Cordella® Clinical Compendium

UPDATED JUNE 2025

An overview of published peer-reviewed literature on the Cordella Pulmonary Artery (PA) Sensor and Heart Failure (HF) System showing consistent results in safety and efficacy.

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PROACTIVE-HF Pivotal Trial 6-Month Results

FDA Approval

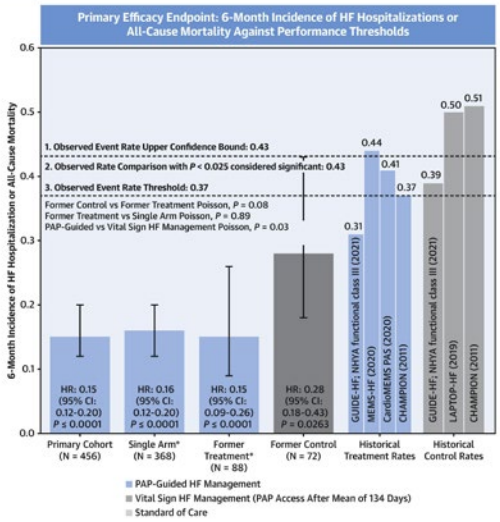
Seated pulmonary artery pressure monitoring in patients with heart failure: results of the PROACTIVE-HF trial

GUICHARD JL ET AL. J AM COLL CARDIOL HF 2024.

Trial Background

- Single-arm, open label trial with blinded endpoint assessment to evaluate the safety and effectiveness of the Cordella PA Sensor and HF System in NYHA class III patients with prior HF Hospitalization (HFH) or elevated natriuretic peptides.
- Study was originally approved as a prospective, randomized, controlled, single blind study but was changed in consultation with the FDA as the clinical evidence around PA pressure-guided HF management increased substantially.
- 456 patients were successfully implanted in a modified intent-to-treat cohort.
  - 80% of cohort had previous HFH within the previous 12 months.
  - Highly diverse cohort (40% female, 24% non-white, 54% HFpEF).
  - 115 unique implanters (52% HF physicians, 48% interventional cardiologists).
- Primary endpoints were evaluated at 6 months.
- Both primary safety endpoints were met.
  - 99.2% freedom from device or safety-related complications (DSRC) (95% CI 97.9%–99.7%) at 6 months.
  - 99.8% freedom from PA sensor failure (95% CI 98.6%–100%) at 6 months.
- Primary effectiveness endpoint was met.
  - Markedly low 0.15 HFH/all-cause mortality event rate at 6 months (95% CI 0.12 to 0.20).*
  - Event rate was less than half and significantly lower than the prespecified performance goal of 0.43, which was determined based on previous PA pressure studies.

CENTRAL ILLUSTRATION: Primary Effectiveness Endpoint for PROACTIVE-HF



Guichard JL, et al. JACC Heart Fail. 2024;12(11):1879-1893.

Key Secondary Endpoints	6-Month Results (Compared to Baseline)
HF Hospitalization Rate	80% reduction
HF Hospitalization/All-Cause Mortality Rate of PA pressure guided HF management group vs formal control group*	44% reduction
KCCQ	+5-point improvement (p<0.0001)
6-Minute Walk Test	+23 meter improvement (p=0.001)
NT-proBNP	Positive trend (p=0.06)
NYHA Functional Classification	32% (n=146) of patients improved (p<0.0001)
Seated mPAP	2.4 mmHg reduction for congested patients
In-office Blood Pressure	5.9 mmHg reduction

Key Takeaways

- For HF patients with NYHA class III symptoms at risk of congestive events, the Cordella PA Sensor and HF System was safe; improved quality of life (QoL), functional class, and functional capacity; and enabled a significant reduction in PAP in patients with elevated baseline seated mPAP.
- Event rates at 6-months were consistent with previously reported event rates for Cordella.
- The ability to remotely monitor seated mPAP with Cordella enabled markedly low event rates compared with earlier trials that evaluated PAP from a supine position.
- High engagement from patients and reviewing clinicians, with 6.2 average patient submissions per week and 2.2 average days between clinician reviews, resulted in high patient compliance.
- Observations of HF medication changes:
  - The majority of medication changes (69%) were oral diuretic changes with the balance GDMT changes, and the number of changes declined over time.
  - Angiotensin Receptor-Neprilysin Inhibitor (ARNi), Aldosterone Receptor Antagonists (MRA) & diuretic doses increased with PAP-guided management.
  - HFpEF patients had more dose adjustments than HFrEF with similar event rates.
  - Higher baseline PAP cohort associated with more medication optimization.

IMPACT

Remote monitoring of seated mPAP in conjunction with daily vital signs with Cordella is safe and effective in achieving lower rates of HF hospitalization and may provide better guidance for treating chronic HF patients.

* Published PROACTIVE-HF study datapoints varied slightly from the FDA Summary of Safety and Effectiveness Data (SSED) due to a change in statistical analysis (0.159 & 49%).

PROACTIVE-HF Pivotal Trial 12-Month Results

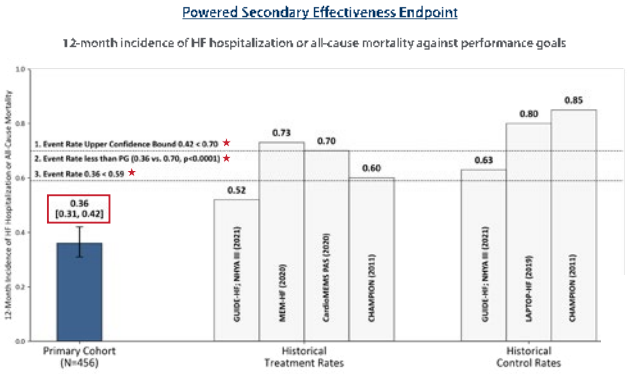
Long-Term Follow Up

Seated Pulmonary Artery Pressure Management in Patients with Heart Failure: 12-Month Outcomes in the PROACTIVE-HF Trial

KLEIN L ET AL. PRESENTED AT HFSA 2024.

Long-Term Follow Up

- Long-term follow-up on PROACTIVE-HF pivotal trial evaluating clinical endpoints over a 12-month period.
- Secondary safety endpoints were met at 12 months.
  - No further DSRC or sensor failures beyond the 6-month primary endpoint (99.2% freedom from DSRC & 99.8% freedom from PA sensor failure).
  - Low incidence of serious adverse events:
    - Acute Kidney Injury (AKI): 2.4%
    - Pulmonary Embolism (PE): 1.0%
    - Bleeding: 0.6%
    - Myocardial Infarction (MI): 0.4%
    - Arrhythmia: 10.1%
    - Hemoptysis: 3.0%
- Powered secondary effectiveness endpoint was met at 12 months.
  - Maintained low 0.36 HFH/all-cause mortality event rate (95% CI 0.31 to 0.43).
  - Event rate was significantly lower than the prespecified performance goal of 0.70, which was determined based on previous PA pressure studies.



Key Secondary Endpoints	12-Month Results (Compared To Baseline)
HF Hospitalization Rate	73% reduction
KCCQ	+5.7-point improvement (p<0.0001)
6-Minute Walk Test	+35 meter improvement (p=0.0004)
NT-proBNP	268 pg/mL decrease (p=0.006)
NYHA Functional Classifications	36% (n=165) of patients improved (p<0.0001)
Seated mPAP	1.4 mmHg reduction for congested patients (p=0.04)

Key Takeaways

- Cordella enabled markedly low rates of HFH and all-cause mortality at 12 months.
- Cordella was safe, improved patient quality of life (QoL) metrics and enabled significant reductions in mPAP for patients elevated at baseline through 12 months of follow up.
- High engagement from patients and reviewing clinicians, with ~6 average patient submissions per week and ~2 avg days between clinician review.

IMPACT

Results support the use of seated mPAP monitoring with the Cordella PA Sensor and adds to the growing body of evidence that PAP-guided management improved outcomes in NYHA class III heart failure patients.

PROACTIVE-HF Substudy

Patient Engagement

Engaging Patients and Clinicians with Remote Pulmonary Artery Pressure Improves Care: A Substudy of the PROACTIVE-HF Trial

COWGER JA ET AL. PRESENTED AT HFSA 2023.

Key Takeaways

- Sub-study of PROACTIVE-HF evaluated the impact of revealing mPAP data from the Cordella HF system to patients and clinicians.
- Changes in mPAP, HF medications, and HF hospitalizations were analyzed before and in the 12 months following unblinding in 63 patients.
  - In the blinded period, average seated mPAP increased significantly.
  - In the unblinded period, average seated mPAP for patients above target (> 20 mmHg) decreased significantly.
  - In the unblinded period, average seated mPAP for patients in target range (5–20 mmHg) were unchanged.
  - The average number of HF hospitalizations was significantly higher in the 12 months prior to Cordella implant than in the 12 months post-unblinding.
  - 78% of patients made lifestyle changes based on their mPAP trends.
  - 86% of patients rated impact of PAP management on their health as positive.
- Virtual access to patient vital signs via the Cordella HF System led to clinically significant improvements in patient mPAPs. Patients prefer to have access to their PAP data, and data access supports clinician interventions directed at mPAP lowering and may enable favorable behaviors in patient self-care.

IMPACT

This was the first study where patients had access to their PAP data which led to clinically significant improvements and favorable changes in patient behaviors.

PROACTIVE-HF Substudy

Medication Change Analysis

Changes in Seated Pulmonary Artery Pressure in Response to Titration of Heart Failure Medications During Ambulatory Monitoring

ZALAWADIYA SK L ET AL. J CARD FAIL. 2025

Key Takeaways

- Sub-analysis of the PROACTIVE-HF 12-month results that evaluated the 14-days before and after isolated changes in medications. Only medications with >10 titrations were analyzed.
- The seated mPAP changed expectedly in response to the titration of loop diuretics (LD), whereas the degree of response varied for angiotensin receptor neprilysin inhibitor (ARNI) and mineralocorticoid receptor antagonist (MRA).
  - Before LD up-titration, mPAP increased by 1.6 ± 1.0 mmHg; afterwards, it decreased by 2.3 ± 1.0 mmHg (p< 0.001), with most reduction occurring within 1 week.
  - Down-titration of LD was followed by an increase of 1.8 ± 1.3 mmHg (p=0.004) over the next several days.
  - ARNI up-titration decreased mPAP by 1.8 ± 1.9 mmHg (p=0.042), whereas down-titration increased mPAP by 1.5 ± 1.4 (p=0.094).
  - MRA up-titration tended to decrease mPAP (1.6 ± 2.5 mmHg, p=0.286,) whereas down-titration was followed by a significant increase in mPAP of 3.2 ± 1.6 mmHg (p=0.001).

IMPACT

The Cordella PA Sensor provides valuable insights into how seated mPAP responds to changes in both diuretics and GDMT in the outpatient setting.

PROACTIVE-HF Trial Design

Rationale and Design of the PROACTIVE-HF Trial for Managing Patients with NYHA Class III Heart Failure by Using the Combined Cordella Pulmonary Artery Sensor and the Cordella Heart Failure System

GUICHARD JL ET AL. J CARD FAIL. 2023

Key Takeaways

- Publication provides overview of the study design of the PROACTIVE-HF trial.
- The PROACTIVE-HF study was originally approved in 2018 as a prospective, randomized, controlled, single-blind, multicenter trial to evaluate the safety and effectiveness of the Cordella PAP Sensor in patients with HF and with NYHA class III symptoms.
- In 2021, PROACTIVE-HF was changed to a single-arm trial with prespecified safety and effectiveness endpoints following the release of robust clinical evidence supporting PAP-guided HF management, making clinical equipoise and enrolling patients into a standard-of-care control arm challenging.
- Key trial hypotheses are that HF management using Cordella PA Sensor in combination with additional vital-sign parameters will provide the dual benefits of congestion management and GDMT optimization and that patient engagement and compliance will positively impact remote medical management decisions and patient outcomes.

IMPACT

PROACTIVE-HF was changed from a randomized controlled trial (RCT) to a single-arm trial mid-study due to the abundance of data demonstrating the positive clinical benefit of PA-pressure-guided therapy for NYHA class III patients. Additionally, the COVID-19 pandemic altered the clinical trial landscape, making patients less willing to subject themselves to risk without immediate clinical benefit.

SIRONA 2 Trial 6-Month Results

Accuracy

Safety and Efficacy of a Wireless Pulmonary Artery Pressure Sensor: Primary Endpoint Results of the SIRONA 2 Clinical Trial

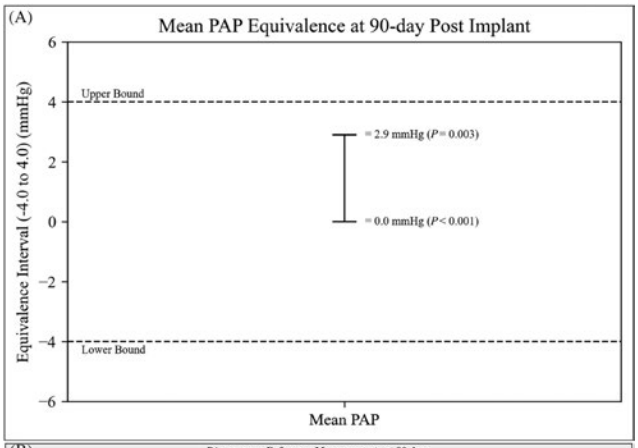
SHARIF F ET AL. ESC HEART FAIL 2022

Key Takeaways

- Prospective, multi-enter, open-label, single-arm trial evaluating the safety and efficacy of the Cordella PA Sensor and HF System in patients with NYHA class III heart failure.
- The primary efficacy endpoint was the accuracy of PA sensor mean PAP measurements, compared with fluid-filled catheter mean PAP measurements obtained by standard right heart catheterization (RHC) at 90 days post-implant.
- The primary safety endpoint was freedom from adverse events associated with use of the Cordella PA Sensor System through 30 days post-implant.
- Key findings include:
  - Equivalence between Cordella and RHC for mean pulmonary artery pressures was excellent with measurements confined within the equivalence bounds of –4.0 to 4.0 mmHg (mean PAP: 0.0 to 2.9 mmHg, p=0.003).
  - The device safety profile was excellent with 98.6% freedom from Device or System-Related Complications (DSRC), defined as invasive treatment, device explant or death.
  - There were no pressure sensor failures.
  - Patients' adherence to daily measurement transmissions of PAP and vital signs was 94%.
- A survey of study patients revealed 97% of patients would recommend the myCordella patient kit to others.

IMPACT

This trial supports the safety and efficacy of the Cordella PA Sensor System and, in conjunction with the Cordella HF System, enables comprehensive HF management in NYHA class III heart failure patients.



(B) PA sensor vs Reference Measurements at 90 days

PAP Parameter	Sample Size	PA Sensor (mmHg)		Reference (mmHg)		Difference		Pearson Correlation Coefficient (r)
		Mean	SD	Mean	SD	Mean	SD	
Mean PAP	58	27.6	12.1	26.1	10.4	1.4	6.7	0.83
Systolic PAP		44.4	19.4	44.7	18.4	-0.3	7.4	0.92
Diastolic PAP		18.1	9	15.8	7.4	2.3	7.7	0.58

SIRONA 2 Trial 12-Month Results

Seated PA Pressure

Twelve-Month Follow-Up Results from the SIRONA 2 Clinical Trial

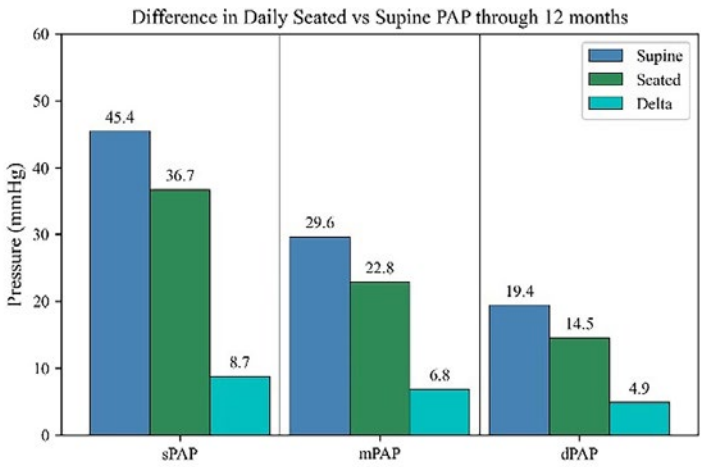
SHARIF F ET AL. ESC HEART FAIL 2024

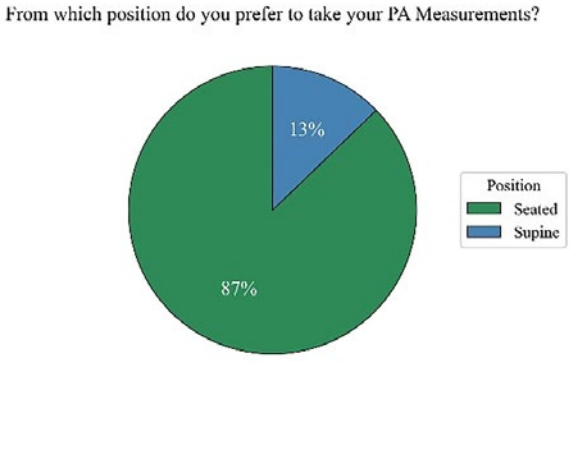
Trial Background

- Prospective, multicenter, open-label, single-arm trial evaluating the safety and efficacy of the Cordella PA sensor and HF system in NYHA class III HF patients with prior HF Hospitalization (HFH) or elevated natriuretic peptides in prior 12 months.
- 70 patients were successfully implanted with the Cordella PA sensor at 7 sites across Europe.
  - Baseline characteristics include 71.4% male, mean age of 71 years and a mean BMI of 28.9 kg/m^2.
- Safety endpoints at 12 months:
  - No pressure sensor failures.
  - 98.4% freedom from device/ system-related complications.
- Efficacy endpoints at 12 months:
  - Good agreement between the Cordella PA Sensor System and right heart cath (RHC), with the average difference for mean PAP being 2.9 ± 7.3 mmHg.
  - HF hospitalizations and mortality were low with a rate of 0.33 event per patient year.
  - Symptoms as assessed by NYHA class ($p<0.0001$) and functional capacity as measured by 6 min walk test ($p=0.02$) were significantly improved.
  - Patients' adherence to daily transmissions of PAP and vital signs measurements was 95%.

Key Takeaways

- First report of long-term (>90 days) use of the implantable Cordella PA sensor.
- Cordella continued to show an excellent safety profile, high patient compliance (95% at 12 months), and low rates of HFH and death.
- Measurement error of the Cordella PA sensor relative to RHC was not significantly different between 90 days and 12 months, suggesting excellent long-term stability of the sensor.
- Patients had access to and were engaged with their vital sign data, suggesting that having access to their health data is an important step in improving knowledge of their HF condition.
- 97% of respondents found the system easy to use.
- 82% noticed and monitored their daily measurements.
- 51% made changes to their lifestyle based on daily readings.
- Cordella enables patients to take their readings in either seated or supine posture.
  - Over 16,000 paired seated and supine measurements were submitted by patients from home with an average difference of 6.8 ± 5.7 mmHg for mPAP; 4.9 ± 4.6 mmHg for dPAP; and 8.7 ± 7.3 mmHg for sPAP.
  - 87% of patients preferred to take their readings in the seated posture.





IMPACT

Use of the Cordella PA Sensor and HF System enables long-term safe and accurate monitoring of HF status in NYHA class III patients. Cordella enables readings to be taken in either seated or supine posture, with patients largely preferring to take their readings in the seated posture.

SIRONA First-In-Human Trial 6-Month Results

Early Clinical Experience

Digital Healthcare Solution for PROACTIVE Heart Failure Management with the Cordella Heart Failure System: Results of the Sirona First-In-Human Study

MULLENS W ET AL. EUR J HEART FAIL. 2020

Key Takeaways

- First-in-human study to evaluate the safety and accuracy of the Cordella PA Sensor and HF System in 15 patients with NYHA class III HF.
- Key findings include:
  - All patients were successfully implanted with the Cordella PA Sensor, without sensor failure.
  - No device system-related complications, defined as invasive treatment, device explant or death, occurred.
  - The primary efficacy endpoint of a mean pulmonary artery pressure at 90 days was met in all but one patient with a cohort difference of 2.7 mmHg (Cordella Sensor 22.5 ± 11.8 mmHg, Swan-Ganz catheter 25.2 ± 8.5 mmHg).
  - Patient adherence to daily measurement, transmission of vital signs and pulmonary artery pressure sensor readings were recorded 99% of the time.

IMPACT

The initial experience of the Cordella HF System incorporating comprehensive vital signs and pulmonary artery pressure monitoring enables safe and accurate monitoring of HF status.

PAP During Exercise

Feasibility of Continuous Non-Invasive Pulmonary Artery Pressure Monitoring Via the Cordella Implantable Pulmonary Artery Sensor in Heart Failure Patients Undergoing Exercise

MULLENS W ET AL JACC-HF 2024

Key Takeaways

- Observational study that evaluated the feasibility of continuously and noninvasively measuring PAP using the Cordella PA Sensor in HF patients undertaking exercise, a 6-minute walk test (6MWT).
- PAP measurements using the Cordella hands-free PA reader achieved excellent signal quality and no adverse effects with significant increase in PAP during the 6MWT.
  - PAP was continuously recorded for a minimum of 17 minutes in all cases (n=12 subjects).
  - PA pressures and heart rate increased significantly during the 6MWT (systolic: +29.2 mmHg [Q1-Q3: 23.1-34.7 mmHg]; diastolic: +13.2 mmHg [Q1-Q3: 9.9-16.4 mmHg]; mean: +21.1 mmHg [Q1-Q3: 9.9-16.4 mmHg]; heart rate: +24.0 beats/min [Q1-Q3: 18.0-36.0 beats/min]; all values of $p<0.05$) and decreased significantly during recovery.
  - Of the measures taken before and after the 6MWT and recovery, only systolic BP increased significantly following the 6MWT (+2.0 mmHg [Q1-Q3: –2.8 to 18 mmHg]; $p<0.05$) and decreased following recovery.

IMPACT

Continuous, noninvasive PAP measurement using the Cordella PA Sensor system is feasible in HF patients during exercise.

Implantation Technique

A Procedural Guide for Implanting the Cordella Pulmonary Artery Pressure Sensor

GUICHARD JL ET AL. J INVASIVE CARDIOL. 2023

Key Takeaways

- Publication provides a summary of the implantation procedure and presents a series of cases detailing the Cordella PA pressure sensor implantation in the United States and Europe.
- Authors describe improved access options, minimal iodinated contrast use, and low procedure times for the Cordella sensor implantation.
- Authors also highlight that Cordella has an anatomic "landmark-based" design meant to be deployed in the right pulmonary artery (RPA) which differs from the "diameter-based" design of other PA sensors that are typically implanted in the left pulmonary artery.
- Location of Cordella in the RPA allows for a short-link distance between the implanted sensor and external reader on the anterior chest to facilitate readings.

IMPACT

Understanding the implantation procedure and technical nuances of the Cordella PA sensor is key to safe, efficient, and effective implantation to allow for successful use over the long term.

NYHA Class III patients: In the US, the Cordella PA Sensor System is Rx Only. CAUTION: Federal law restricts this device to sale by or on the order of a physician. In Europe, the Cordella PA Sensor System is Exclusively for Clinical Investigation.

NYHA Class II patients: The Cordella PA Sensor System is an investigational device and is not currently approved for clinical use in any geography, nor has it been proven safe or effective in NYHA Class II patients. CAUTION – Investigational Device. Limited by Federal (or United States) Law to Investigational Use. Exclusively for Clinical Investigation.

The potential risks of the Cordella PA sensor procedure are similar to other heart procedures. The most serious risks include, but are not limited to death, serious damage to the arteries or valves, serious bleeding, pulmonary embolism/occlusion, allergic reactions, arrhythmias, renal issues, and worsening heart failure. For a complete list visit endotronix.com/safety.

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