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Emergency

In-Hospital Tele-ECG Triage and Interventional Cardiologist Activation of the Infarct Team for STEMI Patients is Associated with Improved Late Clinical Outcomes

Kuan-Chun Chen,[1,2,3] Wei-Hsian Yin,[1,2,4] Mason Shing Young[1,2] and Jeng Wei[2]

Background: Due to recent advances, door-to-balloon time (D2BT) has been reduced significantly for patients with ST-segment elevation myocardial infarction (STEMI). However, whether this reduction can be translated into a concrete mortality or morbidity benefit is still the subject of controversy. We conducted a before-and-after study to determine the impact of in-hospital tele-electrocardiography (ECG) triage and interventional cardiologist activation of the infarct team on D2BT and long-term clinical outcomes in STEMI patients undergoing primary percutaneous coronary intervention (PPCI).

Methods: A total of 272 consecutive patients with acute STEMI undergoing PPCI were enrolled in our study, comprising 102 tele-ECG patients and 170 conventional triage patients. Major adverse cardiovascular and cerebral vascular events (MACCE), including death, recurrent nonfatal MI, nonfatal stroke, and angina-driven target vessel revascularization were recorded during a 3-year follow-up.

Results: The median D2BT of the tele-ECG group was significantly shorter than control group (79 minutes vs. 109 minutes, $p < 0.001$). The tele-ECG triage group had a higher percentage of patients reaching the D2BT goal (< 90 minutes) (78% vs. 55%; $p < 0.001$). The MACCE rate was significantly lower in the Tele-ECG versus the control group (23.5% vs. 38.2%, $p = 0.012$). Tele-ECG group had a lower mortality rate which did not reached statistical significance (2% vs. 5.9%, $p = 0.102$). In multivariable Cox proportional hazards analyses, the implementation of tele-ECG triage (HR = 0.43, $p = 0.003$) and the presence of moderate or severe mitral regurgitation at presentation (HR = 1.87, $p = 0.029$) were discovered as independently associated with MACCE.

Conclusions: In-hospital tele-ECG triage and interventional cardiologist activation can shorten D2BT and is associated with improved late clinical outcomes during a 3-year follow-up in STEMI patients undergoing PPCI.

Key Words: Mortality • Primary percutaneous coronary intervention • ST elevation myocardial infarction

INTRODUCTION

During the treatment of ST-segment elevation myocardial infarction (STEMI), conventional wisdom indicates that timely restoration of the coronary artery blood flow using primary percutaneous coronary intervention (PPCI) can salvage the myocardium and decreases mortality.[1,2] Given the time dependency of survival for patients with STEMI undergoing PPCI, the American College of Cardiology and American Heart Associa-

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[1]Division of Cardiology; [2]Heart Center, Cheng Hsin General Hospital; [3]Institute of Emergency and Critical Care Medicine; [4]Faculty of Medicine, School of Medicine, National Yang-Ming University, Taipei, Taiwan.
Address correspondence and reprint requests to: Dr. Wei-Hsian Yin, Division of Cardiology, Heart Center, Cheng Hsin General Hospital, No. 45, Cheng Hsin Street, Bei-Tou, Taipei 11220, Taiwan. Tel: 886-2-2826-1242; Fax: 886-2-2826-1242; E-mail: yinwh88@gmail.com

tion (ACC/AHA) guidelines for the management of acute myocardial infarction have established a door-to-balloon time (D2BT) of < 90 minutes as a gold standard for PPCI.[1,2] As such, D2BT has been adopted as a key performance measurement for quality of care for patients with STEMI.[3] In the US, a national effort was introduced by the ACC in 2006 to reduce D2BT, and there was a significant improvement in the quality of care observed in those hospitals providing guideline-based standardized care, including D2BT, compared with the control hospitals.[4] More recently, an association between the intervention performed and a reduction in 30-day and 1-year mortality for patients with myocardial infarction was reported.[5,6]

Since 2008, a countrywide campaign seeking to achieve the goal of administering PPCI treatment to 75% of patients with STEMI within 90 minutes of hospital presentation has yielded favorable results in Taiwan. Since 2009, the requirement of achieving a D2BT in 90 minutes or less, and in at least 75% of STEMI patients, has become an important measurement, which is also tied to hospital accreditation by the Taiwan Joint Commission on Hospital Accreditation. This approach was also strongly recommended by the 2012 Guidelines of the Taiwan Society of Cardiology for the Management of STEMI.[7] During the past few years, the National D2BT of Taiwan has dropped significantly for patients with STEMI.[8-10] To adequately address prolonged D2BT before 2009 at our institution, we set up a special task force as a means to improve D2BT and introduced an in-hospital tele-electrocardiography (tele-ECG) transmission system in January 2009. By implementing this system and utilizing other strategies, we were able to significantly shorten D2BT and to treat a larger proportion of patients achieving guideline recommendations.[8]

However, although D2BT is evidently a key indicator for quality performance and has been reduced significantly for patients with STEMI, whether these significant D2BT decreases can be translated into improved mortality or morbidity outcomes remains controversial. Certain studies suggest that the decline may not appear to have translated into reduced in-hospital or long-term mortality; hence, the authors contend that whether D2BT should continue to be a quality measurement needs further investigations.[11-15] In Taiwan, there is scant direct evidence of favorable impact of the serious efforts to reduce D2BT on long-term outcome of STEMI patients. In the present study, we conducted a before-and-after study to determine the impact of implementation of such a strategy of in-hospital tele-ECG triage and interventional cardiologist activation of the infarct team on D2BT and long-term clinical outcomes in STEMI patients undergoing PPCI.

MATERIAL AND METHODS

Study population

The before-and-after study was designed to test the null hypothesis: whether the shortened D2BT and the increased percentage of patients undergoing PPCI within 90 minutes upon arrival after the implementation of Emergency Department (ED) tele-ECG triage and interventional cardiologist activation of the infarct team can translate into long-term clinical benefits.

Patients with STEMI within 12 hours since the onset of chest pain, who had undergone PPCI at the Cheng-Hsin General Hospital between January 2007 and December 2010, were recruited. The diagnosis of STEMI was made based on the presence of both prolonged chest pain lasting for more than 30 minutes, unresponsiveness to nitroglycerin and ECG changes matching the ECG criteria of STEMI. Electrocardiographic criteria of STEMI are ST elevation $\geqq$ 1 mm in $\geqq$ 2 contiguous ECG leads.

The exclusion criteria included: 1) patients who had been diagnosed with STEMI before presentation to our ED (being diagnosed in other hospitals and then transferred to our ED with prior contacts); 2) patients who developed or were diagnosed with acute STEMI post-arrival at our ED; and 3) patients who arrived at our ED with complications or cardiogenic shock needing urgent surgical interventions, cardiopulmonary resuscitation including endotracheal intubation, cardiac massage, intra-aortic balloon pumping, or extra-corporeal membrane oxygenation support.

This retrospective study was approved by the local ethics committee; the informed consent requirement was waived because of the study's retrospective nature.

ED tele-ECG triage and interventional cardiologist activation of the infarct team

A special task force (as mentioned earlier) was set

up in 2009 to improve D2BT in our institution. At first, we identified the interval from ECG examination to a patient's arrival at the catheter laboratory as the time-limiting period of D2BT at our institution, and introduced an in-hospital tele-ECG transmission system. The system can facilitate the process of notification and make a patient's ECG available to the on-call interventional cardiologist. On-call interventional cardiologists are thus enabled to receive and interpret ECG immediately, and then activate the infarct team as necessary. In this way, we could significantly shorten D2BT, which resulted in a larger proportion of patients achieving guideline recommendations. Details of the implementation of the system and how it can improve D2BT in our institution have already been published.[8]

Data collection and patient follow-up

In the present study, all data were retrospectively collected by trained research assistants and taken from our computerized database in a preplanned analysis. We collected data of STEMI patients, who had undergone PPCI two years before and two years after the implementation of the new tele-ECG process. There was no training phase. A total of 102 consecutive patients with STEMI within 12 hours since onset of chest pain, who had undergone PPCI at the Cheng-Hsin General Hospital from January 2009 to December 2010 were recruited as the tele-ECG group in the present study. The other 170 consecutive patients with acute STEMI, who had undergone PPCI from January 2007 to December 2008 before implementation of the tele-ECG protocol, were retrospectively reviewed and served as the historical control group. Clinical follow-up was conducted based on medical records from our computer database, and telephone contacts up to 3 years after the index PPCI procedure for acute STEMI for each patient.

Baseline characteristics, such as comorbidities, vital signs while visiting ED-including blood pressure and heart rate, blood biochemistry as initial plasma creatinine phosphokinase (CK), myocardium specific enzyme (CK-MB), cardiac troponin I levels, complete blood counts and neutrophil/lymphocyte ratio (NLR) obtained from automated blood cell counter, and echocardiographic parameters including left ventricular ejection fraction (LVEF) and the severity of mitral regurgitation (MR), were collected from medical records. Subsequently, the patients' Global Registry of Acute Coronary Events (GRACE) prognosis risk score was calculated according to the previous publication.[16] This score is calculated from eight individual variables: age of the patient, admission systolic blood pressure, heart rate, Killip class, baseline creatinine level, cardiac arrest on admission, ST segment deviation on initial ECG, and elevation of cardiac biomarkers.

Definitions of endpoint

The primary endpoint was defined as the composite endpoints of major adverse cardiovascular and cerebral adverse events (MACCE) regarding death, recurrent nonfatal MI, nonfatal stroke, and angina-driven target vessel revascularization (TVR) during a 3-year follow-up period. TVR was defined as repeat PCI or coronary artery bypass grafting (CABG) of any segment of the target vessel. The target vessel was defined as the entire major coronary vessel proximal and distal to the target lesion.

Statistical analysis

Data were transferred from the database to the Statistical Program for Social Sciences program (version 12.0 for Windows, SPSS Inc., Chicago, IL, USA). Univariate comparisons of demographic parameters and time intervals between these two groups were made. Continuous variables are expressed as mean ± standard deviation or median (interquartile range) and were compared using the Student's t-test or the Wilcoxon rank-sum test. Categorical variables were presented as percent frequency and were compared by the Pearson's chi-square test or the Fisher's exact test. Additionally, MACCE-free survival analysis was performed by the Kaplan-Meier method. A 2-tail p value of < 0.05 was considered to be statistically significant. Independent prognostic determinants of composite MACCE were identified using the Cox proportional hazards analysis, and the hazard ratio (HR) and associated 95% confidence interval were measured for each determinant.

RESULT

Demographic variables, risk factors, and other parameters of the study patients (Table 1)

From January 2007 to December 2010, a total of 272

Table 1. Demographic variables, risk factors, and angiographic parameters of the 272 patients with ST-segment elevation acute myocardial infarction undergoing primary percutaneous coronary intervention

	Tele-ECG group (n = 102)	Control group (n = 170)	p value
Age (years)	62 ± 13	63 ± 14	0.541
Male	85 (83%)	138 (81%)	0.745
Diabetes	33 (32%)	57 (34%)	0.894
Hypertension	58 (57%)	81 (48%)	0.168
Smoking	16 (16%)	30 (18%)	0.740
Hyperlipidemia	40 (39%)	66 (39%)	1.000
Prior myocardial infarction	11 (11%)	23 (14%)	0.573
Prior stroke	4 (4%)	4 (2%)	0.478
Prior CABG	1 (1%)	8 (5%)	0.160
Prior PCI	7 (7%)	9 (5%)	0.603
Prior valvular heart disease	0 (0%)	6 (4%)	0.087
Number of diseased vessels			0.019
1	32 (31%)	27 (16%)	
2	40 (39%)	71 (42%)	
3	30 (29%)	71 (42%)	
Location of lesion			0.430
LAD	45 (47%)	77 (48%)	
LCX	11 (12%)	25 (16%)	
RCA	39 (41%)	59 (37%)	

CABG, coronary artery bypass grafting; ECG, electrocardiography; LAD, left anterior descending artery; LCX, left circumflex artery; PCI, percutaneous coronary intervention; RCA, right coronary artery.

patients matching the inclusion criteria were recruited for the analysis. They were divided into two groups: 102 patients in the tele-ECG triage group (after the implementation of ED tele-ECG triage and interventional cardiologist activation of the infarct team), and 170 patients in the conventional triage group (prior to the implementation of new protocol); i.e., the historical control group.

Table 1 summarizes the baseline clinical characteristics, risk factors, angiographic and other parameters for both groups. The mean age and the incidence of risk factor of cardiovascular disease were similar in both; neither was there any significant difference between the two, regarding the previous history of MI, stroke, CABG, PCI, or valvular heart disease. The angiographic data demonstrated more severe coronary artery disease in the control group than those in the tele-ECG triage one (single vessel disease 16% vs. 31%; p = 0.019), even though the distribution of culprit lesions were similar in both.

D2BT and other parameters of the study patients (Table 2)

Prehospital on-scene times, defined as time from

Table 2. Door-to-balloon time and other parameters of the 272 patients with ST-segment elevation acute myocardial infarction undergoing primary percutaneous coronary intervention

	Tele-ECG group (n = 102)	Control group (n = 170)	p value
Prehospital on-scene time (hours)	2.8 (1-11)	4.8 (1-10)	0.220
D2BT_min, median (IQR)	79 (62-95)	109 (70-121)	< 0.001
D2BT ≤ 90 minutes goal	79 (78%)	93 (55%)	< 0.001
Parameters at presentation			
SBP (mmHg)	134 ± 33	135 ± 29	0.825
DBP (mmHg)	82 ± 22	83 ± 19	0.642
Heart rate (beats per minute)	74 ± 17	78 ± 22	0.208
WBC (/μl)	10,588 ± 3,033	10,833 ± 3,600	0.566
Neutrophil (%)	64 ± 17	69 ± 14	0.008
Lymphocyte (%)	28 ± 14	23 ± 13	0.008
NLR	3.6 ± 3.5	4.7 ± 3.9	0.030
Creatinine (mg/dl)	1.2 ± 1	1.3 ± 1	0.429
Glucose (gm/dL)	178 ± 81	178 ± 93	0.950
Cholesterol (mg/dl)	176 ± 46	179 ± 42	0.600
Triglyceride (mg/dl)	146 ± 136	135 ± 92	0.433
Initial total CK (μ/ml)	501 ± 793	848 ± 1,468	0.029
Initial CK-MB (μ/ml)	26 ± 49	54 ± 93	0.010
Initial troponin I	7 ± 17	12 ± 25	0.124
GRACE score	133 ± 32	139 ± 34	0.182
LV ejection fraction (%)	43 ± 10	42 ± 11	0.639
Mitral regurgitation severity	1.1 ± 0.5	1.2 ± 0.7	0.012
Peak CK (μ/ml)	2,773 ± 2,127	2,424 ± 2,294	0.213
Peak CK-MB (μ/ml)	127 ± 114	130 ± 128	0.865
Peak troponin I (μ/ml)	100 ± 111	74 ± 97	0.044

CK, creatinine kinase; CK-MB, creatinine kinase MB isoenzyme; DBP, diastolic blood pressure; D2BT, door-to-balloon time; ECG, electrocardiography; GRACE, Global Registry of Acute Coronary Events; IQR, interquartile range; LV, left ventricle; NLR, neutrophil-to-lymphocyte ratio; SBP, systolic blood pressure; WBC, white blood cell.

onset of showing symptoms to arrival at the ED, were similar in the tele-ECG and control groups. However, median D2BT of the tele-ECG group was 79 minutes (interquartile range 62 to 95), significantly shorter than the control group's median time of 109 minutes (interquartile range 70 to 121), where p < 0.001. The Tele-ECG triage group had a higher percentage of patients reaching the goal of D2BT in less than 90 minutes than the control group (78% vs. 55%; p < 0.001).

At presentation, the patients' vital signs, serum levels of creatinine, glucose and lipid profiles were similar in both groups. The NLR at presentation and the initial CPK and CPK-MB levels were significantly lower in the Tele-ECG triage group than those in the control group. However, after PPCI, the peak CPK and CPK-MB levels were similar in both again.

There were no significant differences in terms of initial GRACE scores and LVEF in the two groups. However, the patients in the control group had more severe MR upon presentation than those in the other group.

Clinical outcomes

The long-term clinic outcomes following PPCI for STEMI in both groups are presented in Table 3. Clinical follow-up was based on medical records from the computer database and telephone contact up to 3 years after the index PPCI procedure for acute STEMI. Primary endpoint, defined as the composite endpoints of MACCE during follow-up, was significantly lower in the Tele-ECG versus the control group (23.5% vs. 38.2%, p = 0.012). Although a trend of lower mortality rate was demonstrated in the Tele-ECG group, there was no statistical significance (2% vs 5.9%, p = 0.102). The Kaplan-Meier survival curves are shown in Figure 1.

There was no recurrent non-fatal MI or stroke in the Tele-ECG group during the 3-year follow-up; however, 1 patient (0.6%) suffered from recurrent non-fatal MI and 3 others (1.8%) from stroke, during follow-up in the control group. Nineteen patients (18.6%) in the Tele-ECG

Table 3. Long-term outcomes of the 272 patients with ST-segment elevation acute myocardial infarction undergoing primary percutaneous coronary intervention

Event	Tele-ECG group (N = 102)	Control group (N= 170)	p value
Total MACCE	24 (23.5%)	65 (38.2%)	0.012
Death	2 (2%)	10 (5.9%)	0.102
Recurrent nonfatal MI	0	1 (0.6%)	0.429
Recurrent nonfatal stroke	0	3 (1.8%)	0.160
TVR by repeat PCI	19 (18.6%)	50 (31.4%)	0.022
TVR by CABG	3 (2.9%)	1 (0.6%)	0.139

CABG, coronary artery bypass grafting; ECG, electrocardiography; MACCE, major cardiac and cerebral adverse events; PCI, percutaneous coronary intervention; TVR, target vessel revascularization.

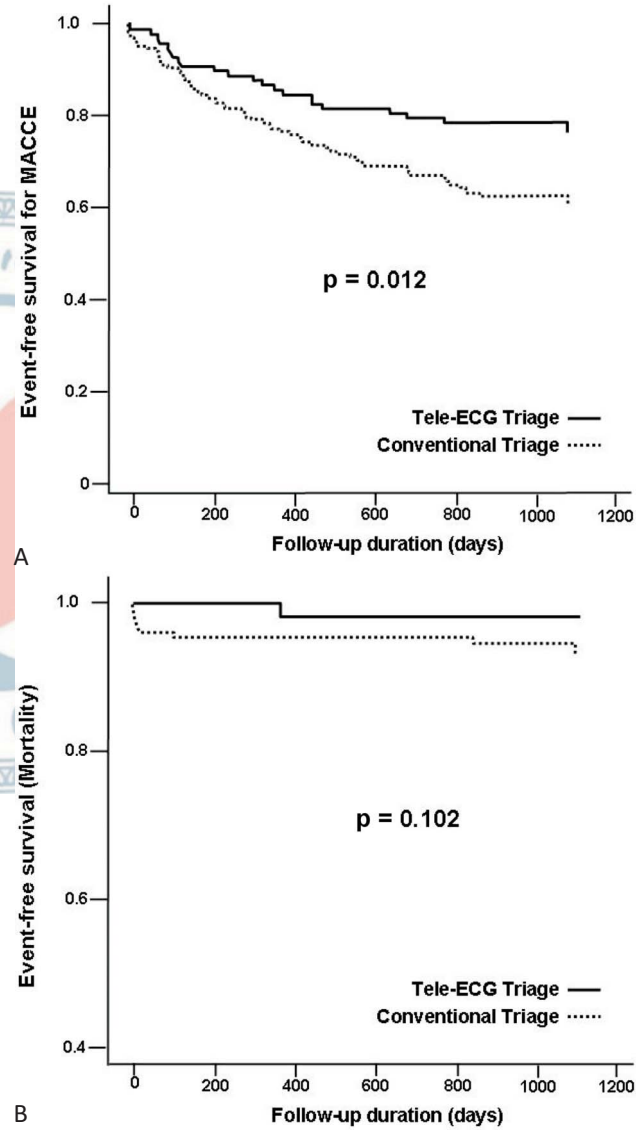

Figure 1. *Cumulative event-free survival curves for major adverse cardiac and cerebral adverse events (MACCE) (A) and mortality (B) in ST-segment elevation myocardial infarction patients of the tele-ECG triage group and the conventional triage (or control) group. ECG ,electrocardiography*

group and 50 (31.4%) in the control group received TVR by repeat PCI (p = 0.022). Three patients (2.9%) in the Tele-ECG group and 1 (0.6%) in the control group received TVR by CABG (p = 0.139). This suggests that the difference of primary end-points between the two groups was primarily driven by repeat PCI for TVR.

Univariate and multivariate analysis

When the 272 patients with STEMI (who had undergone PPCI) were divided into two groups depending on whether a patient had MACCE or not during follow-up, significant differences in the number of diseased vessels, NLR, and the severity of MR were detected between the two groups. Furthermore, significantly more patients in the control group were found to develop MACCE later than did those in the event-free group.

In multivariable Cox proportional hazards analyses (Table 4), the implementation of tele-ECG triage (HR = 0.43, p = 0.003) and the presence of moderate or severe MR (HR = 1.87, p = 0.029) were discovered to be independently associated with MACCE after adjustment for the clinical variables including age, gender, risk factors of MI, number of diseased vessels, vital signs, blood biochemistry parameters, and NLR had been made. Although both D2BT and Tele-ECG triage are significant predictors of later outcomes, these two variables have a positive correlation with each other. Therefore, only tele-ECG triage was indicated in the multivariate analysis.

DISCUSSION

In the present study, we have clearly demonstrated that median D2BT of the tele-ECG group was significantly shorter, and the percentage of patients who reached the goal of D2BT in less than 90 minutes was significantly higher than those of the control group. During a 3-year follow-up period, the primary endpoint of MACCE rate was significantly lower in the Tele-ECG versus the control group, which was mainly driven by reduction of TVR by repeat PCI. Moreover, even though more severe coronary artery disease, higher NLR, initial CPK and CPK-MB levels, and more severe MR at presentation were noted in the control group, after adjustment of those parameters, the implementation of tele-ECG triage to improve D2BT was still discovered to be independently associated with MACCE at the span of 3 years.

There is general consensus that PPCI is the preferred treatment for patients with STEMI, so long as it can be delivered in a timely fashion, by an experienced operator and an infarct team. Since "time is muscle," the sooner treatment begins, the lesser muscle is damaged; that preserves functionality of the heart and quality of life. Therefore, rapidly achieving normal coronary artery flow, at both the macro and micro vascular levels, is the recognized key to aborting the otherwise progressive wavefront of myocardial necrosis.[1,2] Longer D2BT has been associated with increased in-hospital mortality regardless of time of symptom onset or presence of high risk factors.[17] The drive to lower D2BT was underscored by guidelines from the ACC/AHA, and has become the focus of quality-improvement initiatives.[18,19] The proportion of patients with a D2BT of 90 minutes or less has become an important measurement that is also tied to Medicare and Medicaid reimbursement in the US, and studies have identified strategies associated with improved outcomes in achieving better D2BT.[4,20] With the persistent efforts of an integrated multidisciplinary approach nationwide, previous research has suggested that the national D2BT fell sharply in the US.[15] A significant improvement in quality of care was also observed in those hospitals providing guideline-based standardized care, including D2BT, compared with the control hospitals, resulting in an improvement of both short- and long-term mortality for patients with STEMI.[5,6] In Taiwan, previous studies also confirmed that the drive to cut D2BT has been a success; the country's D2BT has fallen sharply since 2008 with the implementation of quality improvement initiatives.[8-10] The present study reconfirms that implementation of an in-hospital tele-ECG transmission system to facilitate the process of infarct team activation by on-call interventional cardiologist and other strategies to shorten D2BT is highly effective, as reported previously.[8] Moreover, its effect is long-lasting, resulting in improved long-term outcomes for STEMI patients.

It is nevertheless noteworthy that this observational cohort study demonstrated significantly reduced D2BT for PPCI patients but no significant improvement in overall mortality during the 3-year follow-up period. In other words, the efforts we had made to reduce D2BT do not appear to have translated into reduced long-term

Table 4. Independent prognostic determinants of composite MACCE by univariate and multivariate analysis

Parameters	MACCE (+) (n = 84)	MACCE (-) (n= 183)	Univariate p value	Multivariate p value
Tele-ECG group	24 (27.3)	78 (42.4%)	0.016	0.003
Age (years)	64.5 ± 14	61.4 ± 13	0.081	
Male	68 (77%)	155 (84%)	0.179	
Diabetes	31 (35%)	59 (32%)	0.680	
Hypertension	48 (54.5%)	91 (49.5%)	0.440	
Smoking	19 (21.6%)	27 (14.7%)	0.169	
Hyperlipidemia	28 (31.8%)	78 (42.4%)	0.111	
Prior myocardial infarction	14 (15.9%)	20 (10.9%)	0.245	
Prior stroke	1 (1.1%)	7 (3.8%)	0.444	
Prior CABG	3 (3.4%)	6 (3.3%)	1.000	
Prior PCI	5 (5.7%)	11 (6.0%)	1.000	
Prior valvular heart disease	1 (1.1%)	5 (2.7%)	0.667	
Number of diseased vessels			0.023	0.128
1	32 (31%)	27 (16%)		
2	40 (39%)	71 (42%)		
3	30 (29%)	71 (42%)		
Location of lesion			0.43	
LAD	45 (47%)	77 (48%)		
LCX	11 (12%)	25 (16%)		
RCA	39 (41%)	59 (37%)		
LAD involved	45 (51.1%)	79 (42.9%)	0.242	
Use of drug eluting stent	25 (28%)	69 (38%)	0.110	
Prehospital on-scene time, hours (IQR)	3.8 (1.63-7.51)	3.2 (1.88-9.6)	0.329	
D2BT_min, median (IQR)	117 (87-182)	91 (75-135)	0.022	
D2BT ≤ 90 minutes goal	29 (35%)	85 (43%)	0.060	
Parameters at presentation				
SBP (mmHg)	130 ± 28	136 ± 31	0.090	
DBP (mmHg)	79 ± 18	84 ± 21	0.058	
Heart rate (per minute)	79 ± 21	75 ± 20	0.102	
WBC (/μl)	11,253 ± 3,642	10,496 ± 3,252	0.085	
NLR, median (IQR)	3.9 (2.2-7.45)	2.9 (1.68-5.2)	0.003	0.372
GRACE score	141 ± 32	132 ± 34	0.047	
GRACE score ≥ 144	41 (48.8)	67 (36.6%)	0.062	
Initial troponin I	13.8 ± 25.4	7.9 ± 20.9	0.060	
Cholesterol (mg/dl)	174 ± 38	180 ± 46	0.299	
Triglyceride (mg/dl)	137 ± 86	141 ± 121	0.795	
Creatine (mg/dl)	1.2 ± 1	1.2 ± 1.1	0.823	
Glucose (gm/dL)	194 ± 105	171 ± 79	0.077	
Peak CK (μ/ml)	2,364 ± 2,201	2,645 ± 2,251	0.333	
Peak CK-MB (μ/ml)	115 ± 2,201	135 ± 2,251	0.234	
Peak Troponin I (μ/ml)	77.3 ± 101.7	86.4 ± 103.5	0.497	
LV ejection fraction (%)	43 ± 10	42 ± 11	0.639	
Moderate to severe MR (%)	19 (23%)	21 (74%)	0.027	0.029

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CK, creatinine kinase; CK-MB, creatinine kinase MB isoenzyme; DBP, diastolic blood pressure; D2BT, door to balloon time; ECG, electrocardiography; GRACE, Global Registry of Acute Coronary Events; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; LV, left ventricle; MACCE, major cardiac and cerebral adverse events; MR, mitral regurgitation; NLR, neutrophil-lymphocyte ratio; PCI, percutaneous coronary intervention; RCA, right coronary artery; SBP, systolic blood pressure; WBC, white blood cell.

mortality. Why was there no apparent change perceived in the risk of death, despite better D2BT? As far as we know, one of the main limitations of the present study was its small sample size, retrospective nature, and before-and-after design. Smaller differences and confounders may exist between the two groups, and may affect the success of either approach if examined in a prospective randomized manner. Moreover, our study excluded STEMI before our ED presentation, patients who developed or were diagnosed with acute STEMI post-arrival at our ED, and patients who arrived at our ED with complications or cardiogenic shock needing resuscitation. Given the fact that advanced age and Killip class were prognostic indicators of mortality in STEMI patients who underwent PCI because older patients typically have more comorbidities; hence, they were more likely to present with atypical symptoms, and have a coronary anatomy unfavourable for PCI.[21-24] Therefore, they were more than likely to be excluded from the present study. Rather unexpectedly, however, the mean ages were relatively young and the mortality rates relatively low in both groups, and there remained very little room for improvement by D2BT reduction.

Survival after acute MI is moreover dependent on several parameters. Some of these parameters act by limiting the infarct size, while others improve the prognosis independent of the final infarct size. Determinants of infarct size are time of vessel occlusion, degree of collaterals and area at risk. The latter two determinants do not offer a therapeutic approach in acute MI. The most important therapeutic intervention remains the restoration of blood flow in the area at risk by either thrombolysis or PCI. Reperfusion within 60 to 120 minutes significantly reduces mortality and infarct size. Within this time frame, changes in left ventricular function correlate with the survival rate. However, this time frame is variable since there are wide variations in the degree of collaterals.[25,26] According to our study, although more severe coronary artery disease, higher NLR, initial CPK and CPK-MB levels, and more severe MR at presentation were noted in the control group than in the tele-ECG triage group, the initial GRACE scores and LVEF, and the peak CPK and CPK-MB levels after PPCI were similar in both groups. That means, even if a later reperfusion was achieved in the control group, it would still be beneficial to survival in certain cases. This is because although the median D2BT of 109 minutes of the control group was longer than that of the tele-ECG triage group, it was still within the time frame. In addition, the improvement in prognosis of patients with sustained patency of the infarct-related artery disproportional to the observed improvement in ventricular function, suggesting that other mechanisms contribute to the beneficial effects of reperfusion in addition to the salvage of ischemic myocardium.[25,26] Experimental and clinical data support the concept that late reperfusion prevents LV dilatation and improves LV function by limiting infarct expansion and ventricular remodeling, and may also prevent severe ventricular arrhythmias. These benefits are independent of any limitation on infarct size.[25,26] Therefore, maintenance of long-term adequacy of reperfusion of the infarct bed may be as important as timing of reperfusion within the narrow time frame during acute heart attack regarding long-term outcomes.[25,26] Hence, although the TVR rate was higher in the control group, the procedures may maintain infarct-related artery patency in the long term and, to some extent, would have reduced the risk of death in those patients.

On the other hand, we have found that the implementation of tele-ECG triage to improve D2BT was still discovered as an independent predictor of better outcomes at the 3-year span. This may imply that although short-term mortality has not been improved, patients having undergone an earlier complete and effective myocardial reperfusion to help reduce infarct size, might recover better and have an improved quality of life after heart attack. In addition, the effects of temporal trends cannot be excluded. This may indicate that strategies to improve the procedural aspects of PPCI and adjunctive medications for reducing residual stenosis, preventing reocclusion, and maintaining infarct related artery patency in the long term are important. For example, rapid platelet inhibition with aspirin and P2Y12 inhibitor is an essential treatment in STEMI.[27,28] Proper use of manual aspiration before stenting can reduce thrombus burden during PPCI, staged PCI for the non-infarct artery to achieve complete revascularization shortly after the initial revascularization of the infarct-related artery for STEMI patients with multivessel disease, use of newer generation DES with thinner struts, reduced polymer thickness, and better drug-releasing pattern are other recommended strategies to improve outcomes of STEMI

patients undergoing PPCI.[27] Moreover, implementation of the tele-ECG protocol formed part of a major continuous quality improvement act initiated in 2009 at our institution, which was expected to result in a Hawthorne effect. Furthermore, a performance monitoring system we established in our hospitals may improve the quality of care and late outcomes of STEMI patients. In the Guidelines Applied to Practice (GAP) intervention aimed at improving quality of care for patients with acute coronary syndromes through the development of standing orders and tool kits, simple hospital discharge contracts designed to ensure that patients left the hospital having received essential medications and education, and systematic data feedback on performance on key quality indicators. Even the GAP initiative was unsuccessful in improving D2BT for PPCI, perhaps due to insufficient attention being placed on the key factors which could influence initial triage and therapy as patients entered ED. The study confirmed that a significant improvement in quality of care was observed in the intervention hospitals compared with the control hospitals, and an association between the intervention performed and a reduction in 30-day and 1-year mortality for patients with MI.[5,29]

As to the D2BT per se, although D2BT have been reduced significantly for patients with a STEMI during the last decade, worldwide, some studies showed that the decline may not appear to have translated into reduced in-hospital or long-term mortality.[11-15] Does it mean that we should abandon D2BT? We believe and have shown in the present study that a substantial reduction in D2BT can be achieved through multi-institutional collaborative initiatives; where, institutions and caregivers work together to identify local action items to focus upon, to implement systems to measure process and outcomes, and to provide timely feedback can provide real residual benefits. However, achieving and maintaining the 90-minute gold standard will require sustained investment on the part of institutions and caregivers alike. The "race against the clock" doctrine may be blinding caregivers to the sometimes complex needs of individual patients, and we should feel comfortable with occasional pauses, treating STEMI patients based on a holistic approach; in other words, the optimal therapy for each STEMI patient should depend on the cardiologist's clinical judgment and preference.

Whether D2BT continues to make sense as a measurement of quality is open to debate. Actually, our finding suggests that other strategies will be needed to cut the risk of death for patients with STEMI. For example, the use of the prehospital ECG to identify patients with STEMI, coupled with a centralized system to alert the cardiac catheterization team in preparation for prompt intervention, has been shown to effectively reduce D2BT when adopted by hospitals and emergency medical services personnel.[30] In Taiwan, PPCI has become the first line reperfusion therapy for STEMI, and almost all STEMI patients received PPCI. This suggests that the major effort now should be focused on decreasing the treatment delay by rapid transfer of STEMI patients with ambulance to PCI-capable hospitals. Any delay in the health care system should be reduced as much as possible from the first medical contact of the STEMI patients.[27] In the future, it is probably more important to cut the "total ischemic time" – the length of time between onset of symptoms and reperfusion with PPCI, for the D2BT takes up a fairly small part of the total ischemic time. Several experimental and human clinical studies have confirmed that infarct size and mortality are strongly correlated with the total ischemic time, and much less so with its subintervals like D2BT.[31-35] To sum up, future efforts should focus on reducing the total ischemic time.[15,32-35]

The present study had some limitations. First, we excluded many higher risk STEMI patients in our study as mentioned earlier. Thus, the study results may be influenced by selection bias and may not be applicable to all STEMI patients. Secondly, the sample was relatively small, and because it was a before-and-after trial rather than a prospective randomized controlled trial, we naturally did not control as many potential confounding variables that might have affected D2BT. Patient data were collected retrospectively and, unavoidably, with all associated limitations of a retrospective medical record review. Finally, because we did not perform cost-effectiveness analyses on implementation of the tele-ECG protocol or consider costs for building the cable network or wireless telephone network, and maintenance of hardware stability, etc., the results presented may not be replicated elsewhere without similar demographics and resources. Nonetheless, this study does provide valuable real-world data on the current practices for STEMI patients by using tele-ECG triage to shorten D2BT. Thanks

to modern technological developments and ever decreasing costs, telecardiology has the potential to save time, money, and lives.

CONCLUSIONS

In-hospital tele-ECG triage and interventional cardiologist activation can shorten D2BT and is associated with improved late clinical outcomes of STEMI patients undergoing PPCI. However, PPCI should not be viewed separately from other equally important targets such as compliance with guideline-driven strategies to improve the procedural aspects of PPCI and adjunctive medications, appropriate secondary prevention measures and risk factor modification, both in hospital and during follow-up.

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