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The CardioMEMS Heart Failure System for chronic heart failure – a European perspective

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ABSTRACT

Introduction: Chronic heart failure (HF) is characterized by high hospital admission rates. The CardioMEMS™ HF System is a pulmonary artery pressure sensor developed for remote hemodynamic monitoring to reduce HF hospitalizations. The device is FDA approved and CE marked, but clinical evidence for the CardioMEMS system is mainly based upon U.S. studies. Because of structural differences in HF care between the U.S. and Europe, it is important to study CardioMEMS efficacy in European setting on top of usual HF care and contemporary therapy. Several observational studies have been performed in Europe, but there is an unmet need for randomized clinical trials.

Areas covered: This review focuses on safety and efficacy data for CardioMEMS remote hemodynamic monitoring in European HF setting, and discusses important upcoming studies.

Expert opinion: For safety, data from European studies are in line with U.S. studies. Efficacy with regard to reduction of HF hospitalizations seems promising, but is merely based upon observational studies comparing pre- and post-implantation event rates. The first European randomized clinical trial (MONITOR HF) will provide efficacy data compared to actual standard care in a high-quality healthcare system with contemporary HF treatment and will provide important generalizable information to other European countries.

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1. Introduction

Chronic heart failure (HF) is characterized by severely impaired prognosis, poor quality of life and high hospital admission rates [1–3]. The worldwide prevalence of chronic HF is estimated at 1–2% of adults and is increasing, especially due to aging of the population and improved treatment of cardiovascular diseases [4–9]. As such, the burden of chronic HF on society and healthcare resources is enormous and expected to rise [2,8]. While major progression has been made in HF treatment and therapeutic options for HF have been expanded, HF patients still require frequent checkup in the outpatient clinic and they are often hospitalized for acute decompensated heart failure [10]. These hospital admissions usually last several days, and one of the major problems in HF care is the high rate of rehospitalization. It is known from previous research that repeated hospital admissions for decompensated heart failure are associated with a decline in myocardial function, renal function and worse survival [3,11,12]. Therefore, one of the most important challenges in HF care alongside reduction of mortality is reduction of HF-related hospitalizations, which is the main target of HF therapy in general. While better HF treatment is urgently needed to reduce worsening HF events, developing strategies for early detection and prevention of these events is important and inevitable to improve prognosis and to preserve healthcare resources. This concept is also referred to as remote monitoring and has been around for many years [13]. While remote monitoring has traditionally been built around noninvasive monitoring (such as structured telephone support), there has been a transition toward monitoring with implantable cardiac devices (such as implantable cardiac defibrillators (ICDs)) and hemodynamic monitoring with specially developed invasive sensors or devices [14–17]. Emphasis has lately been on the latter as clinical evidence for the use of monitoring through noninvasive methods and ICDs has been rather conflicting [15,16]. Hemodynamic monitoring relies on measurement of intracardiac filling pressures, which are the central target of HF therapy. The rationale for hemodynamic monitoring has been discussed before and is mainly based upon the fact that hemodynamic congestion precedes clinical signs and symptoms of HF by several weeks [14,18,19]. The CardioMEMS™ Heart Failure system (Abbott, Sylmar, CA, U.S.A) is a small sensor that is capable of daily measurements of the pulmonary artery pressure [20]. These pressures are comparable to the left ventricular filling pressure. Technical aspects of the device and a detailed description of the implant procedure have been reported previously, as were the limitation associated with this technique [18,21]. Clinical evidence for the efficacy of the CardioMEMS™ HF system has mostly been confined to the U.S. and unfortunately, there is no evidence from randomized clinical trials in Europe. However,

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Article highlights

- After a decade of clinical research, the evidence supporting remote pulmonary artery pressure monitoring with the CardioMEMSTM HF system is promising
- Randomized clinical trials are limited to the U.S. and there is an unmet need for European clinical trial data
- Non-randomized observational studies in European setting have shown promising results for the reduction of HF-related hospitalizations
- Thus far, the CardioMEMSTM HF system has been considered cost-effective, but analyses have been mainly based upon U.S. data
- The MONITOR HF trial (the Netherlands) is the most important upcoming trial that will provide the latest evidence on whether CardioMEMS-guided HF management is safe, efficacious, and cost-effective in a contemporary Western-European setting

important observational work has been performed and clinical trial data from European trials are expected in the near future [22–24]. Pending these results, CardioMEMS is likely to have a considerable impact on HF care and structure in Europe as well. Therefore, this comprehensive review focuses on available data on safety and efficacy of CardioMEMS remote hemodynamic monitoring in European studies, and discusses important upcoming studies and the future perspectives of the CardioMEMS^{TM} HF system, specifically in the European setting.

2. Brief overview of CardioMEMS data from studies performed in the United States

2.1. U.S. clinical trial data

2.1.1. CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients) trial [25,26]

The foundation for CardioMEMS use in clinical practice was laid in 2011 by the pivotal CHAMPION trial, in which 550 patients with chronic heart failure in New York Heart Association (NYHA) class III with an HF hospitalization (HFH) within a year prior to enrollment, had the device implanted [25]. These patients were randomly assigned to either the treatment group (active monitoring group), in which clinicians used the daily PAP readings on top of standard care, or the control group, in which PAP data were not available to clinicians and the patients only received standard HF care. After a mean follow-up of 6 and 15 months, patients in the treatment group had a 28% and 37% lower risk of HF-related hospitalizations as compared to the control group, respectively (hazard ratio (HR) 0.72, 95% confidence interval (CI) 0.60–0.85 and HR 0.63, 95% CI 0.52–0.7, respectively) [25]. After this initial randomized access period, PAP data became available for all patients, and patients were then followed for a mean period of 13 months [26]. During this period, there was a large reduction of heart failure admission rates in the former control (HR 0.52, 95% CI 0.40–0.69) compared with the admission rate in the control group during randomized access [26]. With a total of eight (1%) device-related or system-related complications and seven (1%) procedure-related adverse events, the technique was deemed to be safe and FDA approval for patients in NYHA class III with an HF admission in the previous year was acquired in 2014 [25,26].

In a subanalysis of the CHAMPION trial, information on medication changes was reported separately for the randomized access period [27]. There were significantly more medication changes in the active monitoring group than in the control group (2468 vs. 1061, respectively, $p < 0.0001$). Diuretics were adjusted most frequently in both groups, but significantly more often in the active monitoring group (1547 in the active treatment group vs. 585 in the control group, $p < 0.0001$). Vasodilators and neurohormonal antagonists were adjusted more often in the active group as well. The authors also reported that drug doses were decreased more frequently in the active monitoring group, and that these adjustments consisted mainly of reductions in diuretics doses, which occurred more frequently in the active monitoring group than in the control group. The total daily loop diuretics dose increased in both groups, but this increase was significantly greater in the active monitoring group than in the control group (+27% change vs.+15% change, $p < 0.01$). Importantly, there were no significant changes in serum creatinine or estimated glomerular filtration rate between both groups. Significant increases in ACEi/ARB, beta-blocker and aldosterone antagonist doses between baseline and 6 months were observed in the active monitoring group, but not in the control group. Patients with higher baseline PA pressures in the active monitoring group experienced more frequent drug interventions [27]. This analysis supported the concept of remote hemodynamic monitoring by demonstrating that drug interventions based upon PA pressures may result in a reduction of these pressures, and, consequently, in reduced HF hospitalization rates [27].

2.1.2. GUIDE-HF (Hemodynamic-guided management of heart failure) trial [28]

The second randomized clinical trial in U.S. setting is the GUIDE-HF trial, which was conducted across centers in the U.S.A. and Canada with a design comparable to the CHAMPION trial [28]. Enrollment criteria were expanded as patients in NYHA class II-IV with either a recent heart failure hospital admission and/or elevated natriuretic peptides (prespecified levels) were eligible for participation. A total of 1000 patients had the CardioMEMS implanted and were randomly allocated to CardioMEMS-guided management (treatment group) or usual care (control group). Clinicians did not have access to the PA measurements in the control group [28]. The primary endpoint consisted of all-cause mortality and total HF events (defined as HF hospitalization and urgent HF hospital visit). There was no significant difference in the primary endpoint (HR 0.88, 95% CI 0.74–1.05) nor in the risk of HF events (HR 0.85, 95% CI 0.70–1.03) [28]. However, the COVID-19 pandemic emerged during the follow-up phase of the trial, after enrollment was completed. Therefore, a prespecified pre-COVID-19 sensitivity analysis was performed in which results were analyzed up to the advent of the pandemic. During this period, there was a significant reduction in the risk of the primary endpoint in the active treatment group (HR 0.81, 95% CI 0.66–1.00, p=0.049), which was mainly driven by a reduction in the heart failure event rate (HR 0.76, 95% CI 0.61–0.95) [28]. During

COVID-19, the primary endpoint event rate decreased drastically with 21% in the control group, while the event rate in the treatment group remained unchanged. Therefore, no between-group differences were found during COVID-19 (HR 1.11, 95% CI 0.80–1.55). Importantly, 99% of the patients were free from device or system-related complications [28]. Medication changes occurred frequently in both groups, but more often in the treatment group. Medication changes were not specified in the report, but the proportion of patients receiving GDMT remained fairly stable between baseline and 12 months of follow-up. An overview of completed and ongoing randomized clinical trials is presented in Table 1.

2.2. U.S. observational studies and real-world data

CardioMEMS efficacy and safety were confirmed in the large observational open-label Post Approval Study (PAS) that enrolled 1200 patients with NYHA class III chronic HF who had an HF-related hospitalization one year prior to enrollment [29]. The rate of HFH was significantly lower 1 year after PA pressure monitoring compared to the year prior implantation (HR 0.43, 95% CI, 0.39–0.47) [29]. Recently, the 2-year results of PAS were published. In the total study population, HFH rates decreased from 1.25 to 0.54 at 1 year, and decreased even further to 0.37 during the second year ($p < 0.0001$ for both the 1 and 2-year follow-up). A subanalysis restricted to the 710 patients who completed 24 months follow-up showed a similar pattern. In PAS, the majority of interventions consisted of changes in loop diuretics (in 82.8% of the patients) and temporary addition of thiazide diuretics (37.8% of the patients had changes in thiazide diuretics), whereas there were 356 changes in RAS inhibitors and beta-blockers among all enrolled patients. Therefore, investigators posed that the effects of PA pressure-guided management were most likely the result of optimization of diuretic therapy. Furthermore, the majority of patients with HFrEF already received guideline-recommended medical therapy at baseline [30].

Real-world evidence stems mainly from two large studies that analyzed Medicare data [31,32]. The first study showed that in 1114 patients who received a CardioMEMS, the HFH rate in the period 12 months after implantation was 34% lower than in the 12 months prior to implantation (HR 0.66, 96% CI 0.57–0.76) [31]. In the second study, 1087 patients who received CardioMEMS were matched to 1087 control patients. After 12 months of follow-up, the rate of HFH was lower in the CardioMEMS cohort (HR 0.76, 95% CI 0.65–0.89) [32]. At last, Kishino et al. utilized the U.S. Nationwide Readmissions Database (NRD) to identify patients with a hospital admission for acute HF in a five-year time window [33]. These patients were then divided into those who underwent CardioMEMS implantation, and those who did not. For additional comparison, propensity score matching (1:1 ratio) was performed to construct a control cohort. Both in the matched and unmatched analysis, readmission rates were significantly lower in patients with CardioMEMS compared to those without CardioMEMS at 30, 90 and 180 days. Furthermore, in multivariable regression analyses, CardioMEMS was associated with a lower risk of readmission at 30, 90 and 180 days [33].

3. European observational CardioMEMS data

3.1. Current evidence

3.1.1. MEMS-HF (the CardioMEMS European Monitoring Study for Heart Failure) [34]

In 2020, results from the MEMS-HF study were published [34]. This was an observational prospective non-randomized study performed in centers across Germany. In a later stage, several sites from Ireland and the Netherlands were added for enrollment. Patients with chronic HF were eligible for enrollment if they were in NYHA class III and had an HF-related hospitalization in the year prior to study participation. Outcomes included device or system-related complications (DSRC), sensor failure, quality of life and clinical endpoints such as the annualized HFH rate during 12 months after versus 12 months prior to implant, all-cause mortality rate and PAP changes from baseline [34]. A total of 234 patients had a CardioMEMS sensor implanted of whom 198 completed the 6 months follow-up visit and 180 completed the 12 month visit. After 12 months, 98.3% of the patients were free from DSRC and 99.6% were free from sensor failure. Of the 21 serious adverse events that occurred during 236 implant attempts, 4 were classified as DSCR and 21 as related to the procedure [34]. During the first six months post-implant, the HFH rate decreased by 62% (HR 0.38, 95% CI 0.31–0.48). The reduction over the complete 12-months follow-up period was 66% (HR 0.34, 95% CI 0.26–0.44), which was greater than in the CHAMPION trial [34]. After 12 months of follow-up, 13.8% of the patients had died and none of the deaths were attributed to the device or delivery system. On average, the mean PAP decreased by 3.4 mmHg at 6 months, and 5.5 mmHg at 12 months ($p < 0.0001$) [34]. Additionally, patient reported quality of life scores (assessed by the Kansas City Cardiomyopathy Questionnaire, the Patient Health Questionnaire depression module and the EQ-5D-5 L questionnaire) improved significantly after 6 months, and importantly, these improvements were sustained at 12 months. However, these comparisons were based on inpatient changes from baseline without a comparison group and are therefore less informative. There were a total of 1759 HF medication changes, of which the majority ($N = 1068$) were adjustments to diuretics [34].

It should be emphasized that MEMS-HF was non-randomized and that patients were their own historical control. Therefore, the study was prone to important forms of bias which have limited causal inference. However, safety and durability were confirmed.

Pulmonary hypertension (PH, defined as mean PAP≥25 mmHg) is associated with poor prognosis in HF. A prespecified subgroup analysis from MEMS-HF aimed to study whether the effects of CardioMEMS remote monitoring depended on the presence and subtype of PH [22]. This is an important topic as PH may complicate the interpretation of PA pressures in the context of HF, especially when non-cardiac conditions contribute

Table 1. Overview of completed and ongoing randomized clinical trials.

Study name	Study design	No. of patients	NYHA	Comparator arm	Outcomes	Results	Status
CHAMPION[1] [25]	Single-blind	550	III	CardioMEMS without clinician access to PAP data	Primary efficacy outcome: difference in HFH rate between the two groups after 6 months of follow-up Primary safety outcome: freedom from DSRC and sensor failure	HR 0.72 [0.60–0.85] 98.6% and 100% freedom, respectively	Completed
CHAMPION[1] [26]	Single-blind	347	III	Former control group (cross-over)	Primary efficacy outcome: difference in HFH rate between the control group and former control group during the open access period after 13 months Primary safety outcome: freedom from DSRC and sensor failure	HR 0.52 [0.40–0.69] 98.6% and 100% freedom, respectively	Completed
GUIDE-HF [28]	Single-blind	1000	II-IV	CardioMEMS without clinician access to PAP data	Primary efficacy outcome: composite of all-cause mortality and total HF events at 12 months Primary safety outcome: freedom from DSRC at 12 months	HR 0.88 [0.74–1.05] 99% freedom	Completed
GUIDE-HF [28] Pre-COVID-19[2]	Single-blind	1000	II-IV	CardioMEMS without clinician access to PAP data	Primary efficacy outcome: composite of all-cause mortality and total HF events at 12 months	HR 0.81 [0.66–1.00]	Completed
MONITOR HF [24]	Open-label	340	III	Usual HF care	Primary efficacy outcome: change in quality of life (KCCQ) at 12 months Secondary efficacy outcomes: the number of HFH (among other endpoints)	N.A.	Ongoing

[1]The CHAMPION trial assessed outcomes at two time points; after a median follow-up of 6 months during the randomized access period and 13 months during open the access period, respectively.
[a]The pre-specified COVID-19 sensitivity analysis was significantly different from the main analysis and therefore important to include NYHA, New York Heart Association; PAP, pulmonary artery pressure; HFH, heart failure hospitalization; DSRC, device-related or system-related complications; HR, hazard ratio; HF, heart failure; KCCQ, Kansas City Cardiomyopathy Questionnaire; EQ-5D-5 L, European Quality of Life 5 Dimensions 5-Level.

to elevated PA pressures, and longstanding PH may also result in right ventricular failure, which negatively affects prognosis.

For this subanalysis, 106 study patients with detailed information on PA pressures were analyzed and classified into three groups: 1) no PH ($N = 31$), 2) isolated post-capillary PH (IpcPH, $N = 38$), 3) combined post- and pre-capillary PH (CpcPH, $N = 36$). One patient could not be classified in one of these subgroups [22]. On baseline, patients with CpcPH had the highest PA pressures. Over the total follow-up period (12 months), a significant decline in PAP was observed in every group. The decline in the IpcPH group was significantly greater than in the no PH group, while other between-group differences were non-significant [22]. The improvement of the overall KCCQ summary score was substantial and significant in all groups, whereas the total KCCQ summary score only improved significantly in patients with PH [22]. HF hospitalization rates after CardioMEMS implantation decreased significantly in all groups [22]. Strikingly, the reduction was greatest in patients without PH, while the absolute decline in mean PA pressure was lowest in this group. Patients in the IpcPH and CpcPH groups experienced similar risk reductions [22]. While this subanalysis generated interesting results, it was limited by the small number of patients and observational design. However, as also mentioned by the authors, these data are hypothesis generating and may be helpful for future research.

3.1.2. COAST (CardioMEMS HF System Post-Market Study) study [23]

COAST is an international, prospective, multicenter open-label observational study that is running in the UK, Europe and Australia [23]. COAST aimed to assess the safety, effectiveness and feasibility of CardioMEMS hemodynamic monitoring. Similar to other studies, patients were eligible for enrollment if they had persistent NYHA Class III symptoms and a minimum of one HF hospitalization within 1 year prior to participation, regardless of left ventricular ejection fraction [23]. In 2021, results from a subset of the UK part of the study were published. A total of 138 patients were enrolled and implanted, of whom 103 were consented and 100 underwent successful implantation before the advent of the COVID-19 pandemic. In their report, the authors only reported results of the patients that were enrolled before the pandemic [23].

The primary safety endpoints were freedom from DSRC and sensor failure 2 years after implantation. The primary clinical endpoint was the difference in HF hospitalization rate during the 12 months prior to sensor implantation and the 12 months after implantation which is in line with earlier observational studies [23].

Of the 103 enrolled patients, 3 were not implanted due to hemoptysis, anatomical constraints or inability to gain venous access. Two years after sensor implantation, freedom from DSRC and sensor failure was 100% and 99%, respectively [23]. The event rates before and after implantation were 1.52 and 0.27 per patient year, respectively, which indicated a significant risk reduction of 82% (incidence rate ratio 0.18, 95% CI 0.12–0.28) [23]. PA pressures also declined significantly during follow-up. Similar to earlier studies, medication changes consisted mostly of adjustments to diuretics [23]. As mentioned before, the study design has some important limitations due to its non-randomized design and the lack of a comparator control group (patients were their own historical control).

3.1.3. HEMOVAD study [35–37]

In a small pilot study in the Netherlands, the safety and feasibility of CardioMEMS guided hemodynamic optimization prior to left ventricular assist device (LVAD) implantation was assessed. The rationale for this study was based on the hypothesis that hemodynamic optimization could potentially reduce the risk of renal and RV failure, could aid in optimizing fluid state post-LVAD implantation, and that remote monitoring could be helpful for individualizing patient management in the outpatient phase [35]. As such, the indication for CardioMEMS in this study was different from earlier studies. In summary, this pilot study showed the safety and feasibility of this approach in LVAD patients and was mostly hypothesis-generating [36,37].

3.2. Ongoing European studies

3.2.1. MONITOR HF trial [24]

There is an urgent need for randomized clinical trials in Europe to provide unbiased efficacy data. The Dutch multicenter Monitor HF trial will be the first randomized European study aiming to replicate findings from the pivotal CHAMPION trial [24–26]. This trial is an investigator-initiated, multicenter, randomized clinical trial of patients with chronic HF in NYHA class III and at least one HF hospitalization in the 12 months before trial enrollment. The Monitor HF trial is a reimbursement trial and is sponsored by the Dutch Ministry of Health and National Health Care Institute (Zorginstituut Nederland) [24]. Patients were randomized in a 1:1 ratio to either CardioMEMS PA monitoring or standard HF care. Enrollment started in April 2019, and the study is expected to be completed in the first half of 2023. A unique feature of this study is the fact that the primary endpoint is quality of life as assessed by the Kansas City Cardiomyopathy Questionnaire, which will enable the investigators to link quality of life to hemodynamics [24]. Among secondary endpoints are the number of HF hospitalizations during follow-up and all-cause mortality (Table 1). The trial is scheduled to randomize 340 patients [24]. Importantly, cost-effectiveness analyses will also be conducted to calculate the incremental cost-effectiveness ratio (ICER) per quality adjusted life year (QALY) gained. A set of questionnaires will be used to capture healthcare consumption and quality of life [24].

Based upon available literature, the quality of HF care in the Netherlands is considered to be high, especially with regard to pharmacological treatment, and is at least as good as in other European countries [38–46]. Combined with the comparable HF care organization with dedicated HF outpatient clinics and HF nurses, and patient access to healthcare systems, results from the MONITOR HF trial may be well generalizable to the rest of (Western) Europe. Therefore, this trial may have a large impact on future HF care and CardioMEMS reimbursement in Europe, but also in countries worldwide with comparable healthcare systems and financial structures.

4. Cost-effectiveness of the CardioMEMS HF System

Heart failure care is associated with high costs which are largely attributable to the recurrent hospital admissions [47]. While the CHAMPION trial showed a reduction in HF hospitalization, cost-effectiveness is an important aspect that should be considered when reviewing the CardioMEMS HF System, especially because of the costs of the device and implantation. In this section, studies that focused on cost-effectiveness using efficacy data from the U.S. CHAMPION trial are summarized [25].

In the first report from the CHAMPION trial by Abraham et al., it was estimated that CardioMEMS led to an increase of 0.30 in (discounted) quality adjusted life years (QALYs) and an increase of $4,282 in costs, resulting in an incremental cost-effectiveness ratio (ICER) of $13,979/QALY. The study was based on a Markov model over a time horizon of up to 5 years and from the payer's perspective. It included costs for implant and device, HF-related hospitalization, medications for outpatients, and end-of-life support for those who died [25].

Two other U.S. studies had a perspective and time horizon similar to Abraham et al. and used the European Quality of Life Five Dimensions, three level questionnaire (EQ-5D-3 L) to measure health-related quality of life at baseline and several times during follow-up in the CHAMPION study [48,49]. These studies reported increases in QALYs of 0.40 and 0.58 and increases of $11,644 and $26,108 in costs, respectively. The resulting ICERs were $29,593/QALY and $44,832/QALY [48,49]. These two studies included more comprehensive cost modeling than Abraham et al., including all HF and non-HF hospitalization costs, drug prescriptions, long-term care, and outpatient visits. However, despite using the same sources for hospitalization costs, there was a notable difference in ICERs between these two studies, which stems from the difference in the proportion of those receiving some form of monitoring in the standard of care group, model structure, and input parameters [48,49].

Furthermore, a U.S. study from a societal perspective and with a Markov model of a lifetime horizon that used the results of conversion of the Minnesota Living with Heart Failure (MLWHF) ratings into the EQ-5D scores for the health utility values, estimated an increase of 0.28 in QALYs and a $20,079 increase in costs, resulting in an ICER of $71,462/QALY [50]. This study included all healthcare-related costs, such as costs for hospitalization, outpatient medical costs, device, and implantation costs. Apart from the perspective and modeling of lifetime costs and effects, this study's high estimate of the ICER arose from several assumptions regarding utility values, input parameters, and the model structure [50]. Due to methodological differences, the MLWHF results were lower than those in the EQ-5D responses. Nevertheless, in all US studies, CardioMEMS appears to be cost-effective at a willingness to pay threshold (WTP) of $50,000–$100,000/QALY [51].

In a U.K. study from a payer perspective using a Markov model over a 10-year horizon and utility values based on the CHAMPION trial, CardioMEMS resulted in an increase of £10,916 in costs and 0.57 in QALYs [47]. This study included the costs of the implantation procedure, the device and related complications, HF-related hospitalizations, and standard care costs. The resulting ICER was estimated at £19,274/QALY, which is below the U.K. WTP threshold of £20,000-£30,000/QALY, implying acceptable cost-effectiveness of CardioMEMS [52]. When the same model was applied to four European countries (Germany, the Netherlands, Italy, and Belgium) with country-specific costs, CardioMEMS remained cost-effective [47]. In 2021, the National Institute for Health and Care Excellence published a statement of support for the use of CardioMEMS in the U.K. as evidence on safety and efficacy was deemed adequate [53]. However, actual data to perform cost-effectiveness models and health technology assessments for Europe are lacking.

A cost-effectiveness analysis of CardioMEMS based on a societal perspective, including both healthcare and non-healthcare costs, such as informal care costs in a European setting, is lacking. As discussed, the MONITOR HF trial will provide information on costs, mortality and efficacy, derived from Dutch data, which can be used to perform health technology assessments and cost-effectiveness models for other European countries, such as Belgium, the U.K. and Germany [24].

5. Conclusion

Clinical evidence from randomized trials for the CardioMEMS HF System is convincing as the device has been proven safe, durable and has been associated with a reduction of heart failure related hospitalizations. Thus far, evidence for hemodynamic monitoring of PA pressures with the CardioMEMS system in European setting has been restricted to observational studies. There is an unmet need for data from well-designed European randomized clinical trials with a contemporary standard HF care comparison group for generalizability. Remote care is especially important in light of the COVID-19 pandemic. The Dutch MONITOR HF trial is the most important upcoming trial that will provide the latest evidence on whether CardioMEMS-guided HF care is safe, efficacious, and cost-effective compared to usual HF care.

These data are likely to be of great importance for decision-making on implementation and reimbursement of CardioMEMS PA pressure monitoring in daily clinical practice.

6. Expert opinion: future perspectives for European HF care

In this comprehensive review article, we have discussed the current and upcoming evidence for CardioMEMS PA-guided remote hemodynamic monitoring in Europe. The first results with regard to safety and durability are convincing and in line with studies performed in the U.S.A [23,25,26,28–31,34]. Efficacy with regard to important clinical outcomes, such as reduction of the risk for HF hospitalization, also seems very promising, but evidence is still restricted to observational studies with important limitations [23,34]. The observational non-randomized European studies lacked a comparator arm as patients were their own historical control, which may have introduced various forms of bias.

Results from the Dutch randomized MONITOR HF trial are expected soon. This trial will provide the much-needed evidence that is generalizable to other parts of Europe as well

[24]. The MONITOR HF trial is relevant as its design and the Dutch healthcare structure with dedicated HF outpatient clinics and nurses are representative for a large part of Europe [24]. HF care in the Netherlands has been shown to be of high quality, also in comparison to the U.S [45,54]. Importantly, this trial may provide novel insights into CardioMEMS PA pressure guided management against a background of contemporary HF therapy, including ARNi and SGLT2-inhibitors. Results from the planned cost-effectiveness analyses will be elucidating from an economical point of view [24]. The MONITOR HF trial will be important for the level of recommendation in the European Society of Cardiology Guidelines for Heart Failure [10].

Based upon the overview in this comprehensive review article and upcoming evidence from a randomized clinical trial, we expect integration of the CardioMEMS^{TM} HF system in daily management of European HF patients in due time. However, this largely depends on whether the results of this trial will be in line with U.S. trials considering the significant differences in structure of HF care. Since the advent of the COVID-19 pandemic and its disruptive effects on healthcare systems, even in well-developed countries, the need for remote care has become even more obvious. Chronic heart failure will remain a major health problem, and therefore, policy makers should anticipate by searching for ways to implement proven effective forms of remote monitoring for chronic HF in daily clinical practice to keep patients out of the hospital.

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