Left Main Bifurcation Stenting: Impact of Residual Ischemia on Cardiovascular Mortality

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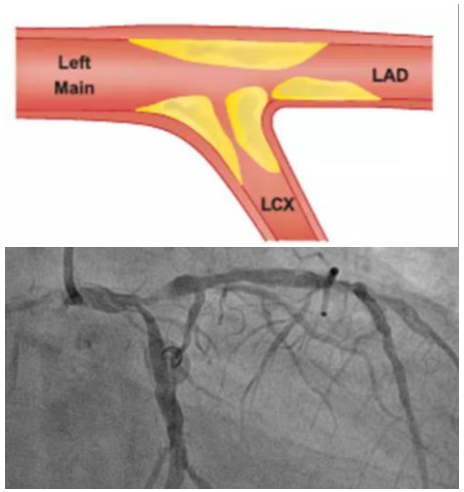
Disclosure

I, (Kefei Dou) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

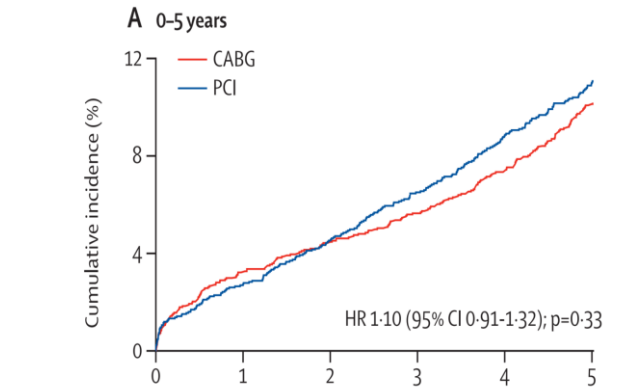
Background

- LM lesion has long been recognized as a **crucial anatomical subset** of CAD associated with **high mortality**
- An individual patient data meta-analysis demonstrated **no significant difference between PCI and CABG with respect to rates of 5-year mortality** among patients with LMCAD
- LMCAD PCI frequently involves **distal bifurcation ,usually** associated with more **complex procedures** and **inferior outcomes** compared with isolated ostial or shaft lesions

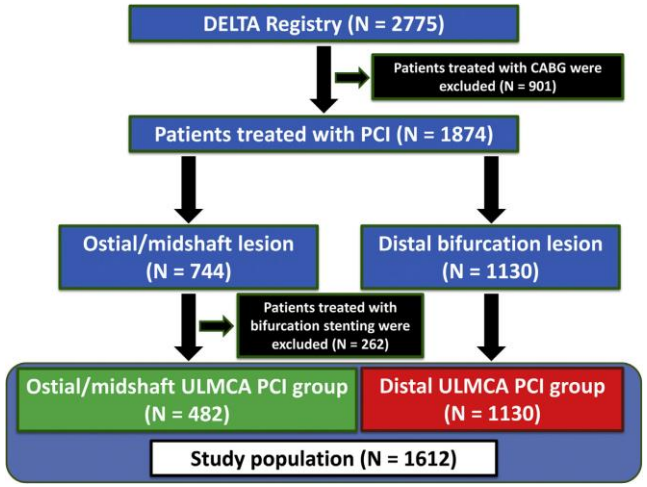
Left Main Bifurcation

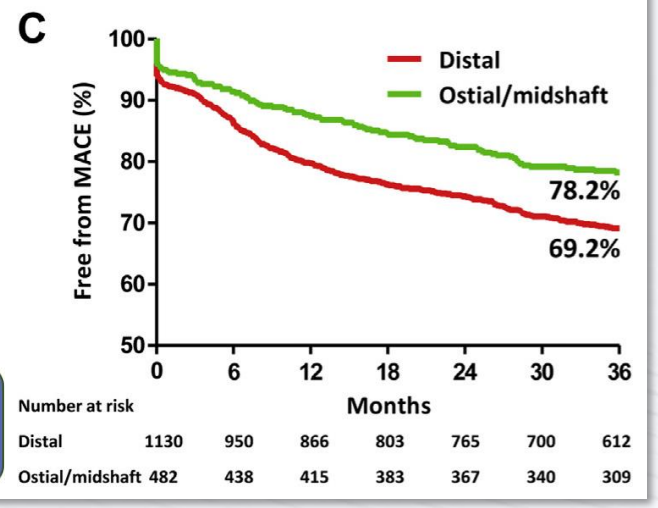


Individual Patient Data Meta-Analysis



DELTA Registry – LM ostial/midshaft lesion vs. distal bifurcation lesion



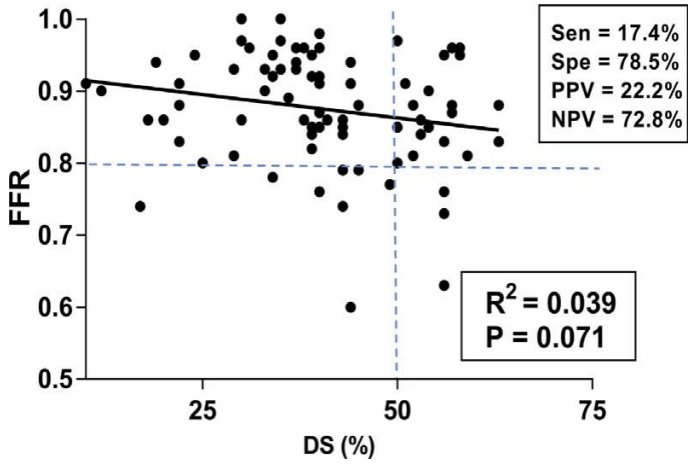


Sabatine M, et al. *Lancet* 2021; Park S, et al. *JACC Asia* 2022; Naganuma T, et al. *JACC Cardiovasc Interv* 2013

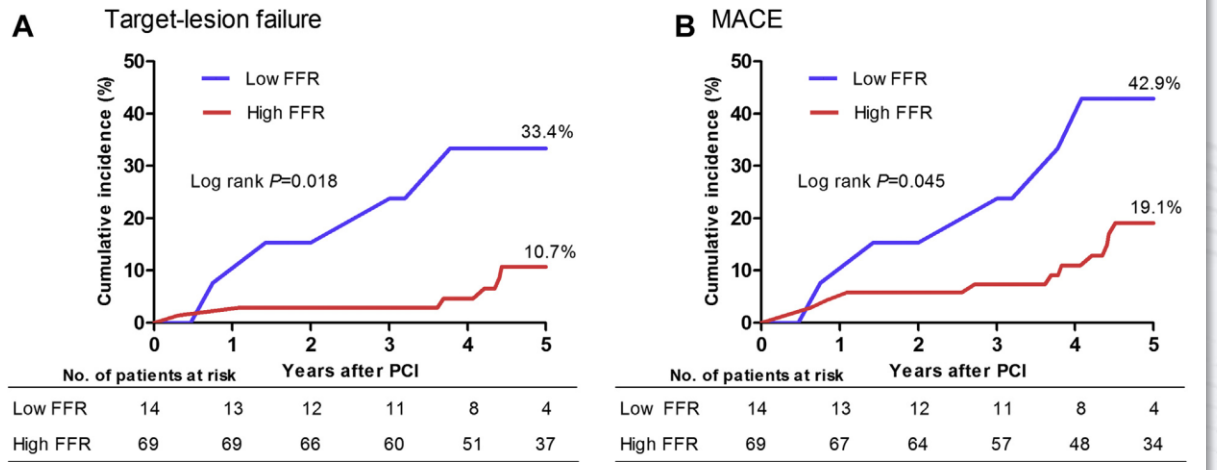
Background

- After LM crossover stenting, LCX residual ischemia was **nearly 16.9%** and associated with poor prognosis ,which is defined by wire-based physiology
- Wire-based physiology is underused due to need of pressure wire, hyperemic agents, prolonged procedural time, and **difficulties to access side branch through stent struts**
- Our study is to determine the rate and prognostic implications of post-PCI physiologically residual ischemia according to **μQFR (a computational physiological index)** after LM bifurcation PCI

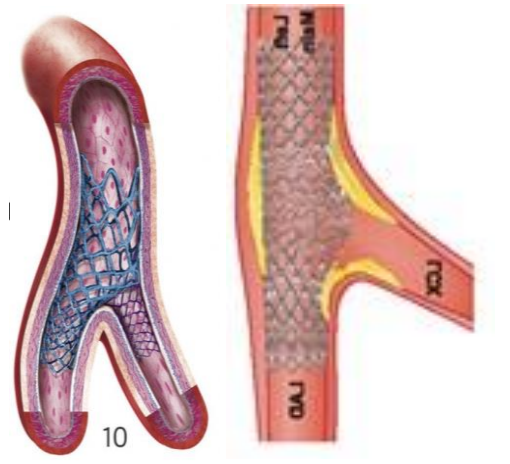
Mismatch Between Anatomy and Physiology after LM Stenting



High FFR in Jailed LCX had Better 5-year Outcomes (small sample size with wire-based physiologic assessment)

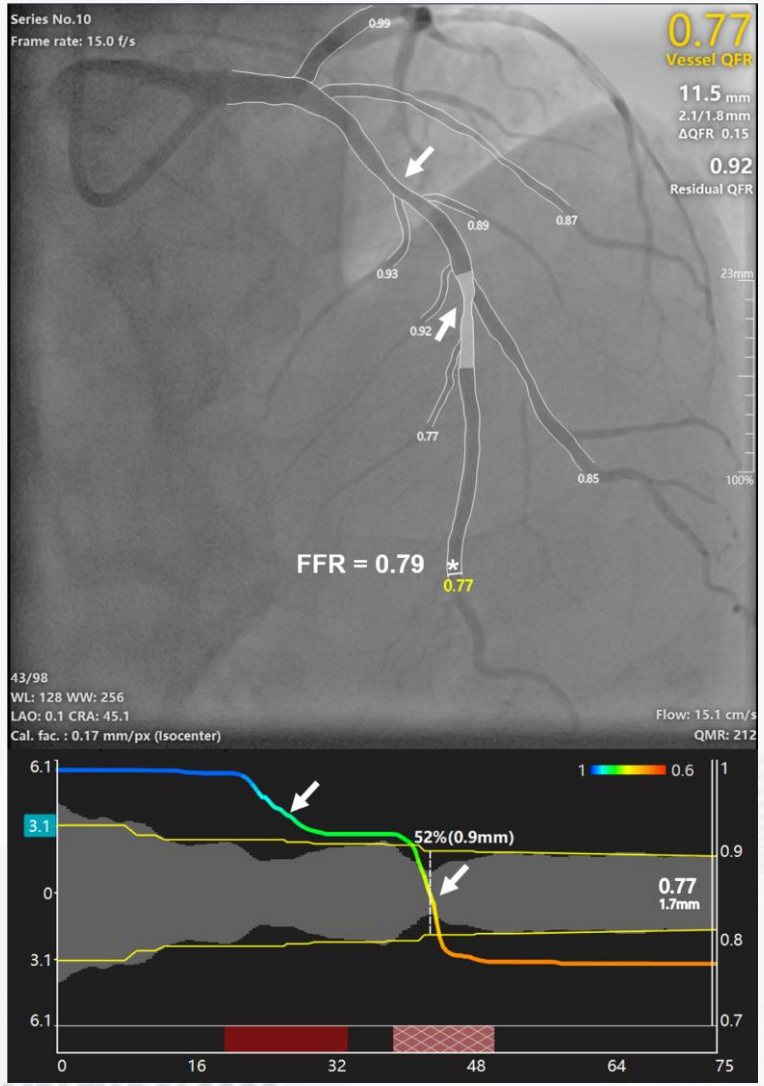


Difficulties to Access Stent Struts (Wire-based Physiology)



Lee CH, et al. *JACC Cardiovasc Interv* 2019; Lee HS, et al. *JACC Cardiovasc Interv* 2022; Armstrong PW, et al. *Eur Heart J* 2022

AI-powered Murray Bifurcation Fractal Law-based QFR (μQFR)



Key features of μQFR

(Powered by AI)

- Support single angiographic view computation
- Support analysis of bifurcation lesions
- Support analysis of all side branches
- AI-powered automation, analysis time ≈ 1 min
- Support analysis of patients with myocardial bridge
- Support analysis of plaque vulnerability: strain

Diagnostic Performance of μQFR

	μQFR ≤0.80	DS% ≥50%
Accuracy, % (95% CI)	93.0 (90.2, 95.8)	76.1 (71.4, 80.7)
Sensitivity, % (95% CI)	87.5 (80.2, 92.8)	57.5 (48.1, 66.5)
Specificity, % (95% CI)	96.2 (92.6, 98.3)	86.7 (81.3, 91.0)
PPV, % (95% CI)	92.9 (86.5, 96.9)	71.1 (61.0, 79.9)
NPV, % (95% CI)	93.1 (88.9, 96.1)	78.1 (72.2, 83.2)
+LR (95% CI)	23.0 (11.6, 45.5)	4.3 (3.0, 6.3)
-LR (95% CI)	0.13 (0.08, 0.20)	0.49 (0.40, 0.60)

Tu S, et al. *Catheter Cardiovasc Interv* 2021; Ding D, et al. *J Soc Cardiovasc Angiogr Interv* 2022

Study Design

Study Population

- A **post-hoc**, **blinded** analysis from a prospective cohort which consecutively enrolled patients with unprotected LMCAD PCI at Fuwai hospital between 2014 and 2016

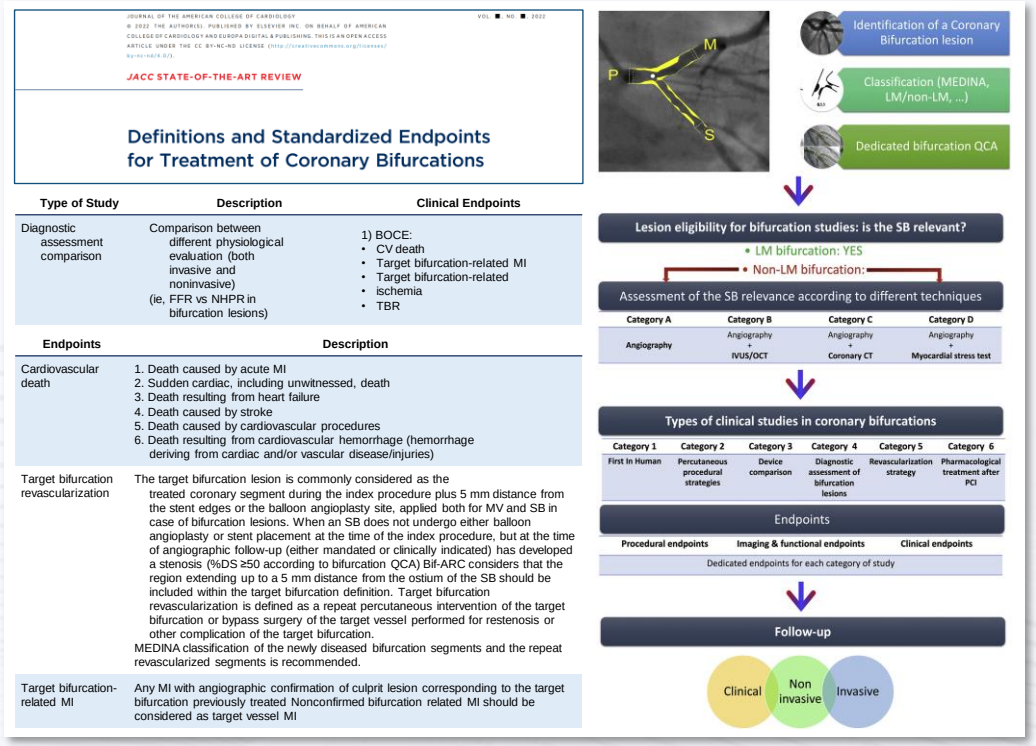
Pre-specified Outcome Definitions

- **Primary outcome:**

  3-year cardiovascular death

- **Major secondary outcome:**

  bifurcation oriented composite endpoint (BOCE), defined as the composite of cardiovascular death, target bifurcation-related MI, or target bifurcation revascularization



JACC STATE-OF-THE-ART REVIEW

Definitions and Standardized Endpoints for Treatment of Coronary Bifurcations

Type of Study	Description	Clinical Endpoints
Diagnostic assessment comparison	Comparison between different physiological evaluation (both invasive and noninvasive) (ie, FFR vs NHPR in bifurcation lesions)	1) BOCE: • CV death • Target bifurcation-related MI • Target bifurcation-related • ischemia • TBR

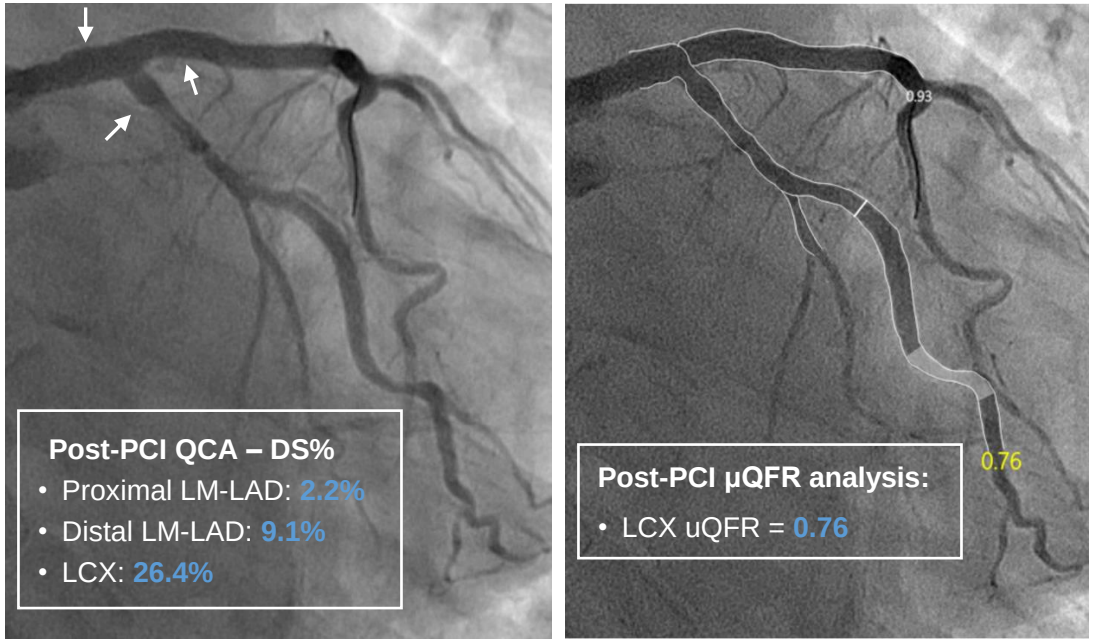
Endpoints	Description
Cardiovascular death	1. Death caused by acute MI 2. Sudden cardiac, including unwitnessed, death 3. Death resulting from heart failure 4. Death caused by stroke 5. Death caused by cardiovascular procedures 6. Death resulting from cardiovascular hemorrhage (hemorrhage deriving from cardiac and/or vascular disease/injuries)
Target bifurcation revascularization	The target bifurcation lesion is commonly considered as the treated coronary segment during the index procedure plus 5 mm distance from the stent edges or the balloon angioplasty site, applied both for MV and SB in case of bifurcation lesions. When an SB does not undergo either balloon angioplasty or stent placement at the time of the index procedure, but at the time of angiographic follow-up (either mandated or clinically indicated) has developed a stenosis (%DS ≥50 according to bifurcation QCA) Bif-ARC considers that the region extending up to a 5 mm distance from the ostium of the SB should be included within the target bifurcation definition. Target bifurcation revascularization is defined as a repeat percutaneous intervention of the target bifurcation or bypass surgery of the target vessel performed for restenosis or other complication of the target bifurcation. MEDINA classification of the newly diseased bifurcation segments and the repeat revascularized segments is recommended.
Target bifurcation-related MI	Any MI with angiographic confirmation of culprit lesion corresponding to the target bifurcation previously treated Nonconfirmed bifurcation related MI should be considered as target vessel MI

Lunardi M, et al. *J Am Coll Cardiol* 2022

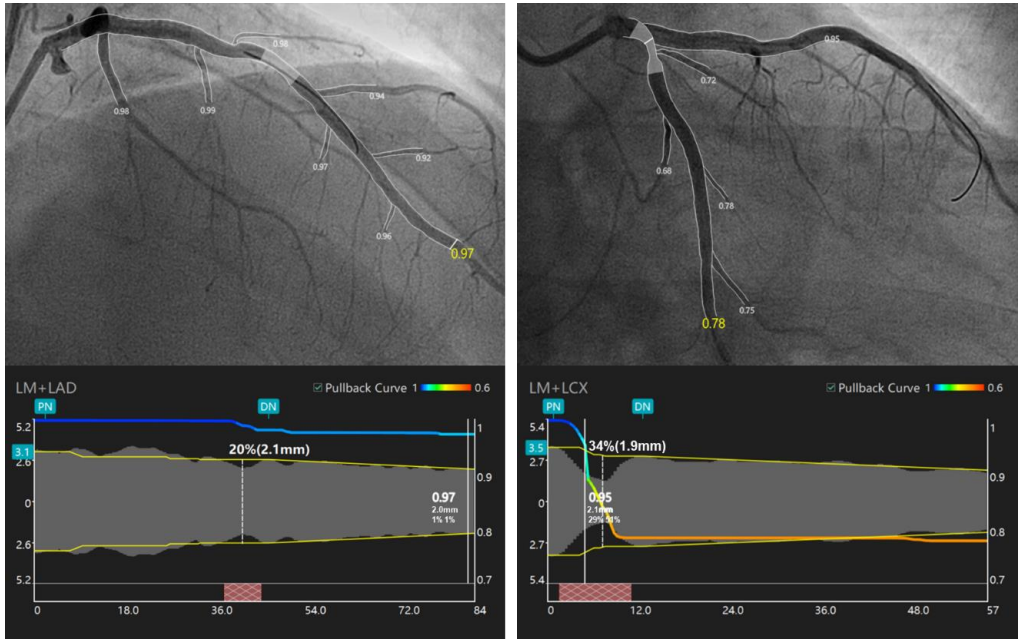
Study Design

- 2D-μQFR assessments were **performed separately in main vessel (LM-LAD) and side branch (LCX)** based on different **single angiographic views**
- **Physiologically significant residual ischemia,** defined by post-PCI μQFR values ≤0.80

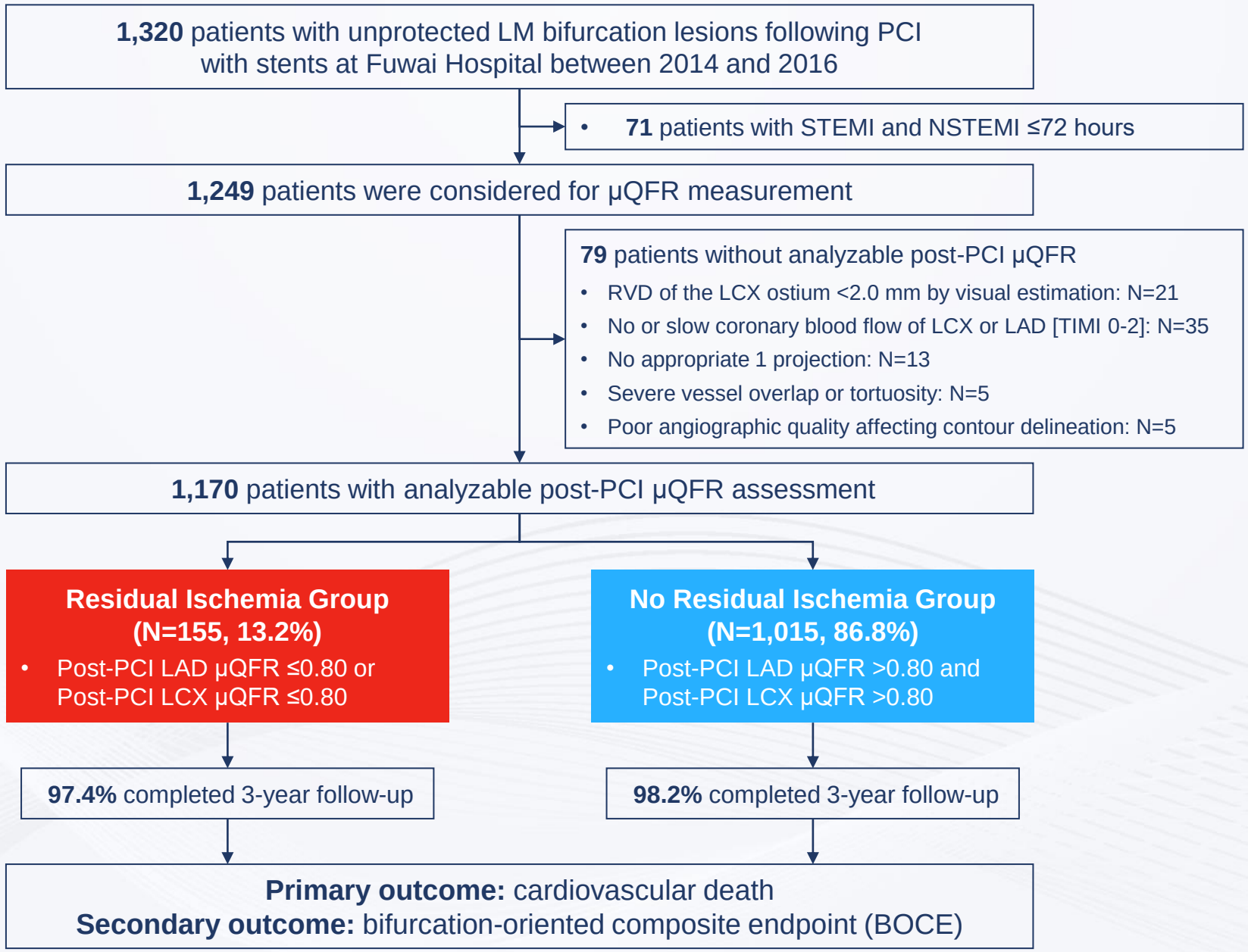
Post-PCI Anatomic QCA and μQFR Assessment



μQFR were assessed separately in LAD and LCX



Study Flow



Distribution of Post-PCI μQFR

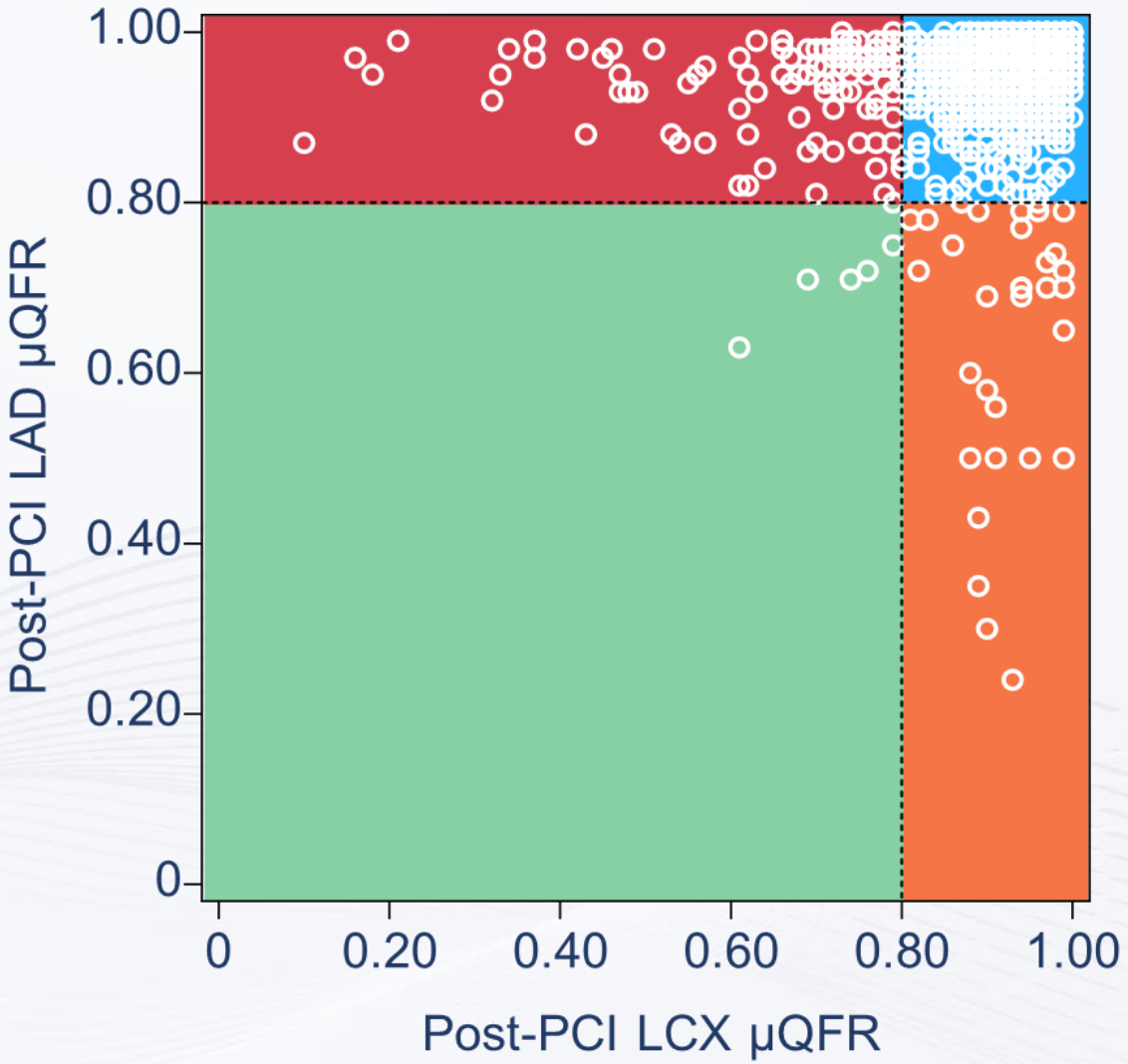
- Post-PCI residual ischemia was detected in **155 (13.2%)** patients after LM bifurcation PCI

LAD μQFR >0.80
LCX μQFR >0.80
N=1,015, 86.8%

LAD μQFR >0.80
LCX μQFR ≤0.80
N=117, 10.0%

LAD μQFR ≤0.80
LCX μQFR >0.80
N=32, 2.7%

LAD μQFR ≤0.80
LCX μQFR ≤0.80
N=6, 0.5%



Key Baseline Characteristics

	Residual Ischemia Group (N=155)	No Residual Ischemia Group (N=1,015)	P value
Age, years	62.1 ± 10.4	60.6 ± 10.2	0.09
Male	77.4%	79.8%	0.49
Diabetes mellitus	**39.4%**	**29.7%**	**0.02**
Hypertension	65.2%	61.2%	0.34
Hyperlipidemia	**76.8%**	**68.3%**	**0.03**
Prior percutaneous coronary intervention	26.5%	23.9%	0.50
Left ventricular ejection fraction, %	**61.2 ± 8.6**	**63.4 ± 7.0**	**0.001**
Acute coronary syndrome	49.0%	50.4%	0.80
LM lesion type - de novo	95.5%	97.5%	0.18
True LM bifurcation	24.5%	28.1%	0.36
DEFINITION criteria - complex bifurcation	32.3%	41.4%	0.33
LM moderate-to-severe calcification	23.2%	17.8%	0.11
Anatomic SYNTAX score	**25.4 ± 7.4**	**22.5 ± 6.7**	**<0.0001**

Key Procedural Characteristics

	Residual Ischemia Group (N=155)	No Residual Ischemia Group (N=1,015)	P value
IVUS guidance	44.5%	52.0%	0.09
Total number of stents per LM lesion	1.75 ± 0.74	1.79 ± 0.76	0.49
Total stent length per LM lesion, mm	34.4 ± 18.9	35.7 ± 19.7	0.44
Provisional stenting technique	**88.4%**	**72.3%**	**<0.0001**
POT performed	57.4%	50.4%	0.11
FKBI performed	**35.5%**	**51.8%**	**0.0002**
Post-dilation performed	89.7%	90.2%	0.83
IABP utilization	3.2%	3.7%	0.75
Angiographic success*	94.2%	95.5%	0.49
Residual SYNTAX score	**7.1 ± 6.5**	**3.8 ± 4.7**	**<0.0001**

*defined as: 1) residual stenosis less than 30% for MV treated with stents and less than 50% for SB treated with balloon angioplasty by visual estimation, with TIMI 3 in both MV and SB for LM bifurcation patients treated with one-stent technique; or 2) residual stenosis less than 30% by visual estimation with TIMI 3 in both MV and SB for LM bifurcation patients treated with two-stent technique.

Predictors of Residual Ischemia

Model 1: Baseline Variables*

Predictors	Adjusted OR (95% CI)	P value
LVEF, per 10% decrease	1.30 (1.02-1.67)	0.03
True LM bifurcation	1.79 (1.15-2.80)	0.01
Side branch – RVD (per 0.1 mm decrease)	1.05 (1.02-1.09)	0.04
Anatomic SYNTAX score (per 1 increase)	1.06 (1.03-1.08)	<0.001
Pre-PCI LCX μQFR (per 0.1 decrease)	1.28 (1.18-1.39)	<0.001

Model 2: Procedural Variables†

Predictors	Adjusted OR (95% CI)	P value
Provisional stenting technique	2.03 (1.12-3.70)	0.02
Side branch – DS% (per 10% increase)	1.18 (1.07-1.30)	0.001
Residual SYNTAX score (per 1 increase)	1.10 (1.07-1.14)	<0.001

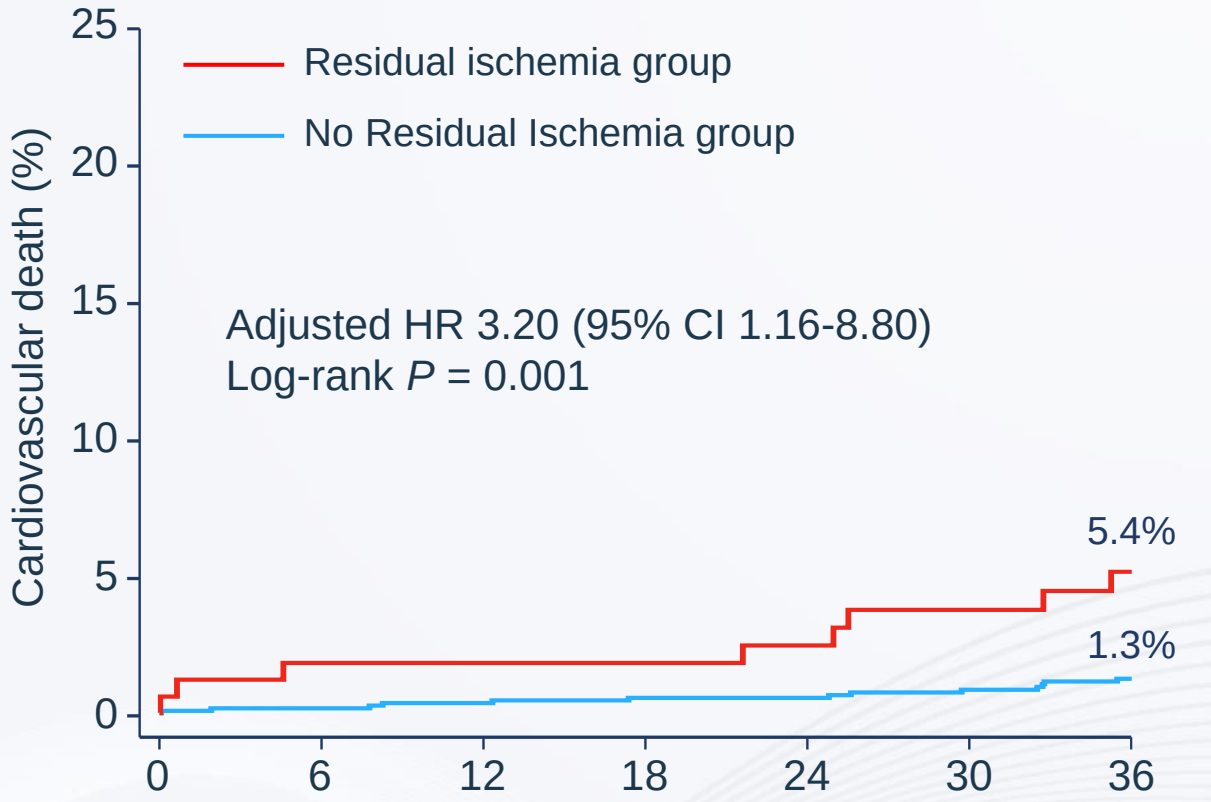
Two multivariable Logistic models were constructed to identified the independent predictors of residual ischemia

*The **15 baseline variables** were incorporated in the **model 1**, including age, male, diabetes, previous myocardial infarction, LVEF, multivessel disease, true LM bifurcation, LM moderate-to-severe calcification, main vessel – RVD, main vessel – DS%, side branch – RVD, side branch – DS%, anatomic SYNTAX score, pre-PCI LAD μQFR, and pre-PCI LCX μQFR

†The **9 procedural variables** were incorporated in the **model 2**, including IVUS guidance, total number of stents per LM lesion, provisional 1-stent crossover technique, POT performed, final kissing balloon inflation, post-dilation performed, main vessel – DS%, side branch – DS%, and residual SYNTAX score

Kaplan-Meier Curves

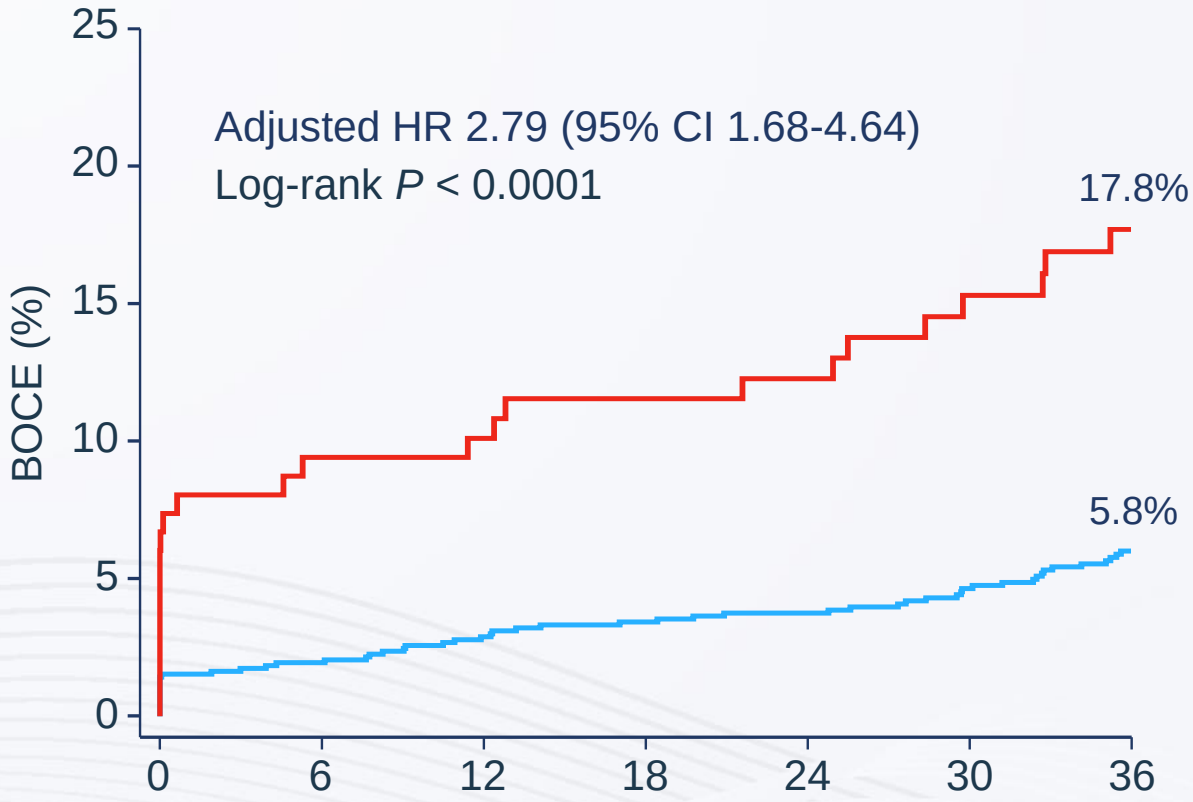
Cardiovascular Death



No. at risk

Ischemia	155	152	150	148	146	137	131
No Ischemia	1,015	1,008	1,003	983	978	952	939

BOCE



No. at risk

Ischemia	155	138	134	128	126	116	109
No Ischemia	1,015	978	961	932	922	890	869

*__Adjusted confounders:__ age, sex, BMI, diabetes, CKD, family history of CAD, previous MI, clinical presentation, LVEF, multivessel disease, SYNTAX score, total stent length in LM, type of DES, post-PCI diameter stenosis in LCX, post-PCI diameter stenosis in LM-LAD

Three-Year Clinical Outcomes

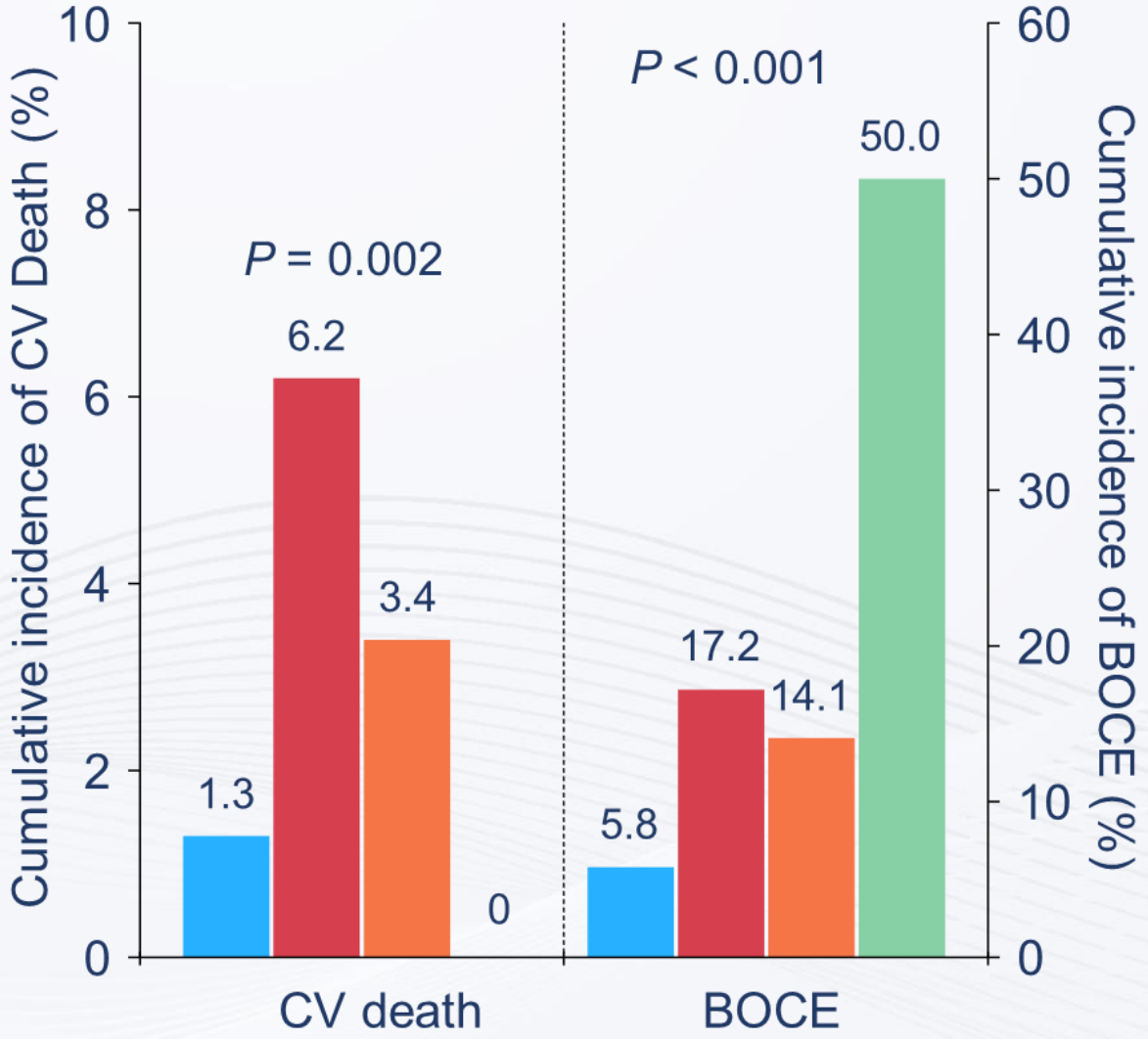
- Residual ischemia regardless of LAD or LCX was associated with worse outcomes

LAD μQFR >0.80
LCX μQFR >0.80
N=1,015, 86.8%

LAD μQFR >0.80
LCX μQFR ≤0.80
N=117, 10.0%

LAD μQFR ≤0.80
LCX μQFR >0.80
N=32, 2.7%

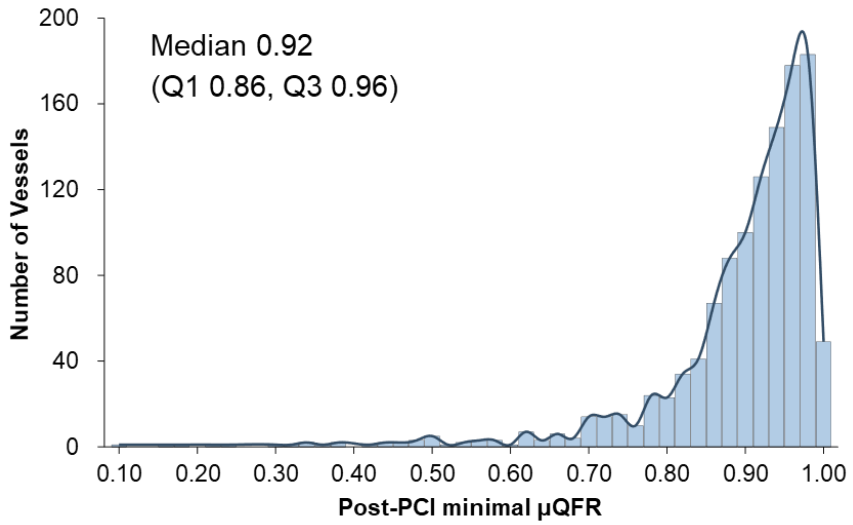
LAD μQFR ≤0.80
LCX μQFR ≤0.80
N=6, 0.5%



Outcomes by Continuous μQFR

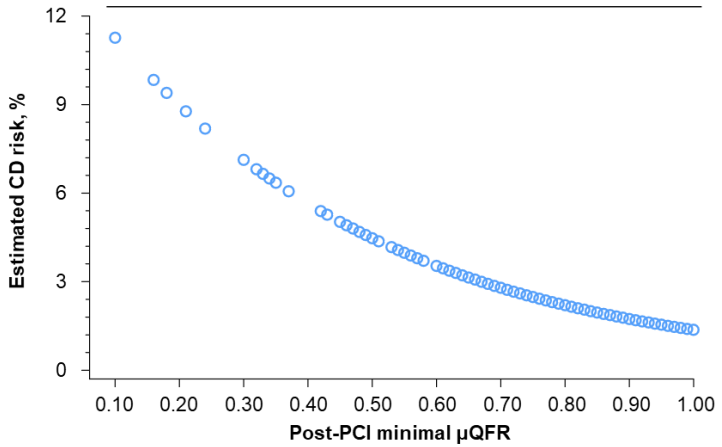
- Clinical outcomes were **inversely and continuously** associated with post-PCI μQFR
- **Per 0.1 decrease** in post-PCI μQFR value, the risk of 3-year cardiovascular death and BOCE increased **27% and 29%**, respectively

Distribution of Post-PCI Minimal μQFR



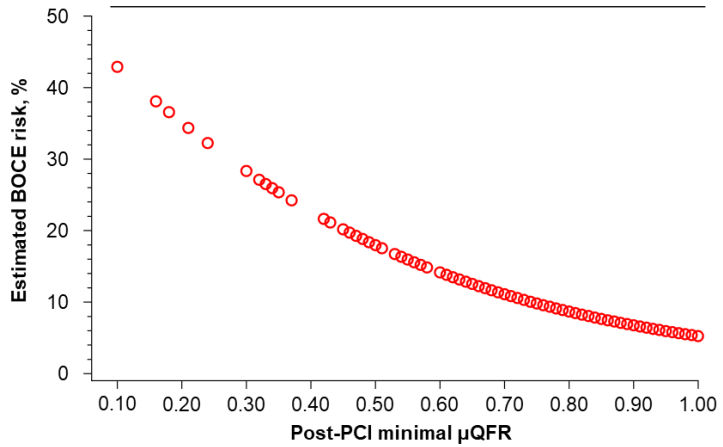
3-year Cardiovascular Death

HR (per 0.1 decrease)	95% CI	*P* Value
1.27	1.00-1.62	0.05



3-year BOCE

HR (per 0.1 decrease)	95% CI	*P* Value
1.29	1.14-1.47	<0.0001



Physiology versus Anatomy

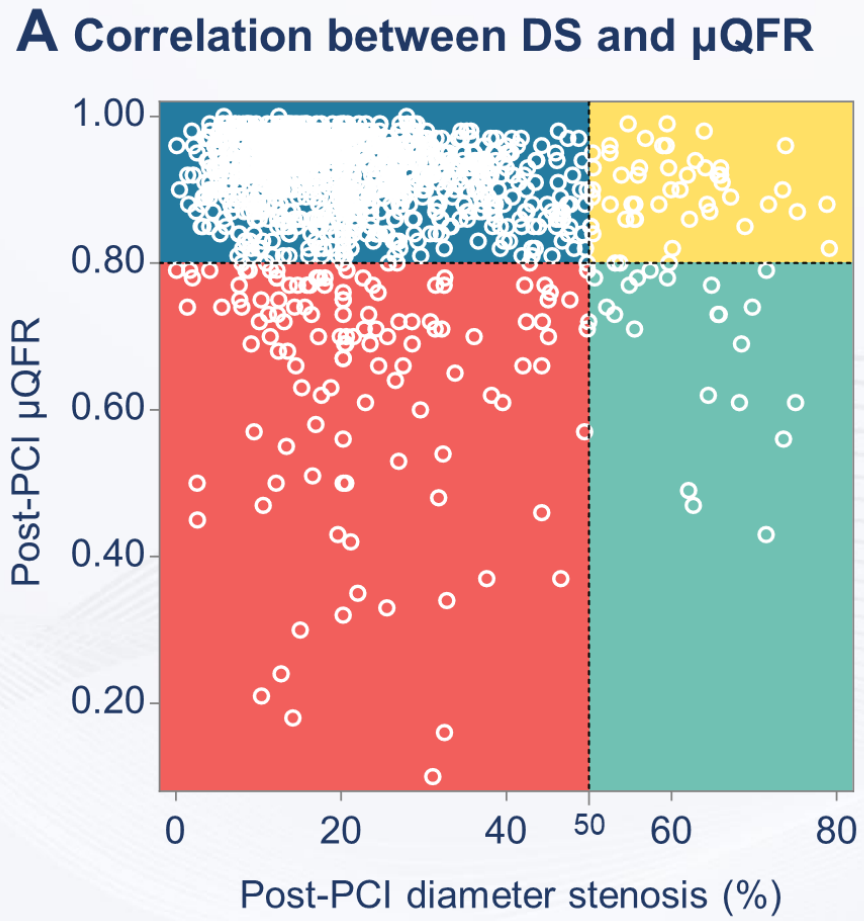
- When using Post-PCI μQFR and %DS for physiological or anatomical significance.
  Mismatched result were found in 177 patients (15.1%).
- Physiological assessment showed superior prognostic value for 3-year clinical outcomes.

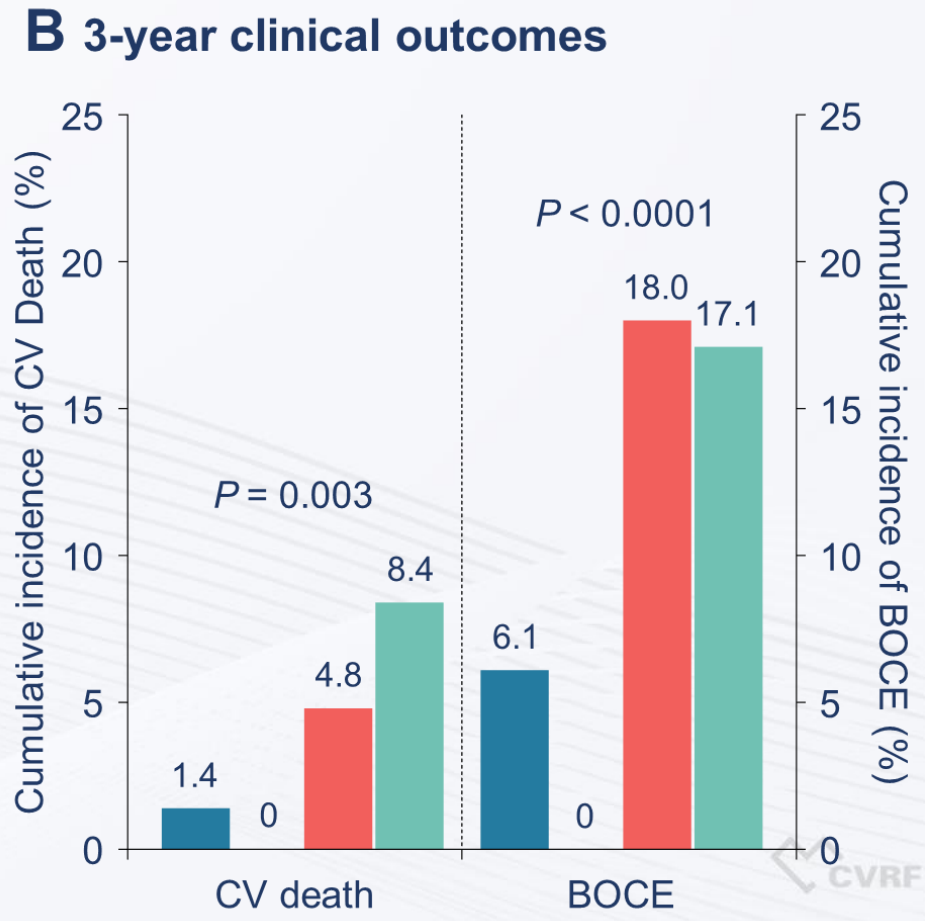
Negative concordance
μQFR>0.80; DS<50%
N=968, 82.7%

Negative mismatch
μQFR>0.80; DS≥50%
N=47, 4.0%

Positive mismatch
μQFR≤0.80; DS<50%
N=130, 11.1%

Positive concordance
μQFR≤0.80; DS≥50%
N=25, 2.1%





Discussion Points

- Why Post-PCI residual ischemia is related to 3-year cardiovascular mortality but not only composite endpoint?
- How to optimize interventions based on post-PCI physiological assessments?

Summary

- After angiographically successful LM bifurcation PCI, residual ischemia assessed by μQFR was identified in 13.2% of patients and was associated with higher risk of 3-year cardiovascular death
- Adopting the strategy of routine post-PCI physiology-based assessment when treating LM bifurcation lesions is necessary, even when PCI appears anatomically satisfactory