Review Article

Prehospital triage and direct transport of patients with ST-elevation myocardial infarction to primary percutaneous coronary intervention centres: a systematic review and meta-analysis

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ABSTRACT

Objective: Percutaneous coronary intervention (PCI) appears to be superior to in-hospital fibrinolysis for most patients with ST-elevation myocardial infarction (STEMI). However, few hospitals have PCI capability. The optimal prehospital strategy for facilitating rapid coronary reperfusion in STEMI patients is unclear. We sought to determine whether direct transport of adult STEMI patients by emergency medical services to primary PCI centres improves 30-day all-cause mortality when compared with a strategy of transportation to the closest hospital.

Methods: We systematically searched MEDLINE, EMBASE, Cochrane "CENTRAL" database (1980–July 2007) and several other electronic databases. Two authors independently assessed citations for relevance. Two authors independently abstracted data from included studies. We included studies that, 1) transported patients directly to a PCI-capable centre for primary PCI, 2) had a control group that was transported to the closest hospital and 3) reported outcomes of treatment time intervals, all-cause mortality, reinfarction rate, stroke rate or the frequency of cardiogenic shock. We used a random effects model to provide pooled estimates of relative risk (RR) when data allowed.

Results: We identified 2264 citations with the search. Five studies, including 980 STEMI patients, met inclusion criteria, and were clinically heterogeneous and of variable quality. Most studies were European (3/5) and involved physician out-of-hospital care providers. There was a trend toward increased survival with direct transport to primary PCI but this was not statistically significant (RR 0.51, 95% confidence interval [CI] 0.24–1.10). One study reported nonsignificant reductions in reinfarction (RR 0.43, 95% CI 0.11–1.60) and stroke (RR 0.33, 95% CI 0.01–8.06) with direct transport for primary PCI.

Conclusion: There is insufficient evidence to support the effectiveness of direct transport of patients with STEMI for primary PCI when compared with transportation to the closest hospital.

Keywords: ST-elevation myocardial infarction, emergency medical services, EMS, reperfusion strategies, primary percutaneous coronary intervention, PCI

RÉSUMÉ

Objectif : L'intervention coronarienne percutanée (ICP) semble donner de meilleurs résultats que la fibrinolyse en milieu hospitalier pour la plupart des patients victimes d'un infarctus du myocarde avec sus-décalage du segment ST (STEMI). Or, peu d'hôpitaux peuvent pratiquer l'ICP. La meilleure stratégie extrahospitalière pour faciliter la reperfusion coronarienne précoce chez ces patients n'est pas claire. Nous avons cherché à déterminer si le transport direct des adultes victimes d'un STEMI par les services médicaux d'urgence à des centres d'ICP primaires (ICPP) réduit davantage le taux de mortalité toutes causes confondues dans les 30 jours par rapport au transport à l'hôpital le plus proche.

Méthodes : Nous avons interrogé systématiquement plusieurs bases de données électroniques, dont MEDLINE, EMBASE, le Registre central Cochrane des essais contrôlés (CENTRAL) (1980 à juillet 2007). Deux des auteurs ont évalué séparément

la pertinence des citations. Deux autres auteurs ont résumé indépendamment les données des études. Nous avons inclus les études qui : 1) portaient sur les patients transportés directement vers un centre d'ICP pour la réalisation immédiate d'une ICPP; 2) comprenaient un groupe témoin ayant été transporté à l'hôpital le plus proche; et 3) ont fait état des résultats relatifs aux délais avant le traitement, à la mortalité toutes causes confondues, au taux de récidive d'infarctus, au taux d'accident vasculaire cérébral (AVC), ou à la fréquence de choc cardiogénique. Nous avons utilisé un modèle à effets aléatoires pour fournir une estimation des données regroupées du risque relatif (RR) lorsque les données le permettaient.

Résultats : Notre recherche des bases de données a permis de repérer 2264 citations. Cinq études, comprenant 980 patients avec STEMI, répondaient aux critères d'inclusion et étaient cliniquement hétérogènes et de qualité variable. La plupart des études étaient européennes (3/5) et mettaient à contribution des médecins extrahospitaliers. Nous avons noté une tendance à la hausse du taux de survie lorsqu'il y avait transport direct à un centre d'ICPP, mais elle n'était pas statistiquement significative (RR à 0,51, intervalle de confiance [IC] à 95 % de 0,24 à 1,10). Une étude faisait état d'une réduction non importante de récidive d'infarctus (RR à 0,43; IC à 95 % de 0,11 à 1,60) et d'AVC (RR à 0,33; IC à 95 % de 0,01 à 8,06) lorsque le patient avait été transporté directement à un centre d'ICPP.

Conclusion : Il n'y a pas suffisamment de preuves pour appuyer l'efficacité du transport direct des patients avec STEMI à un centre en vue d'une ICPP par rapport au transport vers l'hôpital le plus proche.

INTRODUCTION

Background and importance

Each year, diseases of the heart cause approximately 50 000 deaths in Canada[1] and acute myocardial infarction (AMI) accounts for a large proportion of these.[2] A recent report from the Cardiac Care Network of Ontario estimated that 20 000 people were admitted to hospital for AMI in that province during the 2000/01 fiscal year, and more than 6500 of those patients were diagnosed with ST-elevation acute myocardial infarction (STEMI).[3] Approximately 40% of patients with myocardial infarction (MI) are initially cared for and transported by emergency medical services (EMS).[4] Controversy exists about how EMS systems should facilitate timely coronary reperfusion in STEMI patients[5,6] and significant variation in practice is evident.[4]

Primary percutaneous coronary intervention (PCI) appears to be superior to in-hospital fibrinolysis for most patients with STEMI.[7–9] However, most North American EMS protocols for chest pain involve transportation of patients to the closest hospital, most of which do not have PCI facilities.[10,11] As defined in the 2004 STEMI guidelines by the American Heart Association and by the American College of Cardiology,[12] skilled PCI facilities include interventional cardiologist operators who perform more than 75 primary PCI cases per year, and catheterization laboratory support team members who experience more than 36 primary PCI cases per year. Patient outcomes have been found to be associated with operator and facility volume.[12]

Urgent transfer of patients from community hospitals to primary PCI facilities is one potential method of improving access to primary PCI. However, data from the National Registry of Myocardial Infarction in the United States suggest that interhospital transfer delays are excessive and may limit the feasibility of this strategy in many North American communities.[8,13] This registry has demonstrated a median time from presentation at the first hospital to PCI at the second hospital of 180 minutes,[13] which greatly exceeds the current recommendations for 90-minute medical contact–to-balloon interval.[12,14,15]

Another potential solution is a strategy of EMS personnel triage of STEMI patients directly to centres capable of PCI, bypassing closer non-PCI centres as necessary.[16–22] The American Heart Association, in their 2005 Guidelines for Emergency Cardiovascular Care and Cardiopulmonary Resuscitation, was unable to recommend this strategy because of inadequate evidence.[14,15] The ideal strategy for patients who are diagnosed with STEMI by emergency care providers in the prehospital setting remains unclear.

Goals of this investigation

We sought to determine whether direct transport to primary PCI centres improves 30-day mortality when compared with the standard strategy of transportation to the closest hospital for patients diagnosed with STEMI by prehospital emergency care providers.

METHODS

Study design

We performed a systematic review and meta-analysis of the world literature on this topic. We followed the Meta-analysis of Observational Studies in Epidemiology Group (MOOSE) guidelines for reporting our study.[23]

Criteria for considering studies for review

Studies considered for inclusion in the review were randomized controlled trials, quasi-randomized controlled trials, before–after studies and comparative cohort studies. Studies were included only if they reported data on adults (> 18 yr) who were diagnosed with acute STEMI, experienced chest pain for less than 12 hours and were identified by EMS personnel in the prehospital environment. There were no restrictions on the type of EMS system including personnel qualifications or crew configuration. The criterion for the treatment group intervention was that 12-lead prehospital electrocardiography (ECG) was used by EMS personnel to identify STEMI, followed by direct transportation from the scene to an interventional centre for primary PCI. Acceptable comparison groups included patients with STEMI who were identified through a 12-lead prehospital ECG and who received subsequent transportation to the nearest available emergency department (ED) with or without the administration of a prehospital fibrinolytic. Studies needed to report at least 1 outcome of all-cause mortality, reinfarction rate, stroke rate, the occurrence of cardiogenic shock or treatment time intervals including symptom onset to intervention, 911 call to intervention or medical contact to intervention. Intervention time was defined as either the time to needle insertion for fibrinolysis or the time to balloon inflation for PCI. Abstract-only publications were excluded.

Search strategy

We searched the following electronic databases: OVID MEDLINE (1980–July 2007), OVID EMBASE (1980–July 2007), Cochrane "CENTRAL" database of randomized studies (Cochrane Library Wiley Interscience, 1980–July 2007), Web of Science (1980–July 2007), CINAHL on EBSCO (1980–September 2006), OVID HealthStar (1980–September 2006), Proquest Digital Dissertations (1980–September 2006), the NIH CRISP database (1980–September 2006), and clinicaltrials.gov (Jul. 18, 2007). We used modified components of the Cochrane Collaboration Prehospital and Emergency Health Field search strategy.[24] Key search terms included "emergency medical services," "emergency medical technicians," "emergency medicine," "ambulances," "air ambulances," "allied health personnel," "prehospital," "paramedic," "myocardial infarction," "acute coronary syndrome," "chest pain," "transportation of patients," "patient transfer," "angioplasty," "heart catheterization,"

"percutaneous coronary intervention" and "primary angioplasty," in addition to several acronyms (e.g., STEMI) and synonyms for these terms. The full OVID MEDLINE search strategy can be seen in Table 1. There were no restrictions on language of publication.

We hand searched the references of included studies and we attempted contact with the principle authors of included studies for knowledge of relevant studies.

Selection of studies

Two investigators (S.C.B. and K.S.A.) reviewed all English citations independently in a hierarchical manner. They were blinded to author, institutional affiliation, source journal and year of publication. Titles classified as "include" or "indeterminate" by at least 1 of the investigators were included in the next iteration of review by abstract. Similarly, we identified full articles for review. Disagreements during the full-article review were resolved by consensus between the 2 authors. Interrater reliability for each stage of the review process for inclusion was quantified using a κ statistic. An international network of 20 volunteer translators was established to review non-English studies for relevance. The reviewers of non-English articles were not blinded. The volunteers were all health care providers or academic professionals identified through personal contacts of the first author (S.C.B.). In a similar manner to the English reviewers, the reviewers of non-English articles were instructed on the purpose of the systematic review, the inclusion and exclusion criteria and the use of the data form.

Outcome measures

The primary outcome measure for the review was determined a priori to be 30-day all-cause mortality. Based on limited data discovered with the review, a post hoc combination of in-hospital or 30-day mortality was defined as "short-term mortality" and used as the primary outcome. Secondary outcomes, determined a priori, included reinfarction, stroke and cardiogenic shock at 30 days, as well as clinically relevant time intervals including symptom onset to intervention (either time to needle or time to balloon), medical contact to intervention and EMS on-scene time.

Data extraction and analysis

Two investigators (M.W. and L.J.M.) abstracted data independently on the features of study design, interven-

tion and control conditions, patient characteristics and reported outcomes. Data abstraction was standardized between the 2 investigators by using a common data abstraction form that was developed a priori and subject to pilot testing. The quality of the included studies was evaluated independently by 2 investigators (S.C.B. and P.R.V.) using a modified version of the Thomas Quality Assessment Tool for Quantitative Studies.[25] Reviewers for both data abstraction and quality assessment were blinded to source institution, journal, date of publication and author. Disagreements between investigators for each process were resolved by consensus.

The clinical heterogeneity of included trials was explored qualitatively with a detailed examination of study characteristics. The χ^2 test of homogeneity was used with a significance cut-off of 0.10 to test for statistical

Table 1. OVID MEDLINE search strategy			
Line no.	Search term	Line no.	Search term
1	exp Emergency Medical Services	32	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
2	exp Emergency Medical Technicians		
3	exp Emergency Medicine	33	exp Myocardial Infarction/
4	exp Ambulances	34	exp Chest Pain/
5	exp Air Ambulances	35	exp Electrocardiography/
6	exp First Aid	36	exp Coronary Disease/
7	exp Military Medicine	37	exp Angina, Unstable/
8	exp Emergency Medical Service Communication Systems	38	myocardial infarct$.mp.
		39	AMI.mp.
9	exp Allied Health Personnel	40	MI.mp.
10	prehospital.mp.	41	STEMI.mp.
11	pre-hospital.mp.	42	acute coronary syndrome$.mp.
12	paramedic$.mp.	43	acs.mp.
13	ambulance$.mp.	44	ST-segment elevation.mp.
14	out-of-hospital.mp.	45	ST-elevation.mp.
15	out of hospital.mp.	46	chest pain.mp.
16	EMS.mp.	47	33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
17	EHS.mp.		
18	EMT.mp.	48	exp Angioplasty/
19	emergency services.mp.	49	exp Angioplasty, Transluminal, Percutaneous Coronary
20	emergency medical service$.mp.	50	exp Balloon Dilatation
21	emergency technician$.mp.	51	exp Heart Catheterization
22	emergency practitioner$.mp.	52	angioplasty.mp.
23	emergency dispatch$.mp.	53	percutaneous coronary intervention$.mp.
24	emergency despatch$.mp.	54	PCI.mp.
25	first responder$.mp.	55	PTCA.mp.
26	emergency rescue$.mp.	56	primary angioplasty.mp.
27	emergency triage.mp.	57	percutaneous transluminal coronary angioplasty.mp.
28	exp "Transportation of Patients"	58	primary coronary angioplasty.mp.
29	on-scene.mp.	59	48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58
30	on scene.mp.		
31	exp Patient Transfer/	60	32 and 47 and 59

$ = truncation (retrieves unlimited suffix variation); / = medical subject heading designator (retrieves all articles with this particular medical subject heading); acs = acute coronary syndrome; AMI = acute myocardial infarction; EHS = emergency health services; EMS = emergency health services; EMT = emergency medical technician; exp = explode (searches for term and all its conceptually narrower terms within the OVID medical subject heading tree); MI = myocardial infarction; mp = textword search (searches for the word or words in the title, abstract or medical subject headings of articles); PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; STEMI = ST-segment elevation myocardial infarction.

heterogeneity. For all other hypothesis testing, a significance cut-off of 0.05 was used. The I^2 statistic was used to quantify statistical heterogeneity and determine the appropriateness of pooling results across studies. Studies were not pooled if the I^2 was > 50% indicating significant statistical heterogeneity. We used the DerSimonian–Laird method (i.e., the random effects model) to provide pooled estimates of relative risk when the data allowed. Pooled estimates and forest plots were generated using Review Manager 4.2.10 (The Cochrane Collaboration).

RESULTS

Trial flow

The original comprehensive search identified 2264 citations published in 14 languages (Fig. 1). Ninety-eight full articles that were not published in English were reviewed. Five studies met all inclusion criteria and were included in the review.[26–30] Interrater reliability for each stage of the review process for inclusion was quantified using a κ statistic. The κ was 0.55 for titles, 0.68 for abstracts and 0.92 for full articles. One author (S.C.B.) completed an updated search of MEDLINE, EMBASE and the Cochrane library up to May 2008 and no additional relevant studies were identified.

Study characteristics

Table 2 outlines the characteristics of the 5 included studies, which include a total of 980 patients. There were 2 randomized controlled trials,[26,29] 2 prospective observational studies with concurrent controls[28,30] and 1 prospective observational study with a historical control group.[27] Three of the studies occurred in European EMS systems with ambulance medical doctors as the primary prehospital care provider.[28–30] The other 2 studies were Canadian.[26,27] Detailed descriptions of prehospital diagnostic techniques and the process of catheterization laboratory activation were lacking. Prehospital ECG interpretation was not described in one study,[26] performed by the ambulance physician in 2 studies,[28,29] by computer with ambulance nurse confirmation in one study,[30] and by paramedic in one study.[27] Two studies reported that the EMS personnel directly activated the catheterization laboratory,[27,30] whereas the process of activation was unclear in the others.

The method of allocating patients to the intervention or control group varied. The 2 observational studies with concurrent control groups used convenience methods

or patient clinical features to determine group allocation. For example, in the Terkelsen and colleagues study,[28] only patients cared for by an ambulance crew which included a physician were allocated to the PCI arm of the study. In the van Bavel and colleagues study,[30] group allocation was determined by the degree of ST-segment elevation on the prehospital ECG. Quality varied considerably across the included studies (Table 3).

Quantitative data synthesis

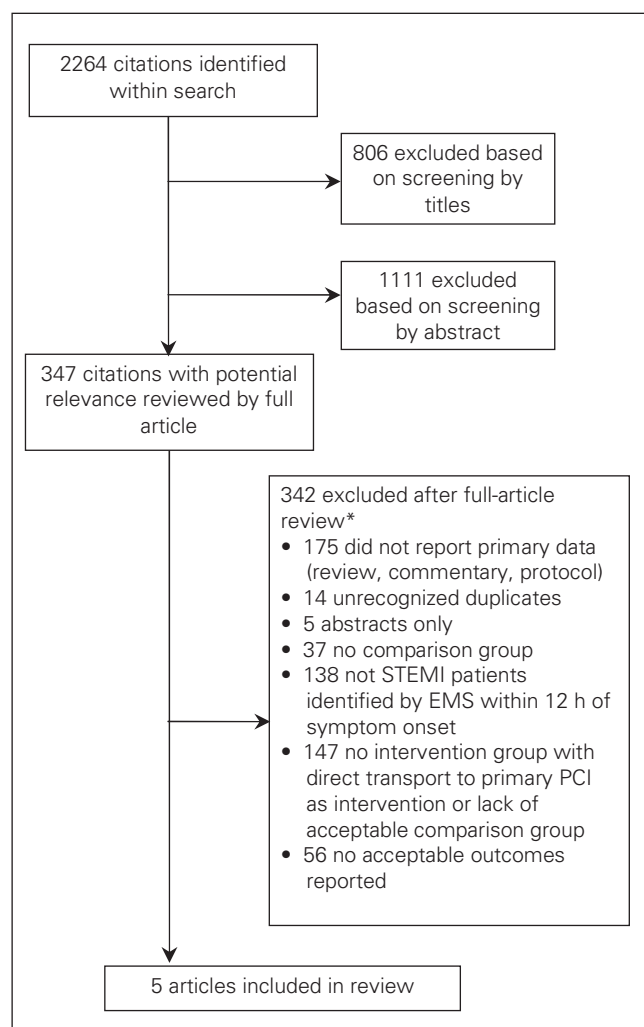Four studies reported short-term mortality[27–30] (Fig. 2).

Fig. 1. Trial flow. After review of 2264 citations by title and abstract, 347 were considered to be potentially relevant. After review by full article, 342 were excluded for various reasons. Five were found to meet criteria for inclusion in the review. EMS = emergency medical services; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction. *Component counts do not sum to total number excluded because many articles had multiple reasons for exclusion.

There was no evidence of statistical heterogeneity among these 4 studies (χ^2 = 2.77, df = 3, p = 0.43 and I^2 = 0%). The pooled relative risk (RR) for short-term mortality demonstrates a trend toward reduction with direct transport for primary PCI, but did not reach statistical significance (RR 0.51, 95% confidence interval [CI] 0.24–1.10). One study[29] demonstrated reductions in the rate of reinfarction (RR 0.43, 95% CI 0.11–1.60) and stroke (RR 0.33, 95% CI 0.01–8.06) at 30 days, which were not statistically significant. None of the included studies reported

rates of cardiogenic shock. Clinical outcome data from the Armstrong study[26] could not be included in the pooled analysis because published data were for the entire study population, which included some patients initially assessed in the ED. Prehospital subgroup data were requested from the primary author, but could not be obtained. Time interval outcome data are displayed in Table 4. All time intervals were reported as medians and therefore weighted means could not be calculated. The relative effect of direct transport to primary PCI on symptom

Table 2. Characteristics of 5 studies included in the review

Study	Design	Intervention group	Control group	Participants	EMS provider type	Relevant outcome data reported
Armstrong[26]	RCT	Direct transport from scene to PCI with clopidogrel 300 mg	PH fibrinolysis with TNK followed by transport to closest ED	n = 200 Age, median (IQR) = IG: 60 (49–71); CG: 58 (51–69) % male = IG: 82; CG: 75 % anterior MI = IG: 42; CG: 42 Exclusions = PCI available within 1 h of diagnosis, CIs to fibrinolysis, prior CABG, GP antagonist within 7 d	Not stated	Symptom onset to intervention time interval, medical contact to intervention time interval
Le May et al.[27]	Prospective observational cohort with historical control group	Direct transport from scene to PCI	• Historical controls • Transport to closest ED	n = 333 Mean age (SD) = IG: 64.3 (14); CG: 64.5 (14.5) % male = IG: 70.4; CG: 66.2 % anterior MI = IG: 44.4; CG: 46.0 Exclusions = VSA, hemodynamic instability, LBBB	Paramedic	All-cause mortality (in-hospital), composite outcome (death or stroke), stroke (at unspecified time point)
Thiele et al.[29]	RCT	PH ½ dose fibrinolysis with reteplase, abciximab, direct transport from scene to PCI	PH ½ dose fibrinolysis with reteplase, abciximab, and transport to ED	n = 164 Median age, yr (IQR) = IG: 65 (57–72); CG: 60 (52–69) % male = IG: 74; CG: 78 % anterior MI = IG: 46; CG: 50 Exclusions = CIs to fibrinolysis	MD	All-cause mortality (30 d, 6 mo), composite (death, reinfarction, stroke) (30 d, 6 mo), on-scene time
Terkelsen et al.[28]	• Prospective observational cohort with concurrent control group • Allocation determined by availability of MD for transport	Direct transport from scene to PCI (only if MD present)	• Transport to closest ED then inter-hospital transfer for PCI • No prehospital diagnosis	n = 106 Median age, yr (IQR) = IG: 63 (54–71); CG: 67 (56–75) % male = IG: 90; CG: 65 % anterior MI = IG: 33; CG: 40 Exclusions = PCI physician did not confirm STEMI, > 12 h symptoms, walk-in patients, unconscious on arrival	MD or ambulance personnel	In-hospital mortality, symptom onset to intervention, on scene time
van Bavel et al.[30]	• Prospective observational study with concurrent control group • Allocation determined by degree of STE on ECG	Direct transport from scene to PCI	PH fibrinolysis followed by transport to closest ED	n = 177 Age, yr = unknown statistic IG: 60.7; CG: 65 % male = IG: 77; CG: 73 % anterior MI = IG: 57; CG: 24 Exclusions = not reported	MD and RN	All-cause mortality (24 h, 30 d, 1 yr), composite outcome (death, reinfarction, stroke, need for revascularization) (30 d, 1 yr)

CABG= coronary artery bypass graft; CG = control group; CIs= contraindications; ED = emergency department; EMS = emergency medical services; GP = glycoprotein; IG = intervention group; IQR = interquartile range; LBBB= left bundle branch block; MD = medical doctor; MI = myocardial infarction; PCI = percutaneous coronary intervention; PH = prehospital; RCT = randomized controlled trial; RN = registered nurse; SD = standard deviation; STE = ST-elevation; STEMI = ST-elevation myocardial infarction; TNK = tenecteplase; VSA = vital signs absent.

onset–to-intervention interval was highly dependent on the nature of the comparison strategy. For example, Armstrong[26] reported a 49-minute additional delay in median symptom onset–to-intervention time when the comparison was prehospital fibrinolysis. In contrast, Terkelsen and colleagues[28] reported a reduction of 46 minutes when the comparison was between transportation to the local hospital followed by interhospital transfer for primary PCI.

Table 3. Results of quality review of the 5 included studies, using the Thomas Quality Assessment Tool

Study	Design	Selection bias	Allocation bias	Baseline confounder	Blinding	Follow-up rate
Armstrong[26]	RCT	Weak*	Moderate†	Strong‡	Strong	Strong
Thiele et al.[29]	RCT	Weak	Strong	Strong	Strong	Strong
Terkelsen et al.[28]	Observational	Moderate	Weak	Weak	Weak	Strong
van Bavel et al.[30]	Observational	Weak	Weak	Weak	Weak	Strong
Le May et al.[27]	Observational	Moderate	Moderate	Strong	Weak	Strong

RCT = randomized controlled trial.
*Poor quality methodology and high risk of bias.
†Moderate quality methodology and moderate risk of bias.
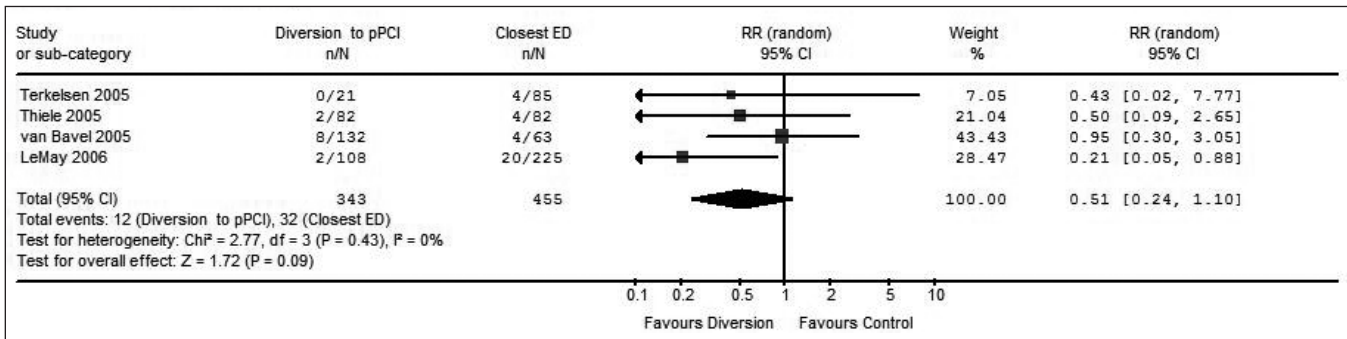‡Strong quality methodology and low risk of bias.

Fig. 2. Short-term mortality comparison between those diverted to primary percutaneous coronary intervention (pPCI) and those transported to the closest emergency department (ED). The short-term mortality (30 d or in-hospital) in patients diverted directly to primary PCI by emergency medical services personnel as compared with those transported to the closest hospital for initial treatment is shown. The relative risk (RR) generated from individual studies (squares) and 95% confidence intervals (CIs) (horizontal lines) are plotted. The diamond represents the pooled RR and 95% CI generated with a random effects model. When the horizontal bars or the diamond cross 1, the effect of direct transport to primary PCI is not statistically different from transportation to the closest hospital. n = number of deaths, N = total number of patients in group.

Table 4. Median time interval data from the 5 included studies

	Time interval, min (IQR)					
	Symptom onset to intervention		On scene		Medical contact to intervention	
Study	Direct to PCI	Closest ED	Direct to PCI	Closest ED	Direct to PCI	Closest ED
Armstrong[26]	140 (115–171) PCI start	91 (70–156) PH fibrinolysis	NR	NR	104 (88–126) ambulance arrival to PCI	46 (35–55) ambulance arrival to fibrinolysis
Thiele et al.[29]	140 (95–220)	NR	NR	NR	NR	NR
Le May et al.[27]	NR	NR	43 (34–52)	41 (35–50)	NR	NR
Terkelsen et al[28]	129 (99–185) PCI start	175 (149–266) PCI start after IH transfer	21 (16–23)	13 (10–17) (no PH ECG)	NR	NR
van Bavel et al.[30]	NR	NR	NR	NR	NR	NR

ECG = electrocardiogram; ED = emergency department; IH = interhospital; IQR = interquartile range; NR = not reported; PCI = percutaneous coronary intervention; PH = prehospital.

Subgroup analysis

A post hoc subgroup analysis was conducted to explore the effect of control group intervention on treatment effect (Fig. 3). We grouped studies by the presence or absence of prehospital fibrinolytic use in control group patients. Among the 2 studies with prehospital fibrinolysis use in the control group, diversion to primary PCI was not associated with a statistically significant reduction in mortality, when compared with transportation to the closest hospital (pooled RR 0.77, 95% CI 0.30–2.01). Among studies involving other control group strategies (e.g., transportation to the closest hospital without prehospital fibrinolysis and interhospital transfer for PCI) short-term mortality was lower with a strategy of diversion to primary PCI versus a strategy of transportation to the closest hospital (pooled RR of 0.24, 95% CI 0.07–0.87).

DISCUSSION

After a comprehensive systematic review of the world literature, we found that there were insufficient data derived from direct comparisons to support the effectiveness of direct transport of prehospital STEMI patients for primary PCI when compared with transportation to

the closest hospital. The sparse data has been produced by 5 heterogeneous studies with major methodological flaws. With respect to contemporary North American emergency medical systems, the generalizability of the data we present in this review is limited, given that only 2 studies were from Canada. Only 1 study described prehospital 12-lead interpretation by a paramedic.

We have discovered that the enthusiasm for direct transport to primary PCI, as demonstrated by implementation in systems across North America, Europe and Australia,[16–18,20–22] is not supported by any studies directly comparing strategies for STEMI patients diagnosed in the prehospital setting. The most recent Canadian report of such an implementation is from Ottawa, Ont.[16] The authors compare a cohort of 135 STEMI patients who were brought directly to a PCI centre by EMS, bypassing local EDs as necessary, with a cohort of 209 patients diagnosed in community EDs and subsequently transferred to a PCI centre for primary PCI. Eighty percent of the field triage patients achieved a door-to-balloon time of less than 90 minutes. Only 11.9% of 209 patients referred from community EDs achieved a door-to-balloon time of less than 90 minutes. These findings are consistent with previous studies demonstrating the time savings associated with the prehospital diagnosis of STEMI.[31–33]
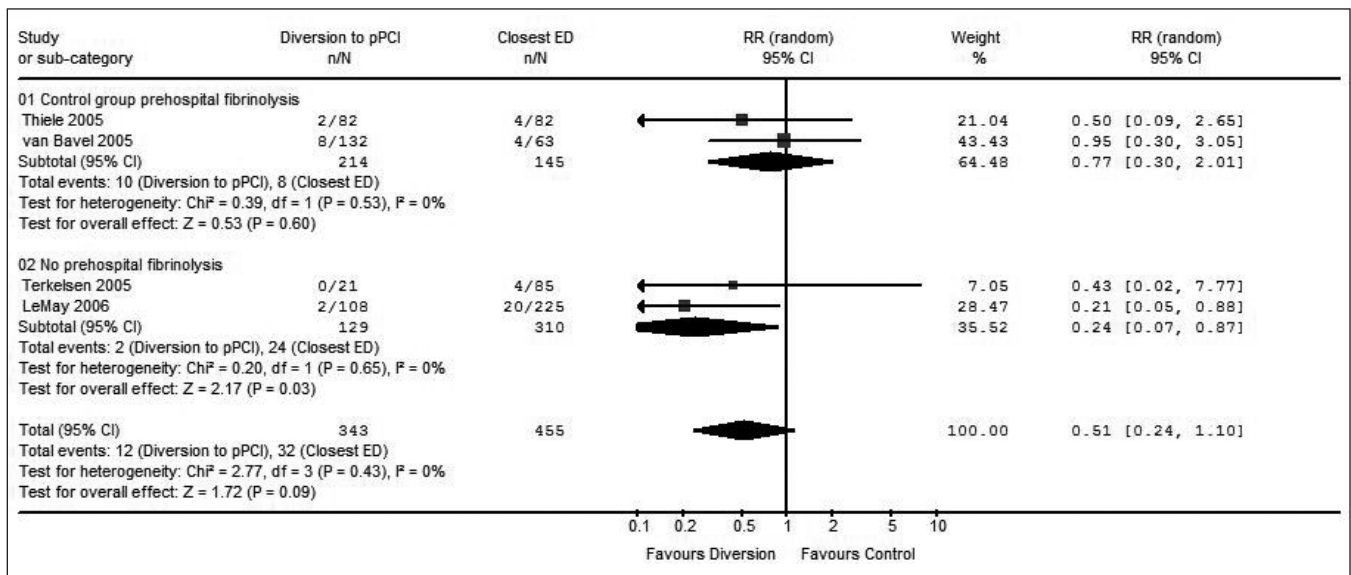

Fig. 3. Short-term mortality outcomes by control group intervention type. The short-term mortality (30 d or in-hospital) in patients diverted directly to primary percutaneous coronary intervention (pPCI) by emergency medical services personnel as compared with those transported to the closest hospital for initial treatment grouped by type of control intervention is shown. The relative risk (RR) generated from individual studies (squares) and 95% confidence intervals (CIs) (horizontal lines) are plotted. Pooled estimates of effect (random effects model) for each subgroup and all studies are represented as diamonds. When the horizontal bars or the diamond cross 1, the effect of direct transport to primary PCI is not statistically different from transportation to the closest hospital. ED = emergency department; n = number of deaths, N = total number of patients in group.

Although it remains unclear whether direct transportation for primary PCI is superior to other strategies involving transportation to the closest hospital, our subgroup analysis (Fig. 3) allows us to hypothesize that direct transport for primary PCI may be superior to strategies involving transportation to the closest hospital only when prehospital fibrinolytic is not used. This is consistent with data from 2 recent French studies, including a registry and randomized controlled trial of prehospital patients with STEMI, which have also cast doubt on the superiority of PCI over prehospital fibrinolysis in certain settings.[34,35]

There are 2 time variables that are hypothesized to be important in determining the optimal reperfusion strategy for any given patient with STEMI: 1) time from symptom onset to reperfusion decision and 2) the "delta" time. The delta is the theoretical time interval between when the patient could receive a fibrinolytic and when the patient could have a PCI balloon inflated across the culprit coronary lesion.

With regard to the time from symptom onset to reperfusion decision interval, there is a hypothesis based on several post hoc subgroup analyses from previous studies that primary PCI may not be superior to fibrinolysis in patients who present very early after the onset of symptoms (e.g., < 2–3 h).[9,36,37] The time data in Table 4 shows that at least 3 of 5 studies (2 did not report) contained a significant number of patients who presented early based on median symptom onset–to-intervention time intervals, but this group of patients was not reported separately.

With regard to the second time variable (i.e., the delta) it remains unclear when the physiologic advantage of primary PCI over fibrinolysis with respect to mortality, reinfarction and stroke is offset by the associated additional delay to reperfusion. In the CAPTIM trial,[35] in which STEMI patients were randomly assigned in the prehospital setting to receive primary PCI or prehospital fibrinolysis, primary PCI caused greater delay between symptom onset to reperfusion (i.e., a median delay of 190 min for PCI v. 130 min for prehospital fibrinolysis) and no clinical advantage was observed with respect to a combined end point of death, reinfarction and stroke at 30 days (6.2% for primary PCI v. 8.2% for prehospital fibrinolysis, p = 0.29). CAPTIM was excluded from this review because both arms of the trial involved direct transport to specialized cardiac care centres with primary PCI facilities. Pinto and colleagues,[38] report data from the National Registry of Myocardial Infarction from 1994 to 2003 for 192 509

STEMI patients admitted to hospital. They analyzed the association between the delta at the level of the hospital (median door-to-balloon interval minus median door-to-needle interval), and the clinical outcome. In-hospital mortality increased 10% with every 30-minute increase in the delta. The adjusted mortality was identical for fibrinolytic therapy and primary PCI when the delta was 114 minutes (95% CI 96–132 min). In contrast, data from the Swedish RIKS-HIA registry[39] on 26 205 consecutive STEMI patients, suggest that even in early presenters (< 2 h symptom duration) the superior strategy is primary PCI, as long as the delta is less than 4 hours. Unfortunately, the data from studies included in this review did not allow for a detailed exploration of the relationship between the relative benefit of the prehospital strategies and these key time intervals.

Although there have been many studies comparing immediate fibrinolysis to primary PCI in admitted patients,[8] we have identified a paucity of prehospital data. This has resulted in data being extrapolated from hospital to the prehospital setting in the creation of guidelines and national initiatives.[14,15,10] There are several reasons why this may be misleading. Compared with patients who self-transport to the ED, patients who call EMS with acute coronary syndrome tend to have had a shorter duration of symptoms before seeking medical care, and are more likely to have a previous history of cardiac disease. They are older, more likely to be female and receive more aggressive management when they reach the hospital.[40] There are many feasibility and safety issues that are unique to the management of STEMI patients in the prehospital setting. These include the diagnostic ability of prehospital providers, the ability to safely administer prehospital fibrinolysis, potential transport delays associated with diversion to a PCI centre, and the ability of a system to effectively activate PCI resources from the prehospital setting.

Prehospital data should be sought before we implement costly large-scale regionalization projects and STEMI "systems of care," which include direct transport for primary PCI. There are certainly sound arguments to pursue further research on direct transportation for primary PCI as a potential strategy for Canadian prehospital STEMI patients for several reasons: current medical contact–to-balloon times in North America are unacceptably long,[38,41,42] there is a clear relationship between reperfusion delay and mortality,[41,42] improved outcomes have been demonstrated in patients transferred from community hospitals to PCI centres for primary PCI when compared with

in-hospital fibrinolysis[7,9] and prehospital fibrinolysis is not available in most North American EMS systems. Future trial design should incorporate specific analyses of patients who present within 2–3 hours of symptom onset and explore whether clinical characteristics such as age and infarct location should influence the choice of reperfusion strategy for the prehospital STEMI patient.

Limitations

Our study has several limitations. We excluded abstract-only reports and may have missed some relevant data. Second, the missing data from the Armstrong (WEST) trial[26] represents 10% of the patients included in the final review and would have allowed for more meaningful pooled estimates. A formal analysis for publication bias was not conducted, because we found no statistically significant effect on our primary outcome, making the calculation of a fail-safe number nonsensical, and there were too few studies to compose a useful funnel plot. We make the conservative assumption that a number of small negative unpublished trials were missed, and our results may be biased toward showing a more positive effect than truly exists.

The studies included in this review had significant potential for bias, and, thus, the results of the meta-analysis have been interpreted with caution. Particular to the studies included in this review, the issue of allocation bias is significant. Several studies did not adequately report important operational details, such as the process of catheterization laboratory activation, making it difficult to compare studies and determine the generalizability of their findings.

We made a post hoc decision to change our primary outcome to a composite of in-hospital or 30-day mortality because few studies reported 30-day mortality. In-hospital mortality was expected to closely estimate 30-day mortality and, accordingly, this change was expected to have little impact on our final conclusions.

Because of the nature of prehospital care, the relative benefit of diversion to primary PCI versus transportation to the closest hospital is very likely to be dependent on a host of particular local variables, such as geography, the relative distribution of hospitals within a region, EMS system configuration and the quality of STEMI management at each of the local hospitals. The results from any investigation exploring this issue need to be considered carefully in the context of local conditions.

CONCLUSION

There is insufficient evidence to support the effectiveness of direct transport for primary PCI when compared with transportation to the closest hospital in patients with STEMI. Further research is needed to determine the optimal prehospital strategy for STEMI patients. There should be a focus on the use of prehospital fibrinolysis as an alternative strategy to direct transport for PCI. Future studies should also address the impact of symptom duration on the relative treatment effect of one reperfusion strategy over the other.

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