CardioMEMS™ HF SYSTEM CLINICAL PROTOCOL EXAMPLE

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Medical Director St. Jude Medical, the former Director Heart Failure Institute at Oklahoma Heart Hospital, shares his experience with patient management of heart failure using PA Pressure.

The following document serves as an example of possible clinical use of the CardioMEMS™ HF System based on experience from Dr. Philip B. Adamson, Medical Director St. Jude Medical, the former Director Heart Failure Institute at Oklahoma Heart Hospital. Medical care of the patient is the sole responsibility of the acting practitioner. This document is not intended to replace the judgement of the acting practitioner nor the establishment of final protocols established within the hospital setting.

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OVERVIEW AND RATIONALE FOR USE

The U.S. Food and Drug Administration approved the CardioMEMS™ HF System, which measures pulmonary artery (PA) pressures and heart rates of patients with New York Heart Association (NYHA) Class III heart failure who have been hospitalized for heart failure in the previous year. The device provides remote monitoring of PA pressures as the basis to change medical management of patients with heart failure and avoid decompensation leading to hospitalization.

This strategy was compared to all available monitoring parameters commonly used in disease management systems in the context of the CHAMPION clinical trial, a multi-center, prospective, randomized, single-blinded trial. This trial demonstrated that pressure-guided heart failure (HF) management was a superior means to maintain stability in high-risk patients, resulting in less need for hospital admission to control decompensation and less readmissions at 30 days following HF hospitalization. The introduction of the CardioMEMS HF System is a significant technologic breakthrough leading to improved outcomes in this very difficult-to-manage population.

System Description

The patient uses the CardioMEMS HF System in the home or other remote location. The CardioMEMS HF System is the first permanently implantable wireless system intended to provide PA pressure measurements, including systolic, diastolic and mean PA pressures. The PA pressure data are reviewed by providers (physicians, Advanced Practice Provider or nurses) who can make decisions regarding the status of the patient and, if necessary, initiate changes in medical therapy with the goal of reducing hospitalization due to heart failure. Changes in medications by nonphysician providers will require establishment of appropriate supervisory protocols according to local licensure laws; an example will be outlined later in Table 1.

The CardioMEMS HF System consists of three parts:

1. A battery-free Implantable Sensor implanted permanently in the PA via right heart catheterization;

2. Delivery System, a transvenous catheter designed to deploy the Implantable Sensor, within the distal PA; and

3. CardioMEMS Hospital and Patient Electronics Systems where the Electronics System acquires and processes signals from the Implantable Sensor/Monitor and transfers PA pressure measurements to a secure database.

Clinical Use

Use of the CardioMEMS HF System is generally divided into four phases: 1) patient selection and implantation, 2) personnel assignment and medication titration to normalize PA pressures, 3) baseline pressure ranges and the email notification system and 4) monitoring pressure deviation from the new baseline.

PHASE 1
PATIENT SELECTION AND IMPLANTATION

Patient Selection

Patient selection is very important when prescribing implantable hemodynamic monitoring as trials clearly have demonstrated that some patients are too well and some patients are too sick to benefit from the management strategy.

The CHAMPION clinical trial enrolled previously hospitalized patients with NYHA Class III symptoms, which means the subjects had dyspnea that limited exertion with minimal effort. There was no ejection fraction criterion for entry to the trial, which makes the CardioMEMS™ HF System the first device-based management strategy that improves outcomes in patients with preserved ejection fraction HF syndromes. The trial specifically excluded patients with ACC/AHA stage D heart failure, deemed in need of advanced therapies such as left ventricular assist device, transplant or continuous or intermittent inotropic support. Even if inotropic support led to improved symptoms, the patient, by definition, had stage D, refractory HF. In addition, renal function was an important exclusion criterion, excluding patients with eGFR less than 25 ml/kg/1.73m^2. Finally, patients who were unable to tolerate Plavix and aspirin therapy were not implanted with the sensor.

It should be clearly noted that patients in the CHAMPION clinical trial received maximally tolerated medical therapy, including appropriate dosing of ACE inhibition or ARB, beta-blocker therapy with a consensus recommended agent, or aldosterone antagonism appropriate for disease state. In addition to medical therapies, patients already benefitted from CRT or ICD therapies in place, if indicated. Drug intolerance should be documented for agents not being used in the patient's care, which would include why they are not receiving maximally recommended doses. Visit https://Clinical.SJM.com for a full list of Clinical Considerations.

Implantation

Once a patient is deemed an appropriate candidate, informed consent is obtained outlining the risks of bleeding, bruising, heart and lung injury, contrast injury, hemoptysis, death, infection, arrhythmias, thrombus, myocardial infarction, transient ischemic attack, stroke, and device embolization. The clinical trial experience can be relayed to the patient: 8 device- or system-related complications in 550 patients implanted. All complications in the trial were resolved. Therefore, risks of implantation should include standard risks associated with right heart catheterization, injection of IV contrast and description of the complications that may occur with sensor implantation. Additionally, the patient should be informed that it may be possible that they will not receive a sensor if their pulmonary anatomy is not suitable to receive the device. See the users manual for a complete list of target implant site criteria.

In the CHAMPION Trial, patients on warfarin, factor Xa inhibitors or direct thrombin inhibitors were managed according to local periprocedural practice, but this level of anticoagulation was continued following implant of the sensor. Patients who were not on warfarin, factor Xa inhibition or direct thrombin inhibitors were instructed to take aspirin 81 or 325 mg daily and clopidogrel 75 mg daily for 1 month after sensor implantation. After 1 month, patients continued with aspirin therapy only, unless clopidogrel was used for another long-term indication.[1] Use of the CardioMems HF System is contraindicated in patients unable to tolerate aspirin or clopidogrel therapy.[2]

After successful implantation of the device, which can be accomplished as an outpatient or during a hospitalization for heart failure, patients are typically observed in the hospital overnight. This time should be used for education and to teach the patient about his or her device, how to interrogate the sensor and troubleshoot. The patient is taught that he or she should upload daily; specific expectations should be directly verbalized about follow-up. The patient should be told that he or she will NOT receive a phone call each time there is an upload; the patient will only hear from the HF clinic if medication changes are needed. After education is complete and competency is demonstrated, the patient is discharged with the interrogation system for follow-up.

During the right heart catheterization, the pulmonary capillary wedge pressure should be compared to right atrial pressure to provide a general understanding of how much volume versus vascular resistance contributes to the elevated PA pressure. Patients with evidence for elevated intravascular volume will likely initially benefit from increased diuretic use. Those with mostly vascular resistance problems may benefit from careful titration of long-acting nitrates as long as they are well perfused and not hypotensive.

PHASE 2
PERSONNEL ASSIGNMENT AND MEDICATION TITRATION TO NORMALIZE PA PRESSURES

Personnel Selection

Heart failure clinical staff trained to use the CardioMEMS™ HF System should be identified as the primary nurse or Advanced Practice Provider responsible for hemodynamic monitoring in each patient. A backup should also be identified, which may be the HF physician or another nurse or Advanced Practice Provider. This person will receive email notifications for pressure excursions and review pressures at least once a week on the Merlin.net™ Patient Care Network (PCN) website. The primary reviewer will also be responsible for medication changes according to the established protocol, which includes discussion and review with the HF physician. The Merlin.net PCN website will be set up using the primary reviewer's email address and contact information along with patient demographics, medications and contact information.

Figure 1 provides an overview of PA pressure data flow in established HF disease management programs.

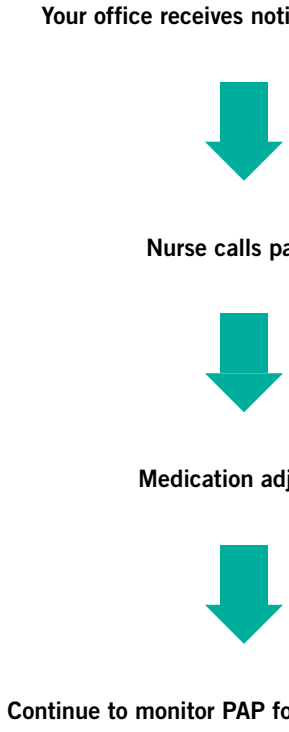


Figure 1. PA pressure data flow in established heart failure disease management programs

Medication Titration to Normalize PA Pressures

The goal of phase 2 medical management is to lower PA pressures to normal. All three pressures monitored (PA systolic, PA diastolic and PA mean) have unique goals and the email alert system thresholds default settings are normal ranges. If initial PA pressures are out of range, and if information at the implant right heart catheterization suggests excess volume, the first action is to intensify diuretic therapy. This may be an increase in loop diuretic dose, change to a more bioavailable agent or the addition of a distally active agent such as metolazone. Electrolyte supplementation should be intensified at the same time of the increase in diuresis.

Pressures should be watched daily or every other day to determine the effect of increased diuretics, and the patient should measure his or her systemic blood pressures at home. Renal function and electrolytes (including magnesium) should be measured within seven days of increasing diuretic and electrolyte therapies. Diuretic dosing should be decreased or discontinued if the patient develops worsening renal dysfunction (increase in creatinine by 20%) or becomes hypotensive. If PA pressures are still high after diuretic intensification, careful addition or intensification of vasodilator therapy should be considered.

The most used vasodilator in the CHAMPION clinical trial was long-acting nitroglycerin often coupled with hydralazine. This drug should be considered in patients with persistently elevated PA pressures after diuretic intensification, as long as they are well perfused and have systemic blood pressures appropriate for this therapy. Vasodilator therapy should be started after physical assessment of the patient focusing on perfusion and systemic blood pressure. Vasodilator therapy should be withheld in patients with evidence for hypoperfusion or hypotension. Once initiated at the lowest dose for the agent chosen, the dose can be uptitrated weekly while following PA and systemic pressures.

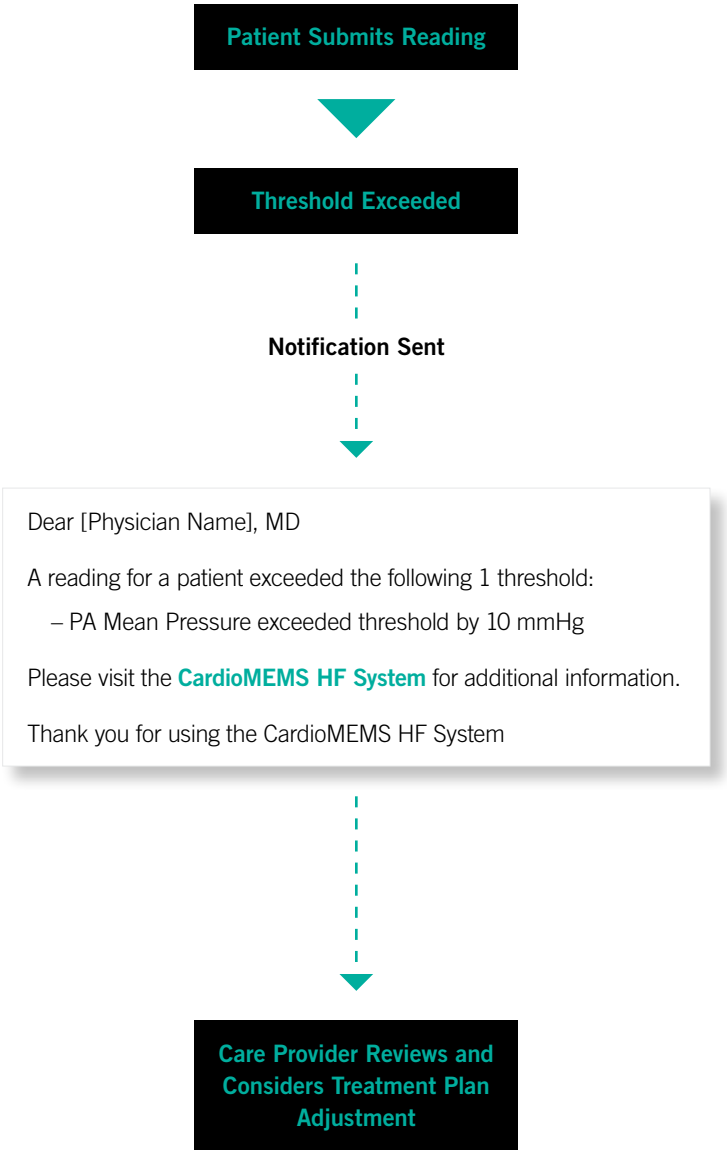
As noted above, the goal of phase 2 is to normalize PA pressures. If those pressures cannot be normalized with diuretic intensification or vasodilator therapy, then pressure ranges should be reset in phase 3.

PHASE 3
BASELINE PRESSURE RANGES AND THE EMAIL NOTIFICATION SYSTEM

Baseline Pressure Ranges

Patients entering phase 3 will be reassessed physically with particular attention to perfusion (exam with orthostatic vital signs) and functional capacity. Also, renal function and electrolytes should be reevaluated. Patients with persistently high PA pressures after phase 2 is completed should have their PA pressure thresholds changed in the Merlin.net PCN website. Attention should be given to each patient's pressure variability, and thresholds should be set to account for natural variability, thereby avoiding unneeded notifications. Each pressure (PA systolic, diastolic and mean) should be individualized for the patient's status and phase 4 starts.

Email Notification System



PHASE 4
MONITORING PRESSURE DEVIATION FROM THE NEW BASELINE

Phase 4 is longitudinal management of the patient and includes development of an individualized prescription, made in collaboration with the HF physician, for sliding-scale diuretic therapy. The goal of phase 4 is to maintain patient stability by empowering the nurse or Advanced Practice Provider with a standing order for diuretic changes in response to observed changes in remotely monitored PA pressures. This process must be individualized for each patient after thoughtful application of phases 1 to 3.

When PA pressures *trend* above the stated threshold, diuretic changes should be made to maintain stability. The concept of trend is based on the observations that PA pressures increase 2 to 3 weeks before patients develop symptoms and require urgent or emergent treatment. Therefore, pressure trend changes are generally not emergent events.

It is important to account for individual PA pressure variability when deciding on a trend of pressure increase or decrease. Generally, pressure readings outside the optimal range that persist for 2 to 3 days should be considered actionable. Over time, it will become apparent when pressure excursions of less duration are important. HF patients with preserved ejection fraction tend to have less "hemodynamic reserve," which means that less time is available from pressure increase to symptom development (typically 10 to 12 days).[3-6] Finally, magnitude of change should be considered in determining response.

There are two pathways of discovering pressure changes. First, the monitoring sequence should include weekly review of uploaded pressures on the Merlin.net PCN website. It should be emphasized that the CHAMPION clinical trial investigators were asked to review pressures weekly and make medication changes if needed. Daily pressure review is not needed for stable patients in whom there have been no recent medication changes.

The second pathway of discovering pressure changes is through email notifications that a specific uploaded pressure is outside the thresholds set up for the patient. Notifications of pressure change allow the user to easily refer to the website in order to verify trends and allow review of medications or notes of previous interventions. Patient demographics are available along with a list of medications. The user has the option to insert a note on the Merlin.net PCN website after deciding on medication change to remind them of what interventions were effective.

Pressure waveforms are also uploaded for review and validation of signal. Nonphysiologic changes, such as progressive decline to negative values, may indicate a need for recalibration. It is always important to consider the physiologic meaning of changes and if the pressures do not make sense, they should be reviewed immediately with the HF physician.

An example of a sliding-scale diuretic prescription is illustrated in Table 1. Frequency of pressure review depends on follow-up of medication changes (see Table 2).

Pressure range	Low	Optimal	High	Very High
mPAP	< 10 mmHg	10-25 mmHg	25-30 mmHg	> 30 mmHg
Diuretic dosing, e.g., torsemide	Half diuretic dose or hold, call MD	50 mg daily	100 mg daily	Twice usual dose or add metolazone, call MD

Other potential actions:

- Add thiazide diuretic or change loop-diuretic.
- See patient and add vasodilator (nitrate or hydralazine), check labs.
- In-office IV furosemide
- Remember to adjust potassium!

Table 1. Example slide-scale diuretic prescription individualized to the patient. Note that pressure ranges must be patient specific.

Subject Status	Weekly	≥ 2-3x per week until optivolemic	≥ 2-3x per week until pressure stabilizes
Optivolemic: minimal symptoms and evidence of poor perfusion. PAS 15-35/ PAD 8-20/ PAM 10-25 mmHg	X		
Hypervolemic: Congestive symptoms. Daily, weekly, acute pressure above optivolemic ranges		X	
Hypovolemic: Poor perfusion in absence of s/s of congestion. Daily, weekly, acute pressure below optivolemic ranges		X	
Medication modification			X
Significant deviations in trend data			X

Table 2. Frequency of uploaded pressure reviews during longitudinal management (phase 4).

PATIENT FLOW

1. Identify patient candidate for the CardioMEMS™ HF System.
   a. Number of readmissions
2. Notify patient's primary care physician or cardiologist of the plan to schedule the patient for assessment with a heart failure clinician.
3. Schedule the patient for assessment visit and consult.
4. Obtain the necessary documents for assessment visit.
   a. Medication list
   b. Insurance coverage
5. Order any lab and diagnostic procedures needed for the assessment visit.
   a. Chest X-ray within the last 12 months
   b. Blood work (CBC, BMP, Magnesium and INR when applicable) within the last 2 weeks
6. Complete the assessment visit and consult and NYHA Class assignment.
7. Determine if the patient meets the criteria for the CardioMEMS HF System.
8. Schedule the patient for the CardioMEMS HF System insertion or reschedule in the heart failure clinic if not a candidate (with primary care physician or primary cardiologists approval).
   a. Educate the patient's primary care physician about the CardioMEMS HF System.
   b. Date
   c. Location
   d. Cardiologist
   e. H & P
   f. Implement preprocedure orders.
9. Provide preprocedure education (see Patient Checklist).
   a. Arrival time
   b. NPO after midnight
   c. Medications to hold
   d. etc.
10. Have the patient arrive at the hospital at the designated day and time.
11. Have the patient check in at Patient Registration.
12. Take the patient to the preprocedure area.
    a. Complete preop documentation.
    b. Prep patient.
13. Perform procedure.
14. Take patient to postprocedure area.
15. Monitor the patient.
16. Provide postprocedure education (see Postprocedure Discharge Education Checklist).
17. Implement discharge orders.
18. Discharge from hospital.
    a. Reinforce the signs and symptoms that would require an immediate call to the nurse practitioner.
19. Home health visit should occur day 1 after discharge.
20. Follow-up with heart failure clinic in 5 to 7 days.
21. Provide ongoing care at the heart failure clinic.
22. Maintain established care with the primary care physician and the cardiologist.

PATIENT CHECKLIST

Before Your Admission

- ☐ Plan to be at the hospital for approximately 8 hours. The amount of time you are monitored in recovery will depend on your care needs.
- ☐ Do not eat or drink anything after midnight except for essential medications _____
- ☐ Stop taking _____ on _____
- ☐ Plan to arrive at _____

What to Bring

- ☐ All current medicines: Please bring every medication you take, including herbal and over-the-counter medications.
- ☐ Insurance card
- ☐ A partner in care, someone from your support network, to:
  - ☐ Participate in the education session and assist where needed with home care
  - ☐ Drive you home

Day of Arrival

- ☐ [Insert Address] _____
- ☐ Go to the main entrance of the hospital and check in at Patient Registration.
- ☐ Patient Registration will direct you to Same Day Surgery.

During Your Stay

- ☐ The physician will review the consent form with you.
- ☐ The right heart catheterization will take approximately 1 hour.
- ☐ You will have 3 to 4 hours of bed rest after the procedure is completed.
- ☐ You will receive patient education and necessary resources for transmissions (special pillow and antennae) prior to leaving.

POSTPROCEDURE DISCHARGE EDUCATION CHECKLIST

Clinician's Initials _____ **Patient Name** _____

☐ **Discharge Instructions**
- ☐ Discharge medications
- ☐ Site care

☐ **CardioMEMS™ HF System Brochure**

☐ **Electronic Unit Review**
- ☐ Watch video
- ☐ Assembly and setup (connections and cables)
- ☐ How to acquire a pressure
- ☐ Schedule for transmissions
- ☐ Antenna and pillow care
- ☐ Phone number for technical support
- ☐ ID card

☐ **Teach-Back Technique for Transmissions**
- ☐ Watch one
- ☐ Do one
- ☐ Teach one

☐ **Setting Expectations**
- ☐ The patient will not receive a call from the nurse practitioner every time he or she transmits.
- ☐ The patient will receive a call if the transmission failed or if medications need to be manipulated.

☐ **Contact Information for the Nurse Practitioner**
- ☐ Reinforce the signs and symptoms that would require an immediate call.

☐ **Follow-up Appointment**

References

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3. Zile MR, Adamson PB, Cho YK, Bennett TD, Bourge RC, Aaron MF, Aranda JM, Abraham WT, Stevenson LW, Kueffer FJ: Hemodynamic factors associated with acute decompensated heart failure: Part 1 – Insights into pathophysiology. *J Card Fail 2011*;17:282-291.

4. Adamson PB, Zile MR, Cho YK, Bennett TD, Bourge RC, Aaron MR, Aranda JM, Abraham WT, Stevenson LW, Kueffer FJ, Taepke RT: Hemodynamic factors associated with acute decompensated heart failure: Part 2 – use in automated detection. *J Card Fail 2011*;17:366-373.

5. Zile MR Bennett TD, St. John Sutton M, Cho YK, Adamson PB, Aaron MF, Aranda JM, Jr, Abraham WT, Smart FW, Stevenson LW, Keuffer FJ, Bourge RC: Transition from chronic compensated to acute decompensated heart failure: pathophysiological insights obtained from continuous monitoring of intracardiac pressures. *Circulation 2008*;118:1433-1441.

6. Zile MR, Bourge RC, Bennett TD, Stevenson LW, Cho YK, Adamson PB, Aaron MF, Aranda JM Jr, Abraham WT, Smart FW, Kueffer FJ: Application of implantable hemodynamic monitoring in the management of patients with diastolic heart failure: A subgroup analysis of the COMPASS-HF Trial. *J Card Fail 2008*;14:816-823.

Rx Only

Brief Summary: Prior to using these devices, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use.

Indications and Usage: The CardioMEMS™ HF System is indicated for wirelessly measuring and monitoring pulmonary artery (PA) pressure and heart rate in New York Heart Association (NYHA) Class III heart failure patients who have been hospitalized for heart failure in the previous year. The hemodynamic data are used by physicians for heart failure management and with the goal of reducing heart failure hospitalizations.

Contraindications: The CardioMEMS HF System is contraindicated for patients with an inability to take dual antiplatelet or anticoagulants for one month post implant.

Potential Adverse Events: Potential adverse events associated with the implantation procedure include, but are not limited to the following: Infection, Arrhythmias, Bleeding, Hematoma, Thrombus, Myocardial infarction, Transient ischemic attack, Stroke, Death, and Device embolization.

Refer to the User's Manual for detailed indications, contraindications, warnings, precautions and potential adverse events.

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