CENTRAL ARKANSAS VETERANS HEALTHCARE SYSTEM

RUTGERS
Robert Wood Johnson Medical School

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

On behalf of co-investigators:

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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 ≤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.*

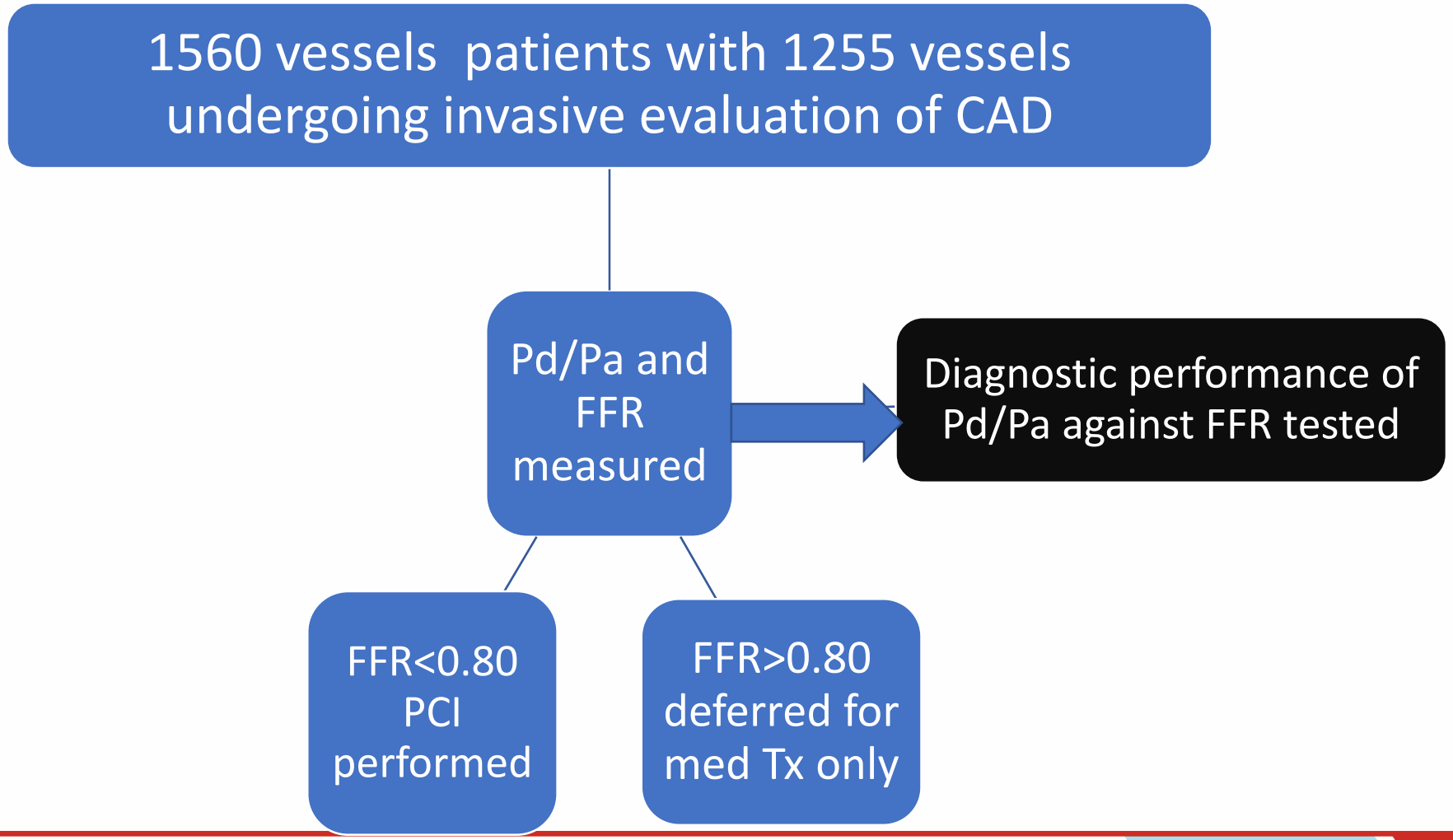
2) **Derivation post-PCI cohort**

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:



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

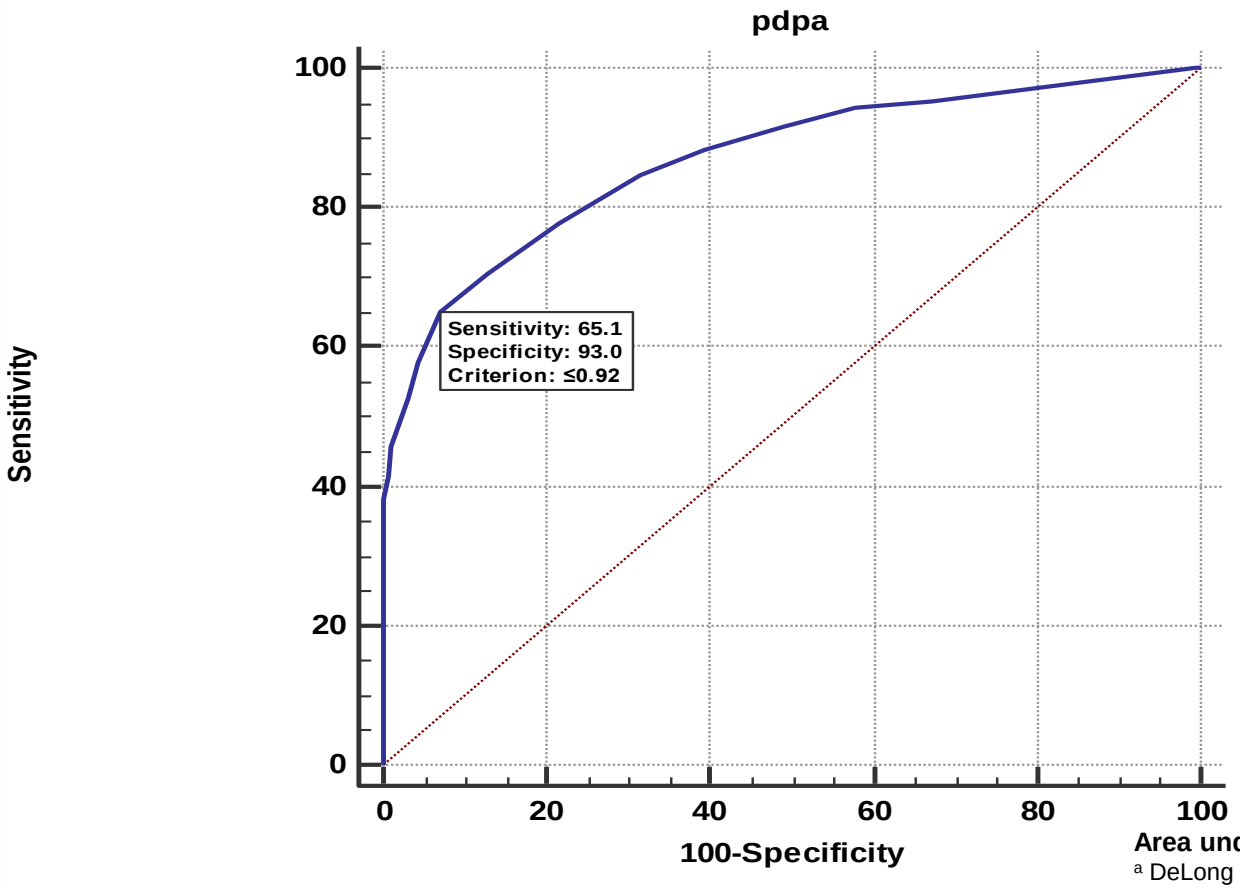
Pd/Pa and FFR measured after PCI result deemed angiographically satisfactory

Diagnostic performance of Pd/Pa against FFR tested post PCI

Baseline characteristics

	Pre PCI Cohort
Age	65 ± 8
Males	96%
Diabetes	47%
Hypertension	96%
CKD	20%
Smoking	42%
Prior revasc.	52%
SIHD	65%
ACS	35%

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

Area under the ROC curve (AUC)
[a] DeLong et al., 1988 [b] Binomial exact
Youden index[a] BC_a bootstrap confidence interval (1000 iterations; random number seed: 978).

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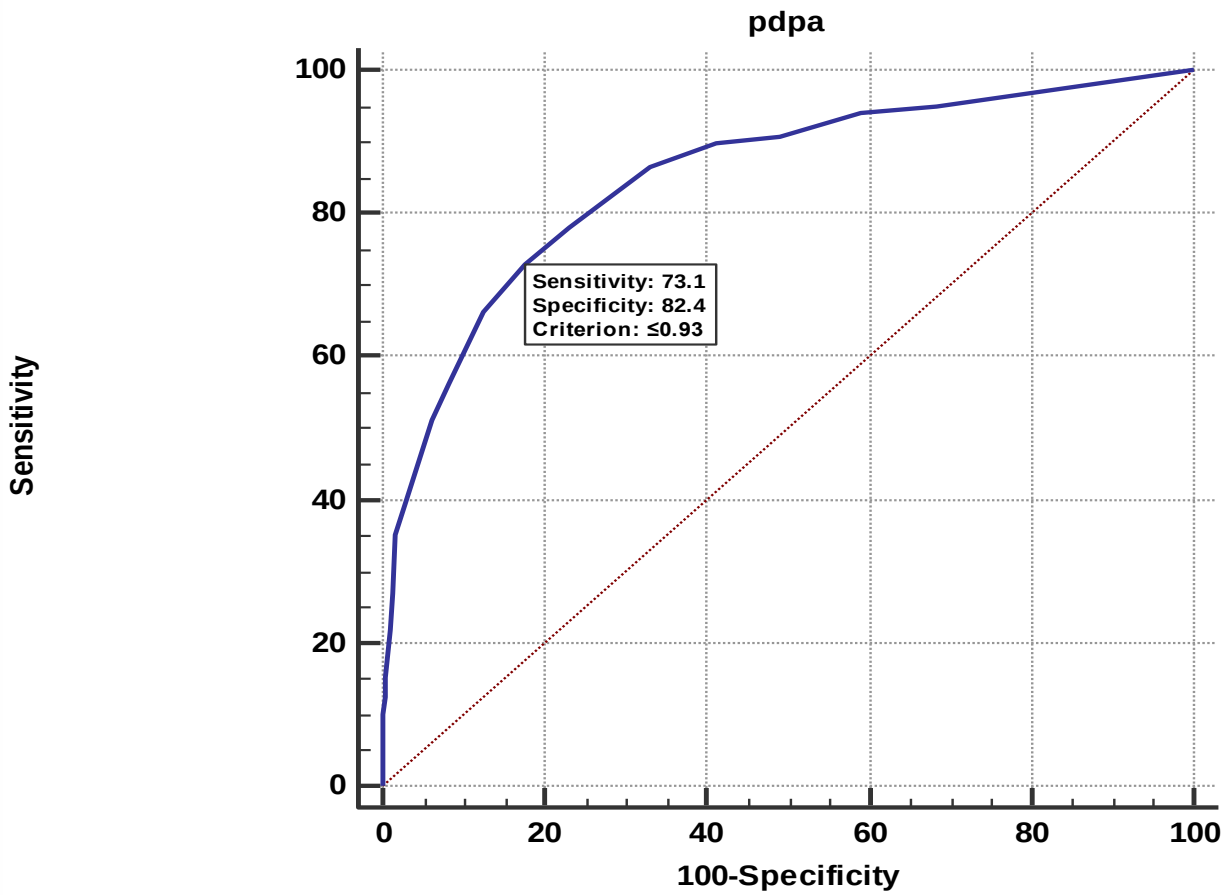
Model II- Derivation post PCI Cohort

Sample size	658
Positive group [a]	119 (18.1%)
Negative group [b]	539 (81.9%)
Area under the ROC curve (AUC)	0.850
Standard Error [a]	0.0208
95% Confidence interval [b]	0.820 to 0.876
z statistic	16.813
Significance level P (Area=0.5)	<0.0001



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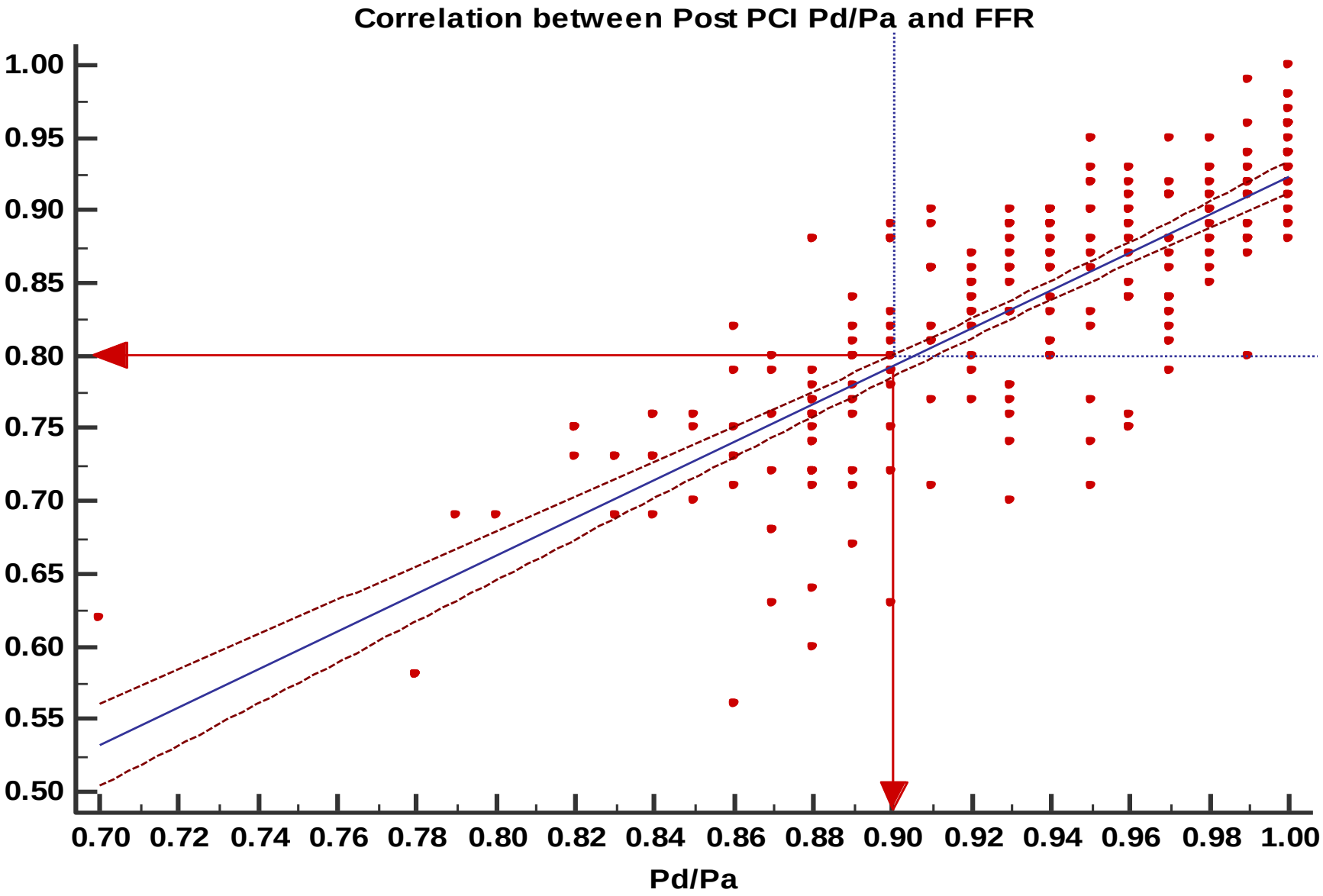
Model 3: Prospective Validation Cohort

Sample size	257
Positive group [a]	93 (36.2%)
Negative group [b]	164 (63.8%)



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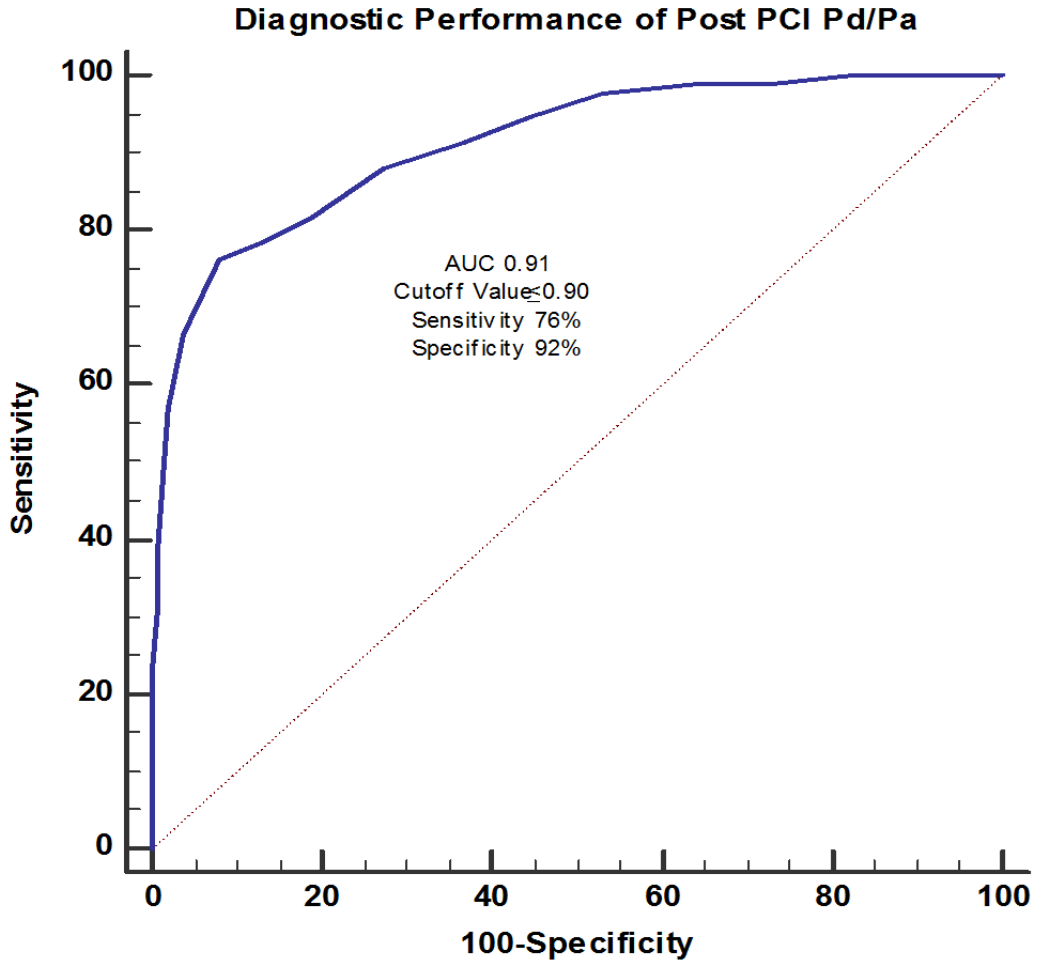
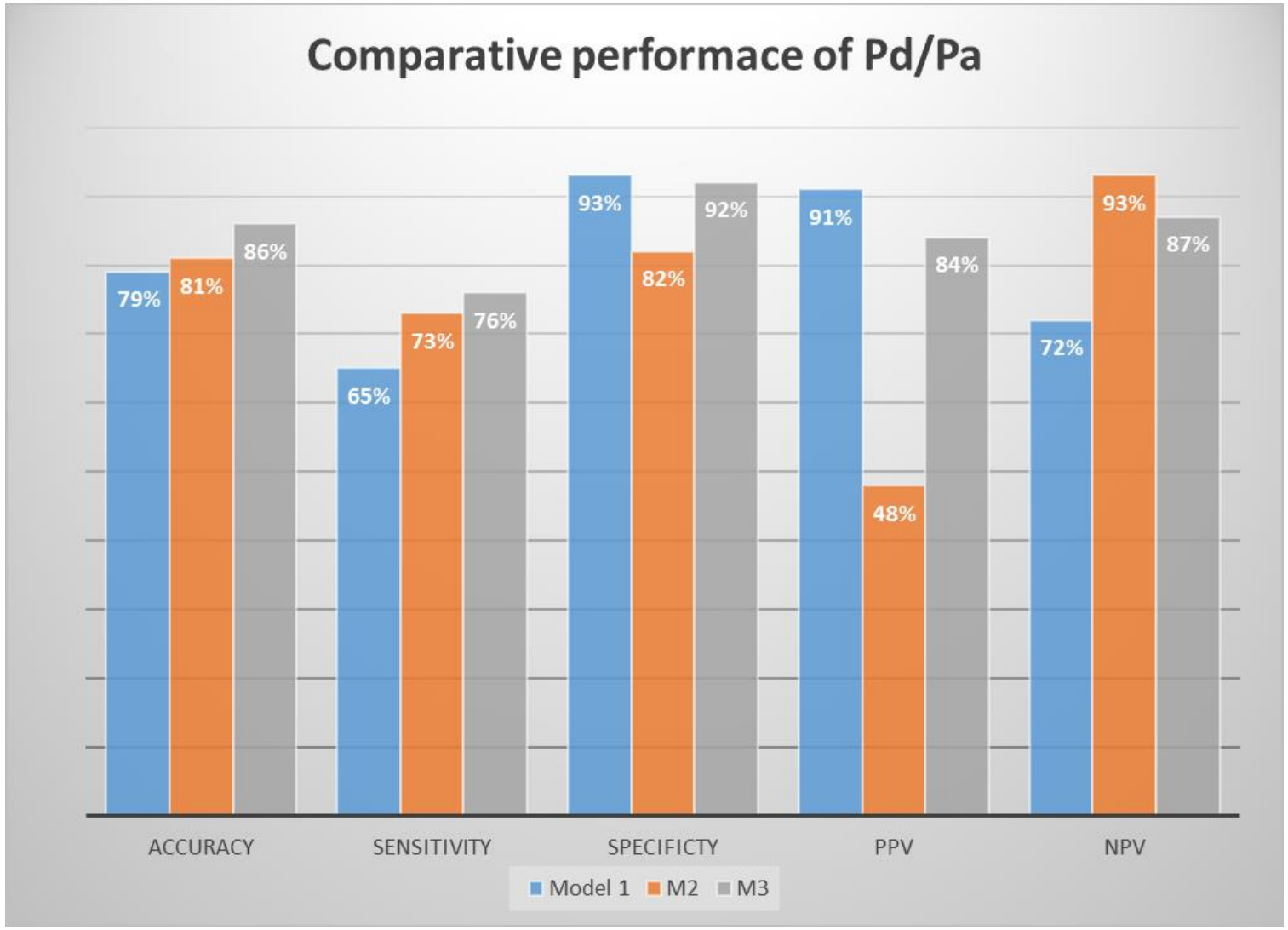
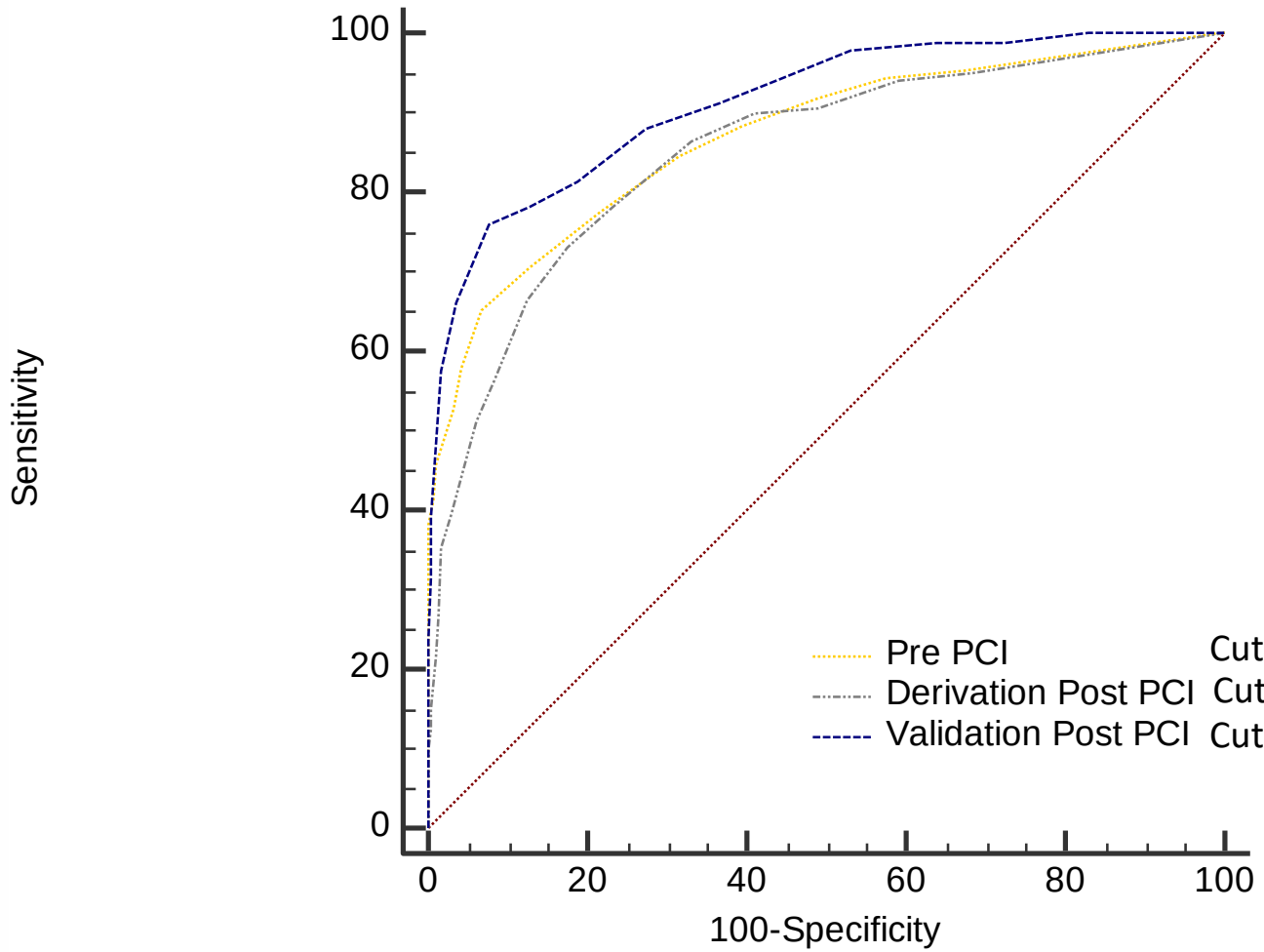
Criterion	Sensitivity	Specificity	+LR	-LR	+PV	-PV
<0.7	0.00	100.00		1.00		63.8
≤0.85	23.66	100.00		0.76	100.0	69.8
≤0.86	31.18	99.39	51.14	0.69	96.7	71.8
≤0.87	38.71	99.39	63.48	0.62	97.3	74.1
≤0.88	56.99	98.17	31.15	0.44	94.6	80.1
≤0.89	66.67	96.34	18.22	0.35	91.2	83.6
≤0.9	76.34	92.07	9.63	0.26	84.5	87.3
≤0.91	78.49	87.20	6.13	0.25	77.7	87.7
≤0.92	81.72	81.10	4.32	0.23	71.0	88.7
≤0.93	88.17	72.56	3.21	0.16	64.6	91.5
≤0.94	91.40	63.41	2.50	0.14	58.6	92.9
≤0.95	94.62	55.49	2.13	0.097	54.7	94.8
≤0.96	97.85	46.95	1.84	0.046	51.1	97.5
≤0.97	98.92	35.98	1.55	0.030	46.7	98.3
≤0.98	98.92	27.44	1.36	0.039	43.6	97.8
≤0.99	100.00	17.07	1.21	0.00	40.6	100.0
≤1	100.00	0.00	1.00		36.2	


Diagnostic Performance of Post PCI Pd/Pa
Sensitivity
100
80
60
40
20
0
AUC 0.91
Cutoff Value≤0.90
Sensitivity 76%
Specificity 92%
0
20
40
60
80
100
100-Specificity


Comparative performace of Pd/Pa
79%
81%
86%
65%
73%
76%
93%
82%
92%
91%
48%
84%
72%
93%
87%
ACCURACY
SENSITIVITY
SPECIFICTY
PPV
NPV
Model 1
M2
M3

Comparative effectiveness



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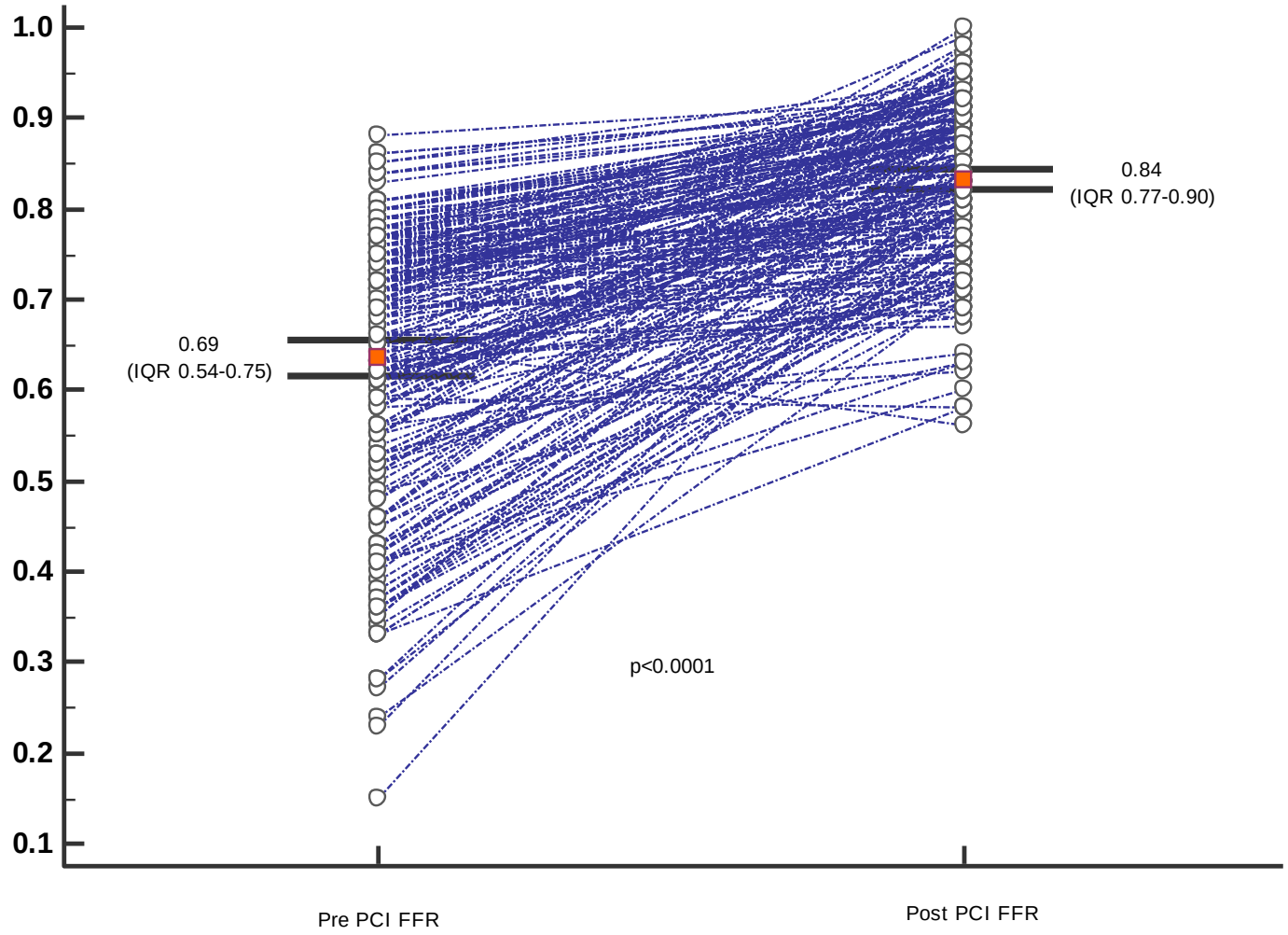
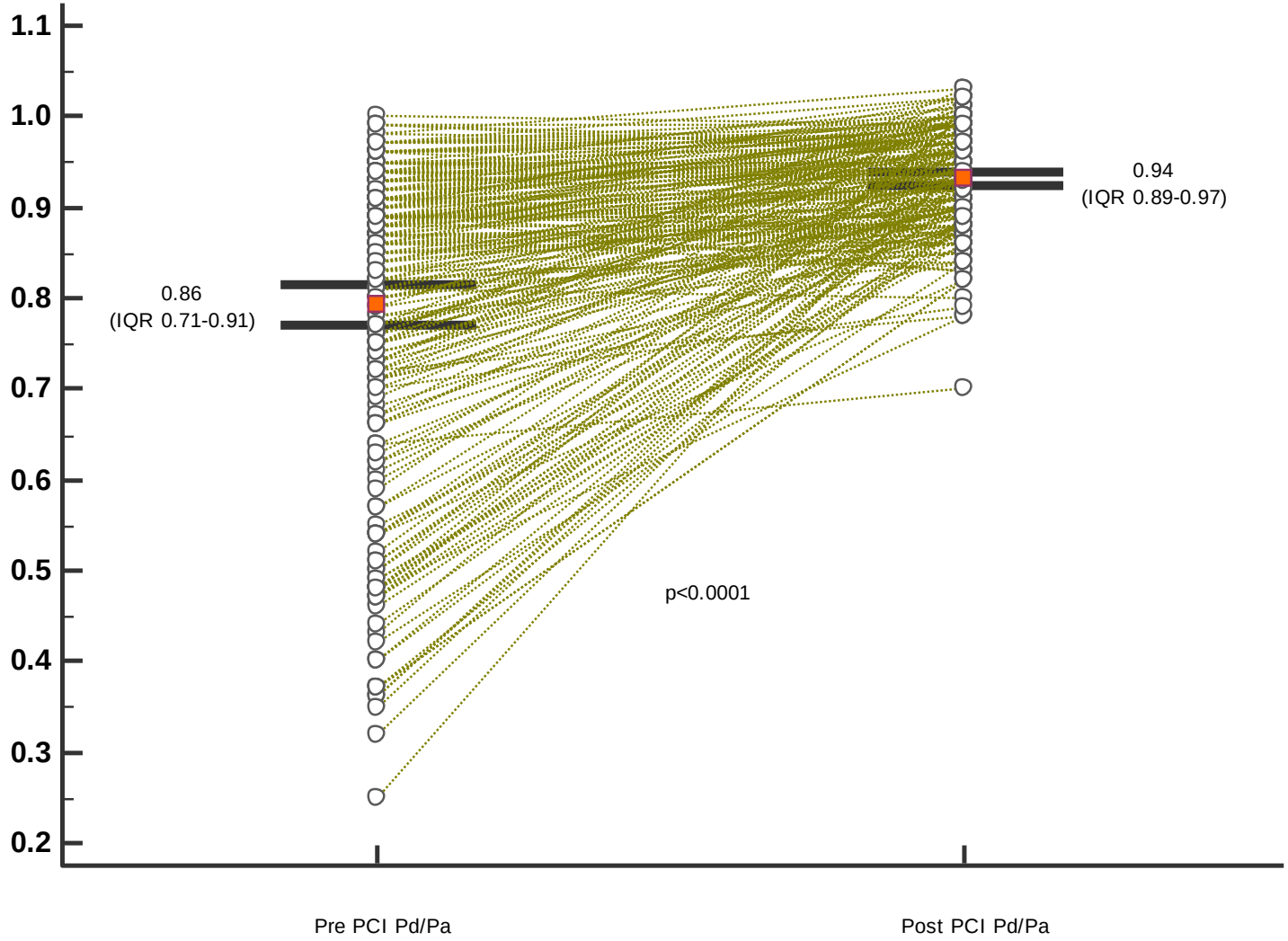
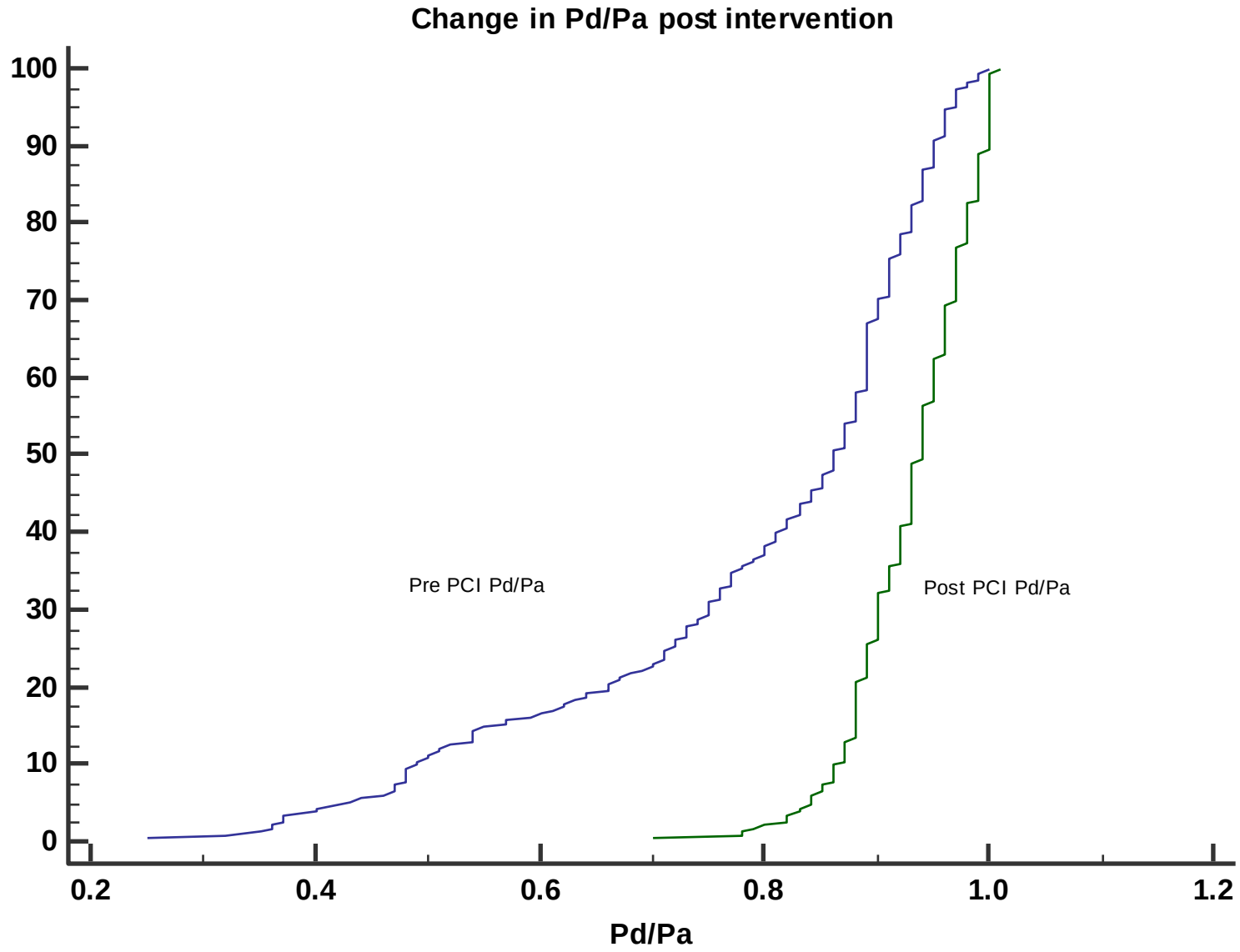
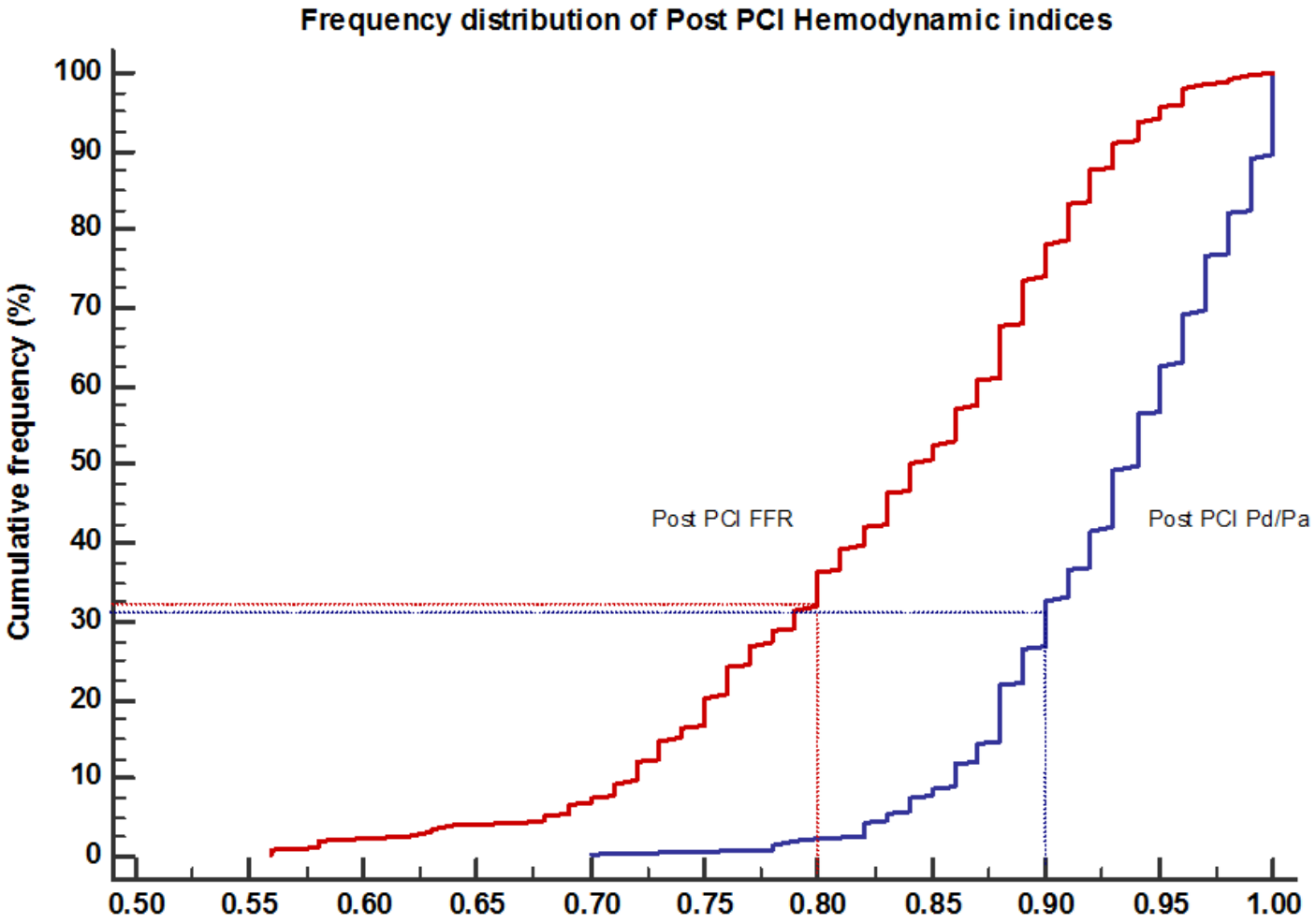
Post PCI FFR to evaluate functional results of PCI

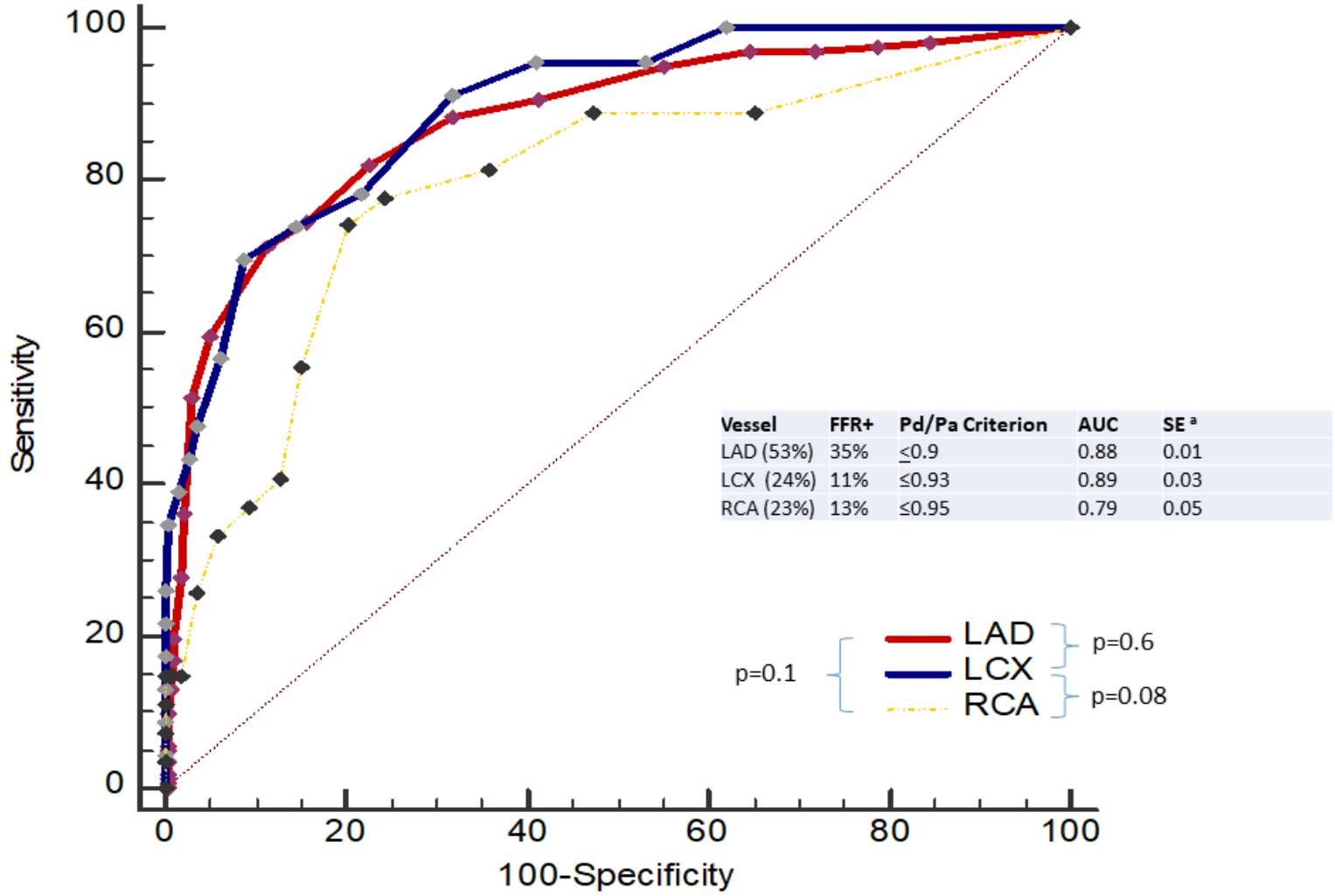


Post PCI Pd/Pa to evaluate functional outcome of PCI

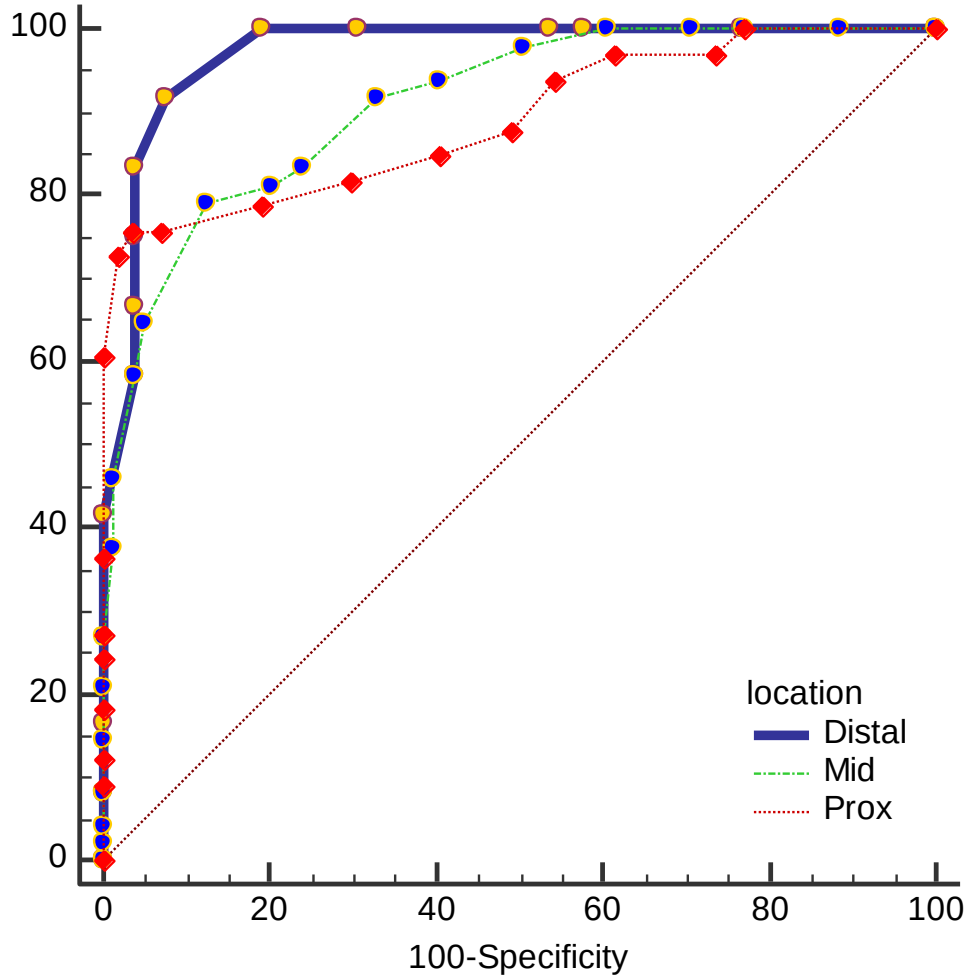



Change in Pd/Pa post intervention
100
90
80
70
60
50
40
30
20
10
0
0.2
0.4
0.6
0.8
1.0
1.2
Pd/Pa
Pre PCI Pd/Pa
Post PCI Pd/Pa


Frequency distribution of Post PCI Hemodynamic indices
Cumulative frequency (%)
100
90
80
70
60
50
40
30
20
10
0
0.50
0.55
0.60
0.65
0.70
0.75
0.80
0.85
0.90
0.95
1.00
Post PCI FFR
Post PCI Pd/Pa



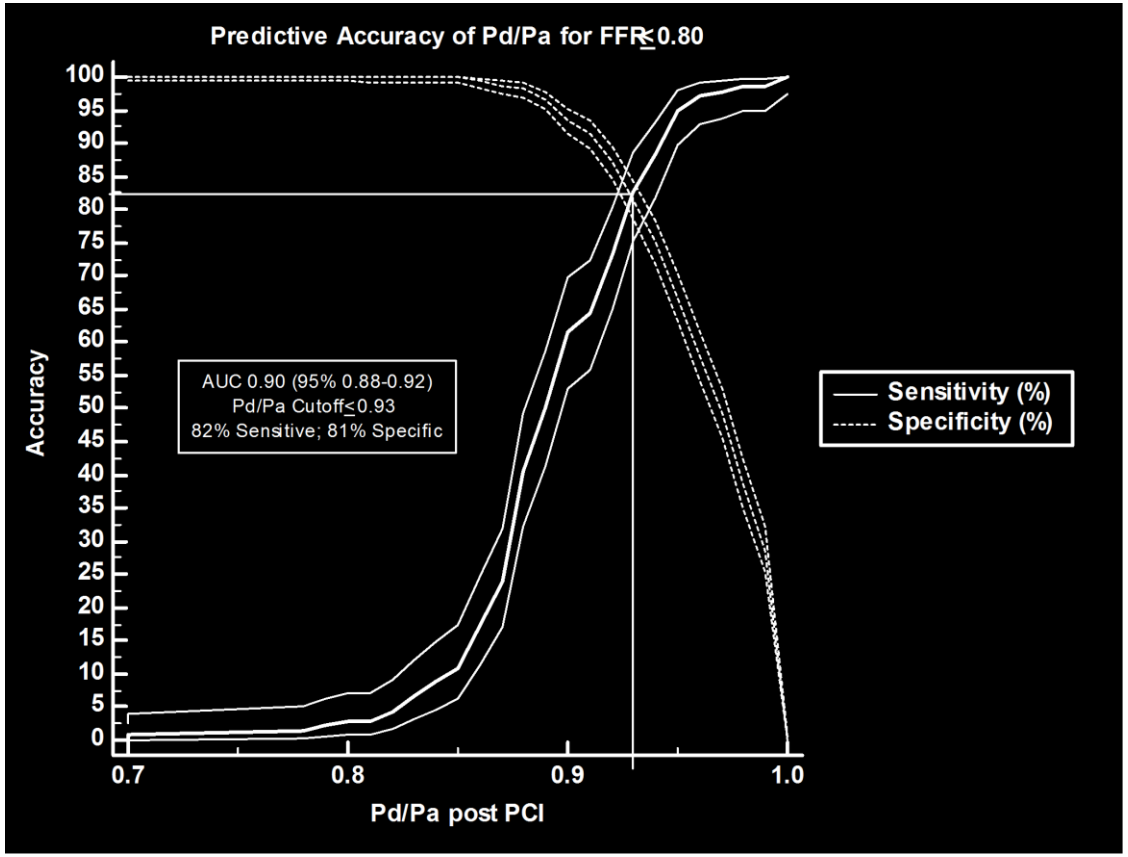
Vessel	FFR+	Pd/Pa Criterion	AUC	SE [a]
LAD (53%)	35%	≤0.9	0.88	0.01
LCX (24%)	11%	≤0.93	0.89	0.03
RCA (23%)	13%	≤0.95	0.79	0.05

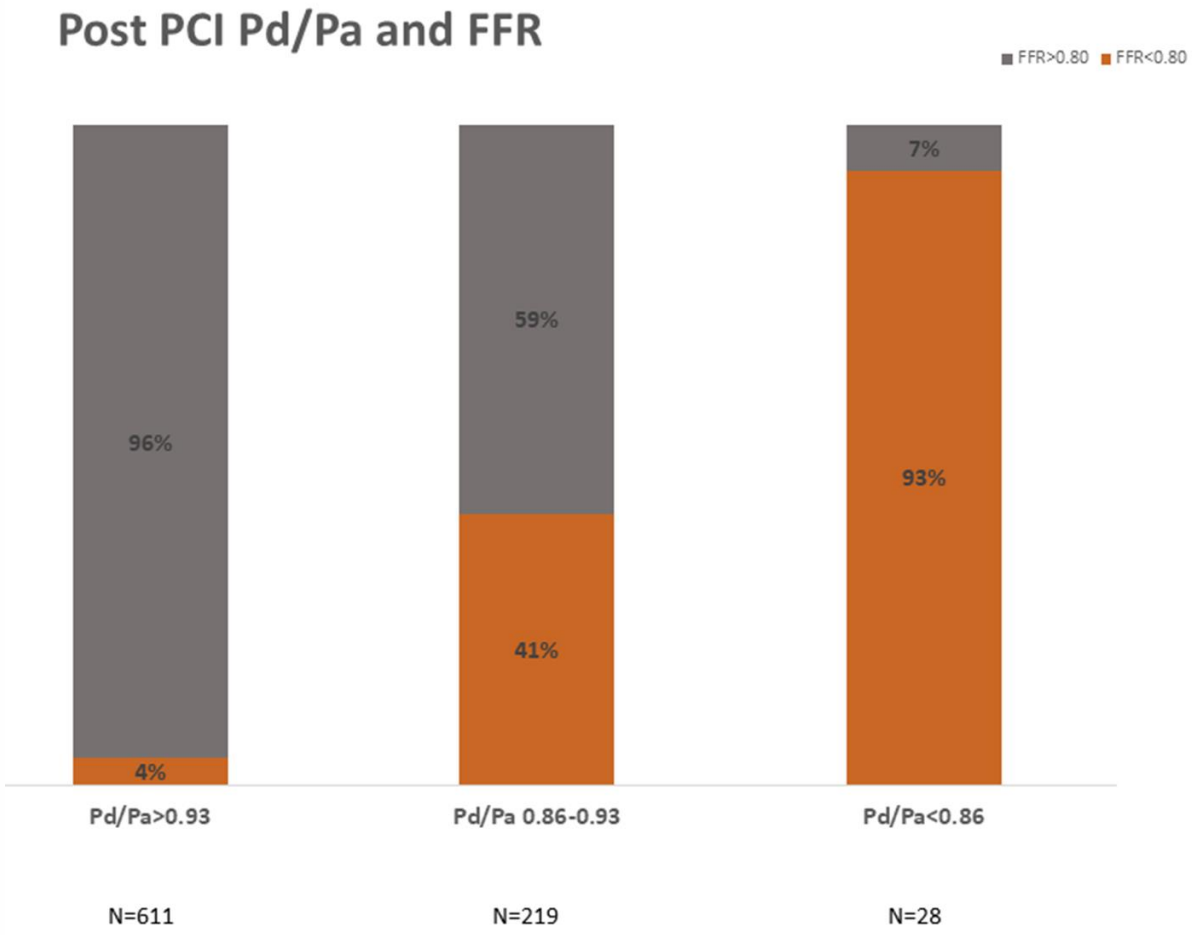


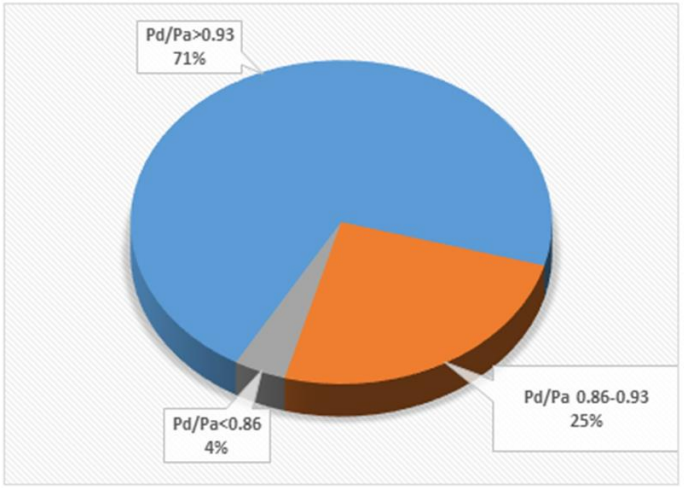
location	AUC	SE [a]	95% CI [b]
Distal	0.971	0.0226	0.858 to 0.999
Mid	0.909	0.0252	0.845 to 0.953
Prox	0.891	0.0391	0.807 to 0.947

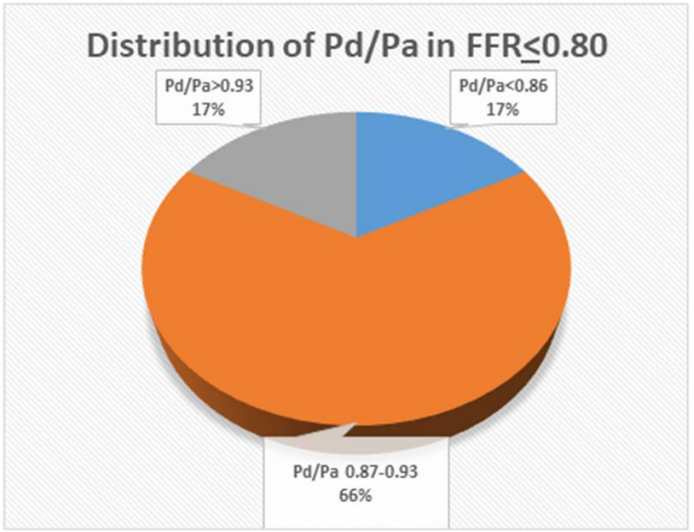
Distal ~ Mid	
Difference between areas	0.0617
Significance level	P = 0.0682
Distal ~ Prox	
Difference between areas	0.0804
Significance level	P = 0.0750
Mid ~ Prox	
Difference between areas	0.0187
Significance level	P = 0.6885

Sequential test strategy:
Pooling Patients from derivation and validation cohorts









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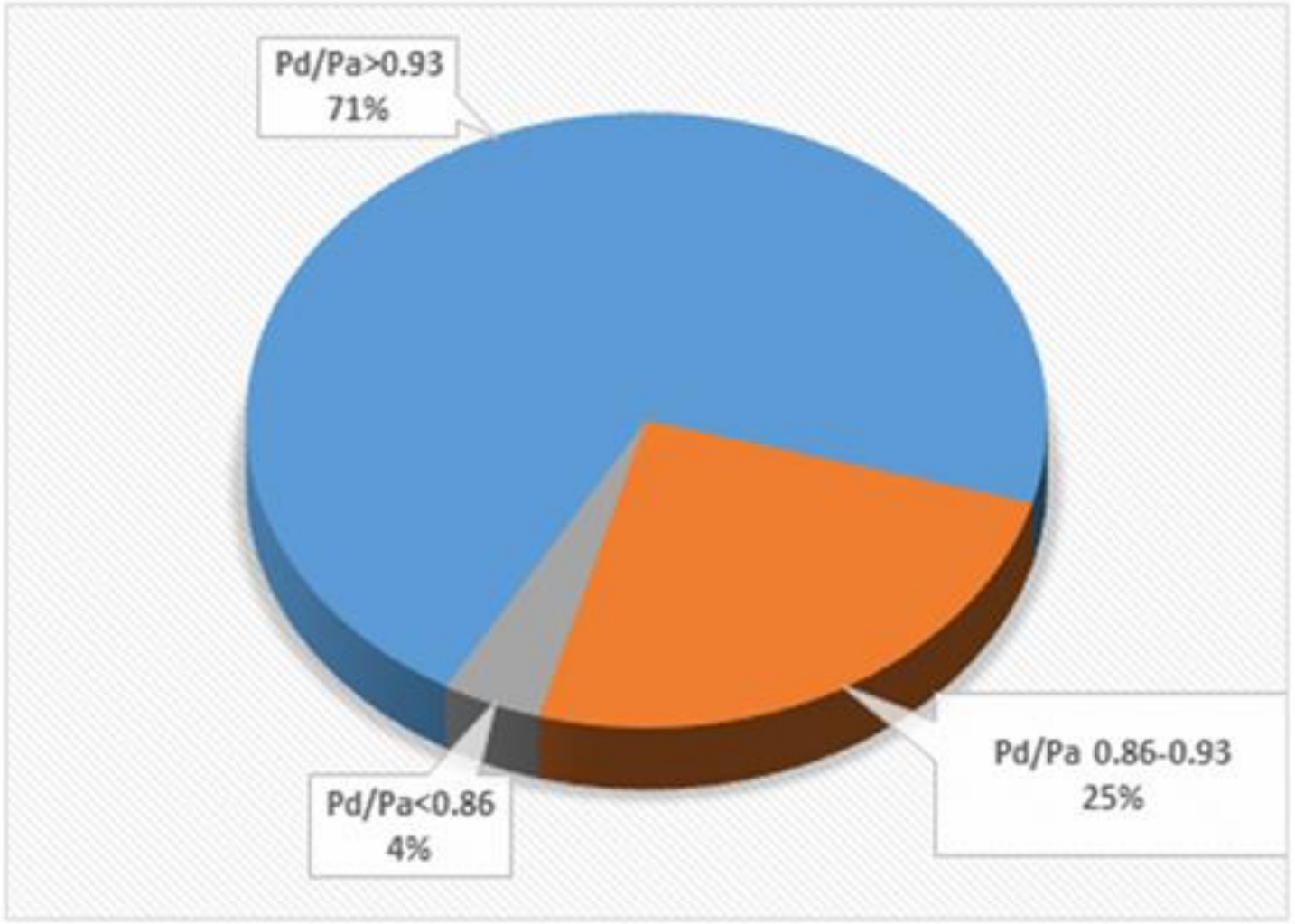

- Using the hybrid strategy, diagnostic accuracy is 95% with Negative Predictive Value (NPV) of 96% to diagnose residual ischemia post-PCI.
- Adenosine can be avoided in >75% patients using this strategy.

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.