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Cardiac resynchronization therapy defibrillators in patients with permanent atrial fibrillation

Antonio Rapacciuolo[1]* [ID], Saverio Iacopino[2] [ID], Antonio D'Onofrio[3], Antonio Curnis[4], Ennio C. Pisanò[5],
Mauro Biffi[6] [ID], Paolo Della Bella[7] [ID], Antonio Dello Russo[8], Fabrizio Caravati[9], Gabriele Zanotto[10],
Valeria Calvi[11], Giovanni Rovaris[12], Gaetano Senatore[13], Daniele Nicolis[14], Matteo Santamaria[15],
Massimo Giammaria[16] [ID], Giampiero Maglia[17], Antonio Duca[18], Giuseppe Ammirati[1],
Salvo Andrea Romano[19], Marcello Piacenti[20], Eduardo Celentano[21], Giovanni Bisignani[22], Paola Vaccaro[23],
Gennaro Miracapillo[24], Matteo Bertini[25], Gerardo Nigro[26], Daniele Giacopelli[27,28] [ID], Alessio Gargaro[27] [ID] and
Caterina Bisceglia[7]

[1]*Department of Advanced Biomedical Sciences, Federico II University of Naples, Corso Umberto I, 40, Naples, 80138, Italy;* [2]*Villa Maria Care & Research, Cotignola, Italy;*
[3]*Ospedale Monaldi, Naples, Italy;* [4]*Spedali Civili, Brescia, Italy;* [5]*Ospedale Vito Fazzi, Lecce, Italy;* [6]*Policlinico Sant'Orsola-Malpighi, Bologna, Italy;* [7]*IRCCS San Raffaele
Scientific Institute, Milan, Italy;* [8]*Ospedali Riuniti, Ancona, Italy;* [9]*ASST dei sette laghi, Ospedale di Circolo, Varese, Italy;* [10]*Ospedale Mater Salutis, Legnago, Italy;* [11]*Policlinico
G. Rodolico, Az. O.U. Policlinico - V. Emanuele, Catania, Italy;* [12]*Ospedale San Gerardo, Monza, Italy;* [13]*Ospedale di Ciriè, Ciriè, Italy;* [14]*Ospedale di Mantova, Mantova, Italy;*
[15]*Gemelli Molise Hospital, Campobasso, Italy;* [16]*Ospedale Maria Vittoria, Torino, Italy;* [17]*Azienda Ospedaliera Pugliese Ciaccio, Catanzaro, Italy;* [18]*IRCCS Neurolesi-Ospedale
Piemonte, Messina, Italy;* [19]*Ospedale di Desio, Desio, Italy;* [20]*Fondazione Toscana Gabriele Monasterio, Pisa, Italy;* [21]*Humanitas Gavazzeni, Bergamo, Italy;* [22]*Ospedale
"Ferrari", Castrovillari, Italy;* [23]*AOR Villa Sofia-Cervello P.O. Cervello, Palermo, Italy;* [24]*Ospedale di Grosseto, Grosseto, Italy;* [25]*University of Ferrara, S. Anna Hospital, Ferrara,
Italy;* [26]*University of Campania "Luigi Vanvitelli," Monaldi Hospital, Naples, Italy;* [27]*Biotronik Italia S.p.a., Vimodrone, Italy; and* [28]*University of Padova, Padova, Italy*

Abstract

Aims   There are conflicting data on the benefit of cardiac resynchronization therapy (CRT) in heart failure (HF) patients with permanent atrial fibrillation (AF). We aimed to compare patient outcomes according to the presence or absence of permanent AF at device implantation.

Methods and results   We retrospectively analysed remote monitoring data from 1141 CRT defibrillators. Propensity score with inverse-probability weighting method was used to balance AF and sinus rhythm (SR) groups. Analysis endpoints included total mortality, appropriate defibrillation shocks, and CRT percentage. There were 229 patients (20.1%) in the AF group and 912 patients (79.9%) in the SR group. Compared with SR patients, AF patients were older (median age, 77 vs. 72 years, $P < 0.001$), more frequently male (82.5% vs. 75.5%, $P = 0.02$), and had higher heart rate (75.7 vs. 71.0 b.p.m., $P < 0.001$). Of the 229 AF patients, 162 (70.7%) received suboptimal CRT ($<$98%) and 67 (29.3%) had adequate CRT ($\geq$98%). During a median follow-up of 24 months, total mortality did not differ between AF and SR groups (propensity-score-weighted hazard ratio, HR 1.32 [95% confidence interval, 0.82–2.15], $P = 0.25$). The risk of appropriate shocks was significantly higher in the AF group with $<$98% CRT than in the SR group (weighted-HR, 1.99 [1.21–3.26], $P = 0.006$) and was similar in the AF group with $\geq$98% CRT versus the SR group (1.29 [0.66–2.53], $P = 0.45$). During follow-up, sinus rhythm was recovered in 23 patients in the AF group (10%) after a median time of 106 (42–256) days. The rate of sinus rhythm recovery in the AF group was 4.5 (95% CI, 2.8–6.7) per 100 patient-years; the rate of permanent AF occurrence in the SR group was 2.5 (95% CI, 1.9–3.3) per 100 patient-years.

Conclusions   Although mortality was similar across patient groups, patients with permanent AF and suboptimal CRT had two-fold higher risk of appropriate shocks than SR patients or AF patients with CRT $\geq$ 98%.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia with well-known association with heart failure (HF).[1] Poorer prognosis in patients with both chronic HF and permanent AF is related to older age, multiple co-morbidities, and significant impairment of cardiac function compared with HF alone.[2,3]

Cardiac resynchronization therapy (CRT) is one of the most successful therapies for symptomatic and severe HF characterized by ventricular dysfunction and wide QRS. According to a recent survey of the European Society of Cardiology, 41% of patients undergoing CRT have history of AF and 47% of the cases are permanent AF.[4] However, the benefit of CRT has not been completely assessed in patients with permanent AF, as the overwhelming majority of randomized controlled trials exclude this condition and the available data are conflicting.[5–7] Observational studies point to comparable efficacy of CRT in AF and in sinus rhythm (SR) when optimal (>98%) CRT delivery is ensured.[8,9] Furthermore, ventricular arrhythmias account for most deaths in HF with reduced ejection fraction, in contrast to HF with preserved ejection fraction,[10] but the incremental benefit of CRT in the context of sudden death prevention with implantable defibrillators remains controversial. More clinical data are needed to clarify these controversial issues.

Methods

Objective and study design

We retrospectively analysed remote monitoring data in patients with CRT-D devices to compare outcomes according to the presence or absence of permanent AF at the time of device implantation. Analysis endpoints included total mortality, appropriate shocks for ventricular arrhythmias, and percentage of CRT delivery (CRT%), including biventricular pacing events and left-ventricular pacing triggered by right-ventricular sensed events. Data on device programming, diagnostics, and arrhythmic recordings were automatically transmitted on a daily basis and stored in the Home Monitoring Expert Alliance (HMEA) database, a nationwide repository of home monitoring (HM) data generated by cardiac implantable electronic devices during ordinary clinical practice.[11]

The present analysis was proposed by the first author and approved by the Executive Committee of the HMEA project. A total of 32 sites contributed to the data needed for this analysis. The HMEA project received approval by relevant Ethics Committees. Patients provided written informed consent before HMEA registration.

Patient selection and study procedures

Patients were included in the analysis if they had a CRT-D device with successfully implanted left ventricular lead, active HM transmissions, and either the biventricular or left ventricular-only pacing mode programmed.

The study cohort was divided into the AF and SR groups, according to baseline assessment. The AF group included patients with therapy-refractory AF for more than 12 months. The SR group included patients in sinus rhythm at implantation, either with or without history of AF, who received a device programmed with an atrial-tracking pacing mode. The AF group was further divided into subgroups of patients who received suboptimal (<98%) and adequate (≥98%) CRT% during follow-up.

Remote monitoring data were collected from implant to the last HM transmission or database freezing. Data on ventricular arrhythmias treated by shocks were reviewed by three electrophysiologists blinded to sites and patient characteristics, and adjudicated by majority vote after visual inspection of intracardiac electrograms (IEGMs) of remotely transmitted episodes. IEGM snapshots included pre-episode, detection, and post-therapy electrograms from atrial, right ventricular, and left ventricular or far-field (coil to case) electrodes. Shock delivery was classified as appropriate if it was triggered by a ventricular arrhythmia (tachycardia or fibrillation). Mortality data were based on clinical records after confirmation of persistent interruption of HM transmissions.

Statistics

Categorical variables are reported as absolute and relative frequencies using non-missing values. Continuous variables are reported as median (interquartile range). The Mann–Whitney U-test for continuous variables, and Pearson-χ^2 or Fisher's exact tests for binary or categorical variables, were used to test differences between study groups. Mortality and incidence of appropriate shock were calculated with the product-limit method and reported with the 95% confidence interval (CI). Kaplan–Meier curves by study group were also generated.

We used the propensity score (PS) with the method of inverse probability of treatment weighting[12] to minimize confounding effects in the comparisons between AF and SR groups. Specifically, weights were assigned to each patient basing on the inverse probability of belonging to the AF group. Variables used for weights comprised age, sex, ischaemic cardiomyopathy, hypertension, diabetes, chronic obstructive pulmonary disease, previous stroke or transient ischaemic attack, chronic kidney disease, history of ventricular arrhythmia, left ventricular ejection fraction, QRS duration, and drug therapy (beta-blockers, diuretics, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, and amiodarone). After PS weighting, AF versus SR hazard ratios (HRs) were

estimated with univariate and multivariable proportional-hazard Cox regressions adjusted by age, sex, ischaemic cardiomyopathy and CRT%. The analysis was performed with the STATA version 11.1SE and the R Studio software version 4.0.3, with a significance level set at $P = 0.05$ in all tests.

Results

Study population and device programming

At the time of database freezing, there were 1226 patients implanted with a CRT-D device. Eighty-five (6.9%) patients were excluded because left ventricular lead was not implanted or HM transmissions were persistently unsuccessful or CRT pacing was switched off. The remaining 1141 CRT-D patients were included in the analysis and had a median follow-up of 24 (13–42) months. The SR and AF groups accounted for 912 (79.9%) and 229 (20.1%) subjects, respectively (*Figure 1*). Compared with SR patients, the AF group was older (77 [70–81] vs. 72 [65–78] years, $P < 0.001$), more frequently male (82.5% vs. 75.5%, $P = 0.024$), more frequently on anticoagulation therapy (82.5% vs. 31.1%, $P < 0.001$), and more often presenting with a (left ventricular dysfunction- or HF-related) CRT indication probably leading to a high right ventricular pacing burden (65% vs. 8%, $P < 0.001$) (*Table 1*). In the AF group, 87 patients (38.9%) received an atrial lead, and 5 patients (2.2%) had undergone atrio-ventricular node ablation at time of device implantation.

Device programming was set according to routine care, with a higher basic rate (70 [60–75] b.p.m. vs. 60 [60–60]

b.p.m., $P < 0.001$) and a more frequent activation of rate responsive function (67.3% vs. 19.9%, $P < 0.001$) in the AF than in the SR group. Tachycardia detection programming did not differ between groups and showed limited inter-individual variability: ventricular fibrillation zone cut-off was programmed to 300 ms in roughly 80% of patients, and ventricular tachycardia zone cut-off to 370 ms in roughly 75% of patients. In all patients, defibrillation shocks were preceded by antitachycardia pacing therapy attempts: one attempt in the fastest zones and at least three attempts in slower zones.

Compared with the SR group, the AF group had higher mean 24 h heart rate (75.7 [71.7–81.9] vs. 71.0 [65.7–76.5] b.p.m., $P < 0.001$) and lower CRT% (96.0 [90.3–98.6] vs. 98.8 [95.4–99.9], $P < 0.001$) (*Table 2*). Adequate CRT% ($\geq 98\%$) was observed in only 29.3% of AF patients ($n = 67$), suboptimal CRT% ($<98\%$) in 70.7% ($n = 162$), and low CRT% ($<90\%$) in 24.4% ($n = 56$).

In the SR group, the median percentage of atrial pacing was 18.1% (2.2%–53.4%). The effect of rate-adaptive pacing on mean heart rate was marginal both in the SR group (71 [66–77] b.p.m. with vs. 72 [67–76] b.p.m. without rate-adaptive pacing, $P = 0.294$), and in the AF group (75 [71–81] vs. 76 [72–83] b.p.m., $P = 0.158$).

Propensity score weighting for outcome analysis

After PS weighting, absolute standardized mean differences between AF and SR groups were ≤ 0.1 for all matching variables (*Figure 2*). During a median follow-up of 24 (13–42) months, 107 (9.4%) deaths were reported: 27 (11.8%) in the AF group and 80 (8.8%) in the SR group, with no significant

Figure 1 Flow chart of patients included in the analysis. Median duration of follow-up was 24 (13–42) months. AF, atrial fibrillation; CRT, cardiac resynchronization therapy; CRT-D, CRT defibrillator; HMEA, home monitoring expert alliance.
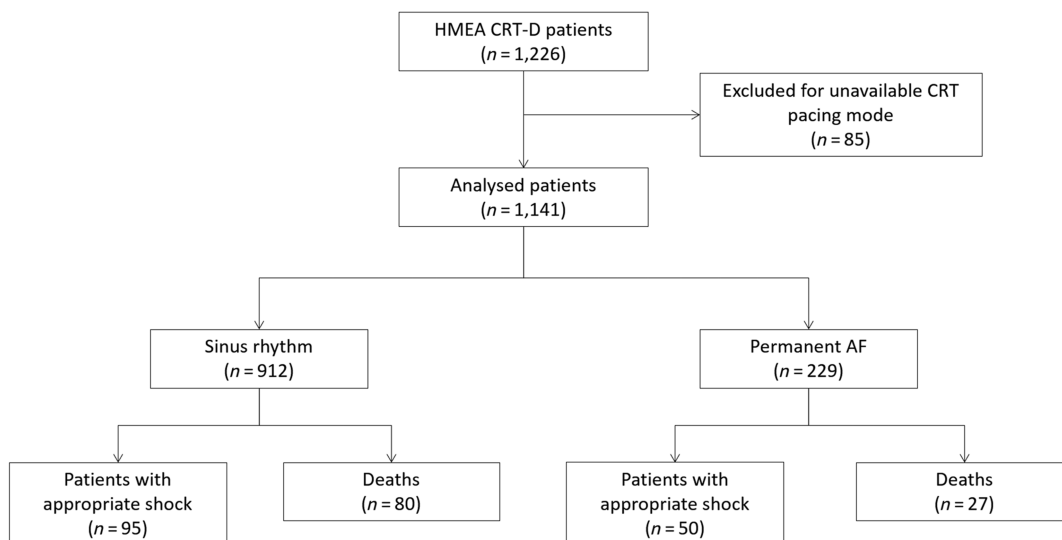
Table 1 Patient characteristics

	All (n = 1141)	Permanent AF (n = 229)	Sinus rhythm (n = 912)	P value
Demographics				
Age, years	73 (66–78)	77 (70–81)	72 (65–78)	<0.001
Female	263 (23.1%)	40 (17.5%)	223 (24.5%)	0.024
Cardiomyopathy				0.084
ICM	529 (46.4%)	93 (40.7%)	436 (47.8%)	-
Non-ICM	612 (53.6%)	136 (59.3%)	476 (52.2%)	-
Co-morbidities				
Hypertension	618 (56.3%)	117 (54.0%)	501 (56.8%)	0.500
Previous myocardial infarction	327 (29.7%)	49 (22.5%)	278 (31.5%)	0.197
Diabetes	302 (27.5%)	52 (24.0%)	250 (28.3%)	0.255
COPD	159 (13.9%)	28 (12.2%)	131 (14.4%)	0.464
Stroke/TIA	88 (8.1%)	9 (4.1%)	79 (9.0%)	0.030
Chronic kidney disease	179 (16.3%)	36 (16.8%)	143 (16.2%)	0.861
History of AF	-	-	14.8%	-
Secondary prevention of SCD	108 (9.8%)	22 (10.3%)	86 (9.7%)	0.787
NYHA class				0.200
I–II	647 (59.5%)	114 (54.5%)	533 (60.5%)	-
III–IV	443 (40.5%)	95 (45.5%)	348 (39.5%)	-
Echocardiography and ECG				
Left ventricular EF, %	30 (25–34)	30 (26–34)	30 (25–33)	0.420
<25	139 (12.7%)	24 (11.5%)	115 (12.9%)	-
25–35	869 (78.9%)	169 (79.7%)	700 (78.7%)	-
>35	94 (8.4%)	19 (8.8%)	75 (8.4%)	-
Intrinsic QRS duration, ms	140 (130–160)	140 (130–155)	142 (130–160)	0.480
<120	87 (8.1%)	15 (7.4%)	72 (8.2%)	-
120–129	110 (10.2%)	17 (8.4%)	93 (10.6%)	-
130–149	426 (38.9%)	99 (47.4%)	327 (37.2%)	-
150–179	377 (34.9%)	55 (26.3%)	322 (36.6%)	-
>180	86 (7.9%)	22 (10.5%)	66 (7.4%)	-
Intrinsic QRS morphology				<0.001
LBBB	566 (50.6%)	81 (36.6%)	485 (53.9%)	-
Non-LBBB	554 (49.4%)	140 (63.4%)	414 (46.1%)	-
Third-degree AV block	50 (4.4%)	13 (5.7%)	37 (4.1%)	0.360
Clinical indication for CRT				<0.001
HF with wide QRS	775 (63.8%)	80 (34.9%)	695 (76.2%)	-
HF or LVD and expected high RV%	225 (25.3%)	149 (65.1%)	76 (8.3%)	-
Other	141 (10.9%)	0 (0%)	141 (15.6%)	-
CHA$_2$DS$_2$-VASc score	4 (3–5)	4 (3–5)	4 (3–5)	0.592
1	48 (4.4%)	12 (5.7%)	36 (4.1%)	-
2	164 (14.9%)	23 (10.7%)	141 (16.0%)	-
3	2787 (25.3%)	57 (26.4%)	221 (25.0%)	-
4	310 (28.2%)	58 (27.0%)	252 (28.5%)	-
≥5	298 (27.2%)	65 (30.2%)	233 (26.4%)	-
Medications				
Beta-blocker	857 (78.1%)	161 (76.4%)	696 (78.5%)	0.563
Digoxin	97 (8.5%)	46 (22.0%)	51 (5.6%)	<0.001
Diuretic	897 (81.7%)	166 (78.6%)	731 (82.5%)	0.240
ACE/ARB	726 (66.1%)	135 (63.8%)	591 (66.7%)	0.472
Anticoagulant	450 (40.3%)	174 (82.4%)	276 (31.1%)	<0.001
Antiplatelet agent	484 (44.4%)	54 (25.4%)	430 (48.5%)	<0.001
Amiodarone	149 (13.6%)	23 (11.1%)	126 (14.2%)	0.294
Device programming				
Basic rate	60 (60–70)	70 (60–75)	60 (60–60)	<0.001
Rate-adaptive pacing mode	335 (29.4%)	154 (67.3%)	181 (19.9%)	<0.001
Follow-up period, months	24 (13–42)	23 (13–40)	24 (12–43)	0.517

Values are median (interquartile range) or number (%) using non-missing values.
ACE, angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin II receptors blocker; AV, atrioventricular; COPD, chronic obstructive pulmonary disease; CRT, cardiac resynchronization therapy; EF, ejection fraction; HF, heart failure; ICM, ischaemic cardiomyopathy; LBBB, left bundle branch block; LVD, left ventricular dysfunction; RV%, proportion of right ventricular pacing; SCD, sudden cardiac death; TIA, transient ischaemic attack; VF, ventricular fibrillation; VT, ventricular tachycardia.

difference (univariate PS-weighted HR 1.32 [95% CI, 0.82–2.15], P = 0.255). Overall, 1 and 4 year mortality rates were 2.6% (95% CI, 1.8%–3.8%) and 13.4% (95% CI, 10.8%–16.6%) (Table 3 and Figure 3).

Appropriate shocks for ventricular arrhythmias were delivered in 50 patients in the AF group (21.8%) and in 95 patients in the SR group (10.4%), with a 79% increased risk in the AF versus SR group (multivariate PS-weighed HR 1.79 [95% CI,

Table 2 Device diagnostics by study groups

	All	Permanent AF	Sinus rhythm	P value
Atrial pacing percentage, %	18.1 (2.2–53.4)	0 (0–0)	18.1 (2.2–53.4)	<0.001
CRT pacing percentage, %	98.5 (94.2–99.8)	96.0 (90.3–98.6)	98.8 (95.4–99.9)	<0.001
Biventricular pacing percentage, %	97.7 (89.8–99.6)	86.4 (60.0–96.5)	98.5 (93.9–99.8)	<0.001
Mean 24 h heart rate, b.p.m.	71.9 (66.7–77.8)	75.7 (71.7–81.9)	71.0 (65.7–76.5)	<0.001

Values were calculated over the second month post-implant and reported as median (interquartile range). CRT pacing percentage is the sum of biventricular events and left-ventricular pacing events triggered by right-ventricular sensed events.
AF, atrial fibrillation; b.p.m., beats per minute; CRT, cardiac resynchronization therapy.

Figure 2 Absolute mean differences for propensity score variables. Variables including missing values are shown before ("Unadjusted") and after ("Adjusted") propensity score by inverse probability of treatment weighting. ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptors blockers; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ICM, ischaemic cardiomyopathy; LVEF, left ventricular ejection fraction; NYHA, New Your Heart Association; TIA, transient ischaemic attack; VF, ventricular fibrillation; VT, ventricular tachycardia.
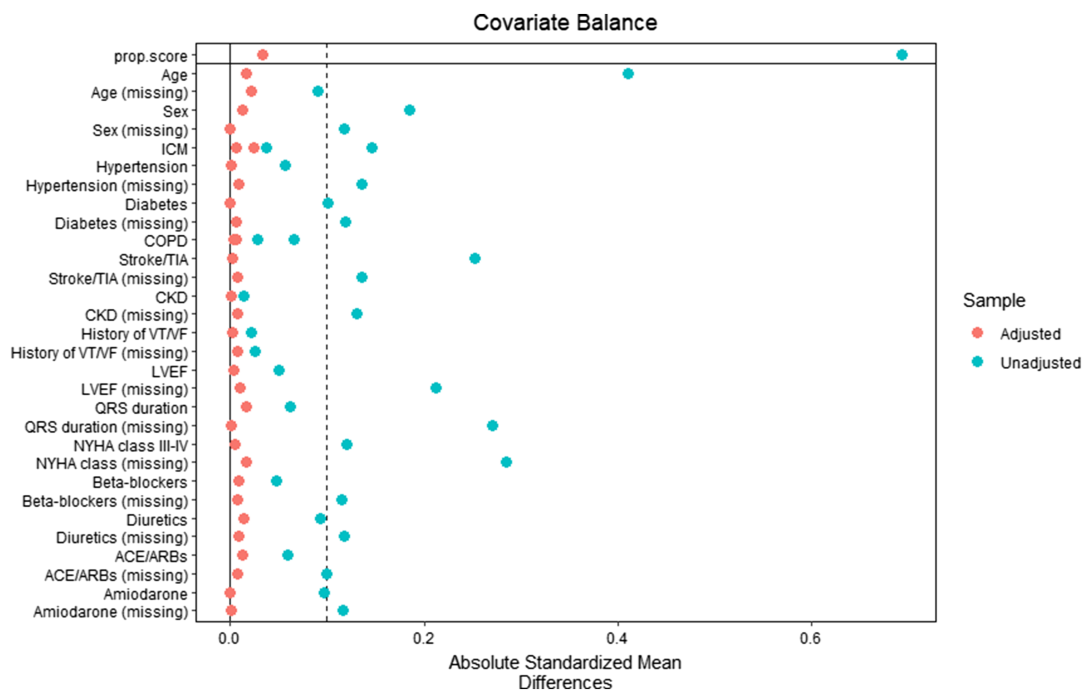
1.15–2.78], $P = 0.01$) (*Table 3*). AF patients who experienced appropriate shocks had similar mean heart rate to AF patients who did not receive shocks (74.0 [71.3–80.1] b.p.m. vs. 75.9 [71.7–82.5] b.p.m., $P = 0.476$), but had lower CRT% (94.9 [86.5–97.7] vs. 96.2 [90.3–98.9], $P = 0.048$). The incidence of appropriate shocks in the AF group with adequate CRT% ($\geq$98%) did not differ significantly from the incidence in the SR group (PS-weighted HR 1.29 [95% CI, 0.66–2.53], $P = 0.455$); conversely, AF patients with suboptimal CRT% (<98%) had a twofold increased risk of appropriate shocks compared with the SR patients (multivariate PS-weighted HR, 1.99 [95% CI, 1.21–3.26], $P = 0.006$). Comparisons are displayed in *Figure 4*.

Inappropriate shocks were delivered in 94 patients: 21 in the AF group (9.2%) and 73 in the SR group (8.0%), with

no significant difference between groups (multivariate PS-weighed HR 1.28 [95% CI, 0.62–2.61], $P = 0.50$). Causes of inappropriate therapy delivery were supraventricular arrhythmias with high ventricular rate (38.3%), electrical noise (38.3%), and T-wave oversensing (23.4%).

Crossover of device programming

During follow-up, sinus rhythm was recovered in 23 patients in the AF group (10%) after a median time of 106 (42–256) days after implantation (recovery was induced by a shock delivery in 4 patients). Twelve patients in this subgroup had already received an atrial lead at implant; in the remaining 11 patients an atrial lead was added after rhythm conversion.

Table 3 Incidence of all-cause mortality and appropriate shocks by study groups

	Time from implant (years)			
	1	2	3	4
Appropriate shock				
All	7.4 (5.9–9.2)	11.8 (9.8–14.1)	16.1 (13.5–19.0)	19.5 (16.4–23.1)
AF group	13.1 (9.2–18.5)	22.1 (16.6–29.1)	28.9 (22.0–37.4)	34.3 (26.0–44.5)
SR group	5.9 (4.5–7.8)	9.2 (7.3–11.6)	12.9 (10.4–16.0)	15.9 (12.7–19.7)
Univariate PS-weighted HR (95% CI)	2.23 (1.55–3.22), $P < 0.001$			
Multivariate PS-weighted HR (95% CI)	1.79 (1.15–2.78), $P = 0.010$			
Covariates				
Age	1.00 (0.98–1.03), $P = 0.670$			
Female	0.52 (0.25–1.09), $P = 0.085$			
ICM	1.11 (0.71–1.73), $P = 0.638$			
CRT pacing percentage	0.99 (0.98–1.00), $P = 0.059$			
All-cause mortality				
All	2.6 (1.8–3.8)	6.4 (4.9–8.2)	11.0 (8.8–13.6)	13.4 (10.8–16.6)
AF group	2.9 (1.3–6.3)	8.2 (4.9–13.5)	13.4 (8.5–20.6)	15.0 (9.6–23.1)
SR group	2.6 (1.7–3.9)	5.9 (4.4–8.0)	10.4 (8.0–13.3)	13.0 (10.2–16.6)
Univariate PS-weighted HR (95% CI)	1.32 (0.82–2.15), $P = 0.255$			

AF group, patients in permanent atrial fibrillation at implantation; CI, confidence interval; CRT, cardiac resynchronization therapy; HR, hazard ratio; ICM, ischaemic cardiomyopathy; PS, propensity score; SR group, patients in sinus rhythm at implantation.

Figure 3 Kaplan–Meier curves for all-cause mortality and appropriate shock occurrence by study groups. AF, atrial fibrillation; HR, hazard ratio; PS, propensity score.
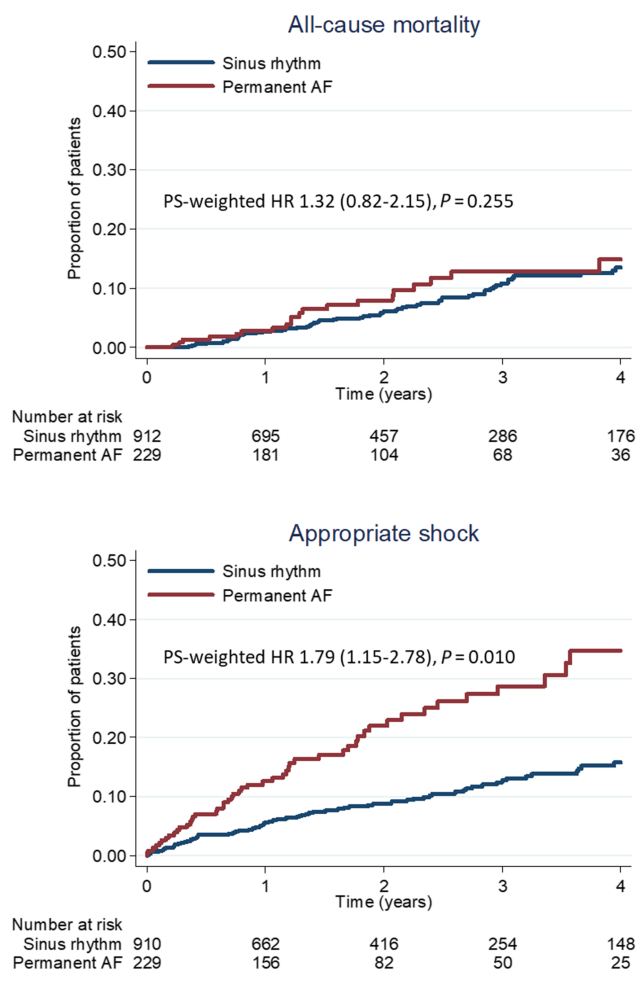

All devices were reprogrammed to a dual-chamber atrial tracking pacing mode. Overall, the rate of sinus rhythm recovery was 4.5 (95% CI, 2.8–6.7) per 100 patient-years. On the other hand, 55 patients in the SR group (6.0%) developed permanent AF with a rate of 2.5 (95% CI, 1.9–3.3) per 100 patient-years. Devices were reprogrammed to a ventricular pacing mode. In the SR group, the median AF burden was 0.94% (0%–2.4%).

Discussion

Our analysis showed that (i) about 20% of patients undergoing CRT-D implantation have permanent AF in ordinary medical practice; (ii) survival in the AF and SR groups was similar, although over 70% of patients in the AF group did not achieve adequate CRT% and exhibited relatively high 24 h heart rates (median, 76 b.p.m.); (iii) patients with permanent AF and suboptimal CRT% had a twofold increased risk of appropriate shocks, but those who achieved CRT% > 98% had a comparable risk of ventricular arrhythmias to the SR patients; (iv) the rate at which sinus rhythm was restored in the AF patients was almost twice the rate at which the SR patients developed permanent AF during follow-up.

The *2016 European Society of Cardiology Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure* provide a IIa class recommendation for CRT implantation in AF patients with a left ventricular ejection fraction ≤35%, NYHA Class III-IV, and QRS duration ≥130 ms, but the emphasis is placed on rate control.[13] The results of our analysis are in line with this recommendation and additionally, show that the known antiarrhythmic effects of cardiac resynchronization[14] are also prominent in patients with permanent AF, as long as adequate CRT% is maintained. As ventricular arrhythmias

Figure 4 Kaplan–Meier curves of appropriate shock occurrence in the SR group and in the AF subgroups with suboptimal (<98%) and adequate (≥98%) CRT pacing percentage. *P = 0.006 versus SR group after PS-weighting analysis. AF, atrial fibrillation; CRT, cardiac resynchronization therapy; PS, propensity score; SR, sinus rhythm.
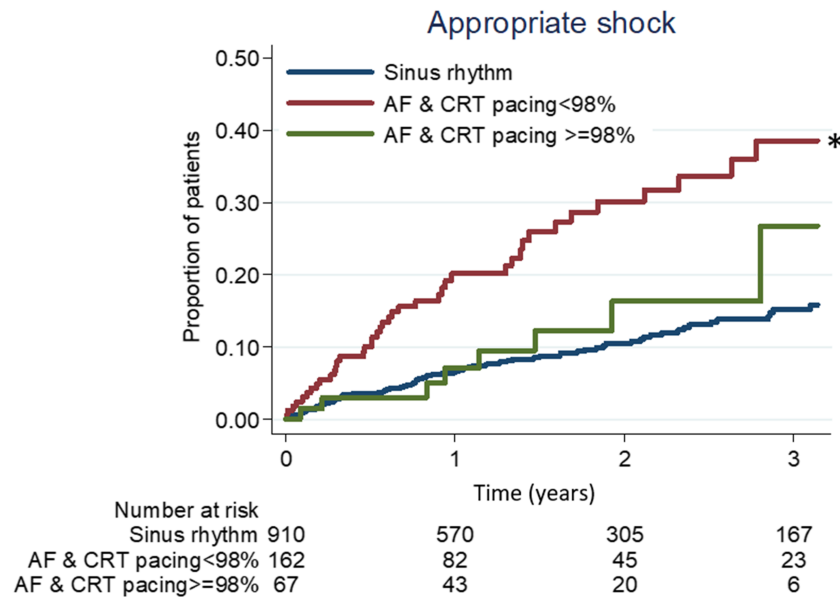
are the prevalent mode of death in HF patients with reduced ejection fraction in contrast to HF patients with preserved ejection fraction,[10] our finding may explain the uncertain results obtained in past randomized trials in CRT patients with permanent AF and implantable defibrillators[6]: if suboptimal CRT% is delivered, the contribution to prevention of ventricular arrhythmias from CRT is lost, but arrhythmic death is still suppressed by automatic defibrillation; conversely, when adequate CRT% is ensured, prevention of ventricular arrhythmias (and consequent reduction of shock deliveries and their negative effects on survival and quality of life) add to the benefit of ventricular remodelling and pump function recovery.

The 98% cut-off value for adequate CRT% has already been established in previous analyses.[9,15] Consistently with other real-world data,[16] the median CRT% was 96% in the AF group of our cohort, significantly lower than in the SR group. This finding confirms that there is still room for improvement. In a previous large observational study, Gasparini et al.[8] had shown similar outcomes for CRT between patients in sinus rhythm and patients with permanent AF undergoing atrioventricular node ablation to ensure 100% CRT. Unlike our analysis, this study found a significantly lower survival even in early follow-up period in the group of patients with permanent AF treated with rate-slowing drugs. However, the 30% of devices without defibrillation function and the CRT% of 87% achieved in this group, which is remarkably lower than in our cohort, likely explain higher mortality and lend support to the central importance of adequate CRT%. Therefore, the need of achieving adequate CRT% in patients with AF is even

stronger if physicians do not opt for defibrillation back-up during CRT system implantation.

According to current guidelines, medical treatment must be optimized before CRT implantation regardless of pacing therapy. In our routine-care cohort, we observed a higher median basic pacing rate in the AF group compared with the SR group (70 vs. 60 b.p.m.). The difference is clearly related to an attempt to maximize the CRT%, but it is probably responsible for higher mean heart rate found in the AF group despite similar rate-slowing drug therapy. The use of rate-responsiveness was more frequent in the AF group compared with the SR group (67.3% vs 19.9%), but the effect on mean heart rate was negligible, suggesting that rate-responsive sensors are unable to modulate heart rate effectively in HF patients who are nearly or totally inactive.

In the AF group, sinus rhythm recovery occurred in 10% of patients, in line with a previous observation[17] and more frequently than permanent AF developed in the SR group. Ventricular remodelling may be at the origin of the sinus rhythm restoration and could facilitate a rhythm control strategy.[18] Recently, a high rate of sinus rhythm conversion and maintenance was reported in a cohort of 328 CRT patients, 44% of whom were found in sinus rhythm at 5 year follow-up despite long-lasting persistent AF in all patients at the time of device implantation.[19] These data raise the question of whether it is appropriate to implant the atrial lead despite overt permanent AF at CRT implantation. Assessing whether the risk of complications related to an apparently useless lead is balanced by the chance of spontaneous sinus rhythm recovery, may not be an easy task. From this perspective, another

option worth considering is a recently introduced CRT system based on a single-pass defibrillator lead with a floating atrial dipole,[20,21] which may ensure immediate atrial tracking in case of unexpected sinus rhythm recovery.

Limitations

This is a retrospective analysis with well-known limitations associated with selection biases. However, the use of inverse-probability PS in the analysis allowed to reduce the effects of confounders in the study group comparisons. The observational design is a major strength, as data were generated in ordinary practice and results reflect common attitudes of clinicians. Follow-up data were retrieved remotely from devices which ensured robust consistency of device data relative to study endpoints (device diagnostics, delivered shocks, heart rhythm, and survival). However, changes in medical therapy during follow-up, hospitalizations in other clinics, or other surgical or medical procedures, including AF or atrio-ventricular node ablation, could not be tracked with the same efficiency. Finally, fusion or pseudofusion beats may have caused an overestimation of actual CRT% values.[22]

Conclusions

In a multicentre registry of routine remote monitoring data from HF patients with CRT-D devices, survival of patients with permanent AF did not differ from survival of patients in sinus rhythm. However, the incidence of appropriate shocks for ventricular arrhythmias was significantly higher in the AF subgroup with suboptimal CRT%. The rate of spontaneous sinus rhythm recovery was nearly twice higher than the rate of permanent AF development in SR patients. These findings confirm the antiarrhythmic effect of CRT and reinforce the recommendation of careful rate control in AF patients undergoing CRT implantation.

Conflict of interest

D.G. and A.G. are employees of BIOTRONIK Italia. All the remaining authors have no conflicts of interest to disclose.

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