DES In-stent Restenosis

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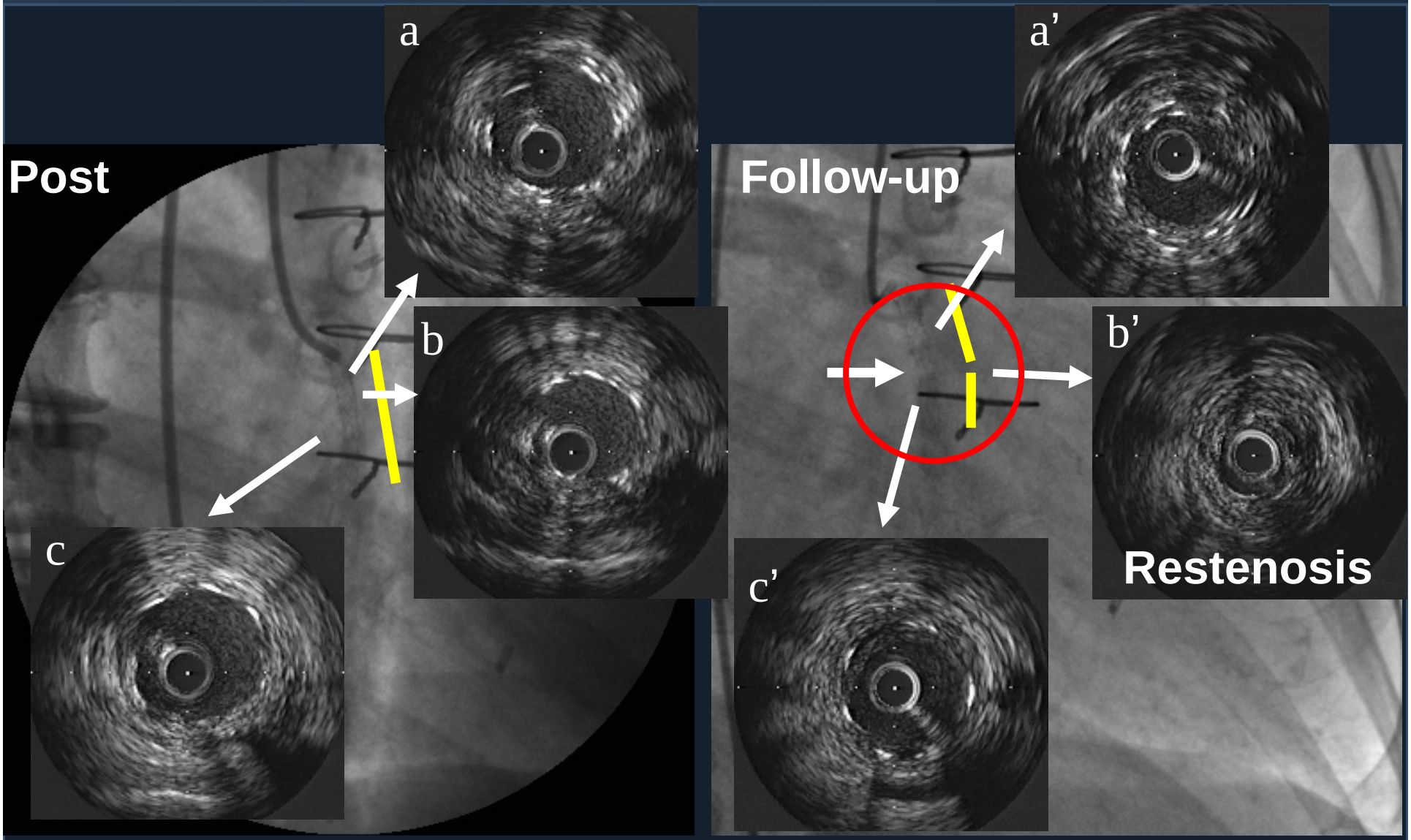
DES Restenosis

- *Mechanisms*
- Predictors
- Morphological patterns
- Therapy approach

Mechanisms of DES Restenosis

- ***Biological factors***
  - Drug resistance
  - Hypersensitivity
- ***Mechanical factors***
  - Non uniform stent strut distribution
  - Stent fractures
  - Polymer peeling
  - Non uniform drug deposition
- ***Technical factors***
  - Incomplete stent expansion
  - Stent gaps or “misses” (uncovered lesion segments)
  - Barotrauma to unstented segments

DES fractures



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Aoki J. et al. *CCI* 2007;69: 380-6

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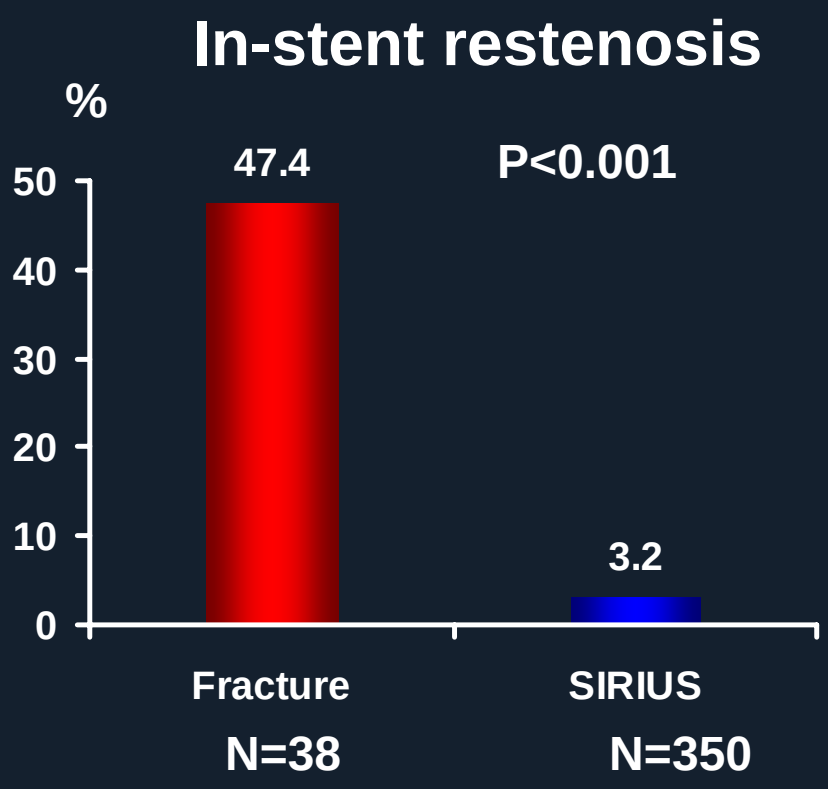
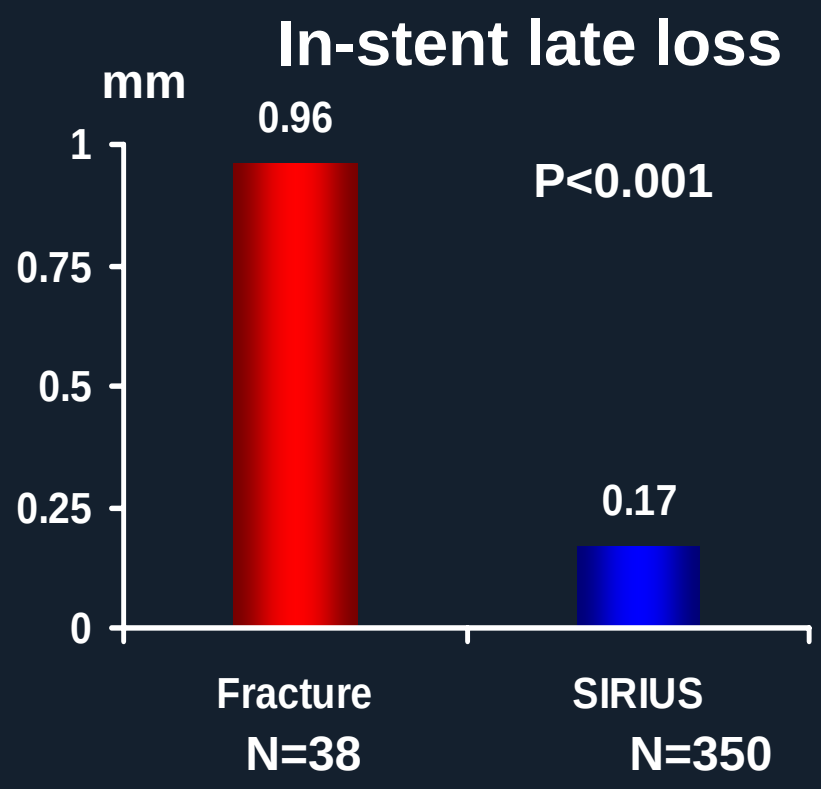
Stent Fracture Analysis

Review of Adverse Event Reports submitted to Cordis between August 2003 - July 2006

Follow-up findings





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Popma JJ. et al. DES revolution IV, 2007

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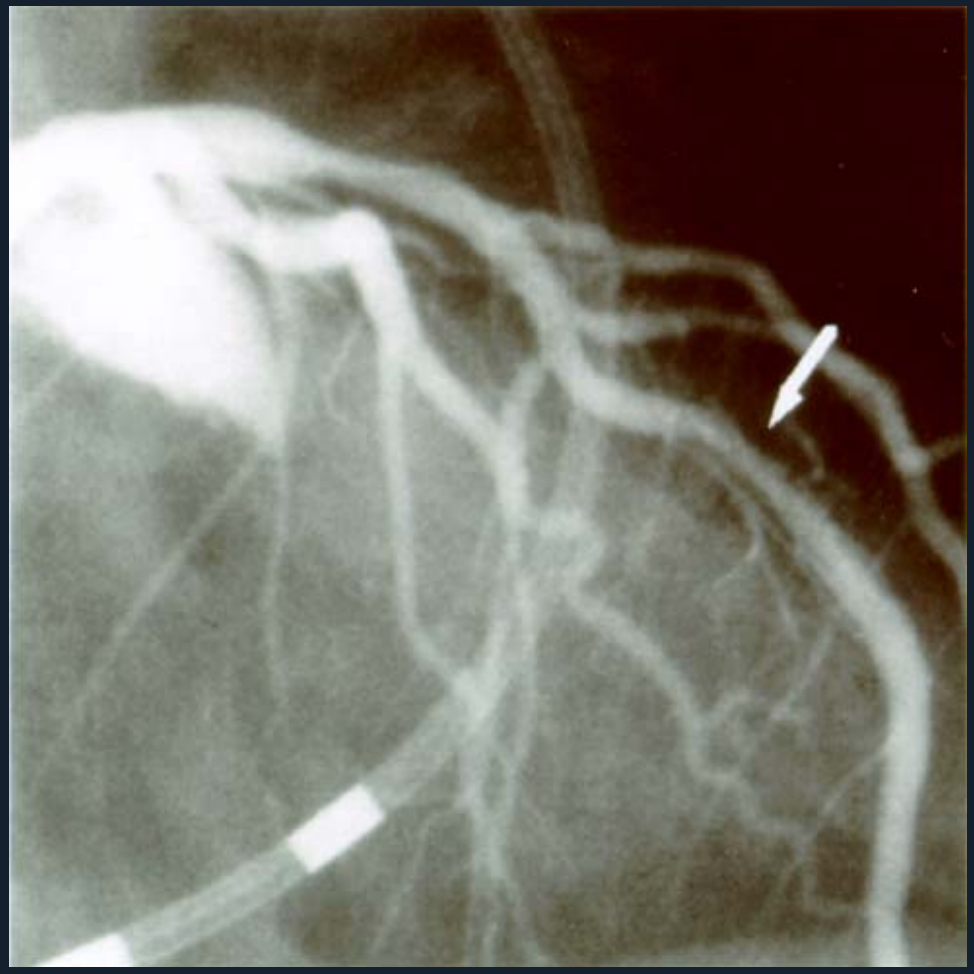
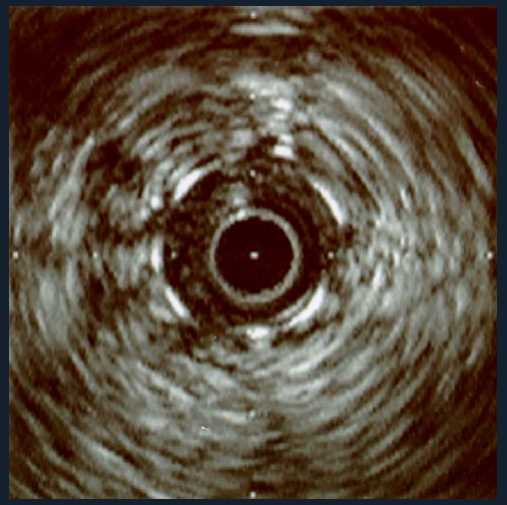
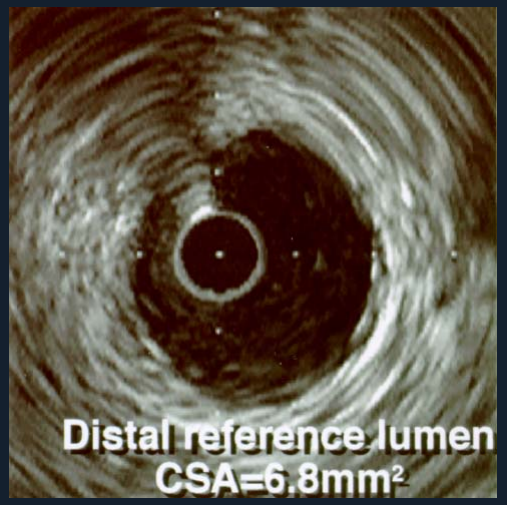
Technical factors

Stent underexpansion







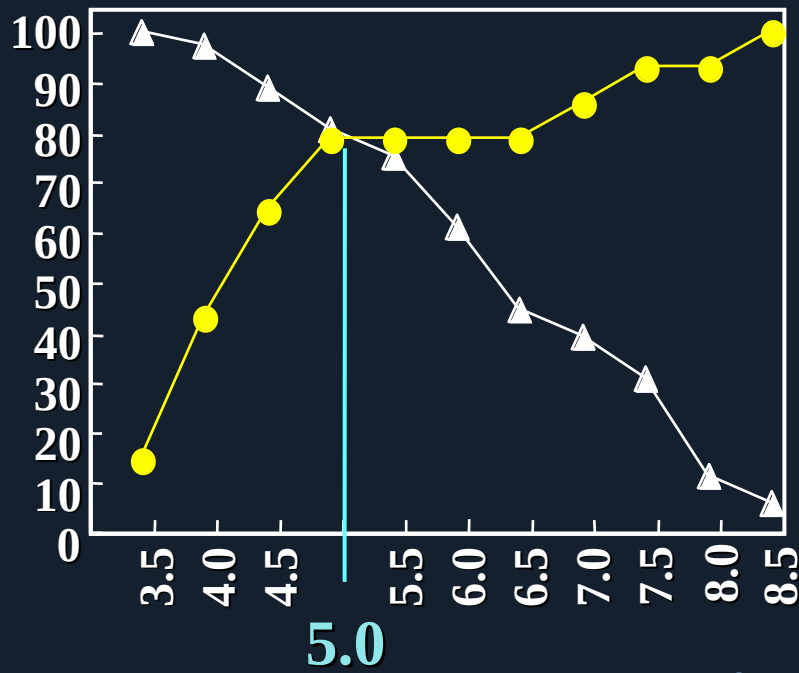
Technical factors

Stent underexpansion

Post-Procedure MSA and Binary Restenosis

(sensitivity and specificity curves)

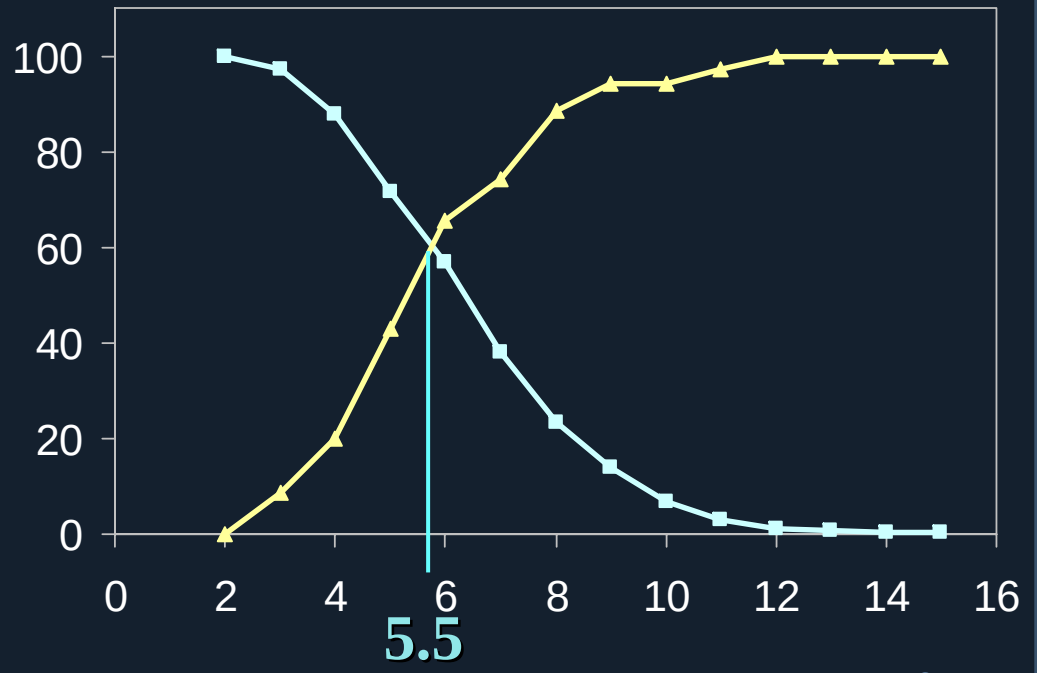
Cypher



Minimum stent area (mm²)

Sonoda S. et al. J Am Coll Cardiol 2004;43:1959-63

Taxus



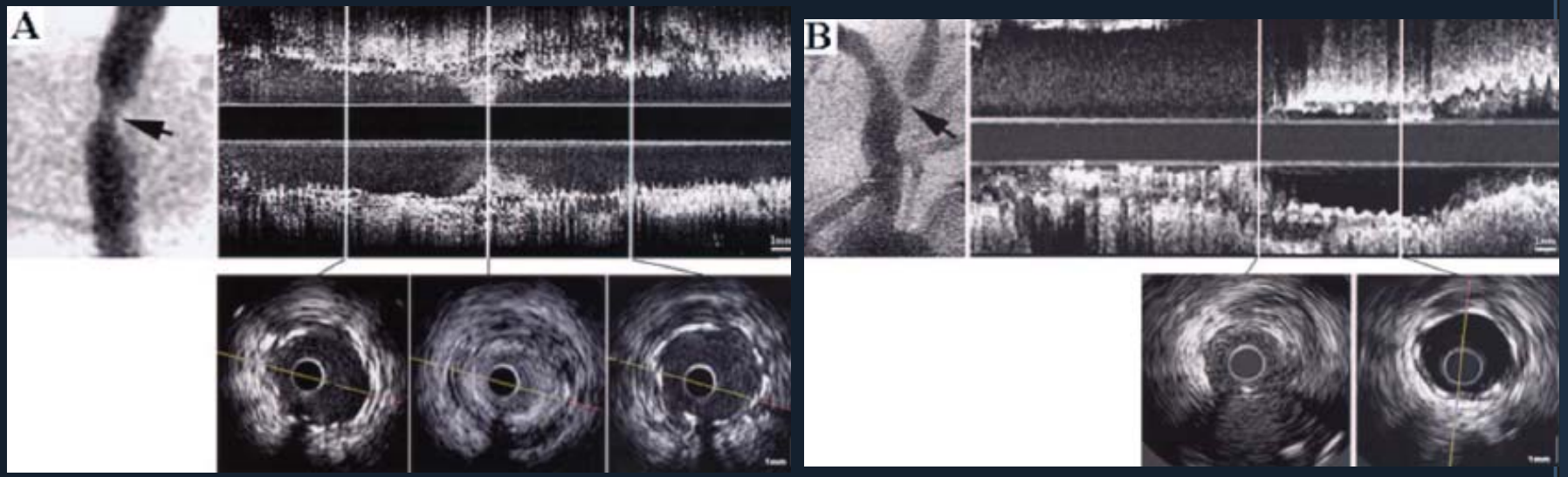
Minimum Stent Area (MSA, mm²)

Weissman N. TCT 2006

Technical factors

Gap

Incomplete stent coverage



Stent edge restenosis is frequently associated with local trauma outside the stent. In-stent restenosis occurs as a localized lesion, commonly associated with a discontinuity in stent coverage.

Lemos A. et al. *Circulation* 2003; 108: 257-60

DES Restenosis

- Mechanisms
- *Predictors*
- Morphological patterns
- Therapy approach

Independent predictors of TLR after DES implantation

Randomized trials (on label)

SES arm in SIRIUS	Odds ratio
✓ Post procedure in-stent MLD	0.1840
✓ Total implanted stent length	1.0270

PES arm in TAXUS IV	Hazard ratio (95% CI)
✓ No study stents implanted	5.86 (1.36 - 25.27)
✓ No prior MI	3.70 (1.11 – 12.50)
✓ Female gender	2.33 (1.08 – 5.00)
✓ Lesion length	1.05 (1.01 – 1.10)

Independent predictors of DES restenosis

Registries (including off-label)

Rotterdam (Circulation. 2004)

- ✓ In-stent restenosis lesion
- ✓ Ostial lesions
- ✓ DM
- ✓ Vessel size
- ✓ LAD

Munich (Circulation. 2006)

- ✓ Vessel size
- ✓ Final Diameter stenosis
- ✓ DES type

Seoul (Am J Cardiol. 2006)

- ✓ DES type
- ✓ Final MLD
- ✓ Lesion length

Washington (ACC. 2007)

- ✓ Age
- ✓ Hypertension
- ✓ Procedural length
- ✓ Lack of IVUS guidance
- ✓ Total stented length

Milan (AHA. 2006)

- ✓ DM
- ✓ Unstable angina
- ✓ Reference vessel diameter
- ✓ Number of stents per lesion

DES Restenosis

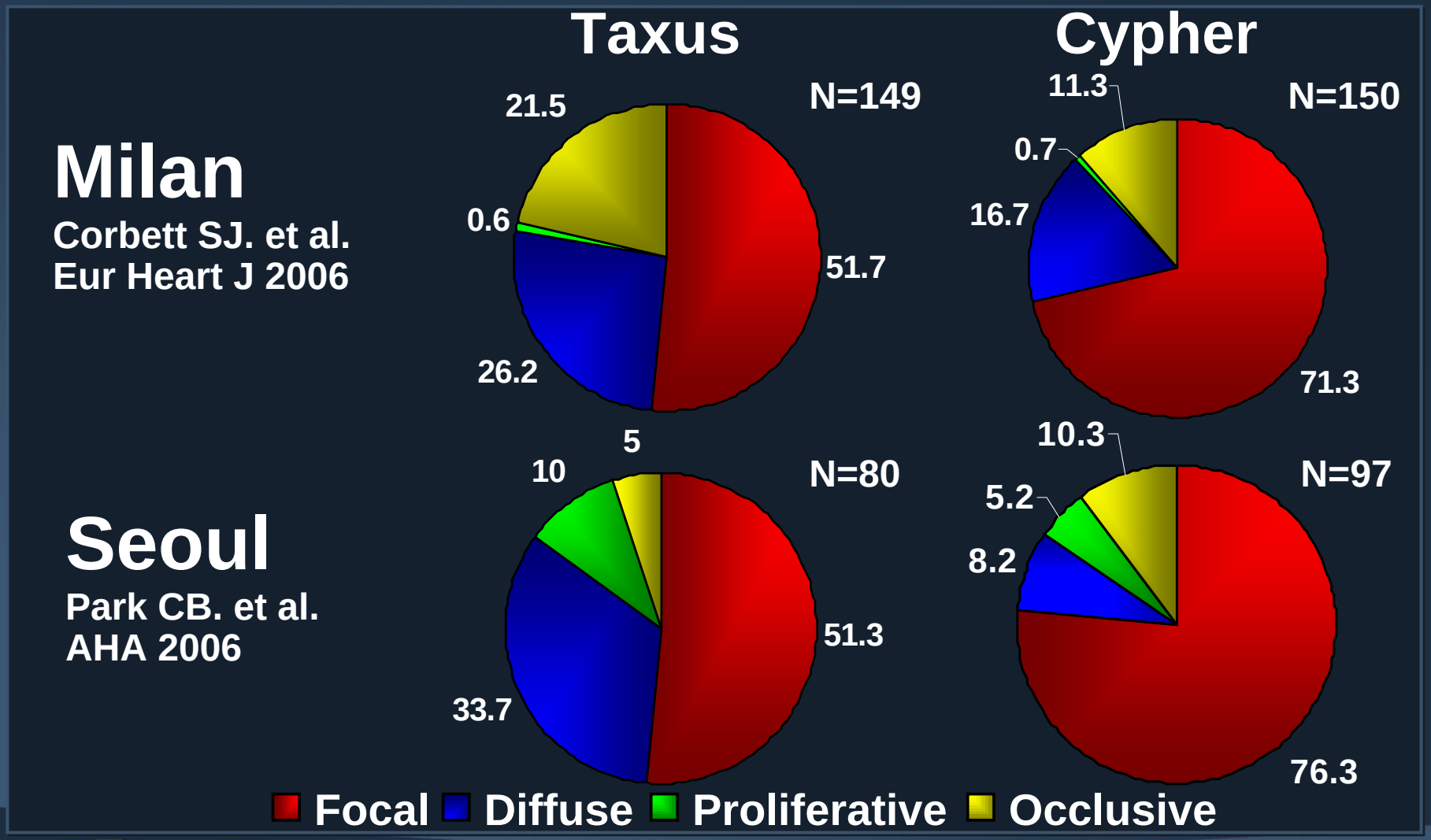
- Mechanisms
- Predictors
- *Morphological patterns*
- Therapy approach
- « Delayed » restenosis

Morphological Patterns of DES In-Stent Restenosis Lesions

SIRIUS	Sirolimus (n=31)	Control (n=128)	P-value
I - focal	*87%*	*42%*	*<0.001*
II/III – diffuse or proliferative	6.5%	50%	<0.001
IV - total occlusion	6.5%	8%	0.895
TAXUS IV	**Paclitaxel (n=16)**	**Control (n=65)**	**P-value**
I - focal	*63%*	*31%*	*<0.001*
II/III – diffuse or proliferative	24%	66%	<0.001
IV - total occlusion	13%	3%	0.245

Patterns of In-Stent Restenosis

Cypher vs Taxus



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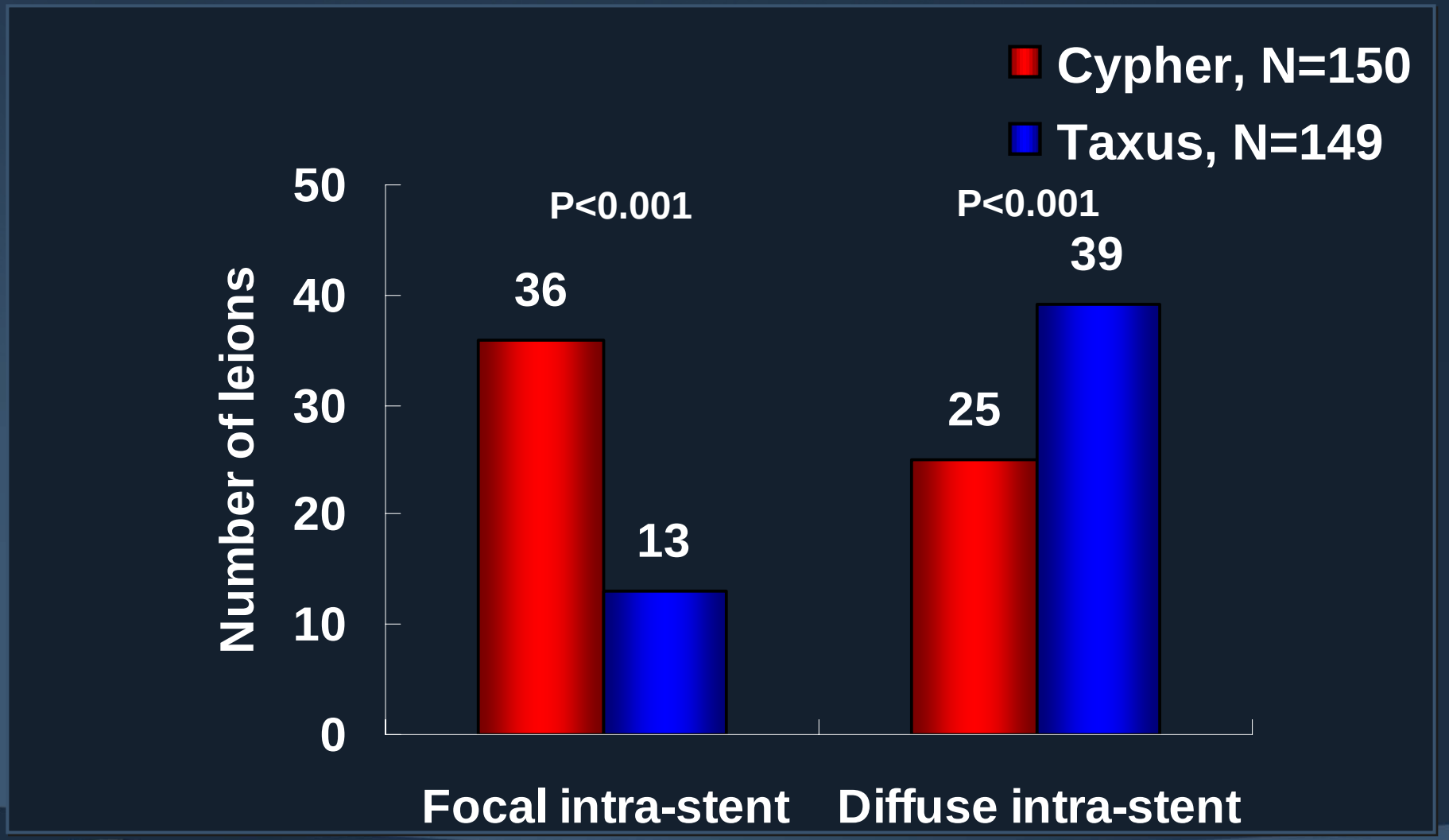
Patterns of In-Stent Restenosis
Milan experience



Corbett SJ. et al. *Eur Heart J* 2006 27:2330-2337

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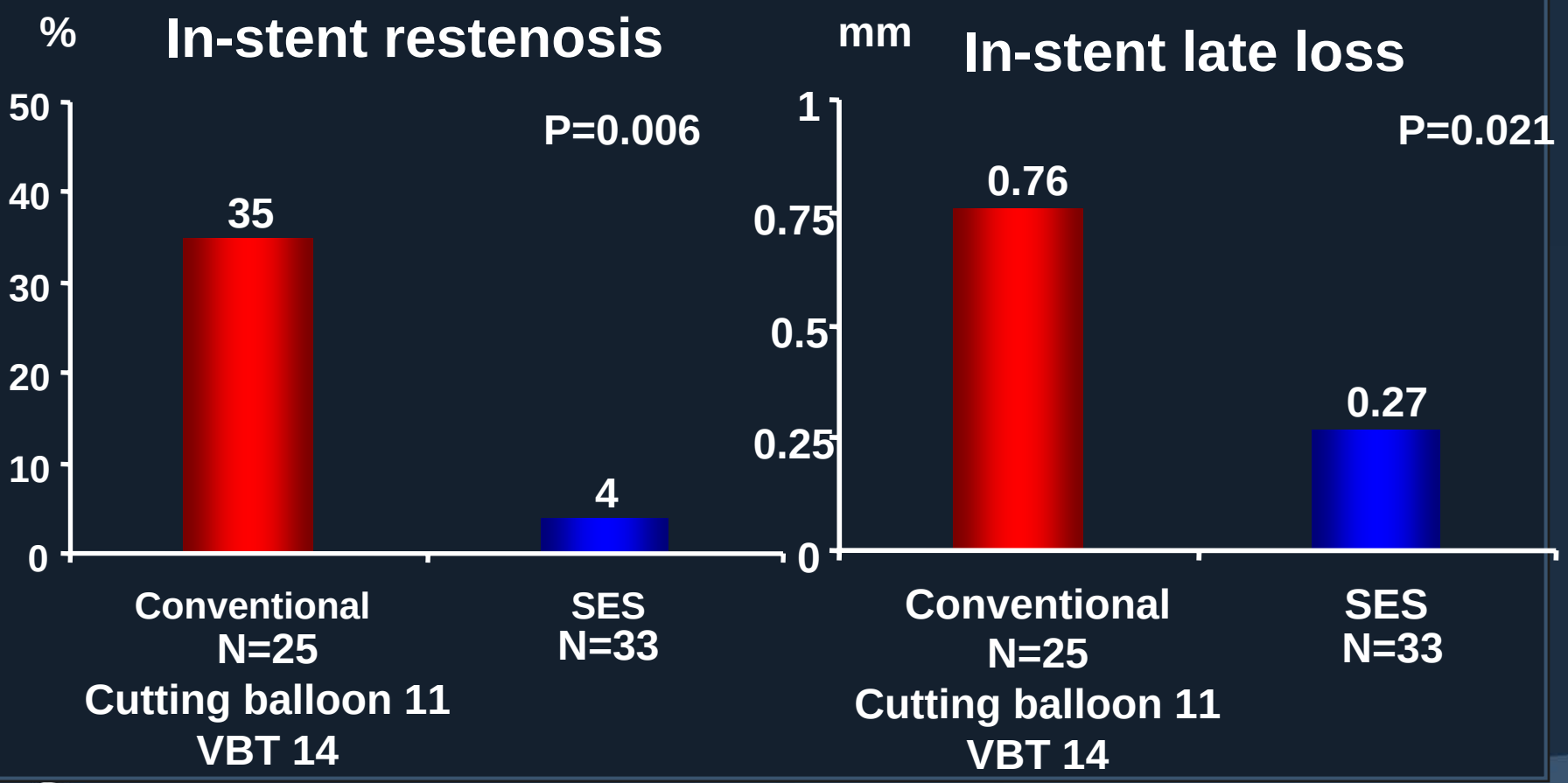
DES Restenosis

- Mechanisms
- Predictors
- Morphological patterns
- *Therapy approach*

Conventional therapies vs SES for DES Failures

6-month angiographic outcomes



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Kim YH. et al. *Am J Cardiol* 2006;98:1451-4

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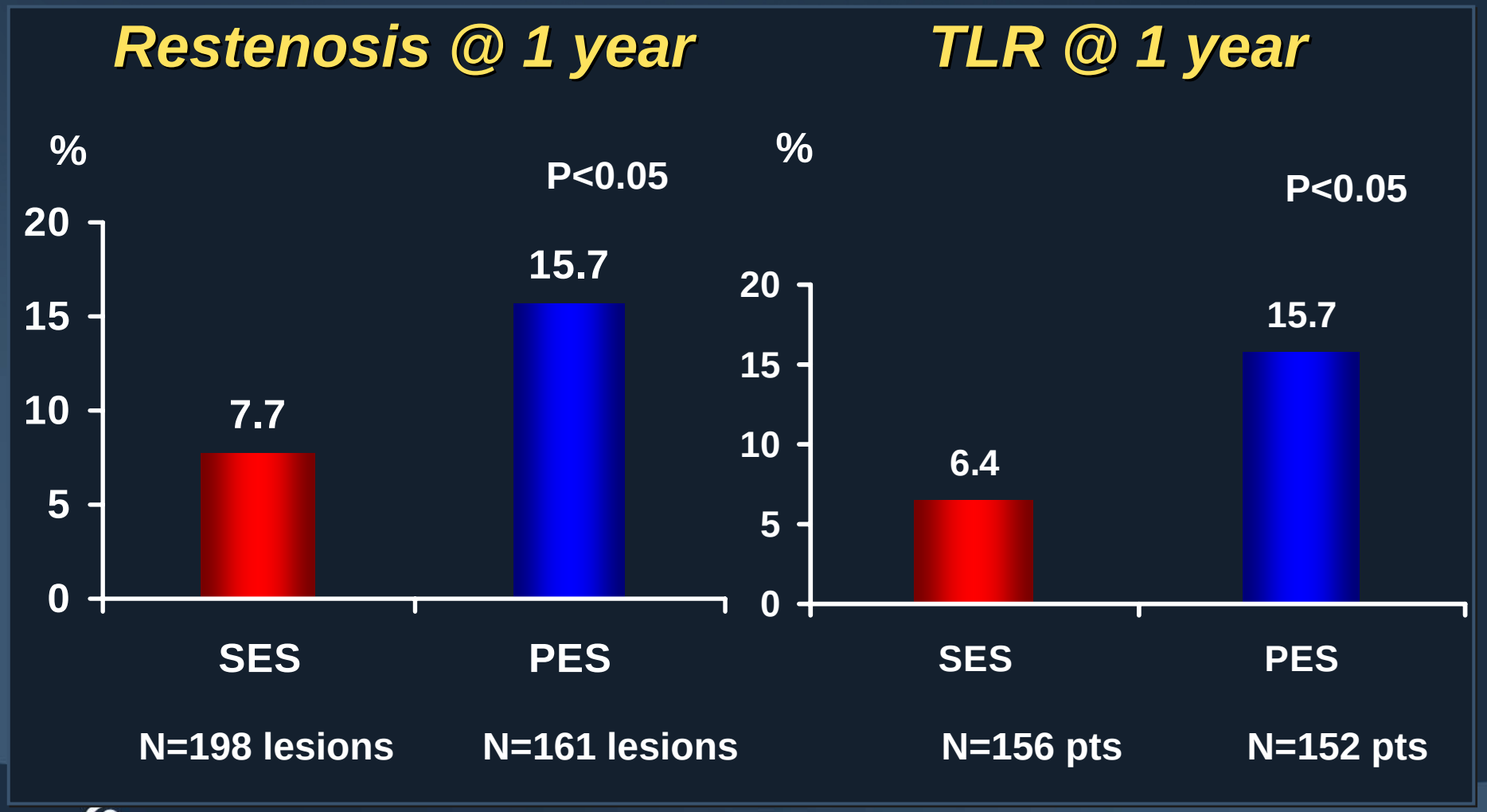
SES vs PES for SES Failures
Multicenter Registry in Asia



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Nakamura S. et al. ACC 2007

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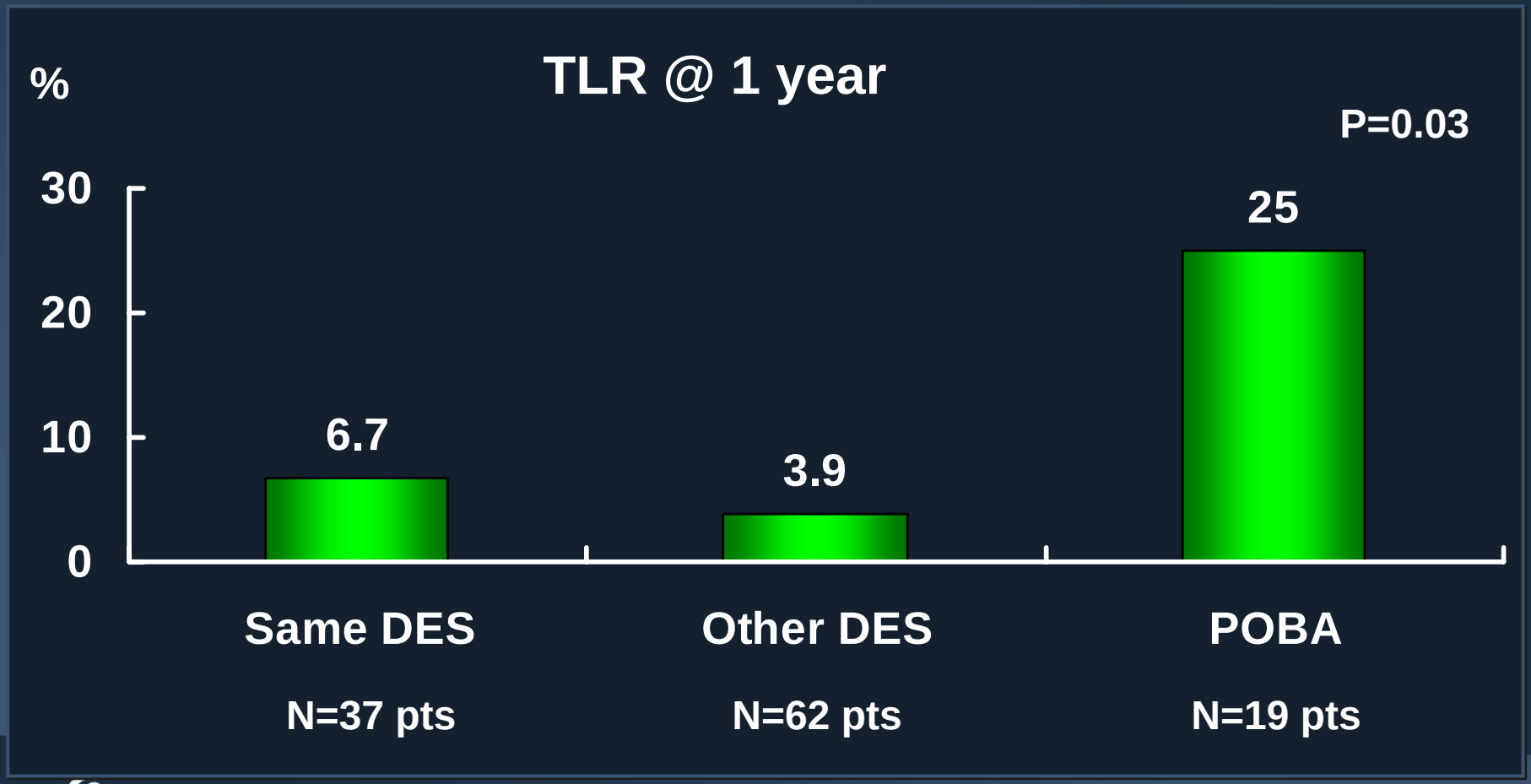
Same DES vs other DES vs. POBA for DES Failures

Does the switch therapy work?



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Solinas E. et al. TCT 2006

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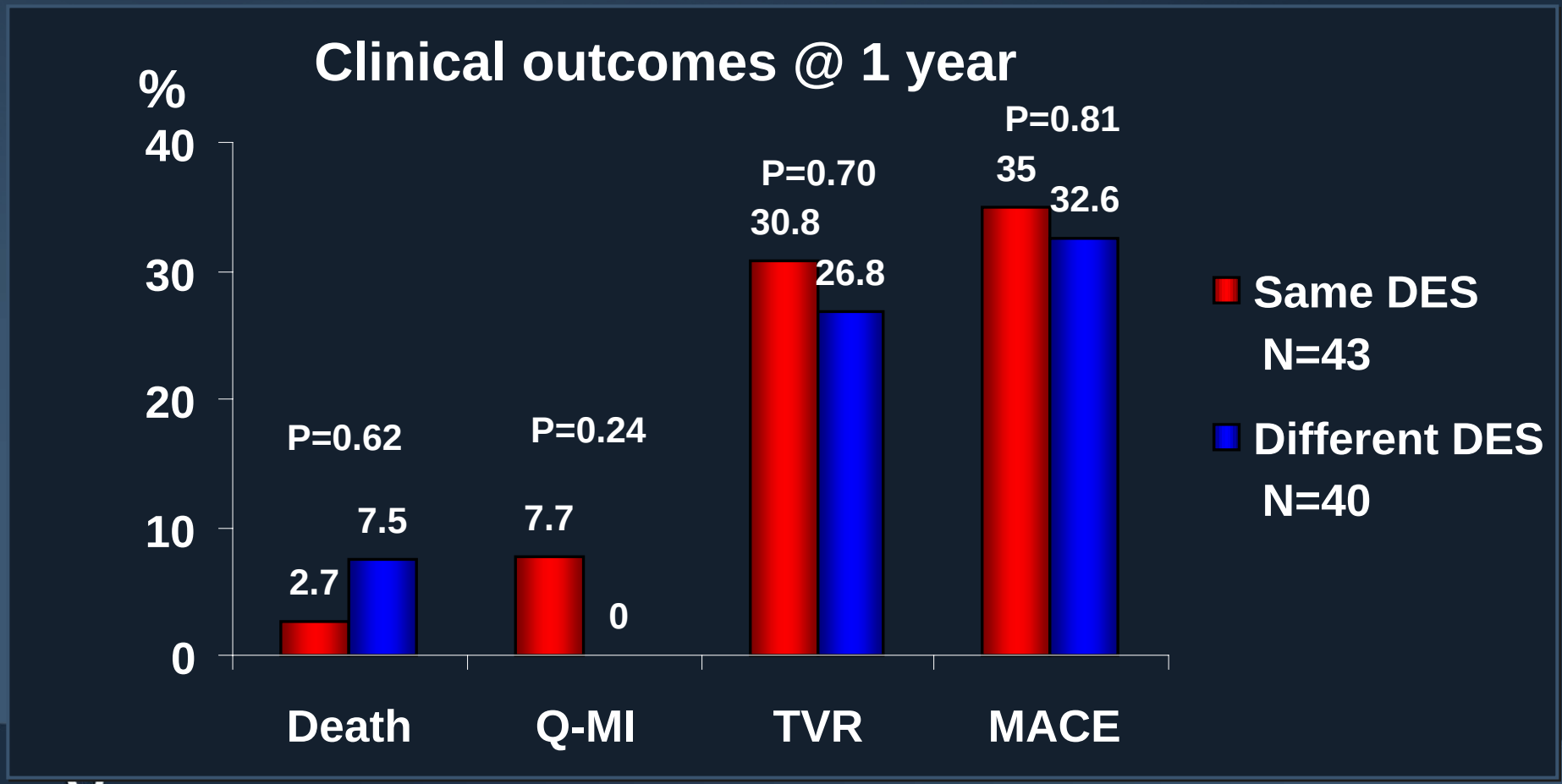
Same DES vs other DES vs. other treatment for DES Failures

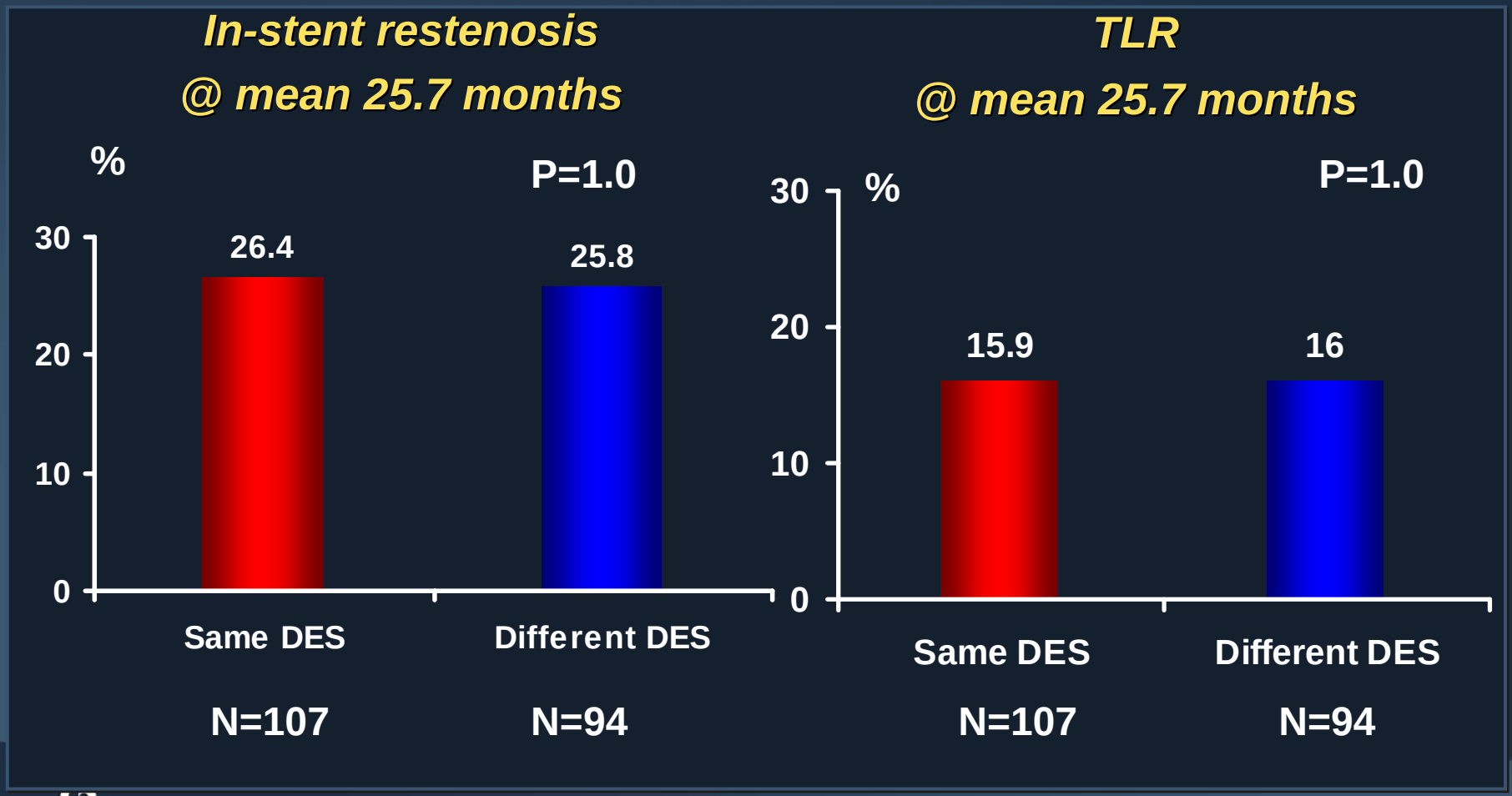
Does the switch therapy work?



Garg S. et al. *CCI*. 2007;70: 9-14

Same DES vs other DES vs other treatment for DES Failures

Does the switch therapy work?



Cosgrave J. et al. *AHJ*.2007;153: 354-9

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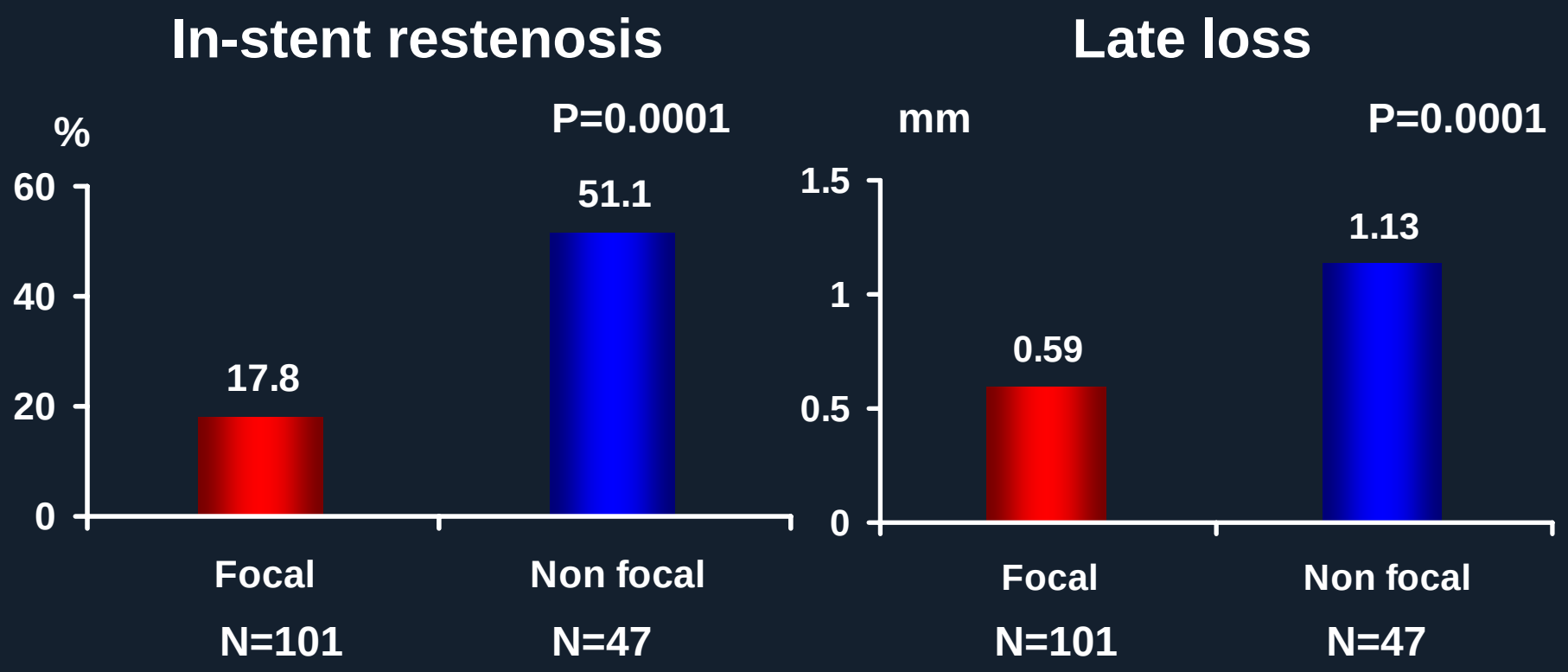
Do patterns of in-stent restenosis predict outcomes in the DES era?

QCA data @ 9 months



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Cosgrave J. et al. *JACC* 2006;47: 2399-404

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Current therapeutic options according to potential mechanisms of DES restenosis

Type of restenosis	Potential mechanisms	Treatment options
Focal in-stent	Underexpansion	BA
	Fracture	DES, BA
	Local vessel biology	DES, BA, atherectomy
	Heterogeneous drug distribution	DES, BA, atherectomy
Focal at stent edge	Geographic miss	DES
	Plaque progression	DES
Diffuse in-stent	Vessel biology / Drug resistance	Different DES, CABG
Proliferative	Vessel biology / Drug resistance	Different DES, CABG

Costa MA. et al. *AHJ*.2007;153: 447-9

DES Restenosis

Summary

- Restenosis after DES still occurs and at a disturbing frequency in the highest risk lesion/patient subsets.
- Underlying mechanism of DES restenosis involve a complex interplay of biological, mechanical, and technical (operator-dependent) factors.
- Strut fractures are more frequent than previously suspected, occurring most commonly at the edge of an overlap segment and they have been implicated in many clinical events, including restenosis, thrombosis, and aneurysm formation .

DES Restenosis

Summary

- The morphologic patterns of DES restenosis are different from BMS, favoring a more focal and easily treated pattern with expected improved clinical outcomes.
- The treatment of DES restenosis is based on appreciation of underlying mechanisms and can vary from simple POBA, to DES when appropriate, to CABG in the most extreme cases.
- Late DES restenosis remains an infrequent clinical event, despite the differing healing patterns relative to BMS.