An early invasive strategy reduced death, myocardial infarction, and hospital readmissions at 2 years in unstable CAD

Lagerqvist B, Husted S, Kontny F, et al. **A long-term perspective on the protective effects of an early invasive strategy in unstable coronary artery disease: two-year follow-up of the FRISC-II invasive study.** J Am Coll Cardiol. 2002;40:1902-14.

QUESTION

In patients with unstable coronary artery disease (CAD), how does an early invasive strategy compare with a noninvasive strategy for long-term effectiveness in reducing death, myocardial infarction (MI), hospital readmissions, and late revascularization?

DESIGN

Randomized {(allocation concealed*), blinded (outcome assessors),*}† controlled trial with 24-month follow-up (The Fragmin and Fast Revascularization during Instability in Coronary artery disease [FRISC-II]) study.

SETTING

58 hospitals in Sweden, Denmark, and Norway.

PATIENTS

2457 patients (median age 65 y, 70% men) with symptoms of unstable CAD, most recent episode of chest pain ≤ 48 hours before the start of dalteparin or regular heparin, and signs of myocardial ischemia (ST-segment depression, T-wave inversion, or raised biochemical myocardial markers). Exclusion criteria included thrombolysis in the previous 24 hours, angioplasty within the past 6 months, previous open heart surgery, and age > 75 years. All patients received aspirin and open-label dalteparin for ≥ 5 days. Follow-up was 99%.

INTERVENTION

Patients were allocated to invasive therapy (coronary angiography, revascularization within 7 d of hospital admission, percutaneous coronary intervention for 1 or 2 lesions, and coronary bypass graft surgery for 3-vessel or left main CAD) {*n* = 1222}† or noninvasive therapy (coronary angiography for refractory or recurrent symptoms despite maximal medical treatment or severe ischemia on a predischarge symptom-limited exercise test) {*n* = 1235}†.

MAIN OUTCOME MEASURES

Composite endpoint of death or MI. Secondary outcomes were death, MI, late revascularizations, and repeated admissions to the hospital.

MAIN RESULTS

Analysis was by intention to treat. Fewer patients in the invasive group had an MI, died, or both, and there were fewer repeated hospital admissions than in the noninvasive group (Table). Although more patients were revascularized at 24 months in the invasive group than the noninvasive group (78% vs 45%, $P < 0.001$), no additional patients were revascularized in the second year of the study. MI, death or MI, and repeated hospital admissions in the invasive group continued to decline during the second year.

CONCLUSION

In patients with unstable coronary artery disease, an early invasive strategy reduced death, myocardial infarction, and hospital readmissions over 2 years.

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*See Glossary.

†The FRISC-II Investigators. Lancet. 1999;354:701-7.

Early invasive vs noninvasive strategies for unstable coronary artery disease at 24 months‡

Outcomes	Invasive	Noninvasive	RRR (95% CI)	NNT (CI)
Death or MI	12%	16%	26% (10 to 39)	24 (14 to 68)
Death	4%	5%	32% (2 to 53)	58 (29 to 1061)
MI	9%	13%	28% (9 to 43)	29 (17 to 94)
Hospital readmission	45%	64%	31% (25 to 36)	6 (4 to 6)

‡MI = myocardial infarction. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The 2-year data from the FRISC-II study by Lagerqvist and colleagues provide convincing evidence that an early invasive approach provide superior outcomes for patients with unstable CAD. At 6 months, the FRISC-II data showed a reduction in the composite endpoint of death and MI in the invasive group. The event curves revealed that this benefit persisted at 1 year, with substantial reductions in death and MI. At 2 years, FRISC-II showed a sustained reduction in the individual endpoints of death, MI, and repeated hospitalization.

The TACTICS-TIMI-18 and RITA-3 studies confirmed the 6-month findings of FRISC-II, that an early invasive strategy reduces the combined endpoint of death, MI, and repeated hospitalization (1, 2). All 3 studies enrolled patients in the glycoprotein IIb/IIIa inhibitor and stent era. Furthermore, results from the TIMI-COOL trial suggest that a period of pharmacologic "cooling off," as used in FRISC-II before proceeding with an early invasive strategy, is generally unnecessary (3).

The 2-year follow-up of the FRISC-II trial, TACTICS-TIMI-18, and RITA-3 provides conclusive evidence that early diagnostic catheterization with subsequent mechanical revascularization is superior to a noninvasive approach for patients with unstable angina/non–ST segment elevation MI, particularly those with chest pain within 48 hours, known CAD, ischemic electrocardiographic changes, or elevated biochemical markers.

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References

1. **Cannon CP, Weintraub WS, Demopoulos LA, et al.** N Engl J Med. 2001;344:1879-87.
2. **Fox KA, Poole-Wilson PA, Henderson RA, et al.** Lancet 2002;360:743-51.
3. **Neumann FJ, Kastrati A, Pogatsa-Murray G, et al.** Circulation 2002;106:2986-a.