



## The prognostic significance of Q waves and T wave inversions in the ECG of patients with STEMI: A substudy of the TOTAL trial

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### ABSTRACT

**Background:** The prognostic significance of Q waves and T-wave inversions (TWI) combined and separately in STEMI patients undergoing primary PCI has not been well established in previous studies.

**Methods:** We included 7,831 patients from the TOTAL trial and divided the patients into categories based on Q waves and TWIs in the presenting ECG. The primary outcome was a composite of cardiovascular death, recurrent myocardial infarction (MI), cardiogenic shock or new or worsening NYHA class IV heart failure within one year. The study evaluated the effect of Q waves and TWI on the risk of primary outcome and all-cause death, and whether patient benefit of aspiration thrombectomy differed between the ECG categories.

**Results:** Patients with Q+TWI+ (Q wave and TWI) pattern had higher risk of primary outcome compared to patients with Q-TWI- pattern [33 (10.5%) vs. 221 (4.2%); adjusted hazard ratio (aHR) 2.10; 95% CI, 1.45-3.04;  $p < 0.001$ ] within 40-days' period. When analyzed separately, patients with Q waves had a higher risk for the primary outcome compared to patients with no Q waves in the first 40 days [aHR 1.80; 95% CI, 1.48-2.19;  $p < 0.001$ ] but there was no additive risk after 40 days. Patients with TWI had a higher risk for primary outcome only after 40 days when compared to patients with no TWI [aHR 1.63; 95% CI, 1.04-2.55;  $p = 0.033$ ]. There was a trend towards a benefit of thrombectomy in patients with the Q+TWI+ pattern.

**Conclusions:** Q waves and TWI combined (Q+TWI+ pattern) in the presenting ECG is associated with unfavourable outcome within 40-days. Q waves tend to affect short-term outcome, while TWI has more effect on long-term outcome.

### Introduction

Both pathological Q waves and T wave inversions (TWI) in the presenting ECG of patients with ST elevation myocardial infarction (STEMI) have an impact on patient outcome. Pathological Q waves have been more consistently associated with worse outcome compared to TWI [1–10]. Numerous pathophysiological mechanisms may be involved in

the development of Q waves and TWI in patients with STEMI. The Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI (TOTAL) showed that routine aspiration thrombectomy was not superior to PCI alone as a treatment strategy in STEMI patients [11,12]. In this substudy of the TOTAL trial, our objectives were to investigate the prognostic significance of Q waves and TWI combined and separately, and whether the patient benefit from routine aspiration

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thrombectomy differs between various combinations of Q waves and TWI.

## Material and methods

### Study population

A total of 10,732 patients were enrolled in the TOTAL trial. The inclusion and exclusion criteria have been described in detail previously [11,12]. The patients of the TOTAL trial had STEMI with symptoms of myocardial ischemia and time from symptom onset  $\leq 12$  hours, had a pre-procedure ECG and underwent primary percutaneous coronary intervention (PCI) with or without manual aspiration thrombectomy after randomization to these two groups. Different ECG substudies of the TOTAL trial, including this one, were pre-planned [11,13]. All the study ECGs were analyzed at the Heart Hospital, Tampere University Hospital by the ECG core laboratory investigators, who were blinded to clinical and angiographic data, as well as treatment assignment. For this substudy we selected all patients who had a pre-procedure ECG available and had an index invasive coronary artery procedure done ( $n=10,064$ ). Patients with left bundle branch block ( $n=62$ ), other broad QRS  $>120$ ms ( $n=486$ ), poor quality of the ECG ( $n=703$ ), missing data of Q wave or TWI ( $n=29$ ) and those where the STEMI criteria were not fulfilled ( $n=953$ ) were excluded. The final study population consisted of 7,831 patients.

### Study outcomes

The primary outcome was a composite of cardiovascular death, cardiogenic shock, recurrent myocardial infarction or new or worsening New York Heart Association (NYHA) class IV heart failure within one year follow-up. Secondary outcome was all-cause death within one year.

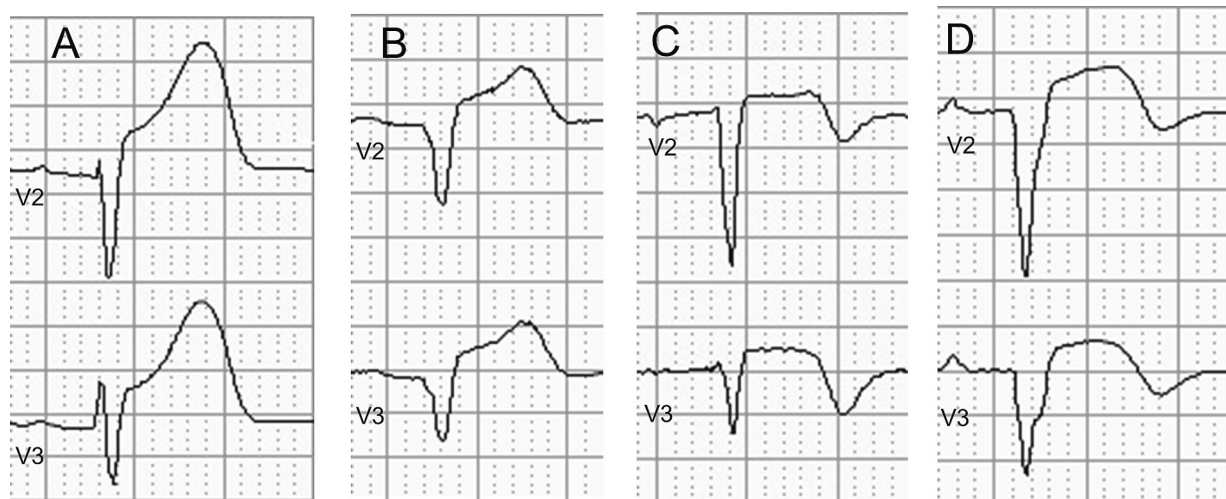
### ECG analysis

ST-elevation (STE) measurements were done from the J point and the TP-segment was used as the isoelectric line. We used a modified cut-off point of 0.2 mV for the leads V2 and V3, because the investigators were blinded with respect to the patients' sex and age. A guideline-based cut-off point 0.1 mV in at least two adjacent leads was used in all other leads [14]. STEMI was defined as anterior (V1-V6), inferior (II, III, aVF) or lateral (I, aVL, V5-6) and/or other. In the leads V2 and V3, pathological Q waves were defined as any Q wave  $\geq 0.02$  sec in duration or a QS configuration. For all other leads, Q waves  $\geq 0.03$  sec in duration and

$\geq 0.1$  mV in amplitude were interpreted as pathological if seen in at least two adjacent leads. TWI was defined as a fully negative T wave or a biphasic T wave with  $\geq 0.05$  mV negative terminal portion. Patients were divided into four groups based on pathological Q waves and TWI, as shown in Fig. 1.

### Statistical analysis

Continuous variables were expressed as mean  $\pm$  standard deviation or median with interquartile range (IQR) and categorical variables as counts and percentages. To determine differences among groups, ANOVA test and Kruskal-Wallis test were used for normally and non-normally distributed continuous variables, respectively. Chi-square test was used for categorical variables. In the analysis of effects of different Q wave and TWI groups on the risk of primary and secondary outcomes, proportional hazards assumption of the conventional Cox model was first evaluated by Schoenfeld residuals. Because of the violation of proportional hazard assumption, an extended Cox regression model with a time-dependent covariate was implemented, where the introduction of an interaction term of Q wave/TWI group variable and dichotomized time-dependent indicator function allowed varying effects in different follow-up periods. The optimal change point  $\tau$  for the dichotomized time-dependent indicator was identified by fitting a set of  $\tau$  values into the model and selecting the one that maximized the log partial likelihood. Hazard ratios (HR) and 95 % confidence intervals (CI) were reported separately for periods before and after change point. Cumulative incidences for primary outcome and all-cause death were explored using Kaplan-Meier curves separately for periods before and after change point. For the multivariable analysis, age, and symptom onset (6–12hrs vs.  $<6$ hrs) were forced into the model. In order to achieve a parsimonious model, other pre-specified risk factors or confounding factors including gender, location of MI, current smoking, hypertension, diabetes mellitus, previous MI, previous PCI, proximal lesion (located at least in one of the following: (1) Right coronary artery (RCA) origin, (2) RCA proximal including right ventricle, (3) Left main coronary artery, (4) 3mm after origin of left anterior descending (LAD), (5) Left circumflex proximal, (6) LAD proximal (first 3mm of the proximal LAD)), heart rate, Killip class  $\geq 2$ , TIMI flow 0 before PCI, thrombus grade (5 vs.  $<5$ ), time from symptom onset to procedure, elevated troponin and cardiogenic shock were tested for inclusion based on their influence and model fit. Variables with p-value  $>0.05$  were excluded using backwards elimination approach. In addition to the above-mentioned analysis of combined Q waves and TWI, Q waves and TWI were also analyzed as two separate variables in a similar way with the



**Fig. 1.** A: no pathological Q waves and no TWI (Q-TWI-); B: pathological Q wave but no TWI (Q+TWI-); C: no pathological Q wave but TWI (Q-TWI+) and D: both pathological Q wave and TWI present (Q+TWI+).

extended Cox regression model. The effect of routine thrombectomy and PCI alone between different Q wave and TWI groups and Q waves and TWI separately on the risk of primary outcome was assessed by likelihood ratio test of interaction term using unadjusted Cox regression model. A two-sided p-value of <0.05 was considered statistically significant. All analyses were executed using SAS Version 9.4 (SAS Institute, Inc., Cary, NC, USA).

*Identification of optimal change point*

The optimal change point  $\tau$  for each model was identified with the method described in statistical analysis section above and ranged between 35 to 45 days depending on the clinical outcomes and whether Q wave and TWI were analyzed jointly or separately. For easy clinical interpretation and presentation, we decided to set the change point to 40 days for all analyses. By short term we refer to cumulative incidence in  $\leq 40$  days and long term from  $>40$  days to up to 1 year.

**Results**

*Baseline characteristics*

The baseline characteristics are shown in Table 1. Patients with the Q-TWI+ pattern were slightly older and were more often females compared with the other groups. There was a trend for higher heart rate and higher blood pressure in patients with the Q+TWI+ pattern. Killip class  $\geq 2$  was more often seen in patients with the Q+TWI- and Q+TWI+ patterns. Patients with the Q-TWI- pattern more often had inferior MI, while patients with Q+TWI- and Q+TWI+ more often had anterior MI. Patients with the Q-TWI+ and Q+TWI+ patterns were more often diabetic, had higher total CK count and a higher rate of elevated troponin levels. There were no differences among the four groups regarding diagnosis of hypertension, previous MI, previous PCI, peripheral artery disease or current smoking. Patients with the Q+TWI+ pattern had a longer time from symptom onset to hospital arrival and onward to the invasive procedure. Enoxaparin and upfront glycoprotein IIa/IIIb inhibitor therapy were more frequently used in the patients with the Q-TWI- pattern. Higher TIMI thrombus grade and a higher rate of TIMI 0 flow before PCI was seen in patients with the Q+TWI- pattern. Median procedure time did not differ among the groups. Ticagrelor was more often used in patients with the Q-TWI- pattern, while clopidogrel was more frequently used in the other groups. Patients with the Q+TWI- or the Q+TWI+ patterns were more frequently on oral anticoagulants.

*Patient outcome in the different Q-wave/TWI categories*

Patients with the Q+TWI+ pattern had the highest risk for primary outcome within 40 days compared to patients with the Q-TWI- pattern [33 (10.5%) vs. 221 (4.2%); aHR 2.10; 95% CI, 1.45-3.04;  $p < 0.001$ ]. Patients with the Q+TWI- pattern also had higher risk for primary outcome within 40 days compared to patients with the Q-TWI- pattern [157 (8.2%) vs. 221 (4.2%); aHR 1.78; 95% CI, 1.44-2.20;  $p < 0.001$ ]. There was no statistically significant difference in the risk of primary outcome between the Q-TWI+ and Q-TWI- patients in the 40-day period [21 (5.9%) vs. 221 (4.2%); aHR 1.08; 95% CI, 0.68-1.71;  $p = 0.743$ ]. Beyond 40 days, patients with the Q-TWI+ pattern had a higher risk for primary outcome compared to the patients with the Q-TWI- pattern [15 (4.6%) vs. 101 (2.0%); aHR 1.82; 95% CI, 1.06-3.14;  $p = 0.031$ ]. There was no excess cumulative incidence for primary outcome after 40 days regarding the Q+TWI+ and Q+TWI- groups compared to the patients in the Q-TWI- group. The patients with the Q+TWI+ pattern also had the highest risk for all-cause death within 40 days compared to the patients with the Q-TWI- pattern [22 (7.0%) vs. 83 (1.6%); aHR 3.50; 95% CI, 2.17-5.65;  $p < 0.001$ ]. A higher risk for all-cause death was also seen in the Q+TWI- group compared to the Q-TWI- group in the 40-day time period [71 (3.7%) vs. 83 (1.6%); aHR 1.96; 95% CI, 1.42-2.72;

**Table 1**  
Baseline characteristics.

Characteristic <sup>a</sup>	Q-TWI- (n=5242)	Q+TWI- (n=1922)	Q-TWI+ (n=354)	Q+TWI+ (n=313)	p value <sup>b</sup>
Age (year)	60.6 ± 11.8	60.4 ± 11.6	63.2 ± 12.3	60.9 ± 13.0	<0.001
Age >75 years	636 (12.1)	217 (11.3)	64 (18.1)	49 (15.7)	0.001
Gender (Male)	3985 (76.0)	1576 (82.0)	240 (67.8)	253 (80.8)	<0.001
Heart rate (beats per minute)	74.3 ± 16.9	80.1 ± 17.5	77.1 ± 19.2	83.6 ± 17.5	<0.001
Systolic blood pressure (mmHg)	134.7 ± 26.5	136.5 ± 25.4	136.9 ± 28.7	138.5 ± 28.3	0.006
Diastolic blood pressure (mmHg)	81.7 ± 16.4	84.5 ± 16.5	81.9 ± 16.5	84.8 ± 17.4	<0.001
BMI, kg/m <sup>2</sup>	27.8 ± 4.7	27.3 ± 4.3	27.4 ± 4.9	26.7 ± 4.6	<0.001
Killip class $\geq 2$	164 (3.1)	109 (5.7)	12 (3.4)	19 (6.1)	<0.001
Location of MI					
Anterior	1480 (28.2)	1222 (63.6)	144 (40.7)	202 (64.5)	
Inferior	3494 (66.7)	626 (32.6)	201 (56.8)	101 (32.3)	
Lateral or other	265 (5.1)	72 (3.7)	9 (2.5)	10 (3.2)	
Hypertension	2604 (49.7)	924 (48.1)	193 (54.5)	149 (47.6)	0.131
Diabetes	944 (18.0)	296 (15.4)	78 (22.0)	70 (22.4)	<0.001
Previous MI	433 (8.3)	185 (9.6)	29 (8.2)	31 (9.9)	0.258
Previous PCI	423 (8.1)	157 (8.2)	26 (7.3)	25 (8.0)	0.964
Peripheral arterial disease	108 (2.1)	41 (2.1)	10 (2.8)	10 (3.2)	0.461
Current smoker	2408 (45.9)	891 (46.4)	149 (42.1)	139 (44.4)	0.478
Total CK (U/L)	189.0 (104.0-514.0)	286.0 (133.0-964.0)	343.0 (153.0-936.0)	575.0 (166.0-1634.0)	<0.001
Elevated troponin	2833 (54.0)	1259 (65.5)	251 (70.9)	241 (77.0)	<0.001
Initial PCI procedure					
Onset to Hospital (min)	114.0 (66.0-190.0)	136.0 (80.0-235.0)	162.0 (82.0-300.0)	185.0 (100.0-360.0)	<0.001
Hospital to procedure (min)	48.0 (21.0-85.0)	50.0 (23.0-84.0)	65.0 (28.0-104.0)	67.0 (31.0-101.0)	<0.001
Enoxaparin Glycoprotein IIb/IIIa inhibitor	453 (8.6)	150 (7.8)	22 (6.2)	12 (3.8)	0.009
Upfront	1380 (26.3)	477 (24.8)	72 (20.3)	70 (22.4)	0.030
Bailout	766 (14.6)	305 (15.9)	52 (14.7)	55 (17.6)	0.336
Initial TIMI thrombus grade					<0.001
0: no thrombus	135 (2.6)	36 (1.9)	17 (4.8)	9 (2.9)	
1: possible thrombus	278 (5.3)	67 (3.5)	24 (6.8)	16 (5.1)	
2: definitive thrombus, <0.5 x vessel diameter	153 (2.9)	40 (2.1)	11 (3.1)	13 (4.2)	
3: definitive thrombus, 0.5-2.0 x vessel diameter	556 (10.6)	179 (9.3)	47 (13.3)	35 (11.2)	
4: definitive thrombus, >2.0 x vessel diameter	727 (13.9)	210 (10.9)	62 (17.5)	56 (17.9)	

(continued on next page)

**Table 1** (continued)

Characteristic <sup>a</sup>	Q-TWI- (n=5242)	Q+TWI- (n=1922)	Q-TWI+ (n=354)	Q+TWI+ (n=313)	p value <sup>b</sup>
5: total occlusion	3390 (64.7)	1389 (72.3)	193 (54.5)	184 (58.8)	
TIMI 0 flow before PCI	3462 (66.0)	1428 (74.3)	194 (54.8)	202 (64.5)	<0.001
Median PCI procedure time (min)	36.0 (27.0- 50.0)	36.0 (26.0- 50.0)	38.0 (28.0- 54.0)	38.0 (29.0- 54.0)	0.062
Clopidogrel	3621 (69.1)	1427 (74.2)	263 (74.3)	225 (71.9)	<0.001
Ticagrelor	1429 (27.3)	422 (22.0)	81 (22.9)	66 (21.1)	<0.001
Oral anticoagulants	249 (4.8)	166 (8.6)	20 (5.6)	22 (7.0)	<0.001

MI, myocardial infarction; PCI, percutaneous coronary intervention.

<sup>a</sup> Values are given as counts and percentage; mean ± SD or median and interquartile range.

<sup>b</sup> p value is from ANOVA test for normally distributed continuous variables, Kruskal-Wallis test for non-normally distributed continuous variable, and Chi-square test for categorical variables.

p<0.001]. Similar to the results of primary outcome, there was no additive risk for all-cause death after 40 days in the Q+TWI+ and Q+TWI- groups compared to the Q-TWI- group. There was no statistically significant difference in the risk of all-cause death between the Q-TWI+ and Q-TWI- groups before or after the 40-day time period. The results are shown in **Table 2**. The cumulative incidences of primary outcome and all-cause death in the time periods ≤40 days and >40 days for the different patient groups are shown in **Figs. 2 and 3**.

*The effect of Q waves and TWI on patient outcome*

The baseline characteristics of patients with/without Q waves and with/without TWI are shown in **Supplementary Table 1**. Patients with pathological Q waves in the pre-procedure ECG had a higher risk for primary outcome and all-cause death within 40 days compared to patients with no Q waves [aHR 1.80; 95% CI, 1.48-2.19; p<0.001 and aHR 2.01; 95% CI, 1.50-2.71; p<0.001, respectively] but there was no additive risk after 40 days either in primary outcome or all-cause death. Patients with TWI in the pre-procedure ECG had a higher risk for the primary outcome after 40 days and higher risk for all-cause death in the time period ≤40 days compared to patients with no TWI [aHR 1.63; 95% CI, 1.04-2.55; p=0.033 and aHR 1.65; 95% CI, 1.13-2.41; p=0.010, respectively]. There was no statistically significant difference between patients with TWI and no TWI regarding the risk for primary outcome within 40 days or all-cause death after 40 days. The results are shown in **Table 2**.

*Effect of aspiration thrombectomy*

The effect of manual aspiration thrombectomy or PCI alone for the risk of primary outcome within different patient groups are shown in **Table 3**. The patients with the Q+TWI+ pattern showed a trend towards a lower risk for primary outcome with thrombectomy, but the result was not statistically significant [HR 0.60; 95% CI, 0.31-1.15]. There was no statistically significant interaction between the different patient groups for the effect of treatments on the risk of primary outcome.

**Discussion**

In this substudy of the TOTAL trial, one of the largest randomized studies of STEMI patients treated invasively, we showed that patients with both Q waves and inverted T waves (Q+TWI+ pattern) in their pre-procedural ECG have an increased risk for the composite endpoint of cardiovascular death, cardiogenic shock, recurrent MI or new or

**Table 2**

Analysis of the effect of different Q wave and TWI categories and Q waves and TWI separately on the primary outcome and all-cause death during time periods before and after 40 days.

Primary outcome	Period 1: ≤ 40 days			Period 2: > 40 days		
	n/N(%)	aHR (95% CI) <sup>a</sup>	p value	n/N(%)	aHR (95% CI) <sup>a</sup>	p value
<b>Model #1</b>						
Q-TWI-	221/ 5242 (4.2)	ref	-	101/ 4970 (2.0)	ref	-
Q+TWI-	157/ 1922 (8.2)	1.78 (1.44- 2.20)	<0.001	34/ 1746 (1.9)	0.96 (0.65- 1.42)	0.838
Q-TWI+	21/354 (5.9)	1.08 (0.68- 1.71)	0.743	15/329 (4.6)	1.82 (1.06- 3.14)	0.031
Q+TWI+	33/313 (10.5)	2.10 (1.45- 3.04)	<0.001	8/277 (2.9)	1.28 (0.62- 2.64)	0.504
<b>Model #2</b>						
No Q wave	242/ 5596 (4.3)	ref	-	116/ 5299 (2.2)	ref	-
Q wave	190/ 2235 (8.5)	1.80 (1.48- 2.19)	<0.001	42/ 2023 (2.1)	0.91 (0.63- 1.30)	0.600
No TWI	378/ 7164 (5.3)	ref	-	135/ 6716 (2.0)	ref	-
TWI	54/667 (8.1)	1.14 (0.85- 1.52)	0.392	23/606 (3.8)	1.63 (1.04- 2.55)	0.033
<b>All-cause death</b>						
	n/N(%)	aHR (95% CI) <sup>b</sup>	p value	n/N(%)	aHR (95% CI) <sup>b</sup>	p value
<b>Model #1</b>						
Q-TWI-	83/ 5242 (1.6)	ref	-	83/ 5118 (1.6)	ref	-
Q+TWI-	71/ 1922 (3.7)	1.96 (1.42- 2.72)	<0.001	28/ 1838 (1.5)	0.85 (0.55- 1.31)	0.455
Q-TWI+	11/354 (3.1)	1.47 (0.78- 2.78)	0.230	12/340 (3.5)	1.65 (0.90- 3.03)	0.106
Q+TWI+	22/313 (7.0)	3.50 (2.17- 5.65)	<0.001	4/290 (1.4)	0.64 (0.24- 1.77)	0.393
<b>Model #2</b>						
No Q wave	94/ 5596 (1.7)	ref	-	95/ 5458 (1.7)	ref	-
Q wave	93/ 2235 (4.2)	2.01 (1.50- 2.71)	<0.001	32/ 2128 (1.5)	0.76 (0.50- 1.14)	0.183
No TWI	154/ 7164 (2.1)	ref	-	111/ 6956 (1.6)	ref	-
TWI	33/667 (4.9)	1.65 (1.13- 2.41)	0.010	16/630 (2.5)	1.31 (0.77- 2.22)	0.323

<sup>a</sup> Adjusted for age, symptom onset, gender, diabetes, previous MI, proximal lesion, heart rate, Killip class≥2, cardiogenic shock

<sup>b</sup> Adjusted for age, symptom onset, diabetes, previous MI, previous PCI, proximal lesion, heart rate, Killip class≥2, cardiogenic shock

worsening NYHA class IV heart failure and all-cause death compared with other combinations of Q waves and TWI.

Although both pathologic Q waves and TWI were associated with an increased risk for adverse outcome, the effect of Q waves seemed to be short term, while TWI had a more long-term effect. These findings

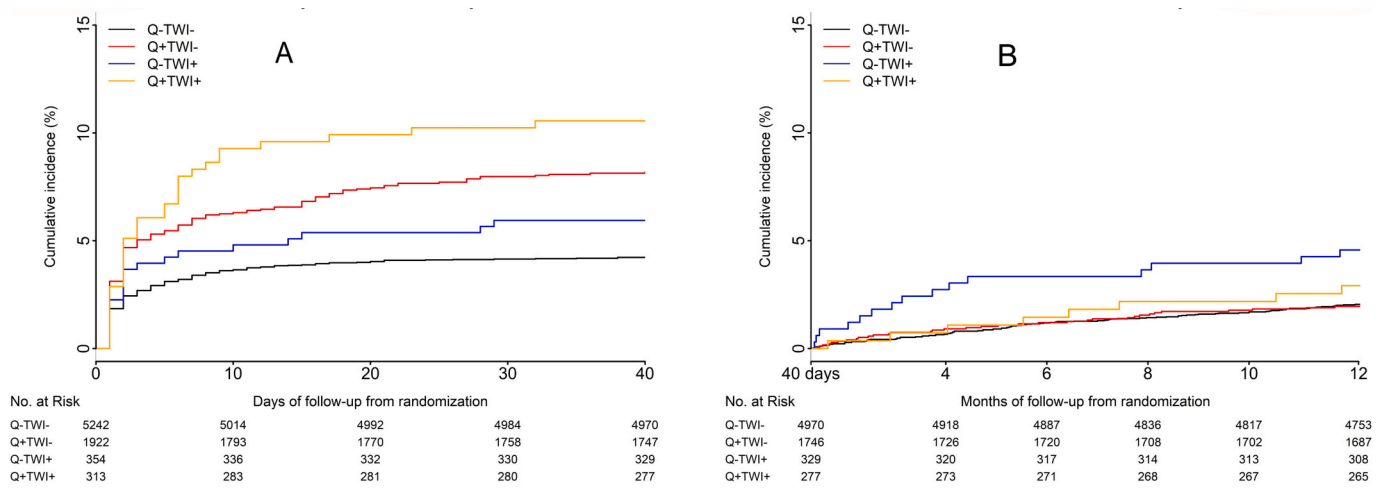


Fig. 2. Kaplan Meier estimate of cumulative incidence of primary outcome for time periods before (panel A) and after (panel B) 40 days.

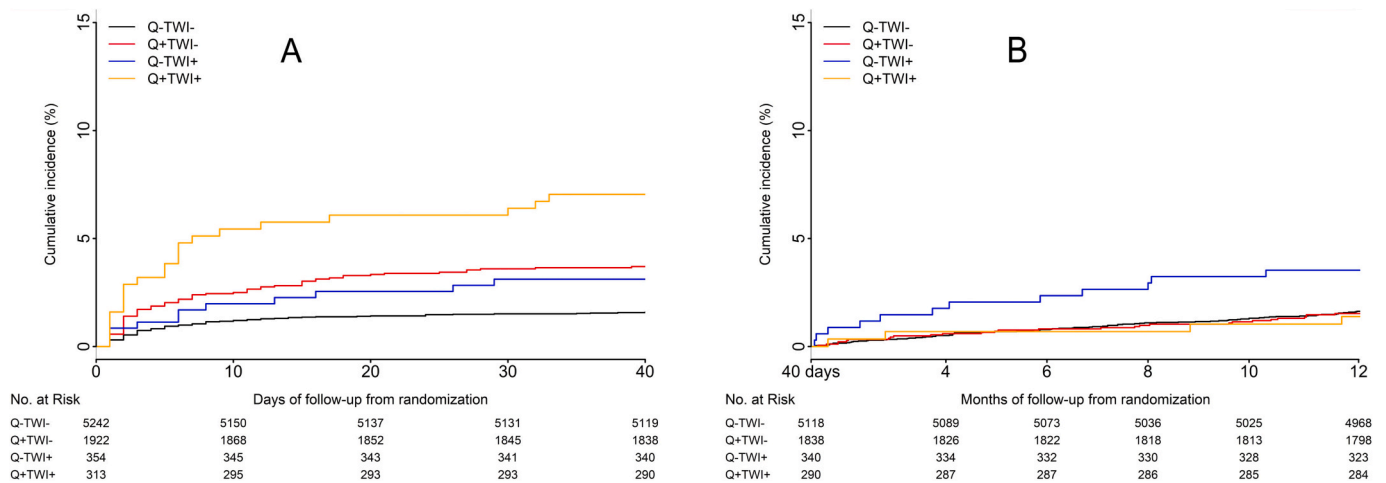


Fig. 3. Kaplan Meier estimate of cumulative incidence of all-cause death for time periods before (panel A) and after (panel B) 40 days.

corroborate those of a previous smaller study [1].

In STEMI patients, pathological Q waves upon admission have been associated with an increased risk for adverse outcome in several previous studies [1–8]. Several pathophysiological mechanisms could provide an explanation for this association. Q waves have been linked to microvascular injury, which, in turn, has been associated with adverse outcome in acute MI [15,16]. Studies have shown that Q waves in patients with acute MI indicate larger infarct size, but not necessarily transmural extension of myocardial injury, and large infarct size is a marker of worse outcome [15,17,18]. In general, anterior infarcts are thought to be larger than inferior infarcts. In our present study, patients with Q waves were more likely to have anterior infarcts, but a higher total CK or troponin level was not explicitly confined to patients with Q waves. A higher TIMI thrombus grade and higher rate of TIMI 0 flow before PCI was also seen in patients with Q waves. Our analysis did take these factors into consideration, showing that they did not affect the outcome of patients with Q waves. Q waves have also been considered as markers of intramyocardial hemorrhage. However, Q waves can be transient, representing myocardial stunning, and they may regress after reperfusion treatment, which is considered as an indicator of improvement in left ventricular ejection fraction [15,17,19,20]. The possible transient nature of Q waves could be one reason for our study findings that Q waves increase the risk of adverse outcome in the early phase but not later on.

TWI in the presenting ECG of STEMI patients has been linked to

patency of the infarct-related artery, but also with non-patency, possibly depending on the time from symptom onset. Patients with TWI had worse outcome at least in the late presenters [9,10,21–23]. In our study, TWI was associated with an increased risk for cardiovascular death, cardiogenic shock, recurrent MI or new or worsening NYHA class IV heart failure, but only after 40 days. Interestingly, TWI was associated with higher risk for all-cause death in the early phase, but not after 40 days. One could speculate that this reflects the effect of T wave normalization on the outcome, analogous to transient Q waves. It has been shown that patients with transient TWI or T-wave normalization after reperfusion treatment have better outcome and less extensive myocardial damage compared to patients with persistent TWI after 4 months [24,25]. TWI with early T-wave normalization could be related to a myocardial stunning, while other studies have demonstrated that TWI could be a sign of myocardial edema in patients with non-ST elevation MI and myocarditis [26–28]. We have no definite explanations for these seemingly contradictory findings. Our study included only the pre-procedural ECG, and therefore, no conclusions can be drawn about temporal changes in the T-wave morphology.

Time from symptom onset has been regarded as a key factor for the outcome of patients with STEMI [29–31]. However, some studies have demonstrated that time from symptom onset is not an independent predictor of outcome [3,5]. Furthermore, Q waves and TWI were previously found to be independently predictive of adverse outcome regardless of time from symptom onset, a finding also observed in our

**Table 3**  
Effect of treatments on 1-year primary outcome subgrouped by Q wave and TWI.

Subgroups	Thrombectomy		PCI alone		HR (95% CI)	p value for interaction <sup>a</sup>
	events/ patients	event rate (%)	events/ patients	event rate (%)		
Q-TWI-	162/2633	6.2	160/2609	6.1	1.00 (0.81-1.25)	0.451
Q+TWI-	97/964	10.1	94/958	9.8	1.03 (0.77-1.37)	
Q-TWI+	20/186	10.8	16/168	9.5	1.13 (0.58-2.18)	0.606
Q+TWI+	14/142	9.9	27/171	15.8	0.60 (0.31-1.15)	
Q wave						
No	182/2819	6.5	176/2777	6.3	1.02 (0.83-1.25)	0.606
Yes	111/1106	10.0	121/1129	10.7	0.93 (0.72-1.21)	
TWI						
No	259/3597	7.2	254/3567	7.1	1.01 (0.85-1.20)	0.343
Yes	34/328	10.4	43/339	12.7	0.80 (0.51-1.26)	

<sup>a</sup> p value for interaction is from likelihood ratio test of interaction term, using unadjusted Cox regression model

study [3,5,10]. While time from symptom onset to hospital arrival and further on to the invasive procedure differed among the patient groups, with the Q+TWI+ patients having the longest delays, Q waves and TWI remained independent predictors of outcome regardless of the time from symptom onset. This implies that different Q and TWI patterns are not simply markers of different temporal stages of the MI disease process, but rather represent different pathophysiological processes associated with acute STEMI.

Routine aspiration thrombectomy was not superior to PCI alone when comparing the different Q wave and TWI groups or when Q waves and TWI were analyzed separately, and therefore, we cannot make recommendations regarding these treatment strategies.

### Limitations

Despite the fact that the analyses were adjusted for numerous confounding factors, some unaccounted factors might still have existed and affected our results. Although the TOTAL trial was one of the largest STEMI trials, the numbers of patients in the Q-TWI+ and Q+TWI+ groups were rather small, which could have affected the results via lack of power, when the follow-up was split into two time periods. Some of the patients had deep inverted T waves, while others had a biphasic T wave with only a minor negative terminal portion. Due to the categorical classification of TWI used in this study, we were unable to account for the differences in TWI morphology and thus this may have affected our results.

### Conclusions

Our study shows that STEMI patients with both Q waves and TWI in the presenting ECG (Q+TWI+ pattern) have worse outcome than patients with neither in their pre-PCI ECG. Q waves mainly affected short-term outcome, while TWI tended to affect long-term outcome, while both ECG parameters independently predicted adverse outcome.

Considering different Q-wave and TWI categories in acute STEMI might be more useful than stratification based on multiple ECG parameters used individually. Conclusive data for tailoring of STEMI treatment based on Q-wave and TWI classification would require prospective studies with randomization according to the ECG changes.

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### CRediT authorship contribution statement

**Joonas Leivo:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Funding acquisition. **Eero Anttonen:** Formal analysis, Investigation, Writing – review & editing. **Sanjit S. Jolly:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Vladimír Dzavík:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Jyri Koivumäki:** Formal analysis, Investigation, Writing – review & editing. **Minna Tahvanainen:** Formal analysis, Investigation, Writing – review & editing. **Kimmo Koivula:** Formal analysis, Investigation, Writing – review & editing. **Kjell Nikus:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Supervision. **Jia Wang:** Methodology, Formal analysis, Writing – review & editing. **John A. Cairns:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Kari Niemelä:** Conceptualization, Methodology, Writing – review & editing, Supervision. **Markku Eskola:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Supervision, Funding acquisition.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jelectrocard.2023.05.010>.

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