OCT Imaging Derived Parameters and Clinical Outcomes after PCI

ILUMIEN IV: OPTIMAL PCI

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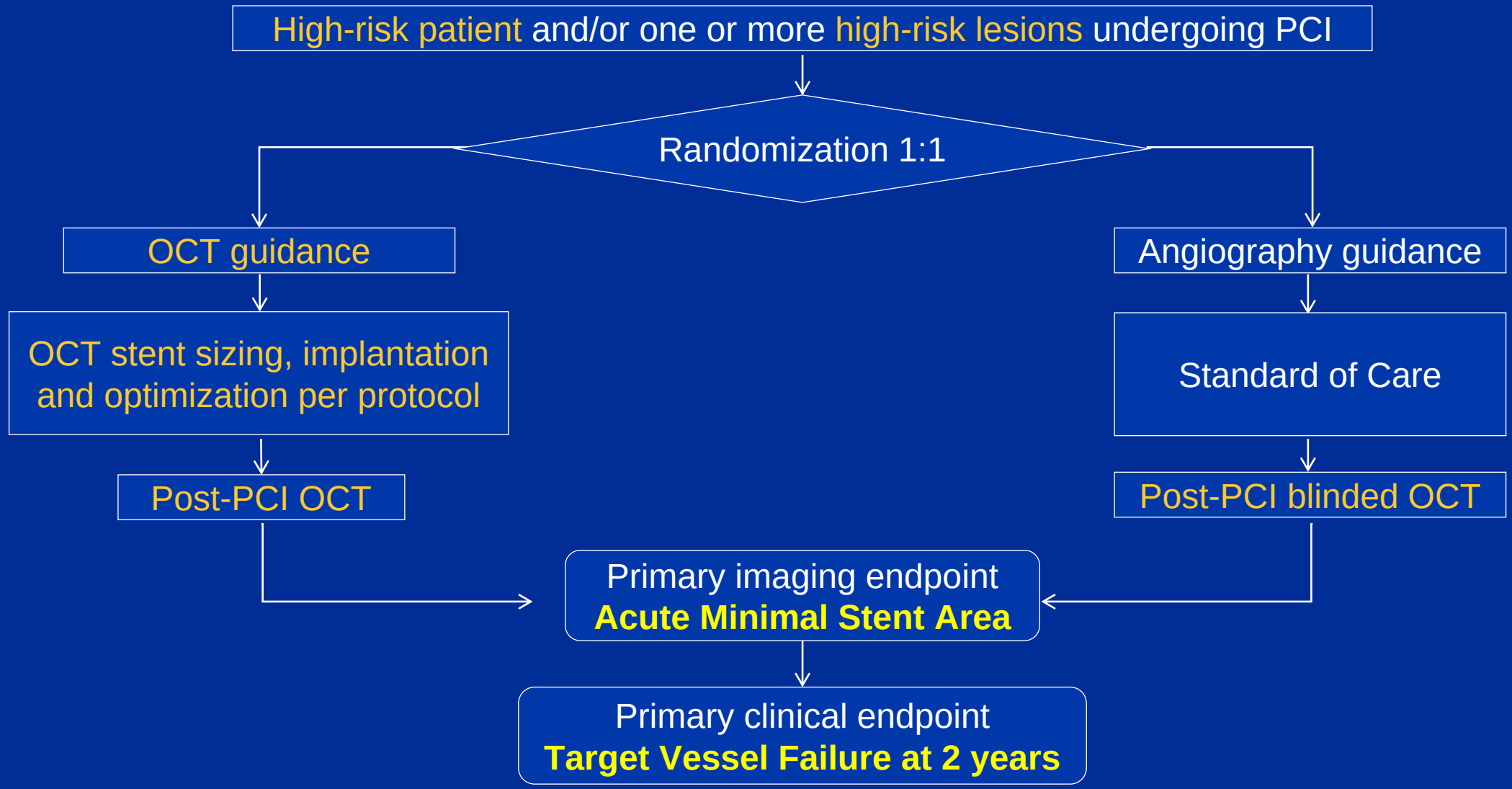
Background

- PCI is most commonly guided by angiography alone
- OCT is a high-resolution intravascular imaging modality that can be used to guide and optimize PCI
- In ILUMIEN III,[1] OCT guidance improved procedural success compared with angiography guidance
  - Greater stent expansion
  - Reduced major malapposition and major dissection
- Whether OCT can improve clinical outcomes is unknown

[1]Lancet. 2016 Nov 26;388:2618-2628.

Study Flow



EuroIntervention. 2021 Jan 20;16(13):1092-1099.

ClinicalTrials.gov #NCT03507777

Qualifying High-risk Criteria

High-risk Patient

- Medication-treated diabetes mellitus

High-risk Lesion

- NSTEMI
- STEMI >24 hours from symptom onset
- Long or multiple lesions (planned total stent length ≥28 mm)
- Diffuse or multi-focal in-stent restenosis
- Angiographic severe calcification
- Chronic total occlusion
- Bifurcation, planned to be treated with 2 stents

EuroIntervention. 2021 Jan 20;16(13):1092-1099.

Endpoints

1. Primary Imaging Endpoint (powered)

Post-PCI MSA assessed by OCT

Superiority of OCT to angiography

Δ 0.4 mm^2, SD 2.2 mm^2, 1600 randomized patients = 95% power at one-sided α 0.025

2. Primary Clinical Endpoint (powered)

TVF during 2-year follow-up

Superiority of OCT to angiography

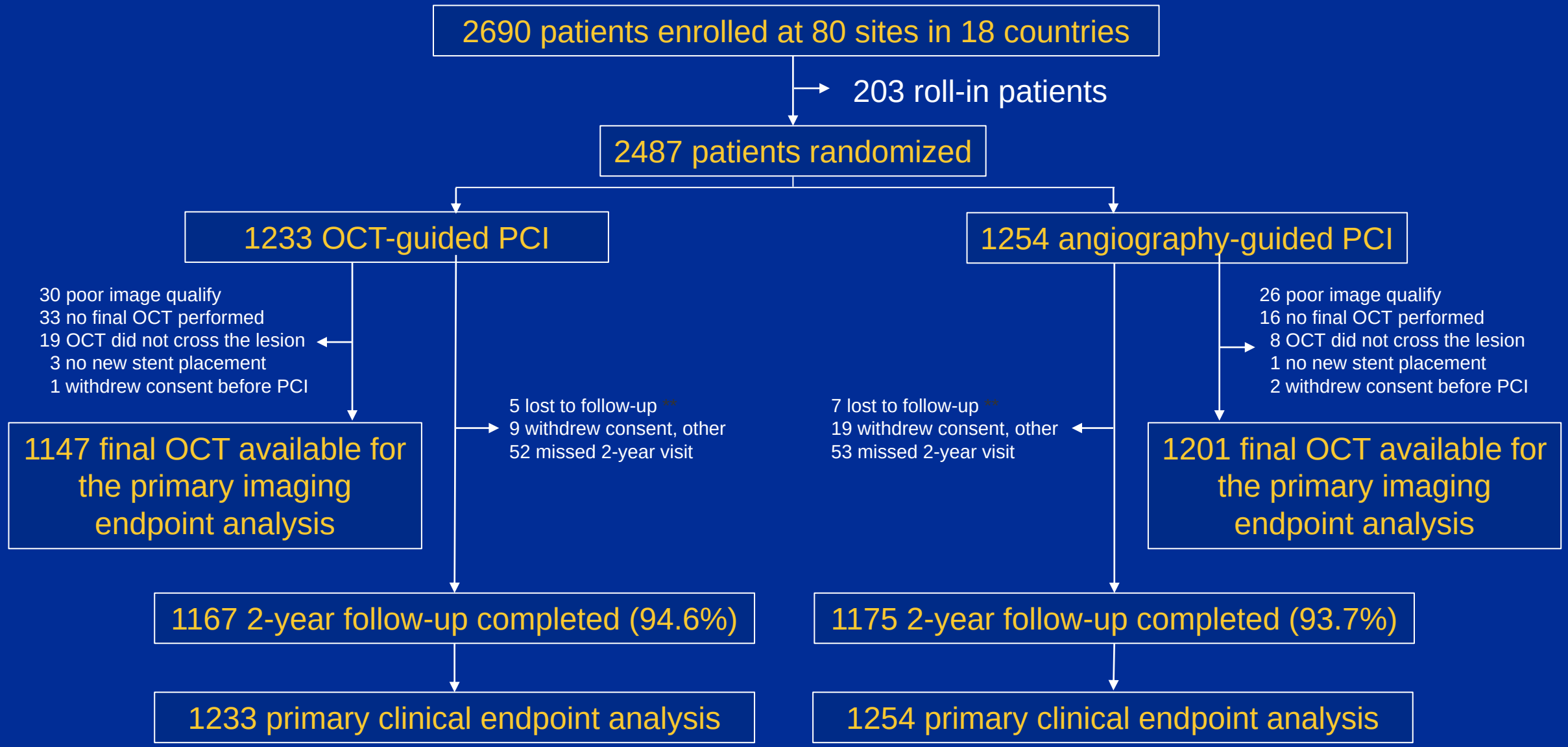
Control TVF 12.0%, HR 0.65, 1230 randomized patients = 90% power at one-sided α 0.025

3. Safety Endpoints (not powered)

Stent thrombosis and procedural complications

EuroIntervention. 2021 Jan 20;16(13):1092-1099.

Randomization and Follow-up



Baseline Characteristics

	OCT (n=1233)	Angio (n=1254)
Age, years	65.5 ± 10.5	65.7 ± 10.3
Male	78.5%	76.2%
Hypertension	71.4%	74.0%
Dyslipidemia	65.5%	68.6%
Diabetes mellitus	42.4%	41.5%
Current smoker	19.6%	19.7%
Serum creatinine, mg/dl	0.96 ± 0.23	0.96 ± 0.25
Silent ischemia	14.0%	15.4%
Stable angina	27.0%	28.5%
Acute coronary syndrome	59.0%	66.1%

Qualifying Characteristics

	OCT (n=1231)	Angio (n=1250)	Difference [95% CI]
Medication-treated diabetes mellitus	40.4%	39.8%	0.5% (-3.3, 4.4)
Long or multiple lesions	69.3%	65.9%	3.4% (-0.3, 7.0)
NSTEMI	24.5%	23.8%	0.6% (-2.8, 4.0)
Angiographic severe calcification	11.4%	11.7%	-0.3% (-2.8, 2.2)
In-stent restenosis (ISR)	10.6%	11.0%	-0.5% (-2.9, 2.0)
Chronic total occlusion (CTO)	7.6%	6.3%	1.3% (-0.7, 3.3)
STEMI (>24 hours from onset)	5.4%	5.6%	-0.2% (-2.1, 1.6)
Bifurcation with 2 planned stents	3.2%	3.4%	-0.2% (-1.6, 1.3)

Angiographic Characteristics

	OCT (L=1320)	Angio (L=1387)	Difference [95% CI]
LAD/LCx/RCA	53.3/ 19.0/ 27.7%	50.9/ 20.6/ 28.5%	--
Thrombus	6.8%	7.4%	-0.6% (-2.6, 1.4)
Calcification (severe)	32.0%	29.7%	2.3% (-1.2, 5.8)
Reference vessel diameter, mm	2.93 ± 0.43	2.90 ± 0.42	0.0 (-0.0, 0.01)
Minimum lumen diameter, mm	0.88 ± 0.43	0.88 ± 0.42	-0.0 (-0.0, 0.0)
Diameter stenosis, %	69.8 ± 13.9	69.6 ± 13.8	0.3 (-0.8, 1.3)
Lesion length, mm	32.9 ± 15.9	29.9 ± 16.1	3.0 (1.7, 4.2)
TIMI III flow	81.4%	79.3%	2.1% (-0.9, 5.2)

Procedural Characteristics

	OCT (n=1233)	Angio (n=1254)	Difference [95% CI]
Stents per patient	1.7 ± 0.9	1.6 ± 0.8	0.1 (0.0, 0.2)
Stent length, mm	44.2 ± 23.8	40.5 ± 24.0	3.8 (1.9, 5.6)
Maximal stent diameter, mm	3.22 ± 0.48	3.11 ± 0.40	0.11 (0.07, 0.14)
Post-dilatation balloons used, n	1.6 ± 1.2	1.3 ± 1.2	0.3 (0.2, 0.4)
Maximum device size, mm	3.67 ± 0.56	3.37 ± 0.47	0.31 (0.27, 0.34)
Maximum inflation pressure, atm	19.8 ± 3.1	18.4 ± 3.3	1.4 (1.2, 1.7)
Procedure duration, min	68.3 ± 38.3	50.0 ± 35.4	18.3 (15.4, 21.2)
Fluoroscopy duration, min	20.9 ± 13.8	17.4 ± 11.8	3.6 (2.6, 4.6)
Radiation dose, Gy	2.01 ± 1.75	1.55 ± 1.36	0.46 (0.32, 0.60)
Contrast volume, mL	231.9 ± 88.2	198.3 ± 81.7	33.7 (27.0, 40.4)

Primary Imaging Endpoint

Final post-PCI MSA by OCT (mm^2)

OCT L=1222	Angio L=1328	Difference [95% CI]	P-Value
5.72 ± 2.04	5.36 ± 1.87	0.36 (0.21, 0.51)	<0.001

Stent Expansion Endpoints

	OCT (L=1228)	Angio (L=1329)	Difference [95% CI]
Min stent expansion, %	80.8 ± 16.8	78.0 ± 16.7	2.9 (1.6, 4.2)
Mean stent expansion, %	111.3 ± 16.3	103.0 ± 17.2	8.2 (6.9, 9.5)
Stent expansion			
- Acceptable (≥90%)	40.5%	23.3%	17.2% (13.6, 20.8)

Post-procedure OCT Findings

	OCT (L=1228)	Angio (L=1329)	Difference [95% CI]
Dissection, any	32.0%	34.2%	-2.2% (-5.9, 1.4)
Major	2.9%	5.1%	-2.2% (-3.9, -0.6)
Minor	22.7%	19.4%	3.3% (-0.1, 6.6)

	OCT (L=1228)	Angio (L=1329)	Difference [95% CI]
Malapposition, any	55.3%	69.7%	-14.4% (-18.1, -10.6)
Major	15.8%	33.2%	-17.4% (-20.6, -14.1)
Minor	39.4%	36.5%	3.0% (-0.8, 6.7)

Post-procedure OCT Findings

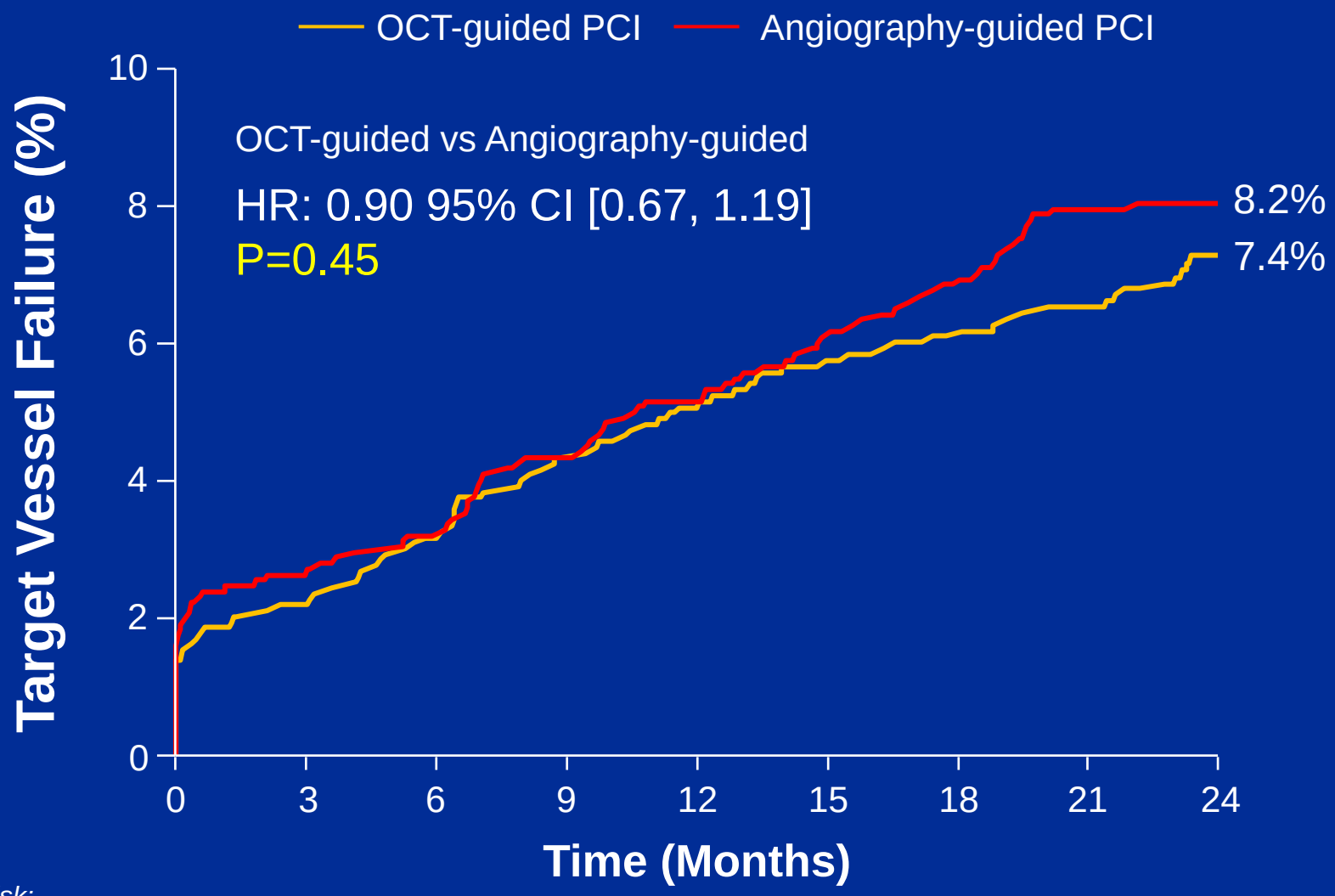
	OCT (L=1228)	Angio (L=1329)	Difference [95% CI]
Tissue Protrusion, any	55.9%	47.0%	8.9% (5.0, 12.8)
Major	5.3%	8.3%	-3.0% (-4.9, -1.0)
Minor	50.6%	38.7%	11.9% (8.1, 15.7)

	OCT (L=1228)	Angio (L=1329)	Difference [95% CI]
Reference Disease, any	17.3%	20.1%	-2.8% (-5.9, 0.3)
Focal	9.5%	12.1%	-2.7% (-5.1, -0.2)
Diffuse	7.8%	8.0%	-0.1% (-2.3, 2.0)

Angiographic Complications (Core Laboratory)

	OCT (I=1320)	Angio (I=1387)	Difference [95% CI]
Final angiographic complications	3.6%	5.3%	-1.7% (-3.3, -0.1)
Dissection ≥ type B	1.2%	1.5%	-0.3% (-1.2, 0.6)
Slow flow or no reflow	0.2%	0.5%	-0.3% (-0.8, 0.2)
Thrombus	0.3%	0.7%	-0.4% (-1.1, 0.2)
Abrupt closure	0.0%	0.0%	0.0% (-0.3, 0.3)
Perforation	0.2%	0.0%	0.2% (-0.1, 0.7)
Distal embolization	0.9%	1.3%	-0.4% (-1.2, 0.4)
Procedure-related stent thrombosis	0.0%	0.1%	-0.1% (-0.4, 0.2)
Procedure-related thrombotic events	2.3%	4.1%	-1.8% (-3.1, -0.4)
Catheter-related complications	0.1%	0.2%	-0.1% (-0.5, 0.3)

Primary Clinical Endpoint – Target Vessel Failure

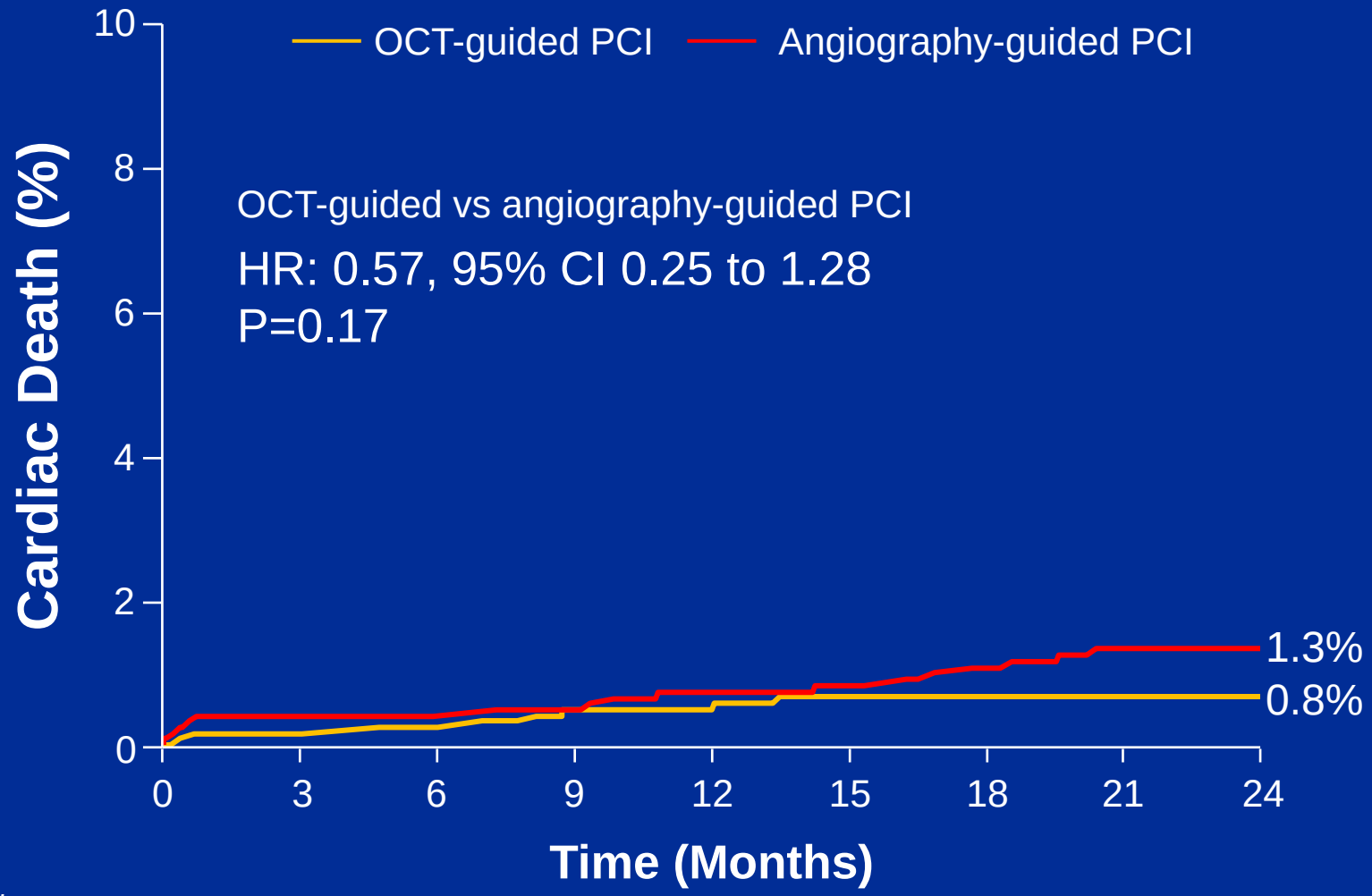


Number at risk:

OCT-guided	1233	1187	1174	1157	1127	1096	1085	1077	560
Angiography-guided	1254	1195	1184	1168	1143	1108	1092	1070	573

ILUMIEN IV

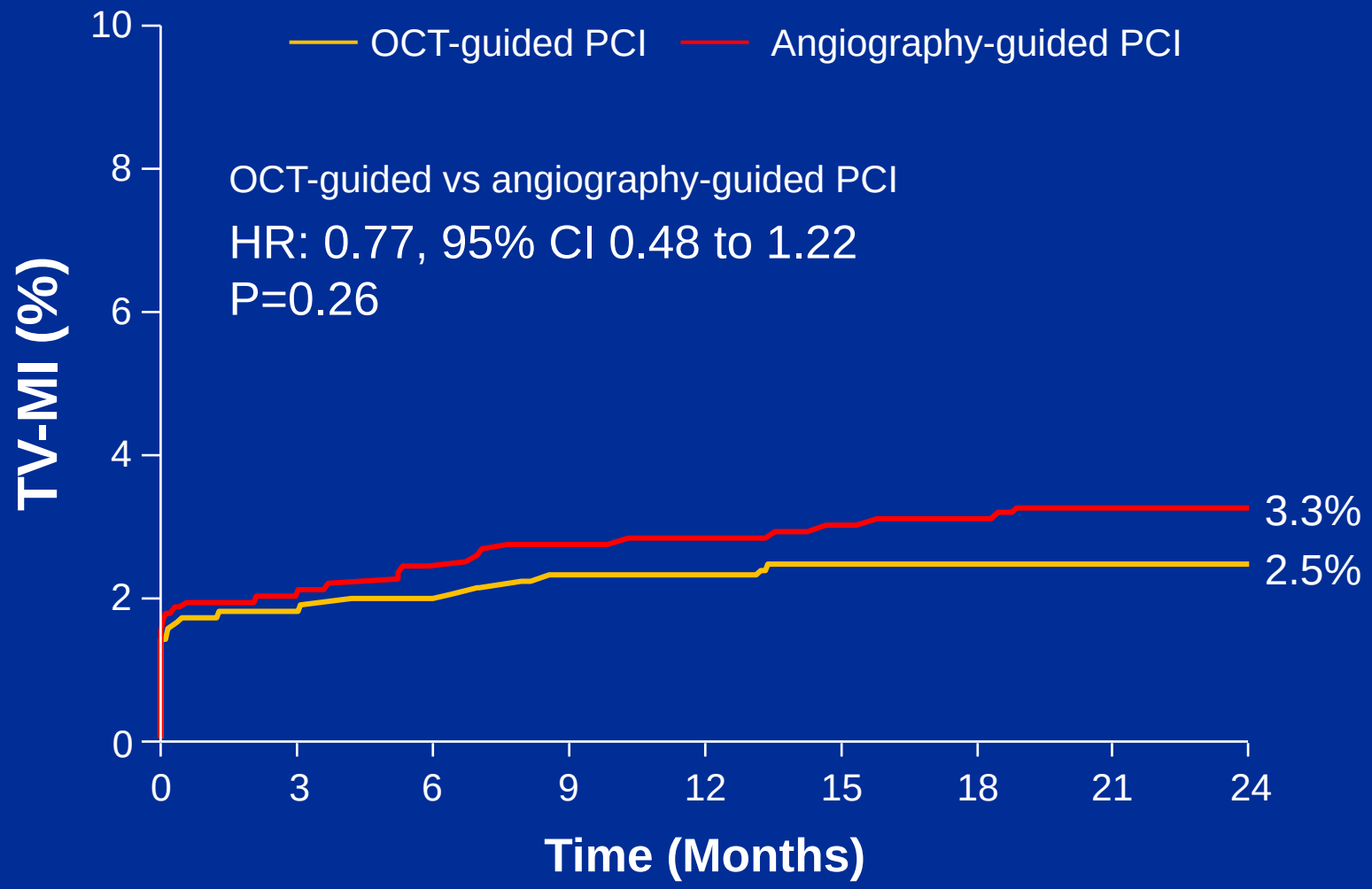
Cardiac Death



Number at risk:

OCT-guided	1233	1211	1208	1201	1180	1152	1146	1143	595
Angiography-guided	1254	1221	1217	1214	1195	1165	1156	1144	609

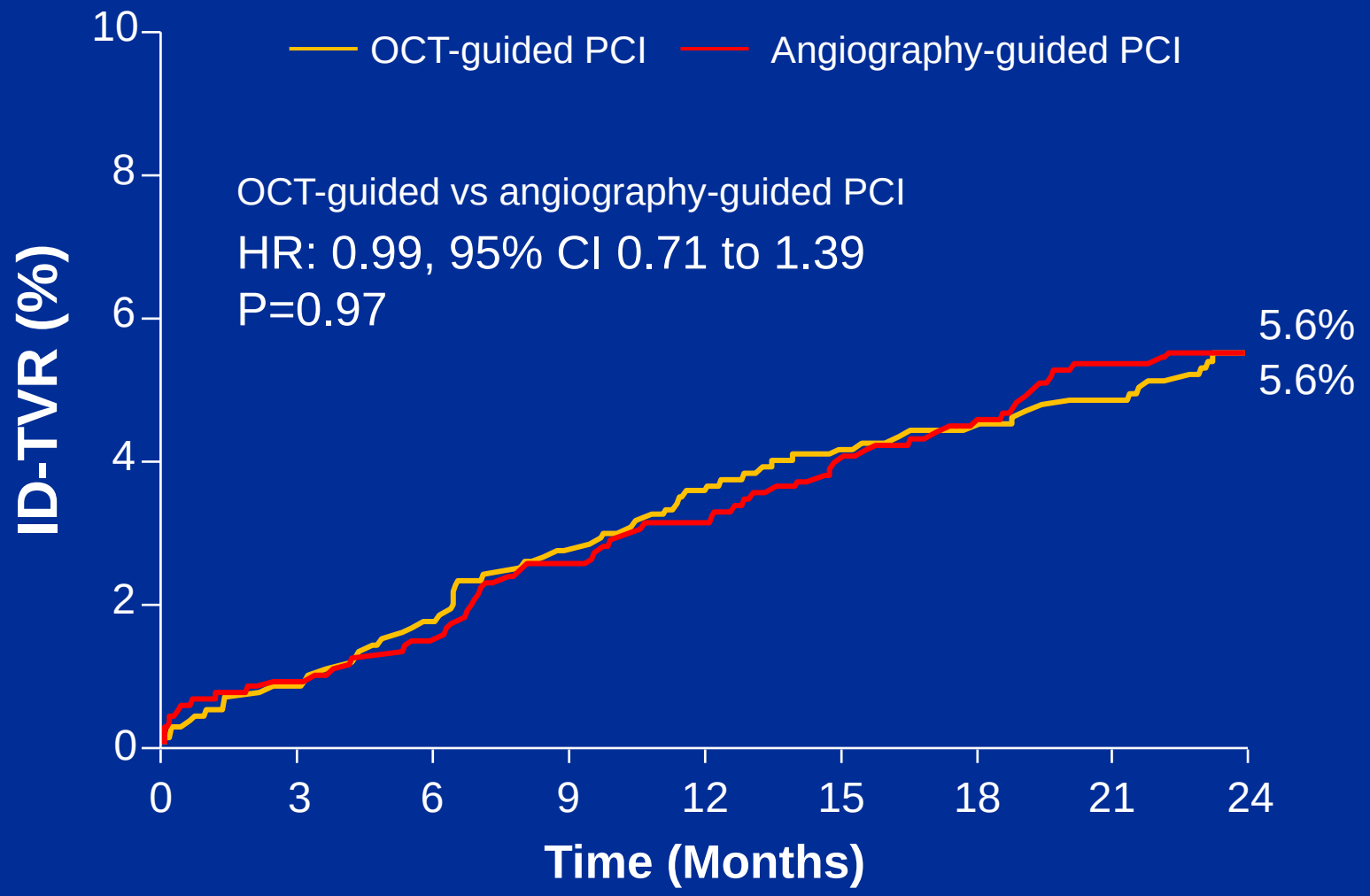
Target-Vessel MI



Number at risk:

OCT-guided	1233	1191	1186	1177	1156	1127	1120	1117	581
Angiography-guided	1254	1201	1192	1186	1166	1136	1126	1112	590

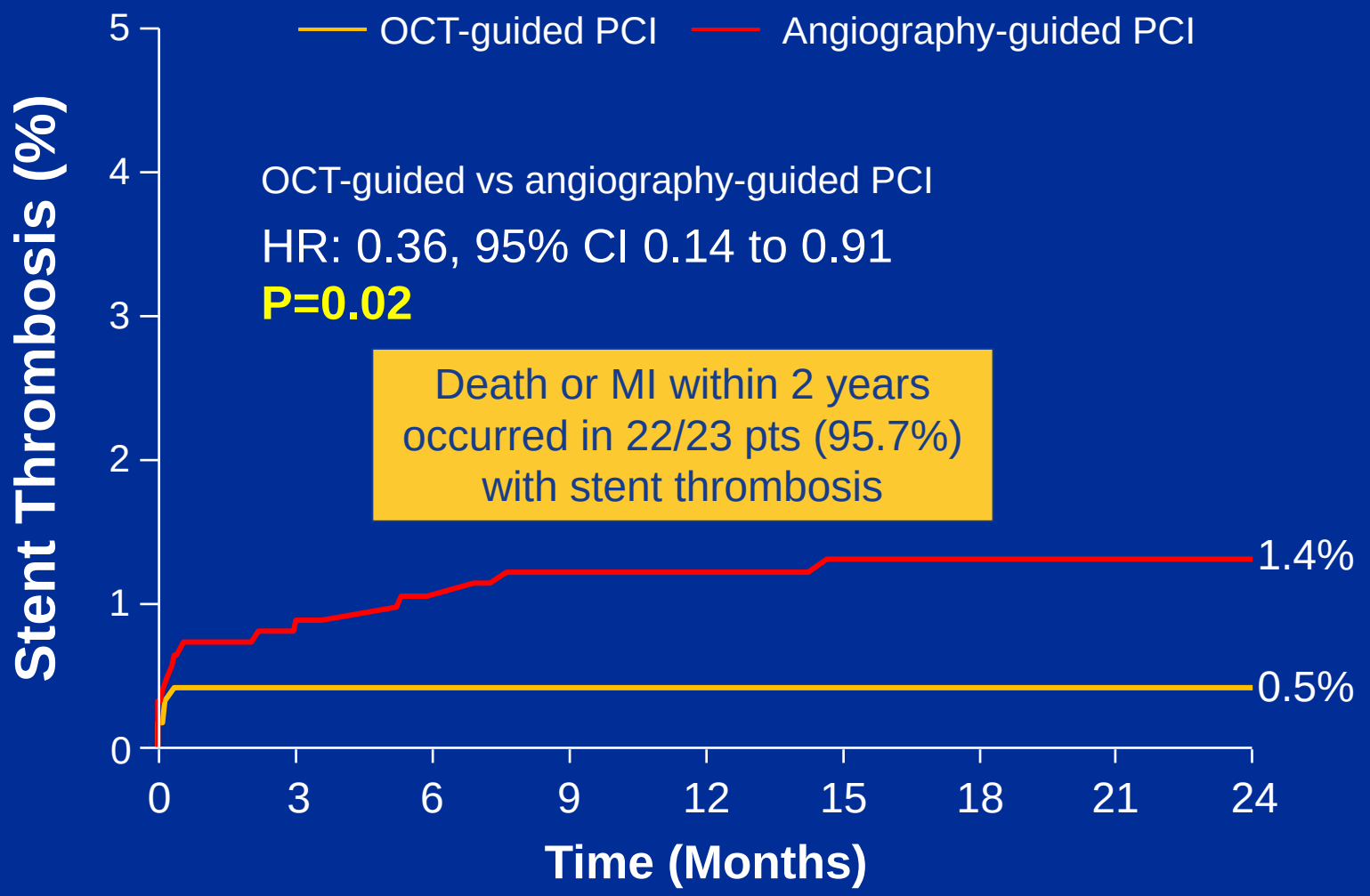
Ischemia-Driven Target Vessel Revascularization



Number at risk:

OCT-guided	1233	1202	1189	1172	1141	1110	1100	1092	569
Angiography-guided	1254	1211	1200	1184	1159	1124	1108	1087	585

Stent Thrombosis (Def/Prob)



Number at risk:

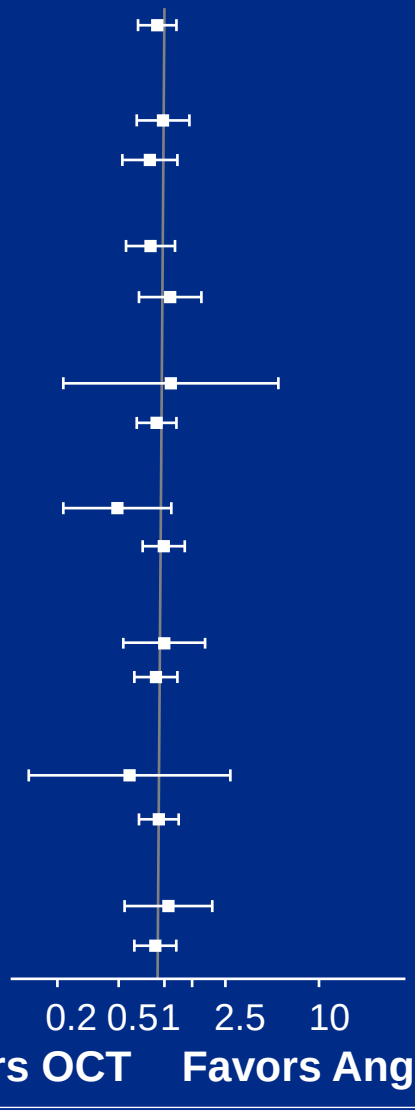
OCT-guided	1233	1207	1204	1197	1176	1149	1143	1140	593
Angiography-guided	1254	1216	1209	1204	1185	1156	1147	1135	607

2-Year Clinical Outcomes

	OCT (n=1233)	Angio (n=1254)	Hazard Ratio (95% CI)
All-cause mortality	2.7%	3.6%	0.73 (0.47, 1.16)
-Cardiac	0.8%	1.3%	0.57 (0.25, 1.29)
-Vascular	0.3%	0.3%	0.76 (0.17, 3.38)
-Non-cardiovascular	1.7%	2.0%	0.84 (0.46, 1.52)
All MI	4.8%	6.0%	0.80 (0.56, 1.13)
-TV-MI	2.5%	3.3%	0.77 (0.48, 1.22)
-Periprocedural MI	1.4%	1.7%	0.82 (0.43, 1.56)
-Non-periprocedural MI	3.4%	4.4%	0.77 (0.51, 1.17)
All revascularization	9.4%	10.1%	0.94 (0.72, 1.21)
- ID-TVR	5.6%	5.6%	0.99 (0.71, 1.40)
- ID-TLR	4.5%	4.3%	1.05 (0.71, 1.54)
- ID-TVR/non-TLR	1.8%	2.4%	0.79 (0.45, 1.38)

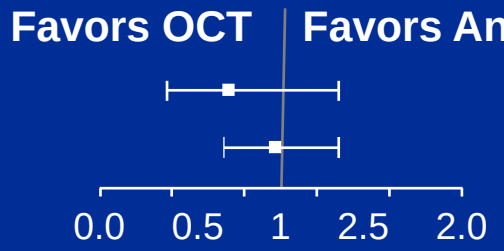
Sub-group Analysis

Subgroup	OCT	Angiography	Hazard Ratio [95% CI]
All Subjects (n=2487)	7.4%	8.2%	0.90 [0.67, 1.19]
Medication-treated diabetes			
Medication-treated Diabetes (n=995)	10.1%	10.1%	0.98 [0.66, 1.46]
Others (n=1486)	5.6%	7.0%	0.80 [0.53, 1.22]
Total stent length ≥28mm			
≥28mm (n=1677)	6.4%	7.9%	0.81 [0.56, 1.16]
<28mm (n=804)	9.7%	8.7%	1.09 [0.68, 1.73]
Two-stent bifurcation			
Yes (n=83)	7.8%	7.0%	1.10 [0.22, 5.46]
No (n=2398)	7.4%	8.2%	0.89 [0.66, 1.19]
Severe calcification			
Yes (n=286)	6.6%	12.7%	0.50 [0.22, 1.11]
No (n=2195)	7.5%	7.6%	0.98 [0.72, 1.34]
NSTEMI/ STEMI >24h			
Yes (n=735)	5.9%	5.9%	1.00 [0.54, 1.82]
No (n=1746)	8.1%	9.1%	0.87 [0.63, 1.21]
CTO			
Yes (n=173)	3.3%	5.4%	0.60 [0.13, 2.69]
No (n=2308)	7.8%	8.4%	0.92 [0.68, 1.23]
Diffuse or multi-focal ISR			
Yes (n=268)	15.2%	13.5%	1.06 [0.55, 2.05]
No (n=2213)	6.5%	7.5%	0.86 [0.63, 1.19]

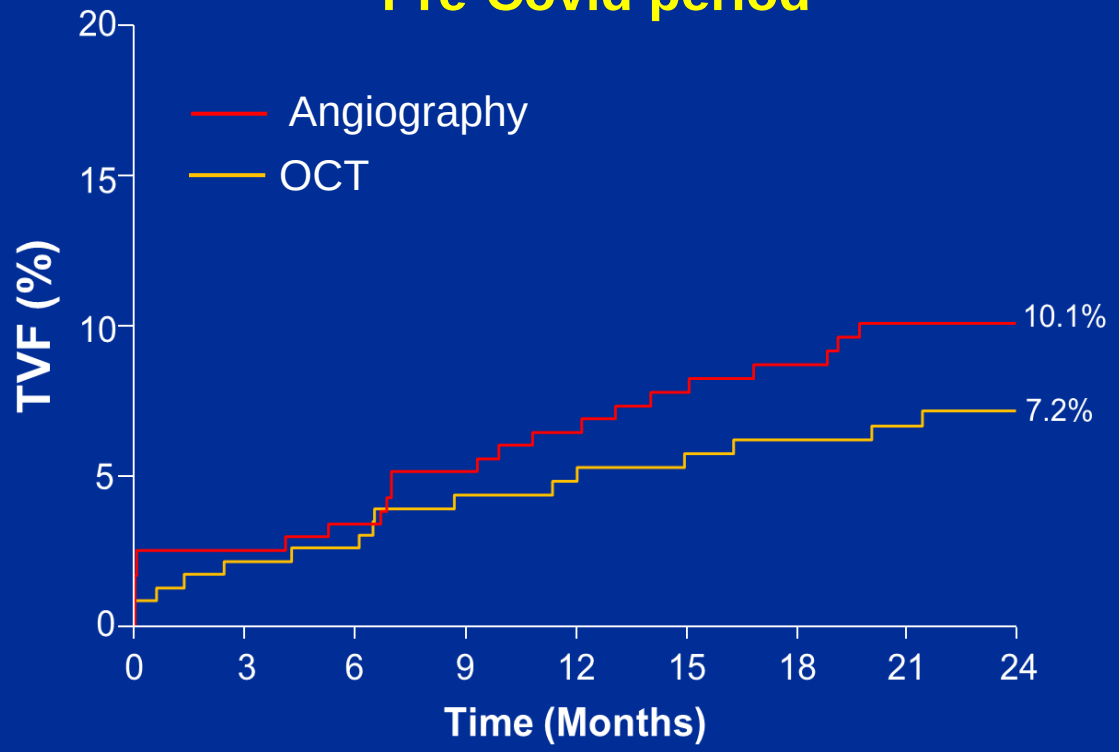


Covid Impact

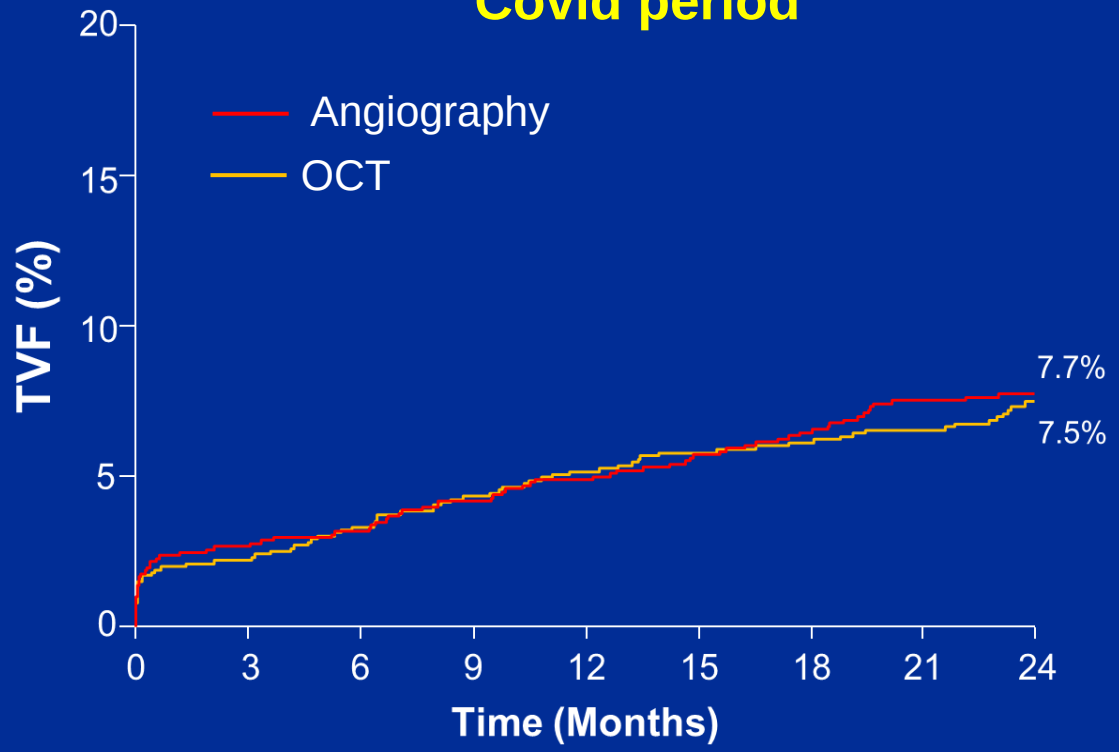
	OCT	Angiography	Hazard Ratio [95% CI]
Target Vessel Failure			
Pre-Covid (n=476)	7.2%	10.1%	0.70 [0.37, 1.32]
Covid (n=2020)	7.5%	7.7%	0.96 [0.69, 1.32]



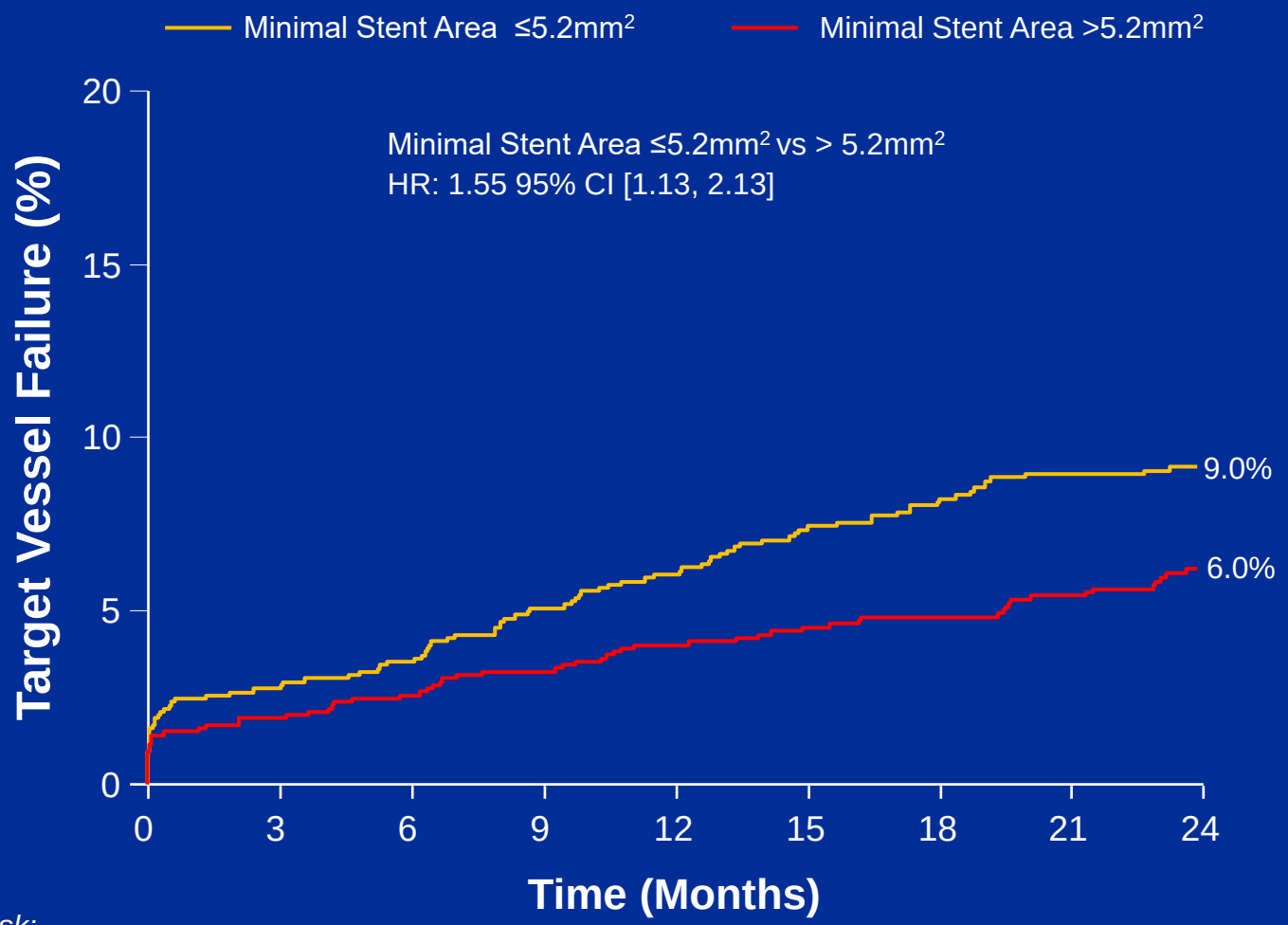
Pre-Covid period



Covid period



Relationship Between MSA and Clinical Outcomes



Number at risk:

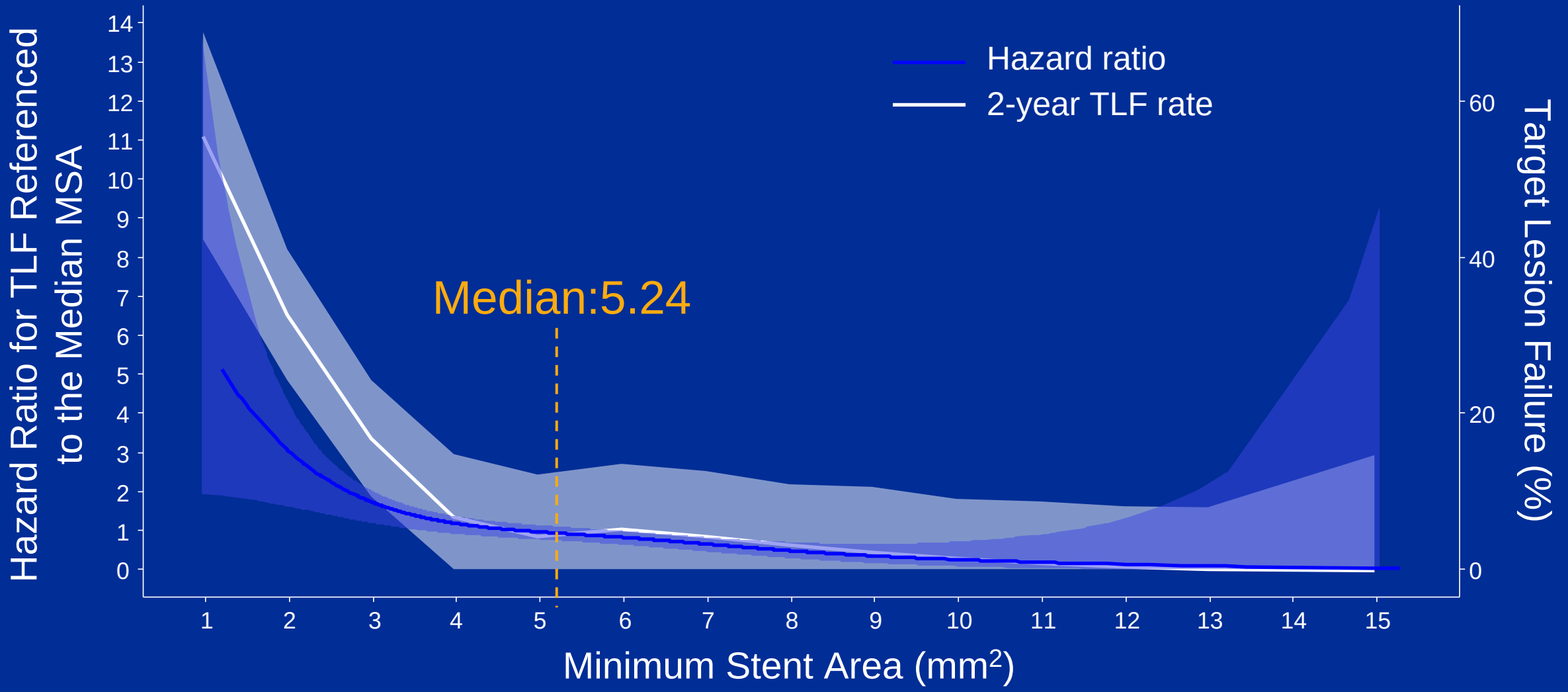
MSA >5.2mm²	1076	1041	1032	1022	996	969	959	949	506
MSA ≤5.2mm²	1083	1032	1022	1004	984	953	941	925	474

* Both study arms combined including only patients with one treated lesion (n=2159)

OCT Findings Independently Associated With Clinical Endpoints (Adjusted Analysis)

Outcome	OCT variable	Hazard ratio (95% CI)	P value
Target lesion failure	Minimal stent area, per 1 mm^2	0.76 (0.68, 0.86)	<0.0001
	Proximal edge dissection, any	1.77 (1.20, 2.62)	0.004
Cardiac death or TV-MI	Minimal stent area, per 1 mm^2	0.82 (0.70, 0.95)	0.009
	Stent length, per 5 mm	1.08 (1.02, 1.15)	0.009
Ischemia-driven TLR	Intra-stent flow area, per 1 mm^2	0.72 (0.62, 0.84)	<0.0001
	Proximal edge dissection, any	1.88 (1.16, 3.03)	0.01
	Plaque or thrombus protrusion, major	1.95 (0.97, 3.92)	0.06
Stent thrombosis	Minimal stent expansion, per 10%	0.71 (0.55, 0.93)	0.01

2-Year Target Lesion Failure (Penalized Spline Analysis)



Conclusions 1

- OCT-guidance resulted in a larger MSA than angiography guidance, with greater stent expansion
- OCT-guidance led to fewer major dissections, major malapposition, major tissue protrusion and untreated focal reference segment disease
- OCT-guidance reduced angiographic complications

Conclusions 2

- The 2-year rates of TVF were not statistically different between OCT-guided and angiography-guided PCI
- OCT-guided PCI significantly reduced stent thrombosis
- There were trends for fewer cardiac deaths and MI with OCT-guidance, consistent with prior intravascular-imaging studies
- Rates of TVR were lower than expected, a finding possibly impacted by the COVID pandemic

Conclusions 3

- The most important OCT-derived post-DES predictors of safety and effectiveness were parameters related to stent area, expansion and flow, proximal edge dissection, and stent length