

Stent Optimization: When to use IVUS and OCT

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IVUS Predictors of BMS Early Thrombosis & Restenosis

| | Thrombosis | Restenosis |
|--|---|--|
| Small MSA or underexpansion | <ul style="list-style-type: none"> • <i>Cheneau et al. Circulation 2003;108:43-7</i> | <ul style="list-style-type: none"> • <i>Kasaoka et al. J Am Coll Cardiol 1998;32:1630-5</i> • <i>Castagna et al. AHJ 2001;142:970-4</i> • <i>de Feyter et al. Circulation 1999;100:1777-83</i> • <i>Sonoda et al. J Am Coll Cardiol 2004;43:1959-63</i> • <i>Morino et al. Am J Cardiol 2001;88:301-3</i> • <i>Ziada et al. Am Heart J 2001;141:823-31</i> • <i>Doi et al. JACC Cardiovasc Interv. 2009;2:1269-75</i> |
| Edge problems (geographic miss, secondary lesions, large plaque burden, dissections, etc) | <ul style="list-style-type: none"> • <i>Cheneau et al. Circulation 2003;108:43-7</i> | <ul style="list-style-type: none"> • <i>Sakurai et al. Am J Cardiol 2005;96:1251-3</i> • <i>Liu et al. Am J Cardiol 2009;103:501-6</i> |
| Stent length | | <ul style="list-style-type: none"> • <i>Kasaoka et al. J Am Coll Cardiol 1998;32:1630-5</i> • <i>de Feyter et al. Circulation 1999;100:1777-83</i> |

IVUS Predictors of DES Early Thrombosis & Restenosis

| | Early Thrombosis | Restenosis |
|--|---|--|
| Small MSA or MLA or underexpansion | <ul style="list-style-type: none"> • Fujii et al. <i>J Am Coll Cardiol</i> 2005;45:995-8 • Okabe et al. <i>Am J Cardiol.</i> 2007;100:615-20 • Liu et al. <i>JACC Cardiovasc Interv.</i> 2009;2:428-34 • Choi et al. <i>Circ Cardiovasc Interv</i> 2011;4:239-47 | <ul style="list-style-type: none"> • Sonoda et al. <i>J Am Coll Cardiol</i> 2004;43:1959-63 • Hong et al. <i>Eur Heart J</i> 2006;27:1305-10 • Doi et al <i>JACC Cardiovasc Interv.</i> 2009;2:1269-75 • Fujii et al. <i>Circulation</i> 2004;109:1085-1088 • Kang et al. <i>Circ Cardiovasc Interv</i> 2011;4:9-14 • Choi et al. <i>Am J Cardiol</i> 2012;109:455-60 • Song et al. <i>Catheter Cardiovasc Interv, in press</i> |
| Edge problems (geographic miss, secondary lesions, large plaque burden, dissections, etc) | <ul style="list-style-type: none"> • Fujii et al. <i>J Am Coll Cardiol</i> 2005;45:995-8 • Okabe et al., <i>Am J Cardiol.</i> 2007;100:615-20 • Liu et al. <i>JACC Cardiovasc Interv.</i> 2009;2:428-34 • Choi et al. <i>Circ Cardiovasc Interv</i> 2011;4:239-47 | <ul style="list-style-type: none"> • Sakurai et al. <i>Am J Cardiol</i> 2005;96:1251-3 • Liu et al. <i>Am J Cardiol</i> 2009;103:501-6 • Costa et al, <i>Am J Cardiol,</i> 2008;101:1704-11 • Kang et al. <i>Am J Cardiol, in press</i> |

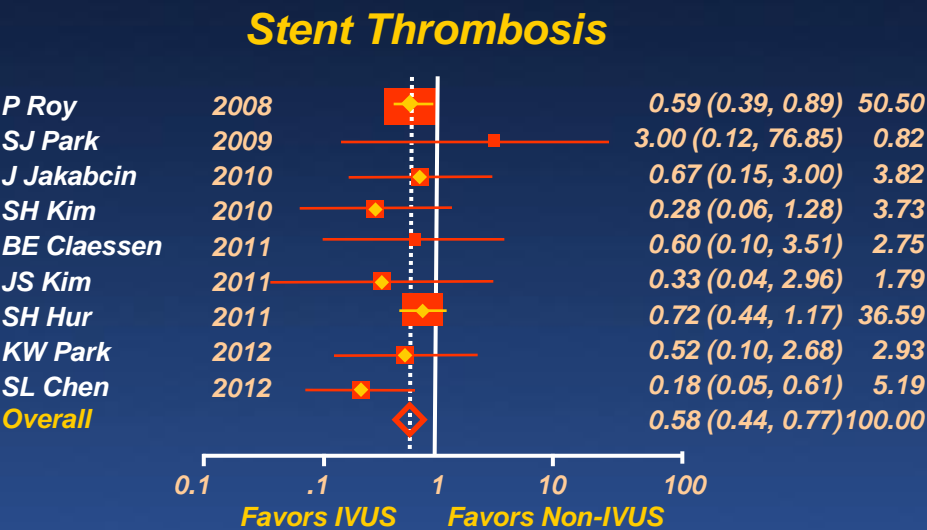
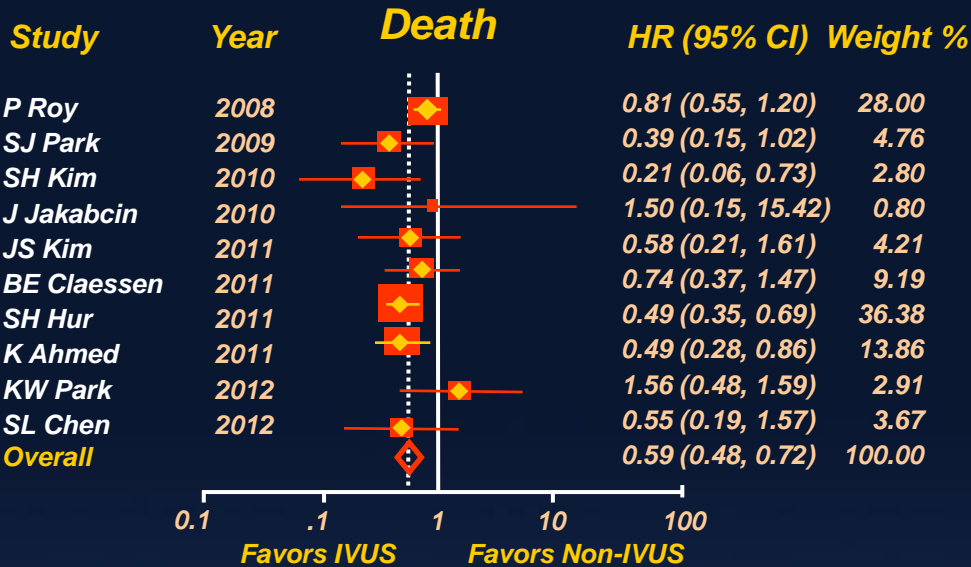
Although it was one of the original Colombo criteria, there is little or no data linking *isolated* acute stent malapposition to adverse clinical events including ST and restenosis.

- **Stent malapposition is associated with *less* intimal hyperplasia – the drug can cross small stent vessel-wall gaps**
 - *Hong et al, Circulation. 2006;113:414-9*
 - *Kimura et al, Am J Cardiol . 2006;98:436-42*
 - *Steinberg et al, JACC Cardiovasc Intervent 2010;3:486-94*
 - *Balakrishnan et al., Circulation 2005;111:2958-65*
- **In the integrated analysis of slow release formulation PES in TAXUS IV, V, and VI and TAXUS ATLAS Workhorse, Long Lesion, and Direct Stent Trial, there was no effect of acute stent malapposition on MACE or ST within the first 9 months – whether BMS or DES**
 - *Steinberg et al, JACC Cardiovasc Intervent 2010;3:486-94*
- **In HORIZONS-AMI, acute stent malapposition was detected in 33.8% of 68 lesions treated with PES and 38.7% of 24 lesions treated with BMS (p=0.7). There was no difference in MACE between pts with versus without acute stent malapposition in either BMS or PES cohorts; and acute malapposition was not a predictor of early ST**
 - *Guo et al. Circulation 2010;122:1077-84*
 - *Choi et al. Circ Cardiovasc Interv 2011;4:239-47*
- **Although acute malapposition was observed in 28/403 pts with LMCA lesions treated with DES implantation, malapposition was not related to MACE at follow-up.**
 - *Kang et al. Circ Cardiovasc Interv 2011;4:562-9*

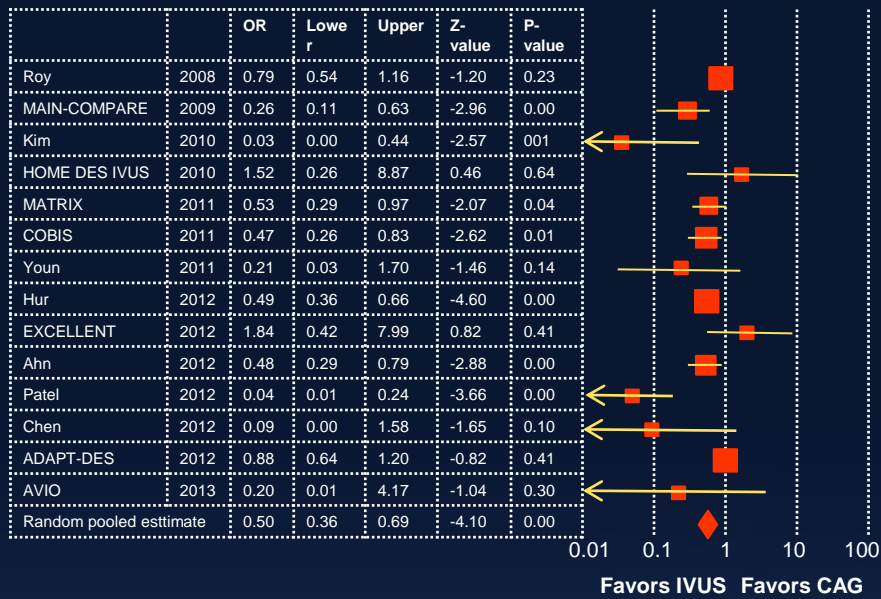
Meta-Analysis of 11 Studies (n=19,619 patients)

Compared with angiography-guidance, IVUS-guided DES implantation was associated with a reduced incidence of

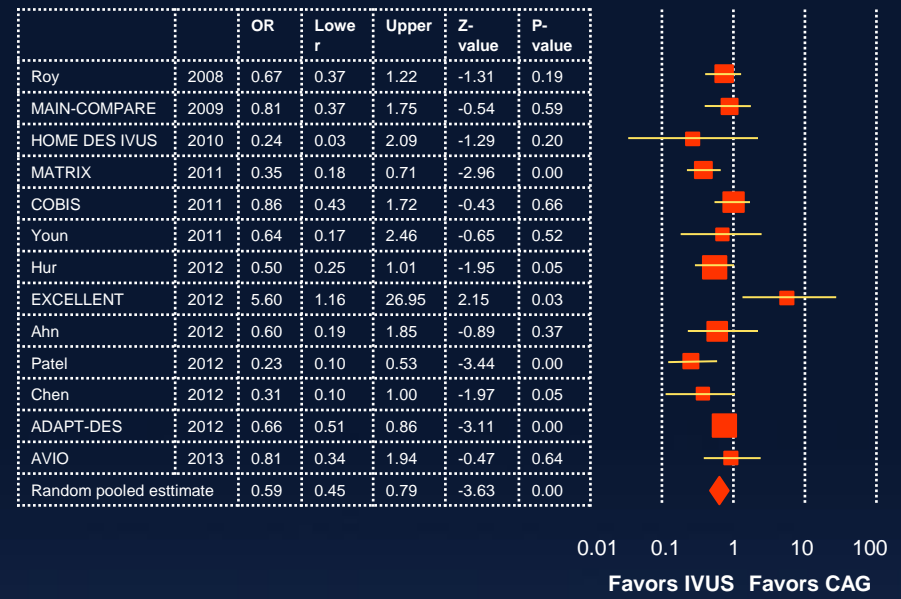
- **Death (HR: 0.59, 95% CI: 0.48-0.73, p<0.001)**
- **Stent thrombosis (HR: 0.58, 95% CI: 0.44-0.77, p<0.0001)**
- **Major adverse cardiac events (HR: 0.87, 95% CI: 0.78-0.96, p=0.008)**



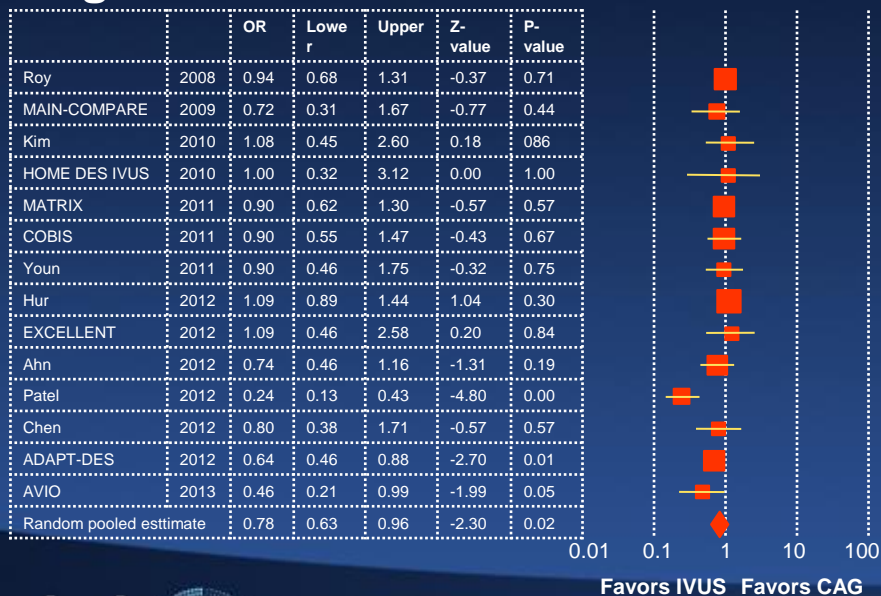
Death from any cause



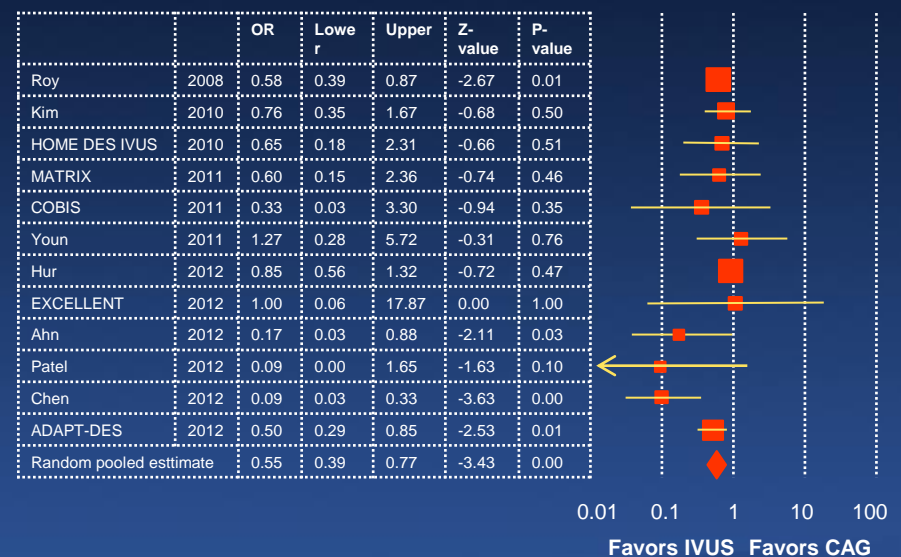
Myocardial Infarction



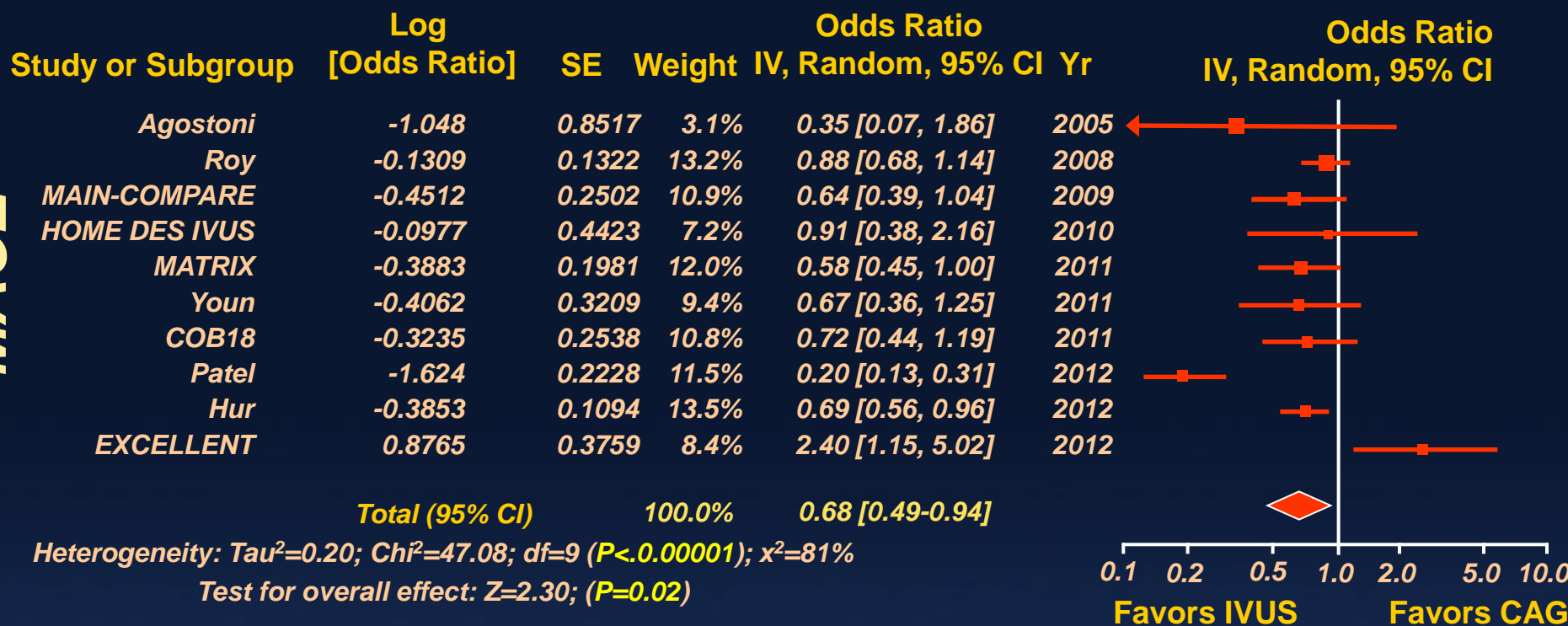
Target vessel revascularization



Stent Thrombosis



MACE



Ten observational and one randomized study (10,916 pts) were included: 5980 IVUS-guided and 4936 angio-guided. Compared with angiography-guidance, IVUS-guided DES implantation was associated with a reduced incidence of

- MACE: OR=0.68 (95% CI 0.49 to 0.94), p=0.02
- Mortality: OR=0.64 (95% CI 0.49 to 0.83), p=0.001
- Myocardial Infarction: OR=0.55 (95% CI 0.35 to 0.88), p=0.01

Agostoni P, Valgimigli M, Van Mieghem CA, et al. Comparison of early outcome of percutaneous coronary intervention for unprotected left main coronary artery disease in the drug-eluting stent era with versus without intravascular ultrasonic guidance. *Am J Cardiol* 2005;95:644-7.

Kim SH, Kim YH, Kang SJ, et al. Long-term outcomes of intravascular ultrasound-guided stenting in coronary bifurcation lesions. *Am J Cardiol* 2010;106:612-8.

Jakabcin J, Spacek R, Bystron M, et al. Long-term health outcome and mortality evaluation after invasive coronary treatment using drug eluting stents with or without the IVUS guidance. randomized control trial. *HOME DES IVUS. Catheter Cardiovasc Interv* 2010;75:578-83.

Youn YJ, Yoon J, Lee JW, et al. Intravascular ultrasound-guided primary percutaneous coronary intervention with drug-eluting stent implantation in patients with ST-segment elevation myocardial infarction. *Clin Cardiol* 2011;34:706-13.

Chieffo A, Latib A, Caussin C, et al. A prospective, randomized trial of intravascular ultrasound guided compared to angiography guided stent implantation in complex coronary lesions: The AVIO trial. 2013;165:65-72.

Kim JS, Kang TS, Mintz GS, et al. Randomized comparison of clinical outcomes between intravascular ultrasound and angiography-guided drug-eluting stent implantation for long coronary artery stenoses. *JACC Cardiovasc Interv* 2013;6:369-76.

Ahn JM, Han S, Park YK, et al. Differential prognostic effect of intravascular ultrasound use according to implanted stent length. *Am J Cardiol* 2013;111:829-35.

Claessen BE, Mehran R, Mintz GS, et al. Impact of intravascular ultrasound imaging on early and late clinical outcomes following percutaneous coronary intervention with drug-eluting stents. *JACC Cardiovasc Interv* 2011;4:974-81.

Chen SL, Ye F, Zhang JJ, et al. Intravascular ultrasound-guided systematic two-stent techniques for coronary bifurcation lesions and reduced late stent thrombosis. *Catheter Cardiovasc Interv* 2013;81:456-63.

Kim JS, Hong MK, Ko YG, et al. Impact of intravascular ultrasound guidance on long-term clinical outcomes in patients treated with drug-eluting stent for bifurcation lesions: Data from a Korean multicenter bifurcation registry. *Am Heart J* 2011;161:180-7.

Roy P, Steinberg DH, Sushinsky SJ, et al. The potential clinical utility of intravascular ultrasound guidance in patients undergoing percutaneous coronary intervention with drug-eluting stents. *Eur Heart J* 2008;29:1851-7.

Park SJ, Kim YH, Park DW, et al. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. *Circ Cardiovasc Interv* 2009;2:167-77.

Park KW, Kang SH, Yang HM, et al. Impact of intravascular ultrasound guidance in routine percutaneous coronary intervention for conventional lesions: Data from the EXCELLENT trial. *Int J Cardiol* 2012; doi:10.1016/j.ijcard.2012.03.059. [Epub ahead of print]

Witzenbichler B, Maehara A, Weisz G, et al. Use of IVUS reduces stent thrombosis: Results from the prospective, multicenter ADAPT-DES study. *J Am Coll Cardiol* 2012;60:B6-B7. Paper presented at: Annual Meeting of the Transcatheter Cardiovascular Therapeutics; October 23, 2012: Miami, FL.

Hur SH, Kang SJ, Kim YH, et al. Impact of intravascular ultrasound-guided percutaneous coronary intervention on long-term clinical outcomes in a real world population. *Catheter Cardiovasc Interv* 2013;81:407-16.

Meta-Analysis of 3 Randomized Trials and 12 Observational Studies (n=24,869 pts) of IVUS vs Angiography-guided DES Implantation

| | IVUS | | Angiography | | OR | 95% CI | Favors | P-value |
|------------------|--------|--------|-------------|--------|--------------------|------------|--------|---------|
| | Events | Total | Events | Total | | | | |
| MACE | 9.0% | 5226 | 11.1% | 5769 | 0.79 | 0.69, 0.91 | IVUS | 0.001 |
| Mortality | 2.0% | 11,461 | 3.3% | 12,930 | 0.64 | 0.51, 0.81 | IVUS | <0.001 |
| MI | 1.2% | 11,316 | 2.2% | 12,785 | 0.57 | 0.42, 0.78 | IVUS | <0.001 |
| TVR | 5.1% | 10,869 | 3.3% | 12,338 | 0.81 | 0.68, 0.95 | IVUS | 0.01 |
| Stent thrombosis | 1.1% | 11,769 | 1.7% | 13,042 | 0.59 | 0.42, 0.82 | IVUS | 0.002 |
| | | | | | IVUS - Angiography | | | |
| | | | | | Mean | 95% CI | | |
| MLD (mm) | | 2415 | | 2308 | 0.12 | 0.08, 0.16 | IVUS | <0.001 |

Comparison of pts undergoing PCI with “OCT guidance” vs angiographic guidance at three high-OCT-volume Italian centers: CLI-OPCI Study

| One year outcomes | OCT | Angiography | p |
|---|------|-------------|-------|
| # | 335 | 335 | |
| Death | 3.3% | 6.9% | 0.035 |
| Cardiac death | 1.2% | 4.5% | 0.010 |
| MI | 5.4% | 8.7% | 0.096 |
| TLR | 3.3% | 3.3% | 1 |
| Definite ST | 0.3% | 0.6% | 0.6 |
| Cardiac death/MI | 6.6% | 13.0% | 0.006 |
| Cardiac death/MI or repeat revascularization* | 9.6% | 15.1% | 0.034 |

****Even after accounting for baseline and procedural differences (OR=0.49, p=0.037)***

IVUS



OCT

**Stent underexpansion
PLUS...**

**Geographical miss
(major edge dissections,
plaque burden >50%)**

***Stent underexpansion
PLUS...***

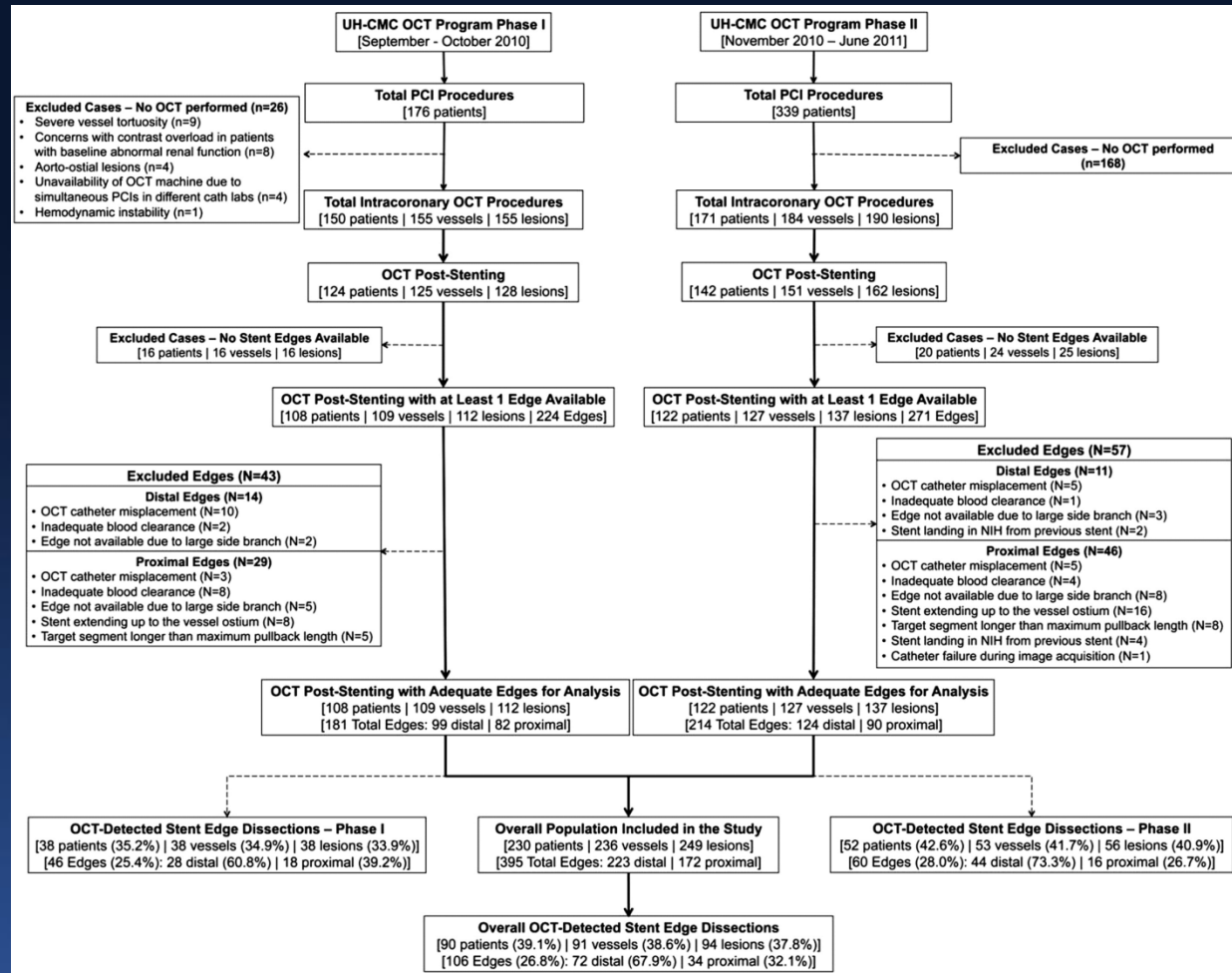
***(Minor) findings not seen
on IVUS***

Malapposition

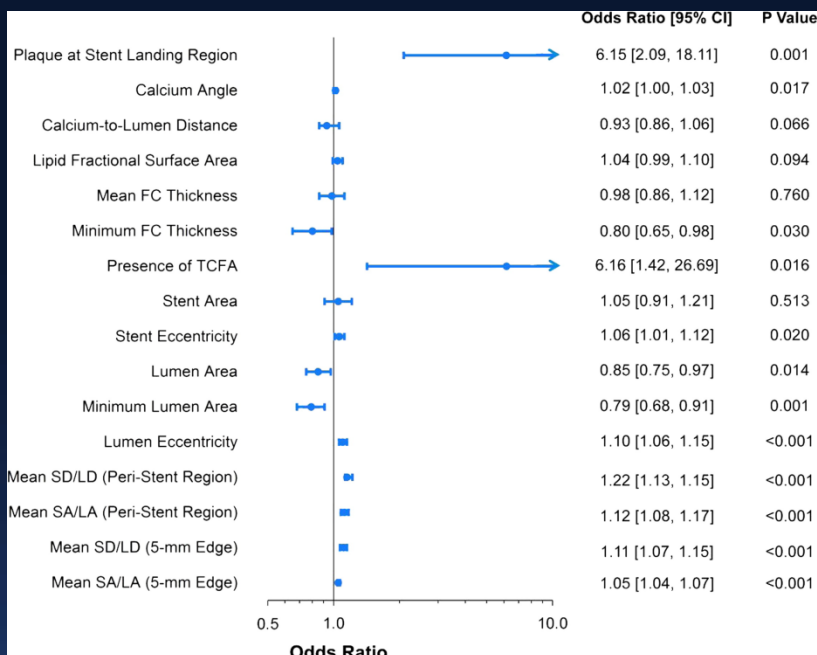
Tissue protrusion

Edge dissections

In total, 395 edges (249 lesions in 230 pts) were analyzed. The overall incidence of OCT-detected edge dissection was 37.8%, and most (84%) were not apparent on angiography.



Independent Predictors of OCT-Detected Stent Edge Dissection



| | Dissection | | | No dissection* |
|-----------------------|------------|----------|-------------|----------------|
| | Overall | Treated | Not-treated | |
| # | 88 | 22 | 66 | 123 |
| MACE | 7 (8.0%) | 1 (4.5%) | 6 (9.0%) | 7 (5.7%) |
| All-cause death | 3 (3.4%) | 0 | 3 (4.5%) | 5 (4.06%) |
| Cardiac death | 1 (1.1%) | 0 | 1 (1.5%) | 4 (3.25%) |
| Nonfatal MI | 4 (4.5%) | 1 (4.5%) | 3 (4.5%) | 3 (2.4%) |
| TVR | 1 (1.1%) | 0 | 1 (1.5%) | 1 (0.8%) |
| TLR | 1 (1.1%) | 0 | 1 (1.5%) | 1 (0.8%) |
| Definite/pr obable ST | 0 | 0 | 0 | 1 |

**p=NS vs untreated dissections*

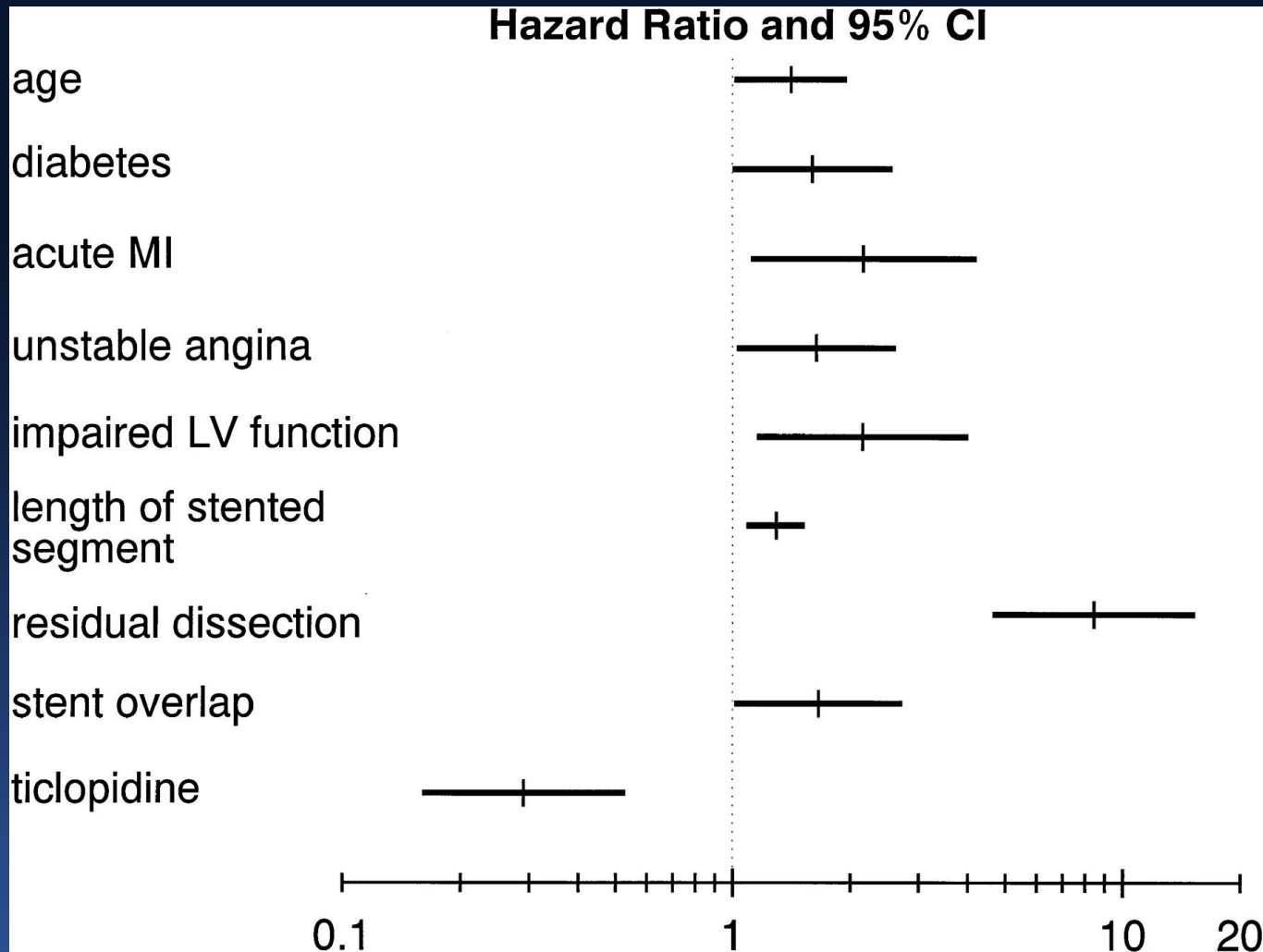
In the dissection group, there were 3 deaths (1 cardiac) and 4 nonfatal MIs, only 1 related to the lesion requiring revascularization. All events occurred > 30 days after the index procedure, and happened in patients in whom the dissections were only seen by OCT, as the majority of dissections seen by both OCT and angiography were treated.

Post-DES and follow-up OCT images from 351 patients (356 lesions). Acute malapposition was observed in 62% of lesions. Follow-up OCT was 175 ± 60 days post-DES; clinical follow-up was 22.7 ± 10.1 months post-DES. (DES included 83 SES, 120 ZES, 30 EES, 123 Biolimus A9-ES.)

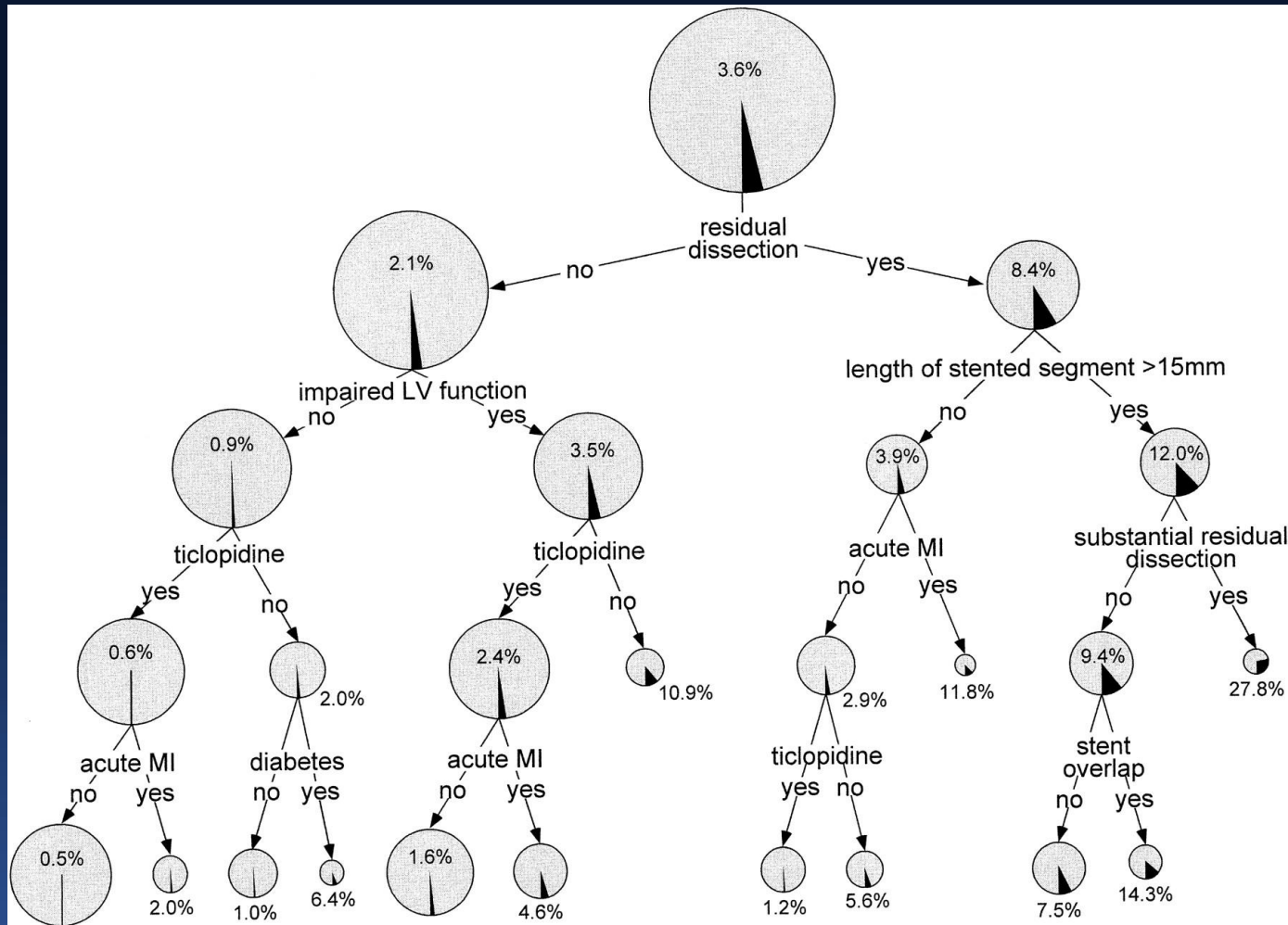
| | Overall | LSM | Acquired LSM | Persistent LSM | No LSM | p |
|------------------------|-------------|------------|--------------|----------------|-------------|------|
| # | 351 | 23 | 31 | 45 | 252 | |
| Follow-up (mos) | 23 ± 10 | 18 ± 4 | 22 ± 9 | 23 ± 0 | 23 ± 11 | 0.15 |
| MACE | 8.3% | 0 | 3.2% | 16.7% | 8.6% | * |
| CV mortality | 1.7% | 0 | 0 | 0 | 2.0% | * |
| Nonfatal MI | 0.3% | 0 | 0 | 0 | 0.4% | * |
| Stent thrombosis | 0 | 0 | 0 | 0 | 0 | * |
| Duration of DAPT (mos) | 14 ± 8 | 12 ± 5 | 16 ± 6 | 14 ± 7 | 14 ± 9 | 0.4 |
| ≥ 12 mos DAPT | 75% | 65% | 87% | 80% | 73% | 0.20 |

* In six pairwise comparisons with 4 different groups of pts, none were statistically significant.

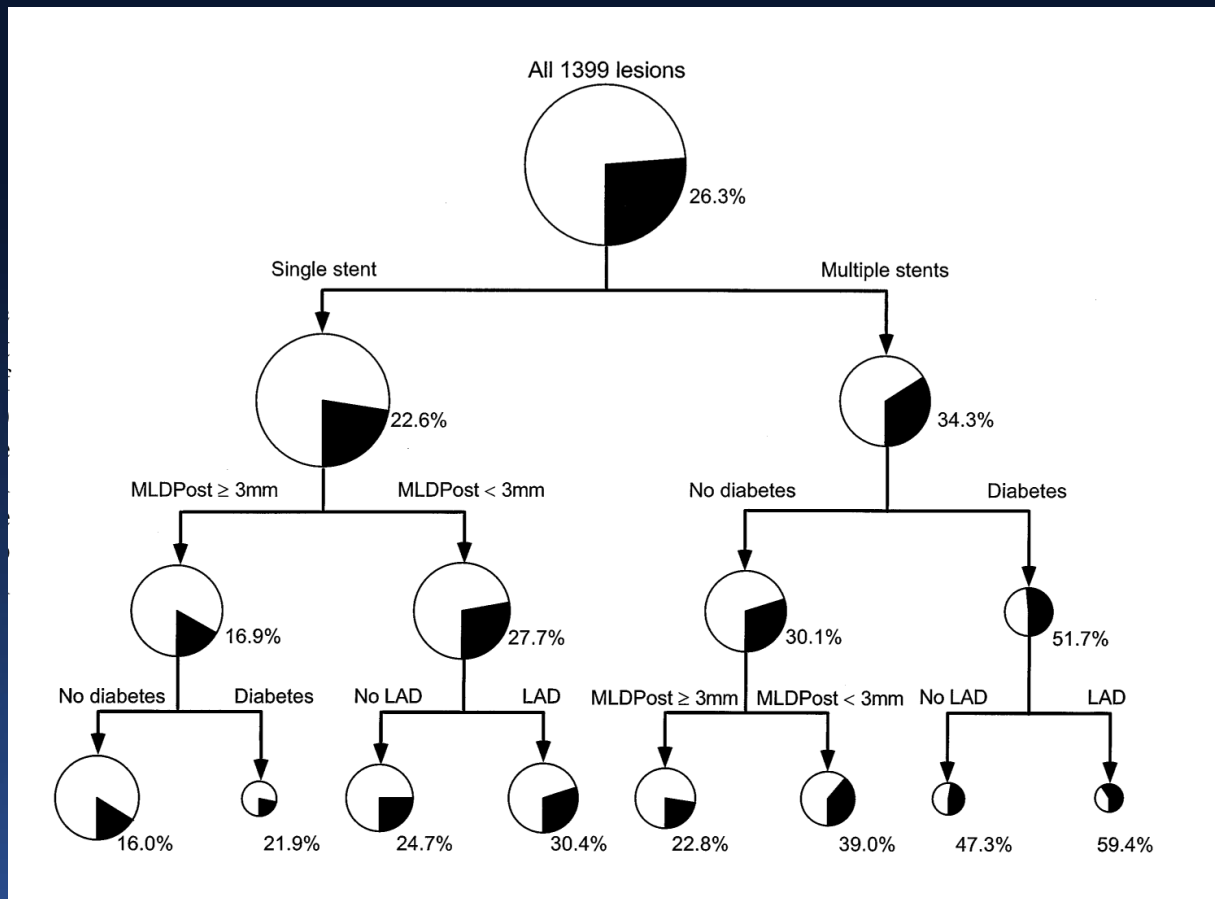
Hazard ratios for independent risk factors for 30 day MACE after successful BMS (n=2894)



Classification and regression tree (CART) model showing the variables that most strongly influence the likelihood of 30 day MACE after succesful BMS (n=2833)



Classification and regression tree (CART) model showing the variables that most strongly influence the likelihood of binary BMS restenosis

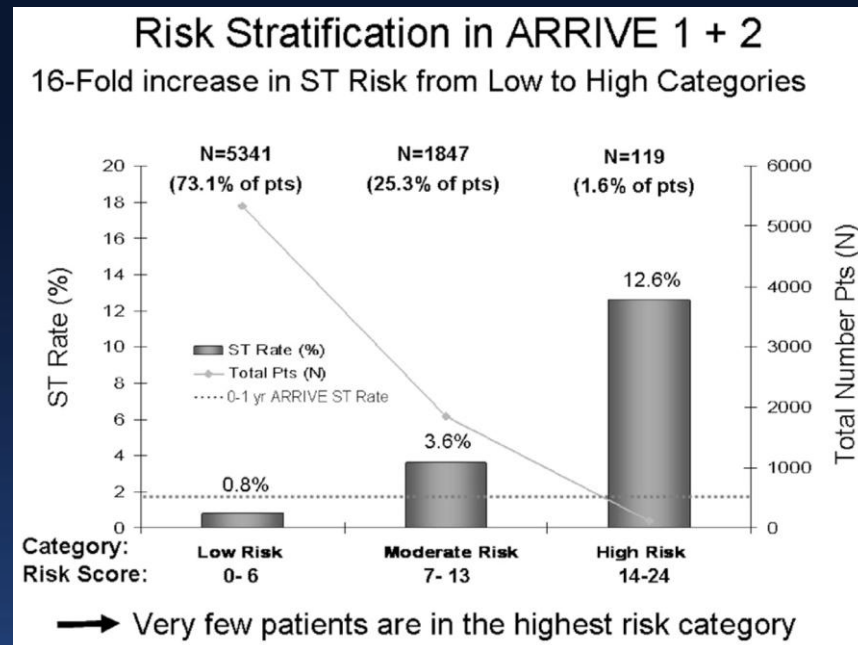


ARRIVE Registry: Predicting DES Thrombosis in routine clinical practice (n=7492 patients)

| | Early ST (n=77) | Late ST (n=51) | Very late ST (n=56) |
|---------------------------|---------------------|--------------------|---------------------|
| Thienopyridine <30 days | 13.78 (8.77, 21.64) | | |
| Multiple stents | 2.21 (1.32, 3.69) | | 2.38 (1.39, 4.08) |
| CHF | 2.15 (1.17, 3.92) | | |
| Mod/severe lesion calcium | 1.83 (1.14, 2.94) | | |
| Lesion length >28mm | 1.77 (1.01, 3.08) | | |
| Prior MI | 1.60 (1.02, 2.52) | | 2.38 (1.39, 4.06) |
| Smoking @ baseline | | 5.86 (3.31, 10.38) | 1.91 (1.09, 3.34) |
| Reference <3.0mm | | 3.43 (1.82, 6.46) | |
| IDDM | | 2.86 (1.45, 5.64) | |
| Post-dilation | | 2.16 (1.23, 3.80) | |
| Thienopyridine <6 mos | | 2.00 (1.07, 3.77) | |
| Multivessel disease | | 1.79 (1.03, 3.13) | |
| Prior VBT | | | 7.32 (1.75, 30.60) |
| Renal disease | | | 3.86 (1.39, 10.73) |
| SVG stenting | | | 2.90 (1.44, 5.83) |

Risk score derived from ARRIVE-1 (n=2487) was validated in ARRIVE-2 (n=4820)

| | HR | Weight |
|--------------------------------------|------|--------|
| Thienopyridine discontinuation <6mos | 5.28 | 5 |
| IDDM | 4.74 | 5 |
| LMCA | 2.73 | 3 |
| Smoking | 2.63 | 3 |
| Lesion length >28mm | 2.35 | 2 |
| Multiple stents | 2.25 | 2 |
| Mod/severe calcification | 1.77 | 2 |
| Reference <3mm | 1.72 | 2 |
| Total possible score | | 24 |



Incidence and predictors of coronary stent thrombosis: Evidence from an international collaborative meta-analysis including 30 studies, 221,066 patients, and 4276 thromboses

- *Most frequently and consistently reported predictors of definite/probable ST were*
 - Early antiplatelet therapy discontinuation
 - Extent of coronary artery disease
 - Stent number/ length
- *Significant, but less consistent predictors of ST were*
 - ACS at admission
 - Diabetes mellitus
 - Smoking status
 - Bifurcation/ostial disease
- *Predictors of ST with relative risk estimates > 5 in at least one study were*
 - Antiplatelet therapy discontinuation before 30 days
 - Residual dissection
 - Antiplatelet therapy discontinuation between 30 days and 180 days,
 - Stent undersizing
 - Prior brachytherapy
 - Left ventricular systolic dysfunction
 - Smoking status
 - Bifurcational/ostial lesion
 - ACS at admission
 - Small vessel coronary disease

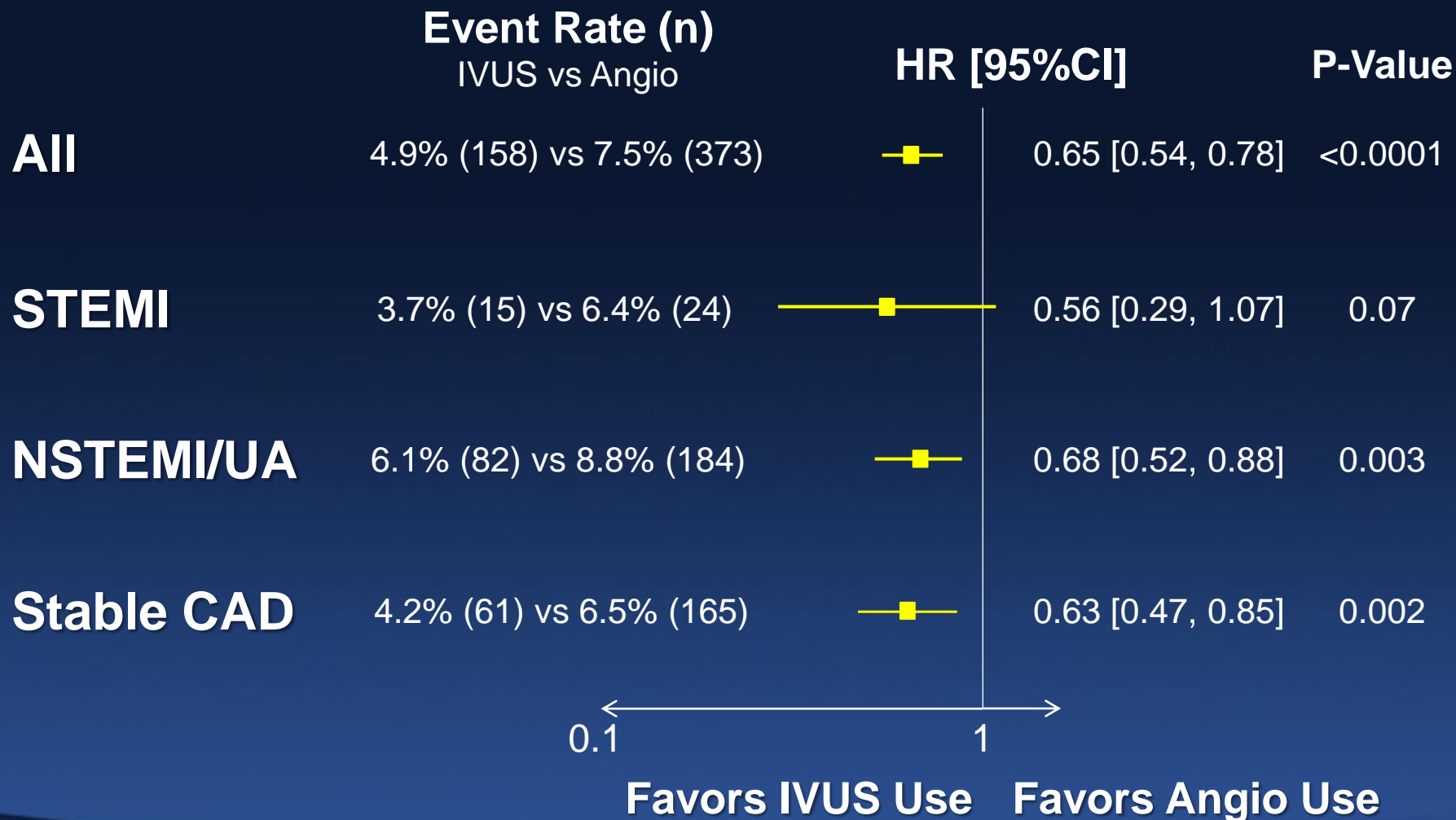
Predicting DES Restenosis in Real-World Clinical Practice: Derivation and Validation of a Risk Model From the EVENT Registry

| | OR | 95% CI | p | Points |
|--------------|------|-----------|---------|--------|
| Age <60 | 1.49 | 1.14-1.95 | 0.0035 | 1 |
| Prior PCI | 1.83 | 1.40-2.39 | <0.0001 | 2 |
| LMCA | 3.14 | 1.30-7.57 | 0.0109 | 3 |
| SVG | 2.40 | 1.62-3.57 | <0.0001 | 2 |
| <2.5mm stent | 1.54 | 1.17-2.02 | 0.0018 | 1 |
| >40mm length | 1.78 | 1.35-2.35 | <0.0001 | 1 |

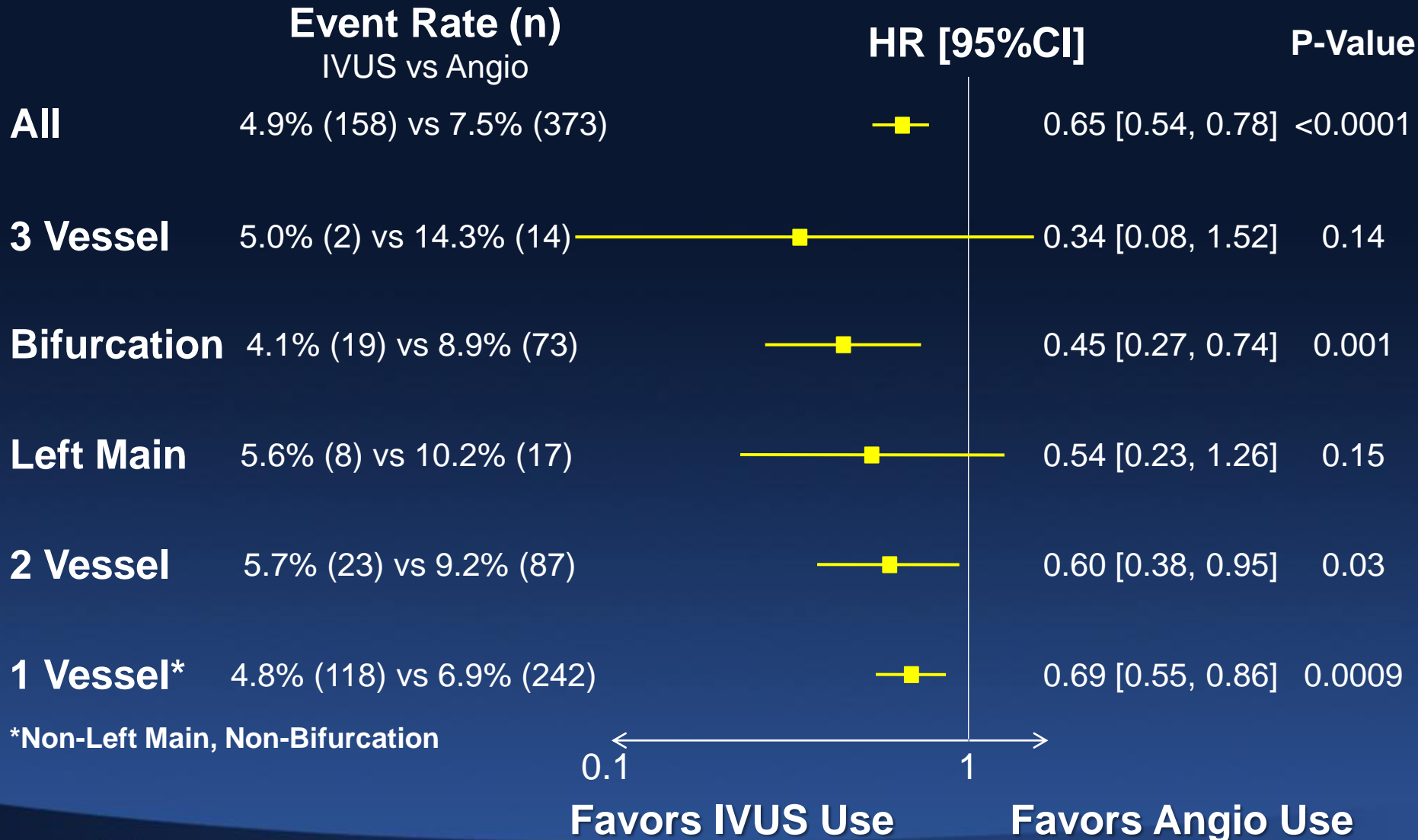
| Points | Predicted TLR | Observed TLR |
|--------|---------------|--------------|
| 0 | 2.3% | 2.2% |
| 1 | 3.5% | 3.3% |
| 2 | 4.4% | 4.3% |
| 3 | 4.9% | 5.5% |
| 4 | 6.3% | 6.7% |
| 5-10 | 9.7% | 7.5% |

At 1 year, TLR occurred in 4.2% of 8829 pts. After excluding stent thrombosis and early mechanical complications, the incidence of late TLR (more likely representing restenosis) was 3.6%

Association of IVUS Use with MACE (Definite/Probable ST, Cardiac Death, MI) in Relation to Index Presentation



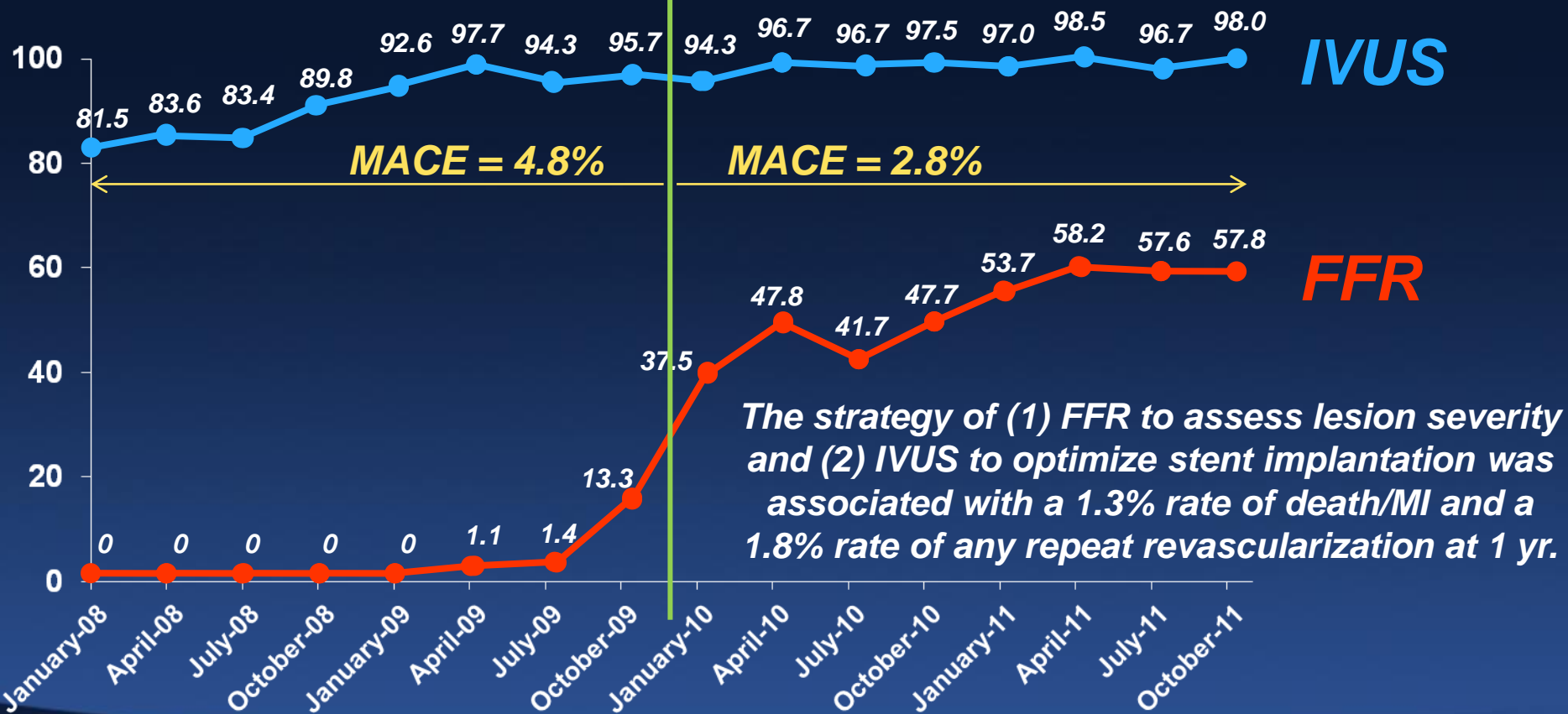
Association of IVUS Use with MACE (Definite/Probable ST, Cardiac Death, MI) in Relation to Lesion Complexity



Between January 2008 and December 2011, 5097 pts underwent PCI at Asan Medical Center, Seoul, Korea and were followed for 1 year.

**Before Routine Use of FFR
(N=2699)**

**After Routine Use of FFR
(N=2398)**



Who should have IVUS (or OCT) guided stent implantation?

Everyone or patients with a high risk of stent thrombosis or restenosis?