# Impact of Intravascular Ultrasound Guidance In Stenting for Unprotected Left Main Coronary Artery Stenosis On Reduction of Long-Term Mortality

## Substudy from the MAIN-COMPARE Registry

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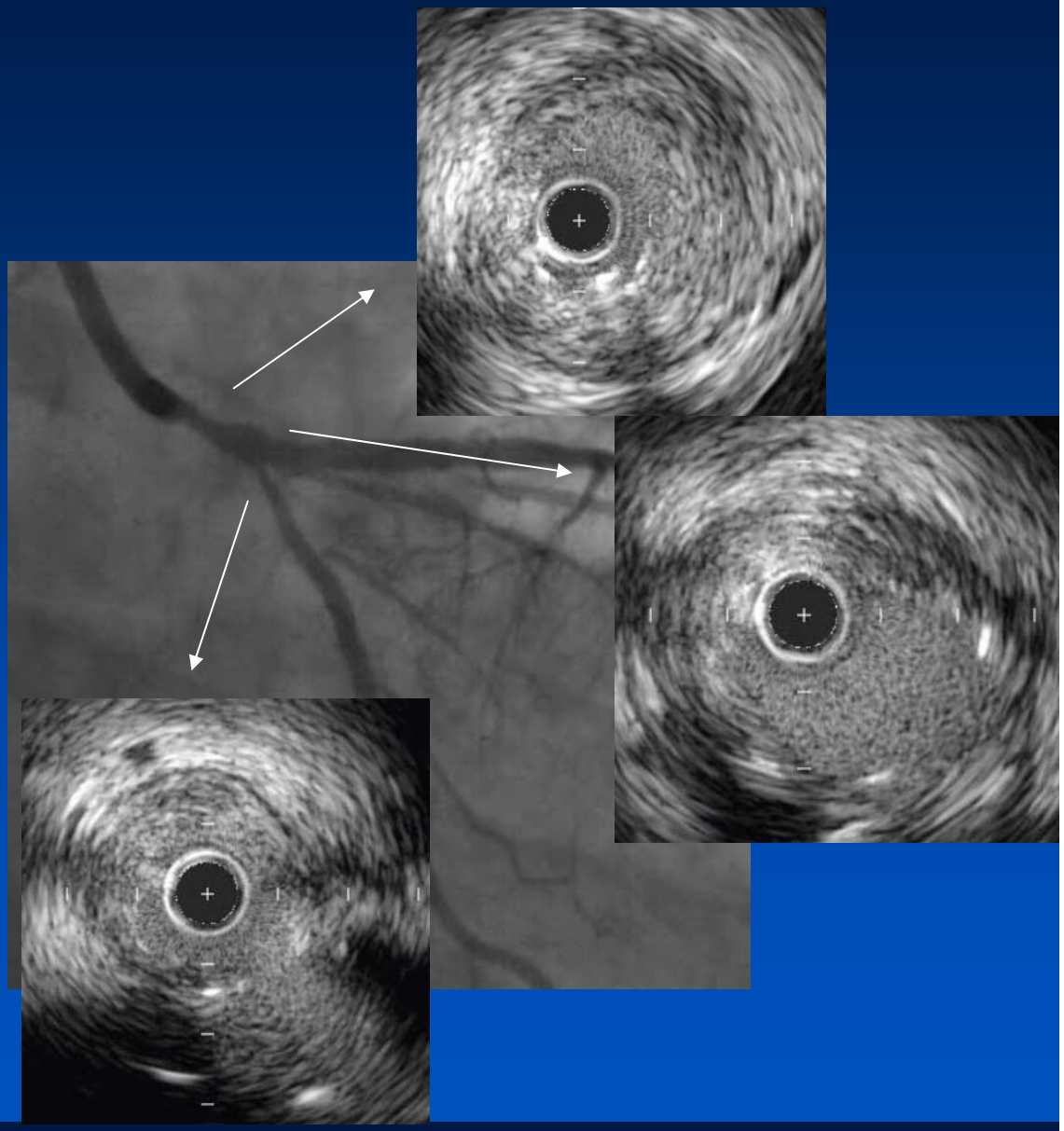
# Limitation of Angiography

- In fact, angiography has limitations in assessing the lesion morphology and true luminal size of LMCA because of aortic cusp opacification, streaming of contrast agent, short length of vessel, and lack of normal reference segment.
- Therefore, IVUS assessment before the procedure provides very useful information not only to detect significant stenosis but also to select appropriate diameter and length of stent.
- In addition, IVUS can be very helpful in optimally expanding stent with or without post-stent balloon dilatation to avoid under- or over-stretch of stent diameter.

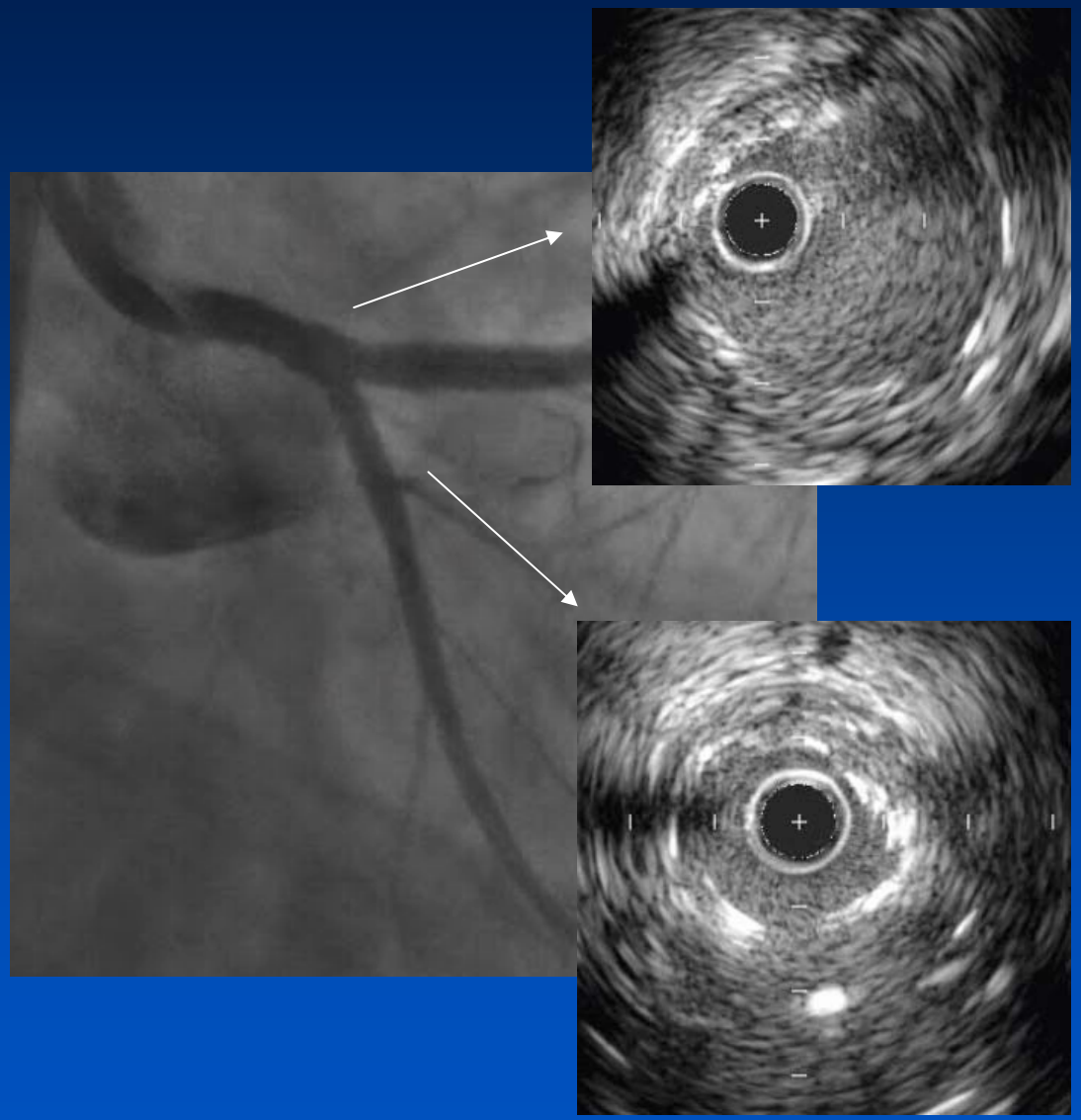
# Left Main Bifurcation Stenosis

- Significant stenosis at the LCX
- Diameter of LCX ~ 3.5 mm
- Diameter of LM ~ 4.8 mm
- Fibrous plaque extended to LM ostium



# LM Stenting with Crush Technique

- Optimal stent expansion in side branch and main vessel
- No inapposition
- Complete lesion coverage



# Purpose

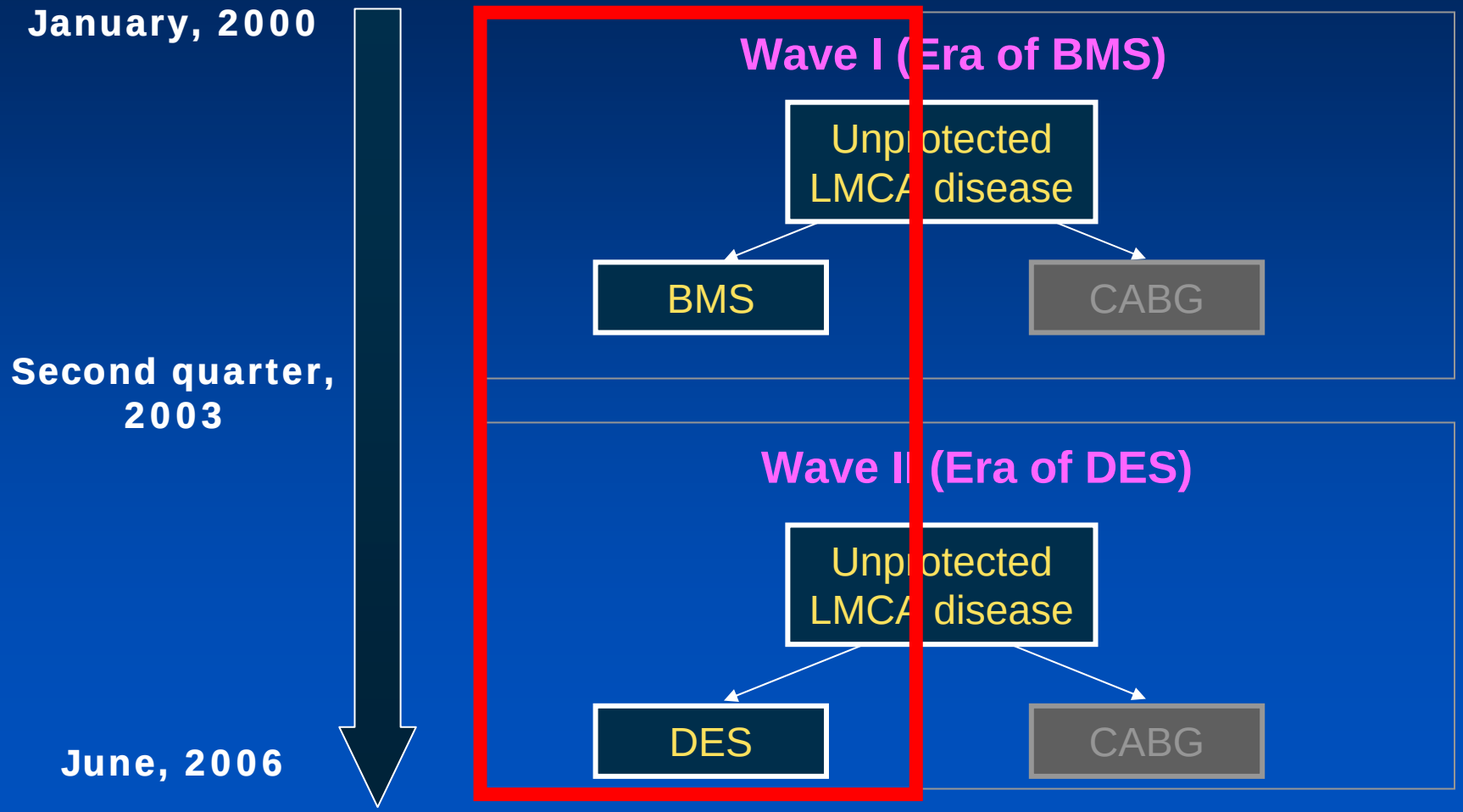
- From the MAIN-COMPARE multicenter registry, we compared long-term outcomes of IVUS-guided stenting versus conventional angiography-guided stenting.

- In addition, the outcomes were further stratified according to the stent type in order to detect differential effectiveness of IVUS in bare-metal stent (BMS) or DES treatment.

# MAIN-COMPARE Registry

## Stenting (BMS vs. DES) vs. CABG

Revascularization for Unprotected Left ***MAIN*** Coronary Artery Stenosis: *COM*parison of *P*ercutaneous Coronary *A*ngioplasty versus Surgical *RE*vascularization from Multi-Center Registry




**12 major academic institutions in Korea**

# Patients

- In the MAIN-COMPARE registry, patients who underwent stenting at the unprotected LMCA were selected and were divided into:
  (1) IVUS-guided group
  (2) Angiography-guided group
- The procedure was considered as IVUS-guided stenting when IVUS examination was performed during the procedure for guidance of optimal stenting.
- Patients who had prior bypass surgery, underwent concomitant valvular or aortic surgery, or presented with cardiogenic shock or myocardial infarction (MI) were excluded.

# Procedures

- The used DES of sirolimus-eluting stent (Cypher) or paclitaxel-eluting stent (Taxus) were selected by the operator’s discretion.
- Use of IVUS was determined by the operator’s discretion.
- Images of IVUS were obtained with a manual or automatic pullback system with commercially available imaging system (40 MHz IVUS catheter, Boston Scientific, Natick, MA: 20 MHz IVUS catheter, Volcano, Rancho Cordova, CA).

# Outcome of Interests

- The primary end point of the study was mortality with any cause.
- All other comparisons with regard to MI, target lesion revascularization (TLR) or composite of events were considered secondary end points of the study.

# Statistics

- Differences between the two groups in baseline clinical, angiographic and procedural characteristics were compared using the *t*-test or Wilcoxon rank sum test for continuous variables, and chi-square test or Fisher exact test for categorical variables, as appropriate.
- Cumulative incidence rates of clinical outcomes were estimated by the Kaplan-Meier method and compared by the log-rank test.
- Univariate and multivariable Cox proportional hazards models were used to examine the association of IVUS-guidance with the risks of clinical events.

# Statistics

- Selection bias for the choice of stent was examined with the use of a propensity model.
- The individual propensity score was incorporated into Cox proportional hazard regression models as a covariate to calculate the adjusted hazard ratios (HR).
- The HR for each outcome were adjusted with all covariates and propensity score.
- Separate Cox proportional multivariable models and new propensity scores were also developed for comparing differential outcomes of IVUS- versus angiography-guidance according to the stent type (BMS versus DES).

# Results

- A total of 975 patients were included in this analysis:
  - 756 patients (77.5%) received IVUS-guided stenting
  - 219 patients (22.5%) received angiography-guided stenting

# Baseline Clinical Characteristics

| Variable | IVUS (n=756) | Angiography (n=219) | *P* |
|---|---|---|---|
| Age (years) | 59.7±11.5 | 65.4±11.1 | **<0.001** |
| Male gender | 522 (69.0) | 159 (72.6) | 0.31 |
| Diabetes | | | |
| Any type | 204 (27.0) | 72 (32.9) | 0.09 |
| Insulin-treated | 39 (5.2) | 21 (9.6) | **0.02** |
| Hypertension | 360 (47.6) | 120 (54.8) | 0.06 |
| Hyperlipidemia | 229 (30.3) | 59 (26.9) | 0.34 |
| Current smoker | 191 (25.3) | 49 (22.4) | 0.38 |
| Family history of coronary artery disease | 58 (7.7) | 11 (5.0) | 0.18 |
| Previous myocardial infarction | 56 (7.4) | 16 (7.3) | 0.96 |
| Previous coronary angioplasty | 130 (17.2) | 52 (23.7) | **0.03** |
| Previous congestive heart failure | 6 (0.8) | 7 (3.2) | **0.006** |

# Baseline Clinical Characteristics

| Variable | IVUS (n=756) | Angiography (n=219) | *P* |
|---|---|---|---|
| Cerebrovascular disease | 50 (6.6) | 22 (10.0) | 0.09 |
| Peripheral vascular disease | 9 (1.2) | 7 (3.2) | **0.04** |
| Chronic lung disease | 15 (2.0) | 4 (1.8) | 0.88 |
| Renal failure | 14 (1.9) | 9 (4.1) | 0.05 |
| Atrial fibrillation | 9 (1.2) | 6 (2.7) | 0.10 |
| Unstable angina | 466 (61.6) | 133 (60.7) | 0.81 |
| Ejection fraction (%) | 62.7±8.5 | 59.4±12.2 | **0.001** |
| Euro SCORE | | | |
| Mean | 3.4±2.2 | 4.4±2.4 | **<0.001** |
| High score ≥ 6 | 124 (16.4) | 71 (32.4) | **<0.001** |

# Angiographic Characteristics

| Variable | IVUS (n=756) | Angiography (n=219) | *P* |
|---|---|---|---|
| **Lesion location** | | | 0.26 |
| Ostium or shaft | 392 (51.9) | 104 (47.5) | |
| Bifurcation | 364 (48.1) | 115 (52.5) | |
| **Extent of diseased vessel** | | | **<0.001** |
| LM only | 227 (30.0) | 31 (14.2) | |
| LM plus 1 VD | 184 (24.3) | 47 (21.5) | |
| LM plus 2 VD | 187 (24.7) | 67 (30.6) | |
| LM plus 3 VD | 158 (20.9) | 74 (33.7) | |
| Right coronary artery disease | 239 (31.6) | 101 (46.1) | **<0.001** |
| Restenotic lesion | 24 (3.2) | 5 (2.3) | 0.49 |

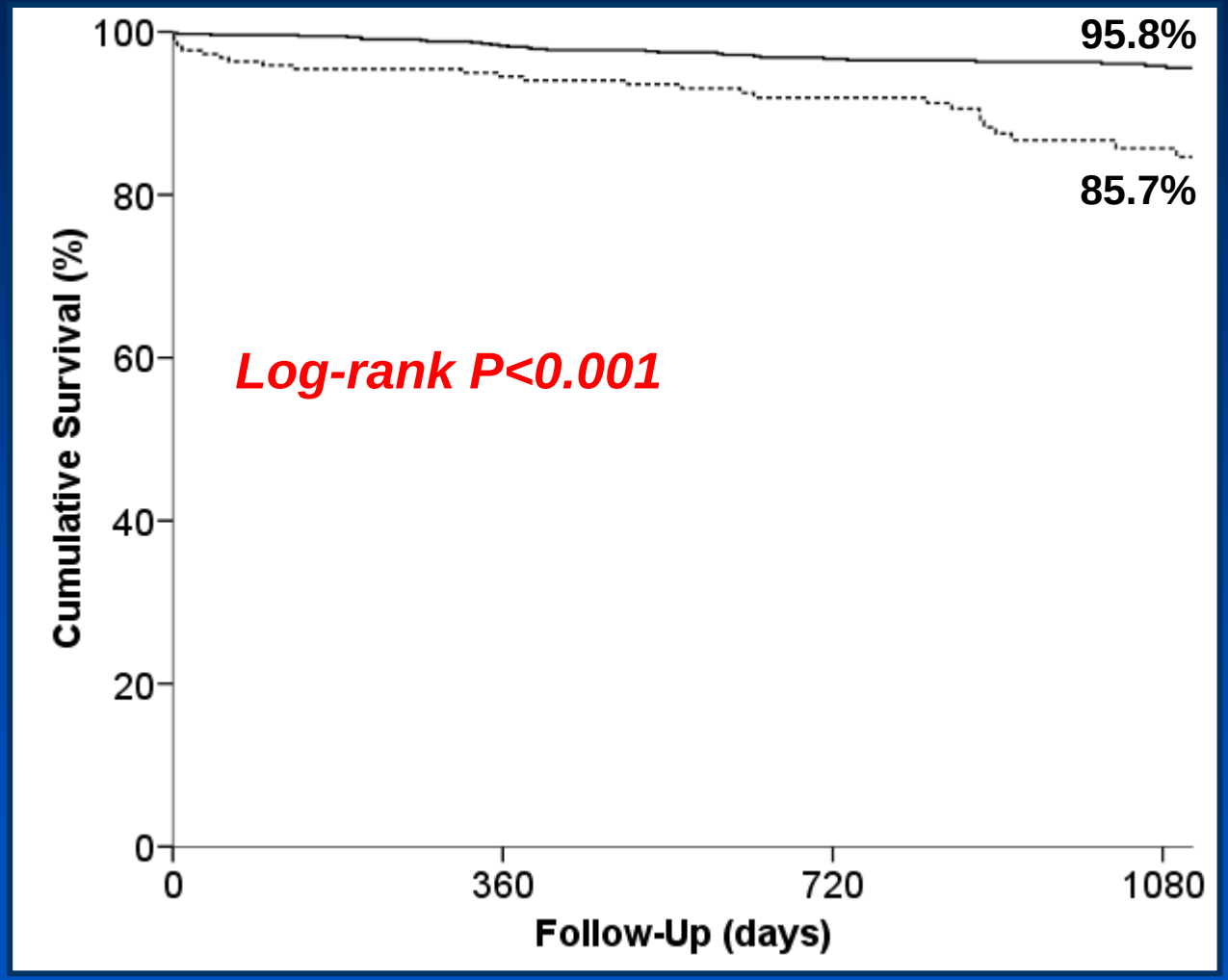
# Procedural Findings

| Variable | IVUS (n=756) | Angiography (n=219) | *P* |
|---|---|---|---|
| Use of GP IIb/IIIa inhibitors | 47 (6.2) | 9 (4.1) | 0.24 |
| Use of intra-aortic balloon pump | 28 (3.7) | 4 (1.8) | 0.17 |
| Direct stenting | 155 (20.5) | 36 (16.4) | 0.18 |
| Number of stents implanted at LM site | 1.2±0.4 | 1.2±0.5 | 0.66 |
| Total stent length at LM site | 27.3±20.9 | 30.1±20.7 | 0.08 |
| Average stent diameter at LM site | 3.6±0.5 | 3.4±0.4 | **0.002** |
| Bifurcation treatment | | | 0.95 |
| Single stenting | 226 (62.1) | 71 (61.7) | |
| Complex stenting (≥ 2 stents) | 138 (37.9) | 44 (38.3) | |

# Unadjusted Outcomes

# 3-Year Survival

## All Patients

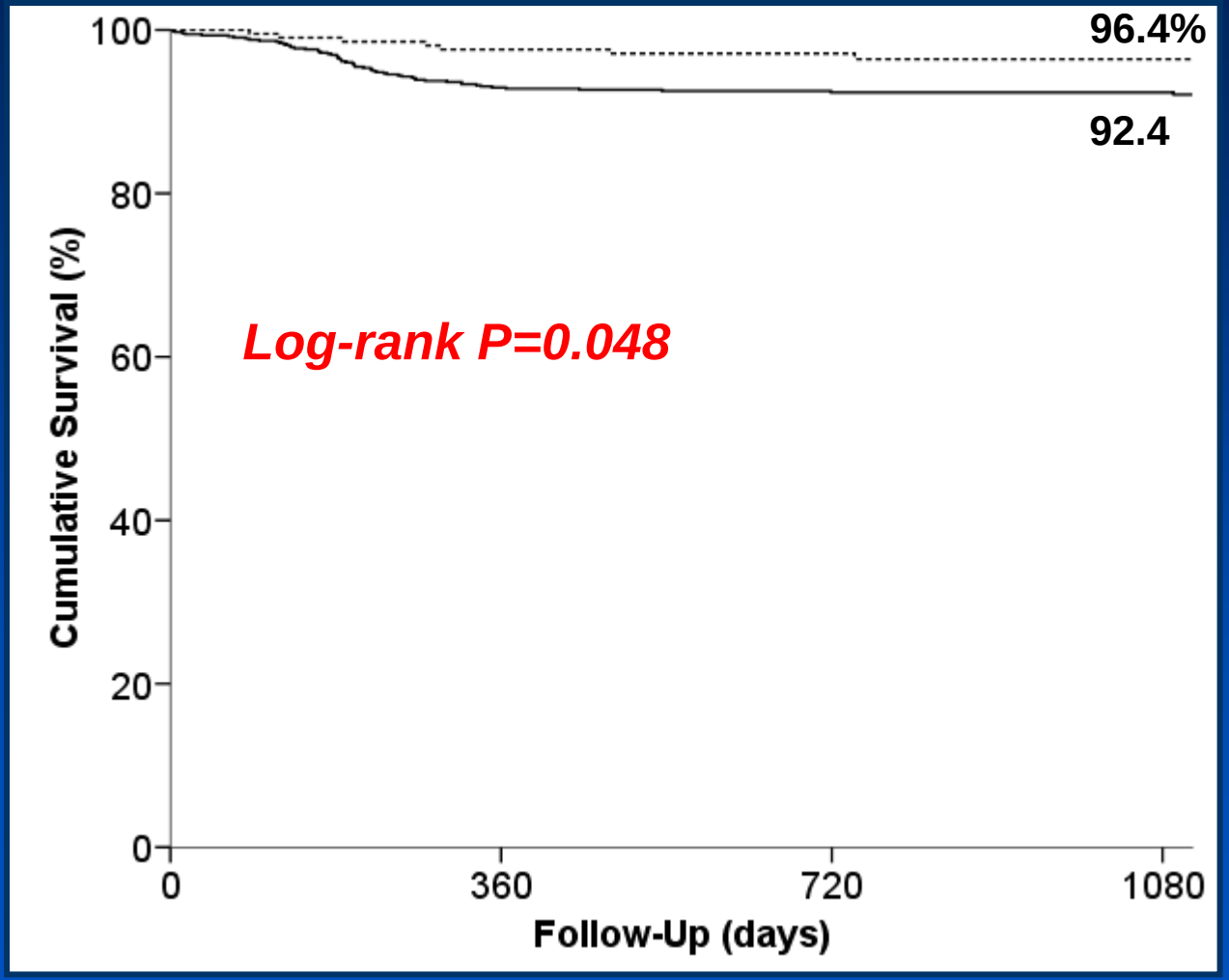



IVUS-guidance

Angio-guidance

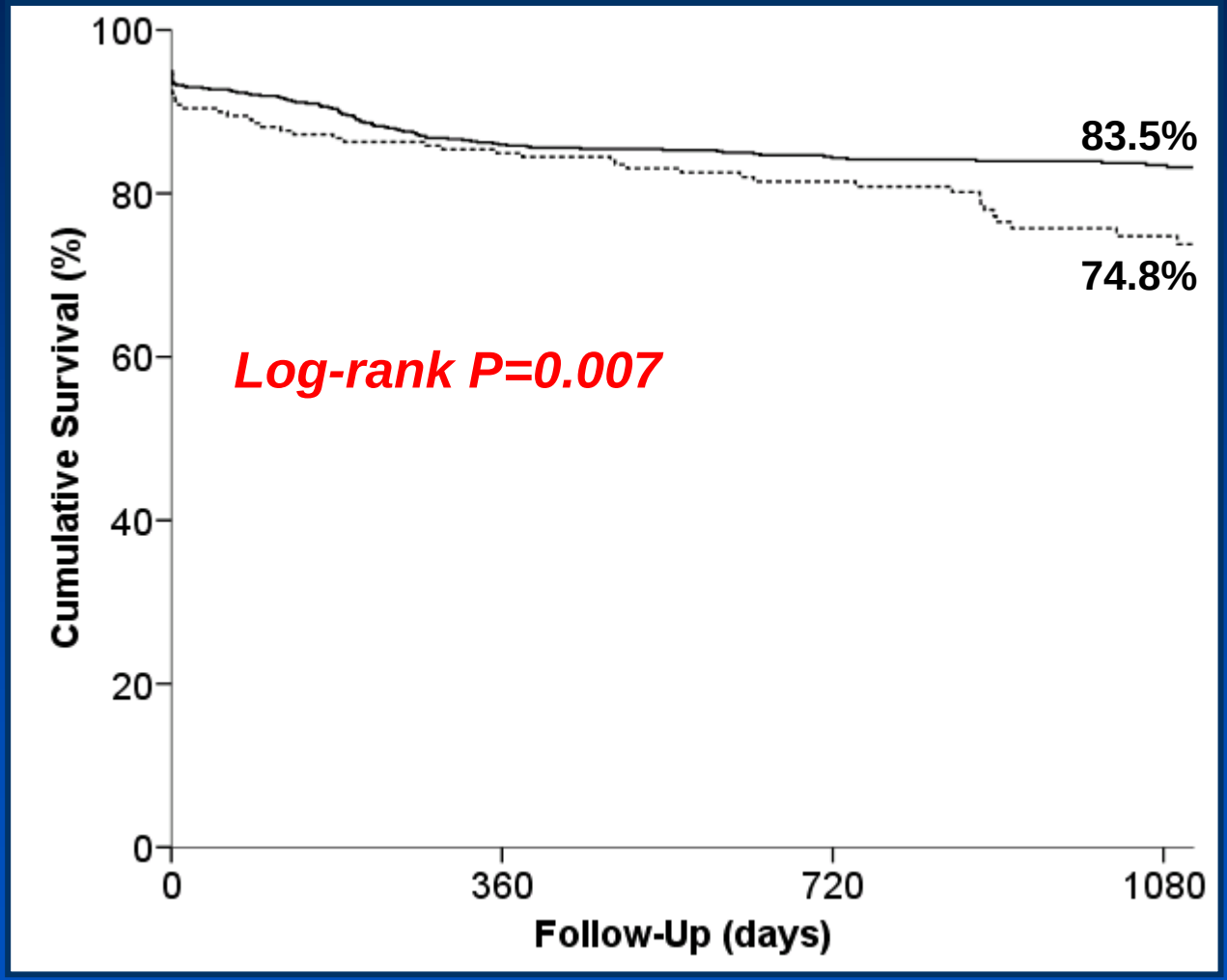
# Survival Freedom from TLR

## All Patients



# Survival Freedom from Death, MI, TLR

## All Patients

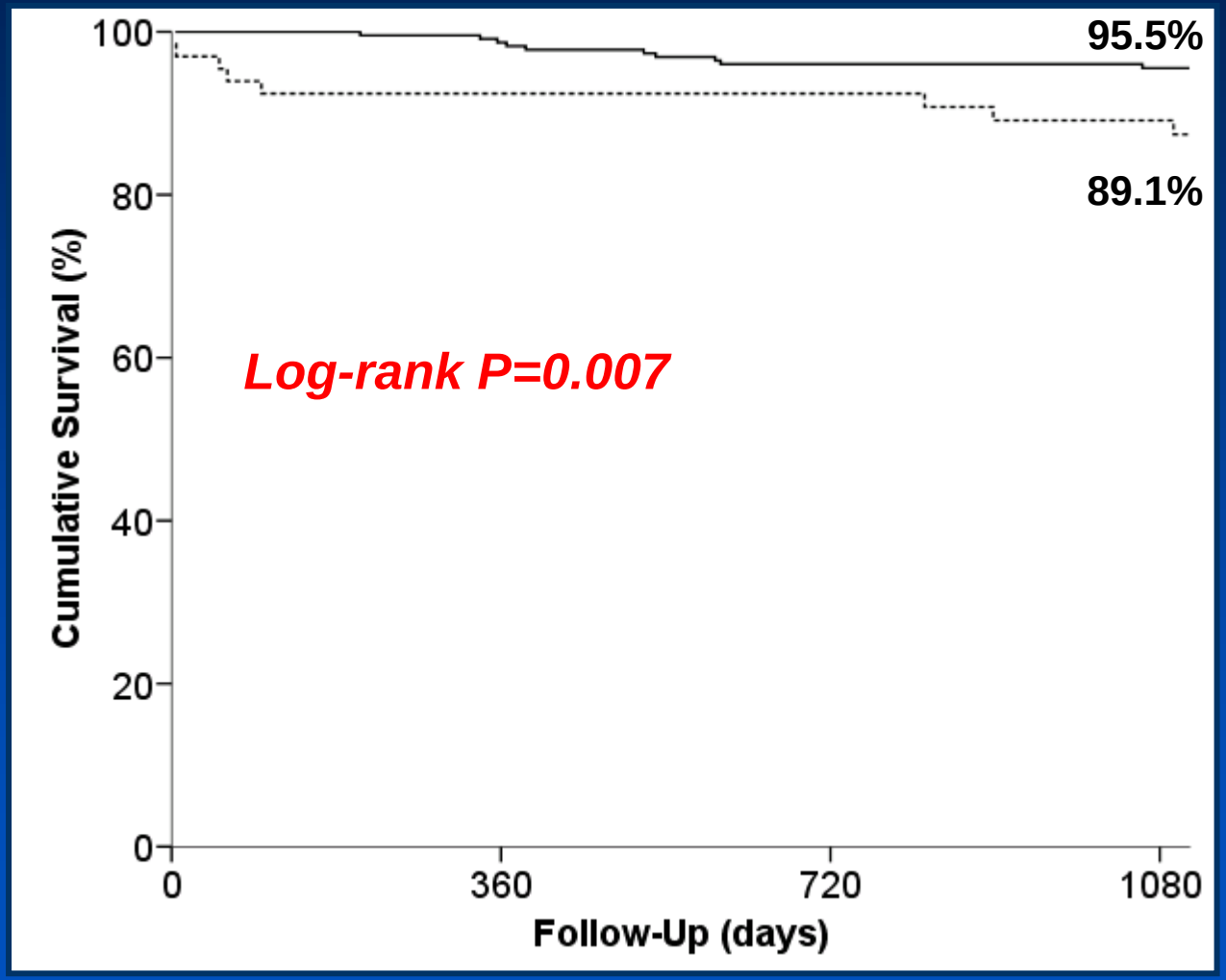



IVUS-guidance

Angio-guidance

# 3-Year Survival

## BMS Patients

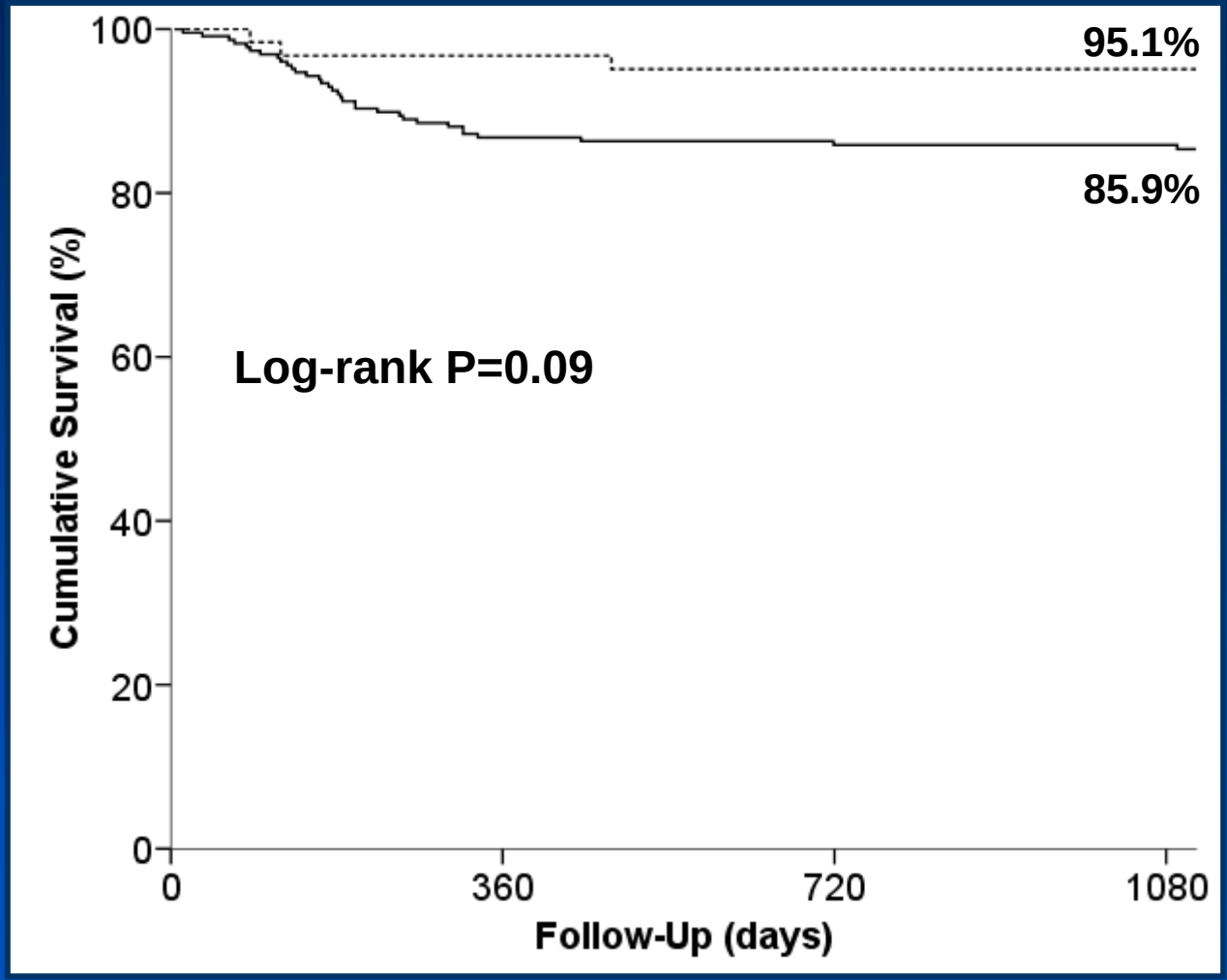



IVUS-guidance

Angio-guidance

# Survival Freedom from TLR

## BMS Patients

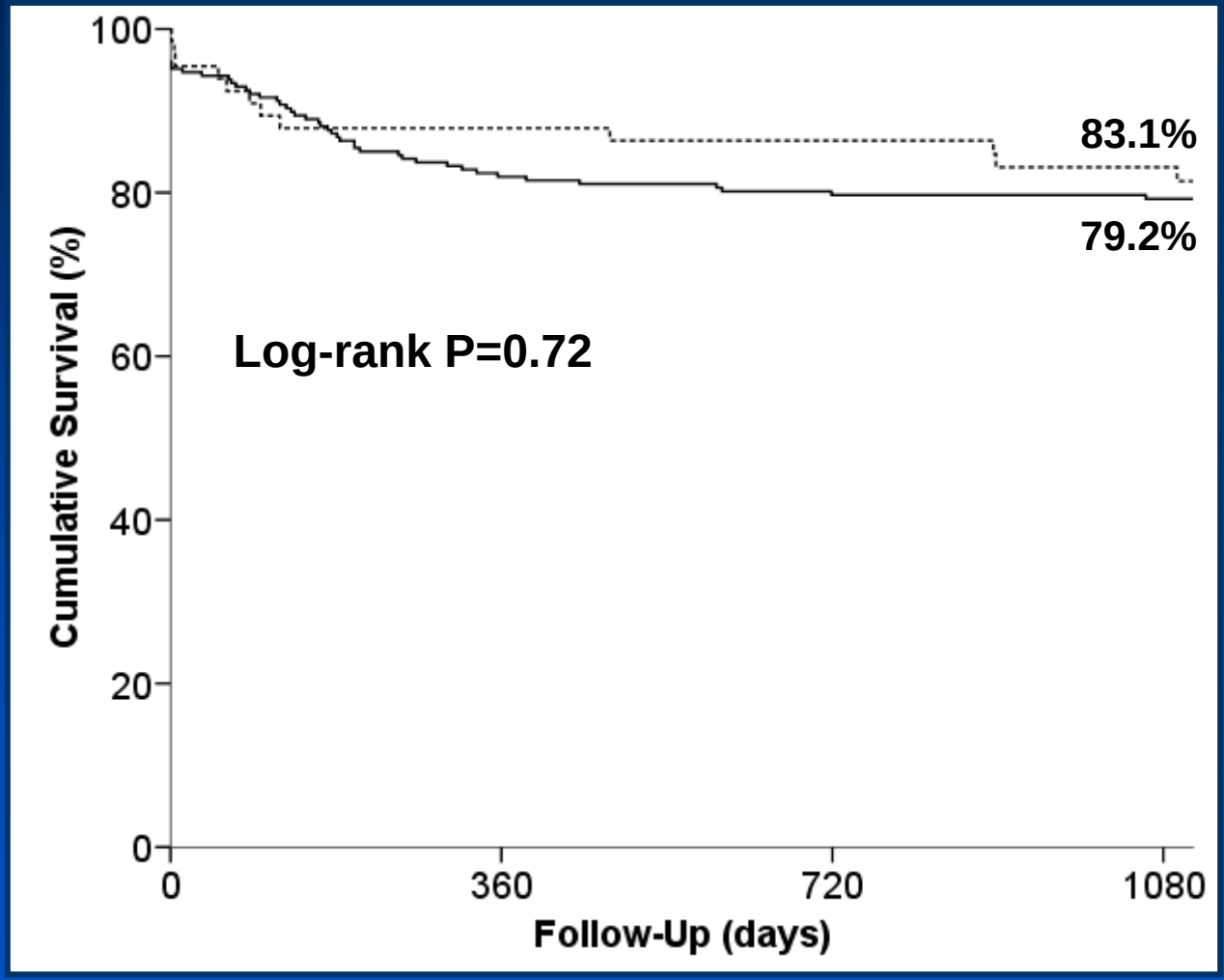



Angio-guidance

IVUS-guidance

# Survival Freedom from Death, MI, TLR

## BMS Patients

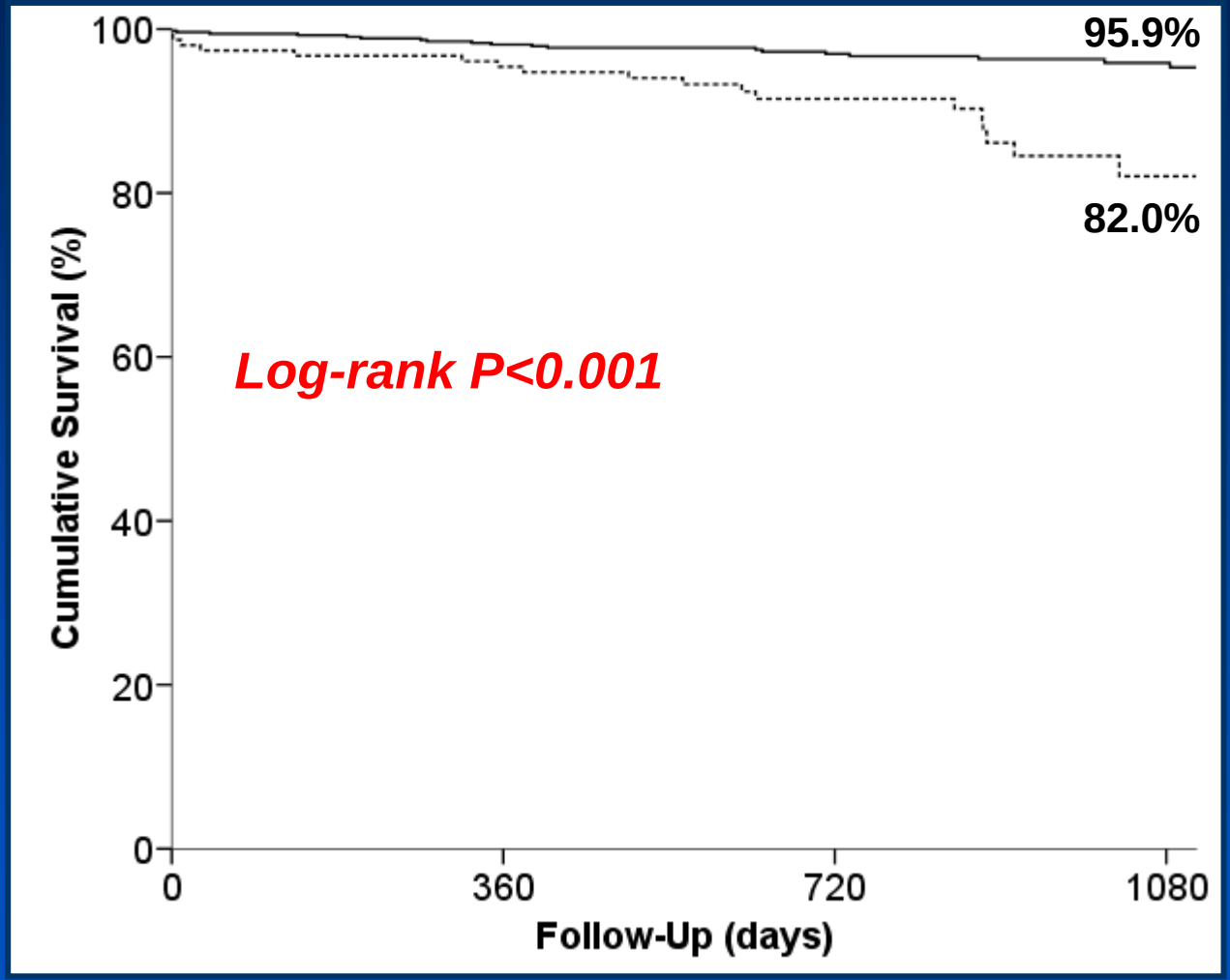



Angio-guidance

IVUS-guidance

# 3-Year Survival

## DES Patients

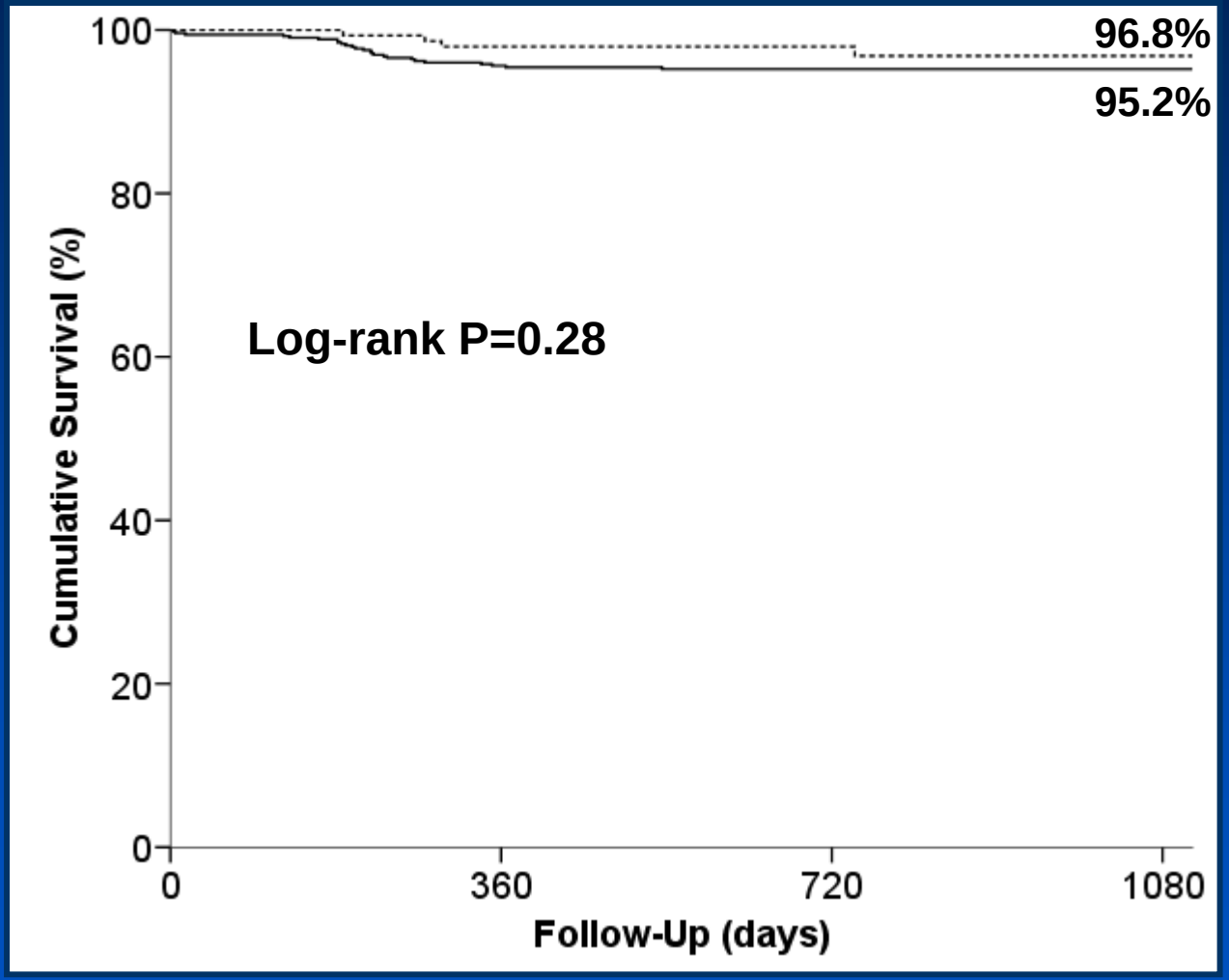



IVUS-guidance

Angio-guidance

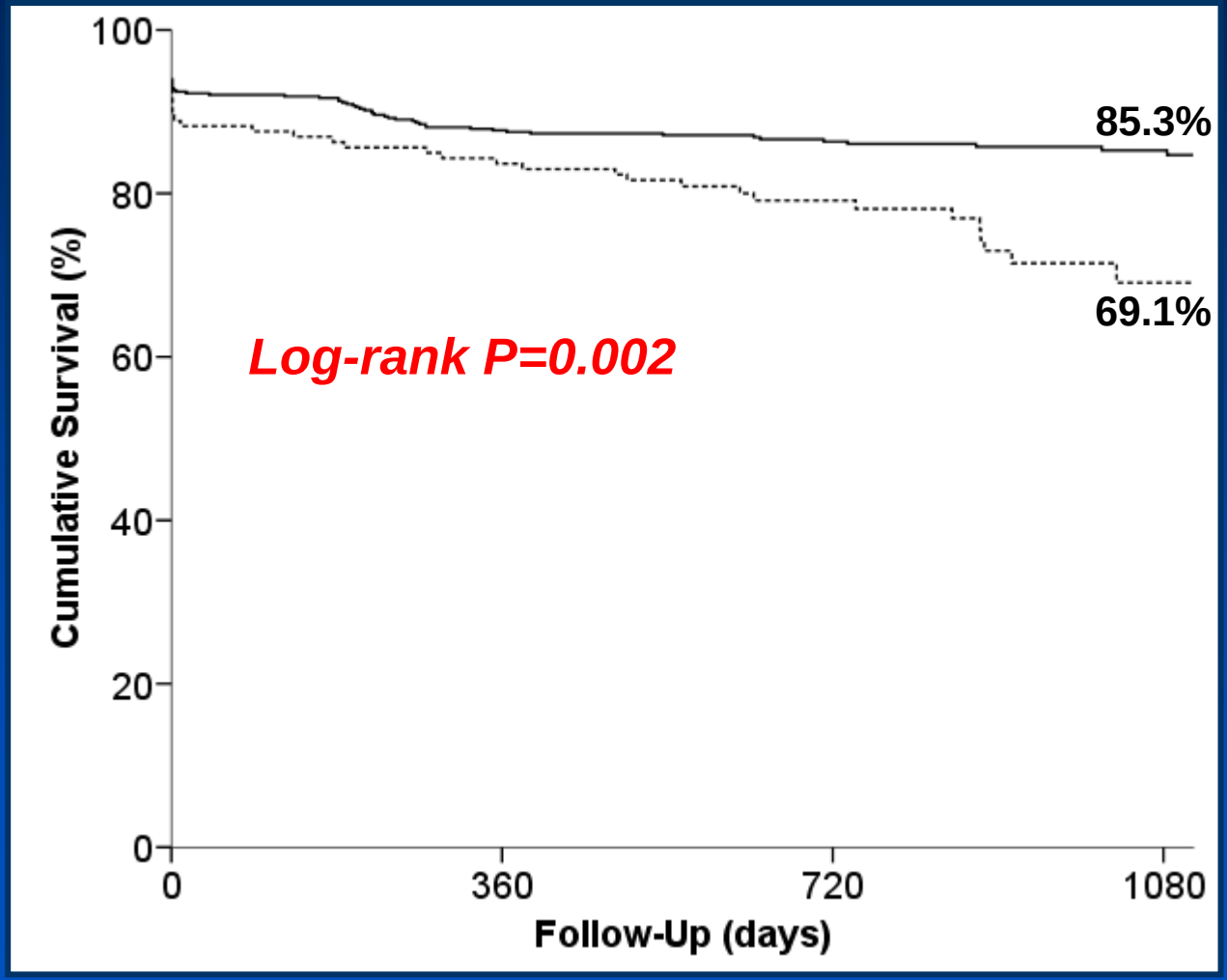
# Survival Freedom from TLR

## DES Patients



# Survival Freedom from Death, MI, TLR

## DES Patients




IVUS-guidance

Angio-guidance

# Adjusted Outcomes

# Cox Model for All Patients

| | Unadjusted | | Multivariable adjusted | | Adjusted for propensity | |
|---|---|---|---|---|---|---|
| Outcome | Hazard Ratio (95% CI) | *P* | Hazard Ratio (95% CI) | *P* | Hazard Ratio (95% CI) | *P* |
| Death | 0.31 (0.19-0.51) | <0.001 | 0.47 (0.27-0.82) | 0.007 | 0.49 (0.29-0.83) | 0.008 |
| Cardiac | 0.29 (0.16-0.52) | <0.001 | 0.44 (0.22-0.86) | 0.016 | 0.45 (0.24-0.84) | 0.013 |
| Noncardiac | 0.36 (0.14-0.89) | 0.03 | 0.55 (0.16-1.88) | 0.34 | 0.60 (0.22-1.59) | 0.30 |
| MI | 0.67 (0.41-1.08) | 0.10 | 0.68 (0.41-1.14) | 0.15 | 0.72 (0.44-1.20) | 0.21 |
| Death/MI | 0.47 (0.33-0.67) | <0.001 | 0.59 (0.40-0.86) | 0.006 | 0.59 (0.41-0.87) | 0.007 |
| TLR | 2.07 (0.99-4.34) | 0.053 | 1.65 (0.77-3.57) | 0.20 | 1.71 (0.80-3.65) | 0.16 |
| Death/MI/TLR | 0.65 (0.48-0.90) | 0.008 | 0.73 (0.52-1.02) | 0.07 | 0.74 (0.53-1.04) | 0.08 |

# Cox Model for BMS Patients

| | Unadjusted | | Multivariable adjusted | | Adjusted for propensity | |
|---|---|---|---|---|---|---|
| Outcome | Hazard Ratio (95% CI) | *P* | Hazard Ratio (95% CI) | *P* | Hazard Ratio (95% CI) | *P* |
| Death | 0.36 (0.16-0.78) | 0.01 | 0.39 (0.13-1.21) | 0.10 | 0.55 (0.21-1.48) | 0.24 |
| Cardiac | 0.27 (0.11-0.67) | 0.005 | —† | —† | 0.35 (0.11-1.10) | 0.07 |
| Noncardiac | 0.78 (0.16-3.85) | 0.76 | —† | —† | 1.86 (0.24-14.28) | 0.55 |
| MI | 0.91 (0.34-2.50) | 0.86 | 0.66 (0.17-2.58) | 0.55 | 1.30 (0.38-4.45) | 0.68 |
| TLR | 2.36 (0.84-6.67) | 0.10 | 3.19 (0.88-11.51) | 0.08 | 3.20 (0.98-10.44) | 0.054 |
| Death/MI | 0.55 (0.29-1.02) | 0.06 | 0.81 (0.35-1.85) | 0.62 | 0.85 (0.39-1.85) | 0.68 |
| Death/MI/TLR | 0.91 (0.53-1.57) | 0.73 | 1.48 (0.73-2.99) | 0.28 | 1.44 0.73-2.82) | 0.29 |

†Could not be estimated.

# Cox Model for DES Patients

| | Unadjusted | | Multivariable adjusted | | Adjusted for propensity | |
|---|---|---|---|---|---|---|
| Outcome | Hazard Ratio (95% CI) | *P* | Hazard Ratio (95% CI) | *P* | Hazard Ratio (95% CI) | *P* |
| Death | 0.27 (0.14-0.52) | <0.001 | 0.38 (0.18-0.81) | 0.012 | 0.49 (0.24-0.98) | 0.044 |
| Cardiac | 0.30 (0.14-0.65) | 0.002 | 0.51 (0.20-1.31) | 0.17 | 0.52 (0.23-1.21) | 0.13 |
| Noncardiac | 0.23 (0.07-0.74) | 0.01 | —† | —† | 0.41 (0.11-1.48) | 0.17 |
| MI | 0.60 (0.35-1.04) | 0.07 | 0.64 (0.35-1.18) | 0.15 | 0.64 (0.36-1.16) | 0.14 |
| TLR | 1.78 (0.62-5.12) | 0.28 | 2.02 (0.66-6.23) | 0.22 | 1.84 (0.61-5.51) | 0.28 |
| Death/MI | 0.43 (0.28-0.67) | <0.001 | 0.51 (0.32-0.83) | 0.006 | 0.54 (0.34-0.86) | 0.009 |
| Death/MI/TLR | 0.54 (0.37-0.80) | 0.002 | 0.62 (0.41-0.95) | 0.03 | 0.66 (0.43-0.996) | 0.048 |

†Could not be estimated.

# Conclusion

- IVUS-guided stenting reduced long-term mortality rate compared with conventional angiography-guided stenting for unprotected LMCA stenosis.
- Such a mortality benefit was identified only in patients receiving DES, but not in those receiving BMS.
- The differential survival rate between IVUS- versus angiography-guidance was more pronounced beyond 1 year after DES placement.
- Therefore, the reduction of the risk of very late stent thrombosis by IVUS-guidance might play a role in improving survival after DES placement.

# Conclusion

- A reduction of late stent thrombosis might be provided by achievement of optimal stent expansion, avoidance of stent inapposition, and selection of optimal stenting technique by use of IVUS.
- A failure of reduction of TLR with IVUS-guidance might be induced by non-randomized study design.
- IVUS-guidance may have been selected for lesions with more complex coronary anatomy, in which ultrasound examination seemed to be necessary.

# Limitations

- Because of a non-randomized registry, unmeasured confounders may have influenced the outcomes.
- Although patients presenting with cardiogenic shock or acute MI were retrieved for fair comparison, IVUS-guided stenting may be preferred for patients in stable hemodynamic condition.
- The participating centers were high-volume tertiary institutions and adopted IVUS as a routine ancillary practice in patients undergoing LMCA stenting.
- Quantitative IVUS or angiographic assessment was not performed.