ORIGINAL ARTICLE

# The burden of atrial fibrillation and its prognostic value in patients with dilated cardiomyopathy

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**KEY WORDS**
atrial fibrillation, dilated cardiomyopathy, outcomes, tachycardia-induced cardiomyopathy

**ABSTRACT**

**BACKGROUND** Atrial fibrillation (AF) is the most common arrhythmia in patients with dilated cardiomyopathy (DCM). However, the epidemiology as well as clinical and prognostic significance of AF in DCM are poorly defined.

**AIMS** We aimed to assess the impact and prognostic value of AF in DCM as well as to investigate the concept of AF-induced DCM.

**METHODS** Hospital records of 285 patients with DCM from 2012 to 2018 with follow-up were analyzed.

**RESULTS** Atrial fibrillation was present in 89 patients (31%). They were older, more frequently male, had higher body mass index, New York Heart Association class, heart rate (HR), creatinine levels, and larger atria (all $P$ <0.05) than patients without AF. During follow-up (mean [SD], 35 [24] months), death occurred in 20 of the 82 available patients with AF and 22 of the 188 patients without AF (24% and 12%, respectively; $P$ = 0.007). Atrial fibrillation was independently associated with a worse outcome (hazard ratio, 2.4; 95% CI, 1.3–4.3) and was found to be the major cause of DCM in 21 patients (24%). The diagnostic accuracy of the most optimal predictive model for AF-induced DCM was 0.935 (95% CI, 0.903–0.967). Despite numerical differences, survival was similar in DCM patients with and without AF ($P$ = 0.15).

**CONCLUSIONS** Almost one-third of patients with DCM had AF. Most of the parameters analyzed differed between patients with and without AF, and AF was found to be an independent prognostic factor of DCM. One-fourth of patients with DCM and AF met the diagnostic criteria for AF-induced DCM.

**INTRODUCTION** Atrial fibrillation (AF) is the most common chronic arrhythmia in heart failure (HF), with an estimated prevalence of approximately 30% to 40%.[1-3] Indeed, AF and HF often coexist, with the presence of one increasing the risk of the other. Moreover, AF worsens the clinical course of HF, which leads to a higher risk of stroke and cognitive impairment, exacerbation of HF symptoms, and more complex management.[4,5] Apart from rhythm or rate control strategy, the vast majority of AF patients require prolonged, or even lifelong, anticoagulation. The introduction of non–vitamin K antagonist oral anticoagulants has greatly improved patient safety and compliance.[6] Nonetheless, the prognostic significance of AF in HF is uncertain.[7-11] Atrial fibrillation is frequently observed independently of HF etiology, whether ischemic or nonischemic, including dilated cardiomyopathy (DCM). The Eurobservational Research Programme (EORP), the largest registry of the European Society of Cardiology (ESC), reported the prevalence of AF in DCM to reach 28%.[12] However, there have been few studies focusing solely on AF in DCM.[13-17]

Tachycardia-induced cardiomyopathy (TIC) is a broad term for a typical phenotype of DCM, characterized by diverse tachyarrhythmias, including supraventricular arrhythmias (such as AF) and ventricular arrhythmias.[18,19] Considering

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**WHAT'S NEW?**

For the first time, atrial fibrillation (AF) is reported to be an independent predictor of all-cause mortality and a composite endpoint in a large cohort of patients with dilated cardiomyopathy (DCM). In almost one-fourth of patients with DCM and concomitant AF, AF was diagnosed to be the main cause of DCM. The clinical characteristics of patients with AF-induced DCM significantly differed from that of patients with concomitant AF. A diagnostic algorithm for AF-induced DCM was developed.

that AF is the most common chronic arrhythmia in HF and other cardiomyopathies, its role as a primary factor in DCM should not be undermined. Prolonged and uncontrolled atrial tachyarrhythmia results in morphological and functional myocyte impairment and inflammation.[20] This is especially the case when prolonged and uncontrolled (or poorly controlled) tachycardia in the form of AF may become the primary cause of DCM (ie, AF-induced DCM). Therefore, the aim of this study was to assess the clinical, echocardiographic, and laboratory profile of patients with DCM, with and without AF. Furthermore, we investigated the prognostic role of AF in DCM as well as the concept of TIC, particularly AF-induced DCM.

## METHODS

### Study population and protocol

Between 2012 and 2018, we retrospectively analyzed 285 consecutive outpatients and inpatients with DCM, who underwent a detailed diagnostic workup: clinical evaluation, blood tests (including N-terminal fragment of the prohormone brain natriuretic peptide [NT-proBNP], high-sensitivity troponin T, hemoglobin, and creatinine levels), electrocardiogram (ECG), echocardiography, and coronary angiography or computed tomography coronary angiography. In addition, some patients underwent magnetic resonance imaging, endomyocardial biopsy, and right-heart catheterization.[21,22] The diagnosis of DCM was established in accordance with the current ESC guidelines, based on: 1) the presence of left ventricular (LV) dilation and impaired LV systolic function (ejection fraction [EF] <45%) on echocardiography, and 2) the exclusion of significant coronary artery disease, arterial hypertension, congenital heart disease, and primary heart valvular disease.[21,23] Patients aged 18 to 70 years with a confirmed diagnosis of DCM and all necessary data were included in the analysis. The study protocol complied with the Declaration of Helsinki.

### Diagnosis of atrial fibrillation and atrial fibrillation–induced dilated cardiomyopathy

Atrial fibrillation was diagnosed according to the current 2016 ESC guidelines.[3] In brief, patients were diagnosed with AF if they fulfilled any of the following criteria: 1) AF pattern on resting 12-lead ECG; 2) documented history of AF, such as previous AF on ECG, in-hospital diagnosis of AF during cardiac implantable electronic device interrogation, or any record of AF ablation; and 3) AF episodes during 48-hour Holter monitoring (Spacelabs Healthcare, Reynolds Medical, Lifecard CF, Snoqualmie, Washington, United States).

The diagnosis of AF-induced DCM was a staged process and was established in line with current practices.[18,24,25] Briefly, it was based on: 1) the presence of fast ventricular rates due to incessant AF (a heart rate [HR] ≥110 bpm at least 90% of the monitoring period); 2) the exclusion of DCM of other etiologies, such as toxic, inflammatory, or familial DCM; and 3) the absence of organic pathology on routine echocardiography or cardiac magnetic resonance.[19,22]

### Definitions of endpoints

The primary endpoint was all-cause mortality, while the composite endpoint included all-cause mortality, urgent heart transplantation, and mechanical circulatory support. Information on the status of patients was obtained from hospital records, outpatient clinics, and via telephone contact.

### Statistical analysis

All parameters were presented as mean (SD) or counts (percentages), as appropriate. All variables were tested for normal distribution with the Shapiro–Wilk test. Continuous parameters were compared with the *t* test if data distribution was normal or with the Mann–Whitney test otherwise. The $\chi^2$ test was used to compare qualitative parameters. The impact of all the analyzed parameters on the presence of AF and AF-induced DCM was assessed with logistic regression models. The most optimal predictive models were established using a backward elimination method. The areas under the receiver operating curve were calculated to assess the validity of the models. To establish the relationship between AF and the long-term outcome, curves were plotted using the Kaplan–Meier method, and the log-rank test was applied. The Cox proportional hazards model was used to analyze multivariate predictors of endpoints. All results were considered significant at a *P* value of less than 0.05. The analysis was conducted with the Statistica package, version 13.0 (StatSoft, TIBCO Software Inc., Palo Alto, California, United States).

## RESULTS

### Baseline characteristics

The study group was divided into patients with AF (n = 89; 31%) and those without AF (n = 196; 69%). Paroxysmal AF was present in 26 patients (29% of the AF group). Patients with AF differed from those without AF in terms of age, sex, body mass index, HR, intensity of HF symptoms, creatinine levels, and echocardiographic parameters such as left and right atrial areas, right ventricular function, and the risk of pulmonary

hypertension (TABLE 1). However, the groups did not differ in terms of EF, LV end-diastolic diameter (LVEDD), right ventricular diameter, as well as NT-proBNP and troponin levels.

**Association between atrial fibrillation and clinical, echocardiographic, and laboratory parameters** Almost all parameters that diferred between the AF-present and -absent groups were found to be associated with AF in a univariate logistic regression analysis, whereas only HR and right atrial area were independently associated with AF in a multivariate analysis adjusted for age, body mass index, the New York Heart Association (NYHA) class, tricuspid annular plane systolic excursion, left atrial area, pulmonary arterial systolic pressure, and creatinine levels (TABLE 2).

**TABLE 1** Baseline parameters in patients with and without atrial fibrillation

| Parameter | AF (n = 89) | No AF (n = 196) | *P* value |
|---|---|---|---|
| Age, y | 58.6 (12) | 51.7 (4.1) | <0.001 |
| Male sex, n (%) | 77 (86.5) | 151 (77) | 0.049 |
| BMI, kg/m$^2$ | 29.0 (3.9) | 26.2 (5.9) | <0.001 |
| NYHA class | 2.7 (0.8) | 2.4 (1.2) | 0.006 |
| Symptom duration, mo | 65.8 (89.4) | 44.2 (61.2) | 0.06 |
| HR, bpm | 91.6 (25.9) | 74.7 (14.1) | <0.001 |
| QRS duration, ms | 116.9 (31.8) | 123.1 (41.2) | 0.47 |
| Diabetes mellitus, n (%) | 24 (27) | 44 (22.5) | 0.4 |
| Hyperlipidemia, n (%) | 60 (68.2) | 118 (60.2) | 0.31 |
| Hypertension, n (%) | 49 (55.1) | 92 (47.0) | 0.09 |
| EF, % | 26.8 (9.9) | 26.4 (10.2) | 0.48 |
| LVEDD, mm | 66.2 (9.9) | 66.4 (10.2) | 0.81 |
| RVD, mm | 39.4 (8.8) | 36.8 (9.2) | 0.05 |
| TAPSE, mm | 16.5 (4.7) | 20 (10.4) | <0.001 |
| LAA, cm$^2$ | 33.1 (8.8) | 27.8 (7.7) | <0.001 |
| RAA, cm$^2$ | 27.1 (7.7) | 20.6 (7.3) | <0.001 |
| Moderate or severe MR, n (%) | 52 (58.4) | 99 (50.5) | 0.17 |
| PASP, mm Hg | 39.8 (5) | 35.1 (15.1) | 0.01 |
| Creatinine, µmol/l | 98.2 (36.4) | 91.2 (41.7) | <0.001 |
| hs-TnT, ng/ml | 1.77 (8.4) | 1.73 (12.1) | 0.39 |
| NT-proBNP, ng/ml | 3549.7 (5237.8) | 3865.9 (9098.2) | 0.12 |
| β-Blocker, n (%) | 87 (98.9) | 190 (97.4) | 0.53 |
| ACEI or ARB, n (%) | 72 (81.8) | 170 (84.6) | 0.14 |
| MRA, n (%) | 82 (93.2) | 174 (89.2) | 0.06 |
| Furosemide dose, mg/d | 44.9 (64.8) | 40.8 (55.1) | 0.99 |
| Anticoagulants, n (%) | 83 (93.3) | 29 (14.8) | <0.001 |
| Digoxin, n (%) | 44 (50) | 20 (10.3) | <0.001 |
| Amiodarone, n (%) | 21 (23.9) | 20 (10.3) | 0.007 |
| ICD and CRT-P / CRT-D, n (%) | 24 (27) | 23 (21.6) | 0.22 |

Data are presented as mean (SD) unless otherwise indicated.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BMI, body mass index; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; EF, ejection fraction; HR, heart rate; hs-TnT, high-sensitivity troponin T; ICD, implantable cardioverter-defibrillator; LAA, left atrial area; LVEDD, left ventricular end-diastolic diameter; MR, mitral regurgitation; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; PASP, pulmonary arterial systolic pressure; RAA, right atrial area; RVD, right ventricular basal diameter; TAPSE, tricuspid annular plane systolic excursion

**TABLE 2** Predictive value of clinical, echocardiographic, and laboratory parameters for the presence of atrial fibrillation in univariate and multivariate logistic regression analysis

| Parameter | Univariate | Multivariate |
|---|---|---|
| Age | 1.05 (1.03–1.08) | 1.08 (0.98–1.20) |
| BMI | 1.11 (1.03–1.19) | 1.04 (0.77–1.41) |
| NYHA class | 1.43 (1.06–1.93) | 0.42 (0.07–2.44) |
| HR | 1.05 (1.03–1.07) | 1.12 (1.01–1.23) |
| TAPSE | 0.89 (0.83–0.95) | 0.88 (0.63–1.21) |
| LAA | 1.09 (1.05–1.13) | 1.25 (0.99–1.59) |
| RAA | 1.12 (1.07–1.16) | 1.25 (1.01–1.54) |
| PASP | 1.02 (1.00–1.04) | 1.05 (0.95–1.16) |
| Creatinine | 1.00 (0.99–1.01) | 0.99 (0.97–1.02) |

Data are presented as odds ratio (95% CI).

Abbreviations: see TABLE 1

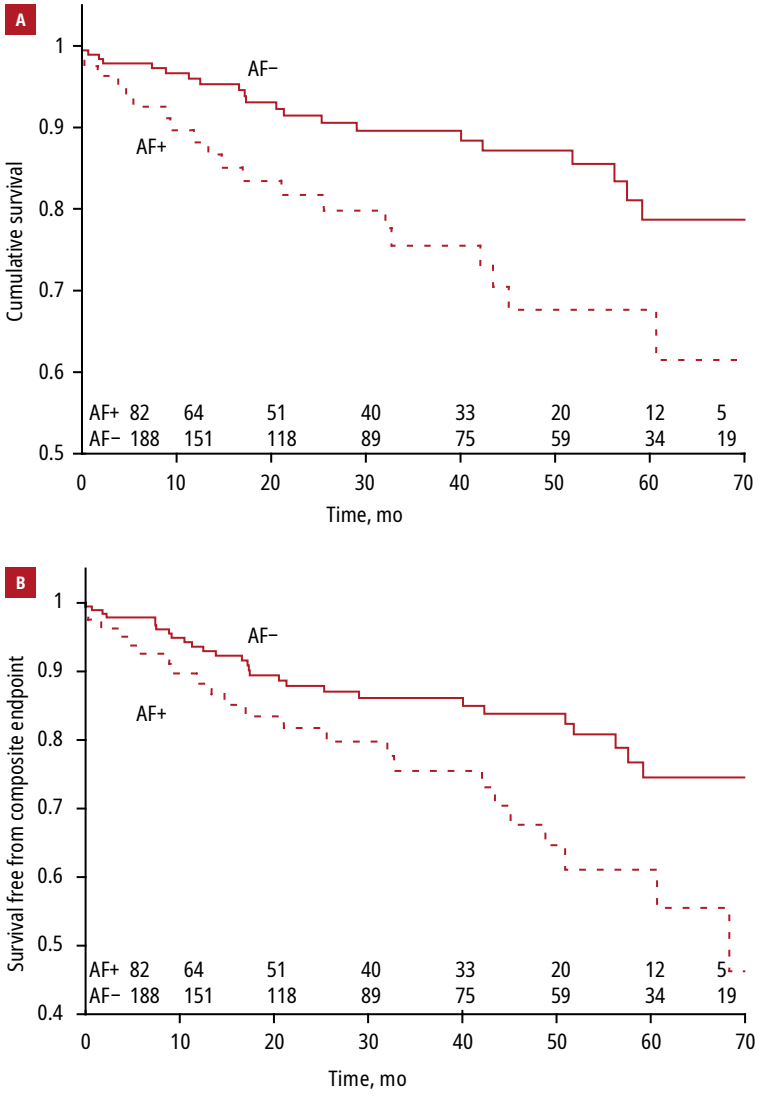


**FIGURE 1** Kaplan–Meier estimates for cumulative survival (**A**) and survival free from composite endpoint (**B**) by the presence of atrial fibrillation

Abbreviations: AF-, without atrial fibrillation; AF+, with atrial fibrillation

## Impact of atrial fibrillation on outcomes

During a mean (SD) follow-up of 33.9 (24) months, reliable information on health status was obtained for 270 patients (94.8%), including 82 (92.1%) with AF and 188 (95.9%) without AF ($P$ = 0.18). During the follow-up, 42 patients (16.2%) died and 54 (20%) reached the composite endpoint (FIGURE 1). In particular, death occurred in 20 patients (24.4%) with AF and 22 (11.7%) without AF (hazard ratio, 2.4; 95% CI, 1.3–4.3), while the composite endpoint was noted in 24 patients (29.3%) and 30 patients (16%), respectively (hazard ratio, 2; 95% CI, 1.2–3.5). In the Cox proportional hazards model, AF was independently associated with death and the composite endpoint (TABLE 3). Among the parameters related to the presence of AF, only the NYHA class and HR were independently correlated with all-cause mortality and the composite endpoint.

**Atrial fibrillation–induced dilated cardiomyopathy** Patients with AF were divided according to the etiology of DCM into those with AF-induced DCM (n = 21, 24%) and those with DCM of other or unknown causes (n = 68, 76%). Patients with AF-induced DCM had a shorter duration of symptoms, lower NYHA class, higher HR, shorter QRS, smaller LVEDD, higher hemoglobin and low-density lipoprotein (LDL) cholesterol levels, and they required lower daily furosemide doses (TABLE 4). The predictive value of these parameters for AF-induced DCM was assessed. All of them were found to be significant predictors in the univariate analysis. Because QRS duration correlated with symptom duration ($R$ = 0.45), LVEDD ($R$ = 0.41), and daily furosemide dose ($R$ = 0.44), it was excluded from the multivariate regression model. Only symptom duration, NYHA class, and HR were found to be predictors in the multivariate analysis adjusted for daily furosemide dose as well as hemoglobin and LDL cholesterol levels (TABLE 5). The best logistic regression model included symptom duration (odds ratio [OR], 0.95; 95% CI, 0.91–0.99), NYHA class (OR, 0.163; 95% CI, 0.04–0.67), HR (OR, 1.08; 95% CI, 1.03–1.14), and hemoglobin levels (OR, 2.03; 95% CI, 0.96–4.26), with a diagnostic accuracy of 0.935 (95% CI, 0.903–0.967). Data are presented in FIGURE 2 and TABLE 5. During follow-up, death occurred in 2 of the 21 patients (9.5%) with AF-induced DCM and 19 of the 61 patients (31.2%) with DCM of other etiologies ($P$ = 0.15), while the composite endpoint was reached by 2 patients (9.5%) and 22 patients (36%), respectively ($P$ = 0.12).

## DISCUSSION

**Study findings** The main findings of the study can be summarized as follows. First, AF was present in almost one-third of

**TABLE 3** Multivariate predictors for outcomes

| Parameter | All-cause mortality | Composite endpoint |
|---|---|---|
| AF | 3.4 (1.57–7.44) | 2.68 (1.32–5.45) |
| Age | 0.99 (0.97–1.02) | 0.99 (0.97–1.02) |
| BMI | 0.95 (0.87–1.03) | 0.94 (0.87–1.02) |
| NYHA class | 1.60 (1.05–2.43) | 1.59 (1.09–2.33) |
| HR | 0.98 (0.96–1) | 0.98 (0.96–0.99) |
| TAPSE | 1.02 (0.93–1.11) | 1.02 (0.95–1.11) |
| LAA | 1.04 (0.99–1.09) | 1.04 (0.99–1.08) |
| RAA | 0.97 (0.92–1.03) | 0.98 (0.94–1.03) |
| PASP | 1.01 (0.97–1.04) | 1.01 (0.98–1.04) |
| Creatinine | 1 (0.99–1.01) | 1 (0.99–1.01) |

Data are presented as hazard ratio (95% CI).

Abbreviations: see TABLE 1

**TABLE 4** Comparison of patients with dilated cardiomyopathy with and without atrial fibrillation

| Parameter | AF-induced DCM (n = 21) | DCM with AF (n = 68) | *P* value |
|---|---|---|---|
| Age, y | 55.2 (9.6) | 59.8 (11.6) | 0.06 |
| Male sex, n (%) | 17 (80.9) | 60 (88.2) | 0.67 |
| Symptom duration, mo | 27.3 (29.8) | 91.5 (100) | 0.002 |
| NYHA class | 2.2 (0.9) | 2.9 (0.9) | 0.006 |
| HR, bpm | 91.6 (25.9) | 74.7 (14.1) | <0.001 |
| QRS duration, ms | 93.3 (19.9) | 121.7 (28.5) | <0.001 |
| EF, % | 28.4 (10.5) | 24.7 (9.4) | 0.19 |
| LVEDD, mm | 62.4 (7.2) | 70.0 (10) | 0.004 |
| RVD, mm | 37.2 (6.3) | 40.2 (9.4) | 0.27 |
| TAPSE, mm | 16.3 (5.2) | 16.5 (4.6) | 0.94 |
| LAA, $cm^2$ | 33.7 (7.8) | 34.3 (9.4) | 0.94 |
| RAA, $cm^2$ | 26.1 (6.3) | 28.4 (9.4) | 0.43 |
| Hemoglobin, g/dl | 14.8 (1) | 13.9 (2) | 0.05 |
| LDL-C, mmol/l | 3.5 (1.3) | 2.7 (1.1) | 0.02 |
| Creatinine, µmol/l | 94.1 (21.4) | 100.9 (45.4) | 0.74 |
| hs-TnT, ng/ml | 0.036 (0.053) | 0.051 (0.095) | 0.79 |
| NT-proBNP, ng/ml | 2776.0 (2974.4) | 4187.1 (6357.2) | 0.19 |
| Statins, n (%) | 9 (42.9) | 29 (42.6) | 0.97 |
| Furosemide dose, mg/d | 14.7 (30.4) | 54.3 (66.8) | 0.01 |

Data are presented as mean (SD) unless otherwise indicated.

Abbreviations: DCM, dilated cardiomyopathy; LDL-C, low-density lipoprotein cholesterol; others, see TABLE 1

patients with DCM. Second, there were significant differences between DCM patients with and without AF. Third, AF was independently associated with the outcome of patients with DCM. Finally, one-fourth of DCM patients with AF met the criteria for the diagnosis of AF-induced DCM.

## Atrial fibrillation in dilated cardiomyopathy

According to the EORP registry on cardiomyopathies, of the 1260 patients with DCM, 353 (28%) were diagnosed with AF.[12] Thus, the current finding on consecutive patients with DCM showing the prevalence of AF of 31% is in line with that result.

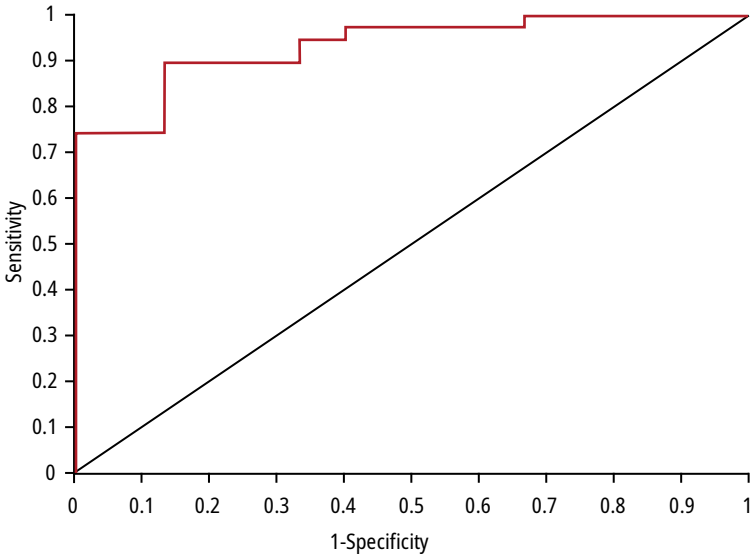


**FIGURE 2** Receiver operating characteristic curve for logistic regression model for the prediction of atrial fibrillation–induced dilated cardiomyopathy

It is widely accepted that the baseline characteristics differ between HF patients with and without AF. Typically, patients with AF are older, have more comorbidities, worse exercise capacity, and more advanced cardiac remodeling.[4,5] Similar to studies on broad populations of HF patients, we observed that our patients with DCM and AF were characterized by older age, higher NYHA class, faster ventricular rates (despite receiving therapy), and dilated atria; however, the left and right ventricular morphology and function as well as laboratory HF biomarkers (NT-proBNP and troponin) were not affected by the presence of AF.

We identified only 4 papers that investigated the characteristics of DCM patients with and without AF.[14-17] The studies largely differed in terms of the size of the study populations, definitions of AF (ie, in most studies, patients with paroxysmal AF were classified as the sinus-rhythm group), and analyzed parameters. Thus, it is difficult to draw any meaningful conclusions based on these data; nonetheless, the general trend indicates that DCM patients with AF are older, more frequently male, have larger atria, higher HR, and higher NT-proBNP levels. Interestingly, in every study, including ours, LV size and EF did not differ between groups. Unlike other authors, we performed a search for independent predictors of AF. Based on the multivariate logistic regression analysis, we observed that only HR and right atrial area were independently associated with the presence of AF in DCM.

**Atrial fibrillation and outcomes in heart failure and dilated cardiomyopathy** Atrial fibrillation worsens clinical course, either alone or in combination with other cardiovascular diseases, such as coronary artery disease or HF.[7,9,10] Rapid and poorly controlled ventricular rates in AF further impair ventricular morphology and function, cause atrial dilation, diminish myocardial perfusion during diastole, and significantly increase the risk of thromboembolic complications, including stroke. Although a considerable body of evidence points towards increased mortality rates in patients with HF and AF, few studies reported similar survival between HF patients with and without AF.[7,8] However, AF was associated with increased mortality in HF patients with a broad range of EF in 2 randomized controlled trials, with modest hazard ratios ranging from 1.29 to 1.79. Still, AF patients were older and had more advanced HF.[1,11]

Of note, patients with DCM differ significantly from typical HF cohorts in terms of age, number of comorbidities, response to therapy, and the risk of reverse remodeling. Therefore,

**TABLE 5** Predictive value of clinical, echocardiographic, and laboratory parameters for atrial fibrillation–induced dilated cardiomyopathy in univariate and multivariate logistic regression

| Parameter | Univariate | Multivariate | Cutoff values (sensitivity / specificity) |
|---|---|---|---|
| Symptom duration | 0.98 (0.96–0.99) | 0.94 (0.88–1) | 30 months (71% / 75%) |
| NYHA class | 0.45 (0.25–0.83) | 0.055 (0.004–0.81) | Class 3 (70% / 70%) |
| HR | 1.05 (1.02–1.07) | 1.1 (1.02–1.2) | 110 bpm (established) |
| QRS duration | 0.95 (0.92–0.98) | 1.17 (0.98–1.76) | 110 ms (61% / 80%) |
| LVEDD | 0.90 (0.83–0.97) | 1.02 (0.79–1.3) | 64 mm (70% / 73%) |
| Hemoglobin | 1.45 (1.01–2.09) | 1.83 (0.7–4.8) | 14.4 g/dl (59% / 65%) |
| LDL-C | 1.75 (1.1–2.78) | 2.93 (0.40–21.3) | 3.3 mmol/l (74% / 58%) |
| Furosemide dose | 0.98 (0.96–0.99) | 0.98 (0.92–1.03) | 10 mg/d (60% / 74%) |

Data are presented as odds ratio (95% CI).

Abbreviations: see TABLES 1 and 4

any investigation of the associations between a clinical course, including hard endpoints, and AF in DCM is worthwhile. Currently, there are few data on outcomes for DCM patients with AF, and at present, no firm conclusions on the associations between AF and survival in DCM can be made. In the literature, there is only one study, by Aleksova et al,[13] that directly investigated the impact of AF on survival in 539 patients with DCM. The authors did not observe any differences in mortality between patients with and without AF. However, there are significant differences between our studies. First, Aleksova et al[13] excluded patients with paroxysmal AF from the group with AF, classifying them as patients with sinus rhythm. Second, their population of patients with AF was small (only 52 of the 539 patients [10%]), and this disproportion may have confounded the results of statistical analysis.

**Atrial fibrillation–induced dilated cardiomyopathy** Establishing the correct etiology of DCM is extremely challenging, and approximately one-third of patients are clinically misdiagnosed.[26,27] Among the various causes of DCM, TIC is an important entity. Although there is lack of robust data, it seems that AF is the most frequent cause of TIC, with the prevalence ranging from 15% to 50%.[28,29] Chronic and rapid ventricular rate during AF causes deleterious atrial and ventricular remodeling, which eventually leads to the DCM phenotype. Restoration of the sinus rhythm and/or appropriate rate control may at least slow down or even reverse the process of cardiac remodeling.[28,29] A rapid HR may be an alarming sign for patients, who may then seek medical help earlier. This might explain the shorter duration of symptoms, a less advanced NYHA class, shorter QRS, and smaller LV cavity in our cohort of patients with AF-induced DCM. It has frequently been highlighted that the diagnostic criteria for AF-induced DCM are imperfect, and physicians struggle to establish the correct diagnosis of DCM on a daily basis.[18,19] Therefore, based on these results, we attempted to develop a diagnostic algorithm for AF-induced DCM. The initial conditions of the model are as follows: the presence of uncontrolled AF (HR >110 bpm) and the exclusion of other common causes of DCM.[22,23] As a result, we constructed a model that consists of symptom duration, assessment of HF severity (NYHA class, daily furosemide dose), indices of electrical and morphological remodeling (QRS, LVEDD), and basic biochemical parameters (hemoglobin and LDL cholesterol levels). The model revealed exceptionally high diagnostic accuracy (FIGURE 3). Although we are fully aware of its numerous shortcomings, such a comprehensive approach to diagnosing AF-induced DCM has not been previously published. No differences in the outcomes of interest were observed between patients with AF-induced DCM and DCM with concomitant AF; however, patients with AF-induced DCM experienced numerically fewer events, though this difference was nonsignificant.

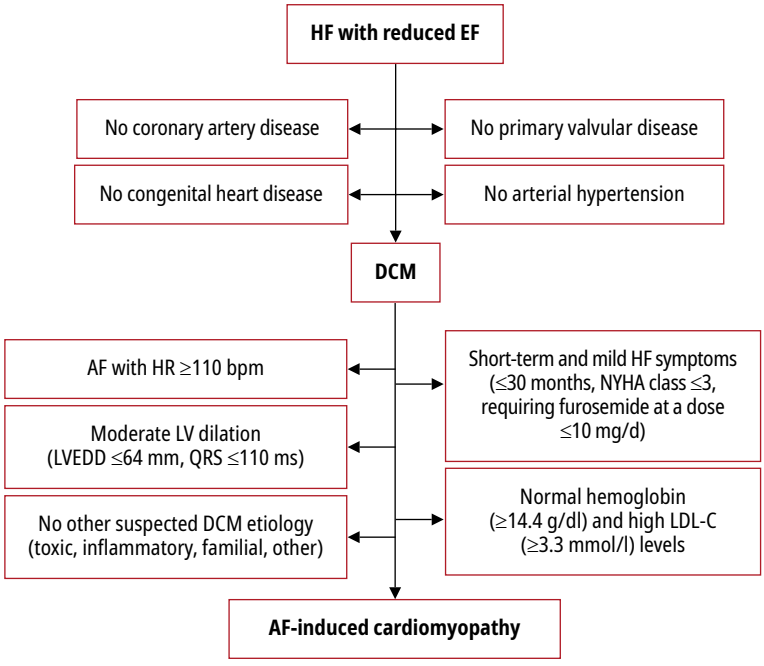


**FIGURE 3** Approach algorithm for a differential diagnosis of atrial fibrillation–induced dilated cardiomyopathy at baseline visit

Abbreviations: HF, heart failure; others, see TABLES 1 and 4

**Study limitations** Although the size of our population is the second largest in the literature investigating AF in patients with DCM, this was a single-center retrospective analysis. We followed the ESC guidelines for AF screening and diagnosis, including 12-lead ECG, 48-hour Holter monitoring, and ECG monitoring during hospitalization. Still, we cannot exclude that some patients with paroxysmal AF could have been missed due to silent AF.[30] The follow-up data were not available for 5% of the study population; however, the distribution of missing data was comparable between patients with and without AF. As there are no clear diagnostic criteria endorsed by the guidelines for TIC, including AF-induced DCM, we followed the most common approach, which may not be fully accurate in some cases.

**Conclusions** Almost one-third of unselected patients with DCM had AF. Various clinical, laboratory, and echocardiographic parameters clearly differentiated patients with AF from those without; however, only HR and right atrial area were found to be independent predictors. Atrial fibrillation was independently associated with outcomes of patients with DCM.

One-fourth of DCM patients with AF were diagnosed with AF-induced DCM. Patients with AF-induced DCM significantly differed from those with DCM and concomitant AF. The prognostic model involving symptom duration, a NYHA class, HR, and hemoglobin levels demonstrated high diagnostic accuracy for establishing AF-induced DCM.

## ARTICLE INFORMATION

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**CONFLICT OF INTEREST** None declared.



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