Best evidence topic - Cardiac general

Is an early invasive approach superior to a conservative strategy in patients with acute coronary syndrome?

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Summary

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was whether an early invasive approach (involving early coronary angiography followed by revascularisation if suitable) is superior to a conservative approach (with revascularisation only in patients with failed medical therapy) in patients with acute coronary syndrome. Altogether 282 papers were found using the reported search, of which seven presented the best evidence to answer the clinical question. The author, journal, date and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these papers are tabulated. We conclude that in patients diagnosed with acute coronary syndrome, an early invasive approach is clearly superior to a conservative approach.

Keywords: Evidence-based medicine; Thoracic surgery; Acute coronary syndrome; Review

1. Introduction

A best evidence topic was constructed according to a structured protocol. This protocol is fully described in the ICVTS [1].

2. Clinical scenario

You are a cardiology registrar who is seeing a 63-year-old builder, admitted 5 days previously to coronary care unit with unstable angina. On admission it turned out that he has had NYHA grade-II angina for 2 years now although he had never mentioned it, and he is a current smoker. He has now been stabilised on oral medical treatment and has been pain free for the last 4 days. He is keen to get home as he had never been in hospital before and has found the whole experience very traumatic. However, you wonder whether an early angiography with revascularisation if appropriate would be safer for him while an inpatient, and if this strategy would increase his long-term prognosis.

3. Three-part question

In (patients diagnosed with acute coronary syndrome) is (early invasive approach) compared to (conservative approach) the best treatment in terms of preventing (myocardial infarction or death).

4. Search strategy

Medline 1966—Feb 2004 using the OVID interface (exp Unstable Angina/ OR unstable coronary-artery disease.mp OR non-ST elevation infarction.mp OR acute coronary syndrom$.mp OR non-Q wave myocardial infarction.mp) AND (exp Myocardial Revascularisation OR Intervention.mp OR exp Coronary angiography OR exp Angioplasty OR exp Coronary Artery Bypass) AND (exp Myocardial Infarction OR myocardial infarction.mp OR Death.mp OR exp treatment outcome) AND randomised controlled trial.pt.
### Table 1: Summary of best evidence papers

<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses/comments</th>
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<tbody>
<tr>
<td>RITA-3 trial (2002), Lancet, UK [2]</td>
<td>N = 1810 patients with non-ST elevation MI or unstable angina from 45 hospitals.</td>
<td>PRCT with blinded outcome measure assessment level 1b</td>
<td>Treatment after randomisation</td>
<td>Early treatment: 865 patients, 311 had PCI at median 3 days, 184 had CAGB at median 22 days. Conservative Rx: 915 patients; 149 patients had PCI, 109 patients had CAGB and 48% of patients had an angiogram within a year.</td>
<td>Median follow-up is currently 2 years although all patients will be followed up for 5 years (results awaited). Well-conducted study.</td>
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<tr>
<td>FRISC-II trial (1999), Lancet, Sweden [3]</td>
<td>N = 2457 patients with unstable angina or non-ST elevation MI (ineligible for thrombolysis) from 58 hospitals randomised to early invasive treatment with revascularisation within 7 days or non-invasive treatment. Note the parallel randomisation to placebo or long-term low molecular mass heparin for 3 months.</td>
<td>PRCT with parallel groups Level 1b</td>
<td>Treatment after randomisation</td>
<td>Invasive group: 1222 patients, 522 had PCI (mean 4 days) and 430 patients had CAGB (mean 7 days). Non-invasive: 1235 patients, 220 had PCI (mean 17 days) and 233 patients had CAGB (mean 28 days). (1) Combined rate of death, non-fatal myocardial infarction, or refractory angina at 4 months. (2) Death or myocardial infarction at 12 months. Death or myocardial infarction at 6 months. Myocardial infarction alone at 6 months. Mortality.</td>
<td>Also of interest: combined endpoint (1) maintained significance at 1 year (risk ratio 0.72; CI 0.58–0.90); 15 MI s in intervention group related to PCI or angiography. The symptoms of angina and use of anti-anginal medication significantly reduced with interventional strategy (P &lt; 0.0001). During the first 6 months, minor elevations in cardiac markers following angioplasty were recorded as myocardial infarction even without any other signs or symptoms. Conservative strategy used very stringent criteria for ischaemia and consequently only 10% of patients underwent cardiac catheterisation during initial hospital admission. Definition of MI was different for those post-PCI or CAGB and those receiving conservative treatment, in terms of CK-MB levels.</td>
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<tr>
<td>FRISC-II trial (2000), Lancet, Sweden [4]</td>
<td>The above-mentioned patients followed for 12 months</td>
<td>PRCT level 1b</td>
<td>Death</td>
<td>Invasive vs non-invasive. 2.2 vs 3.9% P = 0.016 Myocardial infarction. 8.6 vs 11.6% P = 0.015 Composite mortality or MI. 10.4 vs 14.1% P = 0.005</td>
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</table>
| FRISC trial (2002), J Am Coll Cardiol, Sweden [5] | Above patients followed up for 24 months | PRCT level 1b | Reduction in mortality | Invasive vs non-invasive. 3.7 vs 5.4% P = 0.038 MI. 9.2 vs 12.7% P = 0.005 Composite end point of death or MI. 12.1 vs 16.3% P = 0.003. | In contrast to the two earlier reports MIs were now classified as procedural or non-procedural MIs. During the first 6 months two-thirds of MIs were procedure related, most after angioplasty. (continued on next page)
5. Search outcome

A total of 282 papers were found of which seven were deemed to be relevant [2–8]. An additional three randomised trials were found but were not included due to small study size [9–11], one large PRCT was excluded as the patients were recently post-thrombolysed MI [12] and one large study was excluded as treatment arms were significantly out of date [13]. The included studies are summarised in Table 1.
6. Results

The RITA-3 trial [2] showed that among patients with unstable coronary syndromes, the combined endpoint of death, non-fatal myocardial infarction, or refractory angina is significantly reduced in patients assigned to early intervention. These results were significant at 4 months and 1 year. The biggest effect found was on refractory angina but there was a trend towards a significant reduction in death or MI and the 5-year results will give more conclusive evidence for this in 2006. Of note this was a very well-conducted 45-centre trial with good treatment separation among groups and blinded outcome assessment.

The FRISC-2 invasive study reported their results at 6, 12 and 24 months [3–5]. The study showed that in patients with unstable coronary artery disease, an early invasive approach leads to decreased mortality, morbidity, hospital readmissions and need for late revascularisation. Maximum benefit was seen during the first 6 months. This study demonstrated a Number Needed to Treat (NNT) of 28 patients to prevent one cardiac event. Maximum benefit was achieved in high-risk patients with unstable angina or myocardial infarction randomly assigned to an invasive as compared with a non-invasive strategy in unstable coronary-artery disease: the FRISC II invasive randomised trial. FRISC II investigators. Fast revascularisation during instability in coronary artery disease. Investigators. Lancet 1999 Aug 28; 354(9180): 701–7. Erratum in: Lancet 1999 Oct 23; 354(9188): 1478.

The TACTICS-TIMI-18 study [6] showed that in patients with unstable angina or myocardial infarction without ST elevation, an early invasive strategy is superior to a conservative strategy in reducing the incidence of major cardiac events. Maximum benefit was achieved in high-risk patients with troponin T levels greater than 0.01 ng/l. The study showed that in patients with unstable coronary artery disease, an early invasive strategy is superior to a conservative strategy in reducing the incidence of major cardiac events. Maximum benefit was achieved in high-risk patients with unstable angina or myocardial infarction without ST elevation, an early invasive strategy is superior to a conservative strategy in reducing the incidence of major cardiac events. Maximum benefit was achieved in high-risk patients with unstable angina or myocardial infarction randomly assigned to an invasive as compared with a non-invasive strategy in unstable coronary-artery disease: the FRISC II invasive randomised trial. FRISC II investigators. Fast revascularisation during instability in coronary artery disease. Lancet 2000;356(9223):9–16.

The VANQUISH trial [7] had different findings to those above. They demonstrated that in patients with non-Q wave infarction there was no significant difference in outcomes between invasive and conservative approach. However, there were several drawbacks to this study. First the study achieved poor treatment separation with 44% of patients in the invasive group receiving revascularisation and 33% receiving revascularisation in the conservative group. Secondly a significant proportion of those who died in the invasive group died prior to any intervention being performed on them. Lastly this study was in the pre-stenting and pre-gpIIb/IIIa drug era.

7. Clinical bottom line

Current trials clearly show a benefit for the early invasive approach of angiography followed by revascularisation in post-acute coronary syndrome patients with an NNT of around 50 to prevent a death or MI.

References

[8] Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction. Results of the TIMI IIIB Trial.


