaluate the clinical utility of LAP monitoring and dynamically adjusted medical therapy in subjects with chronic heart failure.
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*Circulation.* 2007;116:2952-2959; originally published online December 3, 2007; doi: 10.1161/CIRCULATIONAHA.107.702191

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/116/25/2952

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