Comparison of a Radiofrequency-Based Wireless Pressure Sensor to Swan-Ganz Catheter and Echocardiography for Ambulatory Assessment of Pulmonary Artery Pressure in Heart Failure

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Objectives
The goal of this work was to evaluate the accuracy of a new heart failure (HF) sensor (HFS) (Heart Failure Sensor, CardioMEMS Inc., Atlanta, Georgia) pulmonary artery pressure (PAP) monitoring compared with Swan-Ganz (SG) (Hospira, Inc., Lake Forest, Illinois) catheterization and echocardiography (ECHO) in ambulatory HF patients.

Background
There is an increasing interest in the development of ambulatory monitoring devices aiming to adjust therapy and prevent hospitalizations in HF patients.

Methods
Twelve patients with HF and New York Heart Association functional class II to IV were included in this study. The HFS was deployed into the pulmonary artery under angiography, allowing wireless PAP measurement. Two independent blind operators performed 3 HFS measurements at each visit, with simultaneous ECHO at 2, 14, 30, 60, and 90 days. Swan-Ganz catheterization was performed at 0 and 60 days. Linear regression was used as a measure of agreement. Variability between methods and interobserver variability were evaluated by Bland-Altman analysis.

Results
Mean age was 63 ± 14.6 years. Systolic PAP was 64 ± 22 mm Hg and 58 ± 22 mm Hg for HFS and SG, respectively (p < 0.01). Both methods showed a significant correlation (r² = 0.96 baseline, r² = 0.90 follow-up, p < 0.01), with a mean difference of 6.2 ± 4.5 mm Hg. Diastolic PAP was 23 ± 14 mm Hg and 28 ± 16 mm Hg for HFS and SG, respectively (r² = 0.88 baseline, r² = 0.48 follow-up, p < 0.01), with a mean difference of −1.6 ± 6.8 mm Hg. Systolic PAP was 60 ± 20 mm Hg and 62 ± 12 mm Hg for HFS and ECHO, respectively (r² = 0.75, p < 0.01), with a mean difference of −2.6 ± 11 mm Hg. There was no significant interobserver difference.

Conclusions
The HFS provides an accurate method for PAP assessment in the intermediate follow-up of HF patients.

Congestive heart failure (HF) is a chronic, degenerative condition that impairs the heart’s ability to pump blood at normal filling pressures to adequately meet the metabolic requirements of the body. Nearly 4.9 million Americans suffer from various degrees of HF, with about 400,000 new cases identified each year. Heart failure is the leading cause of hospital admissions in U.S. patients older than 65 years (1). One in 5 HF patients die within 1 year of diagnosis, and only 15% survive more than 10 years (2). The disease is also costly, due in large part to the frequency of acute decompensation episodes, which require emergency treatment and hospitalization.

In nonrandomized studies, acute therapy with vasodilators and diuretics to reduce filling pressures has been associated with improved symptoms and reduction of the degree of mitral regurgitation (3–9). For inpatient HF patients whose signs and symptoms of congestion do not resolve with initial therapy, it appears reasonable to consider invasive hemodynamic monitoring in experienced sites (10,11).

In the outpatient setting, serial laboratory testing and careful clinical follow-up lack the required sensitivity to
identify patients at imminent decompensation risk (12) and often cannot avoid repeated hospitalizations. The currently available methods for routine hemodynamic evaluation (Swan–Ganz [SG] [Hospira, Inc., Lake Forest, Illinois] catheterization and echocardiography [ECHO]) are costly and not suitable for repeated measurements in the ambulatory setting. A considerable amount of investigation has been directed to develop alternative methods for central hemodynamic evaluation in order to adjust therapy in ambulatory patients with severe symptoms despite optimal medical therapy guided only by clinical assessment. Implantable hemodynamic sensors may enable frequent monitoring of hemodynamic changes in HF patients and could be used in tailoring vasodilator or diuretic medication and did not require additional antiplatelet therapy, were included. All patients already on oral warfarin before the randomization were advised to continue their medication and did not require additional antiplatelet therapy. Informed consent was obtained from all patients.

Patients. Twelve HF patients in New York Heart Association (NYHA) functional class III to IV referred to a tertiary center for acute decompensation, with normal ventilation/perfusion lung scan and tricuspid regurgitation signal at ECHO, which allowed for proper PAP determination, were included. All patients already on oral warfarin before the randomization were advised to continue their medication and did not require additional antiplatelet therapy. Informed consent was obtained from all patients. Exclusion criteria were recent acute coronary syndrome, coronary artery bypass surgery, or percutaneous coronary angioplasty within the last 3 months; mechanical right heart valves; pulmonary or tricuspid stenosis, documented pulmonary embolism, or pulmonary infarction within the last 3 months; pregnant women; and active uncontrolled infection. The study protocol was approved by the ethics committees of the participating centers.

HFS delivery system and implantation. The CardioMEMS Heart Failure Sensor (CardioMEMS Inc., Atlanta, Georgia) (Fig. 1) consists of a 3-dimensional coil and a pressure-sensitive capacitor encased within a hermetically sealed, fused silica capsule. Two wired nitinol loops avoid sensor distal migration. The device is 15-mm long and 3-mm wide and is supplied pre-loaded, attached to a tether wire within a delivery catheter.

Implantation was performed under fluoroscopy. A 7-F wedge catheter (Arrow International Inc., Reading, Pennsylvania) was advanced into the deployment site in the pulmonary artery. Then, a 0.025-inch guidewire was advanced through the catheter into the target site; the wedge catheter was retired, and a 12-F sheath was advanced over the guidewire, allowing the introduction of the HFS delivery catheter. Once the target site was reached, the tether wire was pulled to release the sensor. A selective angiography showing the correct position of the device and blood flow distal to it was performed (Fig. 2).

HFS PAP measurement. The coil and capacitor housed within the HFS form a miniature electrical circuit that resonates at a specific frequency. Pressure applied to the sensor causes deflections on the pressure-sensitive surface and results in a characteristic shift in the resonant frequency.

Figure 1 Heart Failure Sensor

The CardioMEMS Heart Failure Sensor consists of electronic components housed within a hermetically sealed, fused silica capsule. Two wire loops of nitinol prevent sensor distal migration.

Methods

Abbreviations and Acronyms

<table>
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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>BNP</td>
<td>B-type natriuretic peptide</td>
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<td>ECHO</td>
<td>echocardiography</td>
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<td>HF</td>
<td>heart failure</td>
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<td>HFS</td>
<td>heart failure sensor</td>
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<td>NYHA</td>
<td>New York Heart Association</td>
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<td>PAdia</td>
<td>diastolic pulmonary artery pressure</td>
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<td>PAP</td>
<td>pulmonary artery pressure</td>
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<td>PASys</td>
<td>systolic pulmonary artery pressure</td>
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<td>RAP</td>
<td>right atrial pressure</td>
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<td>SG</td>
<td>Swan-Ganz</td>
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The CardioMEMS Heart Failure Sensor consists of electronic components housed within a hermetically sealed, fused silica capsule. Two wire loops of nitinol prevent sensor distal migration.
the right atria and right ventricle. Right atrial pressure (RAP) was estimated based on the respiratory motion of the inferior vena cava (18). Systolic pulmonary artery pressure (PAsys) was then calculated as:

\[ \text{PAsys} = 4(V_{TR})^2 + \text{RAP} \]

All determinations were made on an HP Agilent SONOS 4500 (Agilent Technologies, Andover, Massachusetts) by a trained operator blinded for other measurements.

**Patient evaluation and follow-up.** Two independent blinded operators took 3 HFS measurements with a fixed interval of 5 min at each scheduled evaluation. Simultaneously with implantation, each patient underwent SG catheterization. Follow-up schedule consisted in sensor and echo-Doppler PAP measurements at 2, 14, 30, 60, and 90 days. Also, SG measurements were repeated at day 60. All of the evaluations were done by blinded investigators.

**Statistical analysis.** All values are expressed as mean ± SD. Linear regression analysis was used for the comparison of PAP obtained with HFS, SG, and ECHO at baseline and during the follow-up, and for the results of 2 independent operators of the HFS device. Variability between the methods and interobserver variability was expressed relative to the average PAP plus 2 SDs by Bland–Altman analysis; for the former, PAP estimations of both operators were averaged. The Student t test was performed to determine the significance of the differences of the values obtained with different methods. A p value <0.05 was considered statistically significant.

**Results**

Twelve patients were incorporated into the study. Baseline characteristics are shown in Table 1. Implanting procedure was feasible in all patients. Average implantation time was 71 ± 31 min (range 19 to 110 min). The device was deployed in the right pulmonary artery in 8 patients and in the left pulmonary artery in the remaining 4. In 1 patient, device migration from right to left pulmonary artery was observed at day 2. Patients were discharged after 2.6 ± 1.1 days. During follow-up (median 62 days, range 11 to 189 days) no adverse effects attributable to the procedure were observed.

**Comparison of PAP between HFS and SG.** Systolic PAP was 64 ± 22 mm Hg and 58 ± 22 mm Hg for HFS and SG, respectively (p < 0.01). Linear regression and agreement plots for PAsys from HFS and SG as a function of average measurement are shown in Figure 4. A significant correlation was observed for the PAsys measurement between HFS and SG (r² = 0.90 at initial implant and r² = 0.94 at follow-up, p < 0.01), with a mean difference of 6.2 ± 4.5 mm Hg (Fig. 4). Likewise, diastolic pulmonary arterial pressure was significantly lower for HFS than for SG (p < 0.01). The Bland–Altman plots also showed a satisfactory agreement between both systems. The comparison of PAsys from 2 independent operators of the HFS device is shown in Table 2. The mean difference between operators was 6.2 ± 6.5 mm Hg (p < 0.01).

**Figure 2 Pulmonary Angiography During Heart Failure Sensor Implantation**

CardioMEMS Heart Failure Sensor in the left pulmonary artery (A). A selective angiography shows unimpaired pulmonary artery blood flow (B).

**Figure 3 Bedside 6-h Recordings**

On top is the Swan-Ganz reading and at the bottom is the CardioMEMS Heart Failure Sensor pulmonary artery pressure waveform.
artery pressure (PAdia) was 23 ± 14 mm Hg and 28 ± 16 mm Hg for HFS and SG, respectively (p = 0.30). A good correlation was observed between HS and SG (r^2 = 0.88 at initial implant, r^2 = 0.48 at follow-up, p < 0.01) with a mean difference of −1.6 ± 6.8 mm Hg (Fig. 5).

Comparison of PAP between HFS and ECHO. Systolic PAP was 60 ± 20 mm Hg and 62 ± 12 mm Hg for HFS and ECHO, respectively (p = 0.47). Linear regression showed a good correlation between HS and ECHO measurements (r^2 = 0.75, p < 0.01). The limits of agreement analysis for variability between both methods demonstrated a mean difference of −2.6 ± 11 mm Hg, as shown in Figure 6. There was no significant variation over time in the difference between both methods. Echocardiography determination of PAdia was only feasible in 2 patients, showing a known limitation of the method and invalidating further comparison.

Interobserver variability. The results of the interobserver variability assessment for PAsys are shown in Figure 7. No significant difference was present between the 2 independent observers. The limits of agreement analysis for interobserver variability showed a mean difference of −0.8 ± 6.5 mm Hg for PAsys. For PAdia, linear regression analysis showed an adequate correlation (r^2 = 0.79). The limits of agreement analysis demonstrated a mean difference of −2.5 ± 5.7 mm Hg.

Safety. There were no adverse effects associated with device implantation. All patients received intravenous unfractionated heparin during the procedure and remained on oral warfarin for an international normalized ratio between 2.0 to 3.0 afterward. Animal studies with long-term follow-up and histopathological evaluation showed that the sensor is well tolerated by the local pulmonary artery wall and incorporated into the pulmonary artery tissue by stable fibrocellular encapsulation after 3 to 6 months of implantation. There was no propensity for in-situ thrombus formation (unpublished data, K. Robinson et al., 2005). As a precautionary measure, ventilation/perfusion scans were performed at screening and 14 days after implantation to further assess the device’s security.

Discussion

The results demonstrate that this new HFS allows accurate and reliable noninvasive measurement of PAP in HF patients, compared with the currently available methods (SG catheterization and ECHO). In porcine experimental models, the HFS had showed good correlation with invasive pressure evaluations and no evidence of prothrombotic effect on the pulmonary artery. Recently, our group published the first successful implant in an HF patient (19).

A number of studies had shown the limitations of careful clinical assessment of the hemodynamic profile in HF patients (12,20) in order to identify patients at imminent risk of decompensation. The role of B-type natriuretic peptide (BNP) in this scenario requires further clarification. Small clinical studies had suggested that BNP is a useful tool for therapy tailoring in compensated HF patients (21,22); however, normal BNP values show a widespread distribution. Moreover, 21% of symptomatic decompen-sated patients could have BNP levels below the diagnostic threshold (22). Alternative strategies as routine hemodynamic monitoring are a subject of controversy (13,23,24). Kovick et al. (25) were the first to report SG catheterization as a tool for tailoring therapy in decompensated HF, with promising initial results that were repeated in nonrandomized clinical studies (26). The ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) trial (27) was the first randomized clinical trial aimed at evaluating the impact of invasive hemodynamic monitoring compared with standard care in the in-hospital management of HF patients admitted for decompensation, with a history of repeated hospitalizations and systolic dysfunction (left ventricular ejection fraction <30%). Both groups showed significant clinical improvement, without any difference in survival after discharge or

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LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PAP = pulmonary artery pressure; PAPD = diastolic pulmonary artery pressure; PAPS = systolic pulmonary artery pressure.
new hospitalizations. There were, however, a significant number of complications associated with the catheterization. These findings have been reproduced in 2 meta-analyses, evidencing the limitations of SG catheterization for therapy tailoring and establishing the actual recommendation to avoid routine use of invasive monitoring in decompensated HF (28–30).

Another strategy more suitable for outpatient monitoring is repeated ECHO evaluation. The role of echocardiography in the initial assessment of decompensated HF is undisputable and constitutes a current practice in most HF clinics. In the outpatient setting, ECHO allows identification of a group of patients with higher morbidity and mortality (31). In particular, presence of restrictive transmural flow patterns despite optimal management relates with BNP levels and PAP and is associated with a poorer prognosis. However, repeated echocardiograms seem to add little information to the initial prognostic assessment (32).

Implantable devices for ambulatory hemodynamic monitoring appeared the last few years as an alternative for optimizing clinical management of outpatient HF. Initial observational studies showed their usefulness in titrating vasodilation therapy in HF patients. The Chronicle device (Medtronic Inc., Minneapolis, Minnesota) is implanted subcutaneously in the pectoral region. A transvenous electrode with an apical sensor located in the right ventricular
outflow track allows continuous monitoring of right ventricular filling pressures. A first randomized trial with this device (33) enrolled HF patients in NYHA functional class III to IV with standard therapy and repeated hospitalizations in the last 6 months. Right ventricular filling pressures and estimated PAPdia were transmitted to a central station, but they were not available to the clinicians for therapy adjustment in nearly 50% of the cases. In NYHA functional class III patients (85%), guided therapy resulted in a 24% reduction in the number of hospitalizations due to decompenated HF. In a similar trial, Yu et al. (34) evaluated an alternative method for central hemodynamic monitoring with a device capable of sensing transpulmonary impedance, which closely correlates with intrapulmonary water content. Thirty-three patients underwent cardiac resynchronization therapy with an impedance-sensing device (OptiVol, Medtronic Inc.). Consistently, decreases in transpulmonary impedance preceded clinical decompensation. Therapy with diuretics and vasodilators raised impedance to normal levels, correlating inversely with pulmonary capillary wedge pressure.

Our study is the first clinical series of a new implantable device for real-time evaluation of PAP in HF patients. Although PAP changes have not shown a consistent correlation with symptom improvement in the acute HF setting.

Figure 5  Comparison Between Heart Failure Sensor and Swan-Ganz PAdia Determination

Bland-Altman analysis (A) and linear correlation at implant (B) and at follow-up (C) between Swan-Ganz and CardioMEMS Heart Failure Sensor (HFS) diastolic pulmonary artery pressure (PAdia) measurements. In panel A, data and the associated SD’s confidence intervals are combined for the readings taken at initial implant and for the 2 follow-up intervals.
several trials demonstrate the value of PAP as a predictor of morbidity and mortality in ambulatory patients. The lack of direct determination of right ventricular pressures is a known limitation of pulmonary artery devices. However, there is no current data regarding which measurement (PAP or right ventricular pressures) provides the best guide in ambulatory HF patients. The potential of PAP as a therapeutic guidance tool needs to be addressed in further studies. The main objective of this report was to evaluate the accuracy of HFS determinations compared with SG and ECHO, showing an excellent correlation with both new and traditional methods, high reproducibility of the measurements, low interobserver variability, and a favorable safety profile. Systolic pressure as determined with HFS tended to be higher than SG measurements. Because the systolic parameter is derived from the highest frequency part of the waveform, it is the most sensitive parameter to differences in measurement method and sampling rate. The wireless sensor provides a direct pressure measurement at the site, whereas the SG is an indirect measurement transmitted through a column of fluid. When measuring from the external transducer through the column of fluid, there can be a higher level of variation as the frequency (rate of change) of the waveform increases, due to whiplash, ringing, dampening, or other artifacts commonly seen in column of fluid measurements. More precise measurements of pulmonary systolic artery pressure, as can be achieved with a Millar catheter (Millar Instruments Inc., Houston, Texas), could provide a more reliable standard for comparison. The simplicity of device implantation and the absence of a wire lead or the need of battery replacement constitute another comparative advantage to other implantable devices currently available. Data shown in this study are part of a larger phase II trial designed to evaluate the feasibility of device use in humans. In most of the cases, PAP values were put at the disposition of the clinical physician. An incremental use of diuretics and vasodilators and clinical subjective improvement were reported in most patients (data not shown). However, study design and sample size do not allow evaluation of the impact on clinical events.

Conclusions

In summary, there is a growing interest in development of new devices to optimize management and clinical recognition of HF patients at imminent risk of decompensation. The HF device has comparative advantages to other currently available implantable devices in terms of simplicity of implantation procedure, safety profile, and small size, providing
accurate measurements in the follow-up. In our opinion, these findings support the development of a randomized clinical trial to evaluate the clinical usefulness of this device in advanced HF patients.

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