Rome 2020

ROME vs REMI

International Study of Comparative Health Effectiveness With Medical and Invasive Approaches - ISCHEMIA

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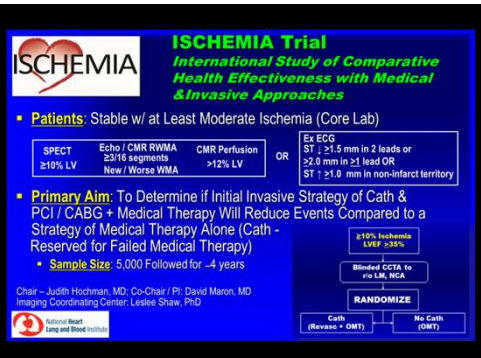

Detailed Results

Primary Endpoint:
Time to CV death, MI, hospitalization for unstable angina, heart failure or resuscitated cardiac arrest

Adjusted Hazard Ratio INV vs CON
0.93 (0.80, 1.08); P-value = 0.34

Detailed Results

Secondary Endpoint:
Time to CV death or MI

Adjusted Hazard Ratio INV vs CON
0.90 (0.77, 1.06); P-value = 0.21

Impressions

The probability of at least a 10% benefit of INV on all-cause mortality was <10%, based on pre-specified Bayesian analysis

Contribution To Literature:

The **ISCHEMIA** trial failed to show that routine invasive therapy was associated with a reduction in major adverse ischemic events compared with optimal medical therapy among stable patients with moderate ischemia.

Description:

The goal of the trial was to evaluate routine invasive therapy (IV) compared with **optimal medical therapy (OMT)** among patients with stable ischemic heart disease and moderate to severe myocardial ischemia on noninvasive stress testing.

Study Design

Randomized

Parallel

Patients with stable ischemic heart disease and moderate to severe ischemia were randomized to **routine invasive therapy** (n = 2,588) versus (OMT) medical therapy (n = 2,591).

In the routine invasive therapy group, subjects underwent coronary angiography and percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) as appropriate.

Study design

In the medical therapy groups, subjects underwent coronary angiography **only** for failure of medical therapy.

Total number of enrollees: 5,179

Duration of follow-up: 3.3 years

Mean patient age: 64 years

Percentage female: 23%

Percentage with diabetes: 41%

Inclusion criteria:

Patients >20 years of age

Moderate to severe ischemia on noninvasive stress testing (nuclear ≥10% ischemia; echo ≥3 segments of ischemia; cardiac magnetic resonance ≥12% ischemia and/or ≥3 segments with ischemia; exercise treadmill test ≥1.5 mm ST depression in ≥2 leads or ≥2 mm ST depression in single lead at <7 METs with angina)

Exclusion criteria:

≥50% left main stenosis (from blinded computed tomography)

Advanced chronic kidney disease (estimated glomerular filtration rate <30 ml/min)

Recent myocardial infarction

Left ventricular ejection fraction <35%

Left main stenosis >50%

Unacceptable angina at baseline

New York Heart Association class III-IV heart failure

Prior PCI or CABG within last year

Angina frequency at baseline:

None, 34%
Several times per month, 44%
Daily/weekly, 22%

Other salient features/characteristics:

Over the entire follow-up period, cardiac catheterization was performed in 96% of the invasive group vs. 28% of the medical therapy group

Over the entire follow-up period, coronary revascularization was performed in 80% of the invasive group vs. 23% of the medical therapy group

Principal Findings:

The primary outcome of cardiovascular death, myocardial infarction, resuscitated cardiac arrest, or hospitalization for unstable angina or heart failure at 3.3 years occurred in 13.3% of the routine invasive group compared with 15.5% of the medical therapy group (p = 0.34). The findings were the same in multiple subgroups.

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Principal Findings:

Invasive therapy was associated:

with

harm within the first 6 months (~2% absolute increase)

and

benefit within 4 years (~2% absolute decrease)

Secondary outcomes:

Cardiovascular death or myocardial infarction: **11.7%** of the routine invasive group compared with 13.9% of the medical therapy group (p = 0.21)

All-cause death: 6.4% of the routine invasive group compared with 6.5% of the medical therapy group (p = 0.67)

Secondary outcomes:

Cardiovascular death or myocardial infarction: **11.7%** of the routine invasive group compared with **13.9%** of the medical therapy group (p = 0.21).

All-cause death: 6.4% of the routine invasive group compared with 6.5% of the medical therapy group (p = 0.67).

Secondary outcomes:

Periprocedural myocardial infarction: (invasive/conservative hazard ratio [HR] **2.98**, 95% confidence interval [CI] 1.87-4.74)

Spontaneous myocardial infarction: (invasive/conservative HR **0.67**, 95% CI 0.53-0.83)

Quality of life outcomes:

Improvement in symptoms was observed among those with angina daily/weekly/monthly, but not in those without angina.

Interpretation:

Among patients with stable ischemic heart disease and moderate to severe ischemia on noninvasive stress testing, routine invasive therapy failed to reduce major adverse cardiac events compared with optimal medical therapy.

Interpretation:

There was also no benefit from invasive therapy regarding all-cause mortality or cardiovascular mortality/myocardial infarction.

Interpretation:

One-third of subjects reported no angina symptoms at baseline. Routine invasive therapy was associated with harm at 6 months (increase in periprocedural myocardial infarctions) and associated with benefit at 4 years (reduction in spontaneous myocardial infarction)

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One-third of subjects reported no angina symptoms at baseline.

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These results **do not** apply to patients with

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Interpretation:

These results do not apply to patients with

1. current/recent acute coronary syndrome
2. highly symptomatic patients
3. left main stenosis
4. left ventricular ejection fraction <35%.

Key findings

The curves cross for the primary endpoint and the major secondary endpoint at approximately 2 years from randomization

- ~2 in 100 higher estimated rate with INV at 6 months
- ~2 in 100 lower estimated rate with INV at 4 years

Procedural MIs were increased with an invasive strategy

Other Endpoints

Cardiovascular Death
Adjusted Hazard Ratio INV vs CON
0.87 (0.66, 1.15); P-value = 0.33

Myocardial Infarction
Adjusted Hazard Ratio INV vs CON
0.92 (0.76, 1.11); P-value = 0.38

Other Endpoints

Procedural MI (Type 4a or 5)
Adjusted Hazard Ratio INV vs CON
2.98 (1.87, 4.74); P-value < 0.01

Spontaneous MI (Types 1,2,4b or 4c)
Adjusted Hazard Ratio INV vs CON
0.67 (0.53, 0.83); P-value <0.01

ClinicalTrials.gov Identifier: **NCT01471522** (opens in new window)

Other Endpoints

All-Cause Death
Adjusted Hazard Ratio INV vs CON
1.05 (0.83, 1.32); P-value = 0.67

Net clinical benefit (stroke added to primary endpoint)
Hazard Ratio INV vs CON
0.95 (0.82,1.10); P-value= 0.50

Interpretation:

Although the overall interpretation of this trial was negative, there were mixed findings with evidence for both harm and benefit. This signals that: 1) invasive therapy for stable ischemic heart disease patients needs to be carefully considered in the context of angina burden and background medical therapy, and 2) likelihood that optimal coronary revascularization can be achieved with low procedural complications.

Key findings

- Spontaneous MIs were reduced with an invasive strategy
- Low all-cause mortality in both groups despite high-risk clinical characteristics, high-risk ischemia and extensive CAD
- No heterogeneity of treatment effect, including by type of stress test, severity of ischemia or extent of CAD
- Very low rates of procedure-related stroke and death

Impressions

- ISCHEMIA is the largest trial of an invasive vs conservative strategy for patients with SIHD
- Overall, an initial INV strategy as compared with an initial CON strategy did not demonstrate a reduced risk over median 3.3 years for
  - Primary endpoint - CV death, MI, hospitalization for UA, HF, RCA
  - Major Secondary endpoint - CV death or MI

References and Sources

Presented by: Judith S Hochman, MD, at AHA Scientific Sessions 2019, Philadelphia, PA

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Hachamovitch R, Rozanski A, Shaw LJ, Stone GW, Thomson LE, Friedman JD, Hayes SW, Cohen I, Germano G, Berman DS. Impact of ischaemia and scar on the therapeutic benefit derived from myocardial revascularization vs. medical therapy among patients undergoing stress-rest myocardial perfusion scintigraphy.*Eur Heart J.* 2011; 32:1012–1024. doi: 10.1093/eurheartj/ehq500

Acute Myocardial Infarction in Young Individuals

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Figure 1

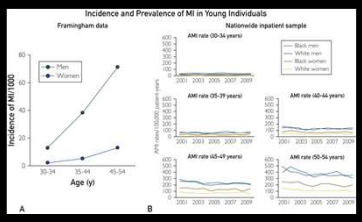

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Figure 2

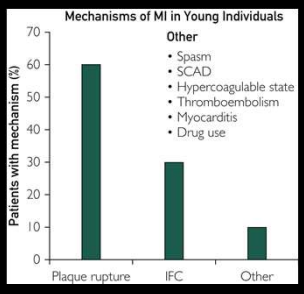

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Figure 4

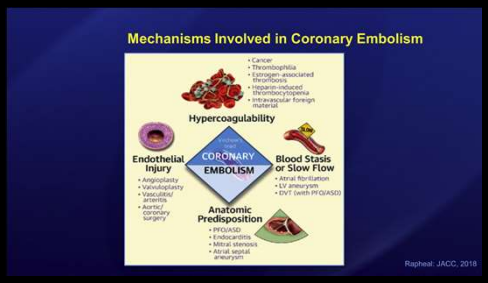

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Figure 6

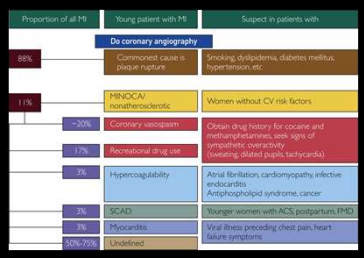

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Figure 8

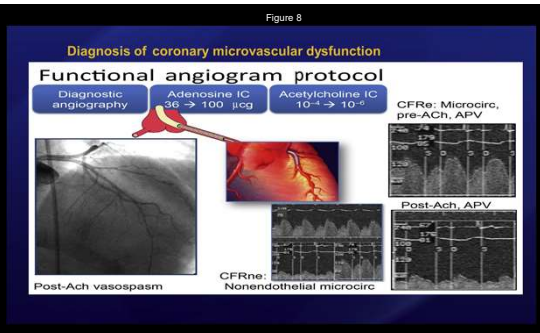

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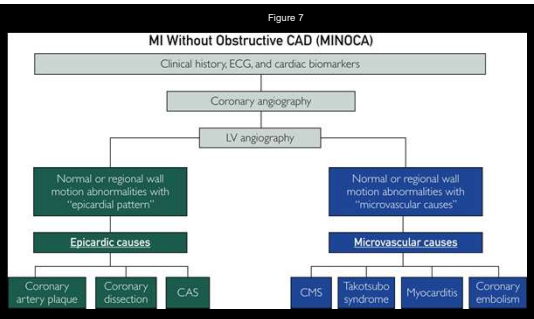
Figure 7



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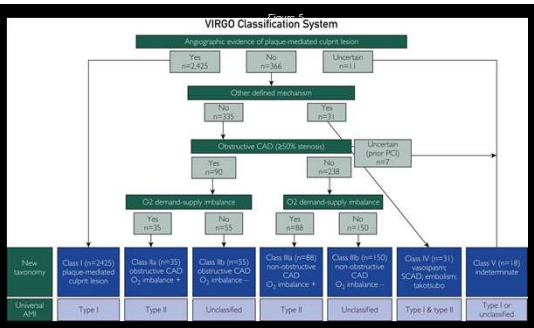

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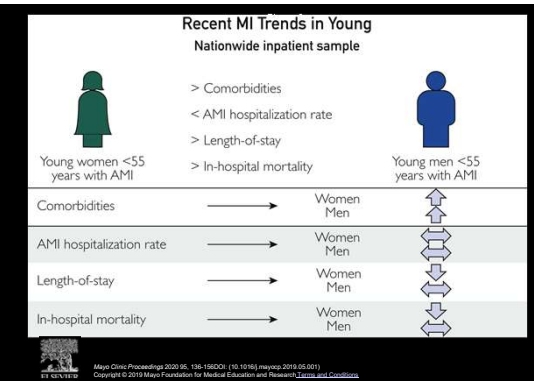

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Myocardial infarction in young individuals

traditional risk factors

2. use of recreational drugs (cocaine and methamphetamine)

spontaneous Coronary artery dissection (SCAD) ,myocarditis or

coronary embolism (CE)

myocardial infarction due to atheromatous coronary artery disease but without critical coronary artery stenosis(MINOCA)

coronary vasospasm

Incidence MI

	Men	Women
Age	per 1000 patients	
30-34 y/o	12.9	2.2
35-44 y/o	38.2	5.2
45-54 y/o	71.2	13.0

Clinical presentation

708 /5127 were silent

Higher prevalence in women

2017 AHA/ACC
Clinical performance and Quality measures for patient's with STEMI and NON-STEMIs

Quality Measures

QM-1 risk stratification of non-STEMI patients with a risk score
QM–2 early invasive strategy (within 24 hours and the high risk Non STEMI patient
QM–3 therapeutic hypothermia for comatose STEMI patients with an out of hospital cardiac arrest
QM –4 aldosterone antagonists prescribed at discharge
QM–5 inappropriate hospital use of NSAIDs
QM–6 inappropriate prescription for Prasugrel at discharge in patients with a history of prior stroke or TIA
QM–7 inappropriate prescription of High Dose aspirin with Ticagrelor at discharge

ACC/AHAPerformance measures

PM–1 Aspirin on arrival
PM–2 Aspirin prescribed at discharge
PM–3 Beta blocker prescribed at discharge
PM–4 High-intensity statin prescribed at discharged
PM–5 Evaluation of LVEF
PM–6 ACE or ARB prescribed for LVSD
PM–7 Time to Fibrinolytic Therapy
PM–8 Time to Primary PCI

ACC/AHA Performance Measures

PM–9 Reperfusion therapy

POM–10 Time from ED arrival at STEMI referral facility to ED discharge from the STEMI referral facility inpatients transferred for primary PCI

PM–11 Time from FMC (at or before ED arrival at STEMI referral facility) 2 primary PCI it's STEMI receiving facility among transferred patient's

PM–12 Cardiac rehabilitation patient referral from an inpatient setting

PL–13 PY 12 receptor inhibitor prescribed at discharge

ACC/AHA Performance measures

PM–14 Immediate angiography for resuscitated out-of-hospital cardiac arrest and STEMI patient's

PM–15 Noninvasive stress testing before discharge and conservatively treated patient's

PM–16 Early cardiac Troponin measurements (within 6 hours of arrival)

PM–17 Participation in > 1 regional or national registries that include patient's with Acute Myocardial infarction Registry

SOAMI

Thank You

Questions?