Fragmented QRS Complex Has Poor Sensitivity in Detecting Myocardial Scar

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Objective: To study the association of the fragmented QRS complex versus the Q wave with myocardial scar and viability.

Background: A prior study has suggested that the fragmented QRS complex on an electrocardiogram (ECG) is a highly sensitive and specific marker of myocardial scar as detected by regional perfusion abnormalities on a nuclear stress test. There is no external validation of this data.

Methods: We correlated the ECG and nuclear perfusion images of 460 consecutive patients with known or suspected coronary artery disease. The presence of fragmented QRS or Q waves in two contiguous ECG leads was correlated with major coronary artery distributions on nuclear perfusion imaging.

Results: For the 1842 evaluated territories, the fragmented QRS complex was not superior to the Q wave in detecting fixed or mixed myocardial defects. The fragmented QRS complex was associated with worse sensitivity (1.7%) in comparison to the Q wave (31.7%) for identifying myocardial scar. The fragmented QRS complex carried a higher false positive rate in patients with normal perfusion scans (15.8%, 221 segments), in comparison to Q waves (1.4%, 17 segments).

Conclusion: In our study population, both the fragmented QRS and Q wave had poor sensitivity and specificity in detecting fixed or mixed myocardial scar. Larger studies are needed to evaluate fragmented QRS as a surrogate of myocardial scar before it can be incorporated into clinical practice.

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Q waves on a 12-lead electrocardiogram (ECG) are considered a classic hallmark of prior myocardial infarction in patients with coronary artery disease. However, Q waves may regress and disappear with time especially in patients treated with reperfusion therapy despite there being continued evidence of myocardial scarring.¹ Furthermore, there are no chronic markers on a 12-lead ECG for identifying a non-Q wave myocardial infarction.

With widespread use of early reperfusion, the incidence of Q wave myocardial infarctions has decreased in recent years.² Studies using contrast-enhanced magnetic resonance imaging have found

low sensitivity of Q waves in predicting overall location of myocardial scar.³

A prior study has suggested that the fragmented QRS complex on an ECG is a highly sensitive and specific marker of myocardial scar as detected by regional perfusion abnormalities on a nuclear stress test.¹ Based on this study, Das et al. concluded that the fQRS complex may be a stronger marker than Q waves in detecting myocardial scar, and specifically non-Q wave myocardial scars.¹

Our study's aim was to define the sensitivity and specificity of fQRS in detecting presence of myocardial scar in a large cohort of patients undergoing nuclear stress testing.

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METHODS

Our study population comprised of 1156 consecutive patients who were referred for myocardial single photon emission computed tomography (SPECT) stress testing at the University of Michigan Cardiovascular Center from September 2006 through June 2007. These patients had either a history of coronary artery disease or were being evaluated for suspected coronary artery disease. Patients with known heart transplants were excluded from the study.

Every patient had a resting 12-lead ECG performed within 3 months of their perfusion study. Patient's ECG and perfusion study were evaluated by different investigators who were blinded to the other test results.

ECG Evaluation

Each patient's ECG was individually reviewed by two blinded investigators, and their corresponding ECG findings (presence of a Q wave or an fQRS) were coded according to a 12-lead designation. The ECG findings were indicated on the reading forms by lead number using American Heart Association classification and correlated with associated nuclear viability scan findings.

ECG Analysis

Of the 1156 consecutive patients, in analysis of the baseline ECG, 17 patients were excluded due to the presence of an incomplete right bundle branch block, 34 patients were excluded due to the presence of a right bundle branch block, 22 patients were excluded on the presence of a nonspecific intraventricular delay, 31 patients were excluded due to the presence of a paced rhythm, 16 patients were excluded due to the presence of a left bundle branch block, 8 patients were excluded due to the presence of baseline ECG artifact, and 491 patients were excluded due to the absence of an ECG available for individual review within the predefined study window.

Four hundred sixty-two resting 12-lead ECGs (GE, Marquette, WI, USA; model Mac 5500; filter range, 20–150 Hz; 25 mm/s, 10 mm/mV) were analyzed by two independent readers blinded to the results of the myocardial perfusion SPECT findings. ECG findings were coded separately for each of the 12 leads, defined by either the absence of any

abnormality or presence of a Q wave and/or fragmented QRS. Leads containing Q waves or fragmented QRS were further subclassified into anterior, inferior, and lateral regions as discussed below. Finally, ECG findings by region were compared to the corresponding findings by region on myocardial SPECT imaging.

ECG Criteria for Fragmented QRS Complex Pattern

As analyzed by the Das et al., the fQRS formation was defined by the presence of a degree of variation of the RSR' pattern in either of the 12 leads.¹ Given that there is no standardization to the depth or degree of R'/r' formation or degree of notching of the nadir of the S wave on a resting ECG independent or dependent on the baseline voltage of ECGs, the RSR' pattern was further specified in this study as having a true negative or positive deflection such that mathematically the first derivative of the ECG at the point is equal to zero. In an individual lead on a continuous 12-lead ECG, the presence of an fQRS was noted only when the fragmentation was detected in >50% of the marched out beats for that specific lead.

Anterior wall myocardial scars were defined by the presence of fQRS in ≥ 2 consecutive leads in V₁–V₅. Inferior wall myocardial scars were defined by the presence of fQRS in at least two of three leads (II, III, or aVF). Lateral wall myocardial scars were defined by the presence of fQRS in at least two of three leads (I, aVL, or V₆).

RSR' patterns were defined as having QRS duration <120 ms (Fig. 1). Bundle branch block patterns (such as right and left bundle branch blocks and incomplete right bundle branch blocks), paced rhythms, and nonspecific intraventricular delay patterns were excluded from the study.

ECG Criteria for Q wave

As dictated by the Das et al. study protocol, in this project, the pathological Q waves were again defined as the presence of a Q wave deeper than one-fourth the size of the voltage of the subsequent R wave, or greater ≥ 0.04 seconds in duration.¹

Anterior wall myocardial scars were defined by the presence of Q wave in ≥ 2 consecutive leads in V₁–V₅ or a Q wave in lead V₂. Inferior wall myocardial scars were defined by the presence of Q wave in at least two of three leads (II, III, or aVF). Lateral wall myocardial scars were defined

Figure 1. Examples of various fragmented QRS complex morphologies.

by the presence of Q wave in at least two of three leads (I, aVL, or V₆).

Posterior Wall Myocardial Scar

The proximal inferolateral scar previously referred to as posterior wall myocardial scar was defined by the presence of an R wave in V₁ that was ≥ 40 ms and ≥ 5 mV.

Nuclear Perfusion Scan Analysis

Gated sestamibi imaging was integrated following an exercise protocol that consisted of symptom-limited maximal upright treadmill testing. Patients' began their exercise stress with either the modified Bruce or Bruce protocols adjusted to their level of fitness, and termination of the test was symptom-limited and occurred only for progressive chest pain, hypotension, symptomatic fatigue, dyspnea, or complex ventricular arrhythmias.⁴

Nuclear perfusion studies acquired using the SPECT technique were performed using either Bruce or Cornell protocol treadmill stress testing, adenosine stress with simultaneous exercise, adenosine alone, or dobutamine protocols. SPECT imaging studies were performed using a gated stress Tc-99m sestamibi rest Tc-99m tetrofosmin protocol. All SPECT studies were acquired with

dedicated SPECT/CT imaging systems (Siemens Symbia T6, Hoffman Estates, IL, USA) and corrected for tissue attenuation and scatter using the manufacture's standard commercially available processing software.⁵

The Corridor4DM (4DM) software application, developed at the University of Michigan Medical Center was used to review and analyze myocardial perfusion SPECT images.⁶ The 4DM allows for the quantification of perfusion or metabolism by constructing polar maps from a maximum search along intensity profiles confined by the endocardial and epicardial surfaces. Images corrected for tissue attenuation and scatter and the corresponding uncorrected images were available for review and quantification and were compared to corresponding databases of corrected and uncorrected radiotracer activity distributions.^{5,7}

Objective myocardial perfusion quantification data are defined by regional classification of the myocardium as being "normal, scar, or ischemic." The latter three terms are defined by measures of perfusion defect severity and reversibility.

Based on the final myocardial perfusion SPECT report, each coronary territory was broken down into categories of viable versus nonviable. Each nuclear medicine scan was coded according to the report in defining the degree of viability in the patient's perfusion imaging findings. Myocardial

Table 1. Sensitivity and Specificity of Q Wave versus fQRS Complex versus Mixed Morphologies in Detecting Myocardial Scar

Q Wave versus fQRS versus Mixed Morphologies in Detecting Myocardial Scar			
	Q Wave	fQRS	^aMixed
Sensitivity	11/60 = 18.3%	19/60 = 31.7%	1/60 = 1.7%
Specificity	1749/1782 = 98.1%	1490/1782 = 83.6%	1763/1782 = 98.9%
^b PPV	11/44 = 25.0%	19/311 = 6.1%	1/20 = 5%
^c NPV	1749/1798 = 97.3%	1490/1531 = 97.3%	1763/1822 = 96.8%

^aDenotes the presence of a Q wave on one lead and an fQRS on a different ECG lead in a specific myocardial territory. ^bPositive predictive value. ^cNegative predictive value.

perfusion scans were defined according to each coronary territory as having: normal perfusion, reversible fully viable defects (majority of defect was denoted to have complete or nearly complete reversibility), mixed viability defects (majority of defect denoted to have significant partial reversibility), and nonviable defects (fixed or minimally reversible defects).

All nuclear perfusion scans were interrogated by a single nuclear cardiologist with over 35 years of nuclear cardiology experience.

Statistical Analysis

Sensitivity was defined by the number of true positives over the total number of patients identified by SPECT imaging to have true myocardial scar. Specificity was defined as the number of true negatives over the total number of patients identified by SPECT imaging to be without evidence of myocardial scar.

Receiver operator curves were used to compare the detection rate of fQRS versus Q wave in detection of myocardial scar.⁸

This study protocol was approved by the Institutional Review Board of the University of Michigan.

RESULTS

The data for the final cohort of 460 patients was analyzed in this study. Each of these patients' 12-lead ECG was analyzed by individual lead/segment classification.

One thousand eight hundred and forty-two ECG segments were examined in this study. A Q wave was present in a total of 66 segments (3.6%) while an fQRS was present in a total of 333 segments (18.1%).

Of the 1842 evaluated territories, 1397 (75.8%) were normal, 152 (8.3%) had a reversible perfusion defect, 50 (2.7%) had a fixed defect, and 152 (8.3%) had mixed reversible and fixed defect. Among patients with normal perfusion, Q waves were seen in 17 segments (1.4%) versus fragmented QRS in 221 segments (15.8%). Among patients with reversible perfusion defects, Q waves were seen in two segments (1.3%), while fragmented QRS were seen in 28 segments (18.4%). Among patients with fixed defects, Q waves were seen in 11 segments (18.3%), while fragmented QRS was seen in 24 segments (40%). Among patients with mixed defects, Q waves were seen in 14 segments (5.8%), while fragmented QRS was seen in 48 segments (19.8%). Sensitivity, specificity, positive predictive value, and negative predictive value for myocardial scar as detected by nuclear perfusion imaging analysis were 18.3%, 98.1%, 25%, and 97.3%, respectively, for the Q wave alone; 31.7%, 83.6%, 6.1%, and 97.3%, respectively, for the fragmented QRS; 1.7%, 98.9%, 5%, and 96.8%, respectively for the Q wave and or fragmented QRS (Table 1). Both Q waves and fragmented QRS performed poorly in detecting fixed or mixed defects.

By regions of myocardial scar, the fQRS has slightly higher sensitivity for detecting anterior scar, but lower specificity than the Q wave. The fQRS had significantly lower sensitivity and specificity for inferior region myocardial scars. The fQRS had greater sensitivity for lateral myocardial scars, but still had worse specificity in comparison to Q waves in this region. The presence of both a Q wave and an fQRS proved of little significance in detecting myocardial scars in any region (Table 2). No fQRS was identified related to posterior myocardial scars (Fig. 2).

Of note, the fQRS had an overall greater frequency of appearance on ECG segments in

Table 2. Sensitivity and Specificity of Q Wave versus fQRS for Detection of Scar by Myocardial Territory

	Q Wave	fQRS	Mixed
Anterior Region			
Sensitivity	4/23 = 17.4%	7/23 = 30.4%	0/23 = 0%
Specificity	428/439 = 97.5%	373/439 = 85.0%	434/438 = 98.8%
^a PPV	4/15 = 26.7%	7/73 = 9.6%	0/5 = 0%
^b NPV	428/447 = 95.7%	373/389 = 95.9%	434/457 = 95.0%
Inferior Region			
Sensitivity	7/16 = 43.8%	6/16 = 37.5%	1/16 = 6.3%
Specificity	428/444 = 96.4%	254/444 = 57.2%	430/444 = 96.8%
^a PPV	7/23 = 30.4%	6/196 = 3.1%	1/15 = 6.7%
^b NPV	428/437 = 97.9%	254/264 = 96.2%	430/445 = 96.6%
Lateral Region			
Sensitivity	0/10 = 0.0%	6/10 = 60.0%	0/10 = 0%
Specificity	449/450 = 99.8%	414/450 = 92.0%	450/0 = ∞
^a PPV	0/1 = 0.0%	6/40 = 15.0%	0/0 = ∞
^b NPV	449/459 = 97.8%	414/418 = 99.0%	450/460 = 97.8%

^aPositive predictive value. ^bNegative predictive value.

comparison to Q waves, with the highest frequency in inferior segments (Fig. 3).

The fQRS was more common across all degrees of viability on nuclear SPECT perfusion scans regardless of whether the studies demonstrate normal, reversible, mixed partially reversible, or fixed myocardial defects (Fig. 3).

DISCUSSION

Our study suggests that fQRS has poor sensitivity in detecting myocardial scar. In our study population, both the fragmented QRS and Q wave had poor sensitivity in detecting fixed or mixed myocardial scar. Thus, we were unable to corroborate the findings of Das and colleagues. Subsequent publications have suggested that when combined together, that is, the presence of a fragmented QRS

and a Q wave in the same leads, to demonstrate higher sensitivity in detecting myocardial scar.⁹ A subset analysis of our retrospective study did not replicate these findings. When patients' ECG segments were analyzed by myocardial territory for (1) the presence of only a fragmented QRS in two ECG leads, versus (2) the presence of one ECG lead with a fragmented QRS and one ECG lead with a Q wave only, versus (3) the presence of two or more ECG leads with a fragmented QRS and one ECG lead with a Q wave only, versus (4) the presence of one ECG lead with fragmented QRS and two or more ECG leads with Q waves, our results showed no correlation with detection of myocardial scar. The combination of multiple ECG leads with fragmented QRS and a Q wave did not correlate with higher sensitivity or specificity in detecting myocardial scar.

Figure 2. Frequency of fQRS versus Q wave in normal versus abnormal nuclear medicine scans by ECG territory.

Figure 3. Frequency of Q wave versus fQRS complex based on perfusion imaging finding.

Limitations

A limitation of our study is that the Q wave sensitivity in our database was less than the expected 30% sensitivity expected from past literature. In this study, the definition of the Q wave followed the criteria set forth in the sentinel study.¹ The criteria utilized for defining a Q wave myocardial infarction by the depth of the Q wave has been recommended to be reviewed. This is largely given the location of the initial vector depolarization may or may not produce the necessary degree of negative deflection to meet the criteria for a Q wave myocardial infarction.^{10,11} In addition, with advancement of modern interventional techniques and early coronary revascularization procedures, the use of thrombolytics, and aggressive medical therapy, Q wave infarcts is less commonly seen today.

In summary, we were unable to validate the prior studies suggesting dramatically high sensitivity and specificity of fQRS complex for predicting myocardial scar. Larger studies are needed to evaluate fragmented QRS as a surrogate of myocardial scar before it can be incorporated into clinical practice.

Disclosures

The authors report no conflicts.

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