Derivation and Validation of Pd/Pa for the Assessment of Residual Ischemia Post-Intervention
A Prospective All Comer Registry

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Disclosures- None
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- Bobbby Ghosh MD  RWJMS
Background

• Functional testing prior to intervention of epicardial CAD has been shown to be efficacious, safe and cost-effective.

• A substantial proportion of vessels (20-30%) show residual ischemia (FFR $\leq 0.80$) after angiographically successful PCI.

• The final post-PCI FFR value is associated with long term outcomes (“higher is better”).

• Further interventions in vessels with low FFR after angiographically successful PCI can improve the functional outcome of PCI.
Non-hyperemic pressure ratios (NHPR) post-PCI

- No NPHR post-PCI has been validated or formally studied prospectively to guide clinical decision-making.

- While the diagnostic performance of virtually all NHPRs including Pd/Pa, iFR, RFR is ~80% when compared with FFR pre-PCI, it is not known whether the comparative effectiveness of NHPRs vs FFR is the same after PCI.
Objectives

- To study
  - a) the **comparative effectiveness** and
  - b) **diagnostic accuracy** of post PCI Pd/Pa
against the reference standard of FFR in identifying residual ischemia (FFR<0.80) in vessels having undergone angiographically successful PCI.
Three cohorts were studied to compare Pd/Pa vs FFR

1) **Reference pre-PCI cohort**
   
   1560 vessels in 1255 patients undergoing pre-PCI Pd/Pa and FFR to study the **diagnostic accuracy of Pd/Pa vs FFR pre-PCI**.

2) **Derivation post-PCI cohort**
   
   655 vessels in 574 patients to study the **diagnostic accuracy of post PCI Pd/Pa in identifying persistent ischemia (FFR<0.80)**

3) **Prospective post-PCI validation cohort**
   
   255 vessels in 230 patients to validate Pd/Pa vs FFR post-PCI
Reference pre PCI Cohort:

1560 vessels patients with 1255 vessels undergoing invasive evaluation of CAD

Pd/Pa and FFR measured

FFR<0.80 PCI performed

FFR>0.80 deferred for med Tx only

Diagnostic performance of Pd/Pa against FFR tested

Diagnostic performance of Pd/Pa against FFR tested
Derivation post PCI Cohort

574 patients undergoing PCI in 664 ischemic lesions

PCI performed

Pd/Pa and FFR measured after PCI result deemed angiographically satisfactory

Diagnostic performance of Pd/Pa against FFR tested post PCI
Validation post PCI Cohort

230 patients undergoing PCI in 255 ischemic lesions

PCI performed

Pd/Pa and FFR measured after PCI result deemed angiographically satisfactory

Diagnostic performance of Pd/Pa against FFR tested post PCI
### Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Pre PCI Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>65 ± 8</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td>96%</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>47%</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>96%</td>
</tr>
<tr>
<td><strong>CKD</strong></td>
<td>20%</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>42%</td>
</tr>
<tr>
<td><strong>Prior revasc.</strong></td>
<td>52%</td>
</tr>
<tr>
<td><strong>SIHD</strong></td>
<td>65%</td>
</tr>
<tr>
<td><strong>ACS</strong></td>
<td>35%</td>
</tr>
</tbody>
</table>

**Post PCI Derivation**

- Age: 64 ± 8
- Males: 97%
- Diabetes: 45%
- Hypertension: 93%
- CKD: 18%
- Smoking: 39%
- Prior revasc.: 49%
- SIHD: 68%
- ACS: 39%

**Post PCI Validation**

- Age: 68 ± 8
- Males: 100%
- Diabetes: 41%
- Hypertension: 94%
- CKD: 19%
- Smoking: 63%
- Prior revasc.: 49%
- SIHD: 61%
- ACS: 39%
Model 1 Reference pre PCI Cohort:

Sample size | 1539
Positive group \(^a\) | 780 (50.7%)
Negative group \(^b\) | 759 (49.3%)

| Area under the ROC curve (AUC) | 0.869 |
| Standard Error \(^a\) | 0.00900 |
| 95% Confidence interval \(^b\) | 0.851 to 0.885 |
| z statistic | 40.955 |
| Significance level P (Area=0.5) | <0.0001 |

DeLong et al., 1988
Binomial exact

Youden index : BC\(_a\) bootstrap confidence interval (1000 iterations; random number seed: 978).
## Model II- Derivation post PCI Cohort

<table>
<thead>
<tr>
<th>Sample size</th>
<th>658</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive group</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>119 (18.1%)</td>
</tr>
<tr>
<td><strong>Negative group</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>539 (81.9%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Area under the ROC curve (AU C)</th>
<th>0.850</th>
</tr>
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<tbody>
<tr>
<td>Standard Error&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.0208</td>
</tr>
<tr>
<td>95% Confidence interval&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.820 to 0.876</td>
</tr>
<tr>
<td>z statistic</td>
<td>16.813</td>
</tr>
<tr>
<td>Significance level P (Area=0.5)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### ROC Curve

- Sensitivity: 73.1
- Specificity: 82.4
- Criterion: ≤0.93

Area under the ROC curve (AU C): 0.850
Standard Error: 0.0208
95% Confidence interval: 0.820 to 0.876
z statistic: 16.813
Significance level P (Area=0.5): <0.0001
Model 3: Prospective Validation Cohort

<table>
<thead>
<tr>
<th>Sample size</th>
<th>257</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive group&lt;sup&gt;a&lt;/sup&gt;</td>
<td>93 (36.2%)</td>
</tr>
<tr>
<td>Negative group&lt;sup&gt;b&lt;/sup&gt;</td>
<td>164 (63.8%)</td>
</tr>
</tbody>
</table>
Correlation between Post PCI Pd/Pa and FFR

![Graph showing correlation between Post PCI Pd/Pa and FFR.](image-url)
<table>
<thead>
<tr>
<th>Criterion</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>+LR</th>
<th>-LR</th>
<th>+PV</th>
<th>-PV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.7</td>
<td>0.00</td>
<td>100.00</td>
<td>1.00</td>
<td>1.00</td>
<td>63.8</td>
<td></td>
</tr>
<tr>
<td>≤0.85</td>
<td>23.66</td>
<td>100.00</td>
<td>0.76</td>
<td>100.0</td>
<td>69.8</td>
<td></td>
</tr>
<tr>
<td>≤0.86</td>
<td>31.18</td>
<td>99.39</td>
<td>51.14</td>
<td>0.69</td>
<td>96.7</td>
<td>71.8</td>
</tr>
<tr>
<td>≤0.87</td>
<td>38.71</td>
<td>99.39</td>
<td>63.48</td>
<td>0.62</td>
<td>97.3</td>
<td>74.1</td>
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<tr>
<td>≤0.88</td>
<td>56.99</td>
<td>98.17</td>
<td>31.15</td>
<td>0.44</td>
<td>94.6</td>
<td>80.1</td>
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<tr>
<td>≤0.89</td>
<td>66.67</td>
<td>96.34</td>
<td>18.22</td>
<td>0.35</td>
<td>91.2</td>
<td>83.6</td>
</tr>
<tr>
<td>≤0.9</td>
<td>76.34</td>
<td>92.07</td>
<td>9.63</td>
<td>0.26</td>
<td>84.5</td>
<td>87.3</td>
</tr>
<tr>
<td>≤0.91</td>
<td>78.49</td>
<td>87.20</td>
<td>6.13</td>
<td>0.25</td>
<td>77.7</td>
<td>87.7</td>
</tr>
<tr>
<td>≤0.92</td>
<td>81.72</td>
<td>81.10</td>
<td>4.32</td>
<td>0.23</td>
<td>71.0</td>
<td>88.7</td>
</tr>
<tr>
<td>≤0.93</td>
<td>88.17</td>
<td>72.56</td>
<td>3.21</td>
<td>0.16</td>
<td>64.6</td>
<td>91.5</td>
</tr>
<tr>
<td>≤0.94</td>
<td>91.40</td>
<td>63.41</td>
<td>2.50</td>
<td>0.14</td>
<td>58.6</td>
<td>92.9</td>
</tr>
<tr>
<td>≤0.95</td>
<td>94.62</td>
<td>55.49</td>
<td>2.13</td>
<td>0.097</td>
<td>54.7</td>
<td>94.8</td>
</tr>
<tr>
<td>≤0.96</td>
<td>97.85</td>
<td>46.95</td>
<td>1.84</td>
<td>0.046</td>
<td>51.1</td>
<td>97.5</td>
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<tr>
<td>≤0.97</td>
<td>98.92</td>
<td>35.98</td>
<td>1.55</td>
<td>0.030</td>
<td>46.7</td>
<td>98.3</td>
</tr>
<tr>
<td>≤0.98</td>
<td>98.92</td>
<td>27.44</td>
<td>1.36</td>
<td>0.039</td>
<td>43.6</td>
<td>97.8</td>
</tr>
<tr>
<td>≤0.99</td>
<td>100.00</td>
<td>17.07</td>
<td>1.21</td>
<td>0.00</td>
<td>40.6</td>
<td>100.0</td>
</tr>
<tr>
<td>≤1</td>
<td>100.00</td>
<td>0.00</td>
<td>1.00</td>
<td>1.00</td>
<td>36.2</td>
<td></td>
</tr>
</tbody>
</table>
Diagnostic Performance of Post PCI Pd/Pa

AUC 0.91
Cutoff Value: 0.90
Sensitivity 76%
Specificity 92%
Comparative effectiveness

Cutoff value < 0.92 AUC 0.87
Cutoff value < 0.93 AUC 0.85
Cutoff value < 0.90 AUC 0.91

p=0.4
p=0.03
p=0.02
Post PCI FFR to evaluate functional results of PCI

Pre PCI FFR
Post PCI FFR

0.69 (IQR 0.54-0.75)
0.84 (IQR 0.77-0.90)
p<0.0001
Post PCI Pd/Pa to evaluate functional outcome of PCI

Pre PCI Pd/Pa

Post PCI Pd/Pa

0.86
(IQR 0.71-0.91)

0.94
(IQR 0.89-0.97)

p<0.0001
Change in Pd/Pa post intervention

Pre PCI Pd/Pa
Post PCI Pd/Pa

Society for Cardiovascular Angiography & Interventions
<table>
<thead>
<tr>
<th>location</th>
<th>AUC</th>
<th>SE</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal</td>
<td>0.971</td>
<td>0.0226</td>
<td>0.858 to 0.999</td>
</tr>
<tr>
<td>Mid</td>
<td>0.909</td>
<td>0.0252</td>
<td>0.845 to 0.953</td>
</tr>
<tr>
<td>Prox</td>
<td>0.891</td>
<td>0.0391</td>
<td>0.807 to 0.947</td>
</tr>
</tbody>
</table>

- **Distal ~ Mid**
  - Difference between areas: 0.0617
  - Significance level: $P = 0.0682$

- **Distal ~ Prox**
  - Difference between areas: 0.0804
  - Significance level: $P = 0.0750$

- **Mid ~ Prox**
  - Difference between areas: 0.0187
  - Significance level: $P = 0.6885$
Sequential test strategy:
Pooling Patients from derivation and validation cohorts
Post PCI Pd/Pa and FFR

- Pd/Pa >0.93: 96% (N=611)
  - FFR >0.80: 4%
  - FFR <0.80: 92%

- Pd/Pa 0.86-0.93: 59% (N=219)
  - FFR >0.80: 41%
  - FFR <0.80: 18%

- Pd/Pa <0.86: 7% (N=28)
  - FFR >0.80: 93%
  - FFR <0.80: 7%

Distribution of Pd/Pa in FFR <0.80
- Pd/Pa >0.93: 17% (66%)
- Pd/Pa 0.86-0.93: 17% (25%)
- Pd/Pa <0.86: 66% (4%)

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• Using the hybrid strategy, diagnostic accuracy is 95% with Negative Predictive Value (NPV) of 96% to diagnose residual ischemia post-PCI.

• Adenosine can be avoided in >75% patients using this strategy.
Conclusions

• Pd/Pa has excellent diagnostic accuracy in identifying residual ischemia and confirming a physiologically successful outcome in patients undergoing angiographically successful PCI.

• Diagnostic accuracy can be further improved by incorporating a hybrid strategy requiring adenosine in only 25% of patients.

• Further studies are needed to establish the role of Pd/Pa in clinical decision-making after angiographic optimization to improve functional outcome of PCI.