International Study of Comparative Health Effectiveness with Medical and Invasive Approaches
Primary Report of Quality of Life Outcomes

Funded by National Heart, Lung, and Blood Institute

John A. Spertus, MD, MPH
Saint Luke’s Mid America Heart Institute/UMKC
On behalf of the ISCHEMIA Research Group
ISCHEMIA QoL Research Question

In a stable patient with at least moderate ischemia, does an invasive strategy...

*improve patients’ health status (their symptoms, function and quality of life)*?
**Study Design**

Stable Patient
Moderate or severe ischemia
(determined by site; read by core lab)

INVASIVE Strategy + OMT

CONSERVATIVE OMT alone (Cath if needed)

1.5m 3m 6m 12m 18m 24m 30m 36m ...

Brief QoL Assessment:
- Seattle Angina Questionnaire – 7
  - Angina Frequency **
  - Quality of Life **
  - Physical Limitations

SAQ Summary Score*

Completion Rates

Con: 91% 88% 94% 93% 92% 90% 91% 89%
Inv: 88% 89% 93% 92% 92% 91% 90% 88%

*Primary QoL Outcome
**Secondary QoL Outcome
Interpreting and Stratifying SAQ Scores

**SAQ Angina Frequency Scale:**

Over the past 4 weeks, how often have you had angina?

- \( \geq 4X/day \) to \( \leq 3X/week \)
- 1-3X/day
- 1-2X/week
- \(<1X/week\)
- None

Daily  Weekly  Monthly  None

Daily/Weekly

ScientificSessi0ns.org#AHA1
Statistical Methods

• Simple descriptive statistics of observed mean scores

• Mixed-effect proportional odds models for all QOL scales
  • Treatment effect = Odds ratio for QOL ≥ X, at each time point
  • Results transformed to individual SAQ scales

• Bayesian methods used for all models to directly estimate probability of treatment effect with posterior means and 95% posterior density intervals

• Analyses performed for all patients and stratified by baseline angina
  • e.g. daily/weekly vs. several times per month vs. no angina
Patient Flow

5,179 Randomized

2,591 Conservative
- 239 improper form completion
- 2,352 Eligible for QOL Analyses
  - 17 no baseline assessment
  - 13 no follow-up assessments
  - 2,322 Included in Analyses of Treatment Effect

2,588 Invasive
- 242 improper form completion
- 2,346 Eligible for QOL Analyses
  - 29 no baseline assessment
  - 22 no follow-up assessments
  - 2,295 Included in Analyses of Treatment Effect
Baseline Health Status

<table>
<thead>
<tr>
<th>Scale</th>
<th>Invasive</th>
<th>Conservative</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAQ Summary Score</td>
<td>73.3±19</td>
<td>74.8±19</td>
</tr>
<tr>
<td>SAQ Quality of Life Score</td>
<td>60.9±27</td>
<td>62.7±26</td>
</tr>
<tr>
<td>SAQ Angina Frequency Score</td>
<td>80.8±20</td>
<td>82.1±19</td>
</tr>
<tr>
<td>Daily/Weekly Angina</td>
<td>21.6%</td>
<td>19.0%</td>
</tr>
<tr>
<td>Several Times per Month</td>
<td>44.1%</td>
<td>44.5%</td>
</tr>
<tr>
<td>No Angina</td>
<td>34.3%</td>
<td>36.6%</td>
</tr>
</tbody>
</table>
Description of Observed Data

SAQ Summary Score

![Graph showing SAQ Summary Score over months]

- **Conservative** (blue line)
- **Invasive** (red line)

Sample sizes at each time point:
- 0 months: N=2321, N=2217
- 6 months: N=2146, N=2170
- 12 months: N=2081, N=2120
- 18 months: N=1822, N=1835
- 24 months: N=1470, N=1482
- 30 months: N=1230, N=1265
- 36 months: N=966, N=982
- 42 months: N=735
- 48 months: N=747
Description of Observed Data

SAQ Angina Frequency

SAQ Quality of Life

N=2292 N=2177 N=2146 N=2080 N=1821 N=1470 N=1229 N=966 N=735
N=2320 N=2212 N=2168 N=2117 N=1831 N=1482 N=1264 N=982 N=747

N=286 N=2171 N=2145 N=2077 N=1816 N=1467 N=1227 N=960 N=731
N=2320 N=2210 N=2166 N=2116 N=1831 N=1481 N=1262 N=977 N=745

Conservative Invasive

Conservative Invasive
Improvement in SAQ Summary Score at 12 Months
Improvement in SAQ Summary Score at 12 Months
Primary Outcome: Benefit of Invasive Rx on SAQ Summary Score

Typical Patient in ISCHEMIA

- **Month 3**: Posterior Mean = 4.1 (3.2, 5.0) *
- **Month 12**: Posterior Mean = 4.2 (3.3, 5.1) *
- **Month 36**: Posterior Mean = 2.9 (2.2, 3.7) *

*95% Highest Posterior Density Interval*
Primary Outcome: Benefit of Invasive Rx on SAQ Summary Score

Typical Patient with Daily to Weekly Angina

- **Month 3**: Posterior Mean = 8.5 (5.8, 11.1)*
  - Favors Invasive
- **Month 12**: Posterior Mean = 7.3 (4.8, 9.9)*
  - Favors Invasive
- **Month 36**: Posterior Mean = 5.3 (3.4, 7.5)*
  - Favors Invasive

*95% Highest Posterior Density Interval
Primary Outcome: Benefit of Invasive Rx on SAQ Summary Score

Typical Patient with at least Monthly Angina

Month 3

Favors Conservative

Favors Invasive

Posterior Mean = 5.5 (4.3, 6.9)*

Month 12

Favors Conservative

Favors Invasive

Posterior Mean = 4.8 (3.4, 6.1)*

Month 36

Favors Conservative

Favors Invasive

Posterior Mean = 3.1 (2.0, 4.2)*

*95% Highest Posterior Density Interval
Primary Outcome: Benefit of Invasive Rx on SAQ Summary Score

Typical Patient with No Angina

Month 3

Posterior Mean = 0.1 (-1.2, 1.4)*

Month 12

Posterior Mean = 1.7 (0.4, 2.9)*

Month 36

Posterior Mean = 1.2 (0.2, 2.2)*

*95% Highest Posterior Density Interval
Probability of No Angina by Baseline Angina Frequency

Month 3

No Difference

NNT = ~3

Baseline SAQ-7 Angina Frequency Score

Probability of No Angina by Baseline Angina Frequency

NNT = ~3
Limitations

• Missing SAQ data, although small (<10%)

• Skewed enrollment towards less symptomatic patients
  • The larger effects in more symptomatic still clearly assessable

• No sham group
  • Nonetheless, angina-free benefits comparable with that seen in ORBITA
Conclusions

• Patients with stable CAD and moderate to severe ischemia had significant, durable improvements in angina control and quality of life with an invasive strategy if they had angina (daily/weekly or monthly)

• In patients without angina, an invasive strategy led to minimal symptom or quality of life benefits, as compared with a conservative strategy

• In patients with angina, shared decision-making should occur to align treatment with patients’ goals and preferences
Thank you....

• Quality of Life Core Lab: Philip Jones, Dan Mark, Khaulala Baloch, Lisa Hatch

• ISCHEMIA Trial Chair & Co-Chair: Judith Hochman, David Maron

• ISCHEMIA Analytic Center and DSMB: Sean O’Brien, Frank Harrell

• ISCHEMIA Site PIs and Data Coordinators

• The Patients volunteering to participate in ISCHEMIA
Backup Slides
SIHD Management after ISCHEMIA

Patients with Stable CAD

Optimal Medical Therapy

None or Satisfied

Residual Symptoms?

Yes

Left Main Disease

PCI

Multi-disciplinary Heart Teams

Cath ± Revasc

Yes

No

CABG

Pt Discussion/Preferences for current Symptoms

Unsatisfied