SYSTEMATIC CARDIAC RISK ASSESSMENT WITH PET/CT MYOCARDIAL PERFUSION IMAGING:
THE INTERMOUNTAIN CARDIAC PET RISK SCORE

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on behalf of the
Intermountain Heart Institute
Cardiac PET Risk Score Research Team
Financial Disclosures - Intermountain Team Members

None
Introduction

Cardiac PET MPI – Powerful tool
• Potential incremental value of ancillary data

Challenges of Increasing Adoption of Cardiac PET
• Appropriate patient selection
• Maintaining accuracy & consistent interpretation
• Providing clear risk assessment & clinical recommendations
The Intermountain Challenge

Focused & Highly Integrated Regional Heart Centers of Excellence

• Intermountain Medical Center
  o Transitioned to Cardiac PET MPI in 2013
  o Currently doing up to 7500 clinical cardiac PET studies annually

• Planned regional implementation of cardiac PET in 2018-2019
Reducing Variation → Higher Quality, Improved Outcomes

The Intermountain Cardiac PET Risk Score
Proposal:
The Intermountain Cardiac PET Risk Score
Consistent, Clinically Meaningful Interpretation
Study Population:
Patients undergoing rest/stress cardiac PET at Intermountain Medical Center from January 1, 2015 to December 31, 2016
N = 8,530 unique consecutive patients

Baseline Characteristics

<p>| | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Age mean ± std</td>
<td>65 y ± 12.7</td>
</tr>
<tr>
<td>Male</td>
<td>4710 (55.2%)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>current</td>
<td>673 (7.9%)</td>
</tr>
<tr>
<td>previous</td>
<td>2351 (27.6%)</td>
</tr>
<tr>
<td>never</td>
<td>5452 (63.9%)</td>
</tr>
<tr>
<td>Hx of Diabetes</td>
<td>2547 (29.9%)</td>
</tr>
<tr>
<td>Hx of Hyperlipidemia</td>
<td>4915 (57.6%)</td>
</tr>
<tr>
<td>Hx of Hypertension</td>
<td>5480 (64.2%)</td>
</tr>
<tr>
<td>Hx of MI</td>
<td>1811 (21.2%)</td>
</tr>
<tr>
<td>Hx of PCI</td>
<td>2052 (24.1%)</td>
</tr>
<tr>
<td>Hx of CABG</td>
<td>896 (10.5%)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>2316 (27.2%)</td>
</tr>
</tbody>
</table>

Imaging Specifications:
Imaging: Siemens 3D Cardiac/PET System
Radiotracer: Rubidium-82
Vasodilator: Regadenason
Software: Corridor4DM (perfusion)
           SiemensSyngo (MBF)
PET/CT Data

Ischemic Burden

- < 5%: 82%
- 5-10%: 10%
- > 10%: 8%

Global CFR

- < 1.5: 39%
- 1.5-2.3: 43%
- > 2.3: 18%

CAC

- Absent: 67%
- Present: 33%

Change in EF

- ≥5%: 57%
- 3%-4%: 27%
- <3%: 16%

TID

- ≤1.00: 51%
- 1.01-1.10: 27%
- ≥1.11: 22%

The Intermountain Cardiac PET Risk Score
Outcomes

Major cardiovascular adverse events (MACE)

- **All-cause death** - based on discharge and linkage with Utah death certificates
- **MI** – based on troponin and diagnosis codes
- **Revascularization** – based on coronary catherization reports and procedure codes.

90-day MACE and One-year MACE examined separately

<table>
<thead>
<tr>
<th></th>
<th>90-day</th>
<th>1-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>820 (9.6%)</td>
<td>1096 (12.8%)</td>
</tr>
<tr>
<td>Revascularization</td>
<td>712 (8.4%)</td>
<td>839 (9.8%)</td>
</tr>
<tr>
<td>Death</td>
<td>114 (1.3%)</td>
<td>277 (3.2%)</td>
</tr>
<tr>
<td>MI</td>
<td>23 (0.3%)</td>
<td>87 (1.0%)</td>
</tr>
</tbody>
</table>
The Intermountain Cardiac PET Risk Score Development Steps

Study Population
Split 70/30

Training Set
n=5971

1. Univariate logistic regression for demographic & PET data
2. Examining impact of missing data
3. Multicollinearity / correlation checking
4. Plausible two-way interactions between PET data examined
5. Stepwise selection for final model

Feature Selection

Deriving Score

1. Multivariable logistic regression beta coefficient ratio used for generating factor weights
2. Receiver operator curve (ROC) and area under the curve (AUC) determined
3. Low, moderate, and high categorization based on rates of MACE by score value

-derived score tested-

Test Set
n=2559

Prediction Comparisons
1. Ischemic Burden
2. Cardiologist Conclusions

FINAL SCORE MODEL

The Intermountain Cardiac PET Risk Score
Development Step Results

Univariate Analysis Variables:

- Age
- Gender
- Comorbidities (DM, HTN *, etc)
- CAD history
- Tobacco use history *
- Coronary Artery Calcium
- Myocardial Blood Flow
- Percent Change in LVEF
- TID
- Ischemic burden

* Not found to be significant

Multivariate Analysis Performed for 90-Day and 1-Year Risk Modeling
The Intermountain Cardiac PET Risk Score – 1 Year MACE

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<tr>
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<td>6</td>
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<td>10</td>
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Stratification of Risk Score – 1 Year MACE

The Intermountain Cardiac PET Risk Score

- Diabetic: 1
- Male: 1
- CFR 1.5 - 2.3: 1
- CFR < 1.5: 4
- CAC Present: 4
- Ischemic Burden 5% - 10%: 6
- Ischemic Burden >10%: 10

Risk Score

- Total Patients
- MACE

Percentage of Patients (Bars)
Percentage with MACE (Line)

Risk Score

0.0% 1.0% 2.0% 3.0% 4.0% 5.0% 6.0% 7.0% 8.0% 9.0% 10.0% 11.0% 12.0% 13.0% 14.0% 15.0% 16.0% 17.0% 18.0% 19.0% 20.0%

0.0% 10.0% 20.0% 30.0% 40.0% 50.0% 60.0% 70.0% 80.0% 90.0%

LOW MODERATE HIGH

Factor
Score
Categorization of Cardiac Risk – PATIENT EXAMPLES

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Low Risk Patient (0-4):
- Not Diabetic +0
- Male +1
- CFR of 2.13 +1
- CAC absent +0
- Ischemic Burden of 2.9% +0

SCORE = 2

Moderate Risk (5-7):
- Diabetic +1
- Female +0
- CFR of 2.39 +0
- CAC absent +0
- Ischemic Burden of 5.8% +6

SCORE = 6

High Risk (≥8):
- Diabetic +1
- Male +1
- CFR of 1.1 +4
- CAC present +4
- Ischemic Burden of 5.8% +6

SCORE = 16
Categorization of Cardiac Risk – PATIENT EXAMPLES – Normal Perfusion

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Low Risk Patient (0-4):
- Not Diabetic +0
- Male +1
- CFR of 2.13 +1
- CAC absent +0
- Ischemic Burden of 0% +0
SCORE = 2

Moderate Risk (5-7):
- Diabetic +1
- Male +1
- CFR of 2.39 +0
- CAC present +4
- Ischemic Burden of 0% +0
SCORE = 6

High Risk (≥8):
- Diabetic +1
- Male +1
- CFR of 1.1 +4
- CAC present +4
- Ischemic Burden of 0% +0
SCORE = 10

88% of patients with ischemic burden of 0% who had a MACE event are scored moderate to high using the Risk Score.
### Performance of Cardiac PET Risk Stratification - Cardiologist

<table>
<thead>
<tr>
<th>Cardiologist Cardiac PET Risk Assessment</th>
<th>Ischemic Burden</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>0-4 %</td>
</tr>
<tr>
<td>Low</td>
<td>6783</td>
</tr>
<tr>
<td>Moderate</td>
<td>441</td>
</tr>
<tr>
<td>High</td>
<td>68</td>
</tr>
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**Weighted Kappa = 0.70**: 95% CI: 0.69, 0.72

**Good agreement Between Cardiologist’s Risk Assessment and Ischemic Burden**
Performance of 90-day MACE Score vs Ischemic Burden

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<td>8</td>
</tr>
<tr>
<td>Ischemic Burden &gt; 10 % &amp; EF change ≥ 3%</td>
<td>13</td>
</tr>
<tr>
<td>Ischemic Burden &gt; 10 % &amp; EF change &lt; 3%</td>
<td>17</td>
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Training (p=0.01)
Score: AUC=0.91 (0.91, 0.92)
Ischemic Burden: AUC=0.90 (0.89, 0.91)

Test (p=0.24)
Score: AUC=0.91 (0.89, 0.92)
Ischemic Burden: AUC=0.90 (0.88, 0.91)
Performance of 1-Year MACE Score vs. Ischemic Burden

Training (p<0.0001)
Score: AUC=0.87 (0.86, 0.88)
Ischemic Burden: AUC=0.83 (0.82, 0.84)

Test (p=0.0005)
Score: AUC=0.85 (0.84, 0.87)
Ischemic Burden: AUC=0.82 (0.80, 0.83)

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Reclassification of 1-Year MACE: Cardiologist vs. Score

Cardiologist Risk Classification
Of those with a MACE event (n=1096)
• 30.7% were high risk
• 35.9% were moderate risk
• 33.4% were low risk

Score Risk Classification
Of those with a MACE event (n=1096)
• 78.4% were high risk
• 17.3% were moderate risk
• 4.3% were low risk
### Reclassification of 1-Year MACE: Cardiologist vs. Score

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</tr>
<tr>
<td>• 33.4% were low risk</td>
<td>• 4.3% were low risk</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Of those without MACE event (n=7434)</th>
<th>Of those without MACE event (n=7434)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>88.9%</strong> were low risk</td>
<td>• 38.5% were low risk</td>
</tr>
<tr>
<td>• 8.9% were moderate risk</td>
<td>• 43.2% were moderate risk</td>
</tr>
<tr>
<td>• 2.2% were high risk</td>
<td>• 18.3% were high risk</td>
</tr>
</tbody>
</table>
Reclassification of 1-Year MACE: Cardiologist vs. Score

Cardiologist Risk Classification
Of those with a MACE event (n=1096)
• 30.7% were high risk
• 35.9% were moderate risk
• 33.4% were low risk

Of those without MACE event (n=7434)
• 88.9% were low risk
• 8.9% were moderate risk
• 2.2% were high risk

Score Risk Classification
Of those with a MACE event (n=1096)
• 78.4% were high risk
• 17.3% were moderate risk
• 4.3% were low risk

Of those without MACE event (n=7434)
• 38.5% were low risk
• 43.2% were moderate risk
• 18.3% were high risk

Sensitivity for high risk was 30.7%
Specificity of low/mod risk was 97.8%

Sensitivity for high risk was 78.4%
Specificity of low/mod risk was 81.7%
Limitations

Single center retrospective study
Simplified score-based model
MACE limited to one year
Lacking external validation cohort
Transforming Nuclear Cardiology

Reducing Variation of Interpretation

• Standardizing risk assessment
• Consistent incorporation of complete imaging data

Identifying Higher Risk Patients
Lesson Learned / Challenges

Developing a Simple yet Effective Risk Scoring Tool

• PET population is diverse, challenging
• PET interpretation should incorporate complete imaging data.
• PET reporting must consistently and clearly convey:
  o 1) Short-term indication for angiography and need for revascularization
  o 2) Longer-term (1 y) risk of overall MACE
Conclusions

The Intermountain Cardiac PET Risk Score

• Excellent prognostic value of ischemic burden alone for 90-day outcomes
• Incorporating complete imaging data provides significant incremental value for 1-year MACE
• The Intermountain Cardiac PET Risk Score provides:
  o Quantification of the incremental value of imaging parameters beyond ischemic burden
  o An opportunity for more consistent PET reading across readers/centers
  o Clearer communication of individual patient’s cardiac risk
Intermountain Heart Institute Cardiac PET Risk Score Team

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1. Poor
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3. Average
4. Good
5. Excellent