Congestive Heart Failure and QRS Duration*

Establishing Prognosis Study

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Study objectives: There is a lack of epidemiologic information about duration of QRS complex in the general heart failure population. We sought to describe age, sex, and clinical subset specific prevalence of QRS prolongation in this population.

Methods: Data were abstracted from the Resource Utilization Among Congestive Heart Failure Study, which identified 29,686 patients with heart failure from a large, mixed-model managed-care organization during 1989 to 1999. A target population of 3,471 had echocardiographic data and ECG data obtained from automated sources during the first year of diagnosis. Systolic dysfunction was defined as heart failure plus a left ventricular ejection fraction < 45%.

Measurements and results: Among the heart failure population, 20.8% of the subjects had a QRS duration > 120 ms. A total of 425 men (24.7%) and 296 women (16.9%) had a prolonged QRS duration (p < 0.01). There was a linear relationship between increased QRS duration and decreased ejection fraction (p < 0.01). A prolonged QRS duration of 120 to 149 ms demonstrated increased mortality at 60 months (p = 0.001), when adjusted for age, sex, and race (p = 0.001). Systolic dysfunction was associated with graded increases in mortality across ascending levels of QRS prolongation.

Conclusions: Approximately 20% of a generalized heart failure population can be expected to have a prolonged QRS duration within the first year of diagnosis, suggesting that as many as 20% of patients with heart failure may be candidates for biventricular pacing.

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Key words: congestive heart failure; mortality; prevalence; prolonged QRS complex; systolic dysfunction

Abbreviations: CHF = congestive heart failure; CONQUEST = Congestive Heart Failure and QRS Duration: Establishing Prognosis; HFHS = Henry Ford Health System; ICD-9-CM = Ninth International Classification of Disease Clinical Modification; LBBB = left bundle-branch block; LVEF = left ventricular ejection fraction; RBBB = right bundle-branch block; REACH = Resource Utilization Among Congestive Heart Failure Study

Congestive heart failure (CHF) is one of the leading causes of morbidity and mortality in Western countries. As the population ages, its prevalence is rising despite improvements in medical therapies and surgical techniques. Many methods are available to determine prognostication in CHF patients, including peak oxygen uptake, left ventricular ejection fraction (LVEF), signal-averaged electrocardiography, and electrophysiologic testing. Deriving prognosis from an ECG is tempting, because the ECG is a relatively inexpensive, noninvasive, rapidly performed test that is commonly ordered. Several studie looking at the QRS duration in patients with CHF have found that a widened QRS indicates a worse prognosis. However, most of these studies were small, comprised of only 34 to 268

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patients. One large study (n = 3,654) analyzed baseline ECG data from the Vesnarinone Survival Trial and found that cumulative survival over 1 year decreased proportionally with widening QRS complex. The risk of the widest QRS group (> 220 ms) was five times greater than the narrowest group (< 90 ms). However, only heart failure patients with drug-resistant dilated cardiomyopathy (LVEF < 30%) were recruited. Consequently, these results cannot be generalized to the overall CHF population. Another study observed 2,263 patients with left ventricular dysfunction, without mention of age, sex, or race stratification. Clearly, analysis of a large community cohort of CHF patients, with both systolic and diastolic dysfunction for prognostication based on the QRS duration, is needed.

New electrophysiologic theories are increasingly being applied in hopes of treating CHF. Although no studies have been conducted regarding its effects in diastolic dysfunction, biventricular pacing can improve acute hemodynamics and interventricular dysynchrony in patients with dilated cardiomyopathy. Randomized clinical trials are ongoing to prospectively substantiate this concept. Furthermore, the QRS duration is a very important, if not the sole, parameter that accurately predicts successful biventricular pacing. If the QRS complex duration is related to survival, this population could be a potential target for biventricular pacing with justifiable hopes of improving clinical outcomes. Therefore, the Congestive Heart Failure and QRS Duration: Establishing Prognosis (CONQUEST) study analyzed a large, urban representative study population to define the prevalence of prolonged QRS duration among patients with heart failure and to determine its relation to all-cause mortality.

**Materials and Methods**

**Setting**

The target population was derived from the Resource Utilization Among Congestive Heart Failure (REACH) study, which has been recently reported. Briefly, Henry Ford Hospital is a 903-bed tertiary care center located in the Detroit metropolitan area and receives patients whose care is provided primarily within the Henry Ford Health System (HFHS), a vertically integrated, mixed-model managed-care organization that includes urban and suburban satellite clinics in Southeast Michigan. The CONQUEST study used data obtained from the REACH study, which identified 29,686 outpatient and inpatient CHF patients within HFHS between the years of 1989 and 1999. An index case of CHF was based on the following: (1) a minimum of two outpatient Ninth International Classification of Disease–Clinical Modification (ICD-9-CM) codes (428.XX, 398.91, 402.01, 402.11, 402.91, 404.00, 404.01, 404.03, 404.10, 404.11, 404.13, 404.90, 404.91, 404.93) for CHF; or (2) one inpatient hospitalization under diagnosis-related group 127 or 124 and one of the above ICD-9-CM codes for CHF in the principal position. Hospital admissions received diagnosis-related group and ICD-9-CM codes from professional coders that were subsequently approved by attending physicians. Outpatient encounters had ICD-9-CM codes assigned directly by the attending physician. The REACH database provided the vehicle by which cases of CHF were identified for the present study of patients.

**Data Management**

A subset of the REACH study identified 4,398 patients with CHF and two-dimensional M-mode echocardiography data obtained from electronically reported studies that were obtained during the first year of diagnosis. The target population was limited to 3,471 patients with an electronically documented ECG stored on the Medical User Systems for Electrocardiography (Marquette Electronics; Rochester, MI) system. All 3,471 patients had LVEFs, as calculated by Simpson’s rule or listed by visual estimate. An average value was obtained if the patient underwent more than one echocardiography study within the first year of diagnosis. These patients were thus classified as having systolic dysfunction based on the presence of CHF and an LVEF < 45%. Conversely, diastolic dysfunction heart failure was defined as the presence of CHF and an LVEF ≥ 45%. Prolonged QRS duration was defined as ≥ 120 ms, because this number has been defined as a critical cutoff value by studies investigating prognostication in CHF, and has been highlighted in biventricular pacing trials. If the QRS duration read is the mean duration among all 12 leads as measured on either a MAC-8 or a PC 5000 computer system (Marquette Electronics). The accuracy and reproducibility of data derived from the electronic-based ECG has been shown previously. All-cause mortality as of December 31, 1999, was confirmed based on any death documented within an HFHS facility or death reported by the State of Michigan Death registry tapes or the National Social Security Death Index.

**Statistical Analysis**

Baseline characteristics of patients within the target population were established, including QRS duration, gender, age, and LVEF, and are reported as mean ± SD where indicated. The prevalence of prolonged QRS duration within the target population with respect to gender, race, age, and LVEF, and its role as a predictor of mortality were compared using χ² test or one-way analysis of variance as appropriate. Cox regression was performed to evaluate the independent effects of QRS duration on race-, age-, and sex-adjusted survival. Statistical significance was established at a nominal α < 0.05 level. All calculations were made using SPSS for Windows software (Release 10.0; SPSS; Chicago, IL).

**Results**

**Baseline Characteristics**

The target population of 3,471 patients with echocardiographic and ECG data were followed up for an average of 32.4 months (Table 1). The average index age was 66.1 years, with 1,723 men (49.6%), 1,748 women (50.4%), 1,429 white subjects (41.2%), and 1,925 black subjects (55.5%). The average QRS dura-
tion of the population was 104 ms, and 721 patients were identified with a QRS duration ≥ 120 ms. Overall, there were 1,798 deaths (51.8%).

Epidemiology of QRS Prolongation

The prevalence of systolic dysfunction was analyzed for each QRS duration group (Fig 1). Systolic dysfunction was present in 42.5% of patients with QRS duration < 120 ms, 60% of patients with QRS duration of 120 to 129 ms, 61.6% of patients with QRS duration of 130 to 139 ms, 67.3% of patients with QRS duration of 140 to 149 ms, and 75.7% of patients with QRS duration ≥ 150 ms (p < 0.01). In the analysis by age group, QRS prolongation was found to be present in 235 patients (16.3%) < 65 years old, 216 patients (22.0%) 65 to 75 years old, 201 patients (25.2%) 76 to 85 years old, and 69 patients (27.9%) > 85 years old (p < 0.01 for trend). Furthermore, as shown in Figure 2, QRS prolongation was present in 157 men (19.9%) and 78 women (11.9%) < 65 years old, in 132 men (26.8%) and 84 women (17.1%) 65 to 75 years old, 104 men (29.6%) and 97 women (21.7%) 75 to 85 years old, and 32 men (34.7%) and 37 women (23.9%) > 85 years old (p < 0.01 for trend for both age and gender).

Survival Analysis

Survival for combined QRS groups (above and below a cutoff of 120 ms) was analyzed in Figure 3 using Cox regression, adjusting for age, sex, race,
and LVEF. Figure 3 demonstrates the lack of a clear separation of survival curves when they are adjusted for age, sex, race, and LVEF at the cutpoint of 120 ms. However, when broken down into subgroups at 60 months, survival was highest among those patients with QRS duration $\geq$ 150 ms (mean age, 69.1 years at initial diagnosis), followed by patients with QRS duration $< 120$ ms (not shown). Patients with a QRS duration between 120 ms and 149 ms had decreased survival ($p < 0.001$).

**QRS Duration, Ejection Fraction, and Mortality**

Mortality with respect to QRS duration and LVEF is shown in Figure 4. Patients with an ejection fraction...
<35% have the highest mortality in most QRS duration groups, with an ejection fraction > 50% associated with the lowest mortality in all groups, demonstrating the smallest influence of QRS duration.

**Discussion**

This study highlights the determinants and utility of QRS duration in the general CHF population. In a prior data validation set, the positive predictive value of the ICD-9-CM coding was 73.8% when chart analysis was performed using both Framingham criteria and National Health and Nutritional Examination Survey-I criteria for CHF. This is similar to the positive predictive value found in a previously published report. The most common cause of CHF in this set was caused by ischemic causes, consistent with other epidemiologic studies with smaller numbers of CHF patients. The contribution of hypertensive heart disease to this population, which contains large numbers of black subjects with CHF, was expected.

CONQUEST had several key features that added to information from prior publications. This was the largest study analyzing QRS duration in the general CHF population, with data on 3,471 patients with both systolic and diastolic dysfunction. This study also incorporated a large number of black subjects (n = 1,925) with CHF, who made up 56% of the study population. Although this may limit external generalizability, it nevertheless represents a view of an urban-based and often understudied CHF population.

A prolonged QRS duration was more common among men (24.7%) than women (16.9%), and mortality trends showed significantly elevated mortality rates in men than women, supportive of previous reports. This trend persisted even among patients with QRS < 120 ms, and it is evident that men with CHF have higher mortality, independent of the QRS duration. Furthermore, the average QRS duration and prevalence of QRS prolongation increased with age. A prolonged QRS duration was found in only 16.3% of CHF patients < 65 years old, as compared with 27.9% of those patients ≥ 85 years old. This significant difference is understandable and is accentuated by the longer duration of exposure to the underlying cardiomyopathy with a progressively worsening myocardial function. Systolic dysfunction occurred more frequently as QRS duration increased. Intuitively, this is acceptable, because left bundle-branch block (LBBB) is a marker of ischemic heart disease, and dilated cardiomyopathy has been shown to have prolonged QRS durations.

Survival analysis demonstrated the lowest adjusted 5-year mortality among patients with QRS ≥ 150 ms, followed by the group with QRS > 120 ms, with highest mortality in those patients with a QRS of 120 to 140 ms. While improved survival in patients with nonprolonged QRS duration is consistent with findings from several previous studies, improved survival has not been reported among patients with more extreme QRS prolongation, as found in this population. The finding of reduced mortality in the extreme QRS duration group, QRS > 150 ms (n = 292), may be attributed to random variation across multiple subgroups. Alternatively, this group may have contained...
individuals without clinical CHF who were captured by the ICD-9-CM codes methodology and had a coincidental ventricular conduction delay. It is possible that those with QRS > 150 ms may have had longer duration of illness and, hence, represent survivors receiving a disproportionate number of life-prolonging therapies (revascularization, medical therapy, implantable defibrillators, etc). Although our database did not classify patients into right bundle-branch block (RBBB), LBBB, and nonspecific intraventricular conduction delay, a large recent study reported that both RBBB and LBBB were associated with elevated and equal all-cause mortality rates in a general population. We found that patients with the lowest LVEF (< 35%) had increased mortality, particularly those with the most prolonged QRS duration. Systolic dysfunction did not seem to have the same association with increased mortality among those patients with normal or only mildly prolonged QRS duration.

This study had multiple limitations. As pointed out by the validation exercise, the use of ICD-9-CM codes will create misclassification bias. This misclassification bias is a tradeoff for evaluation of conditions in large populations using automated sources of data. Furthermore, the subclassification of CHF type, systolic vs diastolic, is subject to current controversy even when complex Doppler imaging methods are used for assessment. We could not make inferences regarding the frequency of QRS widening and the etiology of cardiomyopathy. The use of LVEF from and echocardiographic database with a combination of visual estimates and calculated values has inherent errors with precision and accuracy. Our study did not capture important clinical characteristics, including the use of revascularization, implanted devices, or antiarrhythmics. Of note, a previously reported, random sampling of the parent database REACH found that < 2% of patients were receiving pharmacotherapy for arrhythmias. Furthermore, the type of conduction abnormality (LBBB, RBBB, nonspecific intraventricular conduction delay) was not defined. These limitations, however, taken together, bias our results to the null hypothesis, and hence have been handled reasonably in the analysis.

**Conclusion**

A prolonged QRS duration can be expected in 20% of a generalized heart failure population. Determinants for a prolonged QRS duration are male sex, white race, elderly age groups, and patients with systolic dysfunction. When compared with patients with a normal QRS duration, those patients with the most extreme QRS prolongation have improved survival, whereas patients with intermediate prolongation of the QRS complex (120 to 149 ms) have worse survival. Also, systolic dysfunction seems to have a greater impact on mortality in patients with more prolonged QRS duration. As more data accumulate concerning the potential benefits of biventricular pacing on morbidity and mortality in patients with CHF and QRS widening, the current study provides valuable information regarding the prevalence of QRS widening in a typical, urban CHF population.

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