An early invasive strategy was not better than a selectively invasive strategy for acute coronary syndromes

de Winter RJ, Windhausen F, Cornel JH, et al. **Early invasive versus selectively invasive management for acute coronary syndromes.** N Engl J Med. 2005;353:1095-104.

Clinical impact ratings: GIM/FP/GP ★★★★★☆ Hospitalists ★★★★★☆ Cardiology ★★★★★☆

QUESTION

In patients with high-risk acute coronary syndromes (ACSs), is an early invasive strategy better than a selectively invasive (conservative) strategy?

METHODS

Design: Randomized controlled trial (Invasive versus Conservative Treatment in Unstable Coronary Syndromes [ICTUS]).

Allocation: Concealed.*

Blinding: Blinded (clinical endpoints committee).*

Follow-up period: 12 months.

Setting: 42 hospitals in the Netherlands.

Patients: 1200 patients ≥ 18 to ≤ 80 years of age (median age 62 y, 73% men) who had symptoms of ischemia that were increasing or occurred at rest in the previous 24 hours; elevated troponin T level (≥ 0.03 μg/L); and either ischemic changes documented by electrocardiography or documented history of coronary artery disease. Exclusion criteria included myocardial infarction (MI) with ST-segment elevation in the previous 48 hours, indication for primary percutaneous coronary intervention (PCI) or fibrinolytic therapy, and hemodynamic instability or overt congestive heart failure.

Intervention: Early invasive strategy (n = 604) or conservative strategy (n = 596). All patients received aspirin (300-mg load, 75 mg/d), enoxaparin (1 mg/kg of body weight subcutaneously [maximum 80 mg] twice daily for ≥ 48 h), and abciximab during PCI. The use of clopidogrel and intensive lipid-lowering therapy was recommended. The invasive strategy included coronary angiography within 24 to 48 hours and PCI when deemed appropriate by coronary anatomy. Patients in the conservative strategy group had angiography and revascularization only if they had refractory angina despite optimal medical treatment, hemodynamic or rhythmic instability, or clinically significant ischemia on the predischarge exercise test.

Outcomes: Composite endpoint of death, recurrent MI, or rehospitalization.

Patient follow-up: 99.5%.

MAIN RESULTS

Early invasive and conservative strategies did not differ for the composite endpoint (Table). Groups also did not differ for all-cause mortality (Table). Patients in the early invasive strategy group had higher rates of MI and lower rates of rehospitalization (Table).

CONCLUSION

In patients with acute coronary syndromes and optimized medical therapy, an early invasive strategy was not better than a selectively invasive strategy.

For correspondence: Dr. R.J. de Winter, Academic Medical Center, Amsterdam, The Netherlands. E-mail r.j.dewinter@amc.uva.nl. ■

*See Glossary.

Early invasive vs selectively invasive strategy for acute coronary syndromes at 1 year†

Outcomes	Early invasive	Selectively invasive	RRI (95% CI)	NNH (CI)
Composite endpoint‡	23%	21%	7% (−13 to 33)	Not significant
Myocardial infarction	15%	9.9%	50% (11 to 105)	20 (12 to 79)
			RRR (CI)	**NNT (CI)**
Death	2.5%	2.5%	1.3% (−97 to 51)	Not significant
Rehospitalization	7.4%	10.9%	32% (2.4 to 53)	29 (15 to 463)

†Abbreviations defined in Glossary; RRI, RRR, NNH, NNT, and CI calculated from data in article.
‡Composite endpoint = death, myocardial infarction, or rehospitalization.

COMMENTARY

The study by de Winter and colleagues targeted high-risk patients with troponin-positive (or biomarker-positive) non–ST-segment elevation ACSs. The authors found that an early invasive strategy was not superior to a selective invasive approach with aggressive medical therapy. These results contrast with a recent meta-analysis that concluded that an early invasive approach was superior (1).

The main difference in study design between this study and those included in the meta-analysis is the aggressive medical therapy received. In this study, all patients received aspirin and enoxaparin, as well as abciximab during PCI. Additionally, many patients received clopidogrel (61% in the early and 49% in the selective groups, respectively) and intensive lipid-lowering therapy (90% and 94%). Of the 7 studies included in the meta-analysis, only 1 used glycoprotein IIb/IIIa inhibitors and none used clopidogrel. The value of adding clopidogrel to this high-risk population has been shown (2).

The rates of mechanical revascularization were much higher in this study than in the meta-analysis. de Winter and colleagues reported revascularization rates of 79% in the early invasive group and 54% in the selective invasive group at 1 year, compared with 63% and 41%, respectively, in the meta-analysis.

It is uncertain to what extent the aggressive medical therapy, high revascularization rate, or recruitment of low-risk patients (less diabetes) may have contributed to the low 1-year mortality (2.5% in each group vs 5.5% and 6.0%, respectively, in the meta-analysis) or findings of nonsuperiority of the early invasive approach. This study may prompt another look at the current recommendations for an early invasive approach.

Michelle Welsford, MD, FRCPC
McMaster University
Hamilton, Ontario, Canada

References
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2. **Yusuf S, Zhao F, Mehta SR, et al.** Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med. 2001;345:494-502.