Incidence and prognosis of non-Q-wave vs. Q-wave myocardial infarction following catheter-based reperfusion therapy

A. HALKIN1, D. FOUREY1, A. ROTH1, V. BOYKO2 and S. BEHAR2

From the 1Department of Cardiology, Tel Aviv Medical Center, Tel Aviv and 2Neufeld Cardiac Research Institute, Tel Hashomer, Israel

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Summary

Background: The clinical importance of classifying myocardial infarction (MI) into non-Q-wave (NQWMI) vs. Q-wave (QWMI) subsets is controversial and might depend on the therapeutic reperfusion strategy employed. The prognostic implications of NQWMI development following primary percutaneous coronary intervention (PCI) have not been reported.

Aim: To examine the incidence, determinants and prognostic implications of NQWMI vs. QWMI development following primary PCI.

Design: The ACSIS Registry, a 2-month nationwide survey conducted biennially, prospectively collects data from all MI admissions in Israel.

Methods: Outcomes were compared among patients managed by primary PCI who subsequently developed NQWMI vs. QWMI. Independent predictors of Q-wave development and 1-year mortality were determined by multivariate stepwise logistic regression analysis and Cox proportional hazard model, respectively.

Results: Of 4537 MI patients with ST-segment elevation on admission, 1230 (27%) were treated with primary PCI. A discharge diagnosis of NQWMI was made in 259 (21.1%) patients. The baseline features and PCI strategies employed were similar among NQWMI vs. QWMI patients, though peak creatine kinase levels were higher (median 795 U/l vs. 1681 U/l, P=0.0001) and severe left ventricular ejection fraction (LVEF) impairment (<40%) more frequent (22.6% vs. 43.9%, P<0.0001), in the latter group. Mortality at 1-year was significantly lower in NQWMI vs. QWMI patients (3.9% vs. 10.8%, P log-rank=0.001). By Cox proportional hazard analysis, NQWMI vs. QWMI was an independent predictor of freedom from 1-year mortality [HR = 0.34 (95% CI: 0.15–0.79), P=0.01].

Discussion: The diagnosis of NQWMI after primary PCI is associated with an excellent prognosis independent of established prognosticators, including LVEF.

Acute myocardial infarction (AMI) survivors have been traditionally classified into Q-wave vs. non-Q-wave MI (QWMI vs. NQWMI, respectively) electrocardiographic subsets based upon the development or absence of new Q-waves. However, the prognostic utility of this dichotomous diagnostic scheme remains controversial.1,2 Studies in unselected patients (treated with or without pharmacological reperfusion therapy) have not found an association between Q-wave development and late survival rates.2,3 In patients treated with thrombolysis, a diagnosis of QWMI vs. NQWMI has been shown in most studies,4–7 though not all,8 to portend an adverse prognosis.

Primary percutaneous coronary intervention (PCI) has emerged as the preferred reperfusion modality for acute coronary syndrome patients presenting with ST-segment elevations,9 and has been widely

Address correspondence to A. Halkin, Department of Cardiology, Tel Aviv Medical Center, 6 Weizmann Street, Tel Aviv, Israel. email: ahalkin@netvision.net.il

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adopted in hospitals able to administer this form of therapy in a timely manner. The incidence, determinants and prognostic implications of Q-wave formation (or the absence thereof) following primary PCI have not been studied. We therefore analyzed the database from a large, prospective, national AMI registry to examine the incidence, determinants and prognostic impact of QWMI vs. NQWMI development following primary PCI.

Methods
Details of the Acute Coronary Syndrome Israeli Survey (ACSIS) registry have been previously reported. In brief, the ACSIS Registry is a 2-month nationwide survey conducted biennially that prospectively collects data from all AMI admissions to every 1 of the 25 coronary care units and cardiology departments in Israel. From 1998 to 2006, 4537 patients with ST-segment elevation AMI (STEMI) were included in five ACSIS-enrollment waves. Patient management was at the discretion of the attending physicians. Admission and discharge diagnoses were recorded as determined by the attending physicians based on clinical, electrocardiographic, and biochemical [elevated creatine kinase (CK)-MB and/or troponin levels] criteria. Demographic, historical and clinical data, including medical management, procedures performed and in-hospital complications were recorded on pre-specified forms by dedicated study physicians. The presence or absence of new pathological Q-waves on the pre-discharge or last available electrocardiogram was determined by study physicians. For all enrollment waves, in-hospital, 30-day and 1-year outcome rates were ascertained by hospital chart review, telephone contact and use of the Israeli National Population Registry. In all but six patients, 1-year follow-up was completed.

Endpoints and statistical analysis
Statistical comparisons were undertaken between the QWMI vs. the NQWMI groups. The primary study endpoint was all-cause mortality at 1-year. Continuous data are presented as mean ± 1 SD (or median and interquartile range for variables with skewed distribution), and were compared using Student’s t-test or Wilcoxon rank sum tests, as appropriate. Categorical variables, presented as percentages, were compared using the Chi-square test with Yates’ continuity correction, or the Fisher exact test as appropriate. Predictors of Q-wave development were determined by stepwise logistic regression analysis (entry and exit criteria of \( P < 0.05 \)). The following variables were used in the model: age, gender, smoking status, hypertension, diabetes, previous coronary artery bypass surgery (CABG), previous PCI, prior MI, Killip class, use of stents and glycoprotein IIb/IIIa antagonists, CK levels and ejection fraction. All first-order interactions were examined and found to be nonsignificant. Survival curves were derived using the Kaplan–Meier approach, and unadjusted comparisons of survival curves were performed using the log-rank test. Independent predictors of survival were determined by a Cox proportional hazard model using stepwise selection of clinical and procedural parameters with entry and exit criteria of \( P < 0.05 \). The following variables were available for selection in the model: age, gender, smoking status, hypertension, diabetes, previous CABG, previous PCI, prior MI, Killip class, use of stents and glycoprotein IIb/IIIa antagonists, CK levels and ejection fraction determined during hospitalization. Interactions between QWMI and potential confounders were examined and were found to be nonsignificant. The variability of the proportional hazard assumption was tested and no deviation was found. For all analyses, a two-sided \( P < 0.05 \) was considered statistically significant. Data were analyzed using SAS software, version 8.2 (SAS Institute Inc., Cary, NC, USA).

Results
Baseline features, reperfusion therapy, and NQWMI vs. QWMI
Of 4537 STEMI patients enrolled in the ACSIS registry (1998–2006), 1230 (27.1%) were treated with primary PCI, 1551 (34.2%) patients were treated with thrombolysis, and 1756 (38.7%) received no reperfusion therapy. Rates of primary PCI application increased from 7.3% in 1998 to 47.2% in 2006 (\( P_{\text{trend}} < 0.0001 \)).

The clinical and procedural characteristics of patients with NQWMI vs. QWMI following primary PCI are shown in Table 1. Demographic and clinical features at presentation were similar in both groups, though peak CK levels during hospitalization and the rates of severe impairment of left ventricular ejection fraction (defined as LVEF < 0.40) were lower in NQWMI vs. QWMI patients. Discharge medications are showed in Table 2. Other than anticoagulants (prescribed more frequently to QWMI patients), medication use at discharge was similar in both groups.

Correlates of NQWMI vs. QWMI development following primary PCI
By stepwise logistic regression analysis, the independent predictors of QWMI vs. NQWMI
development were a LVEF < 40% (OR = 1.85, 95% CI: 1.27–2.78, \( P < 0.001 \)) and increasing peak CK levels (OR = 1.03, 95% CI: 1.02–1.04, per 100IU increments, \( P < 0.001 \)). Of the variables listed in Table 1, none of the clinical features or procedural strategies (i.e. stent implantation, glycoprotein IIb/IIIa antagonism) correlated independently with NQWMI vs. QWMI development.

### NQWMI vs. QWMI and outcomes following primary PCI

In-hospital adverse event rates are shown in Table 3. Manifestations of severe heart failure were less likely among NQWMI vs. QWMI patients, with a trend toward lower rates of reinfarction and cerebrovascular events in the former patient group.

In the entire study cohort, 30-day all-cause mortality was 6.4%. The 30-day mortality rate was significantly higher among QWMI vs. NQWMI patients (7.2% vs. 3.1%, respectively; \( P = 0.02 \)). In the entire study cohort, 1-year mortality was 9.3%. Mortality rates at 1-year, presented in the Figure 1, were significantly higher in QWMI vs. NQWMI patients (10.8% vs. 3.9%, respectively, \( P = 0.001 \)). By Cox proportional hazard analysis, NQWMI vs. QWMI was an independent predictor of freedom from 1-year mortality (Table 4).
Discussion
The principal finding of the present analysis is that among patients undergoing primary PCI for an acute coronary syndrome with ST-segment elevation at presentation, 20% subsequently develop a NQWMI. In these patients, NQWMI compared with QWMI development portends an excellent prognosis.

Previous studies
The longstanding notion that NQWMI is a clinical and pathological entity distinct from QWMI has been critically scrutinized, and the prognostic utility of classifying AMI survivors into these electrocardiographic subsets is controversial.

Based on the results of studies preceding the reperfusion era, NQWMI was construed as an entity portending a favorable early prognosis but consequentially taking an unstable course resulting in long-term mortality rates similar to those seen following QWMI. Methodological flaws and the ubiquitous use of reperfusion therapy in modern STEMI management render these studies irrelevant to contemporary practice. Later, after the advent of pharmacological reperfusion, nonselective studies that included patients treated with and without thrombolysis reported conflicting results with respect to the survival differences between NQWMI and QWMI patients. Conversely, most selective thrombolysis studies have reported higher 1-year survival rates among patients with NQWMI compared with QWMI. In these reports, peak CK levels were lower and the LVEF higher among NQWMI compared with QWMI patients. Nonetheless, after adjusting for differences in baseline characteristics and indexes of infarct size, a diagnosis of NQWMI vs. QWMI was independently associated with enhanced early and late survival rates.
Normalized (TIMI-3) flow in the infarct artery is achieved in ~60% of patients following pharmacological reperfusion. Early electrocardiographic markers of successful reperfusion are more commonly observed in patients with NQWMI than in those with QWMI. The Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries (GUSTO)-I investigators reported that early (90 min) angiographic infarct artery patency was more common and that late (1 week) infarct artery re-occlusion was less frequent in NQWMI compared with QWMI patients, confirming similar observations from the earlier Thrombolysis in Myocardial Infarction (TIMI)-II trial. The apparent discrepancy between the findings of thrombolysis studies and nonselective studies might result from differences in the rates of early and complete infarct artery reperfusion, heterogeneity across patient populations and (e.g. inclusion of patients with or without ST-segment elevation at presentation in the nonselective studies), and subsequent medical management.

To our knowledge, previous studies of the incidence and implications of NQWMI vs. QWMI development after STEMI managed by primary PCI (in which TIMI-3 flow is achieved in ≥90% of patients) have not been published.

### QWMI vs. NQWMI and outcomes following primary PCI

Serial electrocardiograms are universally obtained as the standard of care after AMI. As such, characterizing the frequency and prognostic implications of NQWMI vs. QWMI development following primary PCI is of potential clinical utility. The present analysis demonstrates that NQWMI is a predictor of 30-day and 1-year mortality following primary PCI, independent of recognized indexes of infarct size such as LVEF and peak CK levels.

A mechanistic link underlying the independent association between NQWMI development and enhanced survival is unclear, though late (post discharge) left ventricular function might be of importance in this respect. The LVEF data analyzed in the ACSIS registry were obtained by echocardiography during hospitalization. Considering that in the present study NQWMI was an independent correlate of enhanced survival after adjustment for LVEF, it is possible that for a given LVEF determined early after primary PCI greater left ventricular functional recovery might be expected in NQWMI patients compared with those with a QWMI. Since late LVEF data were not collected in the ACSIS registry this issue could not be addressed in the present analysis and further studies are required to investigate whether NQWMI development post primary PCI might be a marker of myocardial ‘stunning’.

In this regard, it is should be noted that certain clinical and angiographic features that have been shown to influence infarct size (e.g. door-balloon time, TIMI flow pre- and post-PCI) were not collected systematically during the early waves of the ACSIS registry and the available data did not permit meaningful analyses. Nonetheless, it is likely that the prognostic impact of these variables was contained within the effects of the determinants of infarct size that were included in the multivariable models (i.e. LVEF, CK levels). With regard to procedural strategies commonly employed during primary PCI, it is noteworthy that glycoprotein IIb/IIIa antagonist use and stenting were not correlates of NQWMI vs. QWMI development in the ACSIS registry. These findings are consistent with previous reports in which these interventions were not found to enhance myocardial salvage or recovery of left ventricular function.

### Limitations

Electrocardiographic analyses in the ACSIS registry were not performed by a core laboratory and thus some degree of erroneous assignments of a NQWMI diagnosis should be considered to have occurred. Nevertheless, the electrocardiographic analyses in the ACSIS registry represent ‘real-world’ clinical practice and are in close keeping with the findings of a large randomized trial of various thrombolytic regimens in which the electrocardiographic classification of QWMI vs. NQWMI was made by a core laboratory. The lack of complete clinical and angiographic data (e.g. door-balloon time, pre- and post-PCI TIMI flow) has been acknowledged. Lastly, the applicability of our findings to patient populations dissimilar to that studied in the present trial or in which alternative strategies for the management of STEMI were utilized (e.g. fibrinolysis, no reperfusion therapy) is unknown. These limitations do not detract from the clinical usefulness of post-PCI serial electrocardiographic evaluation, a noninvasive and inexpensive diagnostic modality that is routinely performed irrespective of healthcare system resources.

### Conclusions and clinical implications

Utilizing serial electrocardiograms, ~20% of STEMI patients managed by primary PCI will be classified as having sustained a NQWMI. Independent of other clinical features and measures of infarct size (including LVEF), the development of NQWMI vs. QWMI following STEMI treated by primary PCI is associated with enhanced long-term survival.
The assessment of serial electrocardiograms after admission for the presence of Q-waves continues to be of prognostic utility in the era of catheter-based reperfusion therapy for STEMI.

Conflict of interest: None declared.

References