

The ISCHEMIA Trial: Is Routine Revascularization Necessary?

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Abstract

Results of the ISCHEMIA study (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches) were presented at the American Heart Association (AHA) Annual Scientific Sessions in November 2019 in Philadelphia [1, 2]. This National Heart/Lung/Blood Institute – funded study compared routine invasive therapy versus optimal medical therapy amongst patients with stable ischemic heart disease and moderate to severe ischemia on stress testing.

Study Design:

- Randomized, parallel, international multi-center trial
- Enrolled 5179 participants; lasted for 7 years
- Routine invasive arm (PCI & CABG): 2588 subjects
 - 96% catheterization; 80% revascularization
- Medical therapy: 2591 subjects
 - 28% catheterization; 23% revascularization

Inclusion criteria:

- Age > 20 years
- Moderate to severe ischemia on noninvasive stress testing:

- Nuclear $\geq 10\%$ ischemia;
- echo ≥ 3 segments of ischemia;
- CMR $\geq 12\%$ ischemia and/or ≥ 3 segments with ischemia;
- GXT ≥ 1.5 mm ST depression in ≥ 2 leads or ≥ 2 mm ST depression in single lead at < 7 METs with angina

Exclusion criteria:

- Left main $\geq 50\%$ stenosis
- GFR < 30 ml/min
- Recent MI
- EF $< 35\%$
- Left main stenosis $> 50\%$
- Advanced angina at baseline
- NYHA III-IV heart failure
- PCI or CABG within last year

Results

Primary outcome: Cardiovascular (CV) death, myocardial infarction (MI), resuscitated cardiac arrest, hospitalization for unstable angina or heart failure at 3.3 years:

- 13.3% of routine invasive group compared with 15.5% of medical therapy group ($p = 0.34$). Findings were the same in multiple subgroups.

Secondary outcomes:

- *CV death or MI:* 11.7% of routine invasive group compared with 13.9% of medical therapy group ($p = 0.21$)
- *All-cause death:* 6.4% of routine invasive group compared with 6.5% of medical therapy group ($p = 0.67$)

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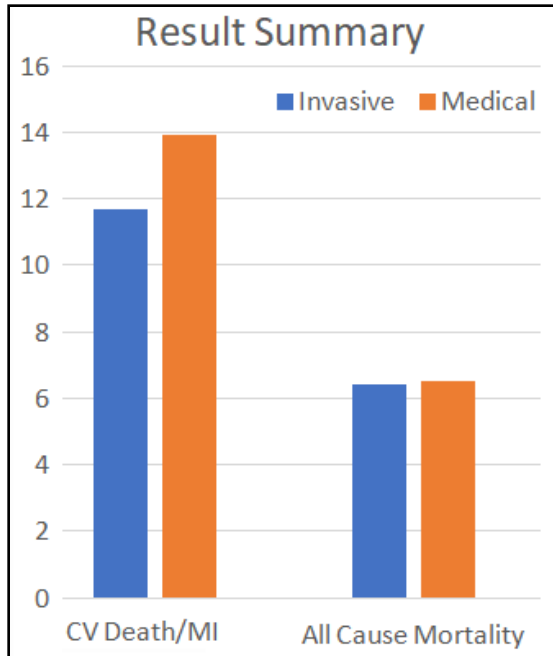
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Quality of Life Outcomes:

- None: 34%
- Several times/ month: 44%
- Daily/weekly: 22%



Discussion

The data from ISCHEMIA trial demonstrates that in stable ischemic heart disease and moderate to severe ischemia on noninvasive testing, routine catheterization and revascularization do not reduce major adverse cardiovascular events when compared to optimal medical therapy alone. However, these results cannot be applied to patients who met exclusion criteria of the study, such as more than 50% left main disease, GFR < 30 ml/min, recent ACS, EF <35%, unacceptable angina at baseline, NYHA Class III-IV heart failure, or revascularization within the preceding year.

The results of the ISCHEMIA trial may not be surprising in light of similar findings from other clinical trials such as the COURAGE trial [3], with its sustained findings up to 15 years [4]. It does, however, present incremental evidence in a larger number of patients that optimal medical therapy remains the cornerstone of treating stable ischemic heart disease, even in the

presence of moderate to severe ischemia demonstrated on noninvasive testing (excluding ACS situations).

Clinical Implications

The field of interventional cardiology has evolved exponentially ever since its inception greater than 40 years ago [5]. This was accompanied by concomitant rapid development of medical therapy which repeatedly proved to be equally protective to PCI or even CABG, especially in patient with stable ischemic heart disease [6, 7, 8]. With these results, cardiologists should focus on aggressive risk factors modification and optimization of medical therapy prior to sending their patients to the catheterization lab, where the main utility is for symptom relief (i.e. those who have failed medical therapy) rather than survival benefit in this population [9].

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