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Appearance of Abnormal Q Waves Early in the Course of Acute Myocardial Infarction: Implications for Efficacy of Thrombolytic Therapy

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Objectives. **The purpose of this study was to determine the time course of the appearance of abnormal Q waves on the electrocardiogram (ECG) over the first 6 h of symptoms of myocardial infarction and to determine what implications, if any, such Q waves have for the efficacy of thrombolytic therapy.**

Background. **Severe myocardial ischemia can produce early QRS changes in the absence of infarction. Abnormal Q waves on the baseline ECG may not be an accurate marker of irreversibly injured myocardium.**

Methods. **Data from 695 patients who had no past history of myocardial infarction and whose admission ECG allowed prediction of myocardial infarct size in the absence of thrombolytic therapy (Aldrich score) were pooled from four prospective trials of thrombolytic therapy. The presence and number of abnormal Q waves on each patient's initial ECG were recorded. Four hundred thirty-six patients had left ventricular infarct size measured using quantitative thallium-201 tomography a mean (±SD) of 52 ± 43 days after admission.**

Results. **Of patients admitted within 1 h of symptoms, 53% had abnormal Q waves on the initial ECG. Both predicted and final infarct size were larger in patients with abnormal Q waves on the initial ECG independent of the duration of symptoms before therapy ($p < 0.001$). Despite this finding, the presence of abnormal Q waves on the admission ECG did not eliminate the effect of thrombolytic therapy on reducing final infarct size ($p < 0.0001$).**

Conclusions. **Abnormal Q waves are a common finding early in the course of acute myocardial infarction. However, there is no evidence that abnormal Q waves are associated with less benefit in terms of reduction of infarct size after thrombolytic therapy.**

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Myocardial infarction is often associated with the loss of R wave voltage in the electrocardiographic (ECG) leads corresponding to the affected area. The magnitude and distribution of QRS changes observed on an ECG performed several days after infarction, including the resulting abnormal Q waves, have been shown to be an accurate indicator of myocardial infarct size in patients not undergoing thrombolytic therapy (1). In contrast, such changes in the QRS complex have not been found to correlate well with ejection fraction, regional wall motion abnormalities or perfusion defect size in patients who have received thrombolytic therapy for acute myocardial infarction (2).

Little is known about the time course or importance of abnormal Q waves present during the first few hours of myocardial infarction and what implications, if any, abnormal Q waves on the admission ECG have for the effectiveness of thrombolytic therapy. Transient changes in R wave amplitude, probably resulting from ischemia-induced intramyocardial conduction delays, have been observed during ischemia induced during coronary angioplasty as well as in experimental animal models of ischemia (3–6). If an ischemia-induced conduction delay resulted in a shift in early electrical forces that would normally be recorded as an R wave to later in the QRS complex, then opposing unaffected electrical forces might result in the inscription of abnormal Q waves (7). Thus, Q waves present early in the course of acute myocardial infarction may not represent irreversibly damaged myocardium. We therefore hypothesized that abnormal Q waves on the admission ECG may not be a reliable marker of reduced potential for myocardial salvage with thrombolytic therapy.

Methods

Patients. Data from patients in four studies of thrombolytic therapy were combined for analysis: the Western Washington Randomized Trial of Intracoronary Streptokinase in Acute Myocardial Infarction (8), Western Washington Intravenous Streptokinase in Acute Myocardial Infarction Randomized Trial (9), Western Washington Myocardial Infarction Registry and Emergency Department Tissue Plasminogen Activator Treatment Trial (10) and Myocardial Infarction

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Table 1. Definition of Abnormal Q Waves

ECG Lead	Criteria	ECG Lead	Criteria
I	≧30 ms	V_2	Any
II	≧30 ms	V_3	Any
aVL	≧30 ms	V_4	≧20 ms
aVF	≧30 ms	V_5	≧30 ms
V_1	Any	V_6	≧30 ms

ECG = electrocardiographic.

Triage and Intervention Pre-Hospital Trial (11). All study patients presented with symptoms of acute myocardial infarction and met standard clinical and ECG eligibility criteria for thrombolytic therapy. In the older two studies (8,9), patients were randomized to undergo thrombolysis with streptokinase or standard therapy for acute myocardial infarction without thrombolysis (9). In the two more recent trials (10,11) recombinant tissue-type plasminogen activator (rt-PA) was utilized in all patients. All patients with a past history of myocardial infarction and those in whom the Aldrich score (see Electrocardiograms) could not be calculated because the initial ECG had bundle branch block or left ventricular hypertrophy were excluded from the analysis. Data on age, gender, duration of chest pain before thrombolytic therapy, systolic blood pressure and heart rate were gathered prospectively and were available for each patient.

Electrocardiograms. The initial ECGs for all eligible patients were reviewed by investigators who were unaware of clinical presentation, hospital course and radionuclide infarct size results. The location of each myocardial infarction was defined on the basis of the ECG leads with the greatest magnitude of ST segment elevation and was recorded as anterior (leads V_1 to V_4) or inferior (leads II, III, aVF). The number of abnormal Q waves, as defined by Selvester et al. (1) (Table 1), on the initial ECG was determined for each patient. In addition, the presence or absence and magnitude of ST segment elevation and depression were recorded. The magnitude and location of ST segment elevation were used to estimate the left ventricular infarct size that each patient was at risk for should thrombolytic therapy not be given. This estimation, the Aldrich score, is calculated by the following formulas: for anterior infarction, 3[1.5(number of leads with ST segment elevation) − 0.4]; and for inferior infarction, 3[0.6(sum of ST segment elevation leads II, III, aVF) + 2.0] (12).

Radionuclide studies. Rest quantitative thallium-201 tomographic imaging was performed a mean (±SD) of 52 ± 43 days after hospital discharge as part of each of the original protocols at a single central nuclear medicine laboratory. The results were analyzed by investigators who had no knowledge of the therapy and hospital course. Quantitative infarct size was measured as a percent of the left ventricle and performed using image acquisition and processing methods that have been previously reported and validated (13).

Statistical analysis. Two-tailed *t* and chi-square tests were used to assess the statistical significance of observed differences in baseline clinical variables of patients with and without abnormal Q waves on the initial ECG. Analysis of variance was used to determine the statistical significance of the effects of time to therapy and the number of abnormal Q waves on infarct size.

Table 2. Baseline Patient Characteristics

	No Abnormal Q Waves (n = 337)	Abnormal Q Waves (n = 358)	p Value
Male (%)	81.3	88.2	0.17
Age (yr)	56 ± 10	57 ± 1	0.21
Initial heart rate (beats/min)	71 ± 16	77 ± 18	<0.001
Systolic blood pressure on admission (mm Hg)	134 ± 27	138 ± 26	0.09
Time from symptom onset to treatment (h)	2.7 ± 1.5	3.0 ± 1.8	0.02
Anterior infarct location (%)	21.7	51.4	<0.001
Sum of ST segment elevation (mm)	8.4 ± 6.2	11.0 ± 8.5	<0.001
Sum of ST segment depression (mm)	7.1 ± 6.3	5.5 ± 5.5	<0.001
No. of abnormal Q waves	0	2.5 ± 1.3	<0.001
Aldrich score (% left ventricle)	17.8 ± 8.5	20.0 ± 8.7	<0.001

Data presented are mean value ± SD, unless otherwise indicated.

Results

Baseline patient characteristics. Six hundred ninety-five of the 1,138 patients enrolled in the four studies met clinical and ECG criteria for study. Reasons for exclusion of the other 443 patients included previous myocardial infarction in 293 (26%) and ECG abnormalities precluding calculation of the Aldrich score in 150 (13%). Baseline characteristics of patients with and without abnormal Q waves on the initial ECG are shown in Table 2. Patients with abnormal Q waves had a higher initial heart rate, were more likely to have an anterior infarction, had greater ST segment elevation, less ST segment depression and a higher predicted infarct size according to Aldrich score.

Abnormal Q waves on initial ECG. Table 3 shows the proportion of patients with abnormal Q waves by time from symptom onset to initial ECG. Over half (53%) of patients seen within the first hour of symptoms had abnormal Q waves on their initial ECG. Overall, the correlation between duration of symptoms before admission and number of abnormal Q waves on the initial ECG was poor (r = 0.11).

Table 3. Presence of Abnormal Q Waves on Initial Electrocardiogram

Time to Admission	Number of Abnormal Q Waves		
	0	1–2	>2
<1 h	90 (47%)	58 (30%)	43 (23%)
1–2 h	133 (50%)	76 (28%)	58 (22%)
2–4 h	77 (45%)	49 (29%)	44 (26%)
>4 h	14 (40%)	8 (23%)	13 (37%)

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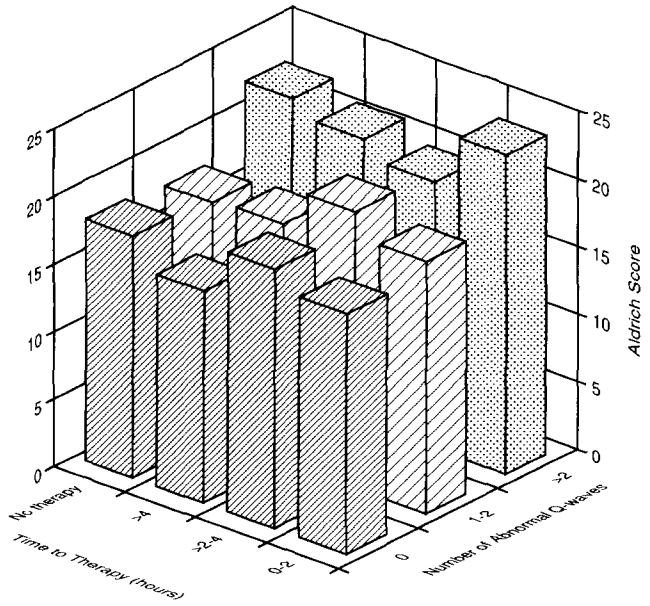

Figure 1. The Aldrich score, predicted infarct size (% left ventricle) were thrombolytic therapy not given, is plotted as a function of duration of symptoms before thrombolytic therapy and number of abnormal Q waves on the initial electrocardiogram (ECG) for 695 patients. By analysis of variance, there was no difference in predicted infarct size as a function of duration of symptoms before thrombolytic therapy ($p = 0.25$). The Aldrich score was higher the more Q waves there were present on the initial ECG ($p < 0.0001$).

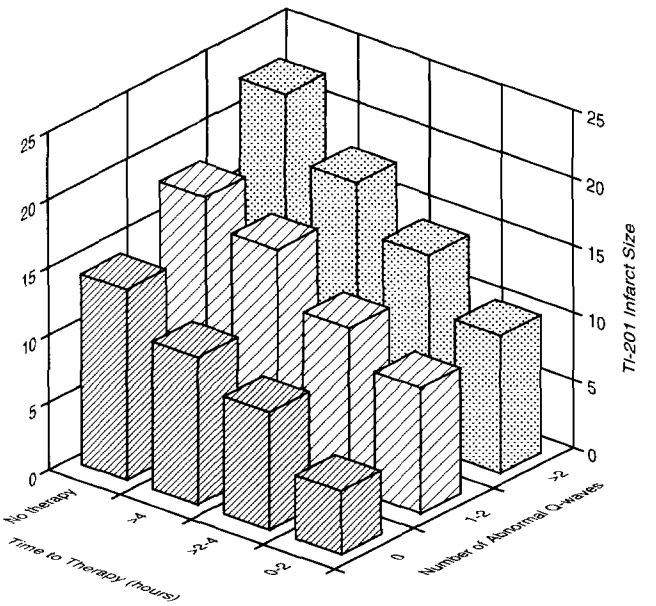

Figure 2. Final infarct size, as measured by quantitative thallium-201 (Tl-201) tomography (% left ventricle), is plotted as a function of duration of symptoms before thrombolytic therapy and number of abnormal Q waves on the initial electrocardiogram (ECG) for 436 patients. By analysis of variance, final infarct size was smaller the earlier thrombolytic therapy was given regardless of whether abnormal Q waves were present on the initial ECG ($p < 0.0001$). Abnormal Q waves were associated with larger infarct size when duration of symptoms before initiation of therapy was taken into account ($p < 0.0001$).

Predicted and final infarct size. In Figure 1, predicted myocardial infarct size had thrombolytic therapy not been given, the Aldrich score, is plotted as a function of time to treatment and number of abnormal Q waves on the initial ECG. There was no significant relation between duration of symptoms before presentation and predicted infarct size, suggesting that if thrombolytic therapy had not been administered there would be no difference in infarct size in these patients as a function of duration of symptoms before hospital admission. The same finding, no association between predicted infarct size and time to admission, was observed when the analysis was limited to the subset of 339 patients who received thrombolytic therapy and had final infarct size measured by thallium tomography.

In Figure 2, final infarct size measured by rest thallium-201 tomography replaces predicted infarct size on the z axis. Unlike predicted infarct size, in which there was no relation to symptom duration, final infarct size was larger in patients treated after a longer duration of symptoms. The largest infarcts were seen in patients randomized not to receive thrombolytic therapy. The presence of abnormal Q waves on the initial ECG was associated with a larger predicted infarct size (Fig. 1, $p = 0.008$) and a larger final infarct size (Fig. 2, $p < 0.0001$) independent of duration of symptoms before initiation of therapy. Despite this finding, the presence of abnormal Q waves on the admission ECG did not eliminate the association between a shorter duration of symptoms before thrombolytic therapy and smaller final thallium infarct size ($p < 0.0001$). Whether there were no, one to two or more than two abnormal Q waves on the initial ECG, final infarct size was smallest in patients treated 0 to 2 h after symptom onset, with progressively larger infarcts in patients treated later and in those who did not receive thrombolytic therapy. The largest mean final infarct size was measured in patients with more than two abnormal Q waves who did not receive thrombolytic therapy (22.5% of the left ventricle). Patients with the same number of abnormal Q waves on their initial ECG treated at 0 to 2 h after symptom onset had a final infarct size of only 10.2%.

Discussion

Origin of early Q waves. Reversible acute myocardial ischemia has been shown to produce R wave voltage changes on the ECG, probably as a result of intramyocardial conduction delays in the ischemic zone of myocardium (3–6). Selvester et al. (7) postulated that proximal or middle occlusions of the left anterior descending coronary artery produce delayed depolarization of myocardium normally activated by the septal and anterior fascicles of the left bundle branch and result in acute reversible R wave diminution or Q wave formation in anterior precordial leads. More distal left anterior descending coronary artery occlusions are postulated to result in conduction delays localized to the apical portion of the anteroseptal wall (leads V_4 to V_6) and delayed right septal

activation, resulting in augmentation of the R wave in the anterior precordial leads.

We observed abnormal Q waves on the initial ECG more commonly in patients with anterior infarction and in those with greater ST segment elevation (i.e., in patients with larger areas at risk). These findings are consistent with the postulate that acute ischemia in regions supplied by the proximal portion of the left anterior descending coronary artery can cause local intramyocardial conduction delays in the regions of the insertion of the specialized conduction system, resulting in early Q wave formation. On the basis of these observations, we postulated that occlusion of arteries supplying large areas of myocardium, especially in the anterior and septal walls of the left ventricle, may be more likely to be associated with delayed activation of the ischemic zone and thus the development of abnormal Q waves within the first hour of ischemia.

Development of abnormal Q waves can occur very early. In the present study, over half (53%) of all patients admitted within the first hour of symptoms had abnormal Q waves on the ECG. The percent of patients with abnormal Q waves did not increase appreciably over the next 6 h. This suggests that factors present very early after arterial occlusion, such as the amount and location of myocardium served by the affected artery, determine whether early abnormal Q waves will develop. If abnormal Q waves observed in this time frame were primarily markers of irreversible infarction, then one would expect a significant increase in the proportion of patients with abnormal Q waves as the duration of symptoms increased and ischemic myocardium became irreversibly infarcted, an association we did not observe.

Impact of early abnormal Q waves on efficacy of thrombolytic therapy. The presence of abnormal Q waves on the admitting ECG was not associated with a lack of benefit from thrombolytic therapy. Neither the presence of one to two nor more than two abnormal Q waves eliminated the finding of smaller final infarct size in patients with versus without thrombolytic therapy or those treated after a longer duration of symptoms. This finding could not be explained by the possibility that patients with abnormal Q waves who received early thrombolytic therapy had less myocardium at risk. The predicted infarct size before therapy (Aldrich score) showed no significant trend as a function of duration of symptoms before treatment whether or not abnormal Q waves were present on the admission ECG.

Patients with abnormal Q waves on the admitting ECG had a larger predicted infarct size before thrombolytic therapy and a larger final infarct size after treatment than those without abnormal Q waves on the initial ECG. This is in part due to the overrepresentation of anterior infarction in patients with an abnormal Q wave but is also the result of abnormal Q waves being a marker for larger areas of myocardium at risk. Finally, we cannot exclude the fact that in some patients, abnormal Q waves represent irreversibly infarcted myocardium, not just reversible conduction abnormalities. Thus, abnormal Q waves on the initial ECG are a marker for larger infarcts but do not preclude significant limitation of infarct size in many patients treated with thrombolytic therapy.

Study limitations. A limitation of the present study is that a substantial proportion (37%) of patients in the four trials otherwise eligible for study did not have radionuclide studies, and thus the findings in our select cohort with infarct size measurements may not be representative of the excluded patients. Follow-up studies were not available for two main reasons: either patients died before the scheduled follow-up or they refused the study, usually because they lived too far from the core laboratory. A comparison of patients not included versus those included in this cohort reveals no significant difference in the number of abnormal Q waves (1.3 ± 1.6 vs. 1.3 ± 1.5, respectively, $p = 0.76$) or predicted infarct size (19.7 ± 8.3 vs. 18.7 ± 8.5, $p = 0.21$), but the excluded patients were treated after a significantly longer duration of symptoms than those who were included (194 ± 103 vs. 143 ± 86 min, $p < 0.0001$). Because these patients were treated later, and many of the deaths probably represent failure of thrombolytic therapy and therefore larger final infarct size, one would expect that their exclusion would cause an underestimation of final infarct size predominantly in patients treated relatively late after symptom onset. If these patients, who had the same number of abnormal Q waves as those with final infarct size measurements, had been included in the analysis, an even more prominent treatment effect of early therapy might have been observed (i.e., an even greater difference in final infarct size between patients treated early versus late, independent of the presence of abnormal Q waves on the admitting ECG).

Another potential limitation of this study is the use of the Aldrich score, an ECG-derived measurement, to estimate infarct size before thrombolytic therapy. Direct measurement of the myocardium at risk using thallium or technetium sestamibi would probably have given a more accurate measurement of predicted infarct size (14). However, the Aldrich score has been shown to have a highly significant correlation with final infarct size in patients not receiving thrombolytic therapy (12,15). In our study patients, we showed that mean predicted final infarct size were thrombolytic therapy not given was unaffected by duration of symptoms before therapy; therefore the Aldrich score was adequate for our purpose. However, the Aldrich score probably does not have a high enough correlation coefficient with final infarct size to be used as a specific measure of myocardium at risk for the determination of myocardial salvage in individual patients.

Finally, the use of a single rest tomographic thallium image acquired immediately after injection may lead to overestimation of myocardial infarct size in some patients because of poor thallium uptake in chronically ischemic but viable myocardium. Two aspects of the protocol would minimize this effect: First, these were rest injections, therefore eliminating any effects of preceding exercise-induced relative hypoperfusion. Second, because of the mean delay of 8 weeks after infarction, overestimation of infarct size as a result of rest ischemia in periinfarct regions is significantly reduced whether or not patients are initially treated with thrombolytic therapy (16,17). We

would thus expect minimal overestimation of infarct size and, furthermore, would expect any such errors to be randomly distributed across the patient groupings. Specifically, it is unlikely that such a false overestimation of infarct size would occur in patients as a function of either the duration of symptoms before therapy or the presence or absence of abnormal Q waves on the initial ECG.

Clinical implications. In the late phase after myocardial infarction, abnormal Q waves often represent infarcted myocardium (1). It is therefore not unreasonable to assume that many clinicians interpret an abnormal Q wave on the admitting ECG in a patient with suspected acute myocardial infarction to be evidence of late presentation, signifying little potential for myocardial salvage. Because of this, many otherwise suitable patients may not be offered early reperfusion therapy. The findings of the present study suggest that Q waves are a poor predictor of symptom duration; ~50% of patients seen within 1 h of symptom onset had abnormal Q waves on the admitting ECG. Furthermore, our findings show that abnormal Q waves on the admitting ECG identify patients with a greater extent of myocardium at risk and that these patients have substantial myocardial salvage after treatment with thrombolytic therapy.

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