Review

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Comparative effectiveness of primary PCI versus fibrinolytic therapy for ST elevation myocardial infarction: a review of the literature

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Aim: To compare the effectiveness of primary percutaneous coronary intervention (pPCI) and fibrinolytic therapy (FL) for the acute management of ST elevation myocardial infarction (STEMI). **Methods**: A review of guidelines and PubMed literature comparing clinical outcomes of patients with STEMI treated with pPCI or FL. **Results**: Earlier trials reported reduced mortality and reinfarction with pPCI. Recent randomized data suggest similar outcomes for delayed pPCI compared with FL, especially in geographically remote areas. Guidelines recommend pPCI as the preferred reperfusion strategy for STEMI, if available within 120 mins of first medical contact. **Conclusion:** pPCI is the preferred treatment strategy for STEMI. However, FL with subsequent percutaneous coronary intervention remains a viable option for those in rural areas.

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Each year, 500 per million hospitalizations in the UK are as a result of ST elevation myocardial infarctions (STEMI) [1], and worldwide, coronary artery disease currently accounts for 12.8% of all deaths [2]. Within the last 30 years, dramatic improvements have been noted in overall mortality owing to both pharmacological and interventional therapies [3], with early access to reperfusion critical to good clinical outcomes. In rural areas, the development of air ambulances have enhanced the care of patients, reducing delays in reperfusion, yet many areas still do not have easy access to percutaneous coronary intervention (PCI).

In the late 1980's, the GISSI [4] and ISIS-2 [5] randomized placebo controlled trials were integral in establishing fibrinolytic therapy (FL) as the standard of care for the acute treatment of STEMI. This continued as the mainstay in treatment until the development of PCI in the 1990s. By 2000, studies including PAMI [6] and GUSTO-IIb [7] had provided randomized evidence for the superiority of primary percutaneous coronary intervention (pPCI) over FL for the acute management of STEMI. It was in 2002 that the DANAMI 2 [8] trial first investigated the outcomes of patients presenting to non-PCI centers with STEMI, and pPCI retained superiority even when delayed due to interhospital transfer.

Both pPCI and FL therapy feature in the national and international guidance for the management of STEMI. Recent research, however, offers differing treatment algorithms and outcomes, especially among patients with STEMI who live in geographically remote areas, and there is evidence that the diffusion of PCI is suboptimal in many countries [9–11].

Therefore, we aimed to review the literature comparing the effectiveness of pPCI and FL for the acute management of STEMI.

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Methods

A review of published literature on PubMed, including randomized controlled trials (RCTs) and observational studies published from 1 January 1985 to 1 September 2015. The following search terms were used: STEMI, myocardial infarction, fibrinolysis, percutaneous coronary intervention, PCI and angioplasty. Data were included if mortality or re-infarction was compared between the two reperfusion strategies. We also reviewed the current American Heart Association, European Society of Cardiology and NICE guidelines.

Results

We reviewed a total of 14 RCTs, one meta analysis of RCTs and four observational studies. Two were published in the 1980's, two in the 1990's and the remainder after 2000. Sample sizes for the RCTs ranged from 212 to 1892 covering a total of 10,221 patients. The meta-analysis included information for 194,040 patients. All but one of the studies included mortality in the composite of the primary end point, but with follow-up of varying durations following STEMI, between 30 days and 5 years. The reporting of other outcomes varied from trial to trial, including re-infarction, cardiogenic shock, arrhythmias, stroke, recurrent ischemia and congestive cardiac failure. Observational studies included a range of countries and cultures, where geographical barriers precluded many patients with STEMI from receiving pPCI within 120 min of first medical contact.

All present-day guidelines are in agreement regarding reperfusion strategies for the acute management of STEMI. That is, pPCI is the preferred treatment option if the onset of the patient's symptoms is less than 12 h and they have the ability to reach a facility with the required expertise within 120 min of first medical contact [1,2,12]. The American Heart Association quotes reduced 6 week ($p = 0.0002$) and long-term ($p \geq 0.0001$) mortality rates among those who received pPCI compared with FL [12] Following FL, all guidelines recommend that patients receive early coronary angiography and, if appropriate, PCI.

Table 1 summarizes the results of the RCTs which have compared reperfusion strategies for STEMI over the last 22 years. In the 1990's, the PAMI [6] and GUSTO IIb [7] trials both concluded a statisically significant reduction in mortality, reinfarction, (and in GUSTO IIb, stroke), 5.1% vs 12% ($p = 0.02$ [6]) and 13.6% vs 9.6% ($p = 0.033$ [7]), respectively, in those treated with pPCI. This remained the case even if pPCI was performed in a hospital without on-site cardiac surgery (C-PORT; 12.4% vs 19.9%; $p = 0.03$ [13]) and accounted for delays in treatment owing to transfer if the patient had presented to a hospital without the facilities to perform pPCI (DANAMI 2; 8% vs 13.7%; $p = 0.002$ [8]). While the negative prognostic effects of delayed transfer for pPCI were deemed minimal [14], it was noted that in the DANAMI trial, although patients were being transferred for pPCI, 96% were transferred in less than 120 min and therefore in fact complying with current guidelines.

Other trials were conducted to assess whether, after FL, outcomes were improved by subsequent PCI, regardless of clinical benefit post FL. The ASSENT-4 trial concluded an increase in 30-day mortality in those patients managed with PCI within 3 h following FL. This suggested a prothrombotic effect of fibrinolysis in early PCI and as a result subsequent trials delayed PCI until at least 3 h post FL [24]. Keeley *et al.* also demonstrated an increase in mortality, reinfaction, revascularization, bleeding and strokes in patients undergoing PCI post FL in a meta-analysis of 17 trials involving 4504 patients and as a result deemed it not suitable for use outside of the context of a RCT [25]. In contrast, CARESS in AMI [17], TRANSFER AMI [19] and NORDISTEMI [21] were all in agreement, that outcomes were improved if patients underwent immediate PCI following FL. CARESS in AMI analyzed a composite of death, re-infarction or refractory ischemia at 30 days (4.4% vs 10.7%; $p = 0.004$ [17]), similarly TRANSFER AMI assessed the same composite, but with the addition of congestive heart failure or shock (11% vs 17.2%; $p = 0.004$ [19]), with NORDISTEMI having a longer follow-up period of a year, with a composite of death, re-infarction and stroke ($p = 0.01$ [21]).

Further to this, RCTs then assessed outcomes according to the timing of PCI following FL. In 2006, the WEST [15] trial failed to demonstrate a significant difference in a composite of 30-day death, re-infarction, refractory ischemia, congestive heart failure, cardiogenic shock and major ventricular arrhythmia between patients who received pPCI, FL and immediate PCI or FL with standard care. In addition, there was still no difference for death and recurrent myocardial infarction between those undergoing pPCI and those managed with FL followed by immediate PCI. These results were echoed in the GRACIA-2 [16] trial in 2007, the 5-year follow-up to the CAPTIM [17] trial in 2009 and the STREAM [22] trial in 2013. In the STREAM trial, patients were randomized if unable to undergo pPCI within the next hour, therefore in keeping with the current guidelines. The recent FAST-MI [23] trial published in 2014 also concluded that there was no significant difference in all-cause mortality depending on whether pPCI or FL was the initial therapy. While a Cox multivariate analysis did show significant survival advantage in the FL group compared with those who underwent delayed pPCI (over 90 min following the

Table 1. Summary of randomized control trials and meta-analyses comparing outcomes of primary percutaneous coronary intervention and fibrinolytic therapy in the management of ST elevation myocardial infarction.

Trial	First named author	Year of publication	Sample size	Study aims	Inclusion criteria	Exclusion criteria	Primary end point	Summary of results	Ref.
PAMI	Grines CL	1993	395	pPCI vs Thrombolysis with tPA	Chest pain with >1 mm ST elevation in two or more leads, onset <12 h	Inability to consent, dementia, complete LBBB, cardiogenic shock, contraindication to thrombolysis	In hospital death and reinfarction	5.1 vs 12% primary end points p = 0.02 in favor of pPCI if within 12 h of symptom onset	[6]
GUSTO IIb	Non cited	1997	1138	Fibrinolytic therapy vs PCI (some plus heparin/hirudin)	Chest pain for >20 min with ST elevation at least 0.2 mV in two leads or LBBB, onset <12 h	Warfarin, active bleeding, CVA, contraindication to heparin, Cr >2mg/dL, SBP>200 mmHg DBP>110 mmHg, Females of childbearing age	Death, reinfarction or disabling stroke within 30 days	13.6 vs 9.6% primary end point in favor of PCI group, p = 0.033	[7]
C-PORT	Aversano T	2002	451	To determine whether pPCI is superior to thrombolysis in hospitals without on-site cardiac surgery	Chest pain, onset <12 h, at least 1 mm ST elevation in at least two leads	Unable to consent, metformin, creatinine >132.6 umol/l (male), >123.8 umol/l (female), contraindications to PCI or thrombolysis	Death, recurrent MI, stroke at 6 months	12.4 vs 19.9% primary end point in favor of pPCI (p = 0.03)	[13]
DANAMI 2	Anderson HR	2003	1572	pPCI vs thrombolysis with Alteplase. Of which 1129 were at non-PCI centers	>18 years, onset 30 min–12 h, cumulative 4 mm ST elevation in two leads	Contraindication to fibrinolysis, LBBB, unsuitable for PCI, previous CABG, Cr >2.83, cardiogenic shock, metformin, unsuitable for transfer	Death, reinfarction or disabling stroke within 30 days	In all, 8 vs 13.7% primary end point in favor of PCI ($p \leq 0.001$). In non-PCI center 8.5 vs 14.2% in favor of PCI (p = 0.002)	[8]
WEST	Armstrong P	2006	304	Thrombolysis (tenecteplase) with immediate PCI vs Thrombolysis and usual care vs PCI	>4 mm ST deviation, onset <6 h, >18 years, chest pain >20 min, new LBBB	If pPCI in 1 h available, contraindications to fibrinolysis, CABG, GIIbIIIa in last 7 days	Death, reinfarction, refactory ischemia, congestive cardiac failure, shock and major arrhythmia at 30 days	24 vs 25 vs 23% primary end points for three groups	[15]

†SBP <100 mmHg; HR>100 bpm; Killip class II or III; 2 mm anterior ST depression; 1 mm ST elevation in V4.
3VD: Three vessel disease; CABG: Coronary artery bypass graft; Cr: creatinine; DBP: Diastolic blood pressure; EF: Ejection fraction; GIIbIIIa: Glycoprotein IIbIIIa inhibitor; HR: Heart rate; LBBB: Left bundle branch block; LV: Left ventricle; LVSF: Left ventricular systolic function; MI: Myocardial infarction; OS: Observational study; PCI: Percutaneous coronary intervention; pPCI: primary percutaneous coronary intervention; PVD: Peripheral vascular disease; RCT: Randomized control trial; SBP: Systolic blood pressure; STEMI: ST elevation myocardial infarction.

Table 1. Summary of randomized control trials and meta-analyses comparing outcomes of primary percutaneous coronary intervention and fibrinolytic therapy in the management of ST elevation myocardial infarction (cont.).

Trial	First named author	Year of publication	Sample size	Study aims	Inclusion criteria	Exclusion criteria	Primary end point	Summary of results	Ref.
GRACIA-2	Fernandez-Aviles F	2007	212	Noninferiority trial to assess if thrombolysis and PCI is a reasonable reperfusion option compared with pPCI	>18 years, onset <12 h, chest pain for >30 min, ST elevation of 0.1 mV in at least two limb leads or 0.2 mV in two precordial leads, LBBB	Contraindication to fibrinolysis, cardiac rupture, shock, terminal illness (life expectancy <1 year), Cr >221 umol/l, neutropenia, thrombocytopenia, hepatic dysfunction, known 3VD, PVD preventing PCI	LVSF at 6 weeks to assess reperfusion, extent of LV myocardial damage	Primary end point p = 0.11. Therefore thrombolysis/PCI does not result in worse outcome compared with pPCI	[16]
CARESS in AMI	Di Mario C	2008	600	Immediate PCI vs standard care post-thrombolysis (half dose reteplase and abciximab)	Extensive ST elevation, new LBBB, previous MI, killip class>2, EF <35%	>75 years	Death, reinfarction or refractory ischemia at 30 days	4.4 vs 10.7% primary end point in favor of immediate PCI group (p = 0.004)	[17]
CAPTIM 5yr follow-up	Bonnefoy E	2009	840	pPCI vs thrombolysis (rt-PA) with immediate transfer to PCI center	Chest pain for 30 min, onset <6 h, ST elevation at least 0.2 mV in at least two leads or LBBB	Contraindication to fibrinolysis, severe renal or hepatic insufficiency, aorto-femoral bypass, cardiogenic shock, CABG, anticoagulated, if >1 h transfer time	Death at 5 years	9.7 vs 12.6% primary end point in favor of thrombolysis (p = 0.18)	[18]
TRANSFER AMI	Cantor W	2009	1059	Immediate PCI vs standard care post-thrombolysis (tenecteplase)	onset<12 h, ST elevation at least 2 mm in anterior leads or 1 mm in inferior leads with high risk characteristics†	Cardiogenic shock, PCI within last month, CABG, option of pPCI with door-to-balloon time <60 min	Death, reinfarction, recurrent ischemia, congestive heart failure or shock within 30 days	11 vs 17.2% primary end point in favor of immediate PCI group (p = 0.004)	[19]

†SBP <100 mmHg; HR>100 bpm; Killip class II or III; 2 mm anterior ST depression; 1 mm ST elevation in V4.
3VD: Three vessel disease; CABG: Coronary artery bypass graft; Cr: creatinine; DBP: Diastolic blood pressure; EF: Ejection fraction; GIIbIIIa: Glycoprotein IIbIIIa inhibitor; HR: Heart rate; LBBB: Left bundle branch block; LV: Left ventricle; LVSF: Left ventricular systolic function; MI: Myocardial infarction; OS: Observational study; PCI: Percutaneous coronary intervention; pPCI: primary percutaneous coronary intervention; PVD: Peripheral vascular disease; RCT: Randomized control trial; SBP: Systolic blood pressure; STEMI: ST elevation myocardial infarction.

Table 1. Summary of randomized control trials and meta-analyses comparing outcomes of primary percutaneous coronary intervention and fibrinolytic therapy in the management of ST elevation myocardial infarction (cont.).

Trial	First named author	Year of publication	Sample size	Study aims	Inclusion criteria	Exclusion criteria	Primary end point	Summary of results	Ref.
Meta-analysis	Huynh T	2009	194,040	Meta-analysis of RCT and observational studies comparing pPCI vs fibrinolytic therapy	Full dose fibrinolytic therapy, had to compare PCI and thrombolysis	Facilitated PCI, intracoronary fibrinolytic therapy, studies who enrolled patients with contraindications to either treatment	All end points analyzed as distinctive events, not a composite. Mortality and stroke	In RCT, 34% reduction in 6 week mortality and 24% reduction in 1 year mortality in pPCI group. No differences seen in long-term outcomes in OS	[20]
NORDISTEMI	Bohmer E	2010	266	Immediate PCI vs standard care post-thrombolysis (tenecteplase)	18–75 years, pain for <6 h, 1 mm ST elevation in limb leads or 2 mm in precordial leads, unable to have pPCI in 1 h, for thrombolysis	Creatinine >250 mmol/l, pregnancy, cardiogenic shock, life threatening arrhythmia, serious disease with life expectancy <1 year, unable to consent	Death, reinfarction, stroke or new ischemia at 1 year	21 vs 27% primary end point in favor of immediate PCI group ($p = 0.19$). If ischemia removed, $p = 0.01$	[21]
STREAM	Armstrong P	2013	1892	pPCI vs thrombolysis (tenecteplase) prior to PCI	ST elevation at least 2 mm in two leads, onset <3 h, unable to have pPCI within 1 h	CABG, LBBB, pacemaker, cardiogenic shock, weight <55 kg, uncontrolled hypertension, anticoagulated, bleeding, renal impairment	Death, shock, congestive heart failure or reinfarction at 30 days	12.4 vs 14.3% in favor of fibrinolysis, $p = 0.21$	[22]
FAST-MI	Danchin N	2014	1492	pPCI vs thrombolysis as initial therapy	STEMI, able to consent, >18 years, <12 h from onset	MI occurring post intervention (CABG, PCI, surgery)	All cause mortality at 5 years	85 vs 88% in favor of PCI when propensity score matched. Not significant	[23]

†SBP <100 mmHg; HR>100 bpm; Killip class II or III; 2 mm anterior ST depression; 1 mm ST elevation in V4.
3VD: Three vessel disease; CABG: Coronary artery bypass graft; Cr: creatinine; DBP: Diastolic blood pressure; EF: Ejection fraction; GIIbIIIa: Glycoprotein IIbIIIa inhibitor; HR: Heart rate; LBBB: Left bundle branch block; LV: Left ventricle; LVSF: Left ventricular systolic function; MI: Myocardial infarction; OS: Observational study; PCI: Percutaneous coronary intervention; pPCI: primary percutaneous coronary intervention; PVD: Peripheral vascular disease; RCT: Randomized control trial; SBP: Systolic blood pressure; STEMI: ST elevation myocardial infarction.

first call), this was not confirmed in a propensity score matched analysis.

Given a number of trials with small sample sizes, Westerhout *et al.* combined the CAPTIM and WEST trial data, and with a larger sample size were able to conclude a survival benefit from FL if delivered within the first 2 h. Yet, if FL was administered after the first 2 h no significant difference was seen between the different modalities of reperfusion [26]. These studies were in contradiction to the results of the PAMI [6] and GUSTO IIb [7] trials, which were performed 20 years earlier favoring pPCI as the preferred modality of reperfusion in STEMI.

As many of these trials included a small sample size, the meta-analysis by Huynh *et al.* [20] in 2009 included all RCTs and observational trials up to 2008. Mortality outcomes in patients managed with pPCI and FL for STEMI were tabulated. The results were in agreement with the original trials, concluding a reduction in mortality both in the short term (34%) and long term (24%) in the pPCI group, therefore, continuing to recommend pPCI as the preferred management option.

Observational studies which attempted to compare outcomes from pPCI with those from FL differed. The WIRE registry [27] in Poland, 2008 found that only those STEMI who received early PCI had long term reductions in mortality. A conclusion echoed in the Middle East by Al-Zakwani *et al.* [28] who demonstrated that those treated with pPCI were less likely to have recurrent ischemic events, (odds ratio: 0.18; 95% CI: 0.06–0.56; p = 0.003). The STEPP-AMI study was a prospective, observational pilot study conducted in India that failed to show any difference in outcomes among those treated with pPCI or FL [29]. The primary end point was a composite of death, cardiogenic shock, re-infarction, repeat revascularization of a culprit artery and congestive heart failure at 30 days (11.1% vs 3.9%; p = 0.07). An Italian study by Manari *et al.* [30], however, concluded that despite longer door-to-balloon times for patients transferred from peripheral hospitals, delayed PCI was associated with favorable short and long-term outcomes.

Discussion

Through the review of published trials, a meta-analysis and observational studies which included cohort from urban and a range of rural areas, we report the comparisons of the effectiveness of pPCI and FL for the acute management of STEMI. While pPCI remains the preferred management option for STEMI [1–2,12,18,20–22], more recent trials have confirmed that in the event of delayed PCI due to transfer times, that FL followed by PCI prior to discharge from hospital provided similar outcomes and is a viable option [16–17,19,23,27]. This finding appears more pertinent to STEMI arising from geographically remote areas, with the current guidelines reflecting this [1–2,12]. As the targeted reperfusion time is currently 120 min from first contact, the STREAM trial randomized patients if they were unable to receive PPCI within the next hour.

Although the more recent trials including STREAM, FAST-MI, GRACIA-2 and WEST [15–16,22–23] have all concluded mortality outcomes in favor of the FL group, it is important to note that none of the results were statistically significant and, therefore, while reperfusion with FL has been demonstrated to have similar outcomes as pPCI, it is not known to have superiority. Westerhout *et al.*, however, did demonstrate reduced mortality in the FL group but only if delivered within 2 h (p = 0.021) [26].

The relevance of these newer trials to clinical practice mainly lies in the heightened recognition of the possibility of early use of FL as the reperfusion strategy for STEMI which, notably, many junior doctors are no longer comfortable in managing independently. This is likely as a result of the current default position of reperfusion for STEMI in many modern healthcare systems (such as UK) being emergency angiography and PCI [31]. Consequent to the introduction of pPCI centers throughout UK, this resulted in 98.5% of STEMI in England and Wales receiving pPCI in 2014, but with wide between-center variation in the adoption of the service [11,32]. Although such a high proportion of patients with STEMI receive pPCI, there are can be delays to reperfusion associated with inter-hospital transfer. The GRACIA-2 and WEST trials concluded that this may in fact negate the benefit of pPCI over immediate FL [15,16]. Therefore, improving confidence in administering FL when the door-to-balloon time is >120 min will subsequently reduce the time to reperfusion and improve outcomes. Delays in reperfusion are known to increase the rates of morbidity and mortality [18] as half of potentially salvageable myocardium is lost in the first hour, and two-thirds lost within 3 h [1]. Hence, the greatest benefit gained from reperfusion therapy occurs within the first 2–3 h of symptom onset. Owing to the delays, however, in time from symptom onset to first medical contact, the current European Society of Cardiology guidelines advise reperfusion with the first 2 h following the first medical contact if the symptom onset is under 12 h.

Other clinical impacts of this research on patient care include the importance of adverse events which may arise from both modes of reperfusion. Reassuringly, in the most recent data, the STREAM trial noted that if a reduced dose of Tenecteplase is used in those over 75 years that there was no statistically significant difference in intracranial hemorrhage between those who

received FL and pPCI [22]. Although not included in our aims, it must be considered too, that if a patient undergoes FL prior to PCI, they become at risk of exposure to adverse events from both modes of reperfusion.

Both demographic and supply factors (such as medical staffing and hospital capacity) are known to be associated with regional variation in pPCI rates [9,10]. Owing to its small area and easily accessible pPCI centers, pPCI is likely to remain the preferred treatment option for those in UK with acute STEMI. For those living in more rural and remote areas, the newer trials have provided reassurance that management with FL, prior to transfer to a PCI-capable center will result in similar outcomes to those who live in cities where there is easy access to pPCI facilities. On the basis of these study results, India, which has the highest burden of acute coronary syndrome in the world [33], has developed a national STEMI program. This incorporates both pPCI and FL followed by coronary angiography (with PCI, if required) within 24 h of first medical contact, depending on location within the country [29]. This aims to improve overall outcomes in India as currently, among adults of working age, nearly 18 million productive years of life are expected to be lost from coronary artery disease by 2030. Remarkably, this is nine times higher than that expected in the USA within the same time-frame [34].

It is possible to debate how pPCI services in UK will evolve, by comparing our care to that delivered in other countries. Sweden for example, has more complete use of evidence-based practice [35], with new technologies introduced at an accelerated rate [36]. As a result, in Sweden, there is much lower hospital variation (interquartile range 16.7% vs 50.7%) [37] in guideline recommended treatment for acute myocardial infarction. In turn, this was associated with a higher 30-day mortality in the UK [37,38], and greater variation in that mortality [37]. A reduction in treatment variation has been associated with the number of physicians and nurses per 100,000 inhabitants, population density and the number of hospital beds per 100,000 inhabitants [9,10].

Thus, to develop a progressive pPCI service, more centers may be required in order to meet demand. However, this will increase staffing requirements, with a greater emphasis on experienced operators working out of regular hours. Alternatively, pPCI may become even more centralized, with larger centers responsible for intervention and perhaps patients undergoing FL at their nearest hospital prior to transfer at a later date. A study by West *et al.* [39] published in 2011 investigated outcomes based on the volume and the proportion of cases of STEMI who received pPCI. The authors demonstrated that although there was no significant difference in mortality depending on the volume of cases undertaken, that in centers where of all the STEMI patients, a smaller proportion (<25%) were treated with pPCI, there was an increase in mortality. In fact, those with a higher volume of cases had a shorter door-to-balloon times. This study therefore, promoted the use of fewer, larger centers.

Finally, any potential changes in the guidelines regarding reperfusion for STEMI will need to assess the financial implications, as increasing the number of patients receiving both FL and subsequent PCI will result in increased costs for the modern healthcare systems. In 2005, Selmer *et al.* [40] conducted a state-transition model that followed patients from the day of STEMI until death, with lifetime costs of €19,250 for pPCI, €24,000 for those undergoing pPCI that required transport from a peripheral hospital and €29,250 for FL. For those treated with FL but subsequent coronary angiography as now recommended in the guidelines, the NHS quote a cost of extra £1284 per patient, with a rise to £3837 for angioplasty (higher if more than one stent required) [41]. While we are unable to formulate comparisons between countries regarding cost of STEMI management as published data is from varying years and with different parameters used, the evidence does largely favor PPCI in Sweden (US$25,315 vs US$27,819) [42], USA (US$24,900 vs US$28,600) [43] and China ($p < 0.05$) [44]. The ZWOLLE trial, however, did conclude that FL while cheaper in the acute setting, by 1 year the difference has resolved (US$16,681 vs US$17,316) [45]. There are limited data from less developed countries regarding the cost effectiveness of the reperfusion options for STEMI management.

Limitations

This was not a systematic review and is therefore not a conclusion based on all available research. We also did not focus on the cost impact of each reperfusion strategy. The focus of this review was on the primary end points of the trials of which the majority were the composite of many outcomes, and didn't focus on adverse events secondary to the treatment such as bleeding, renal impairment, arrhythmias, requiring emergency surgery and allergy. For a more thorough review, each outcome should be analyzed separately and ensure that all trials were managing the treated groups in the same manner.

Conclusion

While pPCI remains the preferred management option for STEMI, more recent trials have confirmed that in the event of delayed PCI due to transfer times, that FL followed by PCI prior to discharge provided similar outcomes and is a viable option, particularly for those living in rural areas. The current guidelines reflect the

available research, yet it is reassuring that in the event of a decline in pPCI services in the future that there remains a viable and evidence based alternative that will result in rates of mortality, re-infarction, recurrent ischemia, cardiogenic shock and heart failure similar to that of pPCI now, albeit at a higher cost.

In order to gain further evaluation of the two treatment options, a meta analysis including the newer trials would provide a more conclusive understanding of their clinical effectiveness.

Future perspective

Over the last ten years, the percentage of patients undergoing pPCI as the mode of reperfusion in STEMI management has increased and this is likely to continue. While pPCI remains the preferred treatment option, the increase in demand will need addressing by diffusion of services and increasing the number of centres providing a 24-h pPCI.

In order to improve patient outcomes further, we should aim to reduce the time between symptom onset and reperfusion by improving patient health behaviours and education. When in spite of this, geographical limitations prevent timely access to pPCI centres, there will always remain a role for FL in management of STEMI and the more recent studies have demonstrated that is a viable option for reperfusion with similar outcomes.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Executive summary

Primary percutaneous coronary intervention for ST elevation myocardial infarctionmanagement

- All current guidelines concur that primary percutaneous coronary intervention remains the preferred strategy for the acute management of ST elevation myocardial infarction.

Fibrinolytic therapy for ST elevation myocardial infarction management

- In some circumstances such as geographically rural areas and delayed access to primary percutaneous coronary intervention, there remains a role for fibrinolytic therapy.
- In patients with ST elevation myocardial infarction unable to undergo primary percutaneous intervention within 60 mins of first medical contact, pre-hospital fibrinolytic therapy with subsequent coronary angiography results in effective reperfusion.

Future perspective

- Further research is required in order to evaluate the most effective mode of reperfusion in those patients facing delays in primary percutaneous intervention for ST elevation myocardial infarction.

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