

Warning system improve the clinical outcomes in transfer patients with ST-segment elevation myocardial infarction

Hsiu-Yu Fang, MD, Wei-Chieh Lee, MD*

Abstract

A warning system included directly faxing electrocardiography information to the mobile phone immediately after an ST-segment elevation myocardial infarction (STEMI) diagnosis was made at a non-percutaneous coronary intervention (PCI) capable hospital. This study aimed to explore the outcomes after using a warning system in transfer STEMI patients.

From October 2013 to December 2016, 667 patients experienced a STEMI event and received primary PCI at our institution. 274 patients who were divided into transfer group were transferred from non-PCI capable hospitals and connected to a first-line cardiovascular doctor by the warning system. Other 393 patients were divided into the non-transfer group.

The transfer group still had a longer pain-to-reperfusion time and presented higher troponin-I level when compared with non-transfer group. There was no significant difference in the use of drug-eluting stent and procedural devices between non-transfer and transfer groups. The prevalence of different anti-platelet agents loading did not differ between non-transfer and transfer groups. Non-significant trend about higher prevalence of statin use was noted in transfer group (78.9% vs 86.1%, $P = .058$). The transfer group presented similar clinical short-term results regarding both cardiovascular and all-cause mortality when comparing with non-transfer group. The transfer group provided non-significant trend about lower one-year cardiovascular mortality (10.7% vs 6.2%, $P = .052$) and lower all-cause mortality (12.2% vs 6.9%, $P = .026$) when compared with non-transfer group. There was a significant difference in the Kaplan–Meier curve of 1-year cardiovascular mortality between the transfer group and the non-transfer group ($P = .049$).

After using the warning system, the inter-facility transfer group had comparable outcomes even though a longer pain-to-reperfusion time and a higher peak troponin-I level when comparing with non-transfer group.

Abbreviations: ECG = electrocardiography, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction.

Keywords: cardiovascular mortality, direct hospital admission, inter-facility transfer, ST-segment elevation myocardial infarction, warning system

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All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later revisions.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Division of Cardiology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung, Taiwan.

* Correspondence: Wei-Chieh Lee, Division of Cardiology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, 123, Ta Pei Road, Niao Sung District, Kaohsiung City, 83301, Taiwan, No.123, Ta Pei Rd, Niao-Sung district, Kaohsiung City, Taiwan (e-mail: leeweichieh@yahoo.com.tw).

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1. Introduction

Primary percutaneous coronary intervention (PCI) is currently class I, level A evidence for the diagnosis of an acute ST-segment elevation myocardial infarction (STEMI) under the American College of Cardiology Foundation/American Heart Association (ACC/AHA) guidelines.^[1] Efforts to improve the door-to-balloon (DTB) interval have achieved a decrease in the USA, but mortality reduction has so far not been observed.^[2,3] The main reason for this is thought to be due to the total ischemic time because of pre-hospital delays in treatment, such as patient awareness and inter-facility transfer delays.^[4–7] The ACC/AHA guidelines in 2013 also recommends an establishment of networks of STEMI-referral (non-PCI capable) and STEMI-receiving (PCI-capable) hospital to implement healthcare system redesign.^[1] The accurate number of STEMI patients referred from non-PCI capable hospitals was unknown, but the estimated percentage was about 20% to 45%.^[8–15] Several studies reported the outcomes of STEMI patients who experienced inter-facility transfer compared with those who presented via direct admission, but the results were inconsistent due to several biases, including different study size protocols.^[8–16] The distance between patients and their closest hospital varies greatly due to the long and narrow terrain of Taiwan. Similar island countries such as Japan reported

significantly worse long-term clinical outcomes for STEMI patients who were referred between facilities for primary PCI.^[17]

The warning system includes a fax machine from a local hospital without the ability to perform primary PCI, a computer with the “Windows fax” function, and a mobile phone. When using this system, we could avoid patients’ privacy leakage. The purpose of the present study was to evaluate the influence of inter-facility transfer on the 30-day and one-year clinical outcomes of STEMI patients undergoing primary PCI after the implementation of the warning system.

2. Materials and methods

2.1. Patients and groups

The reason this study was performed was due to the implementation of a “warning system” (Fig. 1) after October 2013, which included directly faxing electrocardiography (ECG) information to the mobile phone of a first-line duty doctor immediately after a STEMI diagnosis was made at an inter-facility non-PCI capable hospital, where the patient was immediately given medications such as dual anti-platelet therapy

and anti-coagulation therapy. After PCI capable hospital cardiovascular duty doctor confirmed the diagnosis, dual anti-platelet therapy and pre-PCI medications then initiated. The preparation of primary PCI was performed before the patient arrived and directly enter Cath lab for primary PCI. The “warning system” has been used since October 2013 in our institution.

The inclusion criteria were STEMI patients who were transferred from inter-facility non-PCI capable hospitals or admitted to our emergent department directly. We already excluded the patients involving myocardial infarction or the patients experiencing STEMI during hospitalization. From October 2013 to December 2016, 667 STEMI patients were included in our study. The patients were divided into two groups according to whether they were transferred from inter-facility non-PCI capable hospitals (named the transfer group) or presented via directed hospital admission (named the non-transfer group). The transfer group consisted of 274 patients, whereas the non-transfer group consisted of 393 patients.

The study was approved by the Institutional Review Committee on Human Research of Chang Gung Memorial Hospital for retrospective analysis in consecutive patients with

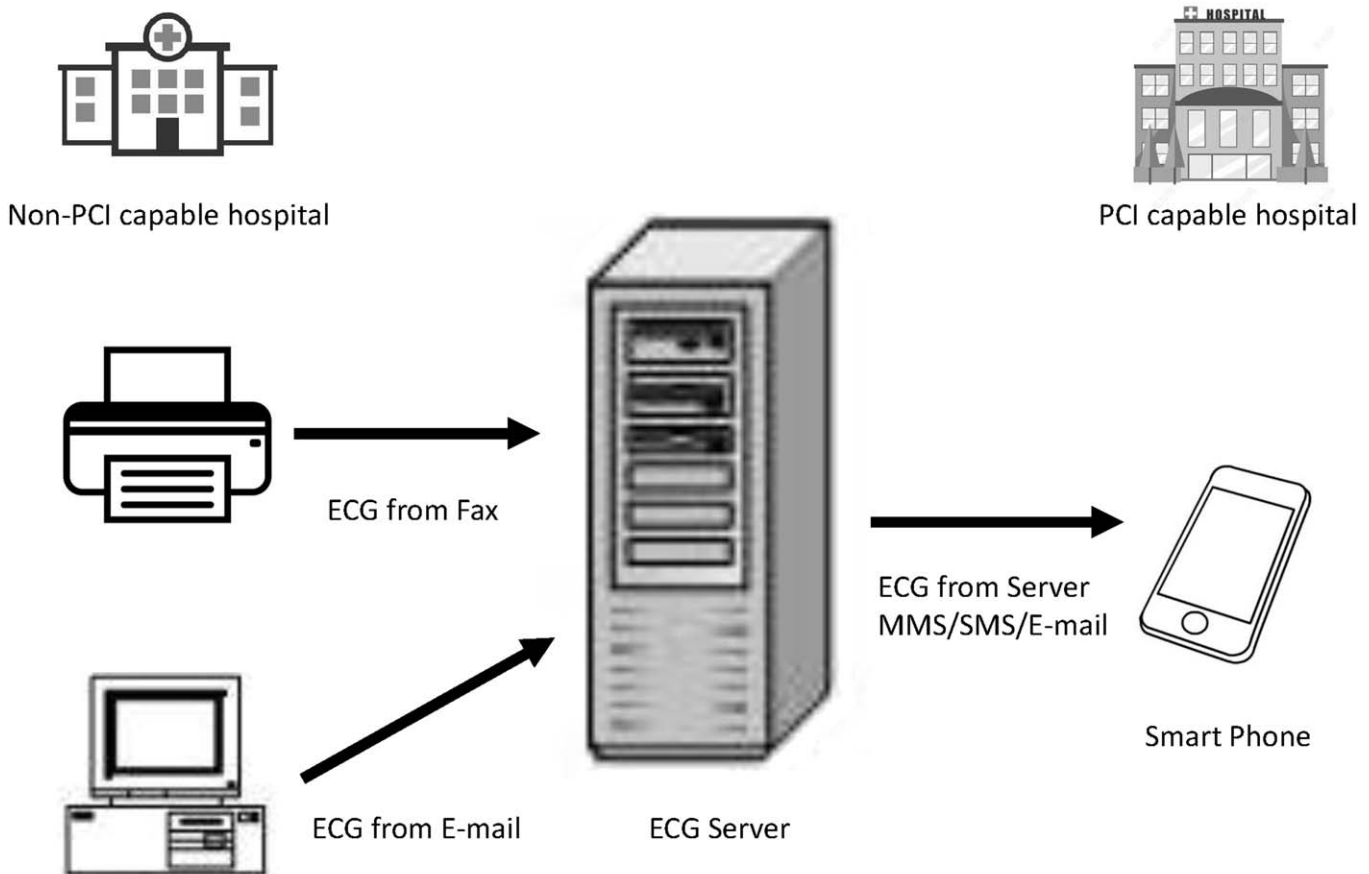


Figure 1. The illustration of the “Warning system.” When a STEMI patient came to a Non-PCI capable hospital, the ECG is sent via the hospital’s system either by Fax or Computer (Windows Fax) system. The ECG will be transferred to the ECG Server. The ECG Server will send the ECG directly to the PCI-capable hospital’s smartphone which is carried by first-line duty cardiovascular doctors by MMS/SMS or e-mail. After the first line duty cardiovascular doctors confirmed the diagnosis of STEMI, dual anti-platelet therapy will be initiated and the patient will be sent immediately from Non-PCI capable hospital to PCI capable hospital without delay. On the other hand, the first line duty cardiovascular doctors will start up the process of emergent PCI in PCI capable hospital. ECG = electrocardiography, MMS = multimedia message service, PCI = percutaneous coronary intervention, SMS = short message service, STEMI = ST-segment elevation myocardial infarction.

STEMI who underwent PCI in our hospital. The approval number was 201701790B0. We focused on the comparison of transfer and non-transfer according to medical record. The raw data was from STEMI registry of Kaohsiung Chang Gung Memorial Hospital.

2.2. Definitions

Our myocardial infarction (MI) definitions were following the most recent universal definition of an MI.^[18] Advanced heart failure was defined, according to the New York Heart Association Classification, as being in a class greater than III. Target vessel revascularization (TVR) was defined as any repeat PCI in a target vessel or coronary artery bypass graft in a target vessel for lesions with a stenosis diameter of $\geq 70\%$.^[19] Cardiovascular mortality was defined as death related to sudden death, ventricular arrhythmia, advanced heart failure, and ischemic or hemorrhagic stroke. All-cause mortality was defined as death from any cause, such as sepsis, and malignancy. The definitions of the primary PCI timing were listed as below: 1. Reperfusion time was defined as the period from patient started the procedure to wire crossing the culprit lesion. 2. Pain to 1st emergency room (ER) time was defined as the period from patient started chest pain to 1st medical contact. 3. Pain to Reperfusion time was defined as the period from patient started chest pain to wire crossing the culprit lesion. The definition of recurrent MI was an acute MI occurs one month after the index MI.

2.3. Study endpoints

The primary endpoints of our study were any recurrent MIs, TVRs, strokes, or cardiovascular mortalities during the 1-year follow-up period. The secondary endpoints included all mortality incidents, regardless of cause, during the one-year follow-up period.

2.4. Statistical analysis

Data were expressed as the mean \pm standard deviation for continuous variables, or as counts and percentages for categorical variables. Continuous variables were compared using independent sample *t*-tests or Mann–Whitney *U* tests. Categorical variables were compared using a chi-square statistic. Kaplan–Meier curves were created to illustrate the 1-year cardiovascular mortality data in each of the groups. All the statistical analyses were performed using SPSS 22.0 (IBM, Corp., Armonk, NY). A *P*-value of less than .05 was statistically significant.

3. Results

3.1. Baseline characteristics

Table 1 demonstrates the baseline characteristics of the study patients. The general demographics between 2 groups were similar, including age, sex, and body mass index, without statistical significance. The comorbidities were also similar between the 2 groups, such as diabetes mellitus, current smoking status, hypertension, prior stroke, end-stage renal disease on hemodialysis, dyslipidemia, and heart failure, without statistical differences, except there was more prior MI experiences in the direct hospital admission group (5.6% vs 2.2%, *P*=.032). The severity of the MI, including systolic blood pressure on arrival and Killip classification III or IV, were also the same without

statistically significant differences (136.31 ± 38.79 vs 139.24 ± 30.13 , *P*=.295) and (22.6% vs 17.9%, *P*=.266).

The parameters of quality control used in PCI centers, such as reperfusion time, pain-to-1st ER time, and pain-to-reperfusion time were also compared. The reperfusion time (18.73 ± 8.84 min vs 18.60 ± 8.59 min, *P*=.848) or the pain-to-1st ER time (153.77 ± 50.31 vs 162.02 ± 76.76 min, *P*=.570) did not differ between groups. However, pain-to-reperfusion times in the transfer group (307.44 ± 99.64 min vs 220.92 ± 126.80 min, *P*=.006) was significantly longer. The average time of transfer from inter-facility non-PCI capable hospitals was 75.54 ± 40.77 minutes.

Only peak troponin I was significantly higher in the transfer group than the direct admission group (48.86 ± 36.09 ng/mL vs 41.67 ± 35.99 ng/mL, *P*=.029). The left ventricular ejection fraction was similar between groups ($54.99 \pm 13.83\%$ vs $56.58 \pm 12.24\%$, *P*=.157) and the infarcted territory was also the same between groups. The anti-platelet loading therapy such as ticagrelor loading was also the same between non-transfer versus transfer patients (85.5% vs 87.6%, *P*=.679). Post-MI medications, such as angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEis)/(ARBs), beta-blockers, and statins were all the same without statistical significance.

3.2. Angiographic characteristics

Table 2 demonstrates the angiographic characteristics of both groups. There was no significant difference in procedure time (42.06 ± 22.53 min vs 39.73 ± 20.52 min, *P*=.167) and contrast volume (132.45 ± 49.95 ml vs 130.93 ± 45.87 ml, *P*=.691). The use of drug-eluting stents (DES) was similar between groups (57.3% vs 53.8%, *P*=.429). The use of intra-aortic balloon pumps (IABP) (18.2% vs 18.8%, *P*=.919) and extracorporeal membranous oxygenation (ECMO) (2.9% vs 4.1%, *P*=.529) were the same between the groups.

3.3. Clinical outcomes

Table 3 illustrates the long-term clinical outcomes between groups. There were no statistically significant differences between the two groups regarding post-PCI acute kidney injury, TVR, or recurrent myocardial infarction. The 30-day mortality, including cardiovascular and all-cause mortality, showed no statistically significant differences between groups (5.5% vs 7.9%, *P*=.277; 5.8% vs 8.4%, *P*=.231). The prevalence of sudden death or ventricular arrhythmia, advanced heart failure, stroke, and sepsis did not differ between 2 groups.

However, the one-year mortality was almost significantly higher between groups, with higher cardiovascular mortality in the non-transfer group (10.7% vs 6.2%, *P*=.052) and a significantly higher all-cause mortality in the non-transfer group (12.2% vs 6.9%, *P*=.026). The prevalence of sudden death or ventricular arrhythmia, advanced heart failure, stroke, sepsis, and malignancy did not differ between two groups.

3.4. Kaplan–Meier curves showing 30-day and one-year cardiovascular mortality data of the two groups

Figure 2A shows a Kaplan–Meier curve illustrating the difference in 30-day cardiovascular mortality between groups. There was no significant difference in 30-day cardiovascular mortality between groups (*P*=.237). Figure 2B shows the Kaplan–Meier curve of the difference in 1-year cardiovascular mortality between

Table 1
Baseline characteristics of study patients.

	Non-transfer (N = 393)	Transfer (N = 274)	P value
General demographics			
Age (yr)	61 ± 12.5	61 ± 13.4	.535
Male sex (%)	317 (80.7)	219 (79.9)	.843
BMI (kg/m ²)	25.80 ± 8.11	25.75 ± 6.26	.932
Comorbidities			
Diabetes mellitus (%)	139 (35.5)	105 (38.3)	.463
Current smoker (%)	219 (55.9)	158 (57.7)	.691
Hypertension (%)	246 (62.8)	153 (55.8)	.078
Prior MI (%)	22 (5.6)	6 (2.2)	.032
Prior stroke (%)	26 (6.6)	15 (5.5)	.624
ESRD on maintenance hemodialysis (%)	17 (4.3)	9 (3.3)	.547
Dyslipidemia with prior statin use (%)	146 (37.2)	117 (42.7)	.171
Heart failure (%)	33 (8.4)	18 (6.6)	.459
The severity of MI			
SBP (mm Hg)	136.31 ± 38.79	139.24 ± 30.13	.295
Killip level (%)			.266
I, II	304 (77.4)	225 (82.1)	
III, IV	89 (22.6)	26 (17.9)	
Timing of primary PCI			
Reperfusion time (minutes)	18.60 ± 8.59	18.73 ± 8.84	.848
Pain-to-1 st ER time (minutes)	162.02 ± 76.76	153.77 ± 50.31	.570
Pain-to-reperfusion time (minutes)	220.92 ± 126.80	307.44 ± 99.64	.006
Laboratory examination			
White blood cell count (x10 ³)	11.1 ± 4.1	11.7 ± 4.1	.069
Blood fasting sugar (mg/dL)	185.66 ± 100.95	190.26 ± 97.32	.581
HbA1C (%)	6.78 ± 1.67	6.91 ± 1.86	.344
Creatinine (except ESRD) (mg/dL)	1.18 ± 0.53	1.15 ± 0.54	.405
Total cholesterol (mg/dL)	175.54 ± 49.25	177.46 ± 44.30	.609
LDL-cholesterol (mg/dL)	106.18 ± 40.18	117.44 ± 37.10	.686
HDL-cholesterol (mg/dL)	40.81 ± 35.98	39.60 ± 10.39	.177
Peak troponin-I (ng/mL)	41.67 ± 35.99	48.86 ± 36.09	.029
LVEF (%)	56.58 ± 12.24	54.99 ± 13.83	.157
Infarcted territory (%)			.237
Anterior wall	214 (54.5)	136 (49.6)	
Non-anterior wall	179 (45.5)	138 (50.4)	
Characteristics of coronary artery disease			
Multiple vessel disease	244 (62.2)	178 (65.0)	.513
Non-culprit lesion stenosis ≥70% (%)	242 (61.5)	159 (58.0)	.559
Left main coronary artery disease (%)	30 (7.7)	19 (6.9)	.765
Non-culprit PCI during index admission (%)	96 (24.4)	86 (31.4)	.116
Loading antiplatelet therapy (%)			.679
Ticagrelor	334 (85.0)	240 (87.6)	
Clopidogrel	59 (15.0)	34 (12.4)	
Post-MI Medications (%)			
ACEI/ARBs	328 (83.5)	238 (86.9)	.073
Beta-blockers	311 (79.1)	228 (83.2)	.205
Statins	310 (78.9)	236 (86.1)	.058

Data are expressed as mean ± standard deviation or as number (percentage).

ARB = angiotensin receptor blocker, BMI = body mass index, CKD = chronic kidney disease, DAPT = dual anti-platelet therapy, ESRD = end stage renal disease, HbA1C = glycohemoglobin, HDL = high density lipoprotein, LVEF = left ventricular ejection fraction, MI = myocardial infarction.

groups. There was a significant difference in the 1-year cardiovascular mortality between the transfer group and the non-transfer group ($P = .049$).

4. Discussion

Due to the improvement of communicative software, more information could be communicated immediately. However, we could not avoid patients' privacy leakage if we used commercial communicative software. Therefore, we introduced a warning system that included directly faxing ECG information to the

mobile phone by a non-PCI capable hospital. In real-world practice, the "warning system" had 3 advantages. First, during the rush time of the STEMI patients, the doctors from non-PCI capable hospital usually not cardiologist always emergency department doctors could send ECG without hesitation. Because the system will help him find the receipt cardiologist by the "warning system" directly. These will shorten lots of communicating time in telephone numbers, who's on duty, who's in charge etc. Second, the ECG often composite with patient's name, identification number, and sex on it. This is an important issue about privacy leakage. After using the "warning system," the

Table 2
Angiographic characteristics of study patients.

	Non-transfer (N = 393)	Transfer (N = 274)	P value
Procedure time (min)	39.73 ± 20.52	42.06 ± 22.53	.167
Contrast volume (ml)	130.93 ± 45.87	132.45 ± 49.95	.691
Primary PCI angiography			
Culprit vessel			
Pre-PCI TIMI flow			.740
≥2 (%)	87 (22.1)	61 (22.3)	
≤1 (%)	306 (77.9)	213 (77.7)	
Pre-PCI stenosis (%)	94.39 ± 9.55	93.85 ± 9.60	.515
Pre-PCI MLD (mm)	0.18 ± 0.09	0.18 ± 0.10	.815
Pre-PCI RLD (mm)	3.14 ± 0.56	3.08 ± 0.65	.336
Post-PCI TIMI flow			1.000
≥2 (%)	387 (98.5)	270 (98.5)	
≤1 (%)	6 (1.5)	4 (1.5)	
Post-PCI stenosis (%)	13.47 ± 10.97	12.63 ± 9.43	.356
Post-PCI MLD (mm)	2.79 ± 0.61	2.78 ± 0.53	.998
Post-PCI RLD (mm)	3.32 ± 0.78	3.26 ± 0.53	.298
Distal embolization (%)	18 (4.6)	9 (3.3)	.433
The use of Drug-eluting stents (%)	212 (53.9)	157 (57.3)	.429
Procedural device			
IABP (%)	74 (18.8)	50 (18.2)	.919
ECMO (%)	16 (4.1)	8 (2.9)	.529

Data are expressed as mean ± standard deviation or as number (percentage).

CABG = coronary artery bypass graft, ECMO = extracorporeal membrane oxygenation, IABP: intra-aortic balloon pumping, MLD = minimal luminal diameter, PCI: percutaneous coronary intervention, RLD = reference luminal diameter, TIMI = thrombolysis in myocardial infarction.

ECG server will only give the time on the ECG to avoid privacy leakage. Third, the precise timing will be documented via the “warning system” such as chest pain onset time, the first ECG time, the loading time of DAPT, and the time of door arrival in PCI capable hospital. These will provide the cardiologist more detail about the patient’s information. In our study, the average time of transfer from inter-facility non-PCI capable hospitals was 75.54 ± 40.77 minutes. Before introduction this system, the STEMI patients may receive fibrinolytic therapy or delay primary PCI if transfer time is near or more than two hours. Sometimes,

unsuitable initiation of primary PCI team may occur if incorrect diagnosis about STEMI in non-PCI capable hospitals. In our study, inter-facility transfer STEMI patients had similar outcomes when compared with non-transfer STEMI patients even though longer pain-to-reperfusion time and higher peak troponin-I level. These results may recommend we accommodate such a warning System in an area such as long and narrow terrain island country in inter-facility transfer for STEMI primary PCI is useful. Also, this system could avoid patients’ privacy leakage and let the patients in non-PCI capable hospitals gain opportunities

Table 3
Clinical outcomes of study patients.

	Non-transfer (N = 393)	Transfer (N = 274)	P value
Post PCI acute kidney injury (%)	54 (13.8)	39 (14.2)	.910
30-d mortality			
Cardiovascular mortality (%)	31 (7.9)	15 (5.5)	.277
Sudden death or arrhythmia (%)	14 (3.6)	8 (2.9)	.620
Advanced heart failure (%)	16 (4.1)	7 (2.6)	.299
Ischemic or hemorrhagic stroke (%)	1 (0.3)	0 (0)	.365
All-cause mortality (%)	33 (8.4)	16 (5.8)	.231
Sepsis (%)	2 (0.5)	1 (0.4)	.851
1-yr target-vessel revascularization (%)	26 (6.6)	14 (5.1)	.508
1-year recurrent myocardial infarction (%)	7 (1.8)	7 (2.6)	.586
1-year mortality			
Cardiovascular mortality (%)	42 (10.7)	17 (6.2)	.052
Sudden death or arrhythmia (%)	22 (5.6)	9 (3.3)	.166
Advanced heart failure (%)	17 (4.3)	7 (2.6)	.247
Ischemic or hemorrhagic stroke (%)	3 (0.8)	1 (0.4)	.523
All-cause mortality (%)	48 (12.2)	19 (6.9)	.026
Sepsis (%)	4 (1.0)	2 (0.7)	.683
Malignancy (%)	2 (0.5)	0 (0)	.242

Data are expressed as number (percentage).

PCI = percutaneous coronary intervention.

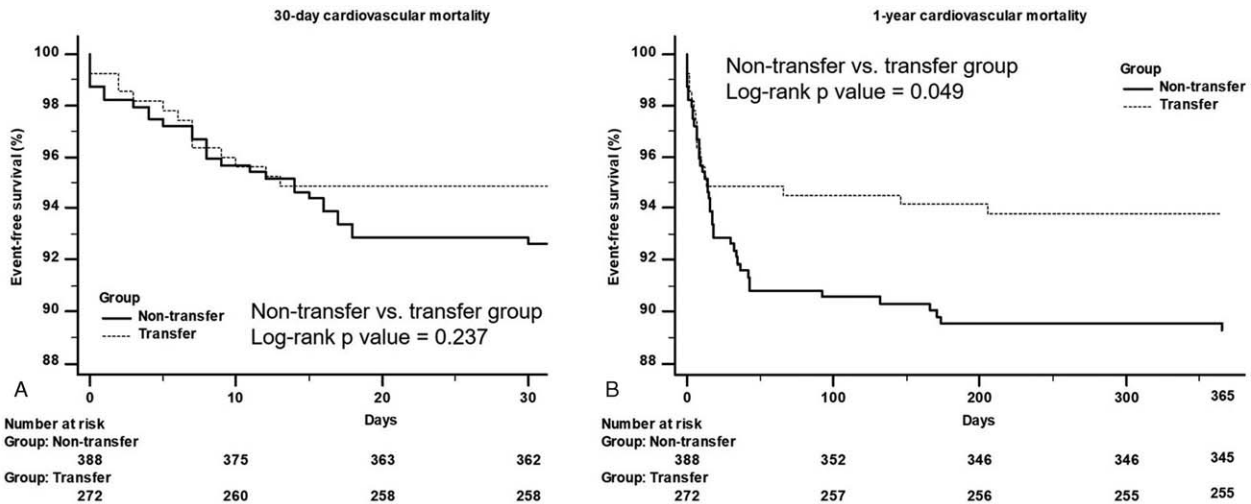


Figure 2. A: A Kaplan-Meier curve of 30-day cardiovascular mortality between groups: There was no significant difference between the non-transfer group and transfer group. ($P = .237$). B: A Kaplan-Meier curve of one-year cardiovascular mortality between groups: There was a significant difference between the non-transfer group and transfer group. ($P = .049$).

for correct information for primary intervention. In addition, over 85% of patients received active drug as ticagrelor for antiplatelet agents loading and this strategy may improve the short-term outcomes in transfer group even though longer pain-to-reperfusion time. Non-significant higher prevalence of statin use may contribute to a non-significant trend of better one-year cardiovascular outcomes.

The impact of total ischemic time and door-to-balloon time on long-term outcomes after STEMI treated with primary PCI

Flynn et al^[2] published the impact of DTB and mortality in 2010, showing unchanged in-hospital mortality even under a dramatic reduction in DTB time in STEMI events treated with primary PCI. One of the largest nationwide registries showed that direct admission to a primary PCI center was associated with a lower 1-year mortality incidence.^[16] The CREDO–Kyoto registry also showed that inter-facility transfer was associated with significantly worse long-term clinical outcomes for patients with STEMI undergoing primary PCI.^[17] However, the DTB times of patients in the CREDO–Kyoto registry were significantly higher in the inter-facility group (78 minutes) compared with our series (58.8 minutes), and the pain-to-ER time of CREDO–Kyoto registry was significantly higher in the inter-facility group (3.5 hours) compared with our series (2.5 hours), indicating that patients from the CREDO–Kyoto registry may have experienced longer transfer times from local hospitals than our series due to geographical barriers. The use of warning system decreased the preparing time and may contribute to comparable outcomes in our study. Also, an early connection gave the primary PCI team more time to prepare well for transfer STEMI patients.

4.1. The impact of inter-facility transfer using the warning system

From the era of reperfusion, experts all over the world were carrying the methods to improve the transferal time. Parikh et al^[20] had used the “single call” broadcast paging of STEMI to improve transferal delay in Texas, U.S.A. Schneider et al.^[21] used the “Drip & Ship” Network Restock in the treatment of transferal acute STEMI patients in Germany. Due to limit

shortening of transferal time, the reperfusion options such as pharmacological strategies were also applied in the U.S.A. for expected delays to primary PCI.^[22] The modifications and changes to current transfer of STEMI patients must be accommodated with regional specificity. In our country, the time range not only affects the clinical short-term and long-term outcomes dramatically due to the significance of the pain-to-reperfusion time, but it also affects treatment strategies. The warning system was implemented to improve the communication time between hospitals unable to perform PCI and PCI-capable hospitals. The warning system did not increase any costs associated with our daily STEMI primary PCI practice, and it has the potential to help to prepare the catheterization laboratory earlier after receiving primary PCI duties. Therefore, the strategy to decrease transfer time or prepare time is very important for improving outcomes about transfer STEMI patients.

4.2. Limitations

This was a retrospective observational study without randomization. Besides, we only provided and analyzed data from a small sample size and single-center experience. Different regions and different transfer situations may not accommodate the result of our study. Our research provides insight into possible improvements in healthcare policies for transferal STEMI patients in the future.

5. Conclusions

After using the warning system, the inter-facility transfer group had comparable outcomes even though a longer pain-to-reperfusion time and a higher peak troponin-I level when comparing with non-transfer group.

Author contributions

Conceptualization: Hsiu-Yu Fang.

Data curation: Wei-Chieh Lee.

Investigation: Wei-Chieh Lee.

Methodology: Wei-Chieh Lee.

Software: Wei-Chieh Lee.

Supervision: Wei-Chieh Lee.

Validation: Wei-Chieh Lee.

Visualization: Hsiu-Yu Fang.

Writing – original draft: Hsiu-Yu Fang.

Writing – review & editing: Wei-Chieh Lee.

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