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Cardiovascular outcomes of early versus delayed coronary intervention in low to intermediate-risk patients with STEMI in Thailand: a randomised trial

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ABSTRACT

Background The benefit of an early coronary intervention after streptokinase (SK) therapy in low to intermediate-risk patients with ST-elevation myocardial infarction (STEMI) still remains uncertain. The current study aimed to evaluate the cardiovascular outcomes of early versus delayed coronary intervention in low to intermediate-risk patients with STEMI after successful therapy with SK.

Methods We randomly assigned low to intermediate Global Registry of Acute Coronary Events risk score to patients with STEMI who had successful treatment with full-dose SK at Lampang Hospital and Maharaj Nakorn Chiang Mai Hospital into early and delayed coronary intervention groups. The primary endpoints were 30-day and 6-month composite cardiovascular outcomes (death, rehospitalised with acute coronary syndrome, rehospitalised with heart failure and stroke).

Results One hundred and sixty-two patients were included in our study. At the 30 days, composite cardiovascular outcomes were 4.9% in the early coronary intervention group and 2.5% in the delayed group ($p=0.682$). At the 6 months, the composite cardiovascular outcomes were 16.1% in the early group and 6.2% in the delayed group ($p=0.054$).

Conclusions The delayed coronary intervention (>24 hours) in low to intermediate STEMI after successful therapy with SK did not increase in short and long-term cardiovascular events compared with an early coronary intervention.

Trial registration number NCT02131103.

BACKGROUND

Primary percutaneous coronary intervention (PCI) is the best reperfusion therapy of ST-elevation myocardial infarction (STEMI). However, the PCI-capable centres and the number of interventionists are limited in many countries, including Thailand. Fibrinolytic therapy, streptokinase (SK), remains the main reperfusion strategy for most patients with STEMI in Northern Thailand. The data of Thailand Registry in Acute Coronary Syndrome (TRACS) showed 42.6% of patients with STEMI received SK and 1% received tenecteplase (TNK), and 50% of the patients underwent coronary angiography (CAG) on hospital admission.¹ Previous randomised controlled trials (RCT) and meta-analyses have shown that early routine post-thrombolysis angiography with subsequent PCI reduced the cardiovascular events when compared

Key messages

What is already known about this subject?

► The early coronary intervention after successful thrombolytic therapy has been shown to reduce cardiovascular events. However, the studies focused on high-risk population and received fibrin-specific agent. The effects on low to intermediate-risk patients who received non-fibrin specific (streptokinase, SK) are still unclear.

What does this study add?

► Delayed coronary intervention (>24 hours) in low to intermediate-risk patients with ST-elevation myocardial infarction (STEMI) did not increase in short and long-term cardiovascular outcomes compared with early coronary intervention.

How might this impact on clinical practice?

► Delayed coronary intervention did not increase composite cardiovascular outcomes in low to intermediate-risk patients with STEMI after successful therapy with SK. In addition, low to intermediate-risk patients with STEMI who underwent early coronary intervention may increase the risk of no reflow, and adequate antithrombotic is important.

with ischaemia-guided angioplasty.^{2,3} Therefore, the current guidelines recommend routine CAG or PCI after successful fibrinolytic treatment (within 24 hours).^{4–8} However, this strategy cannot be timely to perform in our country.

From the previous studies, patients with STEMI mostly received a fibrin-specific agent and the benefit of this strategy was demonstrated especially in high-risk patients with STEMI.^{2,3} The data from subgroup analysis of the Trial of Routine Angioplasty and Stenting After Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI)⁹ and the pooled analysis of previous RCTs¹⁰ showed the greater benefit of an early routine coronary intervention on cardiovascular outcomes in low to intermediate-risk patients than high-risk patients.

The benefit of an early coronary intervention on cardiovascular outcomes in patients with STEMI after SK treatment remains unclear. The objective of the study was to evaluate the short and long-term



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cardiovascular outcomes of early versus delayed coronary intervention in low to intermediate Global Registry of Acute Coronary Events (GRACE) risk patients with STEMI after successful SK therapy.

METHODS

Study design and population

This study was a prospective, randomised, open-label, parallel-group and blinded assessor study among patients who had successful treatment of SK at Lampang Hospital and Maharaj Nakorn Chiang Mai Hospital from June 2015 to January 2017. Patients with STEMI who had successful therapy with the full dose of SK, had a low to intermediate GRACE risk score (<155) and were aged less than 75 years were included. Patients were screened and enrolled after successful SK therapy.

The exclusion criteria were patients who received TNK or alteplase, patients who refused for further interventions, history of coronary artery bypass graft (CABG) surgery and high-risk patients (GRACE score \geq 155). Informed consent was obtained from all individual participants included in the study.

We randomly assigned the patients with STEMI into two groups (early vs delayed coronary intervention groups) by permuted block randomisation (block of 4). The patients in the early coronary intervention group underwent coronary intervention within 3–24 hours after SK, while patients in the delayed coronary intervention group underwent coronary intervention more than 24 hours. The patients in both groups received aspirin 300 mg and clopidogrel 300 mg for a loading dose and maintenance with daily aspirin 81 mg and clopidogrel 75 mg. PCI was performed during persistent occlusion or substantial stenosis of the infarct-related artery (IRA; either stenosis of 70% or more of the diameter of the artery or stenosis of 50%–70% with thrombus, ulceration or spontaneous dissection). Culprit vessel PCI or multivessel PCI was performed under operator's discretion. Stents were implanted during PCI whenever technically possible, and the use of bare-metal stents (BMS) or drug-eluting stents was at operators' discretion. The protocol allowed for the use of glycoprotein IIb/IIIa antagonists during procedure. All of the PCIs were performed using a femoral artery approach. The study flow diagram is shown in figure 1.

The data were collected, including baseline characteristics, medical history, presenting symptoms, baseline GRACE score, time from fibrinolysis to PCI, coronary intervention procedure, complications and clinical outcomes. To assess the relevant clinical cardiovascular outcomes of the patients, the blinded

assessors assessed during hospitalisation, at 30 days and at 6 months after discharge from hospital.

Definitions and outcomes

STEMI was defined as the presence of at least 0.1 mV ST-segment elevation or a new or presumably new left bundle branch block with elevation of cardiac enzyme levels above the reference range. Successful fibrinolytic therapy was defined as the decrease in the elevation of ST-segment \geq 50% at 90 min after treatment. Early coronary intervention was defined as coronary intervention, including CAG and PCI performed within 3–24 hours after successful SK treatment. Delayed coronary intervention means coronary intervention performed more than 24 hours after successful SK therapy. The patients in our study had a low to intermediate risk score (GRACE risk score <155). The primary outcomes were composite outcomes, which included all-cause death, rehospitalisation with acute coronary syndrome, rehospitalisation with heart failure (HF) and stroke at 30 days and 6 months. Culprit vessel PCI was defined as PCI to a culprit vessel lesion only. The multivessel PCI was defined as PCI in lesions in the culprit vessel as well as >1 non-culprit vessel lesion. Secondary outcomes were procedural complications. Abrupt vessel closure was defined as a total coronary occlusion or subtotal occlusion associated with clinical evidence of myocardial ischaemia. No reflow is defined as inadequate myocardial perfusion through a given segment of the coronary circulation without angiographic evidence of mechanical vessel obstruction. Coronary dissection was defined as iatrogenic separation of the coronary artery wall, which creates a false lumen that may or may not be in continuity with the true lumen. New thrombus formation was defined as the presence of a filling defect with either a total occlusion with convex, irregular or hazy distal margins and postinjection contrast retention or staining, or a partial occlusion circumferentially outlined by contrast media during PCI. Coronary perforation was defined as evidence of extravasation of contrast medium or blood from the coronary artery. Contrast-induced nephropathy (CIN) is a 25% relative increase, or a 0.5 mg/dL (44 μ mol/L) absolute increase, in serum creatinine (SCr) within 72 hours of contrast exposure, in the absence of an alternative explanation.

Statistical analysis

Baseline characteristics, procedural details and angiographic data are presented with continuous measures and are expressed as mean \pm SD or median and IQR. The categorical data are expressed as numbers (percentages). Differences in continuous variables were analysed with the Student's t-test or Wilcoxon rank-sum tests. The categorical variables were analysed with χ^2 test and Fisher's exact test. A p value <0.05 was considered statistically significant. Composite outcomes and other clinical outcomes were analysed using time-to-event analysis and estimated according to Kaplan-Meier method. Intention to treat, as treated (PCI) and number needed to treat (NNT) were analysed. We conducted statistical analyses using Stata V.13 (StataCorp, College Station, TX).

The sample size was calculated by base on the data of the previous study of Southwest German Interventional Study in Acute Myocardial Infarction (SIAM-III).¹¹ Death/re-MI at 6 months was 50.6% in the standard treatment strategy and 25.6% in the early PCI group. We estimated 5% loss of follow-up. To achieve a power of 80%, with a type 1 error probability of 5% (one sided), 60 patients were needed in each group. A total of 120 patients were required in this study.

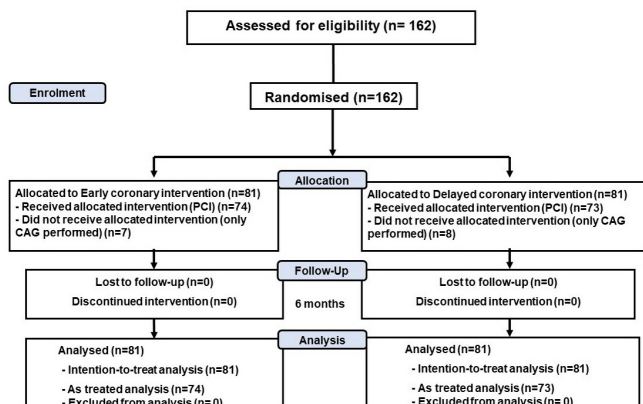


Figure 1 Study flow diagram. CAG, coronary angiography; PCI, percutaneous coronary intervention.

Table 1 Baseline characteristics

Baseline characteristics	Early coronary intervention group (n=81)	Delayed coronary intervention group (n=81)	P value
Age (years), mean±SD	61.8±12.1		0.100
Gender			0.873
Female	32 (39.5)	34 (42.0)	
Male	49 (60.5)	47 (58.0)	
GRACE risk score, mean±SD	107.5±26.1	104.7±21.8	0.463
Medical conditions			
Diabetes	21 (25.9)	24 (29.6)	0.726
Hypertension	45 (55.5)	41 (50.6)	0.637
Dyslipidaemia	29 (35.8)	31 (38.3)	0.875
Smoking	46 (56.8)	40 (49.4)	0.431
Prior MI	2 (2.5)	2 (2.5)	0.690
Congestive heart failure	0 (0)	1 (1.2)	0.500
Stroke	3 (3.7)	4 (5.0)	0.500
Chronic kidney disease	7 (8.6)	3 (3.7)	0.328
Median time from symptom onset to fibrinolysis (hours) (IQR: 25th, 75th percentiles)	2.83 (1.7, 4.3)	2.2 (1.5, 4.0)	0.835
Median time from fibrinolysis to PCI (IQR: 25th, 75th percentiles)	12.0 hours (5.5, 18.9)	2.5 days (1.7, 4)	<0.001
Clinical presentation (%)			0.874
Non-anterior wall	46 (56.8)	48 (59.3)	
Anterior wall	35 (43.2)	33 (40.7)	
LVEF (%)	52.3±12.9	55.7±11.7	0.082
Serum creatinine (mg/L)	1.1±0.5	1.0±0.5	0.310

GRACE, Global Registry of Acute Coronary Events; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention.

RESULTS

Baseline characteristics

One hundred and sixty-two low to intermediate-risk patients with STEMI with successful treatment with SK underwent randomisation. Seven patients in the early coronary intervention group and eight patients in the delayed coronary intervention group were performed only on diagnostic CAG (non-significant stenosis lesions and the lesions were suitable for CABG), as shown in [figure 1](#). All of the recruited patients in both groups completed the follow-up at 6 months.

Baseline characteristics were similar in both groups ([table 1](#)). The mean GRACE risk score was 107.5±26.1 in the early coronary intervention group versus 104.7±21.8 in the delayed group (p=0.463). The baseline left ventricular ejection fraction and SCr were similar in both groups ([table 1](#)). The median time from fibrinolysis to PCI was 12 hours in the early coronary intervention group versus 2.5 days in the delayed coronary intervention group (p<0.001).

Angiographic findings and procedural details

Sixty-four per cent of the patients in the early coronary intervention group (n=52) and 59% of the patients in the delayed group (n=48) had multivessel coronary artery disease (p=0.695). There was a similar target vessel revascularisation between the two groups ([table 2](#)). There were higher rates of pre-PCI TIMI (Thrombolysis in Myocardial Infarction) grade 0–1 flow in the early coronary intervention group than the patients in the delayed coronary intervention group (11.1% vs 4.9%, p=0.247). The rate of thrombus aspiration was higher in patients in the early

Table 2 Angiographic findings and procedural details

Angiographic findings and procedural details	Early coronary intervention group (n=81)	Delayed coronary intervention group (n=81)	P value
Single-vessel CAD	29 (35.8)	33 (40.7)	0.628
Multivessel CAD	52 (64.2)	48 (59.3)	0.628
Target vessel revascularisation (%)			
LAD	39 (48.2)	38 (46.9)	0.500
LCX	5 (6.2)	10 (12.4)	0.279
RCA	36 (44.4)	33 (40.7)	0.751
Left main	1 (1.2)	0 (0)	0.500
Culprit vessel PCI (%)	66 (81.5)	65 (80.2)	0.500
Multivessel PCI (%)	8 (9.9)	8 (9.9)	0.603
Medical treatment or CABG (%)	7 (8.6)	8 (9.9)	0.500
Procedural details			
POBA	5 (6.8)	6 (8.2)	0.765
Thrombus aspiration	9 (12.2)	3 (4.1)	0.129
Bare-metal stent	10 (13.5)	2 (2.7)	0.031
Drug-eluting stent	59 (79.7)	65 (89.0)	0.173
Lesion length (mm), mean±SD	27.0±12.2	24.8±9.6	0.253
Vessel diameter (mm), mean±SD	3.0±0.5	2.9±0.4	0.480
Number of stents used per patient, mean±SD	1.2±0.5	1.2±0.5	0.898
Pre-PCI TIMI flow 0–1 (%)	9 (11.1)	4 (4.9)	0.247
Pre-PCI TIMI flow 2–3 (%)	72 (88.8)	77 (95.0)	0.247
Post-PCI TIMI flow 0–1 (%)	3 (3.7)	1 (1.2)	0.620
Post-PCI TIMI flow 2–3 (%)	71 (95.9)	72 (98.6)	0.500
Low molecular weight heparin (%)	66 (81.5)	73 (90.1)	0.176
Glycoprotein IIb/IIIa inhibitor used (%)	15 (18.5)	10 (12.5)	0.385

CABG, coronary artery bypass graft; CAD, coronary artery disease; LAD, left anterior descending artery; LCX, left circumflex artery; PCI, percutaneous coronary intervention; POBA, plain old balloon angioplasty; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction.

group than patients in the delayed coronary intervention group (12.2% vs 4.1%, p=0.129). A BMS was placed in patients in the early group higher than patients in the delayed group (13.5% vs 2.7%, p=0.031). Post-PCI TIMI flow achieved TIMI 2 and 3 flow in 96% of the patients (n=71) in the early coronary intervention group and 98.6% patients (n=72) in the delayed coronary intervention group (p=0.500). The rate of glycoprotein IIb/IIIa used was higher in the early coronary intervention group patients than in the delayed coronary intervention group patients (18.5% vs 12.5%, p=0.385).

Procedural complications

No reflow phenomenon was higher in the early coronary intervention group patients than the delayed coronary intervention group (12.2% vs 0%, p=0.003) ([table 3](#)). The rates of abrupt vessel closure, new thrombus formation, coronary dissection, side branch occlusion and emergency CABG were similar in both groups ([table 3](#)). Gastrointestinal (GI) bleeding was higher in the early coronary intervention group than the delayed coronary intervention group (6.2% vs 1.2%, p=0.210). Acute kidney

Table 3 In-hospital outcomes and procedural complications

In-hospital outcomes	Early coronary intervention group (n=81)	Delayed coronary intervention group (n=81)	P value
In-hospital mortality (%)	2 (2.5)	1 (1.2)	0.500
In-hospital stroke (%)	1 (1.2)	0 (0)	0.500
Procedural complications (%)			
Abrupt vessel closure	0 (0)	0 (0)	NS
New thrombus formation	1 (1.2)	2 (2.5)	0.500
No reflow	9 (11.1)	0 (0)	0.003
Coronary dissection	0 (0)	0 (0)	NS
Side branch occlusion	1 (1.2)	2 (2.5)	0.500
Emergency CABG	0 (0)	0 (0)	NS
Unsuccessful PCI	1 (1.2)	0 (0)	0.500
Postprocedural complications (%)			
Access site haematoma	2 (2.5)	2 (2.5)	0.690
GI bleeding	5 (6.2)	1 (1.2)	0.210
Needed blood transfusion	2 (2.5)	2 (2.5)	0.690
Acute kidney injury from contrast media	4 (4.9)	1 (1.2)	0.367

CABG, coronary artery bypass graft; GI, gastrointestinal; NS, non-significant; PCI, percutaneous coronary intervention.

injury from contrast media was higher in the early coronary intervention group than the delayed intervention group (4.9% vs 1.2%, $p=0.367$).

Clinical cardiovascular outcomes

In-hospital mortality and stroke were similar in both groups (table 3). None of the patients in either group had a stroke during hospitalisation. At the 30 days, the rates of composite cardiovascular outcomes were similar in both groups (4.9% vs 2.5%, $p=0.682$). At the 6 months, the rates of composite cardiovascular outcomes were higher in the early coronary intervention group than the delayed coronary intervention group (16.1% vs 6.2%, $p=0.054$). None of the patients had a stroke at 30 days and 6 months of follow-up (table 4). The Kaplan-Meier curve of the 6-month composite cardiovascular outcome is shown in figure 2. The univariate and multivariate analyses of 6-month composite cardiovascular outcome were shown in table 5. Intention-to-treat analysis was 16.0% in early coronary intervention group and 6.2% in delayed coronary intervention group, risk difference 9.8% (95% CI 0.31% to 19.4%, $p=0.0043$), as shown in table 6. NNT was 10 (95% CI 6 to 315).

DISCUSSION

Early coronary intervention (<24 hours) after successful reperfusion with fibrinolytic or thrombolytic therapy in patients with STEMI was recommended by several guidelines.⁴⁻⁸ Several RCTs and meta-analyses have shown that early post-thrombolysis PCI reduced the cardiovascular events when compared with ischaemia-guided strategy.^{2,3} However, time to perform coronary intervention in 24 hours after fibrinolytic treatment is not widely available in countries with limited PCI-capable hospitals and interventionists, including Thailand. The data from TRACS showed only 50% of patients with STEMI underwent CAG on index admission.¹ Fibrinolytic therapy (SK) is still the first reperfusion treatment in low-risk patients with STEMI in our country, and especially in Northern Thailand.¹

Table 4 Short and long-term clinical outcomes

Clinical outcomes	Early coronary intervention group (n=81)	Delayed coronary intervention group (n=81)	P value
At 30 days			
Composite cardiovascular outcome (%)	4 (4.9)	2 (2.5)	0.682
Rehospitalised with ACS	0 (0)	0 (0)	NS
Rehospitalised with HF	2 (2.5)	1 (1.2)	0.561
Stroke	0 (0)	0 (0)	NS
Death			
Cardiovascular death	2 (2.5)	1 (1.2)	0.567
Non-cardiovascular death	0 (0)	0 (0)	NS
Loss to follow-up (%)	0 (0)	0 (0)	NS
At 6 months			
Composite cardiovascular outcome (%)	13 (16.1)	5 (6.2)	0.054
Rehospitalised with ACS	2 (2.5)	0 (0)	0.156
Rehospitalised with HF	7 (8.6)	2 (2.5)	0.865
Stroke	0 (0)	0 (0)	NS
Death			
Cardiovascular death	4 (4.9)	2 (2.5)	0.408
Non-cardiovascular death	0 (0)	1 (1.2)	0.320
Loss to follow-up (%)	0 (0)	0 (0)	NS
6-month LVEF (%)	58.6±8.3	59.4±8.4	0.503
Staged PCI in multivessel CAD (%)	7 (9.5)	3 (4.1)	0.327

ACS, acute coronary syndrome; CAD, coronary artery disease; HF, heart failure; LVEF, left ventricular ejection fraction; NS, non-significant; PCI, percutaneous coronary intervention.

In Northern Thailand, the geography of the area means that the patients must be transferred over the long distances. There are also few PCI-capable centres and interventional cardiologists; primary PCI and early coronary intervention were very difficult in this situation. Rescue PCI or primary PCI was performed in patients who were not successful with fibrinolytic therapy or cardiogenic shock at presentation. Fibrinolytic therapy with subsequent coronary intervention strategy is a well-appropriate strategy in management of patients with STEMI in this area.

The data from previous studies such as the SIAM-III,¹¹ the TRANSFER-AMI,¹² the Norwegian Study on District Treatment of ST-Elevation Myocardial Infarction¹³ and the Combined Abciximab Reteplase Stent Study in Acute Myocardial Infarction¹⁴ demonstrated an early PCI after thrombolytic therapy in patients with STEMI showed significant reduction of primary

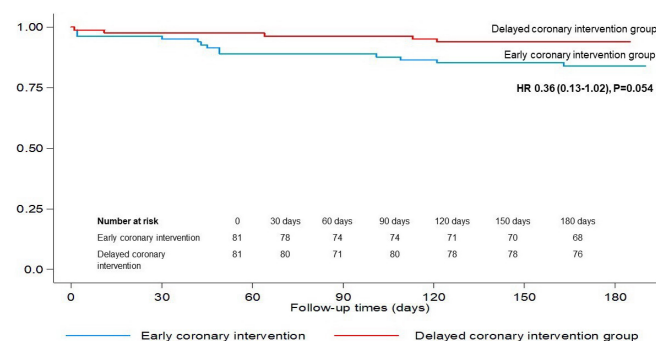
**Figure 2** Kaplan-Meier curve of 6-month composite cardiovascular outcomes.

Table 5 Results of multivariate analysis of 6-month composite outcome in the intention-to-treat populations

Variables	Univariate model		Multivariate model	
	HR (95% CI)	P value	HR (95% CI)	P value
Coronary intervention group (early vs delayed)	0.36 (0.13 to 1.02)	0.055	2.00 (0.49 to 8.16)	0.332
PCI (not performed vs performed)	0.23 (0.08 to 0.65)	0.005	N/A	–
No reflow (absent vs present)	7.79 (2.39 to 25.37)	0.001	5.55 (1.36 to 22.71)	0.017
Thrombus aspiration (not performed vs performed)	5.95 (1.83 to 19.34)	0.003	7.83 (1.67 to 36.59)	0.009
Glycoprotein IIb/IIIa (used vs not used)	1.67 (0.54 to 5.04)	0.371	1.04 (0.24 to 4.47)	0.956
Bare-metal stent (used vs not used)	5.66 (1.74 to 18.42)	0.004	7.43 (1.89 to 29.08)	0.004

PCI, percutaneous coronary intervention; N/A, not applicable.

outcomes, fewer ischaemic complications and a higher long-term survival rate than the delayed PCI.

Previous RCTs were focused on high-risk patients and all of the patients in studies received a fibrin-specific agent for reperfusion therapy.^{2,3} The benefit of an early coronary intervention in low to intermediate-risk patients after non-fibrin specific was uncertain.

A subgroup analysis of TRANSFER-AMI⁹ demonstrated the excellent outcome of an early PCI strategy after thrombolytic therapy was seen only in patients with low to intermediate GRACE risk score (<155), while the early PCI strategy was associated with a worse outcome in high-risk patients. Similarly, the pooled patient-level analysis of seven RCTs of early invasive versus standard treatment in fibrinolytic-treated patients with STEMI¹¹ showed clearly greater beneficial cardiovascular outcomes of an early PCI strategy in low to intermediate-risk patients which was not evident in the high-risk group of patients. From this subgroup analysis, the risk score may also be helpful to guide the best strategy to achieve and maintain myocardial reperfusion after administration of fibrinolytic therapy. Chotchuang *et al*¹⁵ also reported the delayed coronary intervention in intermediate to high GRACE score in non-PCI-capable hospitals was associated with worse cardiovascular outcomes than the low-risk patients. However, there was no randomised trial to evaluate the benefits of the early and delayed coronary intervention in low to intermediate-risk patients receiving SK for reperfusion therapy for STEMI similar to our study.

In our study, the 30-day and 6-month composite cardiovascular outcomes were similar in both groups. Rehospitalisation with HF was the main factor contributing to the 6-month composite cardiovascular outcome in the early coronary intervention group. The explanation of the higher rate of rehospitalisation with HF in the early coronary intervention group was the higher rate of no reflow during the procedure and the higher

rate of post-PCI TIMI 0–1 flow in the early coronary intervention group (3.7% vs 1.2%, $p=0.620$). Similar to our study, no reflow phenomenon is an independent predictor of an adverse clinical outcome after PCI in STEMI and a strong predictor of the worst short and long-term cardiovascular outcomes (as shown in table 5), regardless of infarct size, and is associated with HF and increased mortality in several studies.^{16–20} Morishima *et al*²¹ showed that the patients with no reflow after PCI in acute myocardial infarction had congestive HF ($p<0.0001$) more often than did those with reflow and may be at risk of progressive HF and cardiac death. Kim *et al*²² reported that transient no reflow increased all-cause mortality only compared with the normal reflow group (HR 1.58, 95% CI 1.11 to 2.24, $p=0.010$) and when comparing transient and persistent no reflow, persistent no reflow was associated with increased all-cause mortality (46.7% vs 24.4%, log rank $p=0.033$).

The cause of no reflow in our study may be from the low antiplatelet activity (we used clopidogrel in our study because the patients received SK) or inadequate of anticoagulant in the patients in early coronary intervention group which may be explained by the higher rate of glycoprotein IIb/IIIa used (tables 2 and 5), the type of our fibrinolytic used (a non-fibrin specific), the high volume of plaque burden in the early group patients (may be explained by the higher rate of thrombus aspiration and the lesion length) and the cause of no reflow in the patients (table 5). Our study was limited in collection of the data of platelet reactivity test, intravascular ultrasound for evaluating the burden of plaque volume and cardiac MRI (CMR) for evaluating the degree and severity of ischaemia or IRA in both groups. BMS was used more in the early coronary intervention group than the delayed intervention group (13.5% vs 2.7%, $p=0.0031$) to prevent restenosis because of the high rate of no reflow in our patients and may be one of independent risk factors for 6-month composite cardiovascular outcome, as shown in table 5.

Table 6 Intention-to-treat analysis of 6-month composite cardiovascular outcome after randomisation of the early and delayed coronary intervention

	Allocated (actual) intervention				Risk differences (95% CI)
	Early coronary intervention (PCI) (n=74)	Early coronary intervention (non-PCI) (n=7)	Delayed coronary intervention (PCI) (n=73)	Delayed coronary intervention (non-PCI) (n=8)	
Survivors, n	66	2	68	8	–
6-month composite cardiovascular outcome (n)	8	5	5	0	–
6-month composite cardiovascular outcome (%)	10.8	71.4	6.8	0	–
Intention-to-treat analysis	16.0% (13/81)		6.2% (5/81)		9.8% (0.31% to 19.4%), $p=0.043$ NNT=10 (95% CI 6 to 315)
As-treated (PCI) analysis	10.8% (8/74)		6.8% (5/73)		4.0% (5.1% to –13.1%), $p=0.396$

NNT, number needed to treat; PCI, percutaneous coronary intervention.

There were several factors causing higher upper GI bleeding in the patients of early coronary intervention group such as the fibrinolytic effect and the higher rate use of glycoprotein IIb/IIIa. The incidence of acute kidney injury from contrast media was higher in the early coronary intervention group than the delayed group which may be from inadequate hydration before the procedure in these patients. There was no difference in access site haematoma or required blood transfusions between the two groups.

In this study, we showed that early coronary intervention group had a higher rate of cardiovascular outcomes than the delayed coronary intervention which was the opposite compared with the previous studies. First, the patients in our study received SK (non-fibrin specific) for reperfusion therapy which was different from previous studies.^{2,3} Second, congestive HF was included as a composite cardiovascular outcome in our study, which is different from the previous studies. Because HF is one of leading cardiovascular events after admission with STEMI and after hospital discharge in real-life practice, it was necessary to include HF in composite cardiovascular outcome in our study. Our study also showed the higher rate of no reflow phenomenon in early coronary intervention group, which may contribute to the increased risk of HF in these patients.

The study did not demonstrate the statistical difference between the early intervention and delayed coronary intervention strategy in low to intermediate-risk patients because of the small number of cardiovascular events in our patients (figure 2). The delayed coronary intervention after SK treatment in low to intermediate patients with STEMI was not increased in the composite cardiovascular outcomes and safe for the patients which was confirmed by intention-to-treat analysis and as-treated analysis, as shown in table 6.

Limitations

There were some limitations to our study. The small number of patients was included; exclusive evaluation of no reflow phenomenon needs in our study; the lack of data from the platelet reactivity study; intravascular ultrasound imaging to evaluate the plaque volume; and the data of CMR to evaluate the degree and severity of cardiac ischaemia in the patients. However, the measurement is not routine in clinical practice.

CONCLUSIONS

The delayed coronary intervention in low to intermediate GRACE risk patients with STEMI after SK therapy did not increase in short and long-term cardiovascular outcomes compared with an early coronary intervention. Early coronary intervention in these patients may increase the risk of no reflow which contributed HF, and adequate antithrombotic before procedure is preferred.

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