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Comparison of CardioMEMS and Traditional Medical Management in Reducing Readmissions in Heart Failure Patients

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Abstract

The purpose of this research and literature review is to compare the efficacy of traditional medical management of heart failure patients to management using the implantable CardioMEMS device. The cost-effectiveness of the CardioMEMS device was also evaluated. For the literature review, the data bases of Cochrane, PubMed, Clinical Key, and DynaMed Plus were utilized. Because the CardioMEMS device is relatively new and has not gained widespread use among heart failure patients, there is limited data available in regards to research completed on patients with the implantable device. The time frame of search results related to CardioMEMS was extended to 10 years to include the original clinical trials and research for the device. After a thorough review of the available research, it was concluded that the CardioMEMS device is an effective method for monitoring pulmonary artery pressures as well as for preventing hospital admissions. The research data has also proven the device to be cost-effective as well. However, the device may not be appropriate or cost effective for patients with end stage heart failure or limited life expectancy. Overall, additional longitudinal studies related to the efficacy of the CardioMEMS device would be beneficial.

Keywords: CardioMEMS, heart failure, traditional management, pulmonary artery pressure monitoring, hospital admissions, cost effectiveness, symptom management, natriuretic peptides

Introduction

Heart disease has a significant impact on the lives of many Americans. According to the Center for Disease Control (CDC) (2020), approximately 6.5 million Americans have heart failure and in 2017 it contributed to one out of eight deaths. It is estimated that heart failure has an annual cost of over $30 billion in the United States. Heart disease overall is the leading cause of death not only in the US, but worldwide as well. In a report from The Agency for Healthcare Research and Quality (2014), heart failure was the leading cause for hospital readmissions among Medicare patients in the year 2011 with a total of 134,500 readmissions within 30 days. This number far exceeds readmissions from any other condition. In 2012, The Center for Medicare Services (CMS) implemented the Hospital Readmissions Reduction Program (HRRP) which requires hospitals to track and report data related to hospital readmissions within 30 days of prior discharge. Facilities are penalized for increased readmission rates in the form of reduction in reimbursement for services provided. Determining effective methods to manage heart failure patients and preventing hospital readmissions is important not only for improved quality of life, but for preventing reduction in Medicare reimbursement for care as well.

Statement of the Problem

Heart failure patients have historically been managed and monitored using a variety of methods including at home patient monitoring of blood pressure and weight in conjunction with frequent clinic visits, lab work, and medication therapy. Newer methods include nurse-led heart failure management programs which involve frequent clinic visits and follow up phone calls. One issue with traditional management of heart failure is that it requires patient compliance with treatment plans and recognition of the development of physical signs and symptoms that may indicate acute exacerbations. Data now shows that by the time the patient develops recognizable

physical symptoms, pulmonary congestion and associated complications have already reached levels potentially requiring hospital admission (Adamson, 2009).

In 2014, the United States Food and Drug Administration approved the first of its kind implantable pulmonary artery pressure monitor, called the CardioMEMS. According to Abbott Laboratories (2020), the medical device company that owns CardioMEMS, the device is surgically implanted in a pulmonary artery during a right heart catherization procedure. The device is then able to continuously monitor several data points including heart rate, systolic, diastolic, and mean pressures which are transmitted and collected daily with a pillow-like monitor that the patient lays on. The data is then transmitted via cellular signal, land line, or wifi to an online portal whereby the patient's provider is able to review the data and detect changes in pulmonary pressures that would warrant action. According to Abbott (2020), eligibility criteria for implantation of the CardioMEMS device include NYHA class III heart failure as well as a recent heart failure related hospitalization. The only current contraindication for CardioMEMS therapy identified by the manufacturer is the inability to be on dual antiplatelet or anticoagulation therapy for 1-month post-implantation.

An increase in pulmonary artery pressure is directly associated with increased pulmonary congestion due to worsening heart failure which in turn may result in symptoms of shortness of breath and activity intolerance (Adamson, 2009). Early recognition of increasing pulmonary artery pressure changes allows for earlier intervention with medication adjustments. Appropriate early intervention promotes prevention of acute exacerbations of congestive heart failure which could potentially reduce hospital admissions. The purpose of this study is to compare efficacy of heart failure management with the implantable CardioMEMS device with traditional non-invasive methods in terms of prevention of hospital readmissions.

Research Questions

In patients with heart failure, do interventions based on monitoring pulmonary artery pressures with an implantable CardioMEMS device versus traditional methods lead to decreased hospital readmissions?

Is the CardioMEMS device a cost-effective method for the management of heart failure patients?

Methodology

Through a thorough review of the current available literature, this project compares the efficacy and cost effectiveness of the implantable pulmonary artery pressure monitoring device, or CardioMEMS, with traditional methods of medical management of heart failure patients in preventing hospital readmissions. The medical research databases PubMed, Embase, Cochrane Review, and DynaMed Plus were utilized in obtaining peer-reviewed literature resources. The review included meta-analysis, systematic reviews, randomized controlled trials, and longitudinal studies. Initial search within a 5-year time frame resulted in a total of 87 studies. This was expanded to 10 years to include studies from the original trials on pulmonary artery pressure monitoring devices. The expanded search resulted in 99 studies. A total of 19 studies were reviewed for this study based on inclusion criteria. In order to be included in the review, the studies were peer-reviewed, focused on the efficacy of methods of heart failure monitoring, discussed safety and cost-effectiveness, or summarized results of randomized controlled trials for heart failure management.

Review of Literature

A review of the literature shows extensive research related to traditional methods of the management of heart failure including longitudinal studies. Early monitoring methods were more dependent on patient recognition of developing symptoms or measurement of objective data such as weight and vitals. In recent years, newer, more reliable methods have emerged and have been shown to be more effective in reducing hospitalizations related to heart failure, especially when combining two or more methods. In comparison, there is somewhat limited data available related to the effectiveness of the CardioMEMS pulmonary artery pressure monitor due to the novelty of the device. Research is on-going on this topic however, including longitudinal studies and additional trials which expand inclusion criteria to involve more NYHA classifications of heart failure patients . When looking at the data that is currently available, there is a correlation between early medical intervention of rising pulmonary artery pressures and the reduction in hospital admissions. The CardioMEMS is currently the only FDA approved method of continuous measurement of pulmonary artery pressures outside of the hospital setting. There is a fair amount of research available related to the cost-effectiveness of the CardioMEMS device in terms of reducing cost to the patient and /or the payer due to reduction in hospital admissions over time.

Efficacy of Traditional Medical Management in Heart Failure

Over the years, practitioners have used a variety of methods for management of heart failure. As new advances in medicine allow for improvement in care, it is important to determine the efficacy in comparison to older traditional management techniques. One common method of management of heart failure that has been utilized for years is the home monitoring of daily weights and peripheral edema. Patient education and discharge instructions for heart failure

patients has traditionally included warning signs of increased fluid retention that should prompt the patient to notify their health care provider. Currently, the American Heart Association (AHA), recommends daily weights of heart failure patients, with prompt reporting of weight gain that exceeds 3 pounds in one day or 5 pounds in 1 week.

A study conducted by Howie-Esquivel et al. (2019) evaluated the reliability of weight monitoring in the management of heart failure patients and its reliability in predicting need for hospitalization. This study consisted of a secondary analysis of a randomized REMOTE-HF trial in which 393 patients were asked to track their daily weights along with any symptoms noted using a diary over the course of 24 months. The results of this study did not support relationship between weight gain of $\geq$ 5 pounds in one week with increased risk for hospital admissions (HR 1.01, 95% CI 0.88, 1.16; $p = 0.79$). The symptom of peripheral edema was not a statistically significant predictor for hospital admission (HR 0.89, 95% CI 0.27, 2.92; $p = 0.85$). It was noted however, that an increase in dyspnea over both 7 and 14 days correlated with a greater number of hospital admissions (HR 5.89, 95% CI 1.73, 20.04; $p < 0.004$; HR 3.67, 95% CI 1.15, 11.70; $p < 0.03$). The authors concluded that symptoms of increased dyspnea proved to be a more reliable indicator of worsening heart failure and ED visits as well as hospital admissions. This study was limited by small sample size as well as data was collected only from rural settings. Data was also lacking on differences in medication regimens, dietary habits, and exercise routines which could potentially account for differences in outcomes. Baseline pulmonary function and disease was not assessed which could have influenced results related to dyspnea.

The results indicate that this method of management alone is not enough to provide adequate control of heart failure symptoms, but rather when used in conjunction with other

methods, patient outcomes may be more desirable. This study does highlight the importance of patient education and reinforcement of that education regularly for better understanding of disease process and self-management. Patient understanding of their disease process is essential for effective heart failure management.

Another common traditional method of management of heart failure is monitoring of brain natriuretic peptide (BNP) levels. According to Papadakis and McPhee (2020), BNP is released from cells within the walls of the ventricles of the heart in response to increased stretch. This is typically caused by increased pressure such as with increased intravascular volume. In the acute setting, a BNP of >100 pg/mL is suggestive of heart failure. In patients with chronic heart failure, BNP levels may be chronically elevated, in which case monitoring fluctuations in BNP levels may be helpful in guiding medication management with diuretics, ACE inhibitors, and beta blockers (Papadakis & McPhee, 2020 p. 419).

Myhre et al. (2018) conducted a secondary analysis of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist Trial (TOPCAT) which involved monitoring of natriuretic peptides in 1057 adult subjects with symptomatic heart failure and left ventricular ejection fraction of 45% or more as well as either a heart failure hospitalization in the last 12 months or an elevation in N-terminal brain natriuretic peptide (pro-BNP) of $\geq$ 360 ng/L. Subjects were followed for a mean of 2.4 years in which 300 primary outcome events of either a heart failure related hospitalization, cardiac death, or aborted cardiac arrest occurred.

It was concluded that elevated natriuretic peptide levels were directly associated with risk of a primary outcome (HR 1.36; 95% CI, 1.22-1.54; $p < .001$). This was noted to be true across all subgroups. Subjects who were young, black, obese, had better renal function, and/or no atrial fibrillation, were noted to have lower natriuretic peptide levels on average, however elevation in

natriuretic peptide concentrations was consistently associated with negative cardiovascular outcomes in all subjects regardless of natriuretic peptide distribution levels. Because of this, the authors concluded that monitoring of pro-BNP levels in heart failure patients is an effective way to guide heart failure treatment and predict prognosis, especially in patients with persevered ejection fraction. The study was limited to patients with preserved ejection fraction so generalizations cannot be made for patients with reduced ejection fractions.

In recent years, case management for patients with heart failure has become more popular. Heart failure clinics managed by nurses are becoming increasingly more common and have led to better coordination of care for heart failure patients through close monitoring and collaboration with the primary provider and other members of the healthcare team. McCants et al. (2019) published a retrospective comparative analysis of traditional medical management of heart failure patients compared to those managed with integrated case management provided through a nursing team during a time frame of 2 years from 2015 to 2017. A total number of 68 patients were studied, 49 of whom received the treatment of case management and 19 of whom received treatment as usual (TAU) without case management. Results of the analysis found that for the patients in the integrated case management group, the 30-day readmission rate was 18.4% in comparison to the treatment as usual group in which the 30-day readmission rate was 52.6%. The association between readmission and case management was x (1, n = 68) = 6.372, p = .012. Subjects in the treatment as usual group were found to have a risk of readmission 1.4 times higher than the case management group.

One conclusion that could be made from this review is that integrative case management would be an effective and more conservative treatment alternative for patients that are not appropriate candidates for implantable CardioMEMS device. Limitations of this study include

that it was conducted at one single facility as well the fact that all subjects studied also had the comorbidity of diabetes mellitus. There was also a small sample size of 68 patients.

There is substantial evidence to support the efficacy of beta-adrenergic blocking agents, angiotensin converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs) in reducing mortality and hospital admissions in patients with heart failure. Driscoll et al. (2015) suggest that despite compelling evidence, the trend to optimize these medications in heart failure patients has been slow to come to fruition. One way to maximize medication benefits in the heart failure patient would be to incorporate nurse-led case management using medication titration protocols which has been proven to reduce hospitalizations. Case management would perhaps be a more appropriate method of managing heart failure patients who are not candidates for more invasive monitoring methods.

In a systematic review of randomized trials conducted by Driscoll et al. (2015), outcomes were compared for heart failure patients in a nurse-led medication titration group versus patients who were managed by another health care professional using traditional methods. The focus was the effect of nurse-led up-titration of beta-blockers, ACEIs, and ARBs compared to traditional management and medication titration by the primary care provider. A total of seven studies and 1648 patients were analyzed. Results indicated that heart failure patients who were managed by nurse-led medication titration had a 21% reduction in hospital readmissions from any cause (RR 0.79, 95% CI, 0.71 to 0.88), were 39% less likely to experience a heart failure-related hospital admission (RR 0.51, 95% CI 0.36 to 0.72), and had a 34% reduction in overall mortality (RR 0.66, 95% CI, 0.48 to 0.92) in comparison to heart failure patients managed by traditional means alone by the primary care provider. Limitations include lack of supporting research available

due to limited number of nurse-led heart failure management programs despite evidence for effectiveness. More studies are needed to support these findings.

With advances in technology and emerging discoveries claiming to ensure improved patient outcomes and more effective management methods, it is important to remain objective and evaluate these nuances for reliability and validity. Every patient must be treated individually and managed with methods that will produce optimal outcomes without performing unnecessary or costly procedures. Newer treatment regimens do not always equate to improved outcomes. This may vary from patient to patient. Similarly, older methods of management do not equate to inferior results.

In a meta-analysis performed by Stewart et al. (2019) it was concluded that traditional methods of monitoring heart failure are thought to be just as effective as more intensive intervention programs up to a certain point. The most important factors in predicting effectiveness of preventing readmissions were age and patient complexity. As the heart failure patient ages and comorbidities increase, traditional methods of management become less effective in comparison to the younger heart failure group.

Stewart et al. (2019) noted that the WHICH? and WHICH? II trials were important in that the outcomes were different than what was expected. These trials were multicentered and included 787 heart failure patients who were managed either by traditional monitoring methods or a more intensive program using the GARDIAN tool, structured phone support, and monitoring of brain natriuretic peptide. Interestingly, the more intensive intervention program did not result in fewer hospitalizations and in fact readmissions were slightly increased (18.6 $\pm$ 26.5 versus 16.6$\pm$ 24.8 days; p=0.199) and mortality only slightly reduced (17.7% versus 18.4%; p= 0.848).

The author attributes this finding to the "clinical cascade" phenomenon in which "the harder you look, the more problems you will find" (Stewart, 2019).

Efficacy of CardioMEMS in Management of Heart Failure

In 2014 the US FDA approved the first of its kind pulmonary artery pressure monitor, the CardioMEMS, owned by Abbott Laboratories. This device is surgically implanted into the left descending pulmonary artery during a right heart catheterization procedure. Once implanted, the device monitors the pressure of the pulmonary artery, which is transmitted wirelessly to a secure website where providers are then able to review data. This allows the provider to make adjustments to current medication therapy as needed long before the patient develops symptoms of congestion prompting a clinic or emergency room visit (Abbott, 2020).

Gronda et al. (2020) conducted a meta-analysis to review results of the studies related to the implantable CardioMEMS device in regards to reducing acute exacerbations of congestive heart failure and hospital readmissions. They summarize the results found in the CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in New York Heart Association (NYHA) functional Class III Heart Failure Patients) trial which consisted of 550 NYHA class III heart failure patients. Subjects were included in a single blind, randomized study consisting of the treatment group in which daily measurements of pulmonary artery pressures from the CardioMEMS device were reported to the clinicians (n=270), and the control group in which the patients received traditional heart failure management (n=280). The treatment group was managed with algorithms for specific pulmonary artery pressure targets which addressed both congestion and hypovolemia. Interventions in the treatment algorithms included sodium and fluid restrictions as well as medication regimen modifications. The control group was managed based on clinical symptoms. Results of the trial found a significant

reduction in the rate of hospitalizations related to heart failure in the 6-month study time period (0.44 in the control group compared to 0.32 in the treatment group; relative risk reduction 28%; $p< 0.0002$). A follow up of 17 months in the treatment group found a further reduction in hospitalizations related to heart failure of up to 37% in comparison to the control group. Overall, in the treatment versus the control group there was a decrease in baseline of pulmonary artery pressures, a decrease in hospitalizations, a reduction in overall hospital days, and in improvement of quality of life.

Limitations of the CHAMPION trial include the inability to apply findings to all patients with heart failure due to the specific characteristics of the treatment group of the trial. Average age of patient in the treatment group was 61, compared to an average real-world age of 70 (Gronda, 2020). It was also noted that less than one fourth of the patients in the trial had an ejection fraction of greater than 40%. The results of the CHAMPION trial do support the safety and efficacy of the CardioMEMS device, however more research is need in the area of appropriate patient selection. Gronda et al. hypothesize that a reasonable guide for patient selection based on current data available would include those patients who continue to show evidence of fluid overload at hospital discharge despite efforts to control congestion, patients with an enlarged vena cava and limited respiratory variation, and those with an undesired response to diuretics.

The CHAMPION trial was the first of its kind to evaluate the efficacy of the CardioMEMS device. The results of the clinical trial proved a substantial benefit for use of monitoring in heart failure patients and thus the device was approved for use by the FDA. Because of the novelty of the device, longitudinal studies were lacking. Heywood et al. (2017) performed a retrospective analysis of the first 2000 patients who were implanted with the

CardioMEMS device from June 2014 through June 2016, after FDA approval following the original CHAMPION trial. Participants ranged from 47 states and 416 sites with 427 different physicians performing implantation. To be included in the study, subjects had to have at least 6 months of follow-up. Data was obtained from the St. Jude's Merlin.net database of transmitted device data.

The authors used an area under the curve (AUC) method to evaluate the data transmitted from the CardioMEMS device in 2000 general use patients in order to estimate the mean, systolic, and diastolic pulmonary artery pressures during the first 6-month follow-up time period in comparison to the initial week after implantation pressure readings. By using this method, the authors were able to quantify the frequency and duration of time at which each patient spent below their baseline pulmonary artery pressure reading. These general use results were then also compared to those from the CHAMPION trial treatment and control groups. The mean age of the subjects studied was 70 $\pm$ 12 years. They were followed an average of 333 days $\pm$ 125 days. The mean ejection fraction of the group was 33.5%. Baseline measurements of pulmonary pressures were much higher in the general use group ($p<0.05$).

In the general use subjects, the mean pulmonary artery pressure at time of implantation was 34.9 $\pm$ 10.2 mmHg in comparison to the subjects of the CHAMPION trial which was 32.0 $\pm$ 10.5 mmHg. At the 1-month mark, the general-use patients had and AUC of 32.8 mmHg, -156.2 mmHg at 3 months, and -434.0 mmHg at 6 months post-implantation ($p< 0.001$). These results were significantly lower than treatment group of the CHAMPION trial. When evaluating the treatment group of the CHAMPION trial, the patients with the highest baseline pulmonary artery pressures (>35mmHg) had the biggest impact in negative AUC outcomes with an initial mean baseline pressure of 43.4 $\pm$ 5.7 that was reduced to 37.8 $\pm$ 7.8 mmHg ($p<0.0001$). When

examining the control group of the CHAMPION trial, who were managed based solely on signs and symptoms of heart failure exacerbation, it was noted that patients with baseline pulmonary artery pressures ≤ 35mmHg had an increase in pulmonary pressures at both 1 month and 6 months that was statistically significant for patients with baseline pulmonary artery pressures <25 mmHg (p<0.0001), and for patients with mean pulmonary artery pressures 25- 35 mmHg (p= 0.006). Patients in the control group with baseline pulmonary artery pressures >35mmHg were the only subjects to have a decrease in pulmonary artery pressures from baseline (p=0.0015).

The authors concluded that the results indicate that remote pulmonary artery pressure monitoring is effective and appropriate for the management of heart failure patients as evidenced by a significant reduction in pulmonary artery pressures at 6 months in comparison to baseline pulmonary artery pressures in the general use study group. Furthermore, mortality risk is reduced by 19.2% with just a 3 mmHg reduction in pulmonary artery pressure and by 30% with just a 5 mmHg reduction. On the contrary, there is an increase in mortality risk of 42.8% with a 5 mmHg increase in pulmonary artery pressure (Heywood et al. 2017).

Limitations of the study include lack of data on type of interventions used which may account for some variability in pulmonary artery pressure reduction. It should also be noted that all of the authors have a relationship with St. Jude Medical who is the developer of the CardioMEMS device, thus one cannot conclude that this research is free from bias.

In a retrospective, single-center study conducted at the Keck Medical Center of the University of Southern California, Tran et al. (2019) evaluated the number of hospitalization days in the 1-year period following implantation of an implantable CardioMEMS pulmonary

artery pressure monitor in 78 patients. Another goal of the study was to identify potential variables that may affect hospitalization rates in these patients.

Important findings from this study were the associations between frequency of patient transmission of data from the CardioMEMS devices as well as frequency of provider interpretation of transmitted data in terms of impacting risk of heart failure hospitalizations. There was an exponential relationship between the number of days between data transmission from the CardioMEMS device and number of days spent hospitalized as a result of heart failure. There was also an exponential relationship between mean number of days between data interpretation by health care professionals and heart failure hospitalization days (incidence rate ratio (IRR) = 1.85, 95% CI: 1.14–3.00, p=0.012). It can be concluded from this study that more frequent patient data transmission as well as more frequent data interpretation by health care providers ultimately led to fewer hospitalization days related to heart failure. This is an important reminder that technology alone does not equal improved outcomes, but rather how providers use technologic advances to assist with decisions and interventions related to patient management supports the greatest benefit to overall patient outcomes.

Limitations of this study include the small sample size of 78 patients as well as the single institution studied. Further studies involving multiple institutions and larger patient sample sizes are needed to make definite conclusions.

Until recently, the majority of the research conducted on implantable pulmonary artery pressure monitoring has been within the United States. Angermann et al. (2020) set out to evaluate the safety and efficacy of the CardioMEMS device in health care systems outside of the United States by replicating the CHAMPION trial. The CardioMEMS European Monitoring Study for Heart Failure (MEMS-HF) was conducted in Germany, The Netherlands, and Ireland

and consisted of 234 NYHA class III heart failure patients with a minimum of one heart failure related hospitalization in the year preceding the study. Patients were implanted with the CardioMEMS device at 31 different health care institutions. Data end points of interest included heart failure related hospitalizations, survival rates at 1-year post implant, and freedom of device related complications. Results of the trial concluded that heart failure related hospitalizations were reduced by 62% (HR 0.38; 95% CI 0.31–0.48, P<0.0001). Survival rate at 1-year post CardioMEMS implantation was 86.2%. Freedom from device related complications at 1-year was 98.3% (CI 95%, 95.8-100.0). Also of importance was the reduction in mean pulmonary artery pressure by 5.1 $\pm$ 7.4 mmHg which was similar to results of the original CHAMPION trial. The results of the MEMS-HF trial indicate that the CardioMEMS pulmonary artery pressure monitoring device is a safe and effective method for the management of patients with heart failure in Germany, The Netherlands, and Ireland.

In terms of potential limitations of this study, the authors discuss the possibility of a potential Hawthorne effect in which the subjects being studied are more likely to report potential symptoms of concern because of the realization that they are being studied, thus results may be difficult to correlate to real-life situations. It should also be noted that pulmonary artery pressures less than 15 mmHg were not treated. Only pressures above 15 mmHg were acted upon which likely influenced the end result of patients with higher pulmonary artery pressures were noted to have the greatest reduction in pressures during the study period.

This study is one of the only studies that replicates the conditions of the original CHAMPION trial. It included a large sample size from multiple health care institutions. Also of importance is the similarities in study results despite the difference of trial conduction outside of

the United States. Because similar results were attained from both the CHAMPION and MEMS-HF trials, the efficacy and safety of the CardioMEMS device is further supported.

CardioMEMS for Reducing Hospital Readmissions in Heart Failure Patients

Eurlings et al. (2019), conducted a systematic review of the current evidence related to remote telemonitoring of heart failure in comparison to standard treatment alone by examining the most important trials, meta-analyses and systematic reviews. The most promising results were found were from the CHAMPION trial (2011) which was a single blind multicenter trial with 2 arms: intervention with CardioMEMS and traditional heart failure management. The study consisted of 550 patients for a duration of 15 months. The trial measured three separate endpoints: heart failure related hospitalizations, no device/system complications, and no pressure sensor failure. All three measures had positive results. In preventing heart failure related hospitalizations, the hazard ratio was 0.7; 95% confidence interval (0.60- 0.85); p= 0.002. For the measure of no device system complications, 98.6% of the patients had no complications with a confidence interval of 95% (99.3- 100.0). Lastly, 100% of the subjects had no pressure sensor failure with a confidence interval of 95% (99.3- 100.0).

Limitations of telemonitoring using a CardioMEMS device includes the need for the patient to understand how to use technologic devices and/or applications in order to effectively transmit data. Of note, there is a conflict of interest related to the employer of the authors receiving grant dollars from Novartis, Vifor, Abbott, Medtronic, Servier, and Roche Diagnostics. Several of the authors have personally received grant dollars and funding from AstraZeneca, Abbott, Bristol-Myers Squibb, Novartis, Roche, Trevena, and ThermoFisher GmbH. Because of these associations, one could conclude that the authors are not free from bias in favor of the CardioMEMS device.

Desai et al. (2017) conducted a retrospective study following the FDA approval of the CardioMEMS device. The purpose of the study was to determine effectiveness of the CardioMEMS device beyond the initial clinical trial. Inclusion criteria included implantation of the CardioMEMS device from June 2014 through December 2015. Data was pulled from Medicare claims. The mean age of subjects was 71 $\pm$ 11 years. Hospitalization related to heart failure were significantly lower after implantation with the CardioMEMS device (HR: 0.55; 95% CI: 0.49 to 0.61; $p < 0.001$). Overall reduction of all cases of hospitalizations was decreased at 12 months (HR: 0.77; 95% CI: 0.70 to 0.86; $p < 0.001$). The authors concluded that CardioMEMS device is an effective method for monitoring pulmonary artery pressures that reduces heart failure related hospitalizations.

Limitations of this study include that analysis was based solely on data abstracted from Medicare claims thus patient variables could not be accounted for. Because all centers that practiced CardioMEMS implantation at the time of the study were included in the trial, it is likely that patient background characteristics did not differ significantly. It is important to note that this study consisted of nearly 2000 participants that included a much wider sampling of patients than the CHAMPION trial. Results of this study also further support the efficacy of the CardioMEMS device from the initial CHAMPION trial.

In a systematic Cochrane review conducted by Veenis et al. (2020), data and results of previous studies on invasive and non-invasive methods for monitoring and managing patients with heart failure was evaluated and compared. The review included 41 randomized controlled trials related to non-invasive monitoring of heart failure patients by either structured telephone support (25 studies, 9332 patients) or non-invasive remote telemonitoring (18 studies, 3860 patients) in comparison with heart failure patients managed with standard usual care. Studies

evaluating non-invasive monitoring included methods such as body weight and symptom monitoring, blood pressure, EKG, and pulse oxygenation saturation readings. It was concluded that while there was a modest improvement in all-cause mortality and decrease in heart failure related hospitalizations, there was no significant improvement in all-cause hospitalizations.

In evaluating the data from remote invasive heart failure monitoring, it was concluded that cardiac filling pressures rise up to 2 weeks prior to the patient becoming symptomatic (Veenis et al. 2020). Currently the CarioMEMS is the only FDA approved implantable device for ambulatory pressure monitoring in heart failure patients. The device is not only effective in reducing heart failure related hospitalizations, but safe and durable as well. CardioMEMS pressure readings were validated by two separate studies using Swan-Ganz catherization or echocardiography after initial implantation and again after 6 months post-implantation. Results by Swan-Ganz measurements supported reliability of CardioMEMS pressure readings ($r^2 = 0.90$ at implantation and $r^2 = 0.94$ at 6 months, $p < 0.01$). Results by echocardiography further supported the reliability of CardioMEMS pressure readings ($r^2 = 0.80$ at implantation and $r^2 = 0.75$, both $p < 0.01$ at follow-up). In terms of reduction in heart failure related hospitalizations, CardioMEMS demonstrated a 30% decline when compared to traditional standard of care monitoring as well as a 45% reduction of all-cause hospitalizations at 6 months and 16% at 18 months. In terms of mortality reduction, CardioMEMS showed the most promising results in the reduced ejection fraction cohort ($p = 0.06$).

Veenis et al. (2020) concluded that results for non-invasive heart failure monitoring are inconsistent, perhaps due to the high variability among different provider practices in treatment. The efficacy for CardioMEMS in terms of reducing hospitalizations has been strongly supported however and seems to have the most value for heart failure patients who are more advanced with

reduced ejection fractions. Furthermore, patient with preserved ejection fractions who are low risk and display fewer symptoms of congestion may be more appropriately monitored with traditional methods of management for reasons of simplicity and cost effectiveness.

This study provides data on both traditional non-invasive management methods as well as data from invasive monitoring and offers conclusions on appropriateness of the various monitoring methods in relation to different categories of heart failure patients. This evidence further supports further supports the efficacy of the CardioMEMS device in reducing hospital readmissions. Additionally, results suggest that monitoring and treatment of heart failure patients must be individualized and based on unique patient characteristics and needs.

Cost Effectiveness of CardioMEMS

Studies have proven that the implantable CardioMEMS device is effective at monitoring pulmonary artery pressures and preventing hospital admissions, but does the benefit outweigh the cost? In medicine it is important for providers to recognize when a procedure or therapy is unnecessary or cost prohibitive.

Martinson et al. (2017) conducted a retrospective comprehensive analysis of the CHAMPION trial to determine the cost effectiveness of the CardioMEMS device in comparison to traditional management using a Markov model to estimate the costs related to the course of management reported in the CHAMPION trial. Data points included hospitalization rates, survival rates, and quality of life. Because the majority of patients in the US eligible for implantable pulmonary artery pressure monitoring qualify for Medicare or carry private insurance, the authors focused on cost effectiveness from the perspective of the payer. Data endpoints were cost of treatment and survival. This data was used to calculate a projected cost

per year of life gained as well as cost per quality adjusted life year (QALY) for the treatment versus control group from the CHAMPION trial.

Over a 5-year time frame, the treatment group had a QALYs of 2.56 with estimated total cost of $56,974 compared to the control group who had a QALYs of 2.16 and a total estimated cost of $52, 974. The incremental cost-effectiveness ratio (ICER) was $29,593 per QALY which falls below the US acceptable cost threshold of $50,000 annually. Based on the results of the study, it can be concluded that the CardioMEMS implantable device is a cost-effective way of managing pulmonary artery pressures in the heart failure patient and it was further hypothesized that it will only become increasingly more cost effective in the future in terms of hospitalization reductions.

It should be noted that there is a conflict of interest among the authors of this study and their relationships with St. Jude Medical which is the current marketing company of the CardioMEMS device. Because of this one cannot exclude the possibility of confirmation bias.

In a similar study, Owens et al. (2016) used a Markov model to retrospectively determine the cost effectiveness of the CardioMEMS device based on the data from the original CHAMPION trial. Data points examined included hospitalizations, survival, quality of life, and incremental cost effectiveness ratio among the treatment group. Costs estimates were derived from literature estimates and Medicare reimbursement rates. Another group of lower-risk heart failure patients with preserved ejection fraction was studied and compared to those with reduced ejection fraction in relationship to cost effectiveness.

Results of the study included a lifetime reduction in hospitalizations for the CarioMEMS group (2.18 versus 3.12), increased QALYs (2.74 versus 2.46) and increased costs ($176,648 versus $156,569), yielding a cost of $71,462 per QALY gained and $48,054 per life-year gained.

The cost per QALY gained was $82,301 in patients with reduced ejection fraction and $47,768 in those with preserved ejection fraction. Among the lower-risk sub-group, a 41% reduction in hospitalizations would be necessary for the device to cost less than $100,000 per QALY gained. The device itself costs about $17,750. Use of the device would cost more than $150,000 per QALY gained if it cost more than $34,418 in the reduced ejection fraction subgroup or $59,296 in the preserved ejection fraction subgroup. The average cost of a hospitalization related to heart failure in the US is about $12, 832, but this can vary significantly among facilities.

It was concluded that the CardioMEMS implantable device is cost effective intervention for the management of heart failure as evidenced by improved quality of life and reduced hospitalizations in both the preserved and reduced ejection fraction groups. The cost of therapy was found to be less than the accepted willingness-to-pay threshold in the US ($50,000 per QALY gained). In addition to supporting the cost effectiveness of the CardioMEMS device, there was no identified conflict of interest among the authors of this study.

Ollendorf et al. (2016) conducted a literature review to determine clinical effectiveness, cost effectiveness, and potential budget impact of CardioMEMS implantable pulmonary artery pressure device compared to standard HF management. A 5-year potential budget impact from the payer perspective was estimated based on an annual total hospitalization rate of 45% related toNYHA class III heart failure, with a target population size of 1.4 million. It was estimated that by the end of the 5-year time frame, 25% of the of patient candidates would receive CardioMEMS therapy creating a potential budget impact of $5 million, roughly $1 million annually. Factors such as increase in cost of device and services were accounted for consistent with US economic growth. The overall estimated price of $10,665 if accurate would represent a 40% reduction in average Medicare cost.

The authors felt that evidence from the CHAMPION trial may indicate a net health benefit compared to current traditional management of heart failure as evidenced by reduced hospitalizations, however they also felt that the data was inconclusive due to the potential for confirmation bias related to the CHAMPION trial. It should be noted that this is currently the only trial of its kind and ideally additional studies are needed to make absolute conclusions. The authors conclude that in regards to their cost effectiveness analysis, CardioMEMS seems to be a cost-effective treatment that falls within community accepted cost thresholds. They do note however that budget reduction impact could potentially be absorbed by the healthcare system due to the 40% discount from typical cost to Medicare.

Ollendorf et al. (2016) identified several limitations of the CHAMPION trial that must be recognized including attending physicians were not blinded to treatment allocation, which may have impacted the decision to hospitalize. The authors note that there were methodology concerns brought forth by the FDA related to study personnel relaying possible recommendations for treatment to the treating physicians among the treatment group. Lastly, there was a possible treatment-by-sex interaction but because the number of women in the study was small (n=151), sufficient evidence to make this determination was not available.

Schmier et al. (2017) also examined the cost-effectiveness of the CardioMEMS heart failure management system at up to 5 years compared to traditional medical management in patients with heart failure using a Markov simulation model. This study was important as it also presented data related to mortality rates in the treatment versus control groups from the CHAMPION trial which is lacking in many other studies. This information can further aid in the guidance of shared decision making related to heart failure treatment between the provider and heart failure patients.

Results of the study determined the cost over the 5-year observation period was approximately $162,772 per patient in the traditional medical management group and $188,880 (including the device and implantation) in CardioMEMS treatment group. The difference in quality adjusted life years (QALYs) was 0.58, favoring the CardioMEMS treatment group (2.51 compared to 1.93 in the control group). The model estimated the ICER of treatment with CardioMEMS compared to traditional medical management as $44,832 per QALY. In terms of mortality, 50.4% of the original CardioMEMS patients were dead at 60 months in comparison to the control group which had a mortality rate of 50% at 40 months and 76.2% at 60 months.

The authors concluded that based on the results of their study using a Marcov model, pulmonary artery pressure monitoring using the CardioMEMS HF System was found to be cost-effective in comparison to traditional medical management of heart failure. Findings were consistent across a range of sensitivity analyses. They went on to say that the CardioMEMS HF System may represent a cost-effective medical advancement in heart failure management. It should be noted that there was a conflict of interest rated to authors Jordana K. Schmier and Kevin L. Ong who are employed by Exponent which received a grant from St. Jude Medical to evaluate the cost-effectiveness of the CardioMEMS device. Dr. Fonarow was a consultant to St. Jude Medical. St. Jude Medical has reviewed the manuscript prior to submission, but reportedly did not provide substantial scientific input.

Discussion

Heart failure is a common condition that many health care providers will be tasked with managing among their patients. Medical research related to heart failure management continues to evolve and new advances continue to emerge on a regular basis. As technology continues to be incorporated into these medical advances, monitoring capabilities have become invaluable,

allowing for closer surveillance and more frequent analysis of data. The following section is a discussion of the literature regarding the efficacy of the CardioMEMS device in comparison to traditional medical management.

In heart failure patients, are traditional methods of management effective in terms of preventing hospital admissions?

Data related to several traditional methods of monitoring and managing heart failure patients was examined and found to be most effective when used in combination rather than in monotherapy. A study by Howie-Esquivel et al. (2019) found that home monitoring of weight gain alone is likely not adequate in terms of prevention of heart failure related hospitalizations. This was attributed to the finding that by the time an increase in weight is noticed, the patient has already developed significant pulmonary congestion that may need more intense treatment than what can be provided on an outpatient basis. Results of this study also indicated that increased dyspnea was a better predictor of impending need for hospitalization than weight gain and peripheral edema. It should be noted that management based on symptom development and physical changes alone depends in large part on the ability of the patient to recognize these symptoms. Patient ability to comply and recognize warning signs should be assessed on an individual basis.

In heart failure patients, monitoring of natriuretic peptide levels is a common method of assessing increased intravascular volume and detecting acute exacerbations of pulmonary congestion. Efficacy of monitoring of natriuretic peptides in the management of heart failure patients was assessed in a study by Myhre et al. (2018) and found that elevations in natriuretic peptide levels were directly associated with a heart failure related hospitalization ($p<0.001$) across all patient subgroups. The reliability of this method of management in preventing

hospitalizations would obviously depend directly on the frequency of lab monitoring. Waiting until the patient is symptomatic with dyspnea and peripheral edema would not likely be effective in preventing hospital readmissions.

Case management has become increasingly popular over the years for the management of heart failure patients. This is typically done through heart failure clinics ran by nurses and consists of frequent follow up phone calls, patient participation through monitoring of weight and symptoms, as well as in person clinic visits with physical assessment and lab monitoring of natriuretic peptides. In studies conducted by McCants et al. (2019) and Driscoll et al. (2015), the efficacy of case management of the heart failure patient in terms of reducing hospital admissions was examined and similar conclusions were made. Both studies found that nurse-led case management resulted in a significant reduction in heart failure hospital readmissions. Adjustment of heart failure medications through heart failure case management clinics was associated with a 39% reduction in heart failure related hospital admissions (Driscoll et al. 2015) and similarly, McCants et al. (2015) noted a 34% reduction in heart failure hospital admissions in comparison to the control groups. These results indicate that heart failure case management is an effective method for preventing hospital readmissions.

It can be concluded that for heart failure patients who are not candidates or who decline more invasive methods of monitoring, the most efficacious method of management when looking at the goal of preventing hospital readmissions is case management; This would involve a combination of patient symptom monitoring, frequent follow up phone calls, natriuretic peptide monitoring and associated medication adjustments. This method would allow for a custom-tailored treatment plan based on individual patient needs allowing for interventions in a timely manner through a team-based approach.

In patients with heart failure, do interventions based on monitoring pulmonary artery pressures with an implantable CardioMEMS device lead to decreased hospital readmissions?

The CardioMEMS device is an implantable pulmonary artery pressure monitor that wirelessly transmits data daily to a secure website. The availability of data from the CardioMEMS device allows providers to intervene and make adjustments to heart failure medications early on in the development of pulmonary congestion in order to prevent acute exacerbations and subsequent hospitalizations. The two main clinical trials evaluating the effectiveness of the CardioMEMS device in preventing hospitalizations are the CHAMPION trial conducted in the United States and the MEMS-HF trial conducted in Europe. The trials had similar results indicating that the CardioMEMS device was an effective method of managing heart failure patients and preventing hospital readmissions based on internal monitoring of pulmonary artery pressures. In a study by Gronda et al. (2020) which examined the results of the CHAMPION trial, it was noted that there was a 44% reduction in hospital readmissions in the patients managed with the CardioMEMS device in comparison to the control group. Furthermore, an evaluation of the European MEMS-HF trial indicated a 62% reduction in heart failure related hospitalization in the CardioMEMS treatment group (Angermann et al., 2020).

There are multiple studies that retrospectively examine the continued effectiveness of the CardioMEMS device in the post CHAMPION trial period. Desai et al. (2017) found that in the 1-year time period post CHAMPION trial, heart failure patients monitored with the CardioMEMS device had a 34% reduction in heart failure related hospitalizations ($p<0.001$). Similarly, in a study by Veenis et al., (2020) it was noted that there was a 30% reduction in heart failure hospitalizations at 6 months compared to the control group. These results indicate that

the CardioMEMS device is an effective method for the management of heart failure and should be considered as a treatment option for appropriate patients. Reduction in heart failure readmissions through pulmonary artery pressure monitoring would presumably increase quality of life by limiting symptoms of acute pulmonary congestion, dyspnea, and activity intolerance.

When examining the overall effectiveness of the CardioMEMS device in terms of preventing hospital readmissions, it should be noted that there are many variables that may impact results. This is highlighted in a study by Tran et al. (2019) that found that there was a significant correlation between reduction of hospitalized days and the frequency of patient data transmissions from the CardioMEMS device as well as frequency of provider interpretation of the data. These results serve as an important reminder of the need for evaluation, interpretation, and potential intervention in terms of the overall effectiveness of technologic advances. As CardioMEMS becomes more popular, it may be helpful to incorporate these patients into a heart failure case management clinic for best results. This would ensure timely interpretation of results as well as proper intervention based on pre-determined guidelines.

There are currently several limitations to utilization of pulmonary artery pressure monitoring via the CardioMEMS device. The CardioMEMS is currently FDA approved for New York Heart Association (NYHA) Class III heart failure patients with a heart failure related hospital admission in the previous 12 months. The NYHA defines class III heart failure as causing marked limitation on physical activity characterized by dyspnea, palpitations, fatigue, or angina with less than ordinary activity, but who are asymptomatic at rest. According to Abbott Laboratories, the sole contraindication for CardioMEMS therapy is inability of the patient to take dual antiplatelet or anticoagulant therapy for one month post implantation. Patients who do not meet these criteria may encounter difficulty attaining insurance coverage for the procedure.

There are currently trials underway that will attempt to prove the efficacy of the CardioMEMS device for a broader range of heart failure patients. Approval of the device for the management of patients with less severe heart failure could potentially decrease the progression of heart damage and improve life expectancy if monitored appropriately.

Is the CardioMEMS device a cost-effective method for the management of heart failure patients

Three separate studies evaluating the cost-effectiveness of the CardioMEMS device using a Markov model applied to data from the original CHAMPION trial were examined. All three studies resulted in similar findings and the conclusion that the CardioMEMS device is a cost-effective method for heart failure management (Martinson, 2017; Owen, 2016; Schmier, 2017). All three studies based the determination of cost effectiveness on the commonly used acceptable annual threshold of $50,000 in the United States. Martinson et al. (2017) found that the incremental cost effectiveness ratio was $12,262 per QALY. In a similar study, Owen et al. (2016) found that cost per QALY gained was $47,768 in patients with preserved ejection fraction. Finally, Schmier et al. (2017) concluded that the estimated cost/QALY for treatment with CardioMEMS was $44,832 which places the device in the high-to-intermediate value range according to both the American Heart Association and the American College of Cardiology. Mortality rate was also examined in this study and the authors noted that upon completion of the 60-month trial, 50.4% of the original CardioMEMS patients were dead in comparison to the control group in which 76.2% were dead. These findings suggest that not only is the CardioMEMS a cost- effective method for management, but it may also reduce mortality.

In terms of safety of the CardioMEMS device, several studies evaluate the data from clinical trials and longitudinal studies. These studies all note similar results and that ultimately

the CardioMEMS device is a safe option for the management of heart failure. Overall safety should be discussed with the patient and included as part of the treatment decision making process. Angermann et al. (2020) indicate that when examining data from the original CardioMEMS clinical trial, freedom from device related complications at 1 year was 98.3%. Furthermore, by effectively managing pulmonary artery pressures mortality risk is reduced. A reduction in pulmonary artery pressure by just 5 mmHg is associated with a 30% reduction in overall mortality risk (Heywood et al., 2017). These results indicate that not only is the CardioMEMS device safe, but it may extend life expectancy due to reduction in pulmonary artery pressures and preventing further heart damage and progression of heart failure.

In conclusion, the CardioMEMS device appears to be a safe and cost-effective method in managing heart failure and preventing hospital readmissions. However, due to the limitation of only two major clinical trials evaluating the efficacy of the CardioMEMS device, additional longitudinal studies are needed. Further such trials are currently underway.

Applicability to Clinical Practice

As heart disease continues to be the leading cause of mortality world-wide, it is without question that it is important for health care providers to remain educated on advances in treatment as well as changes in best practices for care. Billions of dollars are spent on the treatment of heart failure on an annual basis in the Unites States alone. Customized treatment regimens tailored to the heart failure patient's individual needs will not only improve quality of life but potentially reduce cost to the patient as well as the payer. Using a shared decision-making model, providers along with their patients can collaborate to determine the most appropriate individualized heart failure treatment and management plan.

Based on the results of the research presented in this review, it can be concluded that the implantable CardioMEMS device is an effective and perhaps under-utilized method of management for the heart failure patient and research has shown that it is cost effective for both the payer and the patient. It should also be noted that there is no one treatment method that has been shown to be superior to other methods in all patient scenarios. In patients with decreased life expectancy, or those who are in need for more advanced interventions such as left ventricular assist device or heart transplant, it may be more appropriate to utilize more traditional methods of medial management and potentially incorporate case management for maximized patient outcomes. The CardioMEMS device may be most appropriate for patients whose life expectancy and quality of life would be predicted to improve significantly with tailored treatment and medication management based on pulmonary artery pressure readings.

One of the limitations of the CardioMEMS device is the current recommendations for eligibility criteria for device implantation are restricted to NYHA class III heart failure patients with a history of hospitalization. For heart failure patients who do not meet these criteria, some resistance may be met in regards to attaining prior authorization for coverage of the device itself as well as expenses incurred related to implantation and continued monitoring. Because of these limitations, the CardioMEMS is most likely underutilized for the management of heart failure. It should be noted that there are studies currently underway that examine the benefit and effectiveness of the CardioMEMS device in a larger range of heart failure patients than just the currently approved NYHA class III patients. If proven effective, the device may potentially become the new standard for the optimization of the management of heart failure patient.

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