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# Use of CardioMEMs HF sensor in management of NYHA Class III heart failure

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**Abstract**

**Objective:** Assess the ability of continuous pulmonary artery pressure monitoring via implantable CardioMEMs HF device to reduce hospitalization in New York Heart Association (NYHA) Class III heart failure patients over the age of 18. **Design:** Systematic literature review. **Methods:** Searches were conducted via PubMed and ClinicalTrials.gov using the single search term "CardioMEMs." Inclusion criteria narrowed results to studies performed in the last 10 years, randomized control trials, cohort studies, and utilizing heart failure related hospitalization as the primary endpoint. **Results:** The current data unanimously asserts that the CardioMEMs HF device is effective at reducing heart failure related hospitalizations, with secondary evidence suggestive of the potential to improve NYHA classification. **Conclusion:** The findings of this literature review support the use of the CardioMEMs HF device in lieu of conventional management, although more data is needed before it can be universally recommended as the new standard of care.

**Introduction**

Heart failure (HF) is a medical condition characterized by a compromised ability of the heart to maintain cardiac output. The condition can be further described as systolic or diastolic failure, or reduced or preserved ejection fraction depending on the specific etiology of the disease. The condition is often caused by damage to the myocardium associated with infarction, but can also be associated with infectious, valvular, and various comorbid etiologies including hypertension and diabetes mellitus[1]. Due to an impaired ability to clear fluid from the heart's chambers, heart failure typically presents with fatigue, dyspnea, orthopnea, and peripheral edema. The severity of these symptoms and the subsequent impact on a patient's quality of life further allow providers to categorize the disease using the NYHA classification of heart failure scale. Broken into four classes, classes I and II are considered asymptomatic to mildly symptomatic with minimal impact on a patient's daily functioning. Class III is defined by moderate symptoms that worsen with minimal physical activity resulting in patients that are only comfortable at rest. Class IV describes patients who are symptomatic even at rest and who experience significant functional impairment in activities of daily living[2]. Classes III and IV are associated with markedly higher rates of acute exacerbation requiring emergent medical attention.

With damage to cardiac tissue being irreversible, management for heart failure focuses on amelioration of symptoms, prevention of disease progression, and maintenance of quality of life. Primary pharmacologic management involves the use of diuretics to prevent fluid overload or hypertension and beta blockers to minimize or prevent cardiac remodeling. Either of these left unaddressed will lead to further compromise of cardiac output, tissue damage, and progression of disease. Angiotensin converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARBs) also have utility in managing hypertension in HF patients, especially in the setting of cardio-renal syndrome. Secondary therapies may include antithrombotic and statin therapy[3]. Heart failure patients are conventionally followed and managed through outpatient cardiology specialists with clinical courses dictated by physical exam, laboratory studies, and echocardiography. Interventions are made in response to a change in presentation, which are most closely associated with worsening of disease. Prevalence of heart failure in the United States is estimated to be upwards of six million people with significantly higher incidence in older adults. Despite well-established outpatient treatment strategies, the condition is associated with frequent hospitalization and acute exacerbation. In 2014, primary heart failure resulted in 1.1 million emergency department visits, 980,000 hospitalizations, and 80,000 deaths. When taking into consideration comorbid conditions these numbers more than triple[4]. The data is suggestive of a medical climate in which progression to class IV heart failure is an inevitability rather than a potential outcome. In addition to an estimated annual cost of 11 billion dollars in related healthcare, there is a clear pattern that current strategies have been inadequate for reliably preventing patient deterioration.

The fundamental problem with the current strategies for management of heart failure is that they are reactive in nature. With advancements in modern technology, strategies are emerging that involve making real time adjustments to patient care as physiologic indicators of worsening disease occur. One of these strategies

involves a permanent implantable device that measures and transmits pulmonary artery filling pressures to the patient's cardiologist. This allows for proactive management of heart failure with the goal of stabilizing symptoms and avoiding the inevitable descent into class IV status. The CardioMEMS HF sensor is a device indicated for class III heart failure patients, approved by the Food and Drug Administration in 2014, but has yet to be widely adopted. The aims of this study are to perform a systematic literature review to assess the efficacy of using real time monitoring through the CardioMEMS implantable device in improving patient outcomes. Outcomes to be assessed include frequency of exacerbation and mortality.

## Methods

A literature search was performed in September of 2021 via PubMed and Clinicaltrials.gov using the single search term "CardioMEMs", resulting in 143 articles for consideration. Further restriction of results using the limitations of publication within the last ten years, randomized control trials, and cohort studies reduced this number to 17 potential publications. A further 14 studies were excluded for examining non-hospitalization related endpoints such as cost-effectiveness, technical accuracy of the device, surgical complications, and focuses on adjuvant therapies. This yielded the final 3 publications that were used for literature review. This process is summarized visually in **Figure 1**.

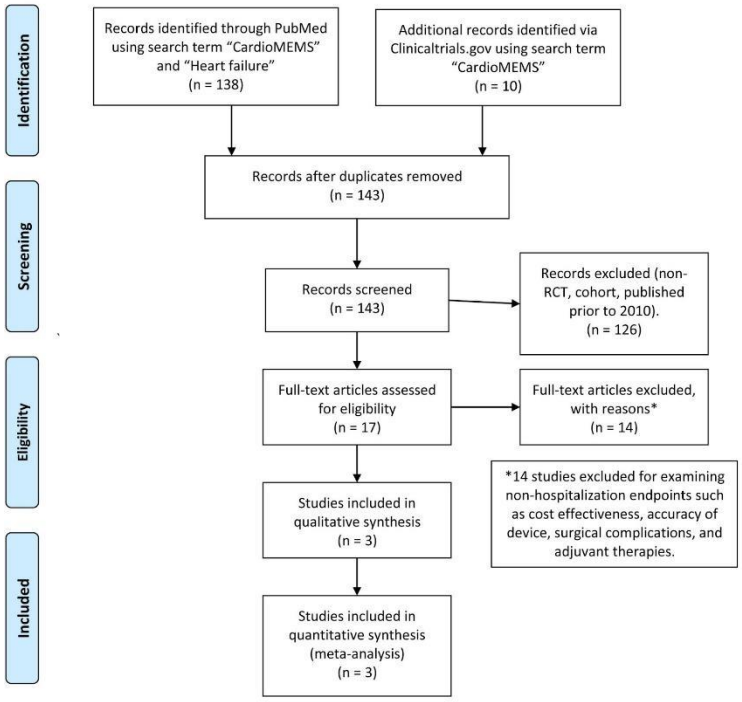


**Figure 1:** PRISMA flow chart depicting the inclusion/exclusion process for literature selection.

## Results

### Study #1

*Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial*

### Study Objective

To evaluate the efficacy of continuous pulmonary artery pressure monitoring via permanent implantable device in reducing the incidence of heart failure related hospitalizations when compared with traditional methods of HF management.

**Study Design**

CHAMPION was a prospective, multicenter, randomized, single-blind clinical trial involving 550 patients with NYHA functional class III HF across 64 clinical sites in the United States. Trial participants were consented and enrolled from September 2007 to October of 2009, with completion of follow-up in March 2010. Procedures were performed to place the CardioMEMS HF sensor in all 550 subjects via femoral vein cannulation and then participants were randomized into treatment and control groups prior to discharge. All participants were directed to obtain daily readings from the sensor via lying supine on the home electronic monitoring unit. These readings were wirelessly transmitted by telephone modem to a secure internet-based database. Management of the treatment group was guided by hemodynamic information from the sensor while the care providers for the control group utilized traditional heart failure methods. Protocols for each treatment regimen were standardized, as were scripts for physicians to follow in order to decrease inadvertent unblinding of the patient population. Frequency of in person follow up appointments were standardized for both treatment and control groups to be month 1, month 3, and month 6. Inclusion and exclusion criteria for the study population are summarized in Tables 1 and 2.

Table 1. Inclusion Criteria

- Written informed consent and authorization to use and disclose health information.
- 18 years of age or older.
- Diagnosis of HF for ≥3 months, with preserved or reduced left ventricular ejection fraction (LVEF).
- Diagnosis of NYHA functional class III HF at screening visit.
- If the subject has a reduced LVEF, they must be receiving a beta-blocker for 3 months and an ACE-I or ARB for 1 month unless, in the investigator's opinion, the subject is intolerant to beta-blockers, ACE-I, or ARB. Beta blocker and ACE-I (or ARB) doses should be stable for 1 month before study entry.
- At least 1 HF-related hospitalization within 12 months of screening visit.
- Body mass index (BMI) ≤35 kg/$m^2$. Subjects with BMI ＞35 kg/$m^2$ require additional screening. If the BMI is >35 kg/$m^2$ and the chest circumference is >52 in and <65 in, the distance from the skin on the subject's back to the pulmonary artery must be <10 cm and confirmed by angiogram of the lateral view during the catheterization before placement of the pressure sensor. If the distance is >10 cm, the subject will not receive a sensor and will not be eligible for the study. Pulmonary artery branch diameter between 7 and 15 mm.
- Female subjects of childbearing age with a negative urine or serum pregnancy test at the screening visit and agreeing to use a reliable mechanical or hormonal form of contraception during the study.

Table 2. Exclusion Criteria

- Active infection.
- History of recurrent (>1) pulmonary embolism or deep vein thrombosis.
- Unable to tolerate a right heart catheterization (RHC), in the investigator's opinion.
- Implantation of cardiac resynchronization device <3 months before enrollment.
- Experienced a major cardiac event (eg, myocardial infarction, stroke) within 2 months of screening visit.
- Glomerular filtration rate (GFR) <25 mL/min or chronic renal dialysis.
- Likely to undergo heart transplantation within 6 months of screening visit.
- Congenital heart disease or mechanical right heart valve(s).
- Diagnosed coagulation disorders.
- Hypersensitivity or allergy to aspirin and/or clopidogrel.
- Enrolled in concurrent studies that may confound the results of this study.
- Clinical condition that would not allow them to complete the study, in the investigator's opinion.

**Study Results**
At 6 months post implantation, the treatment group had experienced a 28% (HR 0.72 95% CI [0.60-0.85]; p=0.0002) decrease in heart failure related hospitalizations when compared with the control group, fulfilling the primary efficacy endpoint. The treatment group also benefited from success in secondary end points such as a greater reduction in pulmonary artery mean pressures, more days alive outside of the hospital, and a better quality of life as measured by Minnesota Living with Heart Failure Questionnaire at 6 months. The duration of heart failure related hospitalization was also reduced when compared with the control group at 2.2 days vs 3.8 (p= 0.02), respectively. Rates of survival in the treatment (255, (94%)) and control groups (260 (93%)) were not significantly different from one another (p= 0.45) at the end of the 6 month period. During the initial 575 implant attempts, there were 15 serious adverse events in which 8 were device safety related complications and 7 were procedure-related adverse events.

**Study Critique**
The CHAMPION trial was the first to attempt monitoring of heart failure through an implantable device and therefore is lacking in comparative safety and efficacy data. The closest safety data available for the implant procedure to be compared with is right heart catheterization and placement of pacemakers or defibrillators, all of which were shown to have similar or decreased safety profiles compared to the percutaneous placement of the CardioMEMs HF sensor. Although results were significant for the primary efficacy and safety endpoints, the sample size of 550 patients for a 6 month monitoring period represents a short window and small population of observation. The short window also prevented conclusions to be drawn about benefit to mortality rates overall. Strengths of the trial include the limited exclusion criteria, and randomized and single-blinded nature of patient assignment. An additional strength of this study lies in the ability of each of the participating facilities to provide standard or above standard level of care to the patients in the control group being managed through traditional means.

*Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. Lancet. 2011;377(9766):658-666.*

**Study #2**
*Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial*

**Study Objective**
To further establish the efficacy of continuous pulmonary artery pressure monitoring at reducing frequency of hospitalization in patients who formerly received traditional heart failure management.

**Study Design**
The methodology of the initial CHAMPION study is described above. This follow up study was a 13 month prospective, non-blinded, multicenter examination of the efficacy of continuous pulmonary pressure monitoring for reducing frequency of hospitalization in the former study populations from the initial CHAMPION study. These groups were made up of the 170 participants that were assigned to the control group that received traditional heart failure therapy and the 177 participants formerly assigned to the treatment group. At the end of the 10 month randomized access trial, pulmonary pressure monitoring data for control group subjects was made available to the facilities participating in the clinical trial. This began the open access 13 month follow up in which the former control group was managed using pulmonary pressure data alongside the treatment group patients. The principal investigators and research sponsors were not directly involved in the protocols of this follow up study.

**Study Results**
Transitioning the former control group to pulmonary pressure guided therapy resulted in a 48% reduction in hospital admissions due to heart failure (HR 0.52 [95% CI 0.40-0.80]; p<0.0001). All-cause hospital admission also decreased by 21% (HR 0.79 [95% CI 0.67-0.92]; p=.00034). Overall risk of death or first hospital admission due to heart failure was 47% lower during the follow up study (HR 0.53 [95% CI 0.38-0.73]; p<0.001). Overall mortality

was not reduced (HR 0.71 [95% CI 0.43-1.17]; p=0.17). Patients reported assessments of quality of life using the Minnesota Living with Heart Failure Questionnaire. This data was used as a secondary end point for perceived quality of life and showed that the former treatment group reported a higher quality of life than the former control group. The former treatment group reported an average score of 47.0 whereas the former control group reported an average score of 56.5 (p=0.0267), with lower scores suggesting heart failure having a less severe impact on the life the patients desire to be living.

**Study Critique**

Strengths of the follow up study include using participants who already met inclusion criteria for the initial CHAMPION study, a relatively large sample size, and a simulated real-world trial where strict compliance is no longer being enforced by the study sponsor or principal investigators. A potential shortcoming of this study is that the removal of strict protocols introduced the new variable of clinical rationale from clinician to clinician. This resulted in some patients receiving medication alterations at higher pulmonary pressures where other patients did not.

*Abraham, et al. 2016. Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. The Lancet. 387: 453-461.*

**Study #3**

*Pulmonary artery pressure-guided therapy in ambulatory patients with asymptomatic heart failure: the CardioMEMS European Monitoring Study for Heart Failure*

**Study Objective**

To evaluate the efficacy of the CardioMEMS HF sensor in reducing heart failure related hospitalizations in Germany, the Netherlands, and Ireland

**Study Design**

MEMS-HF was a prospective non-randomized multicenter study that enrolled 234 patients between May 2016 and March 2018 for implantation of the CardioMEMS HF sensor. Their care was followed for 12 months post implantation and compared with their rates of heart failure related hospitalization in the 12 months prior to implantation. Inclusion criteria for the patients included a consistent experience of NYHA functional class III heart failure symptoms over the last month and at least one heart failure related hospitalization (HFH) in the previous year. Patients that were excluded were candidates for heart transplant, ventricular assist device implantation, or hospice care. Study data was obtained at baseline, during implantation, before discharge, after 6 and 12 months and every 6 months until the last patient completed a 12 month follow up. Post implantation, patients were directed to collect daily pressure readings from the HF sensor via a Patient Electronics Unit and this was transmitted to a secure website. The data was reviewed weekly by study personnel and pharmacological management was modified based on predefined algorithms. Patients were contacted weekly in the first month post implant and then 2-4 weeks thereafter for the remainder of the study period.

**Study Results**

In the 12 month follow up period, 91 (38.9%) patients were hospitalized at least once for heart failure related disease, with 27.8% of incidents occurring in the first six months post implantation. This represented a 62% decrease in HFH from the 12 months prior to implant (0.60 vs 1.55 events/patient-year; [HR= 0.38, 95% CI 0.31-0.48; p<0.0001]. Reductions in hospitalization rate were consistent across all study demographics. Mortality in the study population was 31 (13.8%) patients at 12 months, although none of these deaths were considered device related and occurred outside of the established 30 day safety window. Mean pulmonary artery pressures declined over the 12 month follow up period with a -5.0 +/- 7.3 mmHg (p<0.0001), while the NYHA functional heart failure classification improved in 83 (35.5%) patients and worsened in four (1.7%) patients.

**Study Critique**
Conclusions from the data are limited by the nonblinded and nonrandomized nature of the study design. Information bias is also present in the study population as the rationale for pre-implant hospitalization for heart failure related events was variable. Elevated pulmonary artery pressure (PAP) was not utilized as an inclusion criteria, therefore the largest effect of hemodynamic monitoring guided therapy was in the patients with the highest baseline PAP, lending itself to asymmetrical data as physicians were only prompted to amend therapy when PAP levels surpassed a predetermined threshold per study protocol. Strengths of the study include consistency of improvement in measured outcomes across study populations.

*Angermann CE, Assmus B, Anker SD, et al. Pulmonary artery pressure-guided therapy in ambulatory patients with symptomatic heart failure: the CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF). Eur J Heart Fail. 2020;22(10):1891-1901. doi:10.1002/ejhf.1943*

**Discussion**

The purpose of this paper is to use the available literature to determine if pulmonary artery pressure monitoring leads to improved outcomes for patients diagnosed with NYHA Class III heart failure. The primary outcome of interest was the rate of heart failure related hospital admission which was assessed by all three studies included for review. Abraham 2011 reported a 28% reduction, Abraham 2016 reported a 48% reduction, and Angermann 2020 reported a 62% reduction in hospital admissions due to heart failure when compared with conventional management. These findings unanimously support the efficacy of this new approach to heart failure.

There are additional novel findings in the secondary outcomes monitored in these publications. Angermann 2020, for example, observed that of the 38.9% of study participants that were hospitalized for heart failure, all of these admissions occurred during the first 6 months of the trial. This suggests the possibility that these patients improved as the study proceeded. This suspicion is later corroborated by the finding that 35.5% of study participants moved from NYHA Class III heart failure back into NYHA Class II heart failure by the end of the 12-month monitoring period.

Secondary outcomes such as a decreased mean length of hospital stay observed by Abraham 2011, a 21% decrease in all cause hospitalization, a 47 % decrease in risk of death and first-time hospitalization due to heart failure observed by Abraham 2016, and the findings of the Minnesota Living with Heart Failure Questionnaire are all significant as well. Together these findings strongly suggest a patient population that is more satisfied with its quality of life, less likely to get seriously ill, and experiences exacerbations for shorter amounts of time.

Review of the literature exploring the desired outcomes has revealed weaknesses in the current data supporting this approach however. There are only three published randomized control trials for this intervention and the principal investigators working on these projects are associated with one another and the biotechnology company that owns the patent to the CardioMEMs HF device. This is not excessively rare in very narrow areas of private sector research, but the larger body of data for this intervention would likely benefit from additional investigation by academia.

Future investigation into the value of this management approach should focus on a few key areas. Firstly, the ability to reverse disease progression and move patients back into lower NYHA heart failure classifications and secondly, the efficacy of preventing deterioration at less severe classifications of disease such as NYHA Class II heart failure. Future follow up studies may also be informative as these populations undergo subsequent years of management. Longer timelines may be able to more genuinely assess whether this approach will decrease mortality rates when compared to conventional treatment in addition to improvements in morbidity. The COVID-19 pandemic has highlighted several emerging trends in healthcare. These trends include the increasing need for telehealth care and the ability to manage patients with serious conditions outside of inpatient units. There may be a role for this type of technology-based management for patients in rural areas, or for patients that are too weak

to travel to large medical centers, for ensuring that novel treatment approaches are made the new standard of care.

**Conclusion**

*Does continuous pulmonary artery pressure monitoring via the implantable CardioMEMs HF device when compared with traditional outpatient monitoring reduce hospitalizations in NYHA Class III heart failure patients over the age of 18?*

The CardioMEMs HF device is a safe and effective method of gathering the data necessary to proactively modify the treatment of NYHA Class III heart failure preventing disease advancement and subsequently reducing overall heart failure related hospitalizations, even reversing it to NYHA Class II in certain populations. The wireless and remote nature of the technology allow it to be integrated into a framework of rural health and telemedicine, enabling patients to receive a high standard of care without the burden of frequent travel to and from medical centers. Questions remain about the longevity of the CardioMEMs HF device and its continued efficacy in heart failure management, but there are 20 clinical trials currently in process that when completed may clarify many of these concerns.

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