Cardiac

NON - Q - WAVE MYOCARDIAL INFARCTION

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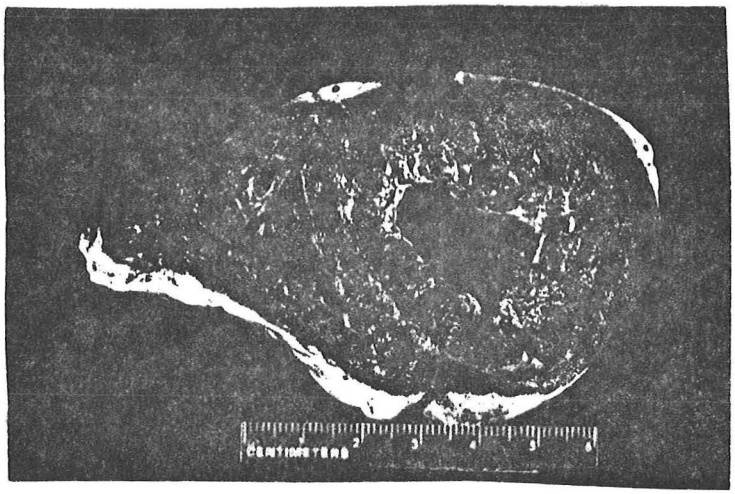
Thursday, 5 June, 1986

Medical Grand Rounds
University of Texas Health Science Center
Dallas, Texas

If language is not used rightly, then what is said is not what is meant. If what is said is not what is meant, then that which ought to be done is left undone.

Confucious



Introduction

For many years, the diagnosis of subendocardial or nontransmural myocardial infarction with ST segment changes without QRS complex changes on the electrocardiogram and relatively small increases in cardiac enzyme levels was of only passing interest. While considered a form of myocardial infarction, it was associated with low morbidity and mortality rates (1). Several studies in the 1970's showed that those assumptions were incorrect and that the prognosis of these patients is identical to those who suffered a transmural myocardial infarction (2-8). Furthermore, at approximately the same time a series of studies reported that the presence or absence of pathological Q waves had no relation to the subendocardial or transmural character of myocardial infarcts (9-15).

This review addresses several issues that have been the subjects of recent reviews (16, 17) including the correct definition of the clinical entity, its prevalence, its diagnosis, and its therapeutic management. For the sake of clarity and consistency, it should be noted at the outset that the myocardial infarction associated with ST-T wave changes without changes in the QRS complex on the electrocardiogram will be referred to uniformly as a non-Q-wave myocardial infarction. The terms "subendocardial" and "nontransmural" will be interchanged with non-Q-wave infarction.

Incidence

Table 1 lists most of the published clinical studies reported during the past 15 years. Of a total of 10,442 patients surveyed, 2,221 or 21 percent were diagnosed as non-Q-wave myocardial infarction. The incidence ranged from 4 to 41 percent.

Pathological reports cannot be included in this list because, as will be seen, the pathological associations of non-Q-wave myocardial infarctions are varied. The methods by which non-Q-wave, nontransmural or subendocardial infarctions have been diagnosed have become more sophisticated during the past 15 years. Nevertheless, the common electrocardiographic finding with all these studies is the clinical presentation of an acute myocardial infarction without Q-waves and with persistent ST-T wave changes.

Although the range of frequency of non-Q-wave myocardial infarction is up to 41 percent, the series of large numbers of patients report an incidence of about 20 percent. Thus, the incidence of a non-Q-wave myocardial infarction among patients admitted to a coronary care unit with a clinical diagnosis of acute myocardial infarction is one in five patients.

Table 1. Incidence of Non-Q-Wave Myocardial Infarction (NQWMI) in Patients Admitted with Acute Myocardial Infarction

Reference	Year	Numbers of Patients: Total	NQWMI	Percent
1. Abbott and Scheinman (3)	1973	230	78	34
2. Madias et al (5)	1974	104	43	41
3. Rigo et al (6)	1975	159	48	31
4. Genovese et al (18)	1976	500	22	4
5. Cannon et al (7)	1976	188	40	21
6. Rothkopf et al (19)	1979	43	10	23
7. Fabricius-Bjerre et al (20)	1979	276	98	36
8. Thanavaro et al (21)	1980	745	124	17
9. Mahony et al (22)	1980	635	141	22
10. Marmor et al (23)	1981	200	58	29
11. BHAT Trial (24)	1982	3837	806	21
12. Krone et al (25)	1983	593	94	16
13. Coll et al (26)	1983	458	28	6
14. Maisel et al (27)	1985	1253	277	22
15. Connolly and Elveback (28)	1985	1221	353	29
Totals		10,442	2,221	
		Average		21%
		Range		4 - 41%

Pathology

It is important to note that there is no specific pathological correlation with a non-Q-wave myocardial infarction.

Prinzmetal et al, originally reported that pure subendocardial infarcts do not significantly alter the depolarization complex (29). This observation has been refuted consistently by subsequent reports (9-15). Durrer et al (9) reported that, after the ligation of coronary arteries in dogs, the smallest subendocardial scar resulted in the occurrence of abnormal Q waves. Further studies (10, 11) confirmed that both experimentally induced and clinical subendocardial infarcts are often accompanied by pathological Q waves. Others (12-15) have confirmed in clinico-pathological correlative studies that both nontransmural and transmural infarcts generate pathological Q waves on the electrocardiogram that are indistinguishable. Furthermore, Raunio et al (16) showed that while half the subendocardial infarctions generated pathological Q waves, half of the transmural infarcts had no Q waves.

Friefeld et al (30) have reported on the autopsy comparisons of 35 Q-wave and 35 non-Q-wave myocardial infarctions. They showed that non-Q-wave infarcts were associated with acute coronary thrombi in the distribution of the infarct in 50 percent of patients and with contraction band necrosis more frequently than with Q-wave infarcts. The importance of this latter finding is that represents evidence for early reperfusion into an infarct. The amount of contraction band necrosis with non-Q-wave infarcts suggest that differing pathophysiological events in the coronary tree are responsible, including thrombotic occlusion, coronary artery spasm, transient hypoperfusion, and reperfusion via spontaneous thrombotic recalalization. These findings concur with previously reported catheterization findings after myocardial infarction and other syndromes of myocardial ischemia (31, 32).

	TMI	NTMI	p Value
All Patients (48 patients)			
Peak CPK level	1,090 ± 210*	290 ± 60*	<0.01
Coronary arteries narrowed > 50 per cent	2.0 ± 0.2	2.0 ± 0.2	NS
Coronary Score	7.9 ± 0.6	8.2 ± 0.7	NS
Patients with First Infarction (32 patients)			
Peak CPK level	1,220 ± 300*	210 ± 40*	<0.05
Coronary arteries narrowed >50 per cent	1.8 ± 0.2	1.4 ± 0.2	NS
Coronary score	6.9 ± 0.6	6.5 ± 0.6	NS

NOTE: Values shown are mean ± SEM. NS = not significant.
* Creatine phosphokinase (CPK) in International Units per liter.

Table II. Coronary anatomy and peak CK levels (33).

Details of the coronary pathoanatomy of patients with non-Q-wave myocardial infarctions have also been recently reported (33-35). Several investigators have shown that in comparing Q-wave with non-Q-wave myocardial infarctions, there was no difference in the extent or number of coronary arteries involved in either type of infarction.

Diagnosis

Electrocardiogram

Because of the previously mentioned pathological findings in the presence and absense of pathological Q waves on the electrocardiogram of patients with either a transmural or nontransmural myocardial infarction, it has been repeatedly suggested that myocardial infarctions be distinguished by the presence or absence of a Q wave.

The Minesota Code Criteria for the diagnosis of non-Q-wave myocardial infarction as proposed by Blackman and associates, is shown in Table III (36). The importance of having a set classification such as this is the need for diagnostic standardization for clinical trials and studies. For example, in the BHAT Trial, the diagnosis of non-Q-wave myocardial infarction required (a) ST segment depression and T-wave inversion, (b) prolonged chest pain, and (c) an appropriate evolution in the plasma enzyme levels (24). In virtually every clinical study, these findings together have been used for the identification of patients with a subendocardial infarction, a nontransmural infarction or a non-Q-wave myocardial infarction.

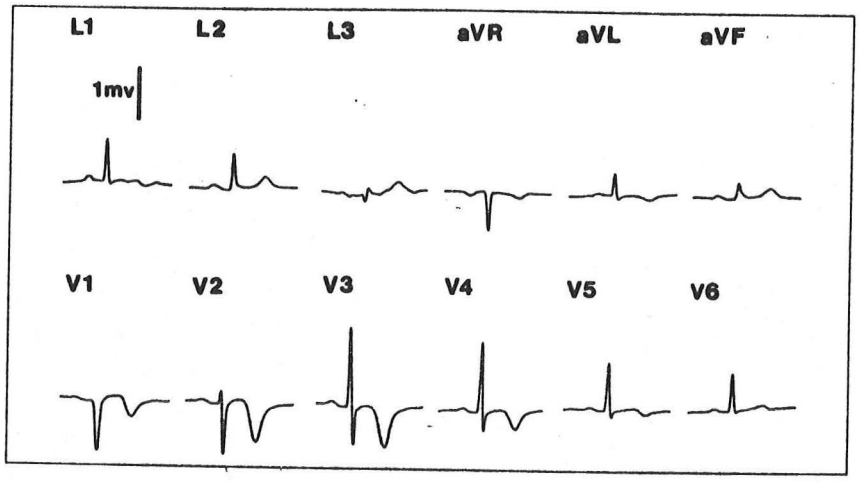


Figure 1. A non-Q-wave myocardial infarction (72).

Table III. Minnesota Code Criteria for the Diagnosis of Non-Q-Wave Myocardial Infarction

1a. ST elevation (ST elevation of 1 mm or more in limb leads or 2 mm or more in leads V1-V4) and ST depression (ST depression of at least 1 mm with ST segment horizontal or downsloping) in the same record.

OR

1b. Increasing or decreasing ST elevation. Our record indicates an ST elevation of 1 mm or more in linb leads or 2 mm or more in V1-V4 and another record does not so indicate such an elevation. Least and greatest ST elevations are compared.

OR

1c. Increasing or decreasing ST depression by comparing the least and greatest ST segment abnormalities. Our record shows no or minor ST depression (ST-J depression less than 0.5 mm with downsloping ST segment of at least 0.5 mm below PR baseline or in ST-J depression of 1 mm or more with upsloping ST segment) and another record showing a major ST segment depression (in ST-J depression at least 0.5 mm with ST segment horizontal or downsloping).

OR

1d. Increasing or decreasing T waves by comparing the least and greatest T wave inversion. One record shows no or minor T wave inversion (T amplitude of less than 1 mm inverted but not positive and another recording showing T-wave inversion (T amplitude negative or inverted at least 1 mm).

PLUS

2. Absence of left bundle branch block and Wolf-Parkinson-White syndrome.

PLUS

3. Elevated levels of serum emzymes

PLUS

4. Typical symptoms of acute myocardial infarction

REFERENCE #36

Enzymatic Diagnosis

The lack of pathological sensitivity and specificity associated with the electrocardiographic changes of a non-Q-wave myocardial infarction has led to the search for more accurate means of making the diagnosis. It is now generally agreed that the diagnosis of non-Q-wave myocardial infarction can only be made with the corroboration of positive isoenzyme or radionuclide studies.

Since Roberts and colleagues (37) identified elevated serum creatine kinase MB-isoenzyme (CK-MB) activity as a high sensitive and specific indicator of myocardial injury, it has been shown that a rapid release of CK-MB isoenzymes is characteristic of an acute non-Q-wave myocardial infarction. Shell et al (38) obtained samples for MB-CK isoenzymes determinations every 10 minutes for 20 minutes and then every 4 hours for 24 hours in 16 patients subsequently diagnosed as non-transmural myocardial infarction. The results showed that CK-MB release occurs earlier in patients with non-transmural infarction compared to those with Q-wave infarctions. These findings are consistent with the more recent observations previously mentioned that non-Q-wave myocardial infarctions are associated with other evidence of early reperfusion of the infarct area (30). Subsequently, Hiller et al have reported that elevated CK-MB isoenzyme activity in the presence of normal serum creatine kinase levels represents definite myocardial injury and is considered consistent with a diagnosis of non-Q-wave myocardial infarction (39).

Rothkopf and colleagues (19) have reported the value of serial CK-MB isoenzymes determinations for the detection of myocardial infarct extension including in patients with non-Q-wave myocardial infarctions.

In summary, the demonstration of early creatine kinase enzyme elevations, and in particular, CK-MB isoenzymes elevations together with symptoms and classical electrocardiographic changes are necessary for confirmation of the diagnosis of non-Q-wave myocardial infarction.

Radionuclide Studies

Willerson and colleagues (40) in 1975 reported that 17 patients admitted with electrocardiographic and enzymatic evidence of non-Q-wave myocardial infarctions had increased technitium 99-M stannous pyrophosphate uptake (PYP) on myocardial scintography. It should be noted that in 11 of the 17 patients, the PYP uptake was designated as 2+ diffuse (out of 4+). Three months later the same group reported on the PYP studies of 202 patients admitted with chest pain of unknown etiology (41). In the 101 patients with ECG and enzymatic evidence of acute myocardial infarction, including 18 patients with non-Q-wave infarcts, PYP scintigrams were positive when done within 6 days of the suspected infarction. In this study, they reported on 7 positive PYP scintigrams of patients subsequently diagnosed as unstable angina. These scintigrams were labeled as 2+ diffuse and comment is made on the similarity of findings between patients with unstable angina and those with non-Q-wave infarctions.

The predictive value of the PYP scintigrams was reevaluated by Berman et al (42). By designating a 2+ diffuse scintigram as equivocal rather than positive for myocardial infarction, they increased the sensitivity and specificity and thus the predictive value of the technique for acute transmural infarctions. However, in their study, the scintigraphic results of 18 patients with ECG and enzymatic evidence of non-Q-wave infarction were: 7 with a positive, 9 with an equivocal and 2 with a negative sentigram. By altering the classification to increase the predictive value of the technique in transmural infractions, they demonstrated its vulnerability as a diagnostic technique in non-Q-wave infarctions.

Subsequently, several studies have confirmed that PYP scintigraphy is a relatively insensitive diagnostic test for non-Q-wave myocardial infarctions. Massie et al (43) agreed that discrete PYP uptake is a sensitive marker for acute myocardial necrosis, but showed in 31 patients that discrete uptake only occurs in a minority of patients with non-Q-wave infarctions. These findings concurred with those presented by Codini et al (44).

The issue of the similarity in PYP scintigraphic findings in patients with non-Q-wave infarction and with myocardial ischemia was addressed by Poliner et al (45), who reported the pathological findings in 52 patients with positive PYP scintigrams. They showed that a positive PYP scintigram is indicative of myocardial injury due to either confluent coagulation necrosis consistent with clinical infarction or to multifocal coagulation necrosis or myocytolysis consistent with unstable angina or recurrent ischemia. A similar clinical study by Jaffe and colleagues (46) showed that some patients admitted with unstable angina confirmed by normal enzymatic determinations have positive PYP scintigraphy, indicating the presence of myocardial necrosis in these patients. The subsequent studies of Freifeld, Schuster and Bulkley (30) referred to above in the discussion on pathology and pathogenesis serve to confirm these earlier suggestions regarding myocardial necrosis.

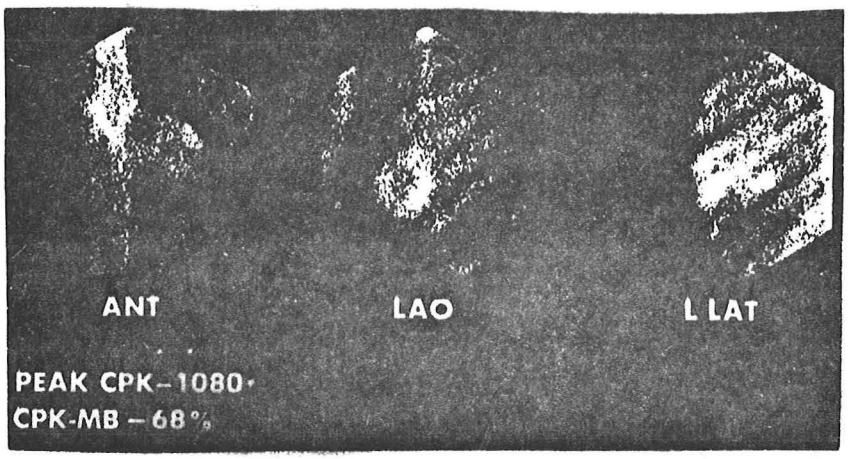


Figure 2. PYP scintigram of a non-Q-wave myocardial infarction (43).

There are a few other items of interest regarding the value of PYP scintigraphy in the diagnosis of non-Q-wave myocardial infarctions. Olsen and colleagues (47) have reported that when evaluating a patient more than 48 hours after the onset of chest pain, and after the CK-MB isoenzyme levels have returned to normal, the positive PYP scintigram has a high sensitivity and specificity for transmural infarcts. The comparative data for non-Q-wave infarctions showed only average sensitivity and specificity. Ahmad et al (48) in a review of acute infarct patients with a doughnut pattern of PYP myocardial uptake found no patients with non-Q-wave infarcts with this characteristic scintigraphic pattern. Corbett and colleagues (49) have recently shown the increased sensitivity of single-photron emission computed tomography (SPECT) compared to planar imaging of PYP scintograms in diagnosing acute non-Q-wave infarcts. Comparative sensitivities in 19 patients with non-Q-wave infarcts were 95 percent by SPECT compared to 67 percent by planar imaging. Furthermore, the same technique has been shown to estimate myocardial infarct size by the same group (50).

The value of PYP scintigraphy in detecting perioperative infarctions after coronary artery bypass has been shown by several investigators (51,52). The absence of Q-waves and the lack of sensitivity of CK-MB isoenzyme determinations in perioperative patients emphasizes the value of PYP scintigraphy in this patient subset.

The value of "cold spot" scanning in acute myocardial infarction was evaluated by Wackers et al (53) using thallium-201 (Tl-201) scintigraphy, where a very high sensitivity for positive scintigraphy within 24 hours of onset of symptoms was found. Pohost and colleagues (54) showed the benefit of serial myocardial scans after a single injection of Tl-201 in distinguishing transiently ischemic from infarcted myocardium. The distinction between a "reversible defect" with reperfusion of an originally nonperfused area reflecting transient ischemia and a "persistent defect" reflecting infarction was demonstrated. Furthermore, the anatomical location of the perfusion abnormality may be used to predict the underlying coronary artery disease (55).

It has been suggested that the Tl-201 scintigram may be less sensitive for identifying non-Q-wave infarctions because both transient ischemia and non-Q-wave infarcts manifest early reperfusion (19,30). Recently, a pattern of so-called "reverse redistribution" on serial Tl-201 scintigraphy has been shown to suggest that this pattern is typical of non-Q-wave infarction, with a patent infarct-related coronary artery (56).

Position-emission tomography has been shown to be promising in detecting and characterizing non-Q-wave myocardial infarctions (57).

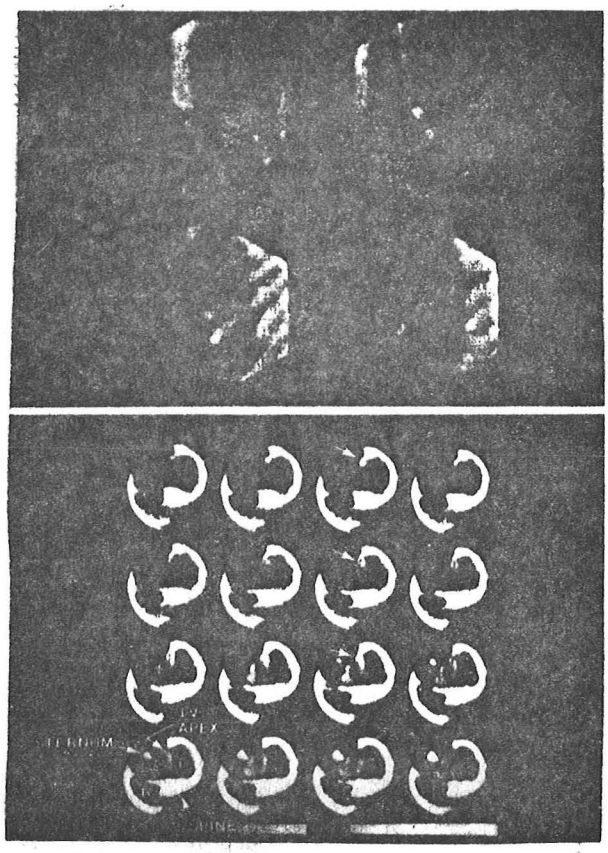


Figure 3. Planar (top) and SPECT images of a non-Q-wave myocardial infarction (49).

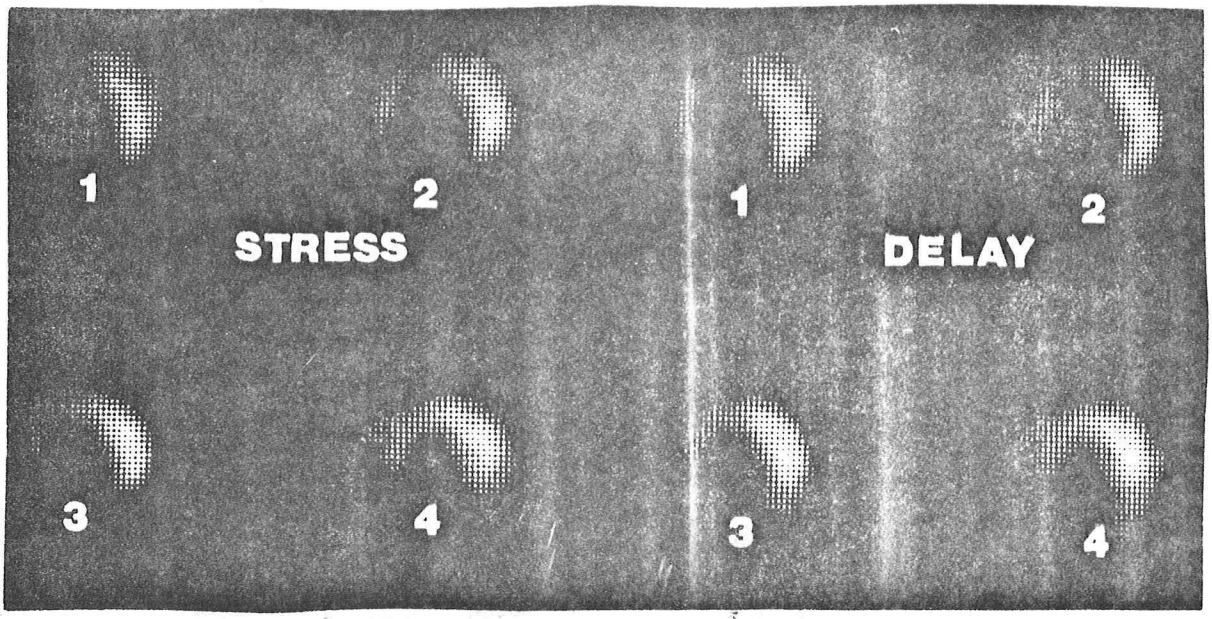


Figure 4. Thallium - 201 images in an acute myocardial infarction showing a persistent defect (55).

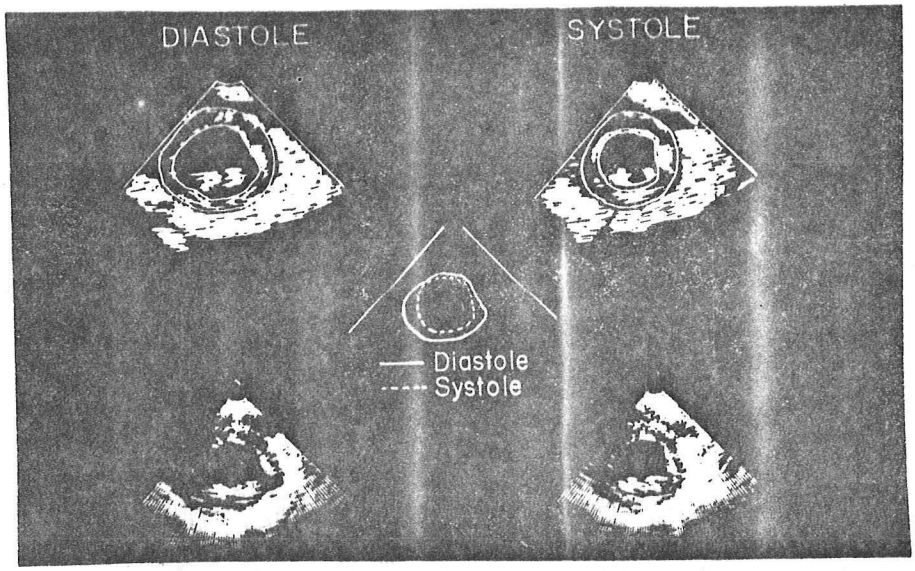


Figure 5. Two-dimensional echocardiogram in an acute anterolateral myocardial infarction (63).

Echocardiography

The value of two-dimensional echocardiographic studies in the detection and characterization of non-Q-wave myocardial infarction remains debatable. Nixon and colleagues (58) reported in a study of patients with both transmural and non-Q-wave myocardial infarctions that left ventricular segmental wall motion abnormalities occurred with less frequency or were absent in patients with non-Q-wave infarctions. The observation that the 2D-echocardiogram was less sensitive in detecting non-Q-wave infarctions has been subsequently confirmed by several investigators (59-62). These variable dynamic echocardiographic findings are consistent with the pathological identification of early vascular reperfusion in non-Q-wave infarction (30). Thus, the similarity in pathogenesis of non-Q-wave myocardial infarction and transient myocardial ischemia, like PYP and TC-201 scintigraphy, affects the sensitivity of the 2E-echocardiogram in both clinical circumstances (63).

Nixon et al (58) also identified, in small numbers of patients, extension of non-Q-wave to transmural infarctions. This is reasonable utilizing a technique with high sensitivity for the detection of wall motion abnormalities in patients with transmural myocardial infarction. Force et al (64) have recently reported the value of 2D-electrocardiography in confirming the occurrence of non-Q-wave perioperative infarctions in patients undergoing coronary artery bypass surgery.

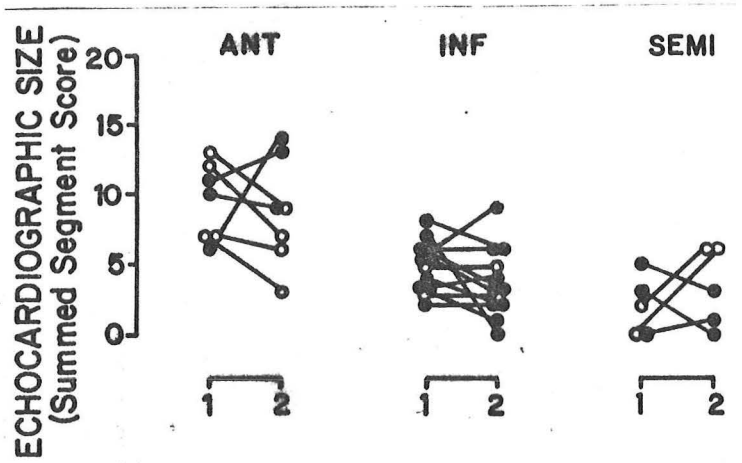


Figure 6. Serial 2D-echocardiograms in anterior (ANT), inferior (INF) and non-Q-wave infarctions (SEMI). Open circles represent infarct extensions.

Magnetic Resonance Imaging

Recently Filipchuk and colleagues (65) have confirmed the capability of magnetic resonance imaging to localize and characterize acute myocardial infarction, including non-Q-wave infarcts, in patients by the identification of increased myocardial signal intensity, increased cavitary signal intensity and reduced myocardial wall thickening.

Clinical Course and Prognosis

Early post-infarction period

Although there were a few small studies with contrary conclusions about the same time (21,22,67), several reports in the early and mid 1970's comparing morbidity and mortality data in transmural and non-Q-wave myocardial infarctions revealed no differences in age or sex distribution and similarities in peri-infarction frequency of supraventricular and ventricular arrhythmias (2,5-7,20,66,68,69). Table IV lists most of the studies comparing early or in-hospital mortality rates of non-Q-wave versus transmural infarctions. The overall in-hospital mortality rate for non-Q-wave infarction is 10 percent, with a range of 2-23 percent. This compares with an in-hospital mortality rate for transmural infarction of 17 percent in the same comparative studies, with a range o 10-30 percent. Several studies, including those of Szklo (68), Thanavaro (21), Hutter (70) and Marmor (23) found the in-hospital rates of the non-Q-wave infarcts to be significantly less than those with transmural infarctions.

Part of this disparity in mortality rates may be attributed to the size of the non-Q-wave infarction. Both Scheimann and Abbott (2) and Rigo et al (6) demonstrated more than 10 years ago that the incidence of complications including death in non-Q-wave infarctions was related to the magnitude of the myocardial enzyme elevations. Thus, the larger the area of myocardial involvement, the greater the likelihood of complications or death.

In 1976, Kossowsky et al (68) reported that 13 (37 percent) of 35 patients admitted to their coronary care unit with non-Q-wave myocardial infarctions progressed during their stay to transmural infarctions. Apart from one or two anecdotes, this was the first report of this significant complication of non-Q-wave infarction. Table IV enumerates the frequency of infarct extension in non-Q-wave infarcts in studies published since the original report. The overall infarct extension rate in these studies is 23 percent, with a range of 8-43 percent, Hutter et al (69) have noted that the frequency of complications such as ventricular arrhythmias and congestive heart failure increases after infarct extension. Furthermore, and of greater importance, several authors including Thanavaro (21), Hutter (70), Marmor (23) and Maisel (27) have reported an increase in mortality rate in patients who have an extension to their original infarction.

In a large prospective study of 200 patients, Marmor and colleagues (23,73) reported infarct extension rates of 8 and 43 percent in transmural versus non-Q-wave myocardial infarctions. They showed that while infarct extension does not materially affect the mortality rate of transmural (Q-wave) infarcts, the occurrence of extension in a non-Q-wave infarct increases the mortality rate from 10 to 16 percent. They also reported the average time as which extension occurred was 10 days after the onset of the initial infarct. Statistical analysis of risk factors revealed that only recurrent chest pain, obesity and female gender were the only predictive variables.

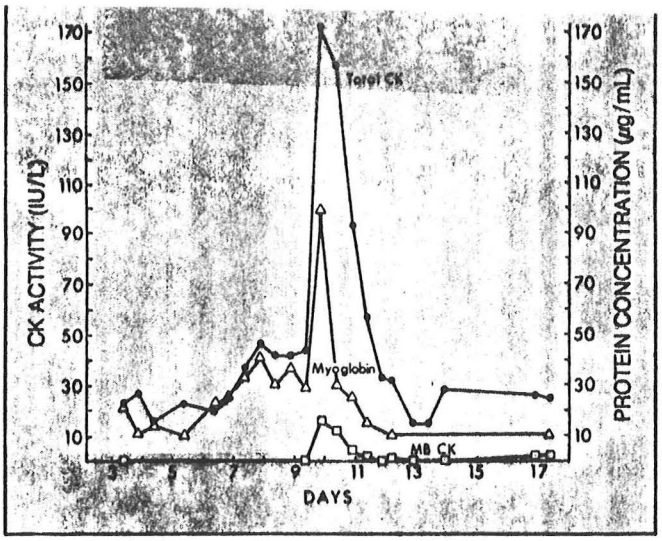


Figure 7. Serial CK-MB determinations in a non-Q-wave infarction showing infarct extension (23).

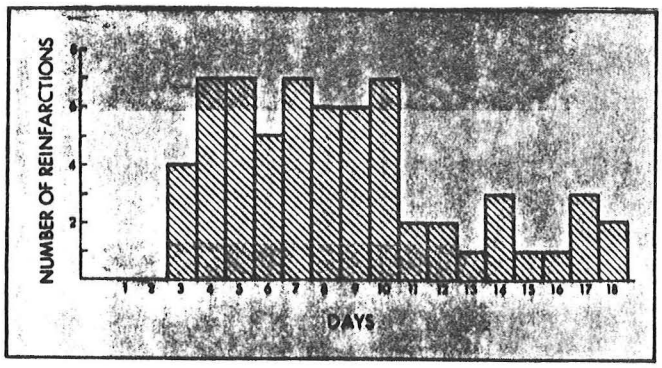


Figure 8. Temporal display of infarct extension in non-Q-wave myocardial infarction (73).

Table IV. Rates of Infarct Extension, Early and Late Mortality in Patients with Non-Q-Wave Myocardial Infarction (NQWMI)

Reference	Year	NQWMI	Infarct Extension	Mortality Early	Mortality Late
1. Scheinman and Abbott (2)	1973	78	-	23%	-
2. Madias et al (5)	1974	43	-	9%	-
3. Rigo et al (6)	1975	48	-	13%	19% (2yr)
4. Madigan et al (65)	1976	50	-	2%	-
5. Cannon et al (7)	1976	40	-	8%	33% (3yr)
6. Kossowsky et al (68)	1976	35	35%	11%	-
7. Szklo et al (69)	1978	283	-	18%	28% (3yr)
8. Fabricius-Bjerre et al (20)	1979	98	-	-	49% (5yr)
9. Rothkopf et al (19)	1979	10	20%	-	-
10. Poehllman and Silverman (8)	1980	50	13%	8%	-
11. Thanavaro et al (21)	1980	124	-	3%	-
12. Hutter et al (70)	1981	67	-	9%	52% (5yr)
13. Marmor et al (23)	1981	58	43%	12%	-
14. Hollander et al (71)	1984	38	18%	21%	-
15. Maisel et al (27)	1985	277	8%	8%	12% (1yr)
16. Connolly and Elveback (28)	1985	353	-	6%	-
17. Zema	1985	28	-	4%	-
Total		1680 patients			
Means: Infarct extension			- 23% (8-43%)		
Early mortality				- 10% (2-23%)	

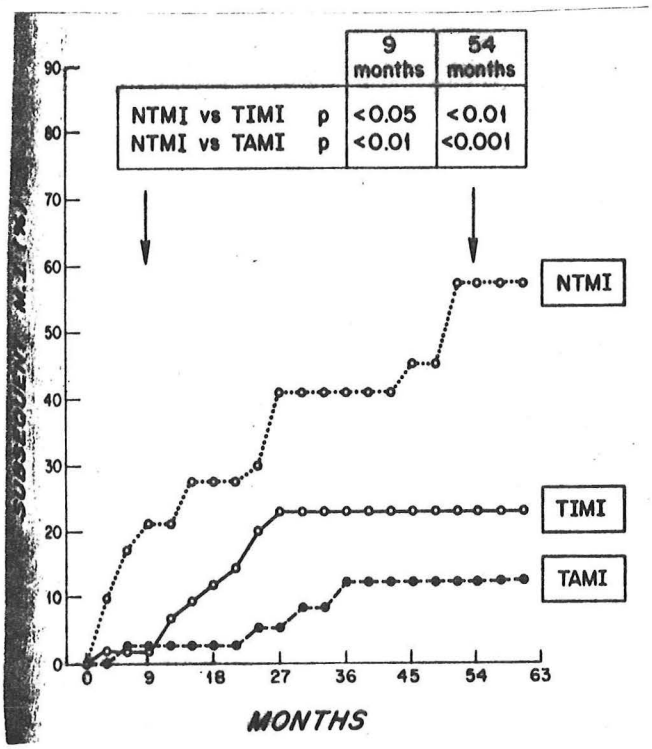


Figure 9. Follow-up data on subsequent myocardial infarction (MI) in transmural anterior (TAMI), transmural inferior (TIMI) and nontransmural (NTMI) groups (70).

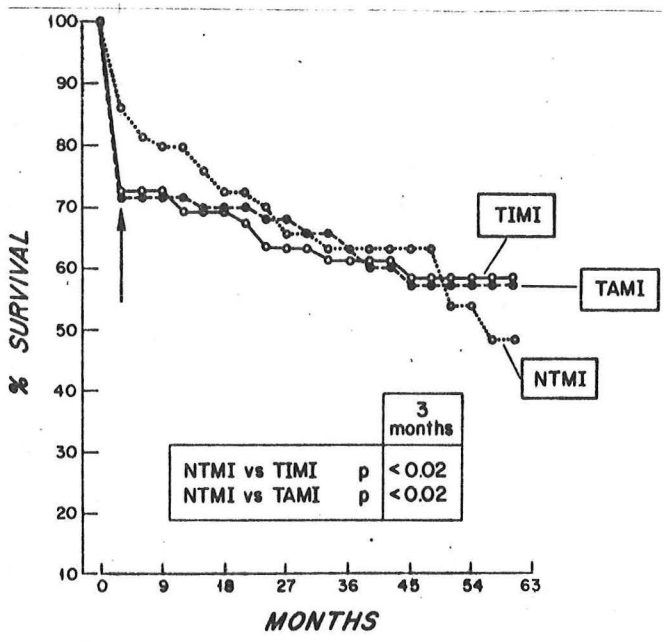


Figure 10. Survival curves of the three patient groups shown in Figure 9 (70).

Late Clinical Course

The recognition of high risk patients after acute myocardial infarction is crucial in the long term management of these individuals. While all patients having a myocardial infarction are at increased risk for recurrence or death, any determination of high risk patient subsets is of immense value.

Several recent studies have shown that the long term prognosis of patients with non-Q-wave myocardial infarctions is very similar to the prognosis with transmural infractions. Table lists the late mortality rates in these reports from 1 to 5 years of variable follow-up. While the numbers of studies are small, the annual mortality rates of pateints with non-Q-wave infarcts are 12 percent at 1 year, 19 percent at 2 years, 31 percent at 3 years and 50 percent at 5 years. The comparative rates in patients with transmural infarctions in these same studies are 12 percent at 1 year, 18 percent at 2 years, 28 percent at 3 years and 52 percent at 5 years, almost identical numbers. Furthermore, Marmor et al (73) and Hutter et al (70) have both demonstrated the increased mortality rate both early and late in the follow up of non-Q-wave infarction patients that suffer an infarct extension after their initial insult.

Meisel et al (74) have recently reported that the documentation of complex ventricular ectopic activity (VEA) on the predischarge 24-hour ambulatory monitoring recording after a non-Q-wave myocardial infarction defines a high risk patient with respect to 1 year survival after infarction. In non-Q-wave infarct patients, 62 percent of those who died had complex VEA compared to 32 percent of survivors. No differences were found in the group with Q-wave infarctions.

It is because of these early and late post-infarction complications that Hutter et al (70) stated that non-Q-wave myocardial infarction is an unstable ischemic event associated with a great risk of later myocardial infarction and a high late mortality rate. A more aggressive diagnostic and therapeutic approach may be warranted in these patients.

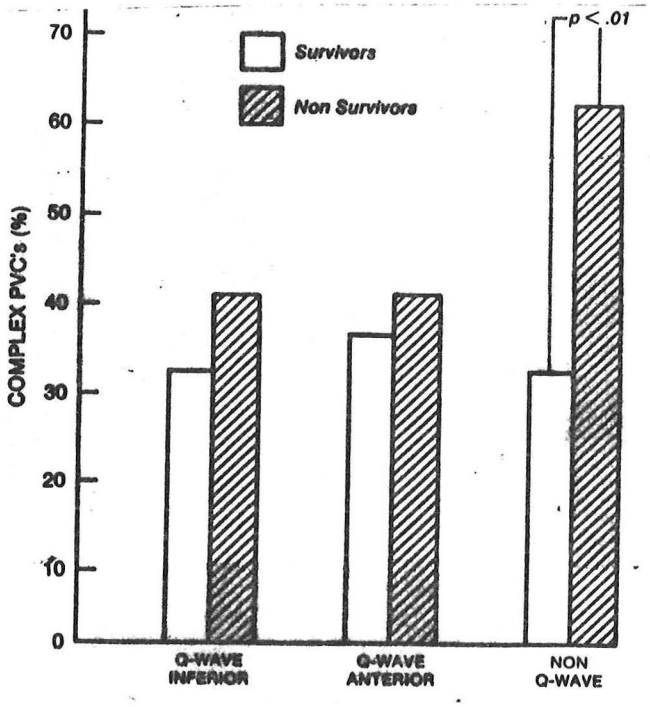


Figure 11. Relationship between complex VEA on discharge monitoring and one year survival (74).

Management

Early care

Although the early course of non-Q-wave myocardial infraction is characteristically benign, conventional coronary unit and post-CCU step down unit care is advocated. The frequency of arrhythmias and cardiac failure in these individuals is similar to patients with transmural infarctions (2, 5-7, 20, 65, 67, 68).

Infarct Extension

The infarct extension rate in patients with non-Q-wave myocardial infarction averages 23 percent, or approximately 1 patient in 4. Thus surveillance for infarct extension is critical. This may be accomplished by serial CK-MB isoenzyme determinations every 12 hours for 14 days (23). Although Marmor et al (73) have shown that recurrent chest pain, female gender and obesity are statistically significant independent predictors of infarct extension, none are 100 percent sensitive. Furthermore, many of these patients suffer ongoing angina without extending their infarction.

Until recently, the therapeutic management of these individuals, particularly in attempting to prevent infarct extension, has been speculative at best. Several beta-blocker trials, including the BHAT Trial (24), have demonstrated that these compounds have no effect on the morbidity or mortality rates of non-Q-wave infarctions, in contrast to the encouraging results with transmural infarctions (75).

The Nontransmural Multicenter Reinfarction Study (76) has been recently completed. They specifically addressed the issue of infarct extension in patients with non-Q-wave infarcts, with the randomized double blind administration of placebo or diltiazem, 360mg per day for 14 days. 576 patients were entered within 24 to 72 hours of onset of their infarction. The investigators reported a significant reduction in the frequency of infarct extension and recurrent angina in the treatment group. Of 41 pateints who suffered infarct extension, 26 (63 percent) were in the placebo group and 15 (36 percent) in the diltiazem treated group ($p < 0.04$). The conclusions of the study are that diltiazem is well-tolerated, safe and effective in the prevention of recurrent infarction and angina in patients with non-Q-wave infarction.

Acute interventional therapy

It has been suggested that the pathogenesis of non-Q-wave myocardial infarction is multifactorial, factors including thrombotic occlusion, coronary artery spasm, transient hypoperfusion, and reperfusion via spontaneous thrombotic recanalization (30). It has been morphologically and clinically demonstrated that intracoronary thrombus plays a significant role in the genesis of a non-Q-wave infarction (30-32,34). These observations naturally raise the issue of acute interventional therapy in these patients (78,79). The effectiveness of streptokinase infusion in patients with non-Q-wave infarcts in recanalizing the occluded coronary vessel has been clearly documented (32,34).

Recently, the findings of the thrombolysis in myocardial infarction (TIMI) trial have shown the efficacy of tissue-type plasminogen activator in recanalizing the occluded coronary vessels of patients entered with sustained angina for more than 30 minutes with 1 mm ST segment elevation in at least two ECG leads (80). It is conceivable that a substantial number of the patients entered into the TIMI trial were evolving a non-Q-wave myocardial infarction. Thus thrombolysis may be considered a therapeutic option in these patients, particularly in those with recurrent or continuing angina.

The precise role of acute interventional therapy in the management of non-Q-wave myocardial infarction will, no doubt, be the subject of further detailed study.

Should coronary artery bypass surgery be necessary in the peri-infarction management of patients with non-Q-wave infarctions, it has been documented that the perioperative morbidity and mortality rates in these patients are both very low, and certainly much better than in transmural infarct patients (81,82).

Predischarge Evaluation

The long term prognosis of patients with non-Q-wave myocardial infarction is similar to transmural infarction in general. Non-Q-wave infarct patients who suffered an infarct extension and those with documented complex ventricular ectopic activity have a worse prognosis than transmural infarct patients (71,75,76). Thus the predischarge evaluation of these patients should be as comprehensive as is feasible, and should include radionuclide ventriculography (MUGA), treadmill exercise testing and 24 hour ambulatory electrocardiographic monitoring. The demonstration of a diminished left ventricular ejection fraction (82), a positive exercise stress test (83) or complex ventricular ectopic activity on ambulatory monitoring (74) are all indicators of high risk patients for subsequent cardiac events after non-Q-wave infarction and such patients require further evaluation including cardiac catheterization.

Long term care

Apart from any management dictated by the results of the predischarge evaluation, the long term management of patients with non-Q-wave myocardial infarction remains a concern, as their prognosis is identical to those with transmural infarctions. Discussion continues on the efficacy of beta-blockers as prophylactic therapy against sudden death in non-Q-wave infarct patients (84). While the Norwegian Multicenter Study using timolol (84) showed a reduction in cardiac mortality, the Beta-blocker Heart Attack Trial (BHAT) (24) showed no statistical reduction in cardiac mortality during the follow-up of non-Q-wave infarction patients. Recently, part II of the Persantin-aspirin reinfarction study (85) has reported the beneficial effects of this therapeutic combination in reducing the incidence of coronary death in the follow up period.

There appears to be no doubt that prophylactic therapy is effective. The selection of a prophylactic agent may remain a personal preference although the argument for using persantin and aspirin would appear to be very strong.

Summary

1. There is no doubt that the diagnosis of non-Q-wave myocardial infarction is important for therapeutic and prognostic reasons.

2. Surveillance of patients for infarct extension is critical for therapeutic and prognostic reasons. This may be done by serial CK-MB isoenzyme determinations for 14 days after the infarction.

3. Where feasible, diltiazem, 360mg per day, should be given to these patients for 14 days after infarction for prophylactic and therapeutic reasons.

4. Acute interventional therapy should be considered in these patients after admission, particularly in those evolving non-Q-wave infarcts with continuing chest pain. The place of acute interventional therapy in all such patients has yet to be determined.

5. Comprehensive predischarge evaluation, including radionuclide ventriculography, stress testing and ambulatory monitoring, is important in these patients for prognostic reasons.

6. Prophylactic therapy in patients should be considered. At present, persantin and aspirin would appear to be the prophylactic agents of choice.

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