QRS Duration Is Associated With Atrial Fibrillation in Patients With Left Ventricular Dysfunction

Angel Leon, Emory University
Jonathan Langberg, Emory University
Mikhael El Chami, Emory University
David De Lurgio, Emory University
MF El-Chami, Emory University
C Brancato, Registrat Inc
DB Delurgio
H Bush, Registrat Inc
L Brosius, Registrat Inc

Journal Title: Clinical Cardiology
Volume: Volume 33, Number 3
Publisher: WILEY | 2010-03-01, Pages 132-138
Type of Work: Article
Publisher DOI: 10.1002/clc.20714
Permanent URL: https://pid.emory.edu/ark:/25593/vdz0k

Final published version: http://dx.doi.org/10.1002/clc.20714

Accessed April 29, 2020 6:52 AM EDT
QRS Duration Is Associated With Atrial Fibrillation in Patients With Left Ventricular Dysfunction

Mikhael F. El-Chami, MD; Candace Brancato, MS; Jonathan Langberg, MD; David B. Delurgio, MD; Heather Bush, PhD; Lynne Brosius, MS; Angel R. Leon, MD
Division of Cardiology, Section of Electrophysiology, Emory University School of Medicine, (El-Chami, Langberg, Delurgio, Leon), Atlanta, Georgia; Registrat, Inc., (Brancato, Bush, Brosius), Lexington, Kentucky; Department of Biostatistics, University of Kentucky (Bush), Lexington, Kentucky

ABSTRACT

Background: QRS duration (QRSd) is associated with higher mortality and morbidity in patients with left ventricular (LV) dysfunction. The association between QRSd and atrial fibrillation (AF) has not been studied in this patient population.

Objectives: To investigate the association between QRSd and AF in patients with LV dysfunction.

Methods: Data were obtained from the National Registry to Advance Heart Health (ADVANCENT) registry, a prospective multicenter registry of patients with left ventricular ejection fraction (LVEF) ≤40%. A total of 25,268 patients from 106 centers in the United States, were enrolled between June 2003 and November 2004. Demographic and clinical characteristics of patients were collected from interviews and medical records.

Results: Mean age was 66.3 ± 13 years, 71.5% were males, and 81.9% were white. A total of 14,452 (57.8%) patients had a QRSd <120 ms, 5,304 (21.2%) had a QRSd between 120 and 150 ms, and 5,269 (21%) had a QRSd >150 ms. Atrial fibrillation occurred in 20.9%, 27.5%, and 35.5% of patients in the QRS groups, respectively (P < 0.0001). After adjusting for potential AF risk factors (age, gender, race, body mass index, hypertension, diabetes, renal failure, cancer, lung disease, New York Heart Association [NYHA] class, ejection fraction, etiology of cardiomyopathy) and the use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β-blockers, and lipid lowering drugs, QRS duration remained independently associated with AF (odds ratio: 1.20, 95% confidence interval: 1.14–1.25).

Conclusion: In this large cohort of patients, QRSd was strongly associated with AF and therefore may predict the occurrence of this arrhythmia in patients with LV dysfunction. This association persisted after adjusting for disease severity, comorbid conditions, and the use of medications known to be protective against AF.

No conflict of interest to report.

Introduction

Atrial fibrillation (AF) affects a significant percentage of patients with heart failure ranging from 5% in patients with New York Heart Association (NYHA) class I–II to 50% in patients with NYHA class IV. The annual incidence of new-onset AF in congestive heart failure (CHF) patients is 2% to 5%. This association between AF and CHF is multifactorial. First, several risk factors for CHF such as age, coronary artery disease (CAD), hypertension (HTN), diabetes mellitus (DM), and obstructive sleep apnea (OSA) are also risk factors for AF. Second, structural, hemodynamic, and electrophysiologic changes seen in CHF such as left atrium enlargement, elevated left atrial pressure, and slow heterogeneous intra-atrial conduction predispose to AF. Interestingly, the mere occurrence of AF in this patient population carries an increased risk of morbidity and mortality. QRS duration (QRSd) is also associated with an increased mortality and morbidity in patients with CHF. A wide QRS in this setting is associated with more myocardial disease and worse left ventricular function (LVEF). We hypothesized that CHF patients with wider QRS will have a higher prevalence of AF.

Methods

Study Population

Patients enrolled in the National Registry to Advance Heart Health (ADVANCENT) registry between June 2003 and November 2004 were included in the study. ADVANCENT is a prospective multicenter, observational registry designed to collect and report data on the histories, diagnostics, and therapies of patients with LV dysfunction (LVEF ≤40%). This registry is sponsored by Boston Scientific, Inc and is managed independently by Registrat, Inc. The registry collects detailed medical and demographic information on enrolled subjects. At the time of data analysis, 25,268 patients from 106 centers in the United States had been enrolled. This registry has served as the source of several publications related to AF but none have addressed the association between QRSd and the risk of this arrhythmia.

Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20714 © 2010 Wiley Periodicals, Inc.

Received: September 27, 2009
Accepted with revision: November 2, 2009
Baseline Data Collection

All patients enrolled in this registry were interviewed by medical personnel (physician, nurse practitioner, or physician assistant). Additional data were obtained from reviewing medical records. Demographic information, details on heart disease and its severity, the presence of comorbidities, and cardiovascular medication were collected. Data on QRSd was available from the index ECG on 25,025 of 25,268 patients (99%).

Statistical Analysis

Patients were divided into 3 different QRS duration groups: the narrow QRS group (QRSd <120 ms), the intermediate QRS group (120 ≤ QRSd ≤ 150 ms), and the wide QRS group (QRSd >150 ms). Continuous variables were reported using the mean and standard deviation and categorical variables were reported using counts and percentages. Cochran-Mantel-Haenszel statistics were used for categorical data and 1-way analysis of variance (ANOVA) was used for continuous data. In addition, bivariate analyses were performed to study the effect of QRSd on AF prevalence in the different NYHA classes and in 3 different LVEF groups (<20%, 20% ≤ EF ≤ 30%, EF >30%). A multivariable logistic regression (MLR) model was constructed to assess the independent impact of QRSd on the prevalence of AF. After accounting for missing values, there were 23,840 (95%) cases completeness observations used in the MLR model. The following statistically significant variables were included in the model: age, gender, race, hypertension, renal failure, cancer, lung disease, LVEF, angiotensin receptor blocker (ARB) use, lipid lowering agent use (statins), nonischemic cardiomyopathy, valvular heart disease, body mass index (BMI), and New York Heart Association (NYHA) class. Nonstatistically significant variables that were also used in the model included: presence of diabetes, β-blocker, and angiotensin-converting enzyme inhibitor (ACEI) use. Age and LVEF were considered continuous variables and NYHA class was considered an ordinal variable. Gender, race, etiology of cardiomyopathy, active cancer, renal failure, DM, and the use of medications known to be protective against AF (ACEI, ARB, β-blockers, and statins) were considered categorical variables. The analysis was performed with QRSd as a categorical variable (ie, comparing QRSd <120 to QRSd >150 and 120 ≤ QRSd ≤ 150 ms to QRSd >150 ms) and as an ordinal variable (treating QRSd as groups: narrow, intermediate, and wide).

All analyses were completed using SAS version 9.2 and a significance level of 0.05 was used for all statistical tests.

Results

Cohort Characteristics

The characteristics of the entire cohort are summarized in Table 1. The mean age was 66.3 ± 13 years. The mean EF was 31.1% ± 10.47%. Coronary artery disease was the most common cause of LV dysfunction (66%). Slightly less than one-third of patients (27.5%) had moderate to severe CHF (NYHA class III or IV); 58% of patients had a QRSd <120 ms, while the remainder of patients were divided equally among the intermediate and wide QRSd groups (21% for each of those groups).

The characteristics of patients in the different QRSd groups are shown in Table 2. Patients with wide QRS were older (P < 0.0001), more likely to be white men (P < 0.0001), more likely to have lower EF (P < 0.0001), and more severe heart failure (P < 0.0001), but less likely to have HTN (P = 0.0066) as compared to the intermediate and narrow QRS groups. Also, this group was less likely to have CAD (P < 0.0001) as the cause of their cardiomyopathy (63.3%) as compared to the intermediate QRS group (67.3%) and the narrow QRS group (66.3%). Patients with wide QRS were also more likely to have valvular heart disease (P = 0.0002). In addition, the groups with intermediate and wide QRS were more likely to have certain comorbidities such as lung disease (P = 0.0074), renal failure (P < 0.0001), and cancer (P = 0.0004) as compared to the narrow QRS group.

The overall use of heart failure medications in the cohort was as follows: 63.4% were on an ACEI, 18.3% were on ARBs, and 79.1% were on β-blockers. There was no difference in the use of ACEI or β-blockers among the 3 groups (Table 2). However, the wide QRS group was more likely to be on an ARB (P = 0.0009), but less likely to be treated with a statin (P = 0.0014) as compared to the intermediate QRS and narrow QRS groups (Table 2).

Atrial Fibrillation Prevalence

One-quarter of patients (25.5%) had AF. Atrial fibrillation was paroxysmal in 46.4%, persistent in 41.1%, and of unknown pattern in 12.5% of patients. Atrial fibrillation was present in 20.9% of patients with QRSd <120 ms, 27.5% of patients in the intermediate QRSd group, and 35.5% of patients in...
Table 2. Cohort Characteristics in Groups of QRS Duration

<table>
<thead>
<tr>
<th>Parameters</th>
<th>QRSd &lt; 120 (n = 14,452)</th>
<th>120 ≤ QRSd ≤ 150 (n = 5,304)</th>
<th>QRSd &gt; 150 (n = 5,269)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (±SD) yrs</td>
<td>64 (13.54)</td>
<td>68.8 (12.06)</td>
<td>70.3 (11.66)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male (%)</td>
<td>10,138 (70.1%)</td>
<td>3774 (71.2%)</td>
<td>3970 (75.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>White (%)</td>
<td>11,491 (79.5%)</td>
<td>4501 (84.9%)</td>
<td>4507 (85.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>EF (±SD) (%)</td>
<td>32.8 (10.49)</td>
<td>29.7 (9.95)</td>
<td>27.7 (9.93)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nonischemic (%)</td>
<td>4872 (33.7%)</td>
<td>1737 (32.7%)</td>
<td>1934 (36.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nonischemic/Valvular (%)</td>
<td>545 (3.8%)</td>
<td>251 (4.7%)</td>
<td>258 (4.9%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>NYHA class III-IV (%)</td>
<td>3224 (22.3%)</td>
<td>1602 (30.2%)</td>
<td>2000 (37.9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HTN (%)</td>
<td>10,528 (72.8%)</td>
<td>3865 (72.9%)</td>
<td>3723 (70.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DM (%)</td>
<td>4574 (31.6%)</td>
<td>1685 (31.8%)</td>
<td>1587 (30.1%)</td>
<td>0.0095</td>
</tr>
<tr>
<td>Lung disease (%)</td>
<td>2389 (16.5%)</td>
<td>977 (18.4%)</td>
<td>896 (17.0%)</td>
<td>0.0074</td>
</tr>
<tr>
<td>Renal failure (%)</td>
<td>812 (5.6%)</td>
<td>355 (6.3%)</td>
<td>394 (7.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cancer (%)</td>
<td>1544 (10.7%)</td>
<td>660 (12.4%)</td>
<td>637 (12.1%)</td>
<td>0.0004</td>
</tr>
<tr>
<td>AF (%)</td>
<td>3022 (20.9%)</td>
<td>1461 (27.5%)</td>
<td>1872 (35.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ACEI</td>
<td>9216 (63.8%)</td>
<td>3354 (63.2%)</td>
<td>3306 (62.7%)</td>
<td>0.3921</td>
</tr>
<tr>
<td>ARB</td>
<td>2583 (17.9%)</td>
<td>937 (17.7%)</td>
<td>1057 (20.1%)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Statins</td>
<td>9736 (67.4%)</td>
<td>3583 (67.6%)</td>
<td>3413 (64.8%)</td>
<td>0.0014</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>11,472 (79.4%)</td>
<td>4774 (87.8%)</td>
<td>4553 (88.8%)</td>
<td>0.4824</td>
</tr>
</tbody>
</table>

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; DM, diabetes mellitus; EF, ejection fraction; HTN, hypertension; NYHA, New York Heart Association.

the wide QRSd group (P < 0.0001). Also, AF prevalence increased with CHF severity, increasing from 21% to 25%, 30%, and 34% for NYHA classes I to IV, respectively (P < 0.0001). In addition, within each NYHA class there was an association found between QRSd and AF prevalence (Figure 1) (P < 0.0001 for class I, class II, and class III, P = 0.0014 for class IV). For example, AF occurred in 18% of NYHA class I patients with narrow QRS and in 31% of NYHA class I patients with wide QRS. Similarly, within 3 different EF groups (<20%, 20% ≤ EF ≤ 30%, and EF >30%) QRSd was associated with AF prevalence (Figure 2).

Multivariable Regression Analysis

There are several factors that co-vary with QRSd including EF, NYHA class, age, gender, race, etiology of cardiomyopathy, and comorbidities (HTN, CAD, DM, chronic obstructive pulmonary disease [COPD], renal failure, malignancy). These factors are also likely to influence the prevalence of AF. To better determine the independent effect of QRSd on AF prevalence, a multivariate analysis accounting for all potential AF risk factors was constructed (Table 3). The model accounted for demographic risk factors (age, gender, race, BMI, height), comorbidities (HTN, COPD, DM, renal failure, cancer), heart disease etiology and severity (nonischemic cardiomyopathy, valvular heart disease, NYHA class, EF), and medications known to be protective against AF (statins, ACEI, ARB, and β-blockers). Even after accounting for all these confounders, QRSd remained associated with AF (odds ratio [OR]: 0.637, 95% confidence interval [CI]: 0.59–0.688 for QRSd <120 vs QRSd >150 and OR: 0.757 95% CI: 0.692–0.827) when comparing the intermediate QRS group to the wide QRS group. When QRSd was used as an ordinal variable, it remained an independent risk factor for AF (OR: 1.20, 95% CI: 1.14–1.25) which indicates that the estimated odds of AF increases by 20.0% as QRSd increases from one group to the next (ie, 20.0% increase in AF prevalence between narrow and intermediate and a 40.0% increase in AF prevalence when comparing narrow to wide QRSd).
Figure 1. Atrial fibrillation frequency according to NYHA class and QRSd. Abbreviations: NYHA, New York Heart Association; QRSd, QRS duration.

Figure 2. Atrial fibrillation frequency according to EF and QRSd. Abbreviations: EF, ejection fraction; QRSd, QRS duration.

Discussion

Comparison to Previous Registries and Reports

Several findings in this study mirror previous reports. The percentage of patients with QRSd > 120 ms in this cohort with LV dysfunction was 42%. Similarly, a post hoc analysis from the Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan (EVEREST) showed that 44.6% of patients had a QRSd > 120 ms.22 Overall, the prevalence of a QRSd > 120 ms in CHF patients averages 30% (14%–47%).21 Also, 21% of patients in the current study had a QRSd > 150 ms. This is comparable to other reports describing that 19% to 29% of CHF patients have a QRSd > 150 ms.

Table 3. Multivariate Analysis Showing the Effect of Different Factors on AF Prevalence

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>120 ≤ QRSd ≤ 150 vs QRSd &gt; 150</td>
<td>0.757a</td>
<td>0.692–0.827</td>
</tr>
<tr>
<td>QRSd &lt; 120 vs QRSd &gt; 150</td>
<td>0.632a</td>
<td>0.59–0.688</td>
</tr>
<tr>
<td>Age</td>
<td>1.535a</td>
<td>1.489–1.582</td>
</tr>
<tr>
<td>Height</td>
<td>1.025a</td>
<td>1.021–1.029</td>
</tr>
<tr>
<td>Gender (female vs male)</td>
<td>0.962</td>
<td>0.876–1.057</td>
</tr>
<tr>
<td>Race (Black vs white)</td>
<td>0.606a</td>
<td>0.546–0.674</td>
</tr>
<tr>
<td>Hypertension (HTN vs no HTN)</td>
<td>1.063</td>
<td>0.99–1.141</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.897a</td>
<td>0.837–0.962</td>
</tr>
<tr>
<td>Renal failure</td>
<td>1.226a</td>
<td>1.082–1.39</td>
</tr>
<tr>
<td>Cancer</td>
<td>0.926</td>
<td>0.843–1.017</td>
</tr>
<tr>
<td>Lung disease</td>
<td>1.19a</td>
<td>1.033–1.212</td>
</tr>
<tr>
<td>LVEF</td>
<td>1.046a</td>
<td>1.014–1.079</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>0.874a</td>
<td>0.812–0.94</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>0.877a</td>
<td>0.816–0.944</td>
</tr>
<tr>
<td>ARB</td>
<td>0.915</td>
<td>0.835–1.003</td>
</tr>
<tr>
<td>Lipid lowering agent</td>
<td>0.684a</td>
<td>0.638–0.734</td>
</tr>
<tr>
<td>Nonischemic</td>
<td>1.321a</td>
<td>1.222–1.427</td>
</tr>
<tr>
<td>Nonischemic/valvular</td>
<td>1.786a</td>
<td>1.543–2.067</td>
</tr>
<tr>
<td>BMI</td>
<td>1.016a</td>
<td>1.01–1.021</td>
</tr>
<tr>
<td>NYHA (ordinal)</td>
<td>1.20a</td>
<td>1.14–1.25</td>
</tr>
</tbody>
</table>

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BMI, body mass index; EF, ejection fraction; HTN, hypertension; NYHA, New York Heart Association; OR, odds ratio; QRSd, QRS duration.

OR for QRSd is comparing: a. QRSd < 120 vs QRSd > 150. b. 120 ≤ QRSd ≤ 150 vs QRSd > 150. OR for age is per 10 years increment. OR for height is per 1 cm increase in height. OR for EF is per 10% increment. OR for BMI is per 1 unit increase in BMI. a Denotes statistically significant.

above 120 ms.32 Furthermore, Sandhu and Bahler noted that mean EF decreased from 41% to 29% and 25% as QRSd increased from <100 ms to 120 ms to 149 ms and >150 ms, respectively.32 Similarly, QRSd correlated with NYHA class.33,35 In more than 5000 outpatients with CHF, 32% of patients with complete left bundle branch block (LBBB) were in NYHA class III or IV as compared to 26% of patients with incomplete LBBB.34 Another study showed that the incidence of QRSd > 120 ms increased from 10% to 32% and 53% as NYHA class worsened from I to II and III, respectively.33
In the current study, more than 80% of the subjects were taking an ACEI or an ARB, and close to 80% were on a β-blocker. This compares favorably to a recently published report from the Acute Decompensated Heart Failure National Registry (ADHERE).  

Atrial fibrillation prevalence in this registry (25.5%) was comparable to AF prevalence in the ADHERE registry (30.9%). Previous reports have shown that AF prevalence in the setting of LV dysfunction varies with severity of CHF and that AF occurs in 4% of asymptomatic CHF patients. This prevalence increases to 10% to 26% in NYHA class II-III and 20% to 29% in NYHA class IV. Furthermore, it has been reported that up to 50% of NYHA class IV patients have AF. Our data show a higher prevalence of AF in patients with NYHA class I (21%). The lower AF prevalence in NYHA class I patients in the Studies of Left Ventricular Dysfunction (SOLVD) prevention and treatment trials may be due to a different system of classification: patients who had a history of AF but were in sinus rhythm at the time of randomization were considered to be in the sinus rhythm group. 

Furthermore, the multivariable analysis results revealed similar findings to previous reports. In our cohort, the odds of AF were less in nonwhite patients compared to white patients (OR: 0.63, 95% CI: 0.54–0.74) and there was a trend in women toward lower AF prevalence compared to men (OR: 0.96, 95% CI: 0.87–1.05). These findings are similar to previous reports. Other factors that were shown to be associated with higher AF prevalence in our cohort included age, BMI, and some comorbid conditions (lung disease and renal failure). These findings are in agreement with previous publications. 

In addition, therapy with neurohormonal modulators (ACEI, ARB, and β-blockers) and statins were protective against AF in this patient population. These findings are in agreement with previous publications. Surprisingly, DM was associated with lower odds of AF whereas hypertension showed a trend toward higher odds of AF that did not reach statistical significance. While HTN and DM are known risk factors for AF in the general population, our cohort had left ventricular dysfunction. Hence, factors that affect left atrial pressure, stretch, and fibrosis such as severity of heart failure or valvular disease and QRSd are possibly more important as determinants of AF. In fact, data from the Cardiovascular Heart Study support these findings. Diabetes mellitus was a risk factor for AF in the general population, but not in patients with cardiovascular disease.

Interpretation of Main Findings and Clinical Implication

QRSd is associated with lower EF and a worse NYHA class. Hence, the association between QRSd and AF seems evident. However, even after accounting for severity of heart failure, EF, and other covariates, a strong association persisted. QRSd is linked to the extent of ventricular fibrosis in patients with cardiomyopathy. It is possible that QRSd also reflects generalized myocardial fibrosis including atrial fibrosis in these patients providing the substrate for AF.

Results of the current study suggest that a simple test (an electrocardiogram) routinely ordered on patients with heart failure could be used to predict the risk of AF. The effect of QRSd on AF prevalence appears to be more potent than NYHA class or EF. For example, AF prevalence in patients with NYHA class I and wide QRS is 31%, a value that is higher than AF prevalence in patients with NYHA class IV and narrow QRS (26%; Figure 1). The effect of these 2 parameters on AF prevalence appears to be additive (Figure 1). Hence, QRSd can conceivably be used in association with other AF risk factors to predict the occurrence of AF in this patient population.

Study Limitations

Because the ADVANCE registry was not intended originally to assess the association between QRSd and AF, it is possible that some confounding variables that could affect this association have not been accounted for. For instance, left atrial size and OSA are 2 important AF risk factors that we did not account for. However, we did account for BMI that strongly correlates with the prevalence of OSA. In addition, we have included height in the multilinear regression model. The latter was found to correlate strongly with left atrial diameter in a subgroup of patients enrolled in the ADVANCE registry. Also, this registry did not include longitudinal data hence it is not possible to determine the association between QRSd and new development of AF.

On the other hand, the large number of patients, the extent and completeness of the data, and the agreement between this study and previous reports on the role of traditional AF risk factors make the conclusion drawn from this study robust and probably reproducible.

Conclusion

To our knowledge, this is the first report in the literature showing an association between QRSd and AF. In this study of more than 25 000 patients with LV dysfunction from more than 100 centers in the United States, QRSd was associated with AF. This association persisted after accounting for several known AF risk factors. Patients with wide QRS and LV dysfunction are at high risk of developing AF. This group of patients could be the subject of future studies addressing AF preventive strategies.

References


