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Rescue PCI in the management of STEMI: Contemporary results from the Melbourne Interventional Group registry ☆

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ABSTRACT

Background: Fibrinolysis is an important reperfusion strategy in the management of ST-elevation myocardial infarction (STEMI) when timely access to primary percutaneous coronary intervention (PPCI) is unavailable. Rescue PCI is generally thought to have worse outcomes than PPCI in STEMI. We aimed to determine short- and long-term outcomes of patients with rescue PCI versus PPCI for treatment of STEMI.

Methods and results: Patients admitted with STEMI (excluding out-of-hospital cardiac arrest) within the Melbourne Interventional Group (MIG) registry between 2005 and 2018 treated with either rescue PCI or PPCI were included in this retrospective cohort analysis. Comparison of 30-day major adverse cardiac events (MACE) and long-term mortality between the two groups was performed. There were 558 patients (7.1%) with rescue PCI and 7271 with PPCI. 30-day all-cause mortality (rescue PCI 6% vs. PPCI 5%, p = 0.47) and MACE (rescue PCI 10.3% vs. PPCI 8.9%, p = 0.26) rates were similar between the two groups. Rates of in-hospital major bleeding (rescue PCI 6% vs. PPCI 3.4%, p = 0.002) and 30-day stroke (rescue PCI 2.2% vs. PPCI 0.8%, p < 0.001) were higher following rescue PCI. The odds ratio for haemorrhagic stroke in the rescue PCI group was 10.3. Long-term mortality was not significantly different between the groups (rescue PCI 20% vs. PPCI 19%, p = 0.33).

Conclusions: With contemporary interventional techniques and medical therapy, rescue PCI remains a valuable strategy for treating patients with failed fibrinolysis where PPCI is unavailable and it has been suggested in extenuating circumstances where alternative revascularisation strategies are considered.

1. Introduction

Fibrinolysis remains an important revascularisation strategy for the management of ST-elevation myocardial infarction (STEMI) when primary percutaneous coronary intervention (PCI) cannot be performed in a timely manner. Current American Heart Association/American College of Cardiology (AHA/ACC) and European Society of Cardiology (ESC) guidelines recommend fibrinolysis for patients presenting with STEMI where time from first medical contact to device across lesion (including transfer to a PCI capable centre) is likely to exceed 120 min[1,2]. Where fibrinolysis is successful, a pharmaco-invasive strategy is recommended where coronary angiography and PCI if indicated is performed between 2 and 24 h after fibrinolysis[3]. In contrast, in patients with failed

☆ The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussion interpretation.

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fibrinolysis, emergent PCI termed 'rescue PCI' is recommended as it is superior to medical therapy for failed fibrinolysis[4–6].

In normal circumstances, primary PCI (PPCI) is the preferred revascularization strategy compared to fibrinolysis when patients present to a PCI capable hospital due to superior ischaemic and bleeding outcomes[7–9]. However, during the current COVID-19 pandemic crisis, fibrinolysis has been suggested as a possible revascularisation strategy in selected STEMI patients with suspected or confirmed infection even in PCI capable centres, to reduce transmission to healthcare workers[10–12]. Furthermore, despite conventional wisdom, whether the risks associated with rescue PCI are truly greater than primary PCI for STEMI in the contemporary era is not known. As such we sought to compare in-hospital, interventional, short- and long-term outcomes post rescue PCI and PPCI for STEMI.

2. Methods

2.1. Study population

Patients 18 years and over undergoing PCI for STEMI since 2005 identified in the Melbourne Interventional Group (MIG) registry were included in the study. A diagnosis of STEMI was based on documentation by the treating cardiologist with compatible symptoms and ST elevation on 12 lead electrocardiogram meeting ACC/AHA defined STEMI criteria[8,13]. Patients presenting with out-of-hospital cardiac arrest were excluded from the analysis.

2.2. Registry design

We used data from the MIG registry that collects procedural and follow up data on patients undergoing PCI across six public (government funded) hospitals in Victoria, Australia. The cohort included consecutive patients undergoing PCI for STEMI from January 2005 to January 2018 enrolled in the MIG registry. Briefly, baseline characteristics, in-hospital laboratory findings, documentation of coronary lesion type according to ACC/AHA (American College of Cardiology/American Heart Association) classifications, in-hospital, 30-day and 12-month outcomes are recorded prospectively using case report forms with standardized definitions for all fields[13]. The Centre of Cardiovascular Research and Education in Therapeutics, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia is responsible for maintaining and coordinating data collection for the registry. Internal validity of the data is regularly evaluated by randomly selecting 5% of the records at each institution with review of several verifiable fields[14]. In the most recent audits, a number of fields were assessed with an overall accuracy of 98%.

Long-term mortality data is available through linkage between the registry and the National Death Index (NDI), which is an Australia-wide database of all patient deaths that have occurred since 1980. This is developed and maintained by the Australian Institute of Health and Welfare.

The ethics committee in each hospital have approved the MIG registry. An opt-out consent process is used whereby patients are provided with an information sheet describing the registry, purposes and routine follow-up.

2.3. Definitions

Major adverse cardiac events (MACE) are the composite endpoint of death, non-fatal myocardial infarction, and target vessel revascularization. Major adverse cardiac and cerebrovascular events (MACCE) are the composite endpoint of death, non-fatal myocardial infarction, target vessel revascularization, and stroke. Rescue PCI was defined as emergent PCI after failed full-dose fibrinolysis where there was one or more of the following; ongoing ischaemic chest pain, haemodynamic instability, ventricular tachyarrhythmias and <50% ST-segment resolution at 90 min. Successful PCI was defined as a final result whereby less than 50% residual stenosis remained after balloon angioplasty or less than 20% residual stenosis after coronary stent implantation at lesion site.

2.4. Study endpoints

The primary endpoint evaluated was 30-day MACE comparing patients who underwent rescue PCI versus PPCI for STEMI. Secondary endpoints include 30-day MACCE, 30-day all-cause mortality and long-term mortality.

In-hospital complications were recorded at the time of death or discharge. 30-day follow up data was obtained either through review of the medical record or after making telephone contact (with confirmation of events from the medical record). Recurrent MI was defined as an increase in creatine kinase more than 3 times the upper limit of normal and/or new significant ST-segment change, development of new Q waves in more than 2 contiguous electrocardiographic leads or new left bundle branch block pattern.

2.5. Statistical analysis

Data collected were reported as either mean ± standard deviation (SD) or as a numbers and percentages for categorical variables. Categorical variables were assessed using Fisher's exact or chi-squared tests as appropriate. Continuous variables were compared using Student's *t*-test. Kaplan-Meier curves were generated for long term mortality comparing patients receiving rescue versus primary PCI. Univariate and multivariate binary logistic regression was performed to evaluate the association between rescue PCI and the primary endpoint of 30-day MACE with adjustment for potential confounding factors. All statistical analyses were performed using Stata 13.1 (StrataCorp LP, College Station, TX, USA). P values < 0.05 were considered statistically significant.

3. Results

Between 2005 and 2018, there were 558 patients (7.1%) receiving rescue PCI after fibrinolysis and 7271 patients receiving PPCI for STEMI within the MIG database during this period. Clinical outcomes at 30 days including the primary endpoint of 30-day MACE was available for 99% of the sample population (7780 patients).

Baseline characteristics in patients undergoing rescue PCI compared to PPCI are presented in Table 1.

Door-to-balloon time was significantly longer in the rescue PCI than PPCI group (145 min vs. 81 min, p < 0.001; see Table 2). 59% of patients in the rescue PCI group had a door to balloon time less than 90 min compared to 71% of patients in the PPCI group (p < 0.001). Symptom to balloon time was also significantly longer in the rescue PCI than PPCI arm (510 min vs. 237 min, p < 0.001). Clinical state on presentation and medications used during PCI are also presented in Table 2.

In terms of angiographic and procedural characteristics, there was greater radial access used for rescue PCI (37% vs. 27%, p < 0.001, see supplementary table 1). There were lower rates of TIMI 0 flow in the rescue compared to PPCI group pre-PCI (36% vs 62%, p < 0.001), higher rates of acute closure (2% vs. 0.7%, p = 0.001) and persistent no reflow (3.7% vs. 1.2%, p < 0.001) in the rescue PCI arm.

Rescue PCI was associated with an in-hospital mortality that was not significantly different than that associated with primary PCI (rescue PCI 5% vs. primary PCI 4.4%, p = 0.48; see Table 3). There

Table 1
Baseline characteristics.

Variable (N = 7829)	Rescue PCI in STEMI (n = 558)	Primary PCI in STEMI (n = 7271)	P value
Age (years),mean ± SD	61 (12)	64 (13)	<0.001
Male, n (%)	436 (78)	5716 (79)	0.79
BMI, mean ± SD	29 (5)	28 (5)	<0.001
Smoking status N = 7609			<0.001
- Current Smoker	230 (43)	2552 (36)	
- Ex-smoker	172 (32)	2032 (29)	
- Never smoker	136 (25)	2487 (35)	
Hypertension, n (%) N = 7824	298 (54)	3829 (53)	0.7
Hypercholesterolemia, n (%) N = 7818	286 (51)	3573 (49)	0.35
Diabetes Mellitus, n (%) N = 7828	87 (16)	1228 (17)	0.43
Family History of CAD, n (%) N = 7293	196 (38)	2287 (34)	0.054
Previous MI, n (%) N = 7826	75 (13)	915 (13)	0.56
Previous PCI, n (%)	56 (10)	773 (11)	0.66
Previous CABG, n (%)	12 (2.1)	169 (2.3)	0.79
Prior Heart Failure, n (%) N = 7828	34 (6.1)	320 (4.4)	0.064
PVD, n (%) N = 7824	12 (2.1)	206 (2.8)	0.35
Cerebrovascular disease, n (%) N = 7824	17 (3)	322 (4.4)	0.121
Creatinine (umol/L), mean ± SD N = 6996	90 (29)	94 (53)	0.1
Atrial fibrillation, n (%) N = 6628	31 (8)	357 (5.7)	0.15

BMI = body mass index; PVD = peripheral vascular disease, CAD = coronary artery disease, PCI = percutaneous coronary intervention, CABG = coronary artery bypass graft surgery, Cr = creatinine; N is number of patients with data available for variable if less than total sample population of 7829 patients.

Table 2
Clinical state on presentation and medications during PCI.

Variable	Rescue PCI (n = 558)	Primary PCI (n = 7271)	P value
Door to balloon inflation time in minutes (SD) N = 7508	145 (207)	81 (75)	<0.001
Symptom to balloon inflation time in minutes (SD) N = 7573	510 (265)	237 (166)	<0.001
Door to balloon time < 90 mins n (%) N = 7508	265 (59)	5038 (71)	<0.001
Cardiogenic Shock, n (%)	67 (12)	503 (6.9)	<0.001
LVEF:			<0.001
- >45%, n (%)	274 (54)	4587 (67)	
- 30–45%, n (%)	219 (43)	2191 (32)	
- <30%, n (%)N = 7395	13 (2.6)	111 (1.6)	
Medications			
IIb/IIIa blockade, n (%) N = 7824	195 (35)	4670 (64)	<0.001
Heparin, n (%) N = 7828	557 (100)	7221 (99)	0.16
LMWH, n (%) N = 7822	210 (38)	1086 (15)	<0.001
Bivalirudin, n (%) N = 7613	1 (0.2)	48 (0.7)	0.187
Aspirin, n (%) N = 7827	553 (99)	7177 (99)	0.25
Clopidogrel, n (%) N = 7824	449 (81)	4076 (56)	<0.001
Prasugrel, n (%) N = 5733	30 (8.6)	724 (14)	0.009
Ticagrelor, n (%) N = 4645	132 (46)	2676 (61)	<0.001

SD = standard deviation, STEMI = ST elevation myocardial infarction, LVEF = left ventricular ejection fraction, IIB/IIIA = Glycoprotein IIB/IIIA inhibitor, LMWH = low molecular weight heparin; Note some patients had change of P2Y12 platelet inhibitor during admission; N is number of patients with data available for variable if less than total sample population of 7829 patients.

was no difference in transfusion of blood products (3% vs. 2%, p = 0.098); however, there were higher rates of major bleeding in the rescue than in the PPCI group (5.9% vs. 3.4%, p = 0.002).

There was no difference in 30-day MACE between the two groups (10% vs. 8.9%, p = 0.26; see Table 3 for clinical outcomes at 30 days and long-term outcomes).

There was a significantly higher rate of stroke in the rescue PCI group (2% vs. 0.6%, p < 0.001). When comparing stroke type, there was an excess of haemorrhagic stroke (1.3% vs. 0.1%, p < 0.001) but not ischaemic stroke (0.7% vs. 0.5%) in the rescue PCI arm. The odds ratio for haemorrhagic stroke in the rescue PCI group was 10.3. There was no difference in long-term mortality between the groups (20% (mean follow up 6.2 years) vs. 19% (mean follow up 5.3 years), p = 0.33). Kaplan-Meier long-term survival estimates in the two groups are presented in Fig. 1.

The unadjusted odds ratio for 30-day MACE in patients with rescue PCI was 1.11 (95% CI 0.82, 1.51, p = 0.484). After adjustment for age, smoking history, coronary artery disease, congestive cardiac failure, cardiogenic shock, ejection fraction, anticoagulation use, access site, culprit artery, stent type, stent count, acute closure and no reflow using a multivariate logistic regression model, the odds ratio for 30-day MACE in patients with rescue PCI remained non-significant (OR 0.74, p = 0.182).

Finally, in our registry analysis, 71% of patients in the PPCI arm had a door to balloon (DTB) time less than 90 min. In order to assess whether longer DTB times compared to optimal contemporary DTB times may have influenced the comparison with rescue PCI, a sensitivity analysis was conducted. In the sensitivity analysis, only patients in the PPCI group with a DTB time less than 90 min were compared to the rescue PCI group for the outcomes of 30 day mortality and MACE. 558 patients in the rescue PCI group and 5038 PPCI patients were included in this sensitivity analysis. There was a trend towards higher mortality at 30 days in the rescue PCI group (6% rescue PCI vs. 4.3% primary PCI, p = 0.07). The 30-day MACE rate was significantly higher in the rescue PCI group compared to PPCI when DTB time was less than 90 min (10.3% rescue PCI vs. 7.7%, p = 0.035).

4. Discussion

The main finding of our analysis is that rescue PCI was associated with an all-cause mortality or 30-day MACE rate at 30 days that was not significantly different to the rates observed with primary PCI. This is despite patients undergoing rescue PCI being more unstable on admission to hospital with greater symptom- and door-to-balloon times and with greater procedural complications. This may be offset by improved pre-PCI TIMI flow in the rescue PCI group even in patients clinically meeting criteria for failed thrombolysis. The other main finding is that patients undergoing rescue PCI and PPCI for STEMI have similar long-term mortality.

A recent publication utilising data from the Canadian Vital Heart Response STEMI Registry explored the utility of a pharmaco-invasive strategy compared to PPCI for STEMI[15]. A secondary analysis in this study demonstrated a similar composite risk of death, heart failure, cardiogenic shock or recurrent MI within one year between rescue PCI and PPCI. Long-term outcome

Table 3
In-hospital, 30-day and long-term Clinical Outcomes.

In-hospital Clinical Outcomes Variable N = 7829	**Rescue PCI in STEMI (n = 558)**	**Primary PCI in STEMI (n = 7271)**	**P value**
Mortality, n (%)	28 (5)	317 (4.4)	0.48
- Cardiac, n (%)	22 (3.9)	287 (3.9)	0.05
- Neurological	2 (0.4)	6 (0.1)	
- Renal	0	3 (0.04)	
- Vascular	0	3 (0.04)	
- Infection	0	3 (0.04)	
- Pulmonary	0	5 (0.07)	
- Other, n (%)	4 (0.7)	10 (0.1)	
New/recurrent MI, n (%) N = 7811	9 (1.6)	88 (1)	0.39
In-hospital unplanned PCI, n (%) N = 7811	8 (1.5)	72 (1)	0.31
Stent thrombosis, n (%) N = 6877	5 (1.8)	51 (0.8)	0.40
In-hospital cardiothoracic surgery, n (%) N = 3414	7 (3.3)	54 (1.7)	0.09
Cardiogenic shock, n (%)	45 (8)	428 (6)	0.04
Arrhythmia, n (%)	99 (18)	1194 (16)	0.42
New heart failure, n (%) N = 7828	61 (11)	564 (8)	0.008
In hospital major bleeding event, n (%)	33 (5.9)	246 (3.4)	0.002
Transfusion of blood products, n (%) N = 7827	17 (3)	146 (2)	0.098
Length of stay, mean ± SD N = 3414	5 (3.7)	4.9 (5)	0.054
30-day Clinical Outcomes Variable N = 7780	**Rescue PCI in STEMI (n = 553)**	**Primary PCI in STEMI (n = 7227)**	**P value**
All-cause mortality, n (%)	33 (6)	380 (5.3)	0.47
Myocardial infarction, n (%)	16 (2.9)	141 (2)	0.13
TLR, n (%)	17 (3.1)	213 (3)	0.87
TVR, n (%)	21 (3.8)	245 (3.4)	0.61
30-day MACE, n (%)	57 (10)	643 (8.9)	0.26
30-day MACCE, n (%)	64 (12)	689 (9.5)	0.12
Haemorrhagic Stroke, n (%)	7 (1.3)	9 (0.1)	<0.001
Ischaemic stroke, n (%)	4 (0.7)	33 (0.5)	NS
30-day readmission, n (%) N = 7421	62 (12)	976 (14)	0.33
Long-term mortality n (%) N = 7829	113 (20)	1352 (19)	0.33
Time to death in days (SD)	2251 (1622)	1952 (1438)	

MI = myocardial infarction, PCI = percutaneous coronary intervention, TLR = target lesion revascularization; TVR = Target vessel revascularization; MACE = major adverse cardiac events; MACCE = Major adverse cardiac and cerebrovascular events; NDI = National death index SD = standard deviation; N is number of patients with data available for variable if less than 7829 patients.

data was not available from this study. Additionally, Welsh and colleagues have previously compared the pharmaco-invasive (scheduled PCI), rescue and PPCI revascularisation strategies as part of a pre-specified post-randomisation analysis of the Strategic Reperfusion Early after Myocardial Infarction (STREAM) study[16]. Whilst data from the PPCI arm were presented, adjusted composite clinical endpoint comparison was performed only between rescue and scheduled PCI rather than primary PCI. As expected, patients with rescue PCI had significantly higher adjusted rates of death, shock and heart failure compared to patients with successful fibrinolysis undergoing scheduled PCI. Finally, several studies have compared a pharmaco-invasive strategy to primary PCI using observational registry based analyses with findings suggesting similar ischaemic outcomes although these studies did not directly compare rescue versus primary PCI[17–21].

In addition, it should be noted that prospective, randomized trials have previously evaluated the role of rescue PCI versus repeat fibrinolysis and conservative management in patients with failed fibrinolysis. The MERLIN trial demonstrated that rescue PCI reduced repeat revascularization rates compared to conservative treatment but not recurrent myocardial infarction[22]. The results of the trial were unexpected in demonstrating a higher 30-day stroke rate (4.6%) in the rescue PCI arm than expected which was difficult to explain. The subsequent REACT trial established rescue PCI as the treatment of choice for patients with failed fibrinolysis when compared to conservative management or repeat fibrinolysis[4]. This multicentre randomized controlled trial (RCT) convincingly demonstrated that in patients with failed fibrinolysis, rescue PCI reduces recurrent acute myocardial infarction compared to conservative management or repeat fibrinolysis. The stroke rate in this subsequent trial in the rescue PCI arm was 2.1% at 6 months which is similar to the rate seen in our study and much lower than that seen in the MERLIN trial.

Despite precautions taken during PCI (e.g. lower use of GP IIIb/IIa inhibitors[23]), there were higher rates of in-hospital major bleeding in patients receiving rescue PCI and higher rates of haemorrhagic stroke. This was not surprising and reflects the main downside to fibrinolysis where previous studies demonstrate a 1.2% risk of significant stroke [24]. Severe bleeding resulting in haemodynamic compromise was seen in 1.8% of patients receiving fibrinolysis in prior studies and moderate bleeding requiring transfusion was seen in 11.4% [25]. The higher use of radial access in rescue PCI may explain the lower proportion and lack of difference in patients requiring blood transfusions in both groups of our

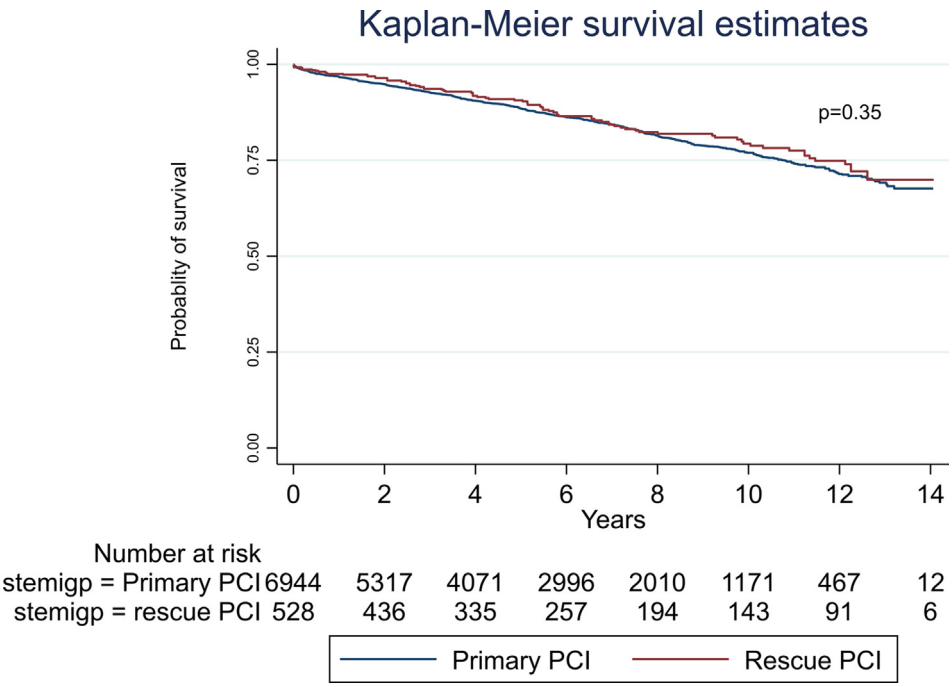

Fig. 1. Central Illustration: Kaplan-Meier Long term survival estimates comparing Primary and Rescue PCI. Primary PCI is represented by the blue line, rescue PCI is represented by the red line. P value not significant. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

study. However, patients undergoing thrombolysis and rescue PCI need to be closely monitored for bleeding complications, particularly haemorrhagic stroke.

Additionally, it was noted that the proportion of patients with optimal DTB times in the PPCI group varied from the most recent targets[7]. This likely reflects changing practice and goals over the 13-year period that is captured in the dataset for this registry-based study. Therefore, to assess whether longer DTB times affected ischemic endpoints in the PPCI group, a sensitivity analysis was conducted where only patients with a DTB time less than 90 min in the PPCI group were included. In this sensitivity analysis, there was a significantly higher rate of 30-day MACE and a trend towards a higher all-cause mortality in the rescue PCI group compared to PPCI. It has previously been shown that shorter DTB times improve ischemic endpoints in patients undergoing PPCI [27]. This sensitivity analysis suggests that when PPCI is optimal, ischaemic endpoints favour PPCI over rescue PCI. This and the reduced risk of major bleeding emphasizes the preference given to PPCI in the management of STEMI where timely access is available.

In the current COVID-19 crisis, fibrinolysis has been suggested as a potential reperfusion strategy for patients with suspected or confirmed infection to reduce risk of spread to healthcare workers. A position statement from the ACC's Interventional Council and Society of Cardiovascular Angiography and Interventions (SCAI) suggests that fibrinolysis can be considered in stable patients with STEMI and active COVID-19 infection when balancing the risks to the patient and risks of transmission to catheterization laboratory staff [12]. This draws on experience and protocols developed in China for managing patients with STEMI that were COVID-19 positive[10,11].

Our study does not address the utility of fibrinolysis during this unprecedented pandemic and as such cannot provide evidence to support or refute this approach. However, we hope it assists in quantifying the risks of bleeding complications in patients requiring PCI post failed fibrinolysis in the contemporary era using real-world data.

4.1. Limitations

There are several limitations to our study. We do not have individual data to compare time from fibrinolysis to PCI in the rescue PCI group. The number of patients in our registry receiving rescue PCI are relatively small compared to those receiving primary PCI; however, we believe this is one of the challenges in evaluating rescue PCI due to the increasing use of primary PCI in STEMI with more timely access to PCI worldwide[26]. As our study is based on a PCI registry, we do not know the actual percentage of patients with successful fibrinolysis as not all of these patients will undergo PCI (some patients post fibrinolysis may have no residual disease).

The presence of TIMI 0 flow pre-PCI was lower in the rescue PCI group than in the primary PCI group, which may have influenced short- and long-term ischaemic outcomes. Whilst this was somewhat unexpected in patients deemed to have had failed thrombolysis, we believe that this reflects the real-world imperfect nature of assessing success of fibrinolysis based on clinical status, symptom and ECG criteria according to current definitions[7].

Finally, the retrospective observational study design may be responsible for an imbalance of confounding factors between the groups. For example, patients in the rescue PCI group were significantly younger and the non-randomized choice to treat with fibrinolysis may reflect unmeasured confounding factors such as a lower bleeding risk in this group. Whilst we utilized multivariate adjustment for known confounders such as age, we are not able to account for these unmeasured confounders. However, we believe this is an appropriate study design to compare these two groups given the small number of rescue PCI procedures performed and the importance of long-term follow up.

5. Conclusions

Fibrinolysis remains an important revascularization strategy in treating patients with STEMI due to the lack of timely primary PCI availability and has been suggested as a potential revascularization strategy during the COVID-19 pandemic. Our study suggests that in

patients with failed fibrinolysis undergoing rescue PCI, traditionally believed to be a high-risk group, short-term ischaemic outcomes and long-term mortality are similar to patients undergoing primary PCI. Whilst these patients represented a more unstable subset on presentation this may have been counterbalanced by improved TIMI flow pre-PCI after fibrinolysis. The increased risk of bleeding complications, particularly haemorrhagic stroke with an odds ratio of 10.3 in our study remains an important disadvantage of fibrinolysis and rescue PCI when fibrinolysis is unsuccessful. However, this appears to be reduced with contemporary PCI techniques and current medical management and in our study did not affect long-term outcomes.

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Declaration of Competing Interest

The Melbourne Interventional Group acknowledges funding from Abbott Vascular, Astra-Zeneca, BMS and Pfizer. These companies do not have access to data and do not have the right to review manuscripts or abstracts before publication. The authors have no conflict of interest to declare.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2021.100745.

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