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Remote haemodynamic-guided heart failure management in France: Results from the CardioMEMS HF System Post-Market Study (COAST) French cohort

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Keywords:

CardioMEMS™ HF System; Clinical trial; Haemodynamic remote monitoring; Heart failure; Pulmonary artery pressure.

X post (Tweet): Demonstration of the safety and the efficacy of the Cardio MEMSTMHF System in the 103 French patients of the COAST study.

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Abstract

Background:

Previous studies have demonstrated the benefit of a haemodynamic-guided management strategy with the CardioMEMS™ HF System. No data from French patients have been published.

Aims:

To analyse the feasibility, safety and clinical benefit of the CardioMEMS™ HF System in 103 French patients included in the CardioMEMS HF System Post-Market Study (COAST).

Methods:

Prospective open-label cohort of New York Heart Association class III patients with at least one heart failure hospitalization in the 12 months before enrolment, regardless of left ventricular ejection fraction. The primary safety endpoints assessed the freedom from device/system-related complications and from pressure sensor failure at 2 years after implantation. The primary efficacy endpoint was evaluated comparing the rate of heart failure hospitalization during the year before and the year after implantation.

Results:

At 2 years, there were no device/system-related complications or pressure sensor failures ($P < 0.0001$). There were 179 heart failure hospitalizations in the year before implantation compared with 79 in the year after implantation (risk reduction 50.3%; rate ratio 0.50, 95% confidence interval 0.38-0.66; $P < 0.0001$). During the 2 years of follow-up, pulmonary artery pressures were lowered significantly (mean pulmonary artery pressure -3.7 ± 6.3 mmHg; $P < 0.0001$), with a significant improvement in functional class and quality of life.

Conclusions:

In the French cohort of the COAST study, we have demonstrated that the CardioMEMS™ HF System is a reliable device, with no device/system-related complications or pressure sensor failures. Patients in this open-label cohort had a significant reduction in pulmonary artery pressures, with an improvement in New York Heart Association classification and quality of life, and a 50% reduction in the heart failure hospitalization rate in the year following implantation compared with the previous year.

1. Abbreviations

CI confidence interval COVID-19 coronavirus disease 2019 DSRC device/system-related complications EQ-5D-5L EuroQol 5-dimension 5-level questionnaire HF heart failure HFH heart failure hospitalization HFpEF heart failure with preserved ejection fraction HFrEF heart failure with reduced ejection fraction ICD implantable cardioverter-defibrillator LVEF left ventricular ejection fraction NYHA New York Heart Association PA pulmonary artery PSF pressure sensor failure RR rate ratio

2. Background

In recent years, and particularly after the worldwide epidemic crisis, medical management of patients is in a transitional phase. In France, as in other countries, the number of caregivers has declined dramatically, and health management offers have been reduced. Remote monitoring and connected tools represent possible solutions to these problems, which could help clinicians to reduce the impact of the diseases. One of the most significant risks after hospitalization for heart failure (HF) is recurrent hospital readmission, mainly for a new HF episode. Studies have shown that 25–50% of patients with HF are readmitted within 30 days of discharge, and the risk of readmission is highest in the first few weeks after discharge [1–4]. The annual mortality rate is approximately 15–35% after the first admission for HF, but increases to almost 50% after the third readmission [5]. Therefore, it is important to reduce the readmission rate of HF, and to adjust the patient's treatments before hospitalization. Remote monitoring devices offer this solution, transmitting the required information from the patient's home directly to the clinician's site. Whereas most randomized controlled trials with non-invasive remote monitoring devices yielded inconclusive results [6, 7], results of meta-analyses found non-invasive remote monitoring to be of significant benefit [8]. However, several studies with implantable remote monitoring devices (such as the Cardio MEMSTMHF System; Abbott Laboratories, Chicago, IL, USA) have demonstrated the effectiveness of such devices [9, 10].

Since the pivotal CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients) trial [9], two other randomized controlled studies have confirmed the efficacy of Cardio MEMSTM in reducing HF hospitalization (HFH) [10,11]. In the Haemodynamic-Guided Management of Heart Failure (GUIDE-HF) study, the reduction in the primary objective (HFH and death) was only significant if the period before coronavirus disease 2019 (COVID-19) was analysed (hazard ratio 0.81, 95% confidence interval [CI] 0.66–1.00; $P = 0.049$), with a non-significant reduction if the entire follow-up period was analysed (hazard ratio 0.88, 95% CI 0.74–1.05; $P = 0.16$) [11]. However, the results of this trial must be interpreted with caution. The analysis before and after the COVID-19 pandemic was prespecified and, unlike in the Remote

Haemodynamic Monitoring of Pulmonary Artery Pressures in Patients with Chronic Heart Failure (MONITOR-HF) study [10], and like the CHAMPION study, GUIDE-HF was a single-blind study, in which all the patients received a Cardio MEMSTMPA Sensor. After randomization, patients did not know whether Cardio MEMSTM data were used for their follow-up. In addition, real-world registries have shown lower HFH rates after the implantation of the Cardio MEMSTMPA Sensor compared with a period (from 6 months to 1 year) before the implantation [12–15].

In Europe, Australia and, particularly, France, the Cardio MEMSHF System Post-Market Study (COAST) was implemented to examine the feasibility, safety and clinical benefit of a haemodynamic-guided management strategy for patients with HF [16]. The aim of this study was to analyse the safety and clinical efficacy of the Cardio MEMSTMHF System in the 103 French patients included in the COAST study

.3. Methods

The COAST study was designed as a prospective open-label cohort with the aim of examining the safety and feasibility of remote management of symptomatic patients with HF using pulmonary artery (PA) pressures frequently assessed with the Cardio MEMSTMHF System in varying healthcare systems outside the USA. Details concerning the rationale and the design of this study, as well as the results from one of its subgroups, have been reported previously [16, 17]. The study protocol was approved by all responsible ethics committees and was conducted in accordance with the principles of the Declaration of Helsinki. The trial was registered at ClinicalTrials.gov (Identifier: NCT02954341). All participants provided written informed consent before any study-related procedure. COAST enrolled patients with persistent New York Heart Association (NYHA) class III symptoms and at least one HFH within the 12 months before enrolment, regardless of left ventricular ejection fraction (LVEF). Patients were considered to have a preserved LVEF (HFpEF) if their LVEF was $\geq 40\%$ and to have a reduced LVEF (HFrEF) if their LVEF was $< 40\%$. Patients with HFrEF were required to be treated with a beta-blocker for 3 months and an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker or angiotensin receptor blocker/neprilysin inhibitor for 1 month, unless the investigator deemed the patient to be intolerant to such therapy. The study inclusion and exclusion criteria are listed in Appendix A.

The COAST study enrolled a total of 321 subjects at 38 sites in six countries; specifically, 103 patients constituted the French cohort of the trial, and were included between May 2018 and July 2020. Following enrolment and implantation, all 103 French patients were instructed in how to operate the Cardio MEMSTM Patient Electronics System in order to obtain daily pressure measurements from the implanted sensor. On the institution side, specific guide-lines regarding euvoelaemic ranges and general strategies to achieve haemodynamic stability were provided to the investigators, as out-lined in the study protocol (Appendix B). The rationale behind these thresholds indicates volume shifts as a contributing factor to PA pressure

variations overtime, with a fluid overload or reduction resulting in a PA pressure increase or decrease outside the patient's baseline, respectively.

3.1. Endpoints

All 103 enrolled subjects were successfully implanted with the Cardio MEMSTMPA Sensor and, thus, all subjects were included in both the primary safety and efficacy evaluations. The primary safety endpoints assess the freedom from device/system-related complications (DSRCs) and freedom from pressure sensor failure (PSF) at 2 years after implantation (details on DSRC and PSF definitions are provided in Appendix A) compared with a prespecified performance goal of 80% and 90%, respectively. The primary clinical impact of haemodynamic monitoring was evaluated by comparing the rate of HFH during the 12-month period before sensor implantation with the 12 months after implantation (primary efficacy endpoint).

To evaluate patients' functional class and quality of life, NYHA functional class assessments were performed, and the EuroQol 5-dimension 5-level questionnaire (EQ-5D-5L) was administered at all study visits. Assessments for both functional class and quality of life were performed at baseline, 6-month, 12-month and 24-month follow-up visits. PA pressure change over time was evaluated using absolute change and with the area under the curve methodology, which quantifies the duration of time that a patient spends at a pressure lower (or higher) than their baseline PA pressure. In addition, pressure changes were also evaluated in subgroups stratified by LVEF.

3.2. Statistical analyses

Data are summarized using univariate statistics (e.g. N, mean, standard deviation, median, minimum and maximum) or frequency (e.g., N, %) as appropriate for continuous or categorical variables, respectively. Enrolment was defined as having a successful sensor implantation. The primary safety endpoints were analysed for 24 months after enrolment, whereas the primary time-point for efficacy analysis was 12 months after enrolment.

The primary safety analysis was based on the following objective performance criteria: (1) the lower limit of the one-sided 97.5% confidence limit interval on the freedom from DSRC rate at 24 months is $> 80\%$; and (2) the lower limit of the one-sided 97.5% confidence limit on the freedom from PSF rate at 24 months is $> 90\%$. The study was deemed to have provided positive safety results if both of the primary safety endpoints were statistically significant (i.e. $P < 0.025$).

The primary efficacy analysis compared the annualized HFH rate at 1 year versus the HFH rate in the year before enrolment using a one-sample one-sided Poisson rate test. The HFH rate in the year before enrolment was defined as all HFHs specified in the hospital records of the patients. The primary clinical impact endpoint was considered met if the one-sided upper

97.5% confidence limit for the rate variable reported after enrolment was less than the rate in the year before enrolment.

Additional analyses included PA pressure changes (systolic, mean and diastolic) for the full cohort and for subjects with HFpEF and HFrEF, home reading daily compliance (defined as the number of days with a reading divided by the total number of days of patient follow-up spent outside the hospital) and weekly compliance (defined as the number of weeks with at least one daily reading divided by the total weeks of patient follow-up spent outside the hospital). Comparisons between quantitative variables were performed by a paired or an unpaired Student's t test. Events were reported by investigators responsible for the patients' clinical care.

3. Results

As part of COAST, 103 French patients were successfully implanted between May 2018 and July 2020 at 12 centres in France. Baseline characteristics are reported in Table 1. The cohort's mean age was 67.2 ± 11.5 years, with a majority of male patients (77.7%) and more than two-thirds with HFrEF (70.9%). Sixty-nine subjects out of 103 (67.0%) had chronic kidney disease in stage 3 or 4. Patients reported an average EQ-5D-5L visual analogue scale score of 54.1 ± 20.5 points. Pharmacological therapy mainly comprised loop diuretics (taken by 94.2% of patients), beta-blockers (80.6% of patients) and angiotensin-converting enzyme inhibitors (70.9% of patients). Demographic data for HFrEF and HFpEF groups are reported in Table 1. Seven patients with HF with moderately depressed LVEF were integrated into the HFpEF subgroup. Fig. 1. Study flow and patient disposition. FU: follow-up; M: month.

4.1. Primary safety endpoint and safety assessments

Visits at 6, 12 and 24 months were completed by 92 (89%), 76 (74%), and 61 (59%) patients, respectively (Fig. 1). The primary safety endpoints of freedom from DSRC and freedom from PSF at 2 years were both 100% (95% CI 96.5–100%), with the lower limit of their confidence interval (96.5%) exceeding the prespecified performance goals of 80% and 90%, respectively ($P < 0.0001$). At 2 years after implantation, 37 patients out of the 103 implanted (35.9%) had died, mainly as a result of cardiac causes (26 patients, 25.2%) and, more specifically, HF (19 patients, 18.4%). Kaplan-Meier analysis indicated an overall 2-year survival of 63.1% (95% CI 52.8–71.8%; Fig. 2). None of the deaths was related to the Cardio MEMSTMHF System or its implantation procedure, according to the reporting physician.

4.2. Primary efficacy endpoint and HFH rates

The rate of HFH during the first year after implantation was significantly lower compared with the year before sensor implantation. There were 179 HFHs (1.59 events/patient-years) in the year before implantation compared with 79 HFHs (0.79 events/patient-years) in the first year after implantation, resulting in a significant risk reduction of 50.3% (rate ratio [RR] 0.50, 95% CI 0.38–0.66; $P < 0.0001$; Fig. 3). Similar results were found in patients with either HFrEF (1.39 vs. 0.76 events/patient-years; RR 0.55, 95% CI 0.40–0.75; $P = 0.0002$) or HFpEF (2.09 vs. 0.87 events/patient-years; RR 0.42, 95% CI 0.24–0.71; $P = 0.0013$; Table A.1). In addition, a dedicated analysis comparing HFH and deaths within the same timeframe confirmed that the death rate did not affect the primary endpoint results (RR 0.65, 95% CI 0.50–0.85; $P = 0.0016$; Table A.2).

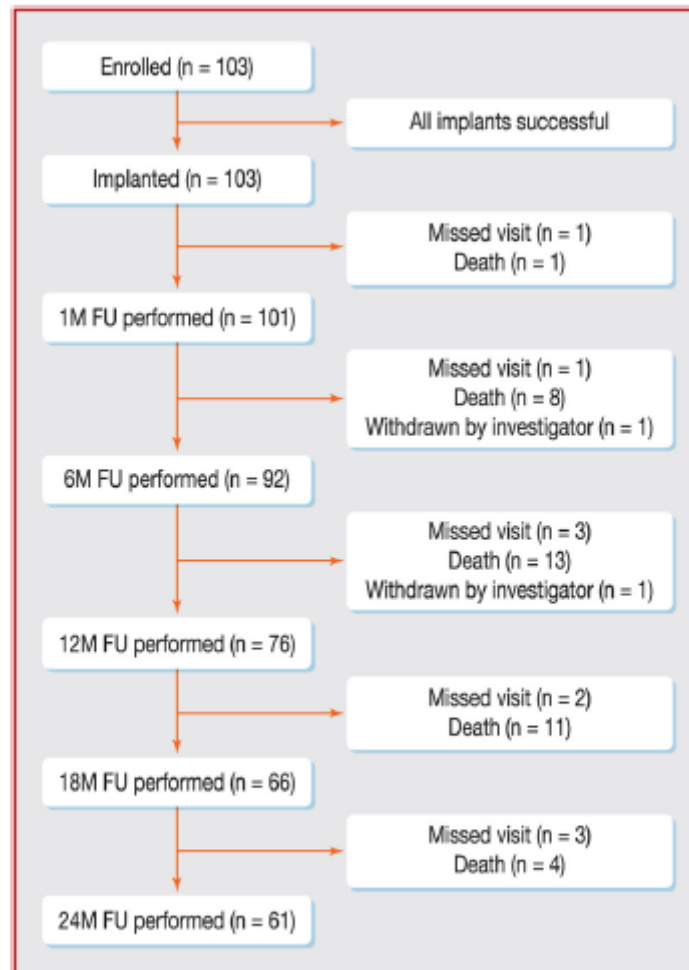


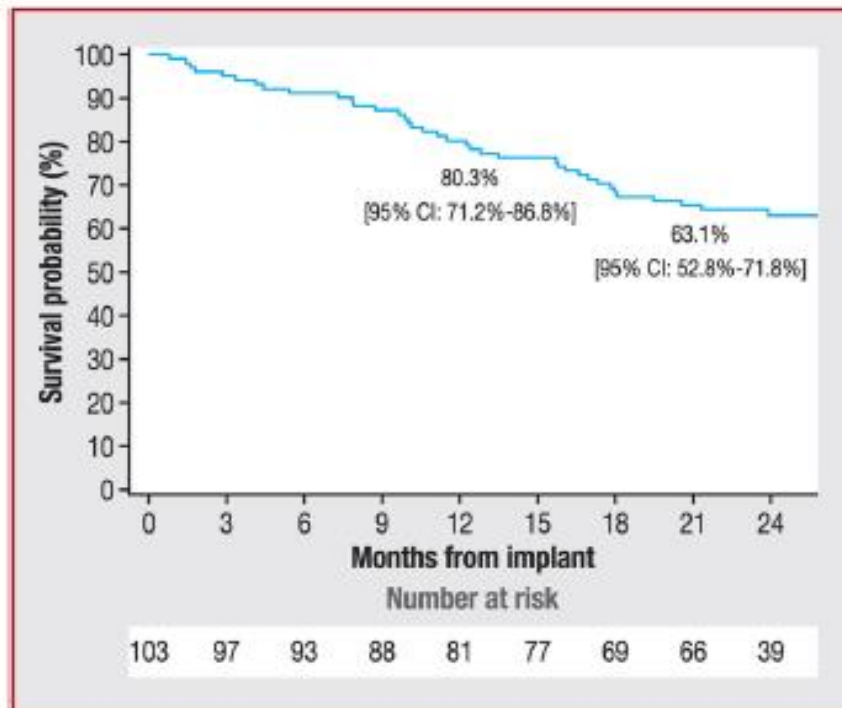
Fig. 1. Study flow and patient disposition. FU: follow-up; M: month.

Table 1

Demographics and baseline characteristics in the whole population and in subgroups according to left ventricular ejection fraction.

Characteristics	Whole population	HFpEF (EF ≥ 40%)	HFrEF (EF < 40%)
	(n= 103)	(n= 30)	(n= 73)
Age (years)	67.2 ± 11.5 69.0 (22.0–87.0)	68.7 ± 15.7 71.5 (22.0–86.0)	66.6 ± 9.4 68.0 (46.0–87.0)
Male sex	80 (77.7)	21 (70.0)	59 (80.8)
Ischaemic cardiomyopathy	56 (54.4)	14 (46.7)	42 (57.5)
HFpEF	30 (29.1)	30 (100)	0 (0)
BMI (kg/m ²)	27.5 ± 4.9 27.0 (16.3–40.6)	28.3 ± 5.3 28.1 (18.6–40.6)	27.2 ± 4.7 26.5 (16.3–37.8)
Hypertension	51 (49.5)	19 (63.3)	32 (43.8)
Diabetes mellitus	47 (45.6)	15 (50.0)	32 (43.8)
Chronic obstructive pulmonary disease	20 (19.4)	9 (30.0)	11 (15.1)
GFR (mL/min/1.73 m ²)	52.7 ± 22.4 46.6 (2.5–139.4)	56.0 ± 27.7 43.0 (26.1–139.4)	51.4 ± 19.8 48.3 (2.5–106.2)
Chronic kidney disease			
Stage 3 (GFR 30–59 mL/min/1.73 m ²)	58 (56.3)	15 (50.0)	43 (58.9)
Stage 4 (GFR 15–29 mL/min/1.73 m ²)	11 (10.7)	3 (10.0)	8 (11.0)
Heart failure medications			
Loop diuretic	97 (94.2)	29 (96.7)	68 (93.2)
ACEi/ARB/ARNi	73 (70.9)	16 (53.3)	57 (78.1)
Beta-blocker	83 (80.6)	22 (73.3)	61 (83.6)
Beta-blocker + ACEi/ARB/ARNi	69 (67.0)	15 (50.0)	54 (74.0)
Mineralocorticoid receptor antagonist	53 (51.5)	14 (46.7)	39 (53.4)
ICD/CRT-D	62 (60.2)	5 (16.7)	57 (78.1)
Pulmonary artery pressures			
Systolic pressure (mmHg)	51.35 ± 15.37	50.91 ± 16.49	51.53 ± 15.00
Mean pressure (mmHg)	36.24 ± 10.88	35.16 ± 10.72	36.69 ± 10.99
Diastolic pressure (mmHg)	26.15 ± 8.47	24.69 ± 8.28	26.75 ± 8.54

Data are expressed as mean ± standard deviation, median (minimum–maximum) or number (%). ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNi: angiotensin receptor blocker/neprilysin inhibitor; BMI: body mass index; CRT-D: cardiac resynchronization therapy-defibrillator; EF: ejection fraction; GFR: glomerular filtration rate; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; ICD: implantable cardioverter-defibrillator.

**Fig. 2.** Overall survival 2 years after implantation, CI: confidence interval.

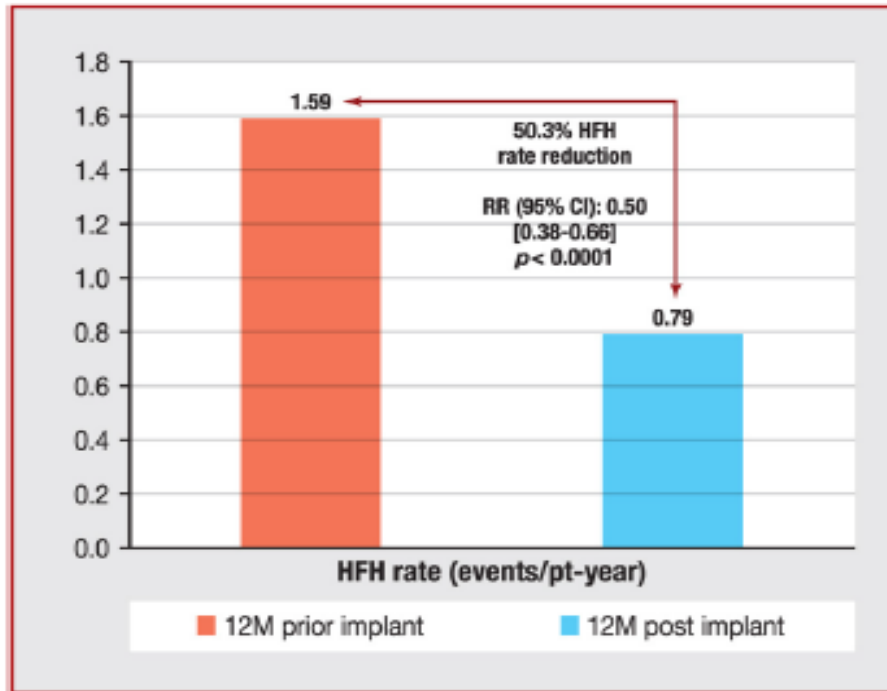


Fig. 3. Heart failure hospitalization reduction. CI: confidence interval; HFH: heart failure hospitalization; M: month; pt-yr: patient-year; RR: rate ratio.

The HFH reduction was also observed in a longer-term follow up of 2 years: 0.46 events/patient-years; RR 0.33, 95% CI 0.21–0.50; $P = 0.12$ (Table A.3).

4.3. Pulmonary pressure changes

The average initial systolic, mean and diastolic pressures were 51.3 ± 15.4 , 36.2 ± 10.9 and 26.1 ± 8.5 mmHg, respectively. At 6 months, the pressures were significantly lower compared with baseline, and these reductions were maintained throughout the 2-year follow-up period. After 2 years of haemodynamic-guided care, systolic PA pressure was reduced, with an average pressure change versus baseline of -4.3 ± 8.43 mmHg ($P < 0.0001$); similar reductions were observed for mean PA pressure (-3.7 ± 6.4 ; $P < 0.0001$) and diastolic PA pressure (-3.2 ± 5.3 ; $P < 0.0001$) as shown in Table 2.

In addition, the area under the curve (mmHg-day) reduction at 2 years was significant for all three PA pressure variables at each follow-up visit (systolic -2707.7 ± 5065.2 mmHg-days; mean -2324.2 ± 3849.5 mmHg-days; diastolic -2069.6 ± 3267.4 mmHg-days; $P < 0.0001$; Table 2 and Fig. 4). The analysis of PA pressure changes in the subgroups of patients with HFpEF ($n = 30$) or HFrEF ($n = 73$) showed a benefit for both groups, but patients with HFrEF had the largest reduction. In the HFrEF group, the PA changes were statistically significant at all timepoints, whereas the same result was not found in the HFpEF group (Table A.4 and

Table A.5). The diastolic PA area under the curve plots for the HFrEF and HFpEF groups are reported in Fig. A.1 and Fig. A.2.

Table 2
Pulmonary arterial pressure changes and area under the curve.

	Baseline (n= 103)	6 months (n= 90)	12 months (n= 76)	24 months (n= 40)
Systolic PA pressure	51.35 ± 15.37	47.54 ± 15.84	43.75 ± 15.37	46.46 ± 13.18
Average pressure change versus baseline (mmHg)	-	-2.08 ± 7.13 (P= 0.0037)	-3.35 ± 7.71 (P<0.0001)	-4.33 ± 8.43 (P<0.0001)
AUC change versus baseline (mmHg-days)	-	-346.54 ± 1261.45 (P= 0.0063)	-1145.08 ± 2600.20 (P<0.0001)	-2707.68 ± 5065.17 (P<0.0001)
Mean PA pressure	36.24 ± 10.88	32.58 ± 11.43	30.15 ± 10.98	31.65 ± 9.69
Average pressure change versus baseline (mmHg)	-	-1.82 ± 5.31 (P= 0.0007)	-2.88 ± 5.74 (P<0.0001)	-3.67 ± 6.35 (P<0.0001)
AUC change versus baseline (mmHg-days)	-	-310.07 ± 939.48 (P= 0.0011)	-994.28 ± 1913.40 (P<0.0001)	-2324.16 ± 3849.46 (P<0.0001)
Diastolic PA pressure	26.15 ± 8.47	22.62 ± 8.70	21.23 ± 8.60	21.78 ± 8.05
Average pressure change versus baseline (mmHg)	-	-1.66 ± 4.34 (P= 0.0002)	-2.59 ± 4.78 (P<0.0001)	-3.24 ± 5.33 (P<0.0001)
AUC change versus baseline (mmHg-days)	-	-290.00 ± 765.56 (P= 0.0002)	-901.21 ± 1588.67 (P<0.0001)	2069.60 ± 3267.40 (P<0.0001)

Data are expressed as mean ± standard deviation (P value). AUC: area under the curve. PA: pulmonary arterial.

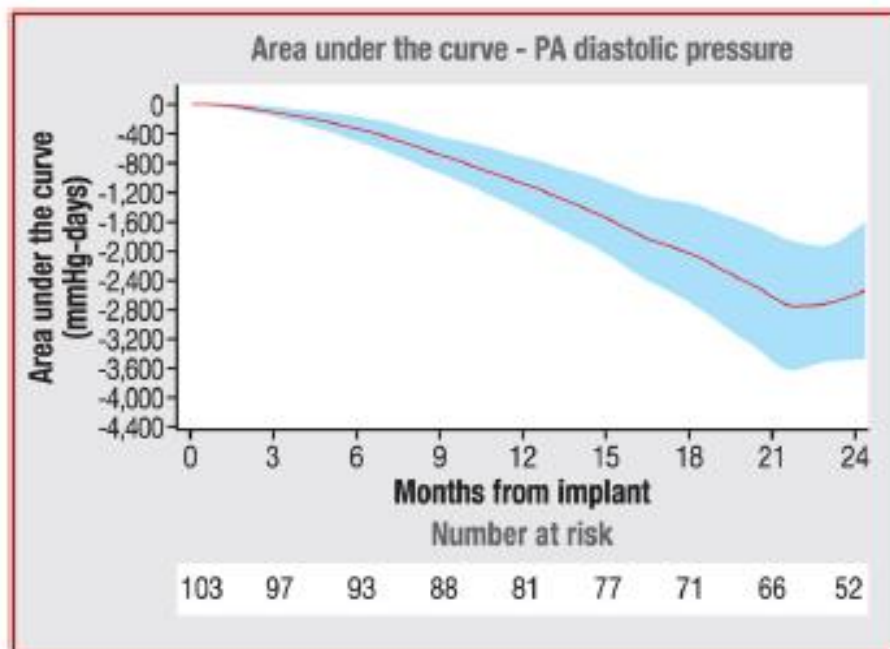


Fig. 4. Area under the curve for diastolic pulmonary arterial pressure, PA: pulmonary arterial.

4.4. Functional class, quality of life and compliance

Functional class improved during follow-up, with 40.8% of subjects improving from NYHA class III to NYHA class I (22.8%) and II (50.9%) after 24 months (Table 3). The patient's quality of life, measured with the EQ-5D-5L, increased steadily at each follow-up visit. A paired analysis of the mean visual analogue scale component of the assessment showed a highly significant improvement when compared with baseline at both 12 months (63.3 ± 191.1 vs. 54.9 ± 21.6 ; $P = 0.0036$) and 24 months (66.1 ± 18.8 vs. 55.3 ± 20.6 ; $P = 0.0005$) (Table 4). Patient reading compliance was high for both daily and weekly measurements: $82.3 \pm$

21.9%(95% CI 78.0–86.5%) and $93.0 \pm 15.3\%$ (95% CI 90.1–96.0%), respectively (Fig. 5). Improvements in NYHA functional class and quality of life, and compliance in patients with HFpEF and with HFrfEF are presented in Tables A.6–A.12.

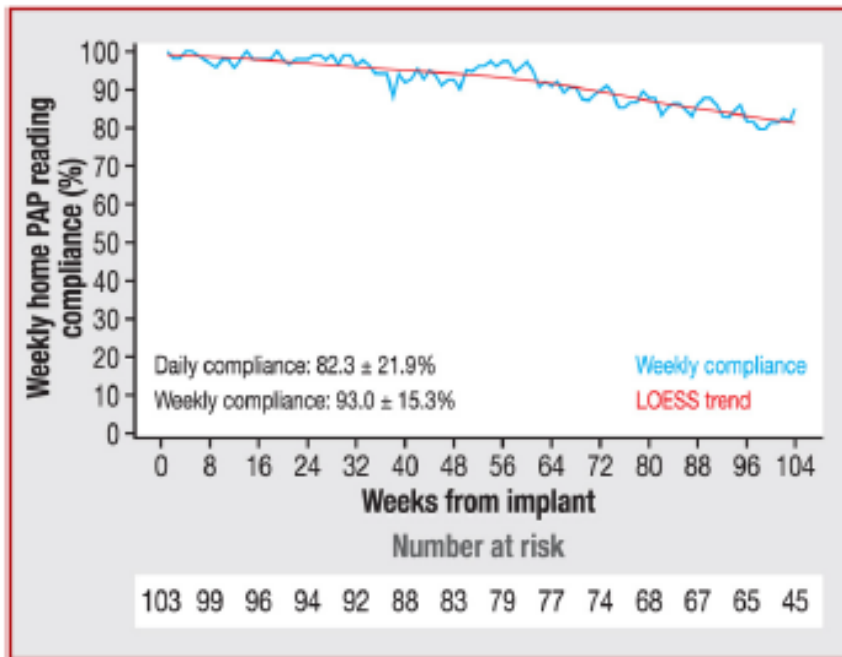


Fig. 5. Weekly home pulmonary arterial pressure reading compliance. LOESS: locally estimated scatterplot smoothing; PAP: pulmonary arterial pressure.

4.5. Medication changes

During the course of the study, 1840 medication changes were made by the treating clinicians, with most changes in the diuretics category (1484 changes, including 742 dosage increases and 681 dosage decreases). Adjustments in neurohormonal antagonists were also observed, with 107 mineralocorticoid receptor antagonist changes (57 dosage increases, 50 dosage decreases), 105 angiotensin receptor blocker/neprilysin inhibitor changes (61 dosage increases, 44 decreases), 68 angiotensin-converting enzyme inhibitor/angiotensin receptor blocker changes (35 dosage increases, 31 decreases) and 75 beta-blockers changes (34 dosage increases, 41 decreases) reported as of 24 months of follow-up.

4. Discussion

The data from the French cohort of the COAST study brings new evidence to the scientific corpus of the Cardio MEMSTMHF System, confirming that device implantation is a safe procedure, and supporting its reliability, as it operated without any reported failure. From a

clinical point of view, these results are similar to those of previous randomized and single-arm studies, showing a significantly lower rate of HFH (50.3%) in the year following Cardio MEMSTMPA Sensor implantation compared with the rate in the previous year, associated with a significant decrease in PA pressures, despite the severity of this study population. Finally, as in previous studies, the rate of daily and weekly data transmission of PA measurements, i.e. compliance rate, remained high at 2 years. In addition, the study showed significant improvement in the NYHA functional classification and quality of life, as estimated by the EQ-5D-5L.

5.1. Safety

There were no unsuccessful implantation attempts, and no DSRCs or PSFs were reported during the 24 months of the study. Previous Cardio MEMSTM studies and registries found similar results, with very few DSRCs or PSFs (Table 5).

5.2. Pulmonary pressures and HFHs

Although a significant difference cannot be demonstrated, French patients in the COAST study were the sickest patients who were included in previous studies with the same device. These patients had higher PA pressures (Table 5) at baseline, with an 18-month death rate close to 32%. In the Optimization of the Ambulatory Monitoring for Patients With Heart Failure by Tele-Cardiology (OSICAT) study, also conducted in France, the death rate at 18 months was 13.4% [7]. Despite the severity of our study population, the HFH rate after implantation of the Cardio MEMSTMHF system was significantly lower than in the year before implantation. Moreover, the HFH rate after implantation is similar to those reported in previous Cardio MEMSTMHF system studies and registries (Table 5). As also demonstrated in these trials, there was a significant reduction in pulmonary pressures, possibly related to changes in the medical treatment guided by the device readings transmitted to the clinicians. However, the precise link between the evolution of pulmonary pressures and changes in medications has not been demonstrated, and specific analyses must be carried out to confirm it.

5.3. NYHA classification, quality of life and compliance

Although the COAST study was an open-label study without a control group, a longitudinal improvement in both quality of life and NYHA classification was observed. During the 24 months of the follow-up period, the number of NYHA class III patients decreased progressively, with very few patients in class IV, despite the severity of the population, whereas the “natural” evolution of severe HF, which tends to worsen inexorably despite treatment, would have increased the number of NYHA class III or IV patients after 2 years. However, a competitive risk cannot be excluded.

The improvement in quality of life, as measured by the visual analogue scale score, demonstrated statistical significance at each follow-up timepoint compared with baseline, regardless of the low initial score. This result was not observed previously in the UK cohort of the same study (COAST UK), which presented less imposing HF symptoms and a higher baseline visual analogue scale score.

However, as the COAST study is an open study without a control group, we cannot exclude that the improvement in patients' NYHA functional class and quality of life was influenced by the global management of the patients in addition to the direct effects of the Cardio MEMSTMHF system.

In the US CardioMEMS Post-Approval study, daily median compliance decreased from 97% in the first month to 85% at 12 months, but weekly median compliance remained at 100% [15]. Similarly, in the retrospective study of the first 2000 patients in the USA implanted with Cardio MEMSTMHF system after the CHAM-PION trial, the median use was 98.4% at 6 months [15]. In the COAST UK study [17], the daily compliance was high ($85.9 \pm 19.3\%$) with a weekly compliance of $94.5 \pm 14.2\%$, which is similar to the compliance reported for the French cohort (daily and weekly measurements: $82.3 \pm 21.9\%$ and $93.0 \pm 15.3\%$, respectively). This outmatches the results obtained with non-invasive remote monitoring, such as the OSICAT trial, where the adherence to daily self-measurement of body weight was $59.9 \pm 35.5\%$ (median 74.6%) and in the Telemedical Interventional Management in HF-2 (TIM-HF2) trial, where 97% of the patients had a daily compliance of at least 70% [6]. Finally, in the Better Effectiveness After Transition-Heart Failure (BEAT-HF) trial, 55.4% of the patients had remote monitoring adherence on $> 50\%$ of days during the first month [18].

5.4. Study limitations

The major limitation of the present study is related to the fact that the study is an open-label single-arm unblinded cohort without a control group. Also, the study population represents a group of patients with severe HF symptoms followed by HF specialists in selected investigational sites, which may have decreased the risk of DSRC or implantation failure and/or improved the management of HF. Thus, these results may not be able to be translated to all patients with HF, who are mainly managed by general practitioners. Medication types and titration changes were collected during the study, but the normalized computation dosage analysis, necessary because of the depth of information, was not performed for this manuscript, which mainly focuses on the principal study end-points and patient-reported outcomes. Additional work is required to analyse the relationships between drug type and titration and HF rates, symptoms and pulmonary pressure changes.

Table 4
EuroQol 5-dimension 5-level questionnaire visual analogue scale score paired analysis.

	Baseline	12 months	24 months
All data	54.1 ± 20.5 (n = 101)	62.8 ± 19.4 (n = 68)	65.8 ± 18.7 (n = 55)
12-month paired analysis versus baseline	54.9 ± 21.6 (n = 67)	63.3 ± 19.1 (n = 67) (P = 0.0036)	–
24-month paired analysis versus baseline	55.3 ± 20.6 (n = 54)	–	66.1 ± 18.8 (n = 54) (P = 0.0005)
12- and 24-month paired analyses versus baseline	55.8 ± 20.8 (n = 46)	65.7 ± 18.9 (n = 46) (P = 0.0067)	66.0 ± 20.0 (n = 46) (P = 0.0023)

Data are expressed as mean ± standard deviation (n) (P value).

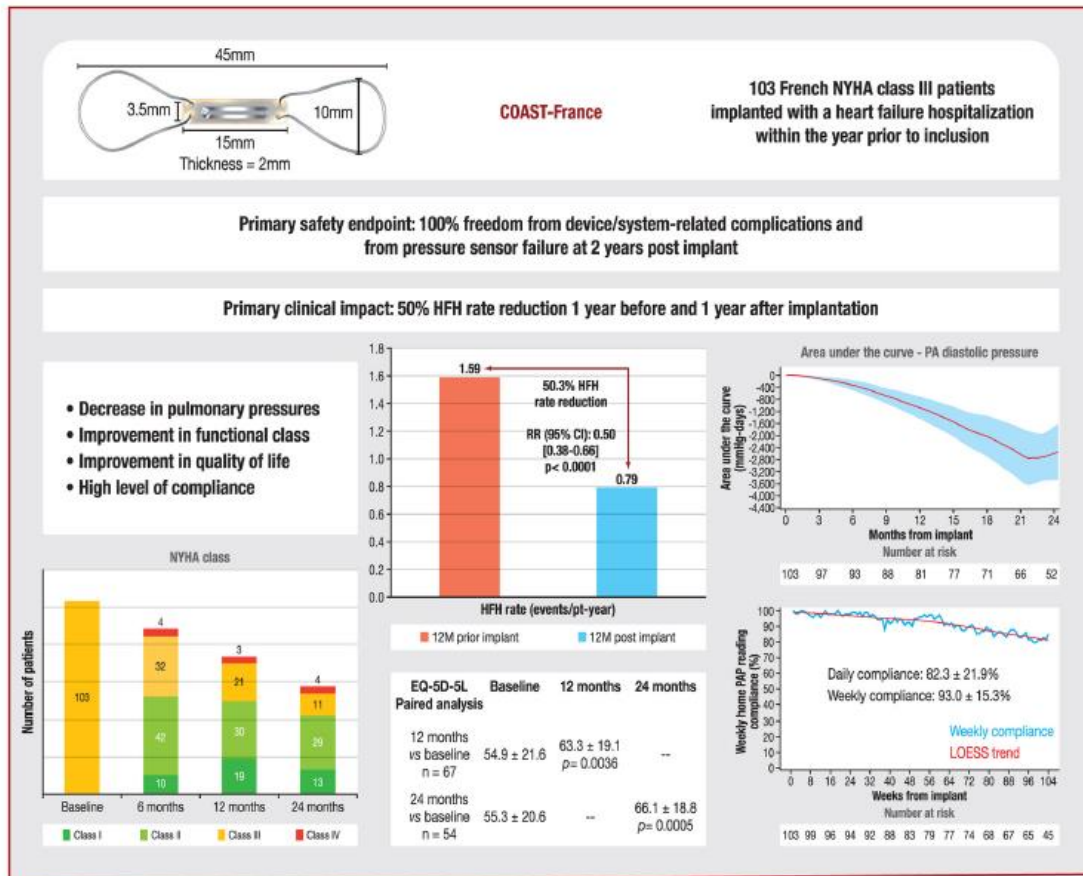
Table 5
Mean pulmonary arterial pressure, primary endpoints and safety endpoints in the different CardioMEMS™ HF System studies and registries.

Study	n	Type of study	Mean PAP S/D/M	Primary endpoint	HR (95% CI) for primary endpoint	Safety endpoints
CHAMPION [9]	550	Prospective; simple blind	44.3/18.6/28.9	HFH (6 months)	0.72 (0.60–0.85); P = 0.002	USI: 0%; DSRC: 1.4%; PSF: 0.1%
GUIDE-HF [11]	1000	Prospective; simple blind	45/22/31	Mortality + HFH (1 year)	0.88 (0.74–1.15); P = 0.16	USI: 0.02%; DSRC: 1%; PSF: 1%
MONITOR-HF [10]	348	Prospective; open	NR/NR/33	Quality of life (1 year)	Significant improvement	USI: 2.3%; DSRC: 2.3%; PSF: 1.2%
				Mortality + HFH (1 year) (secondary objective)	0.63 (0.44–0.90); P = 0.01	
MEDICARE [12]	1114	Retrospective	NR	HFH 6 months before versus after implant	0.55 (0.49–0.61); P < 0.001	USI: NA; DSRC: NR; PSF: NR
MEDICARE [13]	1087/1087	Retrospective; "matched"	NR	Mortality + HFH (1 year)	0.73 (0.64–0.84); P < 0.01	USI: NA; DSRC: NR; PSF: NR
USA Post-Approval [15]	1200	Prospective; open-label; registry	48/20/31	HFH 1 year before and after implant	0.43 (0.39–0.470); P < 0.0001	USI: 0.01%; DSRC: 0.4%; PSF: 0.1%
MEMS-HF [14]	234	Prospective; open-label; registry	47/19/30	HFH 1 year before and after implant	0.38 (0.31–0.48); P < 0.0001	USI: 0.005%; DSRC: 1.7%; PSF: 0.4%
COAST UK [17]	100	Prospective; open-label; registry	49.5/23.3/33.7	HFH 1 year before and after implant	0.18 (0.12–0.28); P < 0.0001	USI: 0.03; DSRC: 0%; PSF: 0.01%
COAST France	103	Prospective; open-label; registry	51/26/36	HFH 1 year before and after implant	0.50 (0.38–0.66); P < 0.0001	USI: 0%; DSRC: 0%; PSF: 0%

CHAMPION: CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients; CI: confidence interval; COAST: CardioMEMS HF System Post-Market Study; D: diastolic; DSRC: device/system-related complication; GUIDE-HF: Haemodynamic-Guided Management of Heart Failure; HFH: heart failure hospitalization; HR: hazard ratio; M: mean; MEMS-HF: CardioMEMS European Monitoring Study for Heart Failure; MONITOR-HF: Remote Haemodynamic Monitoring of Pulmonary Artery Pressures in Patients with Chronic Heart Failure; NA: not applicable; NR: not reported; PAP: pulmonary arterial pressure; PSF: pressure system failure; S: systolic; USI: unsuccessful sensor implantation.

5. Conclusions

The COAST French cohort results demonstrate that implantation of Cardio MEMSTM is safe, and that the system is reliable, with no DSRCs or PSFs up to 24 months after implantation. As in previous open registries, we found that the management of patients with the Cardio MEMSTMHF System was associated with a significant reduction in HFH rate in the first year following device implantation compared with the year before, with a significant decrease in pulmonary pressures. We also found an improvement in the patients' quality of life and functional class, which was maintained to 24months (Central Illustration).



Central Illustration. Major results of the French patients of the COAST study. AUC: area under the curve; CI: confidence interval; COAST: CardioMEMS HF System Post-Market Study; EQ-5D-5L; EuroQol 5-dimension 5-level questionnaire; HFH: heart failure hospitalization; LOESS: locally estimated scatterplot smoothing; M: month; NYHA: New York Heart Association; PA: pulmonary arterial pressure; pt-yr: patient-year; RR: rate ratio.

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Disclosure of interest

P. d. G., C. L., G. H., F. M. and F.R. have received honoraria from Abbott. C. G. and J. H. are Abbott employees. P. A. is an Abbott employee and stock holder. The other authors declare that they have no competing interest.

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