Note: This is a two-article spread with a shared commentary. Please scroll down for the second article.

Rescue angioplasty reduced cardiovascular and cerebrovascular outcomes in acute MI after failed thrombolytic therapy

Gershlick AH, Stephens-Lloyd A, Hughes S, et al. **Rescue angioplasty after failed thrombolytic therapy for acute myocardial infarction.** N Engl J Med. 2005;353:2758-68.

Clinical impact ratings: Hospitalists ★★★★★★☆ Cardiology ★★★★★★☆

QUESTION

In patients with acute myocardial infarction (MI) after failed thrombolytic therapy, does rescue percutaneous coronary intervention (PCI) reduce cardiovascular and cerebrovascular events?

METHODS

Design: Randomized controlled trial (Rescue Angioplasty versus Conservative Treatment or Repeat Thrombolysis [REACT]).
Allocation: {Unconcealed}†.*
Blinding: Blinded (outcome assessors {and data analysis}†).*
Follow-up period: 6 months.
Setting: 35 centers in the United Kingdom.
Patients: 427 patients 21 to 85 years of age (mean age 61 y, 79% men) who had MI with ST-segment elevation ≥ 0.1 mV in ≥ 2 contiguous leads (excluding V_1) and had received aspirin and thrombolysis within 6 hours of symptom onset, and electrocardiogram showed failed thrombolytic therapy at 90 minutes. Exclusion criteria included probable inability to gain femoral access for intervention, left bundle-branch block, < 6 months life expectancy, hemoglobin level > 1.5 g/dL below normal range and platelet count below normal range within the pre-vious 6 hours, elevated blood pressure, cardio-genic shock, and administration of low-molecular-weight heparin in the previous 12 hours.
Intervention: Rescue PCI (n = 144) (coronary angiography, proceeding to angiography if required, and stenting or glycoprotein IIb/IIIa receptor inhibition at discretion of the interventionist), repeated thrombolysis (alteplase or reteplase) (n = 142), or conservative therapy (n = 141).
Outcomes: Composite endpoint of death, recurrent MI, cerebrovascular event, and severe heart failure. Secondary outcomes were components of the primary outcome, bleeding, and revascularization.
Patient follow-up: 93% (intention-to-treat analysis).

MAIN RESULTS

At 6 months, fewer patients in the rescue PCI group had the primary composite endpoint than patients in the repeated thrombolysis group or in the conservative therapy group (Table). Rescue PCI also led to lower rates of mortality, recurrent MI, and revascularization (Table). Rescue-PCI, repeated-thrombolysis, and conservative-therapy groups did not differ for cerebrovascular events, severe heart failure, and major bleeding events, but the rescue PCI group had a higher rate of minor bleeding events than the other 2 groups (23% vs 7.0% vs 5.7%, $P < 0.001$).

CONCLUSION

In patients with acute myocardial infarction (MI) after failed thrombolytic therapy, rescue angioplasty reduced a composite endpoint of death, recurrent MI, cerebrovascular event, and severe heart failure.

Sources of funding: British Heart Foundation and Roche Pharmaceuticals.

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*See Glossary.
†Information provided by author.

Rescue percutaneous coronary intervention (PCI) vs repeated thrombolysis (RT) or conservative therapy (CT) for acute myocardial infarction (MI) after failed thrombolytic therapy at 6 months‡

Outcomes	Comparisons	Event rates	RRR (CI)	NNT (CI)
Primary composite endpoint§	PCI vs RT	15% (22/144) vs 31% (44/142)	52% (24 to 70)	7 (5 to 14)
	PCI vs CT	15% (22/144) vs 30% (42/141)	49% (18 to 68)	7 (5 to 19)
Mortality	PCI vs (RT + CT)	6.3% vs 13%	50% (1 to 76)	16 (11 to 825)
Recurrent MI	PCI vs RT	2.1% vs 11%	76% (37 to 91)	12 (11 to 25)
	PCI vs CT	2.1% vs 8.5%	66% (6.7 to 88)	18 (14 to 176)
Revascularization	PCI vs RT	13% vs 23%	47% (11 to 68)	10 (7 to 41)
	PCI vs CT	13% vs 21%	39% (–3.5 to 64)	Not significant

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from adjusted or unadjusted hazard ratios in article.
§Death (PCI vs RT vs CT = 6.3% vs 13% vs 13%), recurrent MI (2.1% vs 11% vs 8.5%), cerebrovascular event (2.1% vs 0.7% vs 0.7%), or severe heart failure (4.9% vs 7.8% vs 7.0%).

COMMENTARY

Treatment of STEMI with PCI is well-established. However, because of limited facilities for PCI, first-line therapy in 30% to 70% of patients is thrombolytic therapy (1). Although thrombolysis reduces mortality more than placebo, normal blood flow (TIMI grade 3 flow) is restored in only 60% of patients (2). Given the intermediate success rate of thrombolytics in reperfusing the infarct-related artery as well as the high rate of reocclusion/reinfarction, the strategy of routine, early-invasive evaluation with revascularization after thrombolysis has been hypothesized to further improve outcomes.

The REACT trial shows the superiority of rescue PCI over conservative treatment or repeated thrombolysis in patients without clinical reperfusion at 90 minutes after initial thrombolysis. It is important to note that patients who were transferred to a tertiary care center for an interventional procedure also benefited.

In the meta-analysis by Cantor and colleagues, 3 stent-era RCTs showed that the early invasive strategy reduced mortality and recurrent MI more than the conservative strategy after thrombolysis for STEMI. In contrast, meta-analysis of 5 balloon angioplasty-era RCTs did not show benefit of an early invasive strategy. This result reflects some of the improvements in modern PCI, such as smaller guide catheters, low-profile stents, thienopyridines, glycoprotein IIb/IIIa inhibitors, and other adjunctive therapies (and perhaps more experienced operators). These technologies have greatly reduced the early hazard associated with rescue PCI as well as substantially improved the short- and long-term patency of infarct vessels. Mechanistically, an open infarct-related artery and "open myocardium," both early and late, led to myocardial salvage in STEMI; improved infarct healing; and reduced rates of reinfarction, angina, lethal arrhythmias, and heart failure.

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Review: Evidence supporting reduced death and reinfarction by percutaneous coronary intervention after thrombolysis is inconclusive

Cantor WJ, Brunet F, Ziegler CP, Kiss A, Morrison LJ. **Immediate angioplasty after thrombolysis: a systematic review.** CMAJ. 2005;173:1473-81.

Clinical impact ratings: Emergency Med ★★★★★★★ Hospitalists ★★★★☆☆☆ Cardiology ★★★★☆☆☆

QUESTION

In patients with ST-segment elevation myocardial infarction (STEMI) in a prehospital setting or a community hospital emergency department, is immediate or early percutaneous coronary intervention (PCI) after thrombolysis more effective than delayed PCI?

METHODS

Data sources: MEDLINE, EMBASE/Excerpta Medica, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, American Heart Association (AHA) EndNote 7 Master Library, and relevant references (from 1985 to 2004).

Study selection and assessment: Exclusion criteria were PCI done > 24 hours after thrombolysis, no PCI intervention, sample size < 30, or no control group. Assessment of individual study quality was based on 7 levels of evidence (level 1 = highest) and 4 degrees (excellent, fair, poor, and unsatisfactory) of design and methods according to the AHA International Liaison Committee on Resuscitation classification.

Outcomes: Death and a composite endpoint of death and reinfarction at 12 months.

MAIN RESULTS

37 studies met the selection criteria; 18 were randomized controlled trials (RCTs). Meta-analysis (8 RCTs with good or fair degree, $n = 2598$) showed that PCI and delayed PCI groups did not differ for death or the composite endpoint of death and reinfarction within 12 months (1 RCT at 6 mo) (Table). Among these 8 RCTs, meta-analysis of 3 stent-era RCTs ($n = 861$) showed that the PCI group had lower mortality and lower rates of the composite endpoint (1 study at 6 mo) (Table).

CONCLUSIONS

In patients with ST-segment elevation myocardial infarction in a prehospital setting or a community hospital emergency department, evidence from meta-analysis of 8 trials does not show a reduction in death and reinfarction with immediate or early (< 24 h) percutaneous coronary intervention. Stent-era trials show a reduction.

Source of funding: No external funding.

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Immediate or early percutaneous coronary intervention (PCI) vs delayed PCI after thrombolysis for ST-segment elevation myocardial infarction at 12 months (1 study at 6 mo)*

Outcomes	Number of trials (*n*)	RRR (95% CI)	NNT (CI)
Composite endpoint†	8 (2598)	16% (–1.1 to 31)	Not significant
	3 (stent era) (861)	36% (9.1 to 56)	15 (10 to 57)
	5 (prestent era) (1737)	6.0% (–277 to 25)	Not significant
Mortality	8 (2598)	9.8% (–17 to 31)	Not significant
	3 (stent era) (861)	43% (7.2 to 65)	24 (16 to 140)
		RRI (CI)	**NNH**
	5 (prestent era) (1737)	9.0% (–20 to 48)	Not significant

*Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from odds ratios and control event rates provided by author using a fixed-effects model.
†Death and reinfarction.

COMMENTARY *(continued from page 60)*

The results of REACT, the review by Cantor and colleagues, and other studies have several practical implications for clinical practice in patients with STEMI who receive thrombolytics. First, these patients should be considered for immediate transfer to a PCI center such that there is no delay in undergoing angiography if thrombolytic reperfusion is incomplete. A caveat exists from the PRAGUE trial (3) that supports transfer for PCI without administering thrombolytics if PCI will be available in less than 90 minutes. Second, except for patients with severe comorbid conditions, angiography should be done during the index hospitalization.

The optimal timing of angiography in the postthrombolysis patient remains controversial. In REACT, the review by Cantor and colleagues, and other current studies (3-5), angiography or PCI was done within 4 to 24 hours from symptom onset and from 1.5 to 24 hours after thrombolysis. A limitation of these studies is that they do not specifically address the relative benefit that patients may achieve as a function of clinical evidence of successful versus failed thrombolysis. Hence, whether a patient with strong clinical evidence of reperfusion (resolution of symptoms and electrocadiographic changes) would reap the same benefit from an emergency catheterization as a patient without clinical evidence of reperfusion after thrombolysis needs further investigation.

The results of REACT and Cantor and colleagues' study are consistent with most other recent studies comparing an early, invasive strategy with a conservative one across the spectrum of acute coronary syndromes: Routine, early, invasive evaluation improved outcome.

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