THERAPEUTICS

Angioplasty at an invasive-treatment center reduced mortality compared with first-contact thrombolysis

Andersen HR, Nielsen TT, Rasmussen K, et al. **A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction.** N Engl J Med. 2003;349:733-42.

QUESTION

Is the transfer of patients with ST-segment elevation myocardial infarction (STEMI) to an invasive-treatment center (ITC) for primary angioplasty (percutaneous coronary intervention [PCI]) more effective than on-site fibrinolysis for reducing all-cause mortality, reinfarction, or stroke?

DESIGN

Randomized (allocation concealed*), blinded (outcome assessors),* controlled trial with 30-day follow-up (Danish trial in Acute Myocardial Infarction-2 [DANAMI-2]).

SETTING

24 referral hospitals (RHs) and 5 ITCs in Denmark.

PATIENTS

1572 patients ≥ 18 years age (median age 63 y, 73% men) who had STEMI. Exclusion criteria included contraindication to fibrinolysis and left bundle-branch block. Follow-up was 100%.

INTERVENTION

Patients were stratified by hospital and allocated to PCI (n = 567 at RHs and 223 at ITCs) or fibrinolysis (n = 562 at RHs and 220 at ITCs). Patients in the PCI group received heparin, 10 000 U plus aspirin, 300 mg intravenously with immediate transportation to a catheterization laboratory for acute angiography, angioplasty, and primary stenting. Fibrinolytic therapy comprised accelerated treatment with alteplase and was administered by ambulance crews.

MAIN OUTCOME MEASURE

Composite endpoint of all-cause mortality, clinical reinfarction, or disabling stroke.

MAIN RESULTS

Analysis was by intention to treat. 96% of patients allocated to PCI at RHs were transferred to an ITC ≤ 2 hours after admission. Among all patients combined and among patients randomized at RHs or ITCs separately, the rate of the composite endpoint was lower in the PCI group than in the fibrinolysis group (Table).

CONCLUSION

The transfer of patients who have had myocardial infarction with ST-segment elevation to an invasive-treatment center for primary percutaneous coronary intervention was more effective than on-site fibrinolysis for reducing all-cause mortality, reinfarction, or stroke.

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*See Glossary.

Percutaneous coronary intervention (PCI) vs on-site fibrinolysis for myocardial infarction at 30 days†

Outcome	Site of randomization	PCI	Fibrinolysis	RRR (95% CI)	NNT (CI)
Composite endpoint	All patients	8.0%	13.7%	42% (22 to 57)	18 (12 to 38)
	RHs	8.5%	14.2%	41% (17 to 58)	18 (11 to 48)
	ITCs	6.7%	12.3%	45% (0.9 to 70)	19 (9 to 1153)

†Composite endpoint = all-cause mortality, clinical reinfarction, or disabling stroke; RHs = referral hospitals; ITCs = invasive-treatment centers. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

Primary PCI offers advantages over fibrinolytic therapy when done promptly in excellent PCI centers (1). However, the conclusion from DANAMI-2 that hospitals without PCI capability must withhold fibrinolytic therapy and transfer patients for primary PCI because of the reduction in the composite endpoint of death, reinfarction, or disabling stroke compared with on-site fibrinolytic therapy deserves further scrutiny because of study design.

The composite endpoint was driven by the reduction in reinfarction rates with primary PCI. Trends for mortality and disabling stroke reduction with PCI were statistically insignificant. It is important to note that in the fibrinolysis group, rescue PCI was only used in 2% of patients and reinfarction was treated with repeated fibrinolysis instead of angioplasty. With a 30-day mortality rate of 24% after reinfarction, approximately 7 excess deaths occurred in the fibrinolysis group because of this complication. The use of low-molecular-weight heparin instead of unfractionated heparin and a more liberal policy of permitting angioplasty to treat recurrent ischemia in the fibrinolysis group probably would have decreased reinfarction rates and equalized mortality rates. In addition, the stroke rate in the fibrinolysis group was higher than noted in previous fibrinolysis megatrials: Whether the higher-than-currently-recommended unfractionated heparin dosing used in this study or the repeated fibrinolysis infusion in 26 patients contributed to this excess was not discussed. In transfer patients, time to PCI was only 90 minutes because of a superbly organized national MI triage system, compared with 185 minutes in the United States in 2002 (2).

Unless local emergency transport programs can deliver patients to PCI centers within the times observed in this study, fibrinolytic therapy should be the preferred treatment strategy for patients who present to hospitals without PCI capability. In such settings, emergency transfer to PCI centers should be reserved for moderate- and high-risk patients in whom reperfusion fails or for those who develop recurrent ischemia.

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References
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2. The National Registry of Myocardial Infarction-4 Quarterly Report. South San Francisco, CA: Genetech. March 2003.