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Baseline Framingham risk score does not predict future ECG-derived QRS duration over an average of 3.3 years

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Abstract

Background: Prolonged electrocardiogram (ECG) QRS duration has been associated with increased cardiovascular risk. It is unclear whether the main predictor of cardiovascular risk, the Framingham risk score also predicts short-term changes in ECG QRS duration. Our aim is to determine whether baseline Framingham risk score is associated with baseline or changes in QRS duration.

Methods: A retrospective cross-sectional analysis was performed using observational data obtained from two hundred two participants. Framingham risk score was calculated using an online risk calculator. QRS duration was obtained using a 10 s trace from a Welch Allyn PC-based 12-lead ECG system.

Results: Average follow-up duration was 3.3 ± 1.1 years. Mean QRS change was 1.8 ± 11.4 ms. Specifically, among two hundred two participants, there are 104 subjects with a greater QRS duration at follow-up, while 98 subjects had the same or a shorter follow-up QRS duration. Baseline Framingham risk score did not significantly predict an increase in QRSd with an odds ratio of 1.04 ($P = 0.230$). Regression analysis of QRS duration at baseline and Framingham risk at baseline had a weak association ($R^2 = 0.020$; $P = 0.043$). The Framingham risk score at follow-up was likewise has a weak association with follow-up QRS duration ($R^2 = 0.045$; $P = 0.002$).

Conclusions: Our results do not demonstrate a statistically significant association between Framingham risk parameters and future QRS duration changes over longitudinal time. QRS duration had variable changes between baseline and follow-up. This might suggest that a longer period of follow-up is required to document more stable increases in QRS duration associated with ventricular pathology. A larger population study is needed to confirm our observations.

Keywords: ECG, QRS duration, Framingham risk score, Population study, Rural

Introduction

The Framingham Heart study, since its origin in 1948, has enhanced our understanding of how cardiovascular risk factors can predict cardiovascular disease risk [1, 2]. From the Framingham dataset, several online multivariate algorithms have been developed for cardiovascular risk calculations [1, 3]. These calculations offer a prediction score. These algorithms are often utilised as cardiovascular screening tools in communities, as they estimate a patient's predisposition to various cardiovascular-related disease outcomes [1, 3].

There is interest in non-Framingham Heart risk parameters that may be also useful, such as ECG-derived QRS duration [4, 5]. Prolonged QRS duration is generally defined as > 120 ms [6–9]. A prolonged QRS duration has been associated with coronary artery disease (CAD) [7], congestive heart failure (CHF) [8] and increased overall

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mortality [8, 9]. Indeed, one study from the Framingham population study demonstrated that an increased QRS duration was associated with risk of development of new onset congestive heart failure that was independent of baseline adjustments of left ventricular cardiac mass [10]. QRS duration clinically is seen to modestly improve performance assessment of cardiovascular risk models [11].

Despite known relationships between QRS duration and cardiovascular risk, it remains to be determined whether the Framingham risk score can predict future changes in QRS duration. Our aim is to determine whether an elevated baseline Framingham score is associated with change in QRS duration over time in an Australian rural population. Secondary aim is to explore associations with cross-sectional QRS duration and Framingham risk score.

Materials and methods

Study population

Data were retrospectively extracted from a community health-screening project performed at the Albury-Wodonga campus of Charles Sturt University, Australia [12]. Participants attending the clinic were from the Albury-Wodonga area and surrounding districts on the New South Wales-Victoria border. Inclusion criteria included attending health-screening clinic at least twice, with QRS duration and all information required for Framingham risk score calculation recorded for two visits. For participants with more than two relevant clinic visits, data were recorded from the first two visits. Results were screened to exclude subjects who were pregnant, cognitively impaired, non-ambulatory or those who self-reported pre-existing cardiovascular disease (CVD) at baseline. All subjects were greater than 21 years of age. Ethics had been approved by Charles Sturt University (CSU) Research Ethics Committee in accordance with the National Statement of Ethical Conduct in Research Involving Humans.

Demographic information was ascertained through clinical history taking and completion of a self-reported questionnaire on health status. In the questionnaire, participants recorded previous and current medical conditions such as diabetes, cardiovascular disease and hypertension (patients were hypertensive if their blood pressure greater exceeded 140/90 mmHg). Participants answered "yes" to smoking status if they smoked more than five cigarettes per day.

Weight and blood pressure measurement

Blood pressure measurements were obtained using an automatic Welch Allyn mercury sphygmomanometer. Each subject was seated in a relaxed supine position and rested for 5 min prior to measurement. Following this, the blood pressure cuff was placed on the subject's upper arm, while the arm was supported at the level of the heart. Two measurements were taken 1 min apart, and the results for each measurement were averaged in order to determine each subject's systolic and diastolic blood pressure.

Scales were used to record each subject's weight in kilograms, and stature tape was used to record height in metres. BMI was calculated by dividing weight (kg) by squared height (m^2).

12-Lead ECG

Resting 12-lead ECG results were obtained using a Welch Allyn PC-based ECG system. QRS duration was automatically calculated from a 10-s trace (using The Welch Allyn automated MEANS algorithm). QRS change was defined as difference of follow-up QRS duration minus baseline QRS duration. If a subject's QRS change was calculated as >0 ms, they were recorded as having an increased QRS duration. If a subject's QRS change was ≤ 0 ms, they did not have an increased QRS duration.

Biochemistry

Each patient's venous blood was collected and stored in ethylenediaminetetraacetic acid (EDTA) tubes. The samples were then analysed at South West Pathology (Albury) in order to quantify HbA1C, total cholesterol, high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C) and triglycerides.

Framingham risk score

Framingham risk score was calculated in accordance with criteria published on "General Cardiovascular Risk Profile for Use in Primary Care: The Framingham Heart Study", which is recommended by Framingham Heart Study [1] calculates risk based on age, gender, high-density lipoproteins-cholesterol (HDL-c), total cholesterol, SBP, hypertension treatment information, smoking and diabetes.

Statistical analysis

Descriptive data including demographic variables are presented as absolute value or proportions or means with standard deviation (S.D). Univariable logistic regression was applied to calculate the relationship between baseline risk factors and risk of increased QRSd at follow-up clinic visits for each participant. Univariable general linear regression models were applied to evaluate the relationship between cardiac risk factors and QRSd change. Correlations between Framingham risk score and QRS duration at both baseline and follow-up clinic visits were investigated using linear regression. All data analysis was performed using SPSS 22.0 (IBM, Armonk, New York,

Table 1 Demographic and baseline characteristics of subjects

	Male (*N* = 86)			Female (*N* = 116)		
	Min.	Max.	Mean ± SD	Min.	Max.	Mean ± SD
Age (years)	46	90	68.2 ± 9.2	42	86	65.0 ± 9.1
HDL-c (mM)	0.86	2.38	1.21 ± 0.29	0.84	2.98	1.50 ± 0.35
Total cholesterol (mM)	2.60	6.90	4.63 ± 1.06	3.40	8.30	5.38 ± 1.08
SBP (mmHg)	102	165	132.3 ± 14.8	70	200	129.4 ± 19.3
Hypertension (%)	65.1%			56.9%		
Current smoker (%)	3.4%			0.9%		
Diabetes (%)	38.4%			25.0%		
Framingham risk score	7	25	16.6 ± 4.0	0	26	13.1 ± 5.0

Table 2 QRS duration baseline and follow-up data

	All (*N* = 202)			Male (*N* = 86)			Female (*N* = 116)		
	Min.	Max.	Mean ± SD	Min.	Max.	Mean ± SD	Min.	Max.	Mean ± SD
Baseline QRSd (ms)	76	180	101.1 ± 15.5	77	180	106.1 ± 16.0	76	167	97.5 ± 14.1
Follow-up QRSd (ms)	77	177	103.0 ± 16.3	83	163	107.9 ± 16.1	77	177	99.3 ± 15.5
QRSd change (ms)	− 37	67	1.8 ± 11.4	− 37	67	1.8 ± 12.5	− 30	63	1.8 ± 10.7
Interval years (between visits)	0.6	6.0	3.3 ± 1.1	1.0	6.0	3.2 ± 1.1	0.6	5.3	3.3 ± 1.1

This tables provides QRS duration for the two clinic visits (baseline and follow-up). Also the table calculates QRSd change and interval years between the two clinic visits

USA). A two-sided P value < 0.05 was considered statistically significant.

Results

A total of 202 participants were included in our study, of which 42.6% were male and 57.4% were female. Framingham risk score components are presented in Table 1. Mean Framingham risk score for males was 16.6 ± 4.0, with a range of 7–25 and for females 13.1 ± 5.0, with a range of 0–26. Hypertension was prevalent among the population (Table 1).

Follow-up QRS duration is presented in Table 2. Among 202 participants, compared to baseline, there were 104 subjects with an increase in QRS duration, while 98 subjects had the same or a shorter follow-up QRS duration. Average time to follow-up QRS duration was 3.3 ± 1.1 years. Mean QRS duration change was 1.8 ± 11.4 ms, with a range of − 34 to 67 ms and a significant difference from baseline to follow-up in QRSd is reported (P = 0.007). Similar changes in QRS duration were observed for males and females (1.8 ± 12.5 ms and 1.8 ± 10.7 ms, respectively), although females had a shorter mean QRS duration when compared with males at both the baseline and follow-up clinic visits.

For each participant, we separately examined the relationship between age, gender, interval years between the two clinic visits, BMI, baseline Framingham risk score and risk of increased QRS duration (Table 3). While all these factors presented with a possible positive association with increased QRS duration, however, none of these factors researched statistical significance (all P > 0.05). Additionally, these individual factors were not associated with change in QRS duration (between visits) (Table 4).

Table 3 Relationship between factors and risk of increased QRS

	Odds ratio[a]	95% CI	*P*
Baseline age	1.01	(0.98, 1.04)	0.399
Male	0.83	(0.48, 1.45)	0.517
Internal years (year)	1.15	(0.90, 1.47)	0.279
BMI	1.02	(0.96, 1.08)	0.579
Baseline Framingham risk score	1.04	(0.98, 1.10)	0.230

[a] Calculated by univariable logistic regression

However, QRS duration was weakly associated with cross-sectional time points for the Framingham risk score for both the baseline and follow-up clinic visits (P = 0.043 and P = 0.002). At the baseline clinic visit, as Framingham risk score increased by 1, QRS duration increased by 0.44 ms (R^2 = 0.020). At the follow-up clinic visit, QRS duration increased by 0.74 ms for every average increase in the Framingham risk score by 1 point (R^2 = 0.045) (see Fig. 1).

Table 4 General linear model for factors associated with change in QRS duration

	Coefficient[a]	95% CI	*P*
Baseline age	0.02	(− 0.16, 0.19)	0.854
Male	− 0.01	(− 3.23, 3.21)	0.996
Interval to follow-up (years)	0.97	(− 0.45, 2.39)	0.180
BMI	0.26	(− 0.07, 0.59)	0.125
Baseline Framingham risk score	0.28	(− 0.04, 0.61)	0.088

[a] Calculated by univariable general linear model

Discussion

The primary finding in our study is that there is no statistically significant relationship between Framingham risk parameters and future change in QRS duration over an approximate follow-up period of up to 6 years (mean 3.3 years). However, our results showed that an increased Framingham risk score was associated with an increased QRS duration at baseline. Additionally, Framingham risk score at follow-up was associated with increased QRS duration at follow-up.

We thus show that a higher Framingham score is more likely to have a longer QRS duration. This is not surprising, considering variables of the Framingham risk equation (such as SBP) are known risk factors for conditions such as cardiac hypertrophy and ischaemic heart disease [13–15], both of which can slow cardiac conduction and increase ECG QRS duration [16, 17]. For example, hypertension can cause left ventricular hypertrophy, which results in prolonged QRS duration due to prolonged ventricular conduction [18, 19]. On the other hand, progressive increases in cardiac mass do not correlate directly with changes in QRS duration [20]. Given the fact that we did not observe that a Framingham risk score could predict future changes in QRS duration, it may suggest that QRS duration is both related and independent of ventricular mass. It also suggests that there may be some spontaneous improvement in QRS duration with follow-up as we have observed both increases and decreases in QRS duration. If QRS duration is associated with modifiable risk factors (in the Framingham risk score), it will be possible to modify those risk factors.

A limitation to our study is the use of an averaged 10 s, 12-lead ECG lead in order to obtain QRS duration. On the other hand, QRS duration from short ECG recordings has been previously used in large population studies [21, 22]. We do not have data on medications that may have influenced QRS duration in this study. On the other hand, we appreciate that in rural areas of Australia medication use and compliance is low for cardiovascular medications [23, 24]. Additionally, we do not have strict diagnosis of whether bundle branch block was evident at higher QRS durations in our population. Cardiac myocyte gap junction uncoupling as a consequence of LV hypertrophy or fibrosis can give rise to a wide QRS complex with morphological features that are similar to ECG-derived LBBB but are not LBBB [25, 26].

Framingham risk scores may also be an inefficient measure of QRS duration changes within the investigated timeframe (a mean of 3.3 years follow-up). As Framingham score estimates a patient's 10-year cardiovascular risk, it is possible that our study's follow-up interval may have been too short for the purposes of predicting worsening QRS duration. However, we have observed that QRS duration can change significantly during a few years of follow-up, e.g. a significant difference in QRS duration between baseline and follow-up, within participants. Hence, further research could

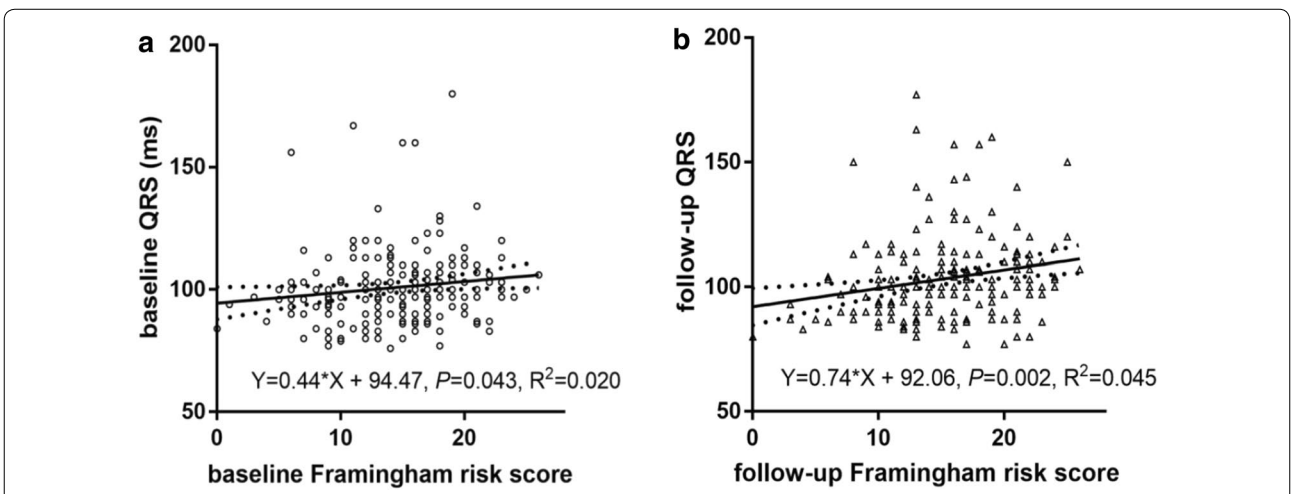

Fig. 1 Cross-sectional association between QRS duration and Framingham risk score at baseline and follow-up clinic visits

ascertain whether greater longitudinal time influences the predictive value of Framingham score with respect to future QRS duration changes. On the other hand, the mean age of our study population was 68.2 years, where central aortic stiffening could theoretically influence systolic blood pressure changes that could increase QRS duration (over a short period of time). A previous cross-sectional study, representative of our study population, demonstrated higher than expected central aortic blood pressure [23] in rural Australia.

Many of the risk factors that comprise the Framingham risk score can influence QRS duration. It is also acknowledged that many pathological cardiovascular changes and cardiac biomarkers are prevalent at earlier stages of sub-clinical cardiac disease development. We cannot ascertain whether our population is relatively healthy; with a mean age of 68.2 several chronic diseases would be prevalent and add to accelerated cardiovascular risk. We believed it was reasonable to evaluate the Framingham risk score with respect to short-term changes in QRS duration. Indeed, QRS duration has been used to predict cardiovascular events in population studies [10, 11].

In summary, from a clinical perspective, our findings do not suggest that Framingham score serves as a predictive measure of worsening QRS duration over a short follow-up period. Our results suggest a higher Framingham score is indicative of prolonged QRS duration. In reverse, this is clinically important as a prolonged QRS duration may suggest modifiable Framingham cardiovascular risk factors that can improve QRS duration. Clinically an increased QRS duration may suggest a need to review blood pressure targets and other cardiovascular risk factors that could influence cardiac conduction or ventricular remodelling.

Abbreviations

BP: Blood pressure; BMI: Body mass index; CAD: Coronary artery disease; CHF: Congestive heart failure; ECG: Electrocardiogram; ms: Milliseconds; %: Percentage; QRSd: QRS duration; SBP: Systolic blood pressure.

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Authors' contributions

ES contributed to drafting the initial manuscript. HJ was responsible for the clinical cohort study. CSM designed the retrospective study and co-drafted the manuscript. YZ was involved in the study design and statistical analysis. All authors contributed to the final reading and editing of the manuscript. All authors read and approved the final manuscript.

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Availability of supporting data

Ethics approval did not consent in sharing of the data, and private requests to share the data will be considered pending governance approvals.

Ethics approval and consent to participate

This study was approved by Human Ethics Committee, Charles Sturt University, Australia, Ethics Protocol number: 2006/042.

Consent for publication for participants in the study

Consent was obtained from all participants in the study for publication.

Competing interests

The authors declare that they have no competing interests.

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