International Study of Comparative Health Effectiveness with Medical and Invasive Approaches – Chronic Kidney Disease

Primary Report of Quality of Life Outcomes

Funded by National Heart, Lung, and Blood Institute

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On behalf of the ISCHEMIA-CKD Research Group
ISCHEMIA-CKD QoL Research Question

In a stable patient with advanced CKD and at least moderate ischemia, does an invasive strategy improve patients’ health status (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

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

SAQ Summary Score*

Completion Rates
Con: 92% 90% 91% 89% 90% 87% 85% 88%
Inv: 88% 85% 90% 85% 87% 86% 82% 80%

*Primary QoL Outcome
**Secondary QoL Outcome
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
  • Joint models to account for drop-outs due to death as a secondary analysis

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

777 Randomized

389 Conservative

368 Eligible for QOL Analyses

358 Included in Analyses of Treatment Effect

21 improper form completion

388 Invasive

367 Eligible for QOL Analyses

347 Included in Analyses of Treatment Effect

21 improper form completion

1 no baseline assessment
9 no follow-up assessments

8 no baseline assessments
12 no follow-up assessments
## 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>75.7±20</td>
<td>76.0±19</td>
</tr>
<tr>
<td>SAQ Quality of Life Score</td>
<td>65.3±28</td>
<td>66.2±27</td>
</tr>
<tr>
<td>SAQ Angina Frequency Score</td>
<td>86.7±18</td>
<td>86.9±18</td>
</tr>
<tr>
<td>Daily/Weekly Angina</td>
<td>11.9%</td>
<td>11.7%</td>
</tr>
<tr>
<td>Several Times per Month</td>
<td>38.2%</td>
<td>40.2%</td>
</tr>
<tr>
<td>No Angina</td>
<td>50.0%</td>
<td>48.0%</td>
</tr>
</tbody>
</table>
Description of Observed Data – All Patients

SAQ Summary Score

![Graph showing SAQ Summary Score over 48 months with data points for different months and patient counts (N=346, N=309, N=288, N=271, N=212, N=123, N=87, N=46, N=20). The graph compares Conservative and Invasive treatment groups.]
Description of Observed Data – All Patients

SAQ Angina Frequency Score

SAQ Quality of Life Score
Probability Distribution of Treatment Benefit from Bayesian Analyses

All Patients

Month 3

Posterior Mean = 2.1 (-0.4, 4.6)*

N=651

Month 12

Posterior Mean = 0.1 (-3.0, 3.1)*

N=589

Month 36

Posterior Mean = 0.5 (-3.6, 4.5)*

N=181

*95% Highest Posterior Density Interval
Probability Distribution of Treatment Benefit on SAQ Summary Score

Daily/Weekly Angina

**Month 3**
- Posterior Mean = 10.1 (0.0, 19.9)*
- N=74

**Month 12**
- Posterior Mean = 2.2 (-8.0, 13.1)*
- N=69

**Month 36**
- Posterior Mean = 0.7 (-13.8, 16.2)*
- N=21

*95% Highest Posterior Density Interval
Probability Distribution of Treatment Benefit on SAQ Summary Score

At Least Monthly Angina

Month 3

Posterior Mean = 2.2 (-2.0, 6.2)*

N=255

Month 12

Posterior Mean = 1.0 (-4.0, 6.2)*

N=232

Month 36

Posterior Mean = 1.5 (-5.1, 8.2)*

N=64

*95% Highest Posterior Density Interval
Probability Distribution of Treatment Benefit on SAQ Summary Score

No Angina

Month 3

Posterior Mean = 0.6 (-1.9, 3.3)*
N=321

Month 12

Posterior Mean = -0.8 (-4.2, 2.8)*
N=287

Month 36

Posterior Mean = 0.0 (-4.2, 4.3)*
N=96

*95% Highest Posterior Density Interval
Predicted Means of SAQ SS with Joint Models
## SAQ-7 Summary Score Odds Ratios

<table>
<thead>
<tr>
<th>Month</th>
<th>Odds Ratios (95% CrIs)</th>
<th>Probability (%) of Any Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>1.20 (0.76, 1.66)</td>
<td>81%</td>
</tr>
<tr>
<td>3</td>
<td>1.48 (0.90, 2.16)</td>
<td>95%</td>
</tr>
<tr>
<td>6</td>
<td>1.13 (0.61, 1.69)</td>
<td>65%</td>
</tr>
<tr>
<td>12</td>
<td>1.06 (0.55, 1.62)</td>
<td>53%</td>
</tr>
<tr>
<td>24</td>
<td>1.59 (0.77, 2.49)</td>
<td>93%</td>
</tr>
<tr>
<td>36</td>
<td>1.16 (0.45, 2.03)</td>
<td>59%</td>
</tr>
</tbody>
</table>
Posterior Distribution of ORs for Main and CKD Trials

94% Probability
CKD OR < Main OR

99% Probability
CKD OR < Main OR

93% Probability
CKD OR < Main OR
Limitations

• Missing SAQ data, although small (<15%)

• Very skewed enrollment towards less symptomatic patients; may not have been able to discern a QoL benefit in more symptomatic patients

• Large mortality rate, but little difference in joint models due to similar mortality in both arms
Conclusions

• In patients with stable CAD, advanced CKD and moderate to severe ischemia, we did not observe a substantial improvement in angina control and quality of life over time.

• However, given the large proportion of asymptomatic patients at baseline, we cannot exclude the possibility of a small benefit in symptomatic patients.
Thank you....

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

• ISCHEMIA-CKD PI: Sripal Bangalore

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

• ISCHEMIA-CKD Site PIs and Data Coordinators

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

• The Patients volunteering to participate in ISCHEMIA-CKD
Backup Slides