Relationships Between Baseline Q Waves, Time From Symptom Onset, and Clinical Outcomes in ST-Segment–Elevation Myocardial Infarction Patients

Insights From the Vital Heart Response Registry

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Background—Using a comprehensive ST-segment–elevation myocardial infarction registry, we evaluated the relationships of baseline Q waves, time from symptom onset, and reperfusion strategy with in-hospital clinical outcomes.

Methods and Results—Consecutive ST-segment–elevation myocardial infarction patients from a defined health region were classified by the presence of baseline Q waves and additionally into primary percutaneous coronary intervention, fibrinolysis, or no reperfusion. ECGs were collected at baseline, after reperfusion, and analyzed for the presence of Q waves using Selvester criteria. Among 2290 ST-segment–elevation myocardial infarction patients, 36.9% had Q waves on their baseline ECG. Patients with Q waves were older (median age, 59 versus 57), were more often male (82.0% versus 75.4%), had higher heart rate (80 versus 72), had higher Global Registry of Acute Coronary Events risk score (129 versus 127), and were with longer time to reperfusion (42 minutes longer). They had higher composite end points (16.3% versus 10.0%), consistent across times from symptom onset to presentation (15.4% versus 9.9% ≤3 hours; 18.5% versus 8.9% >3 to ≤6 hours; 15.9% versus 11.3% >6 hours; Q and no Q, respectively). Baseline Q waves, but not time to reperfusion, were associated with an increased odds of the in-hospital composite end point of death, congestive heart failure, cardiogenic shock, and reinfarction (adjusted odds ratio, 1.65; 95% confidence interval, 1.18–2.30; *P*=0.003). Type of reperfusion did not modify the association of baseline Q waves and in-hospital outcomes (*P* interaction=0.918).

Conclusions—The presence of baseline Q waves, rather than time to treatment, was significantly associated with adverse in-hospital events in real-world patients, regardless of reperfusion strategy used. **(*Circ Cardiovasc Interv*. 2017;10:e005399. DOI: 10.1161/CIRCINTERVENTIONS.117.005399.)**

Key Words: confidence interval ■ fibrinolysis ■ heart rate ■ odds ratio ■ reperfusion

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Time from symptom onset to reperfusion therapy is critical in patients with ST-segment–elevation myocardial infarction (STEMI) because of the direct relationship between duration of coronary occlusion, myocardial necrosis, and clinical outcomes.[1] However, symptom duration is a subjective ascertainment and is therefore a suboptimal metric. The presence of baseline Q waves in the infarct territory on the initial diagnostic 12-lead ECG has been shown to be a simple and objective tool in predicting adverse clinical events in STEMI clinical trials treated with different reperfusion strategies first by Andrews et al[2] and Wong et al.[3] McDonald et al[4] supported this concept in STEMI patients receiving fibrinolytic-facilitated percutaneous coronary intervention (PCI) in the ASSENT-IV study (Assessment of the Safety and Efficacy of a New Treatment Strategy for Acute Myocardial Infarction IV). They demonstrated that this strategy was especially harmful in patients presenting beyond 3 hours from symptom onset with established Q waves on their baseline ECG. Armstrong et al[5] demonstrated that Q waves at baseline were not only a key prognostic marker of clinical outcome in STEMI patients undergoing primary PCI, but were superior to time from symptom onset to treatment in the APEX-AMI trial (Assessment of Pexelizumab in Acute Myocardial Infarction). Siha et al[6] subsequently confirmed these findings in PCI-treated STEMI patients from the PLATO trial (Platelet Inhibition and Patient Outcomes) where a wider entry window (24 hours from symptom onset) and a less stringent ST-segment–elevation entry criteria (1 mm in 2 contiguous leads) were used. However, these associations have not been assessed in a large population of STEMI patients drawn from day-to-day STEMI care

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WHAT IS KNOWN

- In secondary analysis from ST-segment–elevation myocardial infarction patients in clinical trials, the presence of baseline Q waves has been associated with increased adverse clinical events.

WHAT THE STUDY ADDS

- Compared with clinical trial data, in a comprehensive registry with patients receiving primary percutaneous coronary intervention, fibrinolysis pharmacoinvasive approach, and no reperfusion, the presence of Q waves was less frequent and was associated with higher-risk patient profiles, delayed time to presentation, and increased adverse in-hospital clinical events.
- The frequency of baseline Q waves increased with longer time from symptom onset to medical presentation in men but was not observed in women.
- The absence of a baseline Q wave was associated with improved reperfusion success as measured by ST resolution ≥50% ST-elevation resolution and ST-deviation resolution across all 3 time periods of symptom onset to treatment (<3, 3–6, and >6 hours).
- Confirmed previous clinical trial secondary analysis suggested that the presence of a baseline Q wave is a more powerful predictor of adverse clinical events than patient delay to medical presentation in an unselected ST-segment–elevation myocardial infarction population.

where reperfusion is delivered with primary PCI, the fibrinolysis pharmacoinvasive approach, and in those patients who receive no acute reperfusion.

In the present study, using a comprehensive STEMI registry, we evaluated the relationship between the presence of baseline Q waves and time from symptom onset to treatment on in-hospital clinical outcomes. In addition, we assessed whether the applied reperfusion strategy (ie, pharmacological reperfusion, mechanical reperfusion, or no reperfusion) modifies these relationships.

Methods

Data Collection

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

A regional reperfusion protocol in Northern Alberta, Vital Heart Response, was established in 2006 to implement evidence-based guidelines and to deliver expeditious reperfusion therapy for STEMI patients. A linked quality assurance registry tracks all STEMI patients admitted to any of the 5 Edmonton (Alberta, Canada) zone hospitals including 2 tertiary care cardiac catheterization centers and 3 community hospitals. Patients transferred from other community hospitals to the Edmonton referral region are included as well. Although contemporary guidelines for STEMI patients recommend primary PCI as the preferred reperfusion strategy, a large portion of Northern Alberta patients received fibrinolytic treatment at non-PCI capable hospitals because of anticipated delays in achieving timely primary PCI. Detailed data on patient demographics, treatment intervals, mode of reperfusion therapy, hospital management, and clinical events are collected prospectively on consecutive patients by trained analysts.

Reperfusion Strategies, Time to Treatment, and In-Hospital Clinical End Points

STEMI patients were divided into 3 groups according to the reperfusion strategy they received: primary PCI, fibrinolytic treated, and no acute reperfusion. Time to treatment was defined from symptom onset to the first intervention device in the primary PCI group and from symptom onset to time of fibrinolysis administration in the fibrinolytic-treated group. The primary clinical end point included in this study was the composite of death, congestive heart failure, cardiogenic shock, and reinfarction within the index hospitalization. The events were determined by physicians, and no subsequent adjudication on these events occurred.

ECG Analysis

ECGs were collected at baseline, after reperfusion (≈90 minutes after fibrinolysis, 30 minutes post-primary PCI or routine cardiac catheterization). They were then analyzed by experienced ECG readers at the Canadian VIGOUR Centre ECG Core Laboratory (located at the University of Alberta in Edmonton, Alberta, Canada) without knowledge of the reperfusion strategy used or the clinical outcomes according to established protocols.[7,8]

The presence of Q waves was defined at baseline using the Selvester QRS screening criteria[9]: a Q wave of ≥30 ms in lead aVF (inferior); ≥40 ms in leads I and aVL (lateral); or ≥40 ms in ≥2 leads V_4, V_5 or V_6 (apical); or any Q wave ≥20 ms or QS complex in leads V_2 and V_3 (anterior). Q-wave equivalents were defined as follows: R wave ≥40 ms in V_1 (posterior) or R wave ≤0.1 mV and ≤10 ms in V_2 (anterior). In addition to Q waves, ST-segment elevation and depression were measured at the J point with magnified calipers to the nearest 0.05 mV. The sum total across all leads except aVR was used to calculate ST-elevation sums and ST-depression sums. Then the sum ST deviation was calculated by adding ST-elevation sums to ST-depression sums. The prespecified ECG metrics included the worst lead ST elevation at baseline and post-treatment, the worst lead residual ST elevation post-treatment, and the sum ST deviation at baseline and post-treatment. The percent resolution of worst lead ST elevation and sum ST deviation from baseline to post-treatment was dichotomized in accordance with guidelines issued by the European Society of Cardiology and the American College of Cardiology/American Heart Association as either ≥50% or <50%.[10,11]

Statistical Analysis

Categorical variables were reported as percentages, whereas continuous variables were presented as medians with 25th and 75th percentiles. Differences between groups (ie, baseline Q waves and no Q waves) were tested using the χ^2 test for categorical variables and using Wilcoxon rank-sum test for continuous variables. Time from symptom onset to treatment was analyzed as 3-level categorical variable (≤3, >3 to ≤6, and >6 hours) according to clinical guidelines and as continuous variable (Figure I in the Data Supplement) when evaluating the relative association with the primary composite end point.

The relative association between baseline Q waves and time from symptom onset to treatment on the primary composite end point was assessed using a multivariable logistic regression model. This relationship was then adjusted for the Global Registry of Acute Coronary Events risk score,[12] which is an aggregate score based on patients' age, heart rate, systolic blood pressure, creatinine, cardiac arrest at admission, ST-segment deviation, positive cardiac enzymes, and Killip class. A restricted cubic spline function was used to test the linearity assumption when time was considered as continuous variable. To test whether reperfusion strategy modified the relationship between baseline Q waves and the primary composite end point, the interaction between baseline Q waves and reperfusion strategies was estimated. First order of interaction between baseline Q waves and

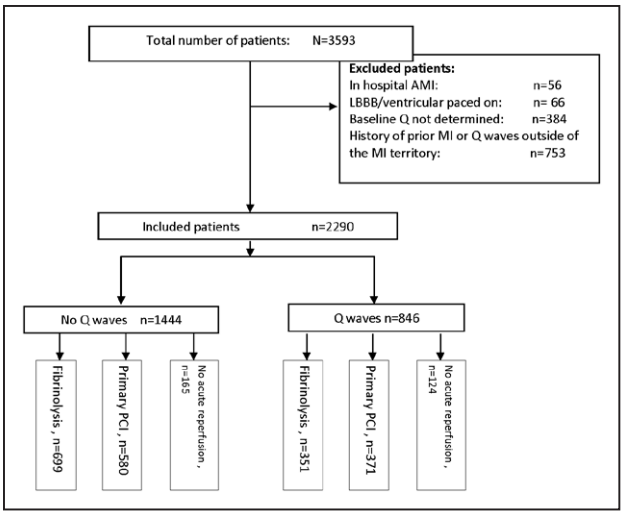

Figure 1. Study cohort. AMI indicates acute myocardial infarction; LBBB, left bundle branch block; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

time, reperfusion strategies, and time were also tested and found not to be statistically significant. Odds ratios and 95% confidence intervals are reported for the associations of baseline Q waves and time to treatment with the primary composite end point.

The study was approved by the University of Alberta Ethics Review Board with individual consent waived because of privacy rules related to this quality assurance registry. All statistical tests were 2-sided with P value <0.05 considered as statistically significant. Statistical analyses were performed using SAS (version 9.4; Cary, NC).

Results

Patient Population

Of the 3593 patients with a STEMI admitted to hospital in Edmonton, Alberta, Canada from October 2006 to October 2011, 2290 patients were included in the current analysis. One thousand three hundred and three were excluded because of the presence of Q waves outside the acute ST-segment–elevation territory (n=797), Q waves not analyzable because of poor quality of ECG (n=384), left bundle branch block or ventricular paced (n=66), prior MI, or initial admission to hospital was not a STEMI event with subsequent in-hospital acute MI occurring (n=56; Figure 1).

Baseline Characteristics According to the Presence/Absence of Baseline Q Waves and Stratification According to Time of Symptom Onset to Treatment

Selected baseline characteristics are presented in Table 1 according to the presence or absence of baseline Q waves. Among all patients (Table 1, left), 36.9% had Q waves in the infarct territory on their baseline ECG. Patients with Q waves were older, were more often male, had higher baseline heart rate, and has higher Global Registry of Acute Coronary Events risk score. They also had a longer time from symptom onset to completion of the baseline ECG (median, 2.4 versus 1.7 hours; P<0.001). In those receiving reperfusion, the time from symptom onset to any reperfusion therapy was ≈42 minutes longer compared with patients without Q waves. The baseline

Table 1. Selected Baseline Characteristics According to Baseline Q Waves and Time From Symptom Onset to Treatment

	All Reperfusion Patients (n=2001)		Sx Onset to Rx, ≤3 h (n=936)		Sx Onset to Rx, >3 to ≤6 h (n=493)		Sx Onset to Rx, > 6 h (n=572)	
	No Q	Q	No Q	Q	No Q	Q	No Q	Q
n	1279	722	638	298	315	178	326	246
Age, y	57.0 (50.0–66.0)	59.0 (51.0–69.0)*	56.0 (50.0–64.0)	58.0 (51.0–65.0)	59.0 (51.0–67.0)	59.0 (50.0–69.0)	59.0 (50.0–69.0)	60.0 (52.0–72.0)
Male, n (%)	964 (75.4)	592 (82.0)†	510 (79.9)	248 (83.2)	238 (75.6)	146 (82.0)	216 (66.3)	198 (80.5)†
Heart rate, bpm	72.0 (60.0–86.0)	80.0 (68.0–94.0)†	70.0 (58.0–83.0)	75.0 (65.0–90.0)†	71.0 (61.0–83.0)	80.0 (67.0–95.0)†	75.0 (64.0–90.0)	86.0 (72.0–98.0)†
Systolic blood pressure, mm Hg	140.0 (119.0–160.0)	141.0 (123.0–159.0)	136.0 (114.0–157.0)	139.0 (121.0–158.0)	144.0 (126.0–163.0)	145.0 (125.5–165.0)	143.0 (121.0–165.0)	142.0 (124.0–159.0)
Hypertension, n (%)	543 (44.5)	302 (44.0)	259 (42.8)	122 (42.1)	133 (44.5)	72 (45.0)	151 (47.9)	108 (45.8)
Diabetes mellitus, n (%)	180 (14.1)	103 (14.3)	84 (13.2)	40 (13.4)	43 (13.7)	24 (13.5)	53 (16.3)	39 (15.9)
GRACE Risk Score	127.0 (108.0–147.0)	129.0 (115.0–152.0)†	127.0 (111.0–146.0)	130.0 (119.0–149.0)*	126.0 (107.5–146.0)	127.0 (115.0–152.0)	127.0 (108.0–149.0)	130.5 (115.0–153.0)*
Sx onset to baseline ECG, h	1.7 (0.9–4.0)	2.4 (1.1–6.9)†	1.0 (0.6–1.4)	1.0 (0.6–1.5)	2.6 (1.8–3.5)	2.9 (2.0–3.5)	7.8 (4.1–16.3)	9.5 (5.8–20.5)†
Anterior MI at baseline, n(%)	378 (29.6)	449 (62.2)†	199 (31.2)	179 (60.1)†	82 (26.0)	115 (64.6)†	97 (29.8)	155 (63.0)†
Sx onset to Rx, hours	3.0 (1.8–6.1)	3.7 (2.1–9.3)†	1.8 (1.3–2.3)	1.9 (1.4–2.4)	3.9 (3.4–4.8)	4.1 (3.5–4.6)	13.0 (8.5–22.1)	15.0 (9.0–25.0)
Length of hospital stay, d	5 (4–7)	6 (4–8)†	5 (4–7)	5 (4–9)	5 (4–7)	6 (4–9)†	5 (4–8)	6 (4–8)

Continuous variables presented as median (25th–75th percentiles). Comparison was made between No Q and Q groups. GRACE indicates Global Registry of Acute Coronary Events; MI, myocardial infarction; Rx, treatment; and Sx, symptom.

*P<0.05

†P<0.01.

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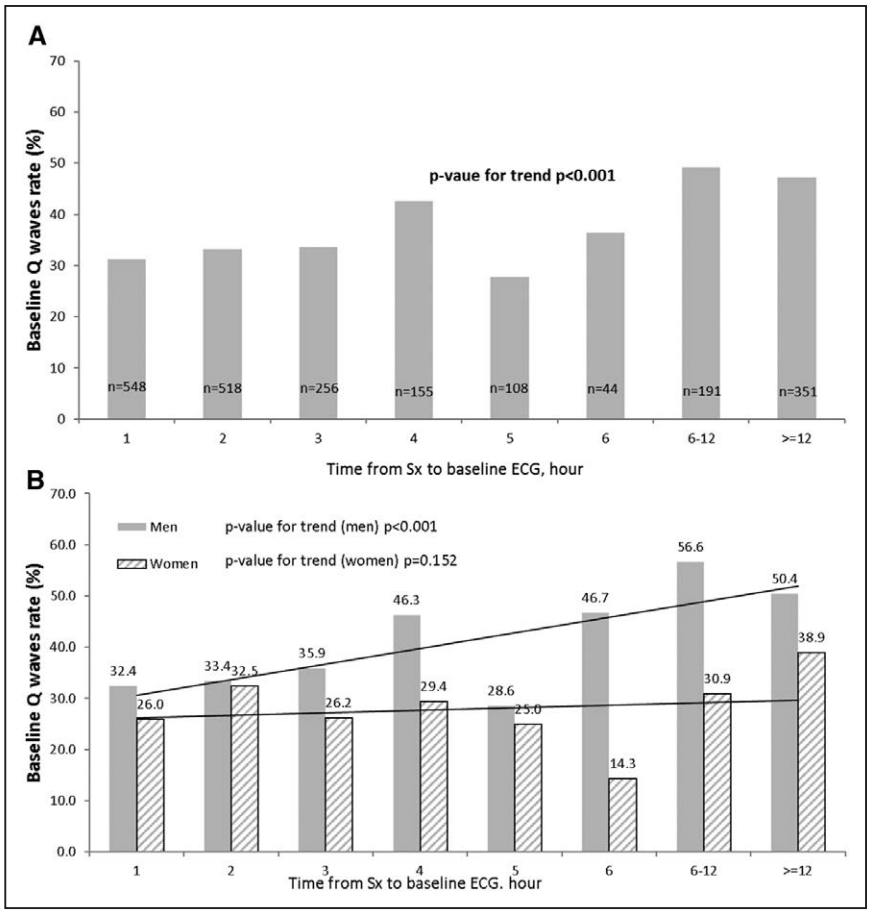

Figure 2. Prevalence of baseline Q waves according to time from symptom onset to baseline ECG. **A**, Baseline Q waves prevalence on all patients and according to time from symptom onset to baseline ECG (119 patients with baseline ECG date/time missing). **B**, Baseline Q waves prevalence on all patients and according to time from symptom onset to baseline ECG and sex (119 patients with baseline ECG date/time missing). Sx indicates symptom.

characteristics shared a similar pattern when the complete cohort was grouped by time from symptom onset to initiation of reperfusion therapy (≤3, >3 to ≤6, >6 hours; Table 1, right). Patients with Q waves had longer length of hospital stay in general but were similar for patients treated within 3 hours of symptom onset.

When patients were stratified according to time from symptom onset to baseline ECG (per hour for first 6 hours and then 6–12 hours and >12 hours), the incidence of baseline Q waves increased with time from symptom onset to baseline ECG (Figure 2A; *P* trend <0.001). When the relationship between time from symptom onset to baseline ECG and baseline Q waves was examined according to sex, the incidence of baseline Q waves increased for men but not for women (Figure 2B).

ECG Metrics According to Presence/Absence of Baseline Q Waves and Stratification According to Time From Symptom Onset to Treatment

ECG metrics at baseline and post-treatment for patients who were treated with reperfusion therapy are shown in Table 2. Patients with Q waves had a greater extent of ST-segment elevation in their worst lead and a greater sum ST-segment deviation on both baseline and post-treatment ECGs. They were also more likely to have exhibited a >2 mm worst lead residual post-treatment. These findings on the presence and absence of Q waves were replicated when patients were grouped by their time from symptom onset to treatment (Table 2). The longer the symptom duration (especially >6 hours) the less likely ST-segment resolution occurred as measured by ≥50% ST-segment–elevation resolution and ST-segment–deviation resolution. Moreover, the absence of baseline Q waves was associated with improved ST-segment resolution as measured by ≥50% ST-segment–elevation resolution and ST-segment–deviation resolution across all 3 time periods of symptom onset to treatment (≤3, >3 to ≤6, and >6 hours).

In-Hospital Clinical Outcomes According to the Presence of Baseline Q Waves

With a similar format, in-hospital clinical outcomes including the composite end point of death, congestive heart failure, cardiogenic shock, and reinfarction, and its components are summarized in Table 3. Notably, patients with Q waves had higher event rates overall and also across the different time periods described previously.

When the relationship between baseline Q waves and time from symptom onset on the composite end point in patients who received acute reperfusion therapies was examined, the presence of baseline Q waves was significantly associated with 65% increased odds, even after baseline adjustment (Figure 3). However, a similar relationship was not observed between time from symptom onset to treatment and the primary composite end point.

Among the total of 2290 patients in this cohort, 951 patients underwent primary PCI, 1050 patients received fibrinolysis, and 289 patients had no acute reperfusion therapy. The

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Table 2. Core Laboratory-Evaluated ECG Characteristics According to Baseline Q Waves and Time From Symptom Onset to Treatment

	All Reperfusion Patients		Sx Onset to Rx, ≤3 h		Sx Onset to Rx, >3 to ≤6 h		Sx Onset to Rx, > 6 h	
	No Q	Q	No Q	Q	No Q	Q	No Q	Q
n	1279	722	638	298	315	178	326	246
Worst lead ST-E at baseline, mm	2.0 (1.0–3.0)	3.0 (1.5–4.0)*	2.0 (1.5–3.5)	3.0 (2.0–4.5)*	2.0 (1.0–3.0)	3.0 (2.0–5.0)*	1.5 (1.0–2.5)	2.0 (1.5–3.5)*
Sum ST deviation at baseline, mm	10.0 (6.0–15.5)	12.3 (8.5–19.0)*	11.0 (7.0–17.5)	13.5 (9.5–20.5)*	9.5 (6.0–14.5)	13.5 (9.5–21.0)*	8.0 (5.0–12.5)	10.0 (7.0–15.0)*
Worst lead residual ST-E post-treatment, n (%)								
< 1 mm	490 (52.4)	179 (31.7)*	219 (48.1)	79 (36.2)*	127 (56.4)	44 (31.9)*	144 (56.3)	56 (26.9)*
1 to < 2 mm	290 (31.0)	202 (35.8)*	140 (30.8)	72 (33.0)	71 (31.6)	46 (33.3)	79 (30.9)	84 (40.4)
≥2 mm	156 (16.7)	183 (32.4)*	96 (21.1)	67 (30.7)	27 (12.0)	48 (34.8)	33 (12.9)	68 (32.7)
Worst lead ST-E resolution ≥50%, n (%)	916 (82.9)	479 (70.6)*	491 (83.5)	220 (77.7)†	225 (86.2)	131 (78.0)†	200 (78.1)	128 (56.4)*
Sum ST-deviation resolution ≥50%, n (%)	620 (66.2)	322 (57.1)*	307 (67.5)	136 (62.4)	157 (69.8)	91 (65.9)	156 (60.9)	95 (45.7)*

Continuous variables presented as median (25th–75th percentiles). Comparison was made between No Q and Q groups. Rx indicates treatment; and Sx, symptom.
*P<0.01
†P<0.05.

baseline characteristics, ECG metrics, and clinical outcomes according to reperfusion strategies are shown in Appendix I in the Data Supplement. Patients not receiving acute reperfusion therapy presented with more frequent comorbidities including older age and more often had hypertension and diabetes mellitus with delayed time from symptom onset to first medical contact. These patients had increased in-hospital clinical events even though they had lower sum ST-segment deviation and lower worst lead ST-segment elevation at baseline when compared with patients who received reperfusion with either fibrinolysis or primary PCI (18.7% versus 10.1% versus 14.7; P<0.001). Reperfusion strategy did not modify the association between baseline Q waves and the primary composite end point (P interaction=0.918; Figure 4).

Discussion

Although several clinical trials have demonstrated the prognostic impact of baseline Q waves in STEMI patients receiving primary PCI, to our knowledge, this has not been evaluated previously in consecutive STEMI patients in general practice. Using a comprehensive Canadian STEMI registry, we found that patients with baseline Q waves had higher baseline clinical risk characteristics including older age, higher heart rate, and higher ECG metrics of risk. These patients also had delayed time for symptom onset to clinical presentation and prolonged time to reperfusion therapy with the frequency of baseline Q waves increasing progressively with patient presentation delay (32% ≤3 hours, 36% within >3 to ≤6 hours, and 43% >6 hours). After adjusted for baseline risk using the Global Registry of Acute Coronary Events risk score, the presence of baseline Q waves was associated with a 65% higher risk of in-hospital death, shock, congestive heart failure, or re-MI. Moreover, the presence of baseline Q waves, but not time to treatment, was significantly associated with the primary composite end point. The association between the presence of baseline Q waves and adverse clinical outcomes was consistent in patients receiving primary PCI, fibrinolysis, and in those patients not receiving acute reperfusion therapy. It is also noteworthy and consistent with prior data that baseline Q waves did not increase in frequency with elapsed time among females—unlike males.[13,14] The possible explanations could be that women tend to develop more atypical or prodromal

Table 3. Clinical Outcomes According to Baseline Q Waves and Time From Symptom Onset to Treatment for All Patients

	All Reperfusion Patients		Sx Onset to Rx, ≤3 h		Sx Onset to Rx, >3 to ≤6 h		Sx Onset to Rx, > 6 h	
	No Q	Q	No Q	Q	No Q	Q	No Q	Q
n	1279	722	638	298	315	178	326	246
Composite of death, congestive heart failure, cardiogenic shock, and re-MI, n (%)	128 (10.0)	118 (16.3)*	63 (9.9)	46 (15.4)†	28 (8.9)	33 (18.5)*	37 (11.3)	39 (15.9)
Death, n (%)	41 (3.2)	34 (4.7)†	18 (2.8)	12 (4.0)	7 (2.2)	10 (5.6)†	16 (4.9)	12 (4.9)
Congestive heart failure, n (%)	36 (2.8)	43 (6.0)*	17 (2.7)	14 (4.7)	8 (2.5)	11 (6.2)†	11 (3.4)	18 (7.3)†
Cardiogenic shock, n (%)	87 (6.8)	79 (10.9)*	47 (7.4)	34 (11.4)†	19 (6.0)	22 (12.4)†	21 (6.4)	23 (9.3)
Re-MI, n (%)	6 (0.5)	8 (1.1)	3 (0.5)	2 (0.7)	1 (0.3)	5 (2.8)†	2 (0.6)	1 (0.4)

Comparison was made between No Q and Q groups. MI indicates myocardial infarction; Rx: treatment; and Sx: symptom.
*P<0.01.
†P<0.05.

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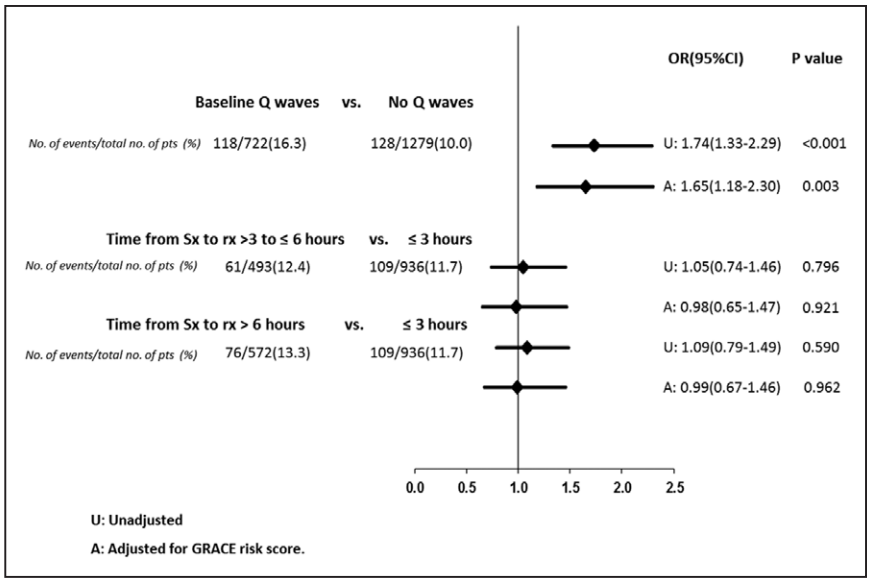

Figure 3. Associations of baseline Q waves and time to treatment on the composite end point of death, congestive heart failure (CHF), shock, and re-MI in hospital for patients who received acute reperfusion therapies. CI indicates confidence interval; GRACE, Global Registry of Acute Coronary Events; MI, myocardial infarction; OR, odds ratio; Rx, treatment; and Sx, symptom.

symptoms, tend to be older than man at the time of presentation which may bias the time of symptom onset, and tend to delay in seeking medical attention.[15,16]

In this study, we found that the prevalence of baseline pathological Q waves was 36.9%, which is lower than previously reported in clinical trials of primary PCI in STEMI (eg, 56% in APEX-AMI trial[5] and 46% in PLATO trial[6]). This may be consistent with the fact that nearly one half of the current cohort presented within 3 hours of symptom onset. Alternatively, it may be that ECG enrollment criteria in clinical trials were used as clinical risk enrichment factors (ie, APEX-AMI trial required a total of 8 mm of ST-segment elevation or depression as an inclusion criterion), altering the frequency of baseline Q waves at presentation. It is also possible that there was a selective bias in the current analysis which excluded many STEMI patients with uninterpretable baseline ECGs. Although these hypotheses are possible, these inclusive observational data provide a closer assessment of the frequency of Q waves in general practice.

Our study supports previous analyses in clinical trial settings where the presence of baseline Q waves was associated with worse clinical outcomes in STEMI patients.[4–6] Our data expand this further to include patients with primary PCI, fibrinolysis, and no acute reperfusion in a STEMI program that delivers the pharmacoinvasive strategy as standard of care. A potential mechanism to explain these associations is related

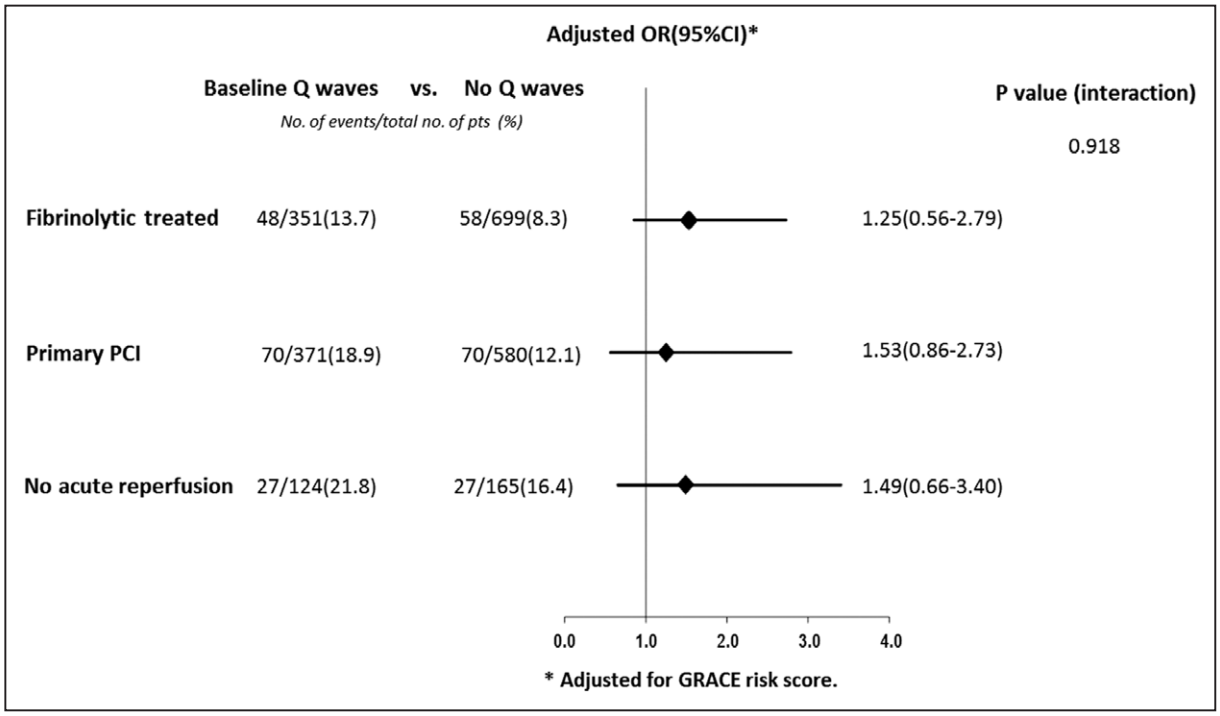

Figure 4. Association between baseline Q waves and reperfusion strategies on the composite end point of death, congestive heart failure (CHF), shock, and re-MI in hospital for all patients. CI indicates confidence interval; GRACE, Global Registry of Acute Coronary Events; MI, myocardial infarction; OR, odds ratio; and PCI, percutaneous coronary intervention.

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to failure of myocardial salvage with tissue-level reperfusion in those with baseline Q waves despite reestablishment of epicardial coronary artery flow. This hypothesis is consistent with our findings and supports previous work on patients with baseline Q waves undergoing primary PCI or facilitated PCI with fibrinolytic therapy in ASSENT-2, ASSENT-4 PCI, APEX-AMI trials, and the PLATO trial where patients were less likely to have reperfusion success in the setting of baseline Q waves.[4–6,17] It is important to note that in this observational study, the presence of baseline Q waves was associated with a decreased chance of reperfusion success as measured by the achievement of ≥50% ST-elevation resolution, which was ≈12% lower in patients receiving reperfusion in the presence of baseline Q waves.[17] These findings are consistent with an analysis of the relationship between the observation of Q waves and reperfusion success measured by cardiac magnetic resonance imaging.[18] Specifically, STEMI patients undergoing primary PCI with baseline Q waves were found to have more microvascular obstruction and less myocardial salvage, although this was still improved with reperfusion. Despite these compelling results, it is even more relevant to acknowledge that reperfusion therapy actually generated ECG evidence of reperfusion success in the presence of baseline Q waves in the majority of patients (specifically 77.7% ≤3 hours, 78.0% >3 to ≤6 hours, and 56.4% >6 hours from symptom onset to reperfusion therapy). From a clinician's point of view, although the presence of baseline Q waves in the infarct territory can modulate prognosis, three quarters of those patients presenting within 6 hours (and ≈50% beyond 6 hours) still achieved successful reperfusion (as measured by ECG metrics).

The current findings provide further evidence supporting the important association of baseline Q waves with adverse clinical outcomes in day-to-day STEMI patient care. These data support the concept that baseline Q waves have a stronger association with clinical outcomes than time to treatment. In fact, the risk of the in-hospital composite events was similar across the time points studied in those without baseline Q waves (9.9% ≤3 hours, 8.9% >3 to ≤6 hours, 11.3% >6 hours) and in those with baseline Q waves (15.4% ≤3 hours, 18.5% >3 to ≤6 hours, 15.9% >6 hours). Although these data do not support lack of efficacy for reperfusion therapy in patients based on the presence of baseline Q waves, we think that it supports the consideration for reperfusion therapy in those patients who may have a delayed presentation yet do not exhibit Q waves in the ST-segment–elevation region of their ECG. These data suggest that although minimizing the time from symptom onset to reperfusion is of key importance to improving STEMI patient outcomes as demonstrated in previous work, accounting for the presence of baseline Q waves enhances prognostic insights and should be considered in the clinical decision-making process of STEMI treatment.

Our study has some limitations. The current study is based on registry data which share the inherent limitations of an observational study. Although adjustment for baseline characteristics was performed, data precision still remains a potential issue. In addition, clinicians managing STEMI patients within the Vital Heart Response program deliver reperfusion therapy based on individual patient assessment, and clinical decisions are influenced by past evidence and international guidelines that focus on temporal variables that influence reperfusion strategies which may bias our time-based analysis. We only examined in-hospital clinical outcomes; longer-term clinical outcomes could be of future research interest.

Conclusions

Within a comprehensive clinical registry of consecutive STEMI patients, we demonstrated that the presence of baseline Q waves was independently associated with adverse clinical events, whereas the time from symptom onset to reperfusion was not. This simple ECG metric which is readily available for every STEMI patient should be taken into consideration in daily practice, and especially in STEMI patients with delayed presentation where the absence of baseline Q waves may influence the clinician's decision to deliver reperfusion therapy. Further systematic research is required to confirm these findings and their impact on clinical practice.

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Disclosures

None.

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Relationships Between Baseline Q Waves, Time From Symptom Onset, and Clinical Outcomes in ST-Segment–Elevation Myocardial Infarction Patients: Insights From the Vital Heart Response Registry

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SUPPLEMENTAL MATERIAL

Supplemental Methods

To validate the adjustment procedure, two sensitivity analyses were performed using different adjustment methods. First, the individual factors of the GRACE Risk Score rather than an aggregate score were included in the multivariable regression model. The variables included in the model were age, heart rate, systolic blood pressure, creatinine, cardiac arrest at admission, ST segment deviation, positive cardiac enzymes, and Killip class.[1] Second, an inverse probability weight (IPW) method was applied in the regression model by using the inverse of propensity score of baseline Q waves as weights.[2] Variables included in the final propensity score logistic regression model were age, sex, heart rate, BMI, systolic blood pressure, creatinine, cardiac arrest at admission, ST segment deviation, positive cardiac enzymes, Killip class, history of hypertension, diabetes, history of heart failure, history of atrial fibrillation. No automated procedure such as stepwise used in the propensity score model. Both sensitivity analyses were conducted for examining the relative association between baseline Q waves and time from symptom onset to treatment on the primary composite endpoint (Supplemental Figure 1 and 3) as well as for testing whether reperfusion strategy modified the relationship between baseline Q waves and the primary composite endpoint (Supplemental Figure 2 and 4). Unadjusted and adjusted or weighted odds ratio (OR) and 95% confidence intervals (CI) were reported. All statistical tests were two-sided with p-value <0.05 considered as statistically significant. Statistical analyses were performed using SAS (version 9.4; Cary, NC).

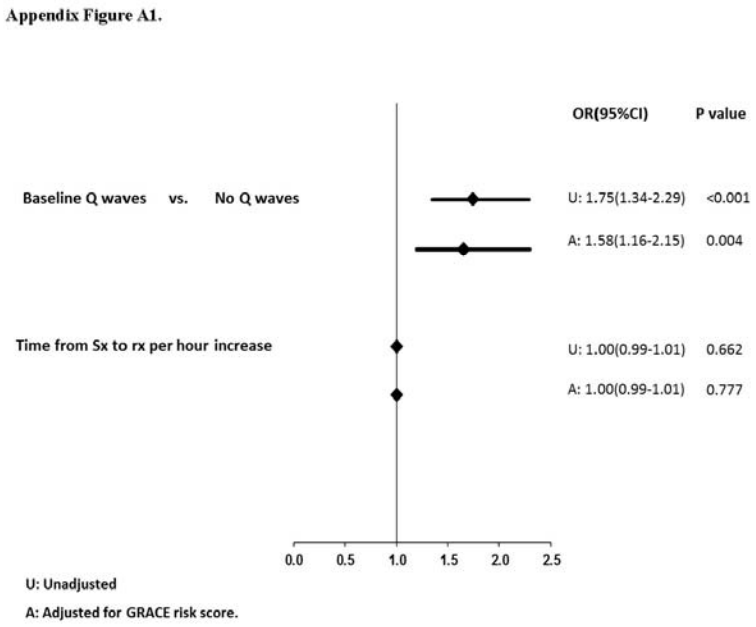
Appendix Table 1. Selected baseline characteristics according to reperfusion strategies.

	Pharmaco-invasive	Primary PCI	No acute reperfusion
n	1050	951	289
Age, years	57.0 (50.0, 65.0)	59.0 (51.0, 70.0)	64.0 (53.0, 76.0)
Male, n (%)	839 (79.9)	717 (75.4)	203 (70.2)
Heart rate, bpm	73.0 (62.0, 87.0)	76.0 (64.0, 92.0)	83.5 (68.0, 100.0)
Systolic blood pressure, mmHg	140.0 (119.0, 159.0)	142.0 (121.0, 161.0)	140.0 (120.0, 160.0)
Hypertension, n (%)	430 (42.7)	415 (46.2)	140 (50.7)
Diabetes, n (%)	141 (13.4)	142 (14.9)	62 (21.5)
GRACE Risk Score	127.0 (108.0, 144.0)	127.0 (115.0, 154.0)	140.0 (122.0, 171.0)
Anterior MI at baseline, n(%)	399(38.0)	428(45.0)	130(45.0)
Symptom onset to baseline ECG, hours	1.8 (0.9, 3.5)	2.2 (0.9, 7.1)	10.3 (1.6, 24.6)
Symptom onset to treatment, hours	2.4 (1.5, 4.2)	4.7 (2.6, 12.4)	5.9 (1.4, 21.3)
Worst lead ST-E at baseline, mm	2.5 (1.5, 3.5)	2.0 (1.0, 3.5)	1.5 (1.0, 2.0)
Q waves at baseline, n (%)	351(33.4)	371(39.0)	124(42.9)
Sum ST-deviation at baseline, mm	11.5 (7.5, 17.0)	10.0 (6.0, 16.0)	7.0 (4.5, 10.0)
Worst lead residual ST-E post treatment, n (%)			
< 1 mm	283 (42.9)	386 (45.9)	81 (57.9)

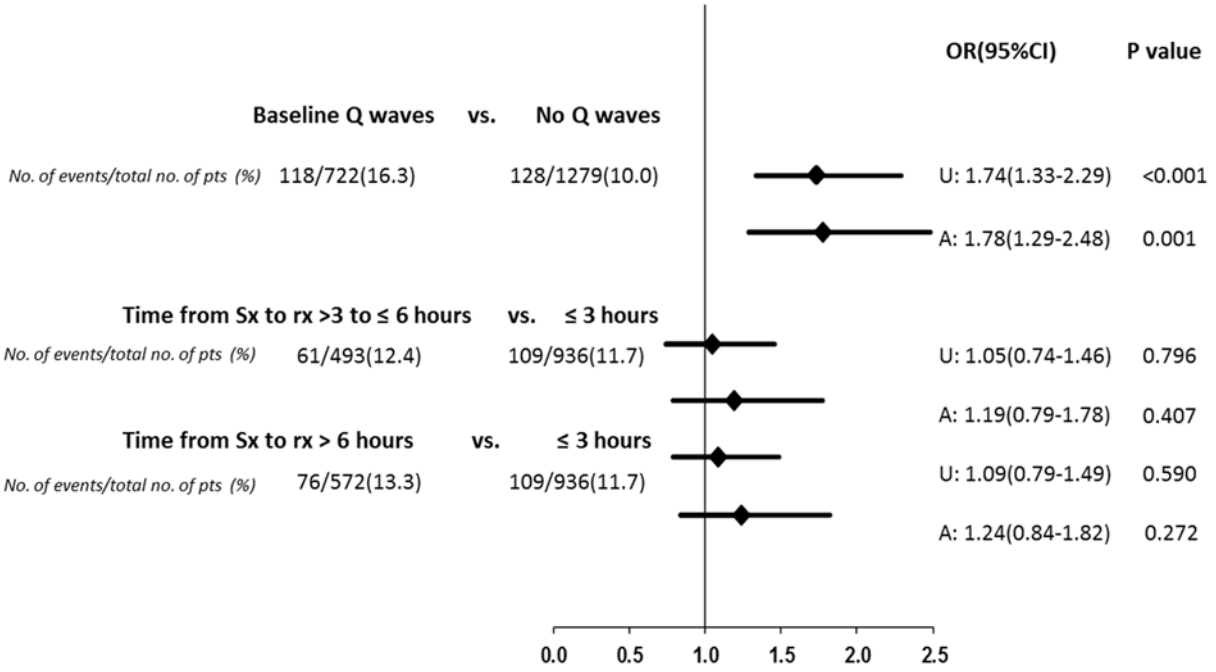
1 to < 2 mm	202 (30.7)	290 (34.5)	47 (33.6)
≥2 mm	174 (26.4)	165 (19.6)	12 (8.6)
Worst lead ST-E resolution ≥50%, n (%)	805 (80.3)	590 (75.6)	87 (72.5)
Sum ST-deviation resolution ≥50%, n (%)	389 (59.0)	553 (65.8)	74 (52.9)
Composite of in-hospital death, congestive heart failure, cardiogenic shock and re-MI, n(%)	106 (10.1)	140 (14.7)	54 (18.7)
Length of hospital stay, days	5(4, 7)	5(4, 8)	7(5, 12)

Supplemental Figures and Figure Legends

Appendix Figure A1. Associations of baseline Q and time to treatment (continuous) on the composite endpoint of death, CHF, shock, and reMI in hospital for patients who received acute reperfusion therapies.



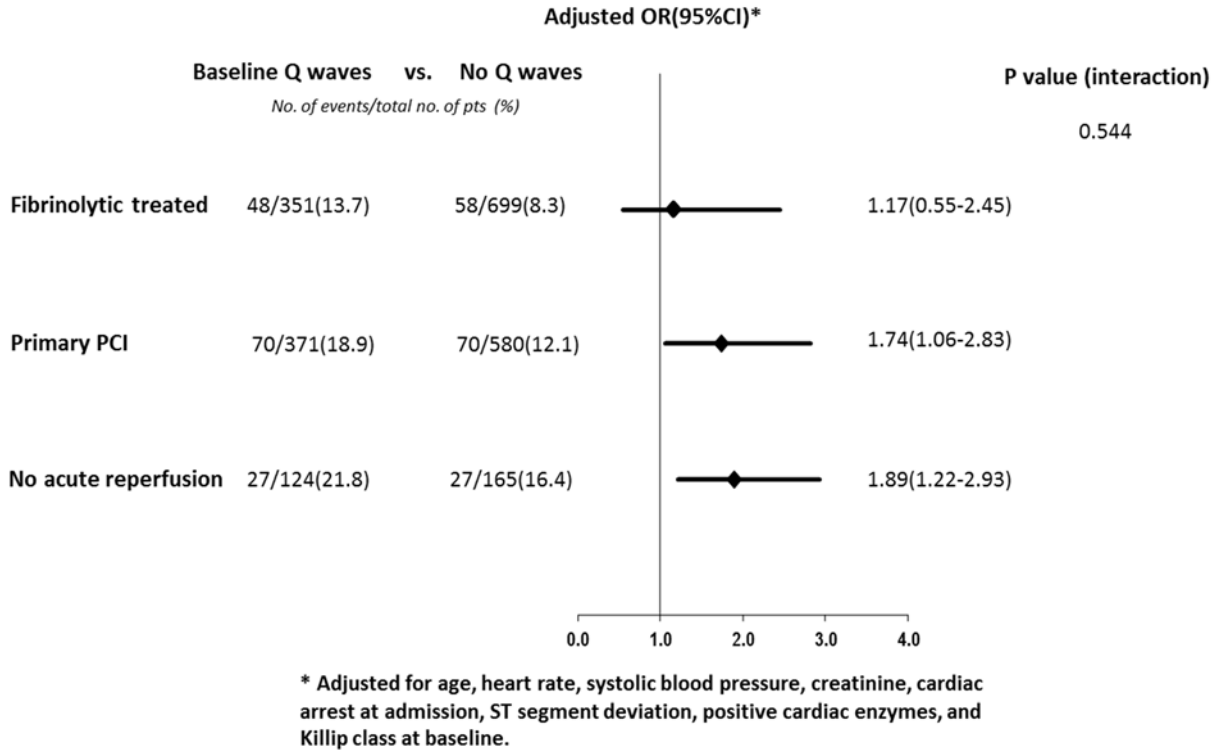
Appendix Figure A2. Association between baseline Q and time to treatment on the composite endpoint of death, CHF, shock, and reMI in hospital for patients received acute reperfusion therapies.



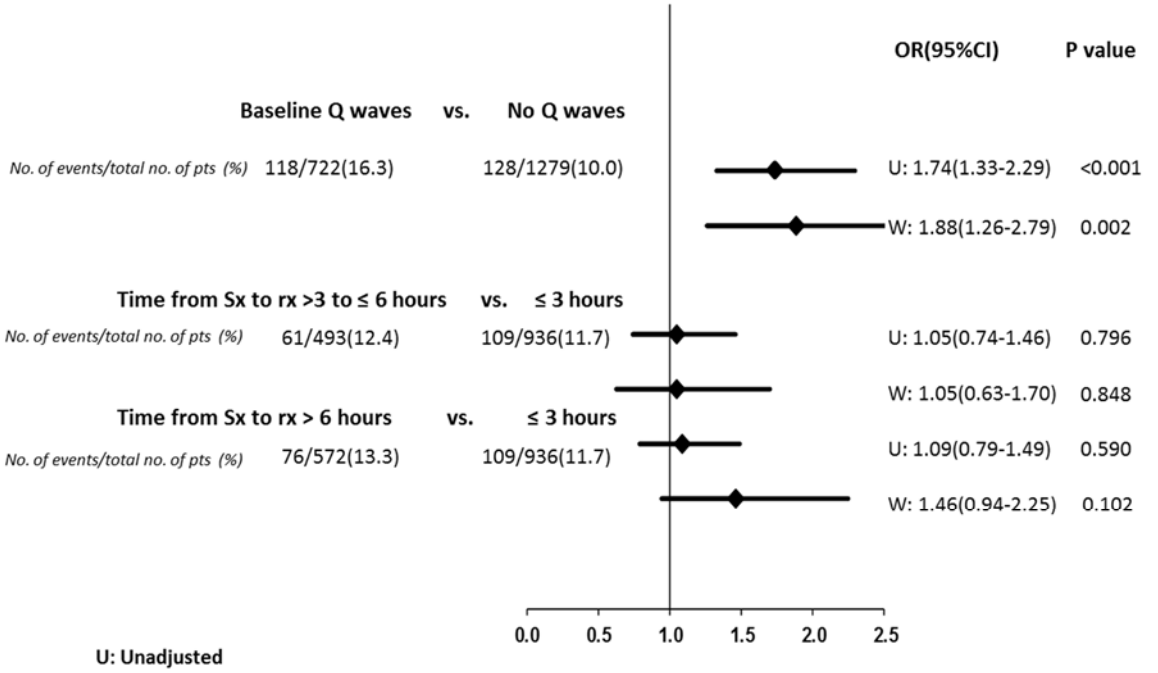
U: Unadjusted

A: Adjusted for age, heart rate, systolic blood pressure, creatinine, cardiac arrest at admission, ST segment deviation, positive cardiac enzymes, and Killip class at baseline

Appendix Figure A3. Association between baseline Q and reperfusion strategies on the composite endpoint of death, CHF, shock, and reMI in hospital for all patients.



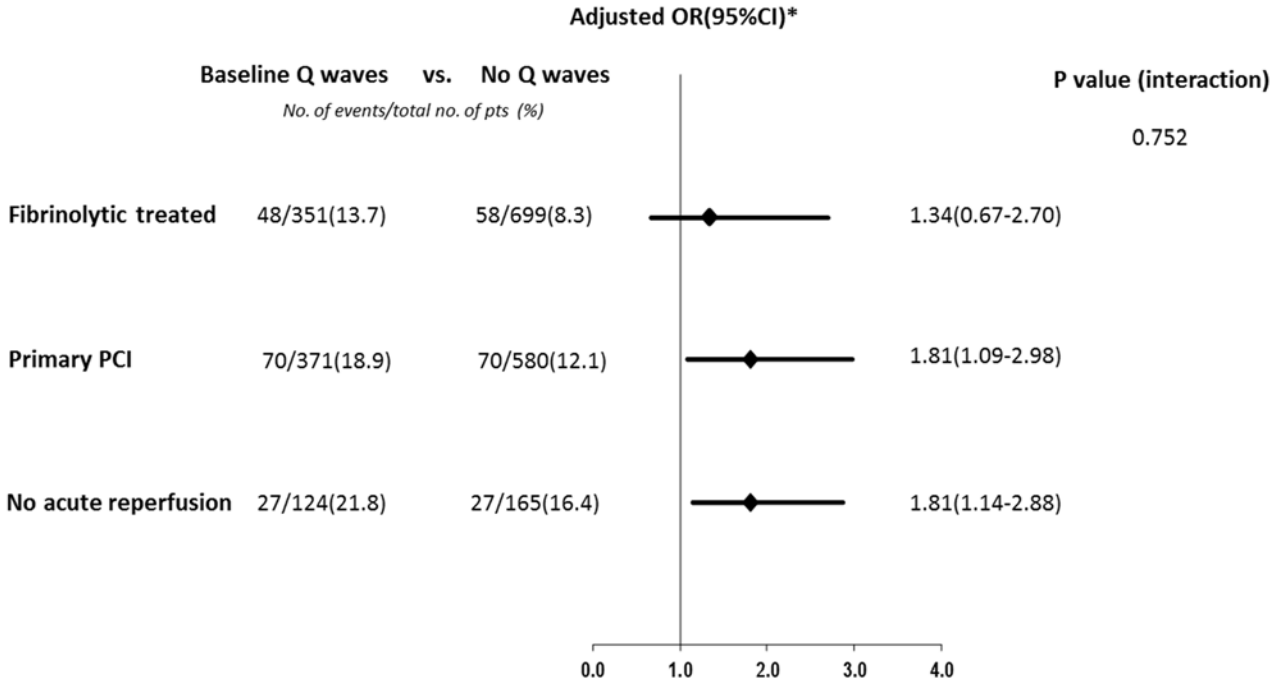
Appendix Figure A4. Associations of baseline Q and time to treatment on the composite of death, CHF, shock, and reMI in hospital for patients received acute reperfusion therapies. Propensity score inverse probability weighted (W) odds ratio.



U: Unadjusted

W: Inverse probability weighted odds ratio using propensity score. Variables included in propensity score model: age, sex, heart rate, systolic blood pressure, creatinine, cardiac arrest at admission, ST segment deviation, positive cardiac enzymes, Killip class at baseline, history of hypertension, diabetes, history of heart failure, history of atrial fibrillation.

Appendix Figure A5. Association between baseline Q and reperfusion strategies on the composite endpoint of death, CHF, shock, and reMI in hospital for all patients. Propensity score inverse probability weighted odds radio.



*** Inverse probability weighted odds ratio using propensity score. Variables included in propensity score model: age, sex, heart rate, systolic blood pressure, creatinine, cardiac arrest at admission, ST segment deviation, positive cardiac enzymes, Killip class at baseline, history of hypertension, diabetes, history of heart failure, history of atrial fibrillation.**

Supplemental References

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