Intravascular Lithotripsy for Treatment of Severely Calcified Coronary Lesions:
1-Year Results from the Disrupt CAD III Study

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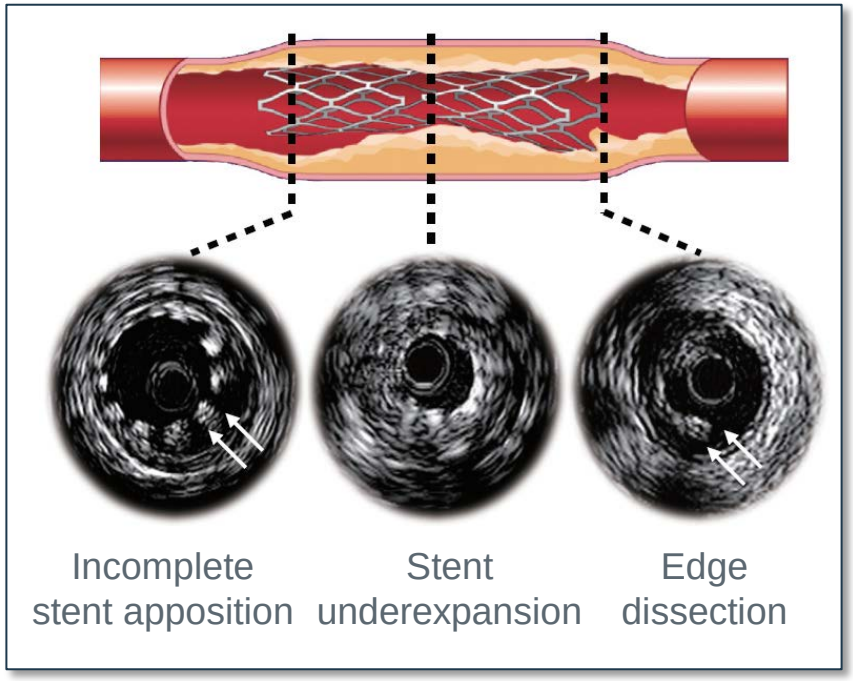
Disclosure Statement of Financial Interest

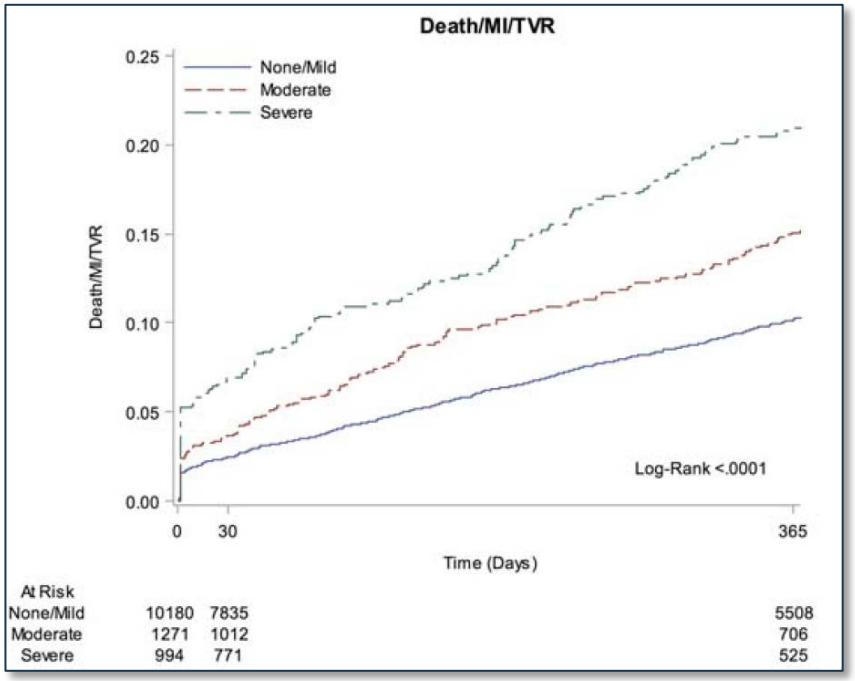
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Consulting Fees	Abbott Vascular Inc
Consulting Fees	Boston Scientific Corporation
Consulting Fees	Shockwave Medical
Stock Shareholder/Equity	Shockwave Medical

Coronary Calcification Impacts PCI Outcomes



CAC may impede optimal stent deployment



Increased risk for MACE at 1-year with moderate-severe CAC

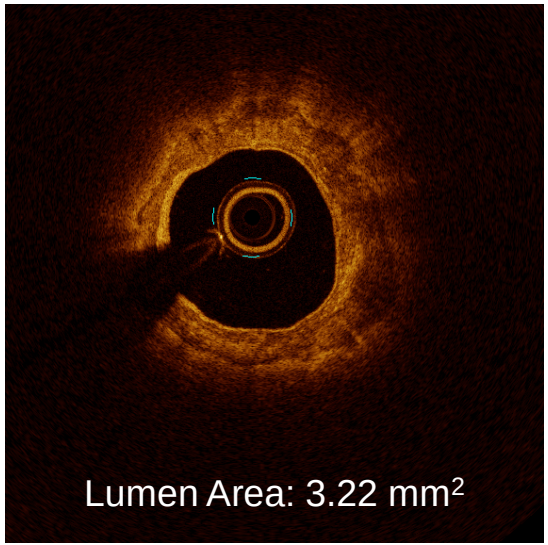
Yoon et al., *KJIM* 2012; Copeland-Halperin et al., *Catheter Cardiovas Interv* 2017

Intravascular Lithotripsy

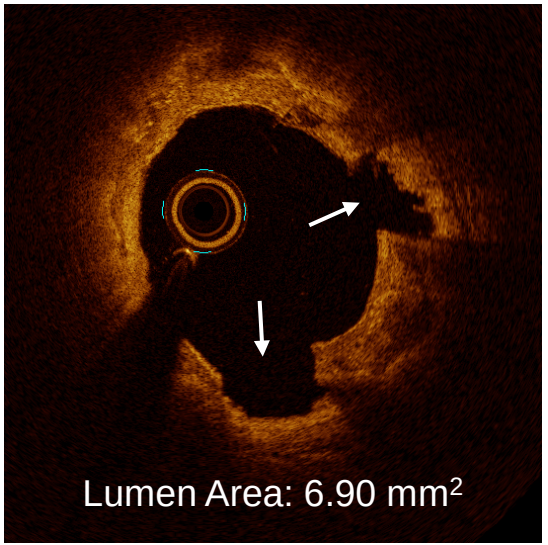
Acoustic pressure waves (1 pulse/sec) travel through tissue with an effective pressure of **~50 atm and fractures both superficial and deep calcium**

Multi-plane Calcium Fracture

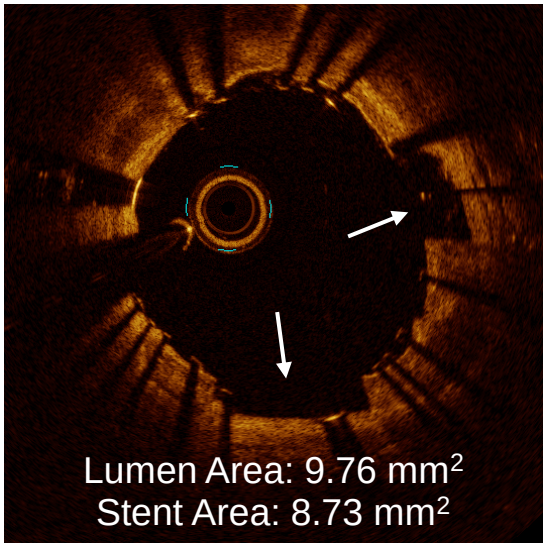
Pre-procedure



Post-IVL



Post-stent



Disrupt CAD III: Study Design*

Prospective, multicenter, single-arm global IDE

NCT03595176

Heavily calcified†, *de novo* coronary lesions
RVD 2.5-4.0 mm, stenosis ≥50%, lesion length ≤40mm
One roll-in patient per site allowed
47 global sites

Roll-in Population
N = 47

ITT Population
N= 384

30-day Follow-up**

OCT Sub-study‡
N= 100

1-year Follow-up

2-year Follow-up

*Kereiakes et al., *Am Heart J* 2020;225:10-18; ‡Shlofmitz R, TCT 2020; **Hill et al., *JACC* 2020;76:2635-46;
†Radio-opacities both sides of vessel ≥15 mm length by angiography or calcium angle ≥270 ° by OCT or IVUS

1-Year Follow-up Analyses

- MACE
  - Cardiac death, myocardial infarction*, or target vessel revascularization
- Target lesion failure
  - Cardiac death, TV-MI, or ID-target lesion revascularization
- Stent thrombosis
- Sub-group analyses for MACE and TVR
- Predictors of MACE and TVR at 1-year

*CK-MB level >3x ULN through hospital discharge (peri-procedural MI) and using the 4th Universal Definition of MI beyond discharge

Key Clinical and Angiographic Eligibility Criteria

DISRUPT CAD III

Inclusion

- Biomarkers (Troponin or CK-MB) normal within 12 hours prior to procedure
- LVEF >25% within 6 months of procedure
- Single *de novo* target lesion with stenosis ≥70% and <100%, or ≥50% and <70% with evidence of ischemia, or FFR ≤0.80, or lumen area ≤4.0 mm^2 by IVUS or OCT
- Target vessel RVD ≥2.5 mm and ≤4.0 mm
- Lesion length ≤40 mm
- Lesion site severe calcification:
  - Angiographic radio-opacities prior to contrast involving both sides of arterial wall with total calcium length ≥15 mm, or presence of ≥270° of calcium on at least one cross section by IVUS or OCT

Exclusion

- Renal failure (serum creatinine >2.5 or chronic dialysis)
- Acute MI within 30 days prior to index procedure

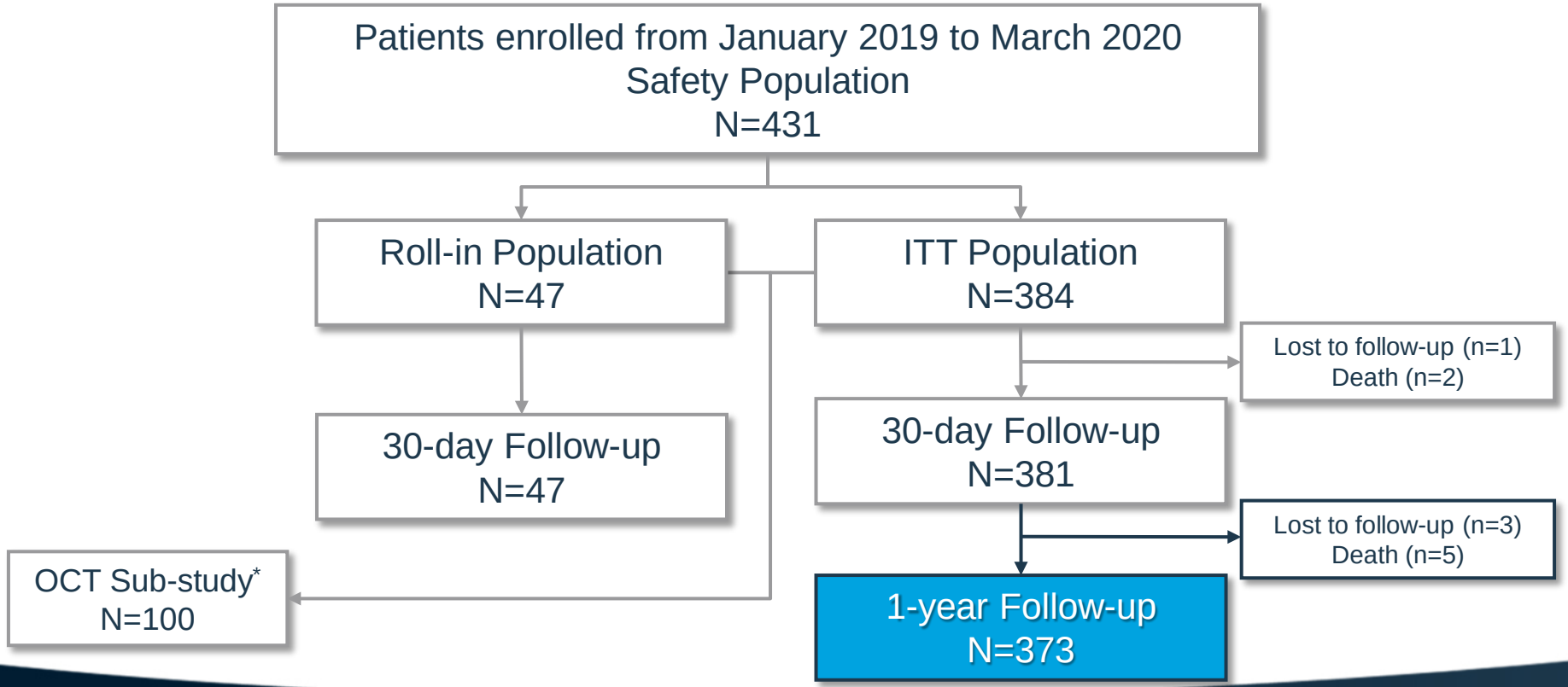
Disrupt CAD III Study Support

Principal Investigators	Dean Kereiakes The Christ Hospital, Cincinnati, OH Jonathan Hill Royal Brompton Hospital, London, UK
Study Chairman	Gregg W. Stone Mount Sinai Heart Health System, New York, NY
Clinical Events Committee	Steven Marx (Chair) Cardiovascular Research Foundation, New York, NY
Data Safety Monitoring Board	Ehtisham Mahmud (Chair) Cardiovascular Research Foundation, New York, NY
Angiographic Core Laboratory	Maria Alfonso (Director) Cardiovascular Research Foundation, New York, NY
OCT Core Laboratory	Akiko Maehara (Director) Cardiovascular Research Foundation, New York, NY

Disrupt CAD III: Top Enrolling Centers

1. Richard Shlofmitz St. Francis Hospital	8. Barry Bertolet North Mississippi Medical Center
2. Andrew Klein Piedmont Heart Institute	9. John Wang MedStar Union Memorial Hospital
3. Robert Riley The Christ Hospital	10. Jean Fajadet Clinique Pasteur
4. Matthew Price Scripps Clinic	10. Alpesh Shah Houston Methodist Hospital
5. Howard Herrmann University of Pennsylvania	12. Sarang Mangalmurti Bryn Mawr Hospital
6. William Bachinsky UPMC Pinnacle	13. Robert Stoler Baylor Heart and Vascular Hospital
6. Ron Waksman MedStar Washington Hospital Center	13. Janusz Lipiecki Clinique des Domes

Study Flow and Follow-up



97.1% Follow-up at 1-year

Baseline Clinical & Lesion Characteristics

DISRUPT CAD III

Characteristic	N=384
Age	71.2 ± 8.6
Male	76%
Hypertension	89%
Hyperlipidemia	89%
Diabetes mellitus	40%
Current smoker	12%
Prior MI	18%
Prior CABG	9%
Prior Stroke	8%
Renal insufficiency*	26%

Core Lab Analysis		N=384
Target vessel	LAD	56.5%
	LCx	12.8%
	RCA	29.2%
	LM	1.6%
Reference vessel diameter, mm		3.0 ± 0.5
Minimum lumen diameter, mm		1.1 ± 0.4
Diameter stenosis		65.1 ± 10.8%
Lesion length, mm		26.0 ± 11.7
Calcified length, mm		47.9 ± 18.8
Severe calcification		100%

*Defined as eGFR <60ml/min/1.73m^2; eGFR=estimated glomerular filtration rate using the MDRD formula

Procedural Characteristics

Characteristic	N=384
Total procedure time, min	59.0 ± 29.6
Pre-dilatation	55.2%
IVL catheters	1.2 ± 0.5
IVL pulses	68.8 ± 31.9
Max IVL inflation pressure, atm	6.0 ± 0.3
Post-IVL dilatation	20.7%
Number of stents	1.3 ± 0.5
Stent delivery	99.2%
Post-stent dilatation	99.0%

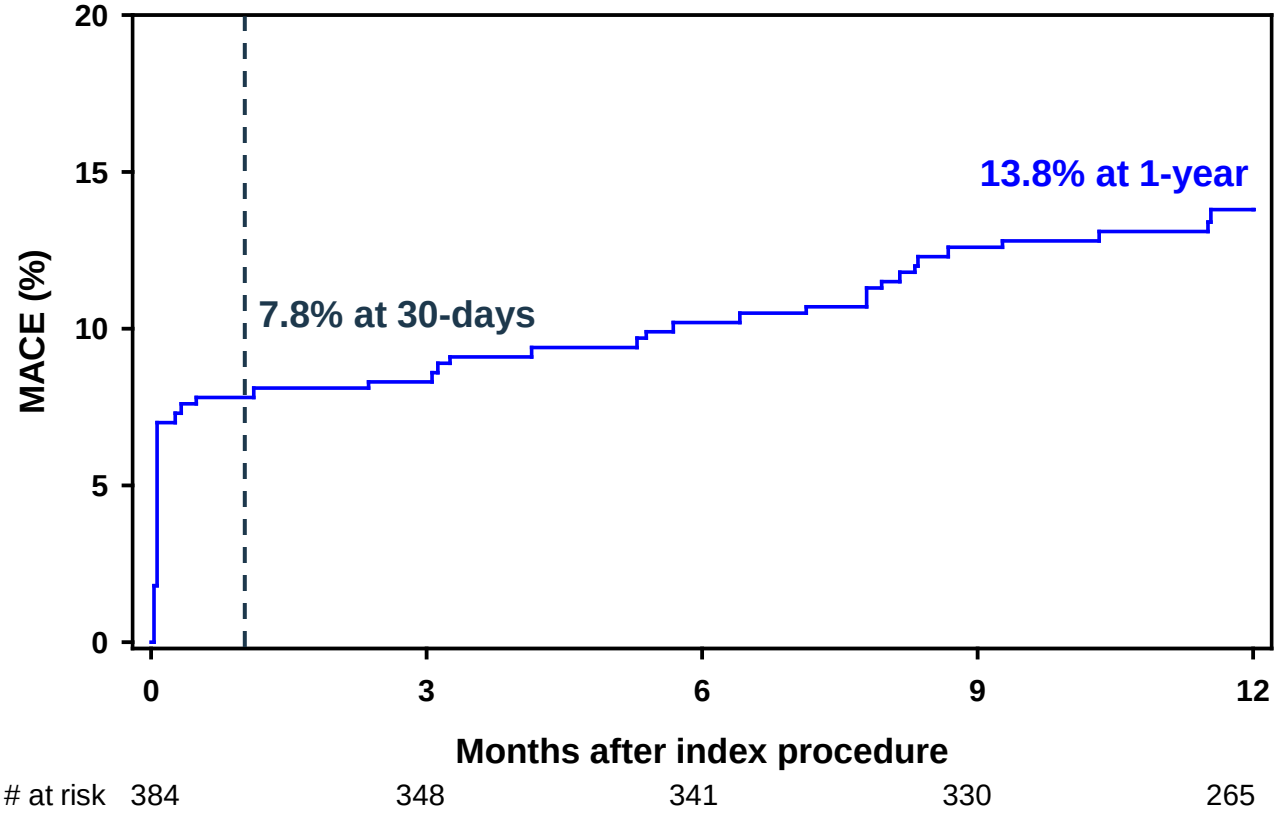
Early Study Results*

Primary endpoints	
Freedom from 30-day MACE	92.2%
Procedural success	92.4%
Angiographic outcomes	
Acute gain, mm	1.7 ± 0.5
In-stent diameter stenosis, %	11.9 ± 7.1
Final serious angiographic complications, %	0.5
OCT outcomes	
Minimum stent area, mm^2	6.5 ± 2.1
Stent expansion at max calcium site, %	101.7 ± 28.9

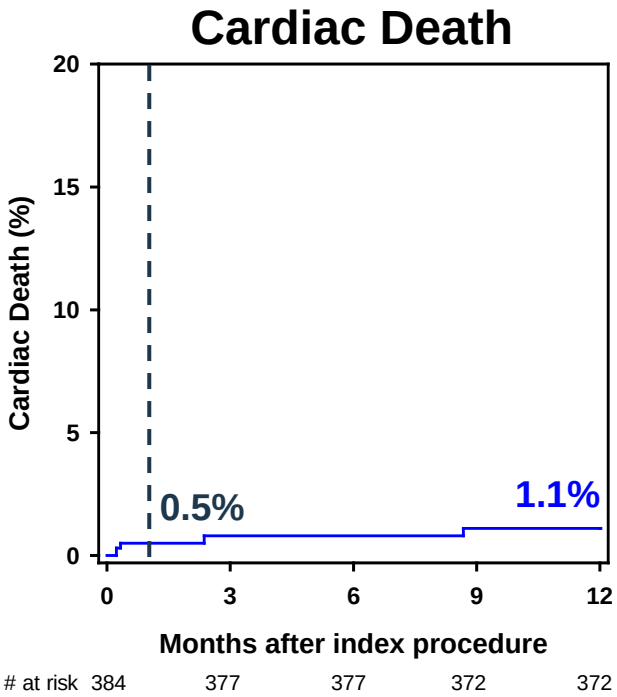
Performance goals and study success were achieved

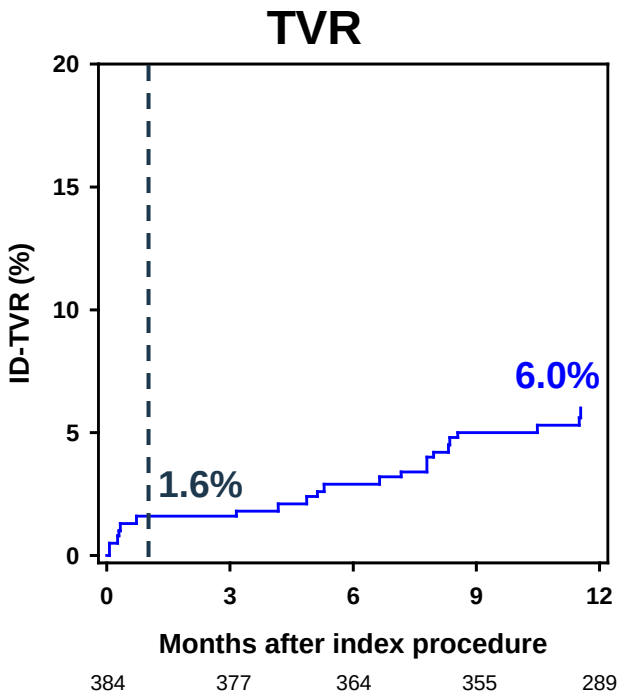
*Hill et al. *JACC* 2020

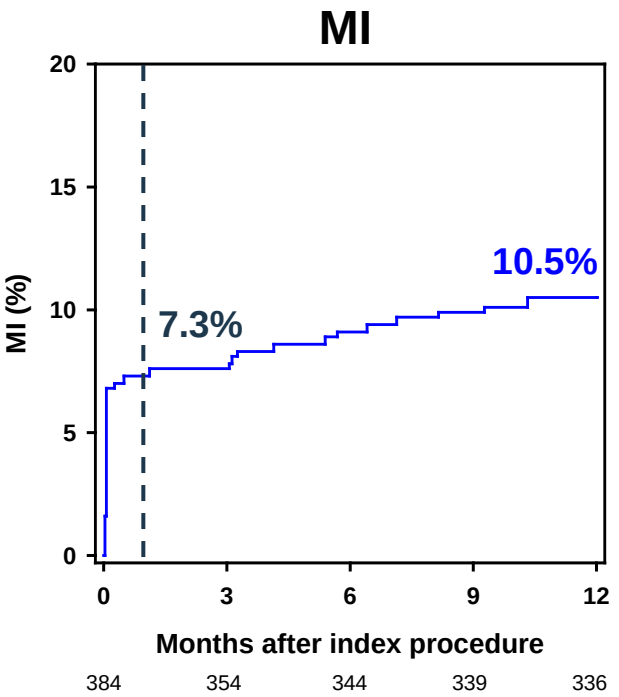
MACE at 1-Year



Components of MACE at 1-Year







CRF TCT

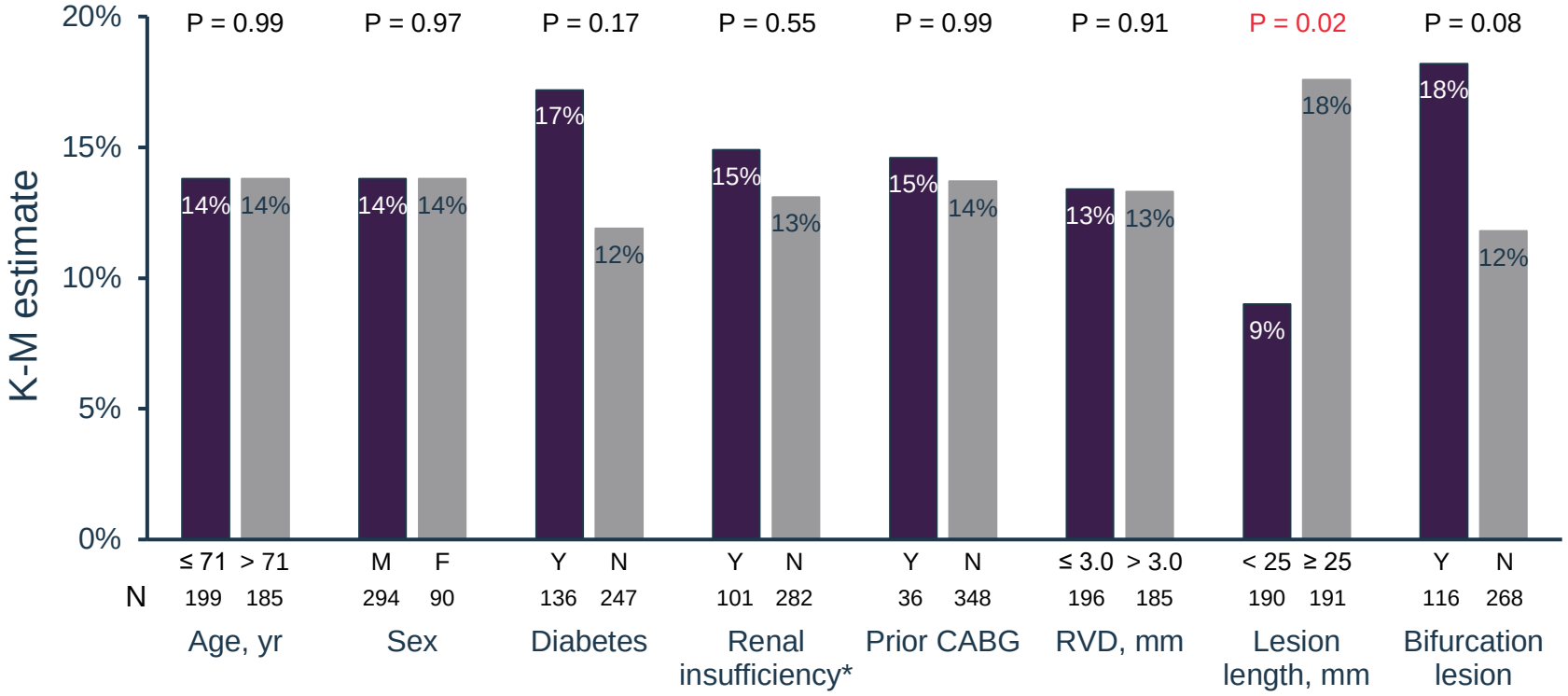
MI at 1-year driven by NQWMI (9.2%) with no Q-wave MI events beyond 30 days

Secondary 1-Year Outcomes

Outcome	1-Year rate (K-M estimate)
All-cause mortality	1.8%
Cardiac death	1.1%
Non-cardiac	0.5%
Vascular	0.3%
Target lesion failure	11.9%
Cardiac death	1.1%
TV-MI	9.9%
ID-TLR	4.3%
Stent thrombosis (definite or probable)*	1.1%

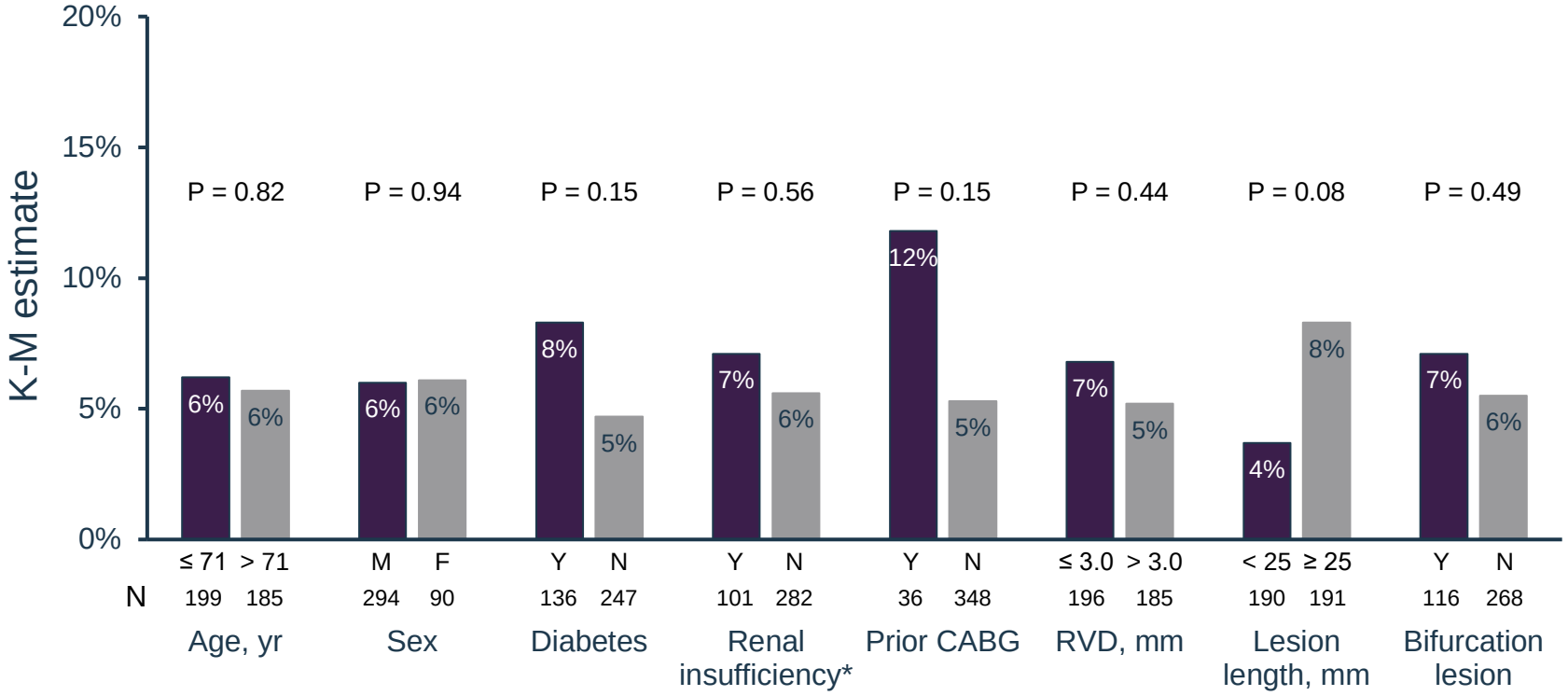
*One stent thrombosis (definite or probable) event beyond 30 days

1-Year MACE by Sub-groups



*eGFR < 60ml/min/1.73m²

1-Year TVR by Sub-groups



*eGFR < 60ml/min/1.73m²

1-Year Outcomes: Multivariable Analysis

	OR [95% CI]	P value
MACE		
Bifurcation lesion	2.69 [1.32 – 5.47]	0.006
Prior MI	2.22 [1.01 – 4.87]	0.048
Current or former smoker	2.21 [1.01 – 4.78]	0.045
TVR		
Prior MI	4.07 [1.20 – 13.77]	0.024

Conclusions

- Disrupt CAD III at 1-year represents the largest and longest clinical follow-up of patients with severely calcified lesions treated with IVL
- Coronary IVL prior to DES implantation resulted in beneficial impact of IVL lesion calcium modification and stent expansion to at least 1 year
- MACE and TVR rates were similar in most sub-groups analyzed
  - Long lesion (>25mm) 1-year MACE driven by rates of peri-procedural NQWMI
- Further study is required to determine if IVL can effectively reduce longer-term (> 1-year) annualized incidence of adverse clinical events