


Impact of lockdown during COVID-19 pandemic on physical activity and arrhythmia burden in heart failure patients

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Abstract

Background: Restricted outdoor activity during COVID-19 related lockdown may accelerate heart failure (HF) progression and thereby increase cardiac arrhythmias. We analyzed the impact of March/April 2020 lockdown on physical activity and arrhythmia burden in HF patients treated with cardiac resynchronization therapy (CRT) devices with daily, automatic remote monitoring (RM) function.

Methods: The study cohort included 405 HF patients enrolled in Observation of Clinical Routine Care for Heart Failure Patients Implanted with BIOTRONIK CRT Devices (BIO|STREAM.HF) registry in 16 countries, who had left ventricular ejection fraction (LVEF) $\leq 40\%$ (mean $28.2 \pm 6.6\%$) and NYHA class II/III/IV (47.9%/49.6%/2.5%) before CRT pacemaker/defibrillator implantation. The analyzed RM data comprised physical activity detected by accelerometer, mean heart rate and nocturnal rate, PP variability, percentage of biventricular pacing, atrial high rate episode (AHRE) burden, ventricular extrasystoles and tachyarrhythmias, defibrillator shocks, and number of implant interrogations (i.e., follow-ups). Intraindividual differences in RM parameters before (4-week period) versus during (4-week period) lockdown were tested for statistical significance and independent predictors were identified.

Results: There was a significant relative change in activity (mean -6.5% , $p < .001$), AHRE burden ($+17\%$, $p = .013$), and follow-up rate (-75% , $p < .001$) during lockdown, with no significant changes in other RM parameters. Activity decreased by ≥ 8 min/day in 46.5% of patients; predictors were higher LVEF, lower NYHA class, no defibrillator

Abbreviations: CRT, Cardiac Resynchronisation Therapy; LVEF, Left ventricular ejection fraction; HF, Heart failure; RM, remote monitoring; AHRE, Atrial high rate episodes; CHF, congestive heart failure; PVC, Premature Ventricular Contractions; NYHA, New York Heart Association dyspnoea classification; GSM, Global System for Mobile Communication; ICD, Implantable Cardioverter Defibrillator; IQR, Inter Quartile Range; CRT-D, Cardiac Resynchronisation Therapy with defibrillator; HM, HomeMonitoring®; HR, Heart rate; OR, Odds ratio; SD, Standard deviation; TIA, Transient ischemic attack; VT, Ventricular tachycardia; VF, Ventricular fibrillation; PP, Atrial-atrial interval; CRT-P, Cardiac resynchronisation therapy without defibrillator; CL, Confidence limit.

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indication, and more activity before lockdown. AHRE burden increased by ≥ 17 min/day in 4.7% of patients; predictors were history of atrial fibrillation, higher LVEF, higher body mass index, and activity decrease during lockdown.

Conclusion: Unfavorable changes in physical activity, AHRE burden, and follow-up rate were observed during lockdown, but not in ventricular arrhythmia.

KEYWORDS

arrhythmia burden, cardiac resynchronization therapy, COVID-19 lockdown, heart failure, physical activity, remote monitoring

1 | INTRODUCTION

The outbreak of the Coronavirus Disease 2019 (COVID-19) pandemic has forced many countries to impose "lockdown," including restrictions of outdoor activity, as a preventive measure against coronavirus transmission. The associated decrease in physical activity can be deleterious especially in patients with congestive heart failure (CHF), in whom outdoor exercise and other forms of activity generally improve and stabilize cardiac function.¹⁻³ Most CHF patients are equipped with a cardiac implantable electronic device, such as implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy (CRT) pacemaker/defibrillator. Normally, CHF patients benefit from regular in-hospital follow-up visits; nowadays, most of implanted devices can be monitored remotely. Telemonitoring offers many options to check on CHF patients, not only in terms of device conditions but also on heart failure (HF) issues. In addition to the greatly improved medical treatment options in last years, another important cornerstone of CHF treatment is heart training group meetings.^{2,3} These training meetings have been restricted by lockdown measures or by patients' fear of coronavirus infection with poor outcome.

The COVID-19 related lockdown can accelerate HF progression, which may then increase the occurrence of cardiac arrhythmias, such as atrial fibrillation, premature ventricular contractions (PVCs), and even ventricular tachycardia and ventricular fibrillation. In the present study, we evaluated the impact of lockdown on physical activity and arrhythmia burden in CHF patients treated with CRT devices with remote monitoring (RM) function.

2 | METHODS

The analysis was performed in a subgroup of CRT patients enrolled in the Observation of Clinical Routine Care for Heart Failure Patients Implanted with BIOTRONIK CRT Devices (BIO|STREAM.HF) registry, who had a left ventricular ejection fraction (LVEF) $\leq 40\%$ and a New York Heart Association (NYHA) functional class II-IV before CRT implantation, and automatic, daily RM data transmission during ≥ 12 weeks before and ≥ 4 weeks after the lockdown onset in the early 2020.

2.1 | The BIO|STREAM.HF registry

The BIO|STREAM.HF registry is a prospective, large, international (18 countries in Europe, Australia/Oceania, Asia, and Africa), open, non-controlled observational registry enrolling patients since May 14, 2018. The patients indicated for (de novo or upgrade) implantation of a CRT pacemaker (CRT-P) or defibrillator (CRT-D) according to current clinical guidelines are being enrolled if they accept Home Monitoring system (Biotronik SE & Co. KG, Berlin, Germany) and are not minors, pregnant, or breastfeeding. The primary objective of the registry is to assess the long-term outcome, efficacy, and residual safety aspects of CRT in an unselected, real-life clinical set-up. All patients gave written informed consent for study participation, data collection, and data processing. Each investigational site either accepted a central ethics committee's vote or obtained a separate local approval. The study is registered with ClinicalTrials.gov, number NCT03366545.

2.2 | The analysis population

For the present analysis, the registry database was frozen on November 22, 2020. Of a total of 1073 registry patients who had received a CRT-P/D by that time, 668 were excluded for the following reasons:

- Enrolment after December 21, 2019 (too short run-in period between implantation and lockdown) ($N = 460$);
- Study termination before May 5, 2020 (insufficient follow-up after lockdown) ($N = 86$);
- Enrolment in Taiwan (no lockdown during early 2020) ($N = 1$);
- LVEF $> 40\%$ or NYHA class $< \text{II}$ before CRT implantation ($N = 79$); and
- Insufficient number of Home Monitoring messages: not at least 3 daily messages within at least 1 week during 12 weeks pre-lockdown and at least 1 week during 12 weeks post-lockdown ($N = 42$).

TABLE 1 Countries, number of patients, lockdown dates

Country	N = (% of 405)	Lockdown date in early 2020 ^a
Germany	109 (26.9)	22 March
Czech Republic	57 (14.1)	14 March
Portugal	44 (10.9)	18 March
Israel	41 (10.1)	19 March
Slovakia	37 (9.1)	08 April
Hungary	24 (5.9)	16 March
Australia	20 (4.9)	19 March
France	16 (4.0)	16 March
South Africa	13 (3.2)	26 March
Spain	12 (3.0)	13 March
Latvia	10 (2.5)	16 March
Belgium	6 (1.5)	13 March
Austria	5 (1.2)	16 March
Switzerland	5 (1.2)	16 March
Poland	4 (1.0)	20 March
Great Britain	2 (0.5)	23 March
Total (16 countries)	405 (100)	13 March–8 April

^aEvery country's lockdown was different and the wide range of measures adopted by different governments is difficult to summarize. The Oxford University's Blavatnik School of Government created a database of pandemic-response policies and derived an index of the measures' overall stringency at the website (last assessed on May 6, 2021): <https://ig.ft.com/coronavirus-lockdowns/>.

The remaining 405 patients constituted the analysis population. Table 1 delineates the patient distribution per country.

2.3 | Home monitoring data

All implanted CRT-P/D devices used the Home Monitoring technology characterized by daily automatic data transmissions over the Global System for Mobile Communication (GSM) network to the manufacturer's central repository, the Home Monitoring Service Center.^{4–6} The following Home Monitoring data were analyzed:

- Physical activity detected by accelerometer sensor, expressed as percentage of 24 h or min/day during which the patient moves;
- Mean heart rate during 24 h;
- Mean heart rate at rest (between 1:00 and 5:00 am);
- PP variability, calculated as standard deviation of the 5-min average atrial–atrial intervals recorded every 5 min within 24 h;
- CRT%, calculated as percentage of paced biventricular or left ventricular beats among all ventricular events within 24 h;
- Atrial high rate episode (AHRE) burden, determined as percentage of 24 h or min/day in atrial fibrillation or with otherwise high atrial rate (programmable cut-off rate with a default value of >200 beats/min);

- Number of PVCs per hour within 24 h;
- Number of ICD shocks;
- Number of ventricular fibrillation episodes;
- Number of ventricular tachycardia episodes;
- Intrathoracic impedance measured between right ventricular lead and device case, reflecting thoracic fluid level; and
- The counter of implant interrogations (i.e., follow-ups).

2.4 | Data analysis and statistics

For each country, the date of the beginning of the most rigorous COVID-19 related restrictions in the early 2020 was determined (Table 1). The weekly mean and median values for Home Monitoring data were then calculated in each patient and evaluated as intraindividual graphical trends. The period of interest covered 12 weeks before and 12 weeks after the country-specific lockdown date.

In the statistical analysis, the 4-week period after the beginning of lockdown was compared with a 4-week period before lockdown, including weeks –6 to –3 and excluding weeks –2 and –1 because patient behavior in the last 2 weeks before lockdown might have been influenced by an increasing fear of coronavirus infection or by local/regional restrictions or pre-announcements of restrictions. The 4-week periods with data transmissions occurring on <50% of days were excluded from the analysis.

The intraindividual differences in Home Monitoring parameters pre- versus post-lockdown were tested for statistical significance by the Wilcoxon signed-rank test. As most patients had a constant AHRE burden (0% or 100%), distorting the mean and median values, we repeated the AHRE analysis in a subset of patients with a varying burden during the observational period. For the significantly changed clinical or physiological Home Monitoring parameters, predictors among baseline variables were identified by logistic regression and a stepwise approach using an entry criterion of $p < .20$ and a stay criterion of $p \leq .10$.

Otherwise, p -values $< .05$ were considered statistically significant. Data are presented as mean \pm standard deviation, median (interquartile range [IQR]), or absolute and relative frequencies. The analysis was performed using the SAS (SAS Institute Inc., USA) and R (R Development Core Team, <https://www.R-project.org/>) statistical software.

3 | RESULTS

3.1 | Patients

The 405 patients in the analysis population were 69.3 ± 10.3 years old (median 70 [IQR 63–77]) and predominantly male (75.3%). The patients were in NYHA class II (47.9%), III (49.6%), or IV (2.5%) and had an LVEF of 28.2 ± 6.6 % (median 30 [IQR 25–33]) before CRT implantation. Less than half (41.0%) of patients had ischemic cardiomyopathy, and 42.0% had a history of atrial fibrillation.

TABLE 2 Impact of lockdown on home monitoring parameters

Home monitoring parameter	Lockdown			p-value
	Before (4 weeks)	During (4 weeks)	Change	
Physical activity (% of 24 h)	9.1±4.5 (376) 8.8 (5.9–12.0)	8.6±4.7 (368) 8.0 (4.9–11.3)	−0.5±2.0 (361) −0.5 (−1.6 to 0.5)	<.001
Physical activity (min/day)	132±65 (376) 126 (85–173)	124±68 (368) 115 (71–163)	−8±29 (361) −7 (−23 to 8)	<.001
Relative decrease (%)	–	–	−6.5±21.9 (359) −5.7 (−20.8 to 6.8)	<.001
Mean HR during 24 h (bpm)	72.2±8.2 (383) 70.9 (66.4–77.5)	71.9±8.1 (374) 71.0 (66.9–76.9)	−0.2±3.3 (367) −0.1 (−1.3 to 0.9)	.14
Mean HR at rest (bpm)	64.8±8.0 (291) 61.8 (60.0–70.0)	64.4±7.8 (287) 61.8 (60.0–69.8)	−0.1±2.3 (282) 0 (−0.6 to 0.4)	.24
PP variability (ms)	69.8±29.7 (313) 70.9 (51.4–89.0)	68.5±31.1 (309) 68.2 (49.1–86.7)	−0.8±12.3 (301) −0.4 (−4.8 to 4.2)	.26
CRT% (%)	96.7±8.7 (381) 99.5 (97.0–100.0)	96.9±9.1 (372) 99.4 (97.2–100.0)	0.0±5.7 (368) 0 (−0.3 to 0.3)	.89
AHRE burden (% of 24 h)	8.3±26.9 (356) 0 (0–0)	10.0±29.2 (349) 0 (0–0)	1.2±9.0 (342) 0 (0–0)	.013
AHRE burden (min/day)	119±387 (356) 0 (0–0)	144±420 (349) 0 (0–0)	17±130 (342) 0 (0–0)	.013
AHRE burden in subset of patients from Figure 1B ^a (min/day)	326±555 (46) 10 (0–183)	534±636 (43) 86 (1–1368)	142±361 (40) 4 (−2 to 78)	<.001
Mean PVC (number/h)	71±146 (362) 16 (1–66)	65±134 (354) 15 (1–61)	−3±74 (347) 0 (−9 to 4)	.22
Intrathoracic impedance (Ohm) ^b	75.1±11.0 (222) 74.8 (69.0–82.8)	75.7±11.4 (215) 75.8 (68.3–82.8)	0.8±3.6 (211) 0.8 (−0.8 to 2.0)	<.001
Follow-ups per patient	0.22±0.54 (386) 0 (0–0)	0.06±0.29 (381) 0 (0–0)	−0.16±0.56 (374) 0 (0–0)	<.001

Data are shown as mean ± SD (number of patients) median (interquartile range). See Figure 1 for the definition of 4-week periods before versus during lockdown. Significant p-values are indicated in bold (Wilcoxon signed-rank test). AHRE, atrial heart rate episode; CRT%, percentage of paced biventricular or left ventricular beats; HR, heart rate; PP, atrial–atrial; PVC, premature ventricular contractions; SD, standard deviation.

^aSubset of patients who had an AHRE burden different from 100% or 0% (no permanent atrial fibrillation and no complete absence of atrial arrhythmia).

^bIntrathoracic impedance is available only in patients with a defibrillator and if the measurement of the values is programmed ON. Despite the statistical significance, the relative numerical difference of ≈1% appears too small to be of clinical relevance.

CRT devices were implanted for standard CRT indication (LVEF <35%, QRS ≥130 ms) in patients with sinus rhythm (65.9%) or atrial fibrillation (18.3%), for conventional pacing in a reduced LVEF (14.4%), or for other reasons (1.4%). Three quarters (74.6%) of patients had an indication for CRT defibrillator (CRT-D).

3.2 | Impact of lockdown

Figure 1A illustrates the impact of lockdown on physical activity. As seen, activity decreased abruptly during the first 2 weeks of lockdown, to increase gradually in weeks 3–7, and then exceed the pre-lockdown level in weeks 8–12. The AHRE burden slightly increased prior and during the first 4 weeks of lockdown, after exclusion of patients with a fixed AHRE burden of 0% or 100% during the studied period of 24 weeks (Figure 1B).

Table 2 shows a statistically significant impact of lockdown on patient activity (decreased from a mean 132 to 124 min/day, $p < .001$),

AHRE burden (increased from a mean 120 to 144 min/day, $p = .013$, for all patients), and follow-up rate (decreased from 0.22 to 0.06 follow-ups per patient in the period of 4 weeks, $p < .001$). Also the change in intrathoracic impedance was statistically significant, but the numerical difference appears too small to be of clinical relevance. There was no significant impact of lockdown on heart rates, PP variability, CRT%, and PVC frequency.

The incidence of ICD shocks and ventricular tachyarrhythmia episodes was low and data are summarized in a separate Table 3 (there were no significant differences). The proportions of patients receiving shocks and having ventricular arrhythmia were 0.7% and 1.0%–1.4% in each 4-week period, and 2.8% and 3.1%–3.8% in each 12-week period, respectively (Table 3).

Lockdown had a substantial impact on patient follow-up rate, with 18.1% (70/386) versus only 4.5% (17/381) of patients having at least one follow-up within the referent 4-week periods and 60.5% (237/392) versus 41.7% (161/386) of patients having at least one follow-up within 12 weeks pre- versus post-lockdown.

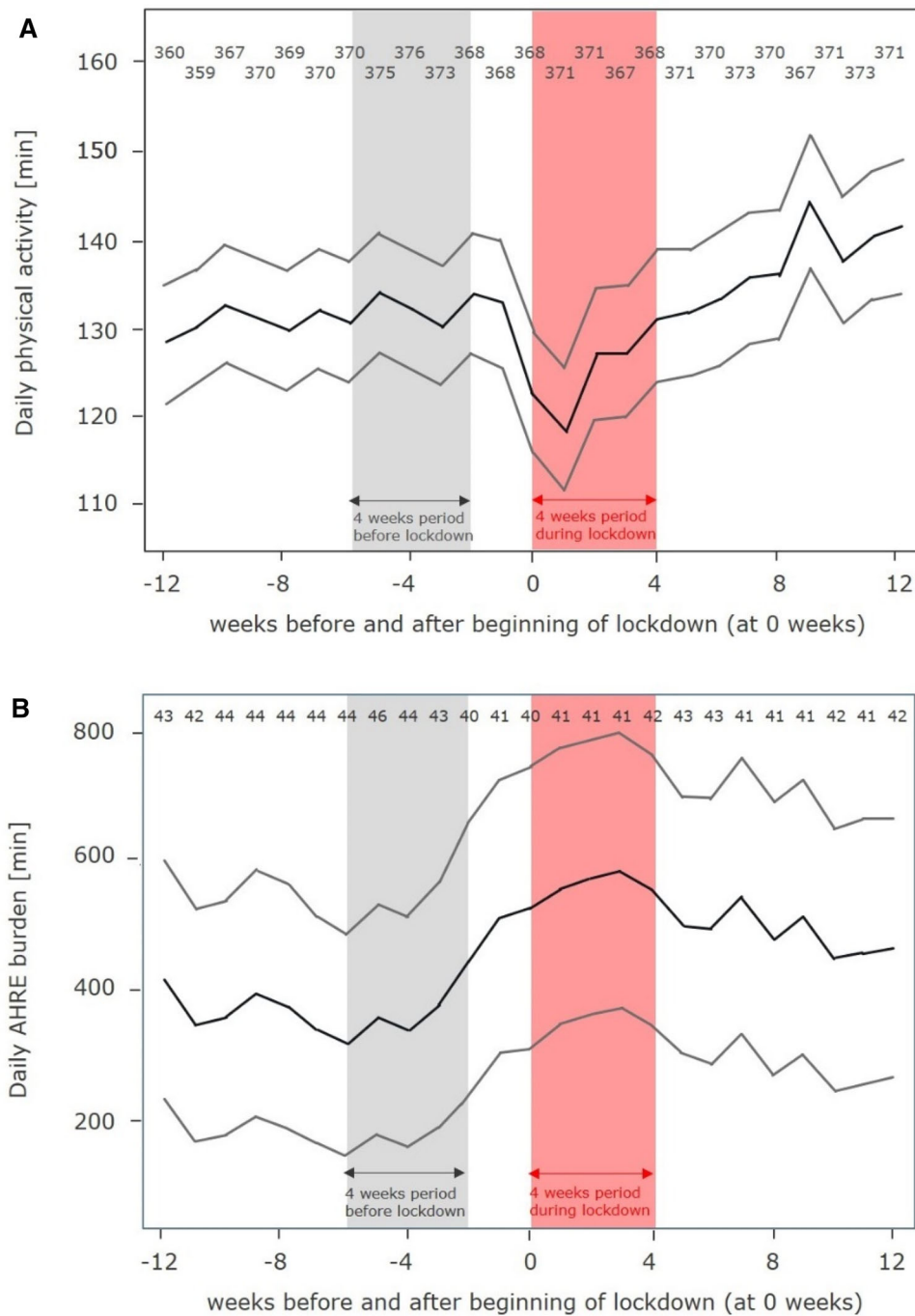


FIGURE 1 (A) Trend of physical activity measured by the implanted devices. (B) Trend in atrial high rate episode (AHRE) burden in patients who did not have permanent atrial fibrillation (100% AHRE burden) or absence of atrial arrhythmia (0% AHRE burden) during the studied period of 24 weeks. Data are shown as minutes during 24 h, averaged per week in the period from 12 weeks before to 12 weeks after the beginning of lockdown (the 0-point). The lines are mean values and 95% confidence intervals. The numbers on the top are included patients. The shaded areas indicate the 4-week periods before (gray) and during (red) lockdown used in the statistical analyses in Table 2. The white area in-between the shaded areas represents the last 2 weeks before lockdown, which are excluded from considerations due to possibly disturbing effects of local/regional restrictions (or pre-announcements of restrictions) and of an increasing patients' fear of coronavirus infection

TABLE 3 Patients with ventricular tachyarrhythmia episodes and defibrillator shocks

	Number (%) of patients			
	4-week period		12-week period	
	Before lockdown (N = 293) ^a	During lockdown (N = 291) ^a	Before lockdown (N = 291) ^a	During/after lockdown (N = 290) ^a
Patients with a device-detected VT or VF episode	4 (1.37)	3 (1.03)	11 (3.78)	9 (3.10)
VT episode	3 (1.02)	1 (0.34)	5 (1.72)	4 (1.38)
VF episode	1 (0.34)	2 (0.69)	6 (2.06)	5 (1.72)
Patients with a shock for VT/VF	2 (0.68)	2 (0.69)	8 (2.75)	8 (2.76)

VF, ventricular fibrillation; VT, ventricular tachycardia.

^aNumber of patients who had a cardiac resynchronization therapy defibrillator and valid data in the given period.

TABLE 4 Intraindividual change in physical activity and AHRE burden

Change during versus before lockdown	N (%)
Physical activity decrease	N (% of 361)
≥8 min/day	168 (46.5)
≥30 min/day	69 (19.1)
Any decrease	229 (63.4)
AHRE burden increase	N (% of 342)
≥5 min/day	20 (5.8)
≥17 min/day	16 (4.7)
≥30 min/day	14 (4.1)

AHRE, atrial heart rate episode.

Regarding hospitalizations for worsening HF or arrhythmia, the number of affected patients was 2/405 versus 1/405 within 4 weeks and 17/405 versus 12/405 within 12 weeks pre- versus post-lockdown. No study patient had COVID-19 up to 12 weeks post-lockdown.

3.3 | Predictors of activity decrease and AHRE burden increase

Physical activity decrease was at least 8 min/day in nearly half of patients (46.5%) (Table 4). These patients had a mean of 31 min/day less activity post-lockdown as compared to a mean of 12 min/day more activity post-lockdown in the rest of patients, which was also accompanied with a greater reduction in mean heart rate and in PP variability (Table 5).

When comparing baseline characteristics of the ≥8-min/day versus <8-min/day activity decrease groups, patients with greater decrease had a significantly higher LVEF, lower NYHA class, less frequent ICD indication, and more physical activity before lockdown (Table 5). Except for LVEF, these variables were also independent predictors of ≥8-min/day (or ≥7% relative) activity decrease (Tables 6 and 7).

The intraindividual AHRE burden increase during lockdown was ≥17 min/day in 16 (4.7%) patients (Table 4). A history of atrial fibrillation, higher LVEF, higher body mass index, and physical activity decrease during lockdown were independent predictors (Tables 6 and 7).

4 | DISCUSSION

As physical inactivity poses an additional risk to CHF patients, we evaluated the impact of COVID-19 related lockdown in March/April 2020 on 405 CHF patients with remotely monitored CRT-P/D devices. There was a significant decrease in patient activity (−6.5% on average) and increase in AHRE burden (+17%). Patients presented less frequently for in-hospital follow-up (−75%) during the first 4 weeks of lockdown, with no significant changes in other remotely monitored parameters.

By comparison, in a study of 180 Italian patients (67% ICD, 33% CRT-D) who were forced to spend an extended time in home quarantine, Mascioli et al.⁷ reported a 21.6% relative decline in physical activity, along with a significant decrease in mean heart rate by 1.3 beats/min and a minor increase in thoracic impedance by 0.5 Ohm. In contrast to our study, they did not observe a significant change in atrial arrhythmia burden, likely due to the smaller cohort size and different inclusion criteria, and did not assess follow-up frequency. They included all patients with RM, without focusing on CRT/CHF conditions, which is more conclusive to our data in a subgroup of patients with less severe HF symptoms, who had more pronounced decrease in activity. In line with our study, there was also no significant change in resting heart rate, PP variability, CRT%, PVC frequency, and the occurrence of ventricular tachyarrhythmias or ICD shocks.⁷

Very similar results were obtained by Bertagnin et al.⁸ from 211 Italian patients (59% ICD, 41% CRT), who had an average 25.9% decline in physical activity, a 1.6-beats/min (2.2%) decrease in mean heart rate, and a 0.5-Ohm (0.6%) increase in thoracic impedance during home quarantine. Furthermore, three studies assessed only physical activity decrease during lockdown in three countries: Italy (26.1% relative activity decrease in 184 ICD/CRT-D patients),⁹ Saudi Arabia (27.1% decrease in 82 ICD/CRT patients),¹⁰ and the USA (16%–27% decrease in 9924 pacemaker/ICD patients, depending on the city).¹¹ Overall, the 6.5% activity reduction in our international study was remarkably lower than the 16%–27% reduction in previous single-country studies. As none of the previous studies looked exclusively at CRT patients, our data are the first dedicated to CRT/CHF in a large international cohort. In addition, the prospective character of our registry is different from the study by Lu et al.,¹¹ who analyzed a

TABLE 5 Comparison of patients with activity decrease ≥ 8 -min/day versus < 8 -min/day

Parameter	Physical activity decrease ≥ 8 min/day		p-value
	Yes (N = 168)	No (N = 193)	
HM data change during versus before lockdown ^a			
Physical activity (min/day)	-31 \pm 20 (168) -26 (-43 to -15)	12 \pm 19 (193) 7 (-3 to 21)	<.001
Mean HR during 24 h (bpm)	-0.6 \pm 2.9 (168) -0.5 (-1.7 to 0.3)	0.2 \pm 3.4 (193) 0.2 (-0.7 to 1.4)	<.001
PP variability (ms)	-3.0 \pm 11.4 (136) -1 (-7 to 3)	1.2 \pm 12.6 (163) 0 (-4 to 6)	.008
Clinical baseline data (before implantation)			
Age (years)	69.8 \pm 9.7 (168) 71 (63-77)	68.8 \pm 9.9 (193) 71 (63-76)	.46
Body mass index (kg/m ²)	28.9 \pm 5.5 (161) 28 (26-31)	28.9 \pm 5.6 (188) 28 (26-31)	.89
Left ventricular ejection fraction (%)	29.3 \pm 6.2 (165) 30 (25-34)	27.6 \pm 6.5 (165) 30 (23-32)	.034
NYHA functional class			.003
II	95 (56.5)	79 (40.9)	
III	70 (40.7)	108 (56.0)	
IV	3 (1.8)	6 (3.1)	
Gender, male	129 (76.9)	145 (75.1)	.81
History of myocardial infarction	43 (25.6)	49 (25.4)	.45
History of atrial fibrillation	68 (40.5)	78 (40.4)	1.00
History of TIA/stroke	21 (12.5)	28 (14.5)	.65
Hypertension	129 (76.8)	146 (75.6)	.81
Valvular heart disease	112 (66.7)	145 (75.1)	.08
Diabetes	61 (36.3)	65 (33.7)	.66
Renal insufficiency	45 (26.8)	58 (29.0)	.72
ICD indication	117 (69.6)	159 (82.4)	.006
HM data before lockdown ^a			
Physical activity (min/day)	143 \pm 61 (168) 136 (98-182)	122 \pm 65 (193) 117 (74-163)	.001
Mean PVC (number/h)	53 \pm 110 (164) 12 (1-52)	85 \pm 171 (182) 17 (2-86)	.053

Data are shown as N (%) or as mean \pm SD (number of patients), median (IQR). Significant p-values are indicated in bold (Mann-Whitney-Wilcoxon U test). HM, Home Monitoring; HR, heart rate; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; NYHA, New York Heart Association; PP, atrial-atrial; PVC, premature ventricular contractions; SD, standard deviation; TIA, transient ischemic attack.

^aNo other HM parameters showed statistical significance.

huge number of patients retrospectively, using an RM platform and with limited medical information. In our opinion, the reasons for the lower physical activity reduction in BIO|STREAM.HF patients than in the previous studies are two-fold: different stringency and duration of home quarantine in different countries and the already limited baseline activity (mean 9.1%/day) in our CHF patients with NYHA class II-IV than in previous studies (10%–16%/day) that also included patients with less severe HF symptoms in whom more pronounced activity drop is possible during lockdown.⁷⁻¹⁰

After COVID-19 restrictions were eased, physical activity in our study exceeded the pre-lockdown level. Among previous studies, only

one covered the period after the end of lockdown and found that patient activity did not return to pre-restrictions levels for several months.¹¹ This is an interesting finding, as this group also compared the post-lockdown period to the same time a year ago (2019), to compensate for a possible seasonal effect on patient activity during 2020. Since our patients returned to normal and even exceeded the previous values, we might only hypothesize if it is because of the seasonal spring effect all over the Europe, circumstances related to urban areas versus unselected living sites, or/and a compensation for restrictions. Physical inactivity may lead to deconditioning and decreased exercise tolerance in a CHF population that already has limited reserve. In this

context, insufficient patient activity and sedentary behaviour have been associated with frailty and several metabolic and mental effects that can increase the risk of cardiovascular disease.^{9,12,13} As mental and physical abilities influence each other, this might have led to the above-mentioned activity decline even in the post-lockdown era.¹⁴

Our study is the first to show the association of lockdown with an increase in AHRE burden, which started already 4 weeks before the lockdown. This may be the effect of psychological stress resulting from increasing social isolation and fear of getting infected.⁷ Isolation and self-quarantine are associated with depression, anger, and chronic stress.¹⁵ As described by Mattioli et al.,^{12,13} negative feelings and stress are associated with changes in neurohormonal, hemodynamic, and coagulation systems, potentially leading to systemic inflammation, endothelial dysfunction, tendency to adopt an unhealthy lifestyle, and activation of the adrenergic system. All this can influence cardiovascular system in many ways: increase blood pressure, increase systemic and coronary resistance, promote thrombus formation, and increase the risk of arrhythmias.¹² Since atrial fibrillation (the most common arrhythmia underlying an AHRE) is linked to poorer prognosis especially in HF patients,¹⁶ a lockdown-related increase in AHRE may be an important finding and will be analyzed in the future. Holt et al. described a 47% reduction in registered new-onset atrial fibrillation cases during the lockdown in Denmark (general population); however, history of HF, vascular disease, and cancer were more prevalent among the atrial fibrillation patients diagnosed during lockdown.¹⁷ These findings suggest that lockdown restrictions have a relevant health influence on HF patients and those with some other comorbidities rather than on the general population.

In our study, there was no change in other monitored cardiac parameters, except for AHRE burden. This overall low impact of restrictions may be due to a relatively short lockdown, but the long-term effects of such a situation are not clear. A longitudinal study is needed, including clinical outcomes.

We could show that the rate of follow-ups markedly decreased during the lockdown period. HF patients and other carriers of cardiac implantable electronic devices are prone to serious COVID-19 infections and it is important to keep these patients out of contagious areas. On the other hand, close monitoring is of great importance in HF management, promoting automatic daily RM as essential tool for patients predisposed to the infection.¹⁸⁻²⁰ In 2014, Hindricks et al. could show the benefit of telemonitoring in HF patients⁴; as this proved the benefit of technical and patient status surveillance, it can be assumed that an acute and long-term benefit is even more pronounced during COVID lockdown.

4.1 | Predictors of activity decrease and AHRE burden increase

The three independent predictors of activity decrease in our study were NYHA class II (vs. III/IV), no ICD indication at the time of CRT implantation, and more physical activity before lockdown. These findings may be explained by the fact that patients with a lower NYHA class

are generally more physically active than more symptomatic patients and can therefore be more affected by restrictions. The same is true for patients that were more physically active before lockdown irrespective of the NYHA class. Regarding the indications for CRT-P (but not CRT-D) implantation, they are very heterogeneous between countries and also between physicians in clinical practice. Many CRT-P implantations are upgrades of a pacemaker system due to pacing-induced left ventricular dysfunction or left-bundle-branch-block-induced left ventricular dysfunction. We can speculate that these groups will have a better response to resynchronization and therefore better functional status and greater ability to exercise in normal conditions. Altogether, lockdown had less of an effect on activity in higher risk patients (advanced NYHA class, sedentary lifestyle) who tend to be inactive whether locked down or not.

By comparison, in previous studies, Mascioli et al.⁷ sought predictors of activity decline during lockdown and found that patients with marked ($\geq 25\%$) relative reduction in physical activity were more likely men than women. Likewise, Malanchini et al.⁹ found that the percentage decrease in activity level was greater among men (28.2%) than women (19.4%) ($p = .038$). This result, obtained in the setting of Italy, was likely attributable to habitual lower levels of physical activity in women, but our international study did not confirm that gender predicts activity decline.

The four independent predictors of AHRE burden increase were history of atrial fibrillation, higher LVEF, greater body mass index, and reduced physical activity during lockdown. The predictive value of atrial fibrillation history and activity decrease appears logical because they indicate greater patient susceptibility to AHRE and unhealthy change in lifestyle, respectively. However, we have no explanation for the "negative" role of a higher LVEF and body mass index at baseline in this context.

4.2 | Study limitations

This study has several limitations worth noting. The lockdown measures were a mixture of different restrictions in different countries and not a uniform condition in all study patients. There is no information on the type and intensity of activity or any other factors that might have affected activity level in individual patients. There is also no information on potential coronavirus infection in study patients. The BIO|STREAM.HF registry is projected for 3000 patients, which is too large cohort to be able to collect data on medication changes systematically; however, medication change in a fraction of patients is not expected to have a substantial impact on pooled results for a large patient cohort

5 | CONCLUSIONS

Unfavorable changes in physical activity, AHRE burden, and follow-up rate were observed during lockdown, but not in ventricular arrhythmia or any other RM parameter. Prognostic implications of reduced

TABLE 6 Predictors of activity decrease and AHRE burden increase: logistic regression

Baseline parameter	Activity decrease ≥ 8 min/day		AHRE burden increase ≥ 17 min/day	
	p-value	OR (95% CL)	p-value	OR (95% CL)
Clinical, continuous				
Age (years)	.88	1.00 (0.97–1.03)	.63	0.98 (0.90–1.07)
Body mass index (kg/m ²)	.87	1.00 (0.96–1.05)	.011	1.16 (1.03–1.31)
Left ventricular ejection fraction (%)	.24	1.02 (0.99–1.06)	.004	1.25 (1.07–1.45)
Clinical, dichotomized				
Gender: male versus female	.69	1.12 (0.64–1.95)	.65	1.49 (0.27–8.34)
NYHA class: III/IV versus I/II	.009	0.55 (0.35–0.86)	.34	1.97 (0.49–7.85)
Clinical, dichotomized: yes versus no				
History of sick sinus syndrome	.90	0.95 (0.44–2.08)	.91	0.89 (0.14–5.75)
History of atrioventricular block	.75	1.09 (0.63–1.88)	.95	0.94 (0.16–5.48)
History of atrial fibrillation	.93	1.02 (0.63–1.66)	.003	24.1 (3.04–191)
History of ventricular arrhythmias	.75	0.91 (0.50–1.64)	.66	0.66 (0.10–4.15)
Hypertension (including well-controlled)	.85	1.06 (0.61–1.82)	.98	1.02 (0.13–7.78)
Valvular heart disease	.23	0.73 (0.44–1.22)	.59	1.53 (0.32–7.20)
History of TIA/stroke	.87	0.95 (0.49–1.82)	.57	0.50 (0.05–5.44)
Renal insufficiency ^a	.63	0.88 (0.53–1.48)	.61	1.45 (0.36–5.86)
Diabetes mellitus	.62	1.13 (0.70–1.83)	.22	0.37 (0.07–1.83)
ICD indication	.017	0.48 (0.26–0.88)	.99	1.01 (0.15–7.04)
HM data change: during versus before lockdown				
Physical activity, continuous (min/day)	–	–	.056	0.98 (0.95–1.00)

AHRE, atrial heart rate episode; CL, confidence limits; ICD, implantable cardioverter-defibrillator; NYHA, New York Heart Association; OR, odds ratio; TIA, transient ischemic attack.

^aDefined as an estimated glomerular filtration rate < 60 mL/min/1.73 m².

TABLE 7 Independent predictors of activity decrease and AHRE burden increase^a

Independent predictors	p-value	OR (95% CL)
For activity decrease ≥ 8 min/day		
Clinical parameters only		
NYHA class: III/IV versus I/II	.003	0.52 (0.34–0.80)
ICD indication	.002	0.44 (0.26–0.74)
Clinical and HM parameters		
Activity before lockdown	.041	1.06 (1.00–1.11)
NYHA class: III/IV versus I/II	.004	0.51 (0.32–0.80)
ICD indication	<.001	0.34 (0.19–0.60)
For AHRE burden increase ≥ 17 min/day		
Activity change during versus before lockdown	.040	0.97 (0.95–1.00)
Body mass index	.004	1.15 (1.05–1.27)
Left ventricular ejection fraction	.002	1.23 (1.08–1.40)
History of atrial fibrillation	<.001	19.1 (3.47–105)

AHRE, atrial heart rate episode; CL, confidence limits; ICD, implantable cardioverter-defibrillator; HM, Home Monitoring; NYHA, New York Heart Association; OR, odds ratio.

^aBy a stepwise method.

activity and increased AHRE burden have to be analyzed. Telemonitoring enables physicians and caregivers to better detect changes and treat patients with congestive HF during pandemic situations. Tailored remote cardiac rehabilitation program and telemedicine for controlling physical exercise at home may be the new frontier for implementing cardiac exercise in this fragile population of patients.

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CONFLICT OF INTEREST

Jörn Schmitt declares speaker honorarium by Biotronik and study support. Beate Wenzel and Bernd Brüsehaber are employees of Biotronik. Other (co-)authors declare having no conflicts of interest.

CLINICAL TRIAL REGISTRATION

The study is registered with ClinicalTrials.gov, number NCT03366545.

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