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Device-Detected Atrial Tachyarrhythmias Predict Adverse Outcome in Real-World Patients With Implantable Biventricular Defibrillators

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Objectives The purpose of this analysis was to evaluate the correlation between atrial tachycardia (AT) or atrial fibrillation (AF) and clinical outcomes in heart failure (HF) patients implanted with a cardiac resynchronization therapy defibrillator (CRT-D).

Background In HF patients, AT and AF have high prevalence and are associated with compromised hemodynamic function.

Methods Forty-four Italian cardiological centers followed up 1,193 patients who received a CRT-D according to current guidelines for advanced HF, New York Heart Association functional class ≥II, left ventricular ejection fraction ≤35%, and QRS complex ≥120 ms. All patients were in sinus rhythm at implant.

Results During a median follow-up period of 13 months, AT/AF >10 min occurred in 361 of 1,193 (30%) patients. The composite end point (deaths or HF hospitalizations) occurred in 174 of 1,193 (14.6%). Multivariate time-dependent Cox regression analyses showed that composite end point risk was higher among patients with device-detected AT/AF (hazard ratio [HR]: 2.16, p = 0.032), New York Heart Association functional class III or IV compared with II (HR: 2.09, p = 0.002), and absence of beta-blockers (HR: 1.36, p = 0.036). Furthermore, the composite end point risk was inversely associated with left ventricular ejection fraction (HR: 1.04, p = 0.045), increasing by a factor of 4% for each 1% decrease in left ventricular ejection fraction.

Conclusions In HF patients with CRT-D, device-detected AT/AF is associated with a worse prognosis. Continuous device diagnostics monitoring and Web-based alerts may inform the physician of AT/AF occurrences and identify patients at risk of cardiac deterioration or patients with suboptimal rate or rhythm control. (Italian ClinicalService Project; NCT01007474) (J Am Coll Cardiol 2011;57:167–72) © 2011 by the American College of Cardiology Foundation

Among chronic heart failure (HF) patients, atrial tachycardia (AT) or atrial fibrillation (AF) are common comorbidities and are associated with a worse prognosis (1–3). For patients with HF, systolic dysfunction and cardiac dyssynchrony, cardiac resynchronization therapy (CRT), through biventricular pacing, reduces the risk of death, reduces complications, and improves symptoms and quality of life (4,5). Benefits of CRT have also been demonstrated in patients with AT/AF (6,7).

Only a few studies have evaluated the incidence and clinical consequences of AT/AF in HF patients with CRT pacemakers (8) or CRT implantable cardioverter-defibrillators (CRT-D) (9). Device diagnostics allows a continuous monitoring of cardiac arrhythmias and an accurate evaluation of AT/AF occurrence and duration. The aim

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Abbreviations and Acronyms

AF = atrial fibrillation
AT = atrial tachycardia
BIVP% = biventricular pacing percentage
CI = confidence interval
CRT = cardiac resynchronization therapy
CRT-D = cardiac resynchronization therapy defibrillator
HF = heart failure
HR = hazard ratio
LVEF = left ventricular ejection fraction
NYHA = New York Heart Association

of our research was to characterize patients' AT/AF profiles, in terms of maximum AT/AF duration, and to evaluate the correlation between AT/AF and clinical outcomes, such as survival or HF hospitalizations, in a large population of patients with CRT-D.

Methods

Patient population. Patients were included consecutively by 44 cardiological centers that participate in the Italian ClinicalService Project, a national medical care project aiming to evaluate and improve the use of implantable cardiac devices in clinical practice. Each patient signed an informed consent approved by each site's institutional review board.

All patients received a CRT-D, according to current guidelines (10,11), namely, advanced HF (New York Heart Association [NYHA] functional class II, III, or IV), depressed left ventricular function (left ventricular ejection fraction [LVEF] ≤35%), and wide QRS complex (≥120 ms). A history of AT/AF was defined as ≥1 AT/AF episode, documented by electrocardiogram or Holter monitor, in the period preceding implantation. Patients with permanent AT/AF or treated by pulmonary vein AT/AF ablation were excluded from the analysis.

Follow-up and end points. In-hospital follow-up visits were scheduled according to each center's clinical practice. Patients' clinical management, such as treatment of AT/AF episodes, was performed according to expert cardiologists' discretion.

Information about clinical outcomes such as hospitalizations and deaths were collected during scheduled or unscheduled hospital visits, or by phone calls for patients who missed programmed visits.

The incidence and duration of AT/AF was derived by device data, which comprise the total time spent by the patient in AT/AF for each day of the follow-up period. The AT/AF detection and its sensitivity and specificity, in the CRT-D used, have been previously described (12). Patients were considered to have experienced AT/AF episodes if the device detected a cumulative AT/AF duration >10 min in a day, a cut-off duration recognized as appropriate to discard false detections (8). As a function of the duration of the longest AT/AF period, observed during the follow-up period, each patient was classified according to 5 AT/AF profiles, whose length was >10 min, >6 h, >24 h, >7 days, and >6 months; the first 3 cut-offs characterize different forms of paroxysmal AT/AF, whereas the last 2 mimic persistent and permanent AT/AF, respectively.

Biventricular pacing percentage (BIVP%) was estimated as the number of paced biventricular beats divided by the number of paced or sensed ventricular beats over given time periods; in particular, BIVP% was estimated both during the whole lifetime of the device and during AT/AF periods.

Device programming. The pacing mode was atrial-synchronous ventricular pacing. The automatic mode-switch feature was enabled in all patients to switch the pacing mode to a nonatrial tracking mode during AT/AF. The detection and therapy programming of the defibrillator was left to the clinical practice of each center.

Statistical analysis. Descriptive statistics were reported as mean and standard deviation for normally distributed continuous variables, or median with 25th and 75th percentiles in the case of skewed distribution. Categorical variables were reported as percentages. Comparisons of categorical variables were performed by means of the Fisher exact test or chi-square, as appropriate.

Survival analysis was performed by the Kaplan-Meier method, and the log-rank test was applied to evaluate differences between survival trends.

Hazard ratios (HRs) and their 95% confidence intervals (CIs) were computed by means of time-dependent Cox regression models, where AT/AF during follow-up was considered as a time-dependent covariate and baseline predictors as fixed covariates. After checking for collinearity, we included in the multivariate Cox models any baseline variable with $p < 0.05$ on univariate analysis, and age and sex regardless of their p values. For statistical analysis, Stata/SE version 11.0 for Windows (StataCorp LP, College Station, Texas) were used.

Results

The baseline characteristics of the 1,193 patients are shown in Table 1.

AT/AF type and incidence during follow-up. The median follow-up period was 13 months (25th and 75th percentile: 8 and 20 months). AT/AF lasting longer than 10 min occurred in 361 of 1,193 (30%) patients. Figure 1 shows the number of patient with AT/AF occurrence, as a function of their AT/AF profile. Among 882 patients with no previous history of AT/AF, 178 (20%) had a new-onset AT/AF.

Clinical outcomes. The incidences of the composite end point and its components—deaths and heart failure hospitalizations—are summarized in Table 2, for various patient subgroups identified as a function of AT/AF occurrence, duration, and type.

Table 3 shows results of multivariate time-dependent Cox regression analyses performed to evaluate predictors of death, HF hospitalizations and the composite end point. In the whole population, the median value of the lifetime BIVP% was 98% (25th and 75th percentiles: 95% and 99%).