Review: Invasive management after unstable angina or non–ST-segment elevation MI does not reduce risk for death or MI

Choudhry NK, Singh JM, Barolet A, Tomlinson GA, Detsky AS. **How should patients with unstable angina and non-ST-segment elevation myocardial infarction be managed? A meta-analysis of randomized trials.** Am J Med. 2005;118:465-74.

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

QUESTION

In patients with unstable angina or non–ST-segment elevation myocardial infarction (NSTEMI), is initial management with an invasive strategy better than a conservative strategy?

METHODS

Data sources: MEDLINE and EMBASE/Excerpta Medica (1966 to September 2003), and bibliographies of relevant articles.

Study selection and assessment: Randomized controlled trials (RCTs), published in English, that compared invasive and noninvasive strategies for early management of patients with unstable angina or NSTEMI; had ≥ 3-month follow-up; and reported mortality, reinfarction, or rehospitalization. The quality of the included trials was assessed for blinding, allocation, withdrawals, and standardization of assessment, based on the Cochrane Handbook.

Outcomes: Mortality, reinfarction, and rehospitalization.

MAIN RESULTS

7 RCTs (n = 9212, mean age 62 y) met the selection criteria. 6 RCTs were of high methodological quality. Meta-analysis of all 7 RCTs, using a random-effects model, showed no difference between strategies for all-cause mortality or the combined outcome of reinfarction or death (Table). Meta-analysis of 4 RCTs showed no difference between groups for nonfatal MI; 3 RCTs showed a reduction in fatal or nonfatal MI with the invasive strategy (Table). Risk for hospital readmission was also reduced with the invasive strategy (Table).

CONCLUSION

In patients with unstable angina or non–ST-segment elevation myocardial infarction (MI), an early invasive strategy reduces rates of fatal or nonfatal MI and rehospitalization more than a conservative strategy, but not all-cause mortality or the composite outcome of death or nonfatal MI.

Source of funding: Canadian Institutes of Health Research.

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Invasive vs noninvasive strategies for early management of unstable angina or non–ST-segment elevation myocardial infarction (MI) at 6 to 23 months*

Outcomes	Number of trials (n)	Weighted event rates		RRR (95% CI)	NNT (CI)
		Invasive	Noninvasive		
All-cause mortality	7 (9212)	5.2%	5.5%	3.8% (–25 to 27)†	Not significant
Death or nonfatal MI	7 (9212)	14%	16%	14% (–2 to 28)†	Not significant
Nonfatal MI	4 (3062)	8.1%	10%	19% (–14 to 44)	Not significant
Fatal or nonfatal MI	3 (6150)	7.5%	10%	25% (11 to 37)	41 (28 to 92)
Rehospitalization	5 (6482)	21%	28%	26% (4 to 44)†	14 (9 to 82)

*Abbreviations defined in Glossary; weighted event rates, RRR, NNT, and CI calculated from odds ratio in article using a random-effects model.
†Statistically significant heterogeneity present.

COMMENTARY

The choice of an "invasive" or "conservative" strategy for the initial management of patients with acute coronary syndromes (ACSs) has been evaluated in 7 RCTs, the results of which have been summarized by 2 groups using meta-analysis. Although it seems that the 2 meta-analyses reached different conclusions, both groups supported the invasive strategy in their respective discussion sections. Several trial limitations have confused the debate on what used to be a contentious subject, but the evidence now favors percutaneous coronary intervention (PCI) for NSTEMI.

First, the terms that describe the strategies need to be clarified. The "invasive strategy" refers to the routine use of cardiac catheterization, not coronary revascularization with PCI or coronary artery bypass graft (CABG) surgery. The "conservative strategy" limits the use of cardiac catheterization to patients with spontaneous or provokable ischemia, but the term does not convey the fact that 50% of patients allocated to this strategy also received cardiac catheterization. Therefore, these trials tested overlapping diagnostic risk-stratification strategies and did not randomize patients to cardiac catheterization versus control or coronary revascularization versus control.

Second, significant heterogeneity was present in the trials. Large differences existed among trials for men (62% to 97%), cardiac enzyme elevation (18% to 100%), electrocardiogram (ECG) ST-depression (21% to 47%), multivessel or left main disease (40% to 74%), and adjunctive drug therapy. Most important is the fact that patients with positive biomarkers or dynamic ECG changes almost always have plaque rupture, thrombosis, and vascular inflammation present, whereas a large proportion of patients with "unstable angina" in fact have noncardiac chest pain from anxiety, acid reflux, or another cause and do not really have an ACS. Therefore, the invasive strategy in many patients with "unstable angina" defines normal coronary arteries, and has no chance of changing death or MI rates.

Third, the trials were done in different eras and in different health care systems. The TIMI group did 2 of the studies in U.S. hospitals; 1 recruited patients from 1989 to 1992 and the other recruited from 1997 to 1999. 3 studies were done in Europe. VANQWISH was done in Veterans Affairs medical centers 10 years ago (1). Updated American College of Cardiology/American Heart Association guidelines on this topic have been released twice since these studies were completed.

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Review: Routine invasive management after unstable angina or non–ST-segment elevation MI reduces risk for death or MI

Mehta SR, Cannon CP, Fox KA, et al. **Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials.** JAMA. 2005;293:2908-17.

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

QUESTION

In patients with unstable angina or non–ST-segment elevation myocardial infarction (NSTEMI), is initial management with a routine invasive strategy more effective than a selective invasive (conservative) strategy?

METHODS

Data sources: MEDLINE and the Cochrane Library (1970 to June 2004), conference abstracts, and bibliographies of relevant articles.

Study selection and assessment: Randomized controlled trials (RCTs) that compared routine invasive and selective invasive strategies for early management of patients with unstable angina or NSTEMI. Studies that were quasirandomized or determined eligibility based on the results of coronary angiography were excluded. Study quality was assessed for allocation concealment. Data were confirmed and additional data provided by the principal investigators of the original trials.

Outcomes: Mortality, reinfarction, and rehospitalization.

MAIN RESULTS

7 RCTs (n = 9212) met the selection criteria. Meta-analysis of all 7 RCTs, using a fixed-effects model and including all events from randomization to the end of follow-up, showed no difference between strategies for all-cause mortality (Table). The routine invasive strategy reduced risks for nonfatal MI and the combined outcome of MI or death (Table). In patients who received the routine invasive strategy, risk for MI or death increased before first hospital discharge (OR 1.36, 95% CI 1.12 to 1.66), but decreased after hospital discharge (OR 0.64, CI 0.56 to 0.75). Hospital readmission was reduced with the routine invasive strategy (Table).

CONCLUSION

In patients with unstable angina or non–ST-segment elevation myocardial infarction (MI), a routine invasive strategy reduces risk for death or nonfatal MI compared with a conservative strategy.

Sources of funding: Canadian Institutes of Health Research; Heart and Stroke Foundation of Ontario; Charles University Research Project.

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Routine invasive vs selective invasive strategies for early management of unstable angina or non–ST-segment elevation myocardial infarction (MI) at mean 17 months*

Outcomes	Number of trials (n)	Weighted event rates		RRR (95% CI)	NNT (CI)
		Routine invasive	Selective invasive		
All-cause mortality	7 (9212)	5.5%	6.0%	7.6% (–8 to 22)	Not significant
Death or nonfatal MI	7 (9212)	12%	14%	16% (6 to 25)	44 (28 to 115)
Nonfatal MI	7 (9212)	7.2%	9.4%	23% (11 to 33)	46 (33 to 97)
Rehospitalization	7 (9147)	32%	41%	23% (19 to 28)	11 (9 to 13)

*Abbreviations defined in Glossary; weighted event rates, RRR, NNT, and CI calculated from odds ratios in article using a fixed-effects model.

COMMENTARY

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Therefore, these trials may not be applicable to the current era, in which platelet GP IIb/IIIa–receptor inhibitors and drug-eluting stents are used during PCI and clopidogrel and statins are recommended for all patients.

Fourth, the choice of revascularization strategy is important. For the past 2 decades, emergency CABG in patients with ACS has been associated with a greater mortality risk than elective CABG, whereas patients rarely die during PCI in the current era. In the VANQWISH trial, there were 2 deaths (1.3%) in the 153 patients having PCI (both in the conservative strategy group) compared with 14 deaths (7.7%) in 182 patients receiving CABG (1). Therefore, PCI should be separated from CABG as a revascularization strategy when outcomes are analyzed.

It may be time to redefine the term "ACS" because it interferes with evidence-based utilization of invasive cardiology resources. Patients with positive biomarkers (NSTEMI) or dynamic ST segments have an unstable coronary artery lesion putting them at risk for death or MI, and they should receive cardiac catheterization with the goal of proceeding to PCI. If CABG is required, it should be done electively, if possible. Patients with unstable angina can be considered for either cardiac catheterization or noninvasive stress testing, depending on the clinical assessment of risk. It is important to note that computed tomography angiography may soon replace cardiac catheterization as a noninvasive means of defining normal coronary arteries in patients with "unstable angina" who seem to be at low risk.

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Reference

1. **Boden WE, O'Rourke RA, Crawford MH, et al.** Outcomes in patients with acute non-Q-wave myocardial infarction randomly assigned to an invasive as compared with a conservative management strategy. Veterans Affairs Non-Q-Wave Infarction Strategies in Hospital (VANQWISH) Trial Investigators. N Engl J Med. 1998;338:1785-92.