What's new insight from Korean CTO registry?

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… based on the Korean-CTO (K-CTO) registry

1. **Outcomes between successful vs. failed CTO ?**

2. **Clinical outcomes following CTO intervention?**

3. **Impact of risk factors on outcomes after successful CTO intervention & on-going K-CTO random trial**

Today's Talk
… based on the Korean-CTO (K-CTO) registry

1. **Outcome between successful vs. failed CTO ?**

2. **Comparison of clinical outcomes following CTO intervention?**

3. **Impact of risk factors on outcomes after successful CTO intervention & on-going K-CTO random trial**

CTO PCI, Rationale and Dilemmas co-exist …

- Reduction in ischemic burden
- Enable complete revascularization
- Improvement of symptoms & LV function
- Reduced predisposition to arrhythmic events and ischemic events
- Avoidance of procedures and reduced medications
- Survival benefit ???

- Technical and procedural challenges
- Misperceptions regarding viability, collateral flow
- Uncertainty regarding which patients may benefit balanced by
- Concern for complications in patients who may not derive clinical benefit

✓ **Regarding the impact of successful revascularization of CTO on clinical outcomes, it still remained controversy.**

Korean CTO registry data?

Original Contribution

J Invasive Cardiol. 2014;26:255-9.

Clinical Outcome of Successful Percutaneous Coronary Intervention for Chronic Total Occlusion: Results From the Multicenter Korean Chronic Total Occlusion (K-CTO) Registry

Byeong-Keuk Kim, MD[1*]; Sanghoon Shin, MD[1*]; Dong-Ho Shin, MD[1]; Myeong-Ki Hong, MD[1]; Hyeon-Cheol Gwon, MD[2]; Hyo-Soo Kim, MD[3]; Cheol Woong Yu, MD[4]; Hun Sik Park, MD[5]; In-Ho Chae, MD[3]; Seung-Woon Rha, MD[6]; Seung-Hwan Lee, MD[7]; Moo-Hyun Kim, MD[8]; Seung-Ho Hur, MD[9]; Yangsoo Jang, MD[1]

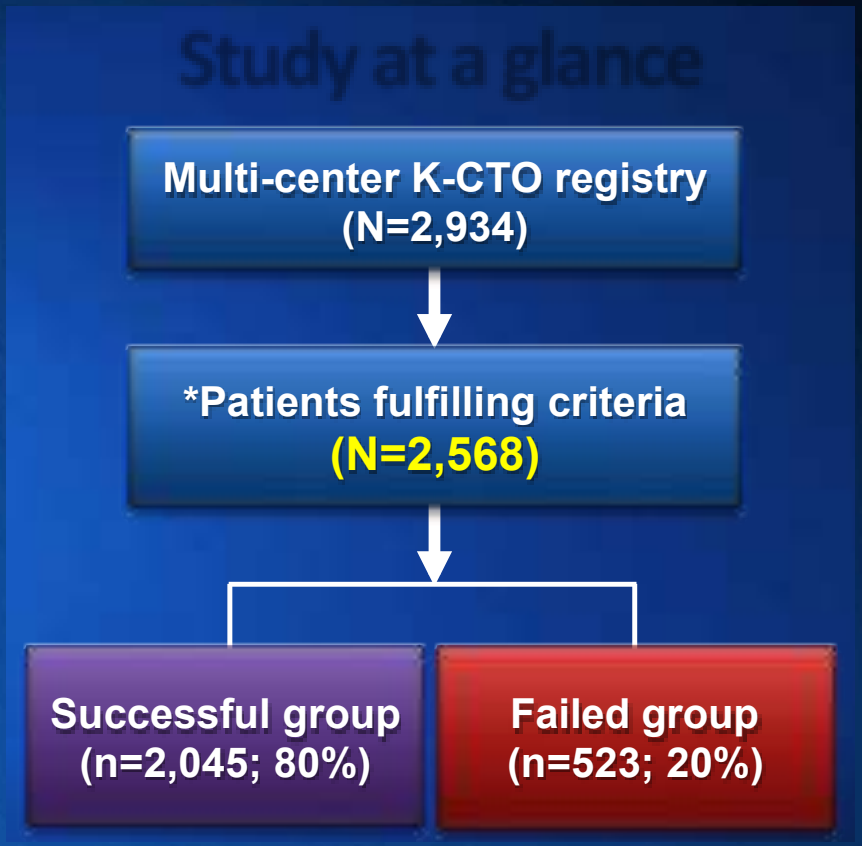
- *Objective*

To investigate the **impact of the success or failure of CTO intervention** **on** **long-term clinical outcomes** from a larger cohort of the Korean patients (K-CTO registry) undergoing CTO PCI in the era of DES.

- **Study population;**
  - From 2007 to 2009, a total of ***2,568 patients with true*** CTO who underwent PCIs and met the criteria of this study were enrolled in the multicenter K-CTO registry, consisting of 26 Korean centers.

    … K-CTO registry; All comer CTO registry

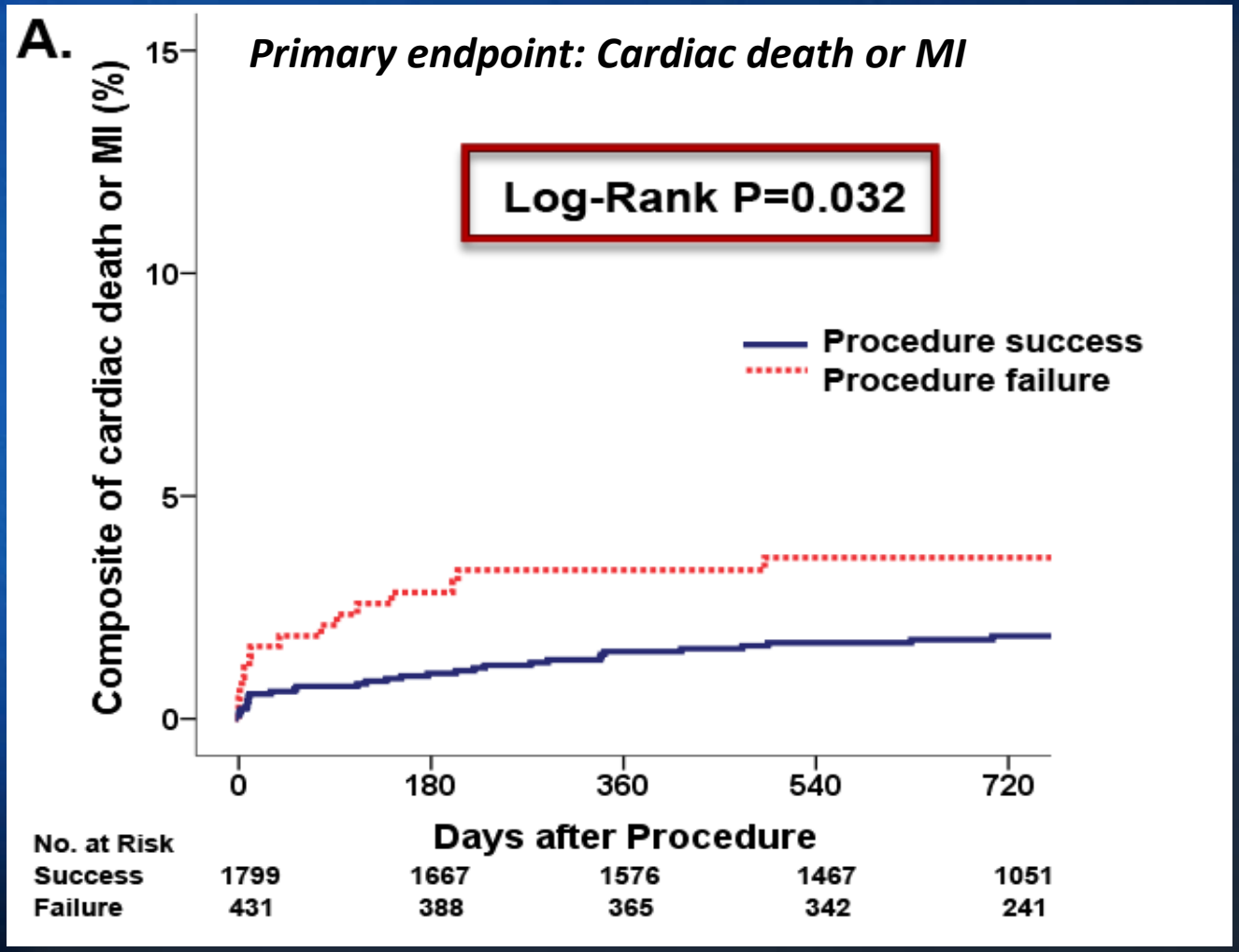
    - Regardless of success or failure of PCI
    - No specific exclusion for the directly reflecting "Real-world clinical practice of CTO intervention"



- **Endpoints;**
  - **Primary endpoint: Occurrence of Cardiac death or MI between "Successful-CTO group" vs. "Failed-CTO group"**

    ✓ *Kaplan Meier analysis and Cox's proportional hazard model for the comparison of the events*

Occurrence of the primary endpoint by comparing using Kaplan Meier Analysis



Risk factors for the occurrence of cardiac death or MI?

	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	**1.08 (1.05-1.12)**	**<0.001**	**1.09 (1.05-1.14)**	**<0.001**
Hypertension	0.82 (0.46-1.45)	0.496		
Diabetes mellitus	1.31 (0.74-2.33)	0.355	1.73 (0.88-3.41)	0.114
Previous PCI	0.80 (0.40-1.61)	0.538		
Previous MI	0.43 (0.13-1.37)	0.152	0.56 (0.17-1.84)	0.337
LVEF < 40%	**3.50 (1.74-7.02)**	**<0.001**	**2.34 (1.02-5.53)**	**0.029**
Multi-vessel diseases	1.49 (0.79-2.82)	0.219	0.89 (0.44-1.81)	0.749
Procedural success	**0.48 (0.27-0.86)**	**0.018**	**0.51 (0.29-0.92)**	**0.035**
Lesion length	1.00 (0.98-1.02)	0.892	1.00 (0.98-1.02)	0.827

Kim BK, et al. J Invasive Cardiol. 2014;26:255-9.

In the Successful CTO group, Predictors for the occurrence of the fatal events?

(occurrence of *Cardiac death, MI or ST)*

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Age ≥65 years	**2.073 (1.223-3.514)**	**0.007**	**1.769 (1.025-3.052)**	**0.041**
Male gender	0.871 (0.496-1.531)	0.632		
Diabetes mellitus	**2.140 (1.284-3.567)**	**0.004**	**1.773 (1.043-3.012)**	**0.034**
LVEF <40%	**5.069 (2.811-9.141)**	**0.001**	**4.242 (2.335-7.705)**	**0.001**
Left main disease	2.621 (0.949-7.236)	0.063	2.181 (0.782-6.085)	0.136
Total stent length ≥20 mm	0.948 (0.430-2.086)	0.893		
Stent diameter (mm)	0.837 (0.485-1.147)	0.525		
No. of DES ≥3	1.134 (0.487-2.639)	0.770		
First- vs. New-gen DES	1.029 (0.607-1.744)	0.915		

Kim et al. 2017 CAD in-press

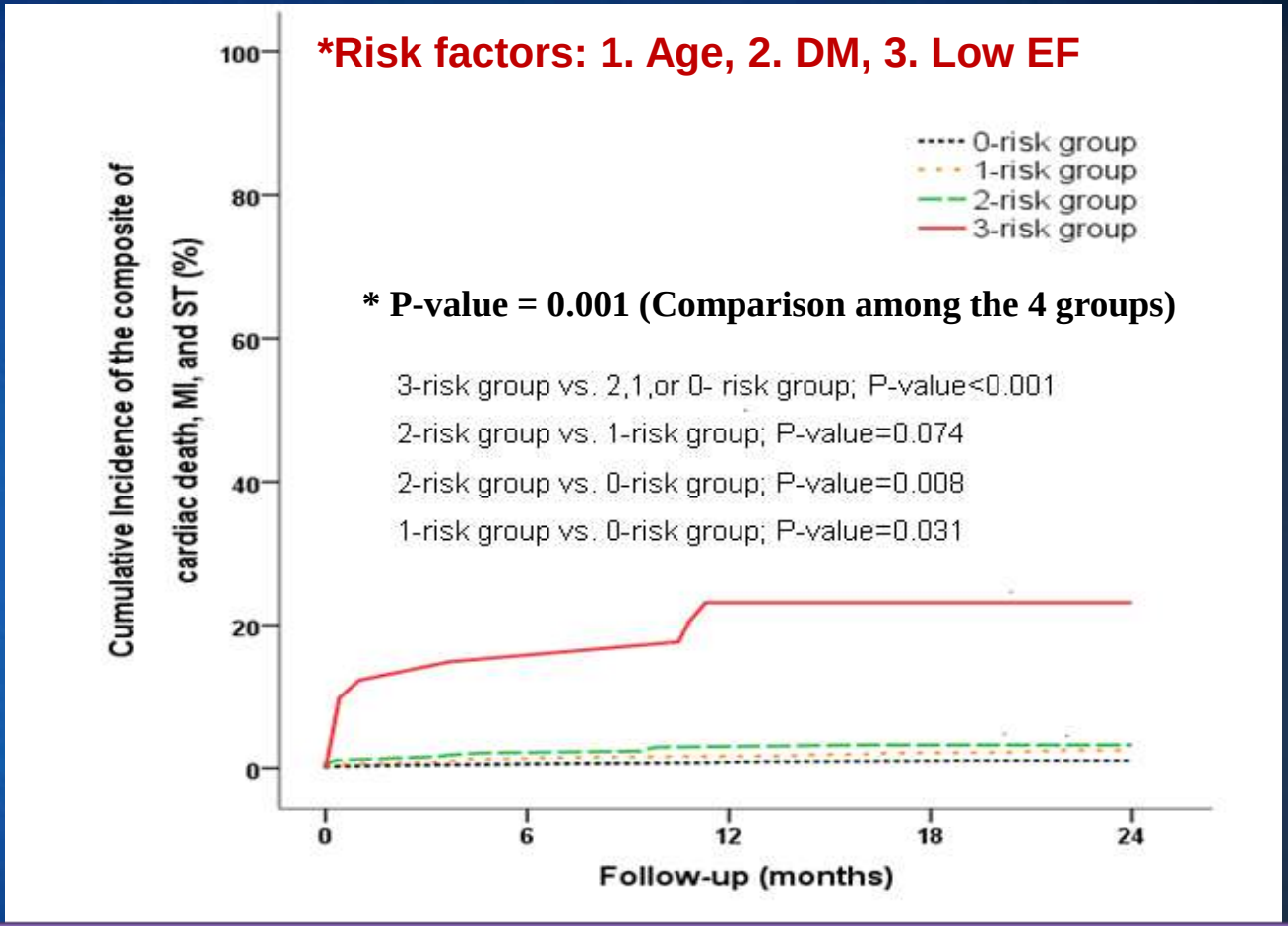
Predictors for the occurrence of TVR in the successful CTO group ?

	Adjusted HR	95% CI	P
Lesion length ≥ 20 mm	**1.626**	1.129-2.340	**0.009**
Number of implant			

✓ **Clinical parameters** (such as age, diabetes, and heart failure) were independent predictors of **the composite of cardiac death, MI, and ST,** whereas **angiographic or procedural parameters** (such as **lesion length and number of implanted stents**) were predictors of **TVR**.

Manuscript submission

Comparison of the according to the No. of risk factors



- ✓ The incidence of the primary endpoint was **significantly higher in patients with multiple risk factors** than in those with a single risk factor.

2017 in-press

Long-Term Survival Benefit of Revascularization Compared With Medical Therapy in Patients With Coronary Chronic Total Occlusion and Well-Developed Collateral Circulation

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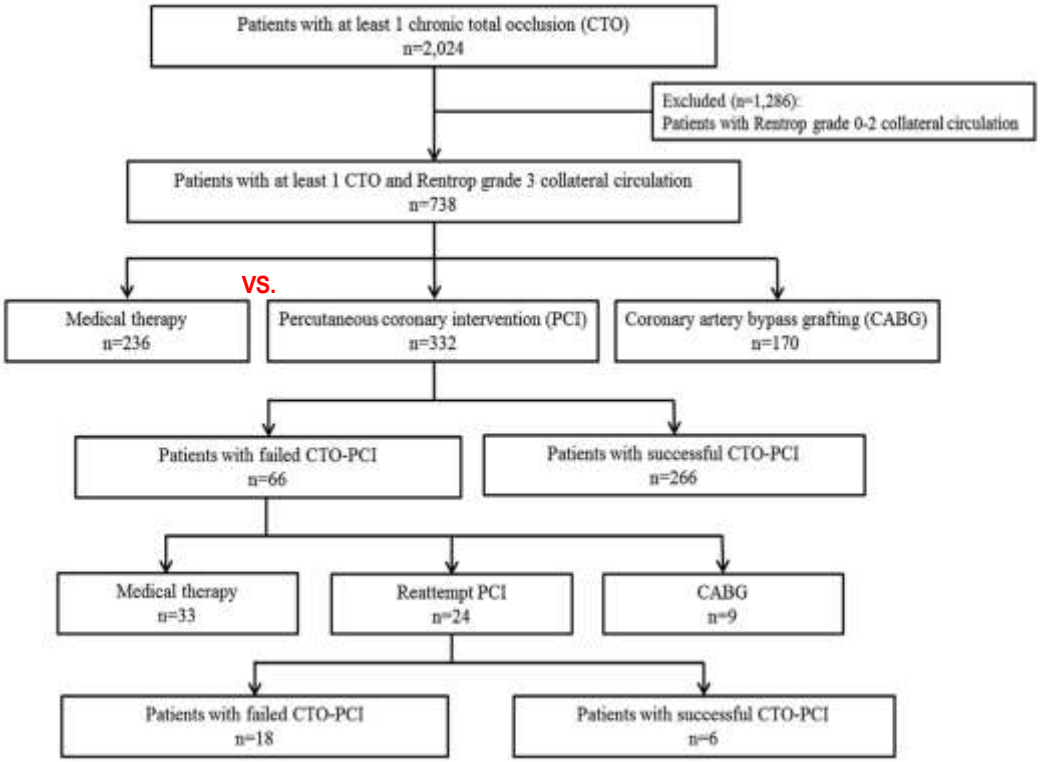
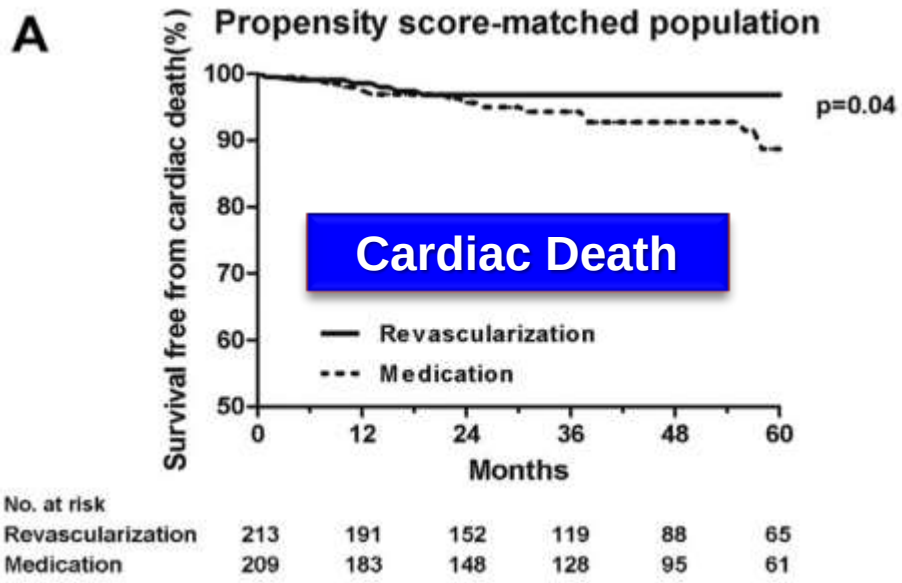
- **Objectives**
  - to compare the long-term clinical outcomes of patients with **CTO and well-developed collateral circulation** treated with **revascularization vs. medical therapy.**
- **Study Population**
  - From 2003 to 2012, 738 Pts. with Rentrop Gr 3 collaterals

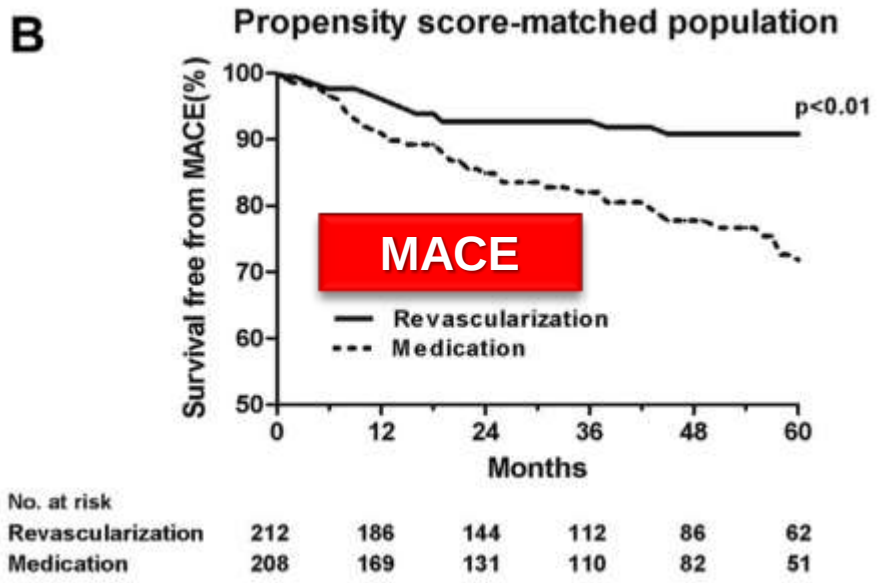


Choi SH et al., ***JACC Intv.***, 2015

Clinical Outcomes in PS-matched population

	Medication (n = 215)	Revascularization (n = 215)	HR (95% CI)	p Value
All-cause death	39 (18.1)	16 (7.4)	0.23 (0.10-0.53)	<0.01
Cardiac death	20 (9.3)	9 (4.2)	0.27 (0.09-0.80)	0.02
MI	1 (0.5)	2 (0.9)	2.00 (0.18-22.06)	0.57
Repeat revascularization*	33 (15.3)	14 (6.5)	0.59 (0.27-1.29)	0.18
MACE†	53 (24.7)	23 (10.7)	0.44 (0.23-0.82)	0.01





- **Well-developed collaterals** may preserve **viable myocardium**
- **Revascularization** in these pts. reduces the risk of **cardiac death and MACE**

Choi SH et al., ***JACC Intv.***, 2015

Today's Talk

1. Outcome between successful vs. failed CTO?

2. Clinical outcomes following successful CTO intervention?

3. Impact of risk factors on outcomes after successful CTO intervention & on-going K-CTO random trial

Question;

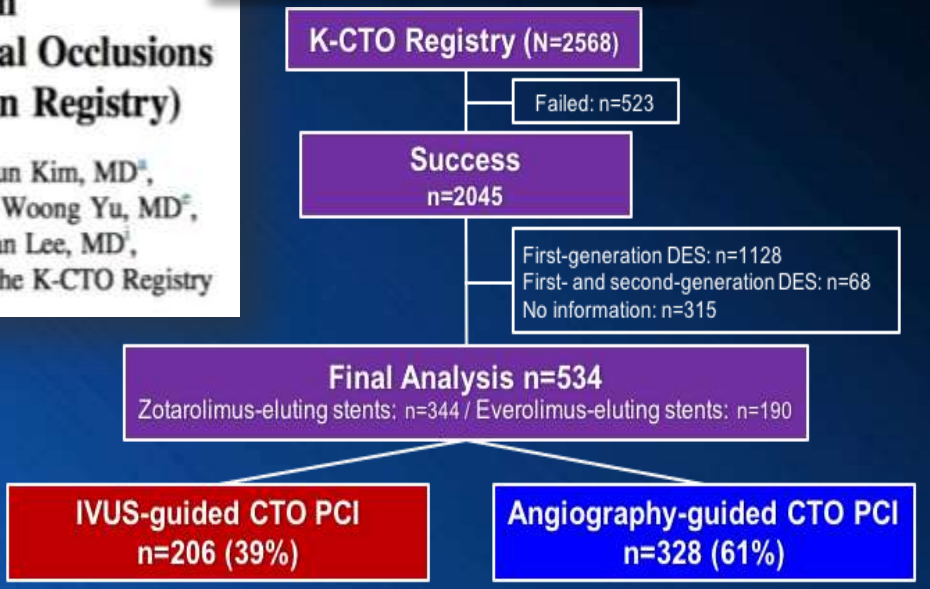
Could IVUS improve clinical outcomes after PCI?

- ✓ **A lack of evidence** regarding the **"the beneficial role of IVUS-guided CTO intervention using current-generation DES for the improved clinical outcomes"** after stent implantation.

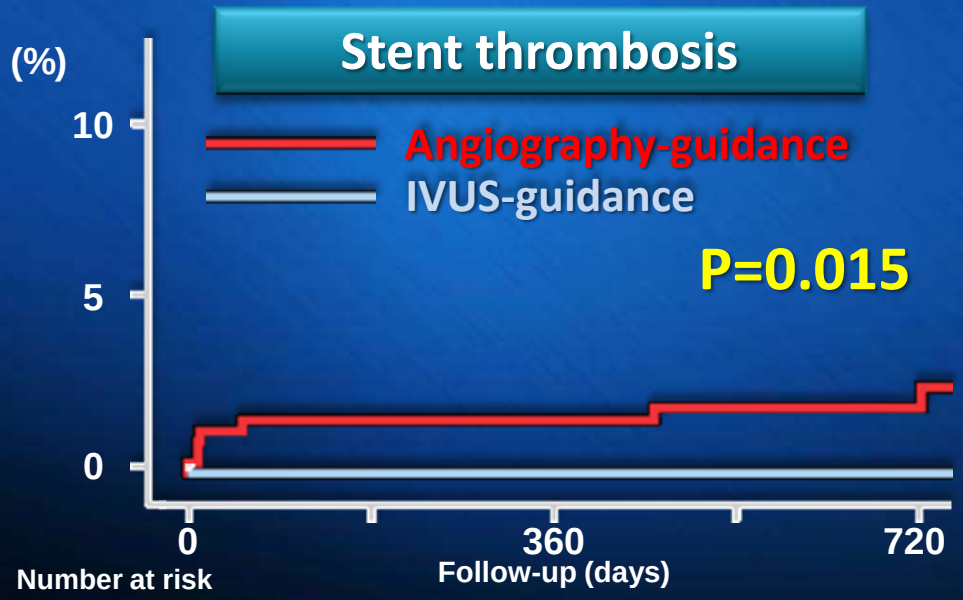
Usefulness of Intravascular Ultrasound Guidance in Percutaneous Coronary Intervention With Second-Generation Drug-Eluting Stents for Chronic Total Occlusions (from the Multicenter Korean-Chronic Total Occlusion Registry)

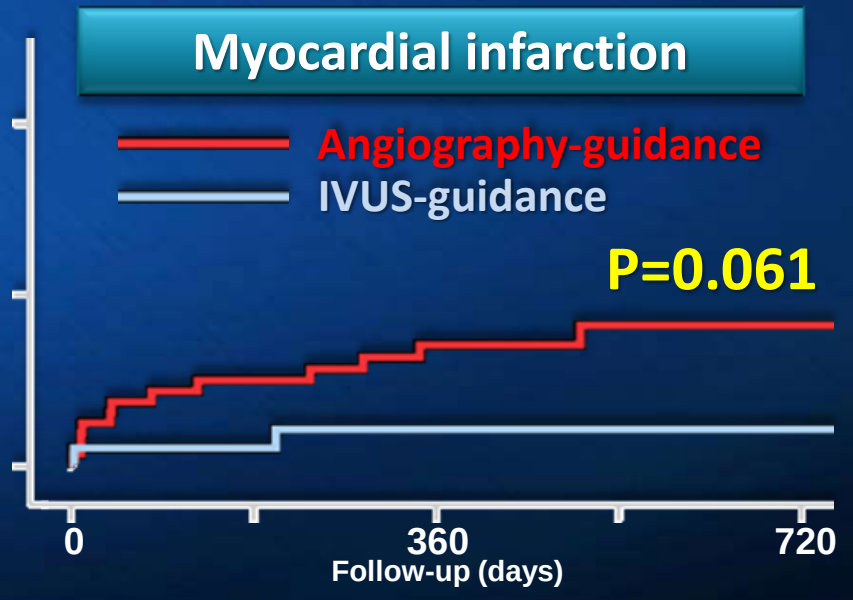
Sung-Jin Hong, MD[a], Byeong-Keuk Kim, MD[a], Dong-Ho Shin, MD[a], Jung-Sun Kim, MD[a], Myeong-Ki Hong, MD[a,b], Hyeon-Cheol Gwon, MD[c], Hyo-Soo Kim, MD[d], Cheol Woong Yu, MD[e], Hun Sik Park, MD[f], In-Ho Chae, MD[g], Seung-Woon Rha, MD[h], Seung-Hwan Lee, MD[i], Moo-Hyun Kim, MD[j], Seung-Ho Hur, MD[k], and Yangsoo Jang, PhD, MD[a,b,*], for the K-CTO Registry

K-CTO registry study



- Primary endpoint; *Definite or probable ST after propensity-score matching*





Number at risk						
Angio	201	180	112	201	180	110
IVUS	201	170	116	201	170	115

Randomized CTO-IVUS study

Coronary Interventions

Clinical Impact of Intravascular Ultrasound–Guided Chronic Total Occlusion Intervention With Zotarolimus-Eluting Versus Biolimus-Eluting Stent Implantation

Randomized Study

Byeong-Keuk Kim, MD; Dong-Ho Shin, MD; Myeong-Ki Hong, MD; Hun Sik Park, MD; Seung-Woon Rha, MD; Gary S. Mintz, MD; Jung-Sun Kim, MD; Je Sang Kim, MD; Seung-Jin Lee, MD; Hee-Yeol Kim, MD; Bum-Kee Hong, MD; Woong-Chol Kang, MD; Jin-Ho Choi, MD; Yangsoo Jang, MD; for the CTO-IVUS Study Investigators*

Background—There have been no randomized studies comparing intravascular ultrasound (IVUS)–guided versus conventional angiography–guided chronic total occlusion (CTO) intervention using new-generation drug-eluting stent Therefore, we conducted a prospective, randomized, multicenter trial designed to test the hypothesis that IVUS-guided CTO intervention is superior to angiography-guided intervention.

Methods and Results—After successful guidewire crossing, 402 patients with CTOs were randomized to the IVUS-guided group (n=201) or the angiography-guided group (n=201) and secondarily randomized to Resolute zotarolimus-eluting stents or Nobori biolimus-eluting stents. The primary and secondary end points were cardiac death and a major adverse cardiac event defined as the composite of cardiac death, myocardial infarction, or target-vessel revascularization, respectively. After 12-month follow-up, the rate of cardiac death was not significantly different between the IVUS-guided group (0%) and the angiography-guided group (1.0%; *P* by log-rank test=0.16). However, major adverse cardiac event rates were significantly lower in the IVUS-guided group than that in the angiography-guided group (2.6% versus 7.1%; *P*=0.035; hazard ratio, 0.35; 95% confidence interval, 0.13–0.97). Occurrence of the composite of cardiac death or myocardial infarction was significantly lower in the IVUS-guided group (0%) than in the angiography-guided group (2.0%; *P*=0.045). The rates of target-vessel revascularization were not significantly different between the 2 groups. In the comparison between Resolute zotarolimus-eluting stent and Nobori biolimus-eluting stent, major adverse cardiac event rates were not significantly different (4.0% versus 5.7%; *P*=0.45).

Conclusions—Although IVUS-guided CTO intervention did not significantly reduce cardiac mortality, this randomized study demonstrated that IVUS-guided CTO intervention might improve 12-month major adverse cardiac event rate after new-generation drug-eluting stent implantation when compared with conventional angiography-guided CTO intervention.

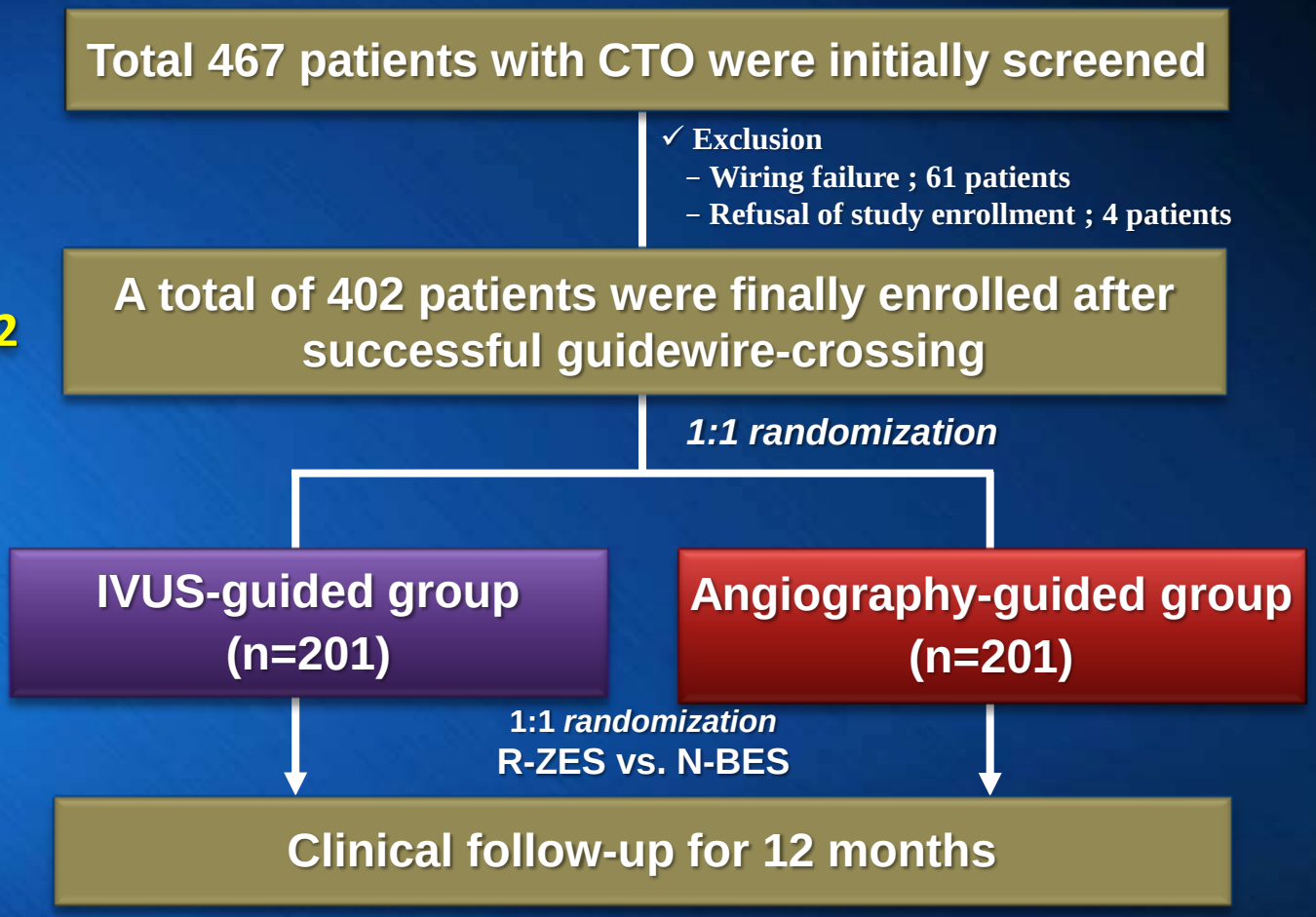
Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01563952.

(*Circ Cardiovasc Interv*. 2015;8:e002592. DOI: 10.1161/CIRCINTERVENTIONS.115.002592.)

Randomized CTO-IVUS study

A prospective, multi-center (20 centers in Korea), randomized trial

 # Primary endpoint;
Composite of Cardiac death, MI, ST, & TVR at 12 months



Recommendation in the IVUS-guided group: 1) MSA ≥distal reference LA; 2) SA at CTO segment ≥5 mm^2 as far as vessel area permits; and 3) complete stent apposition.

Kim BK, et al. Circ Interv 2015

Procedural summary & QCA

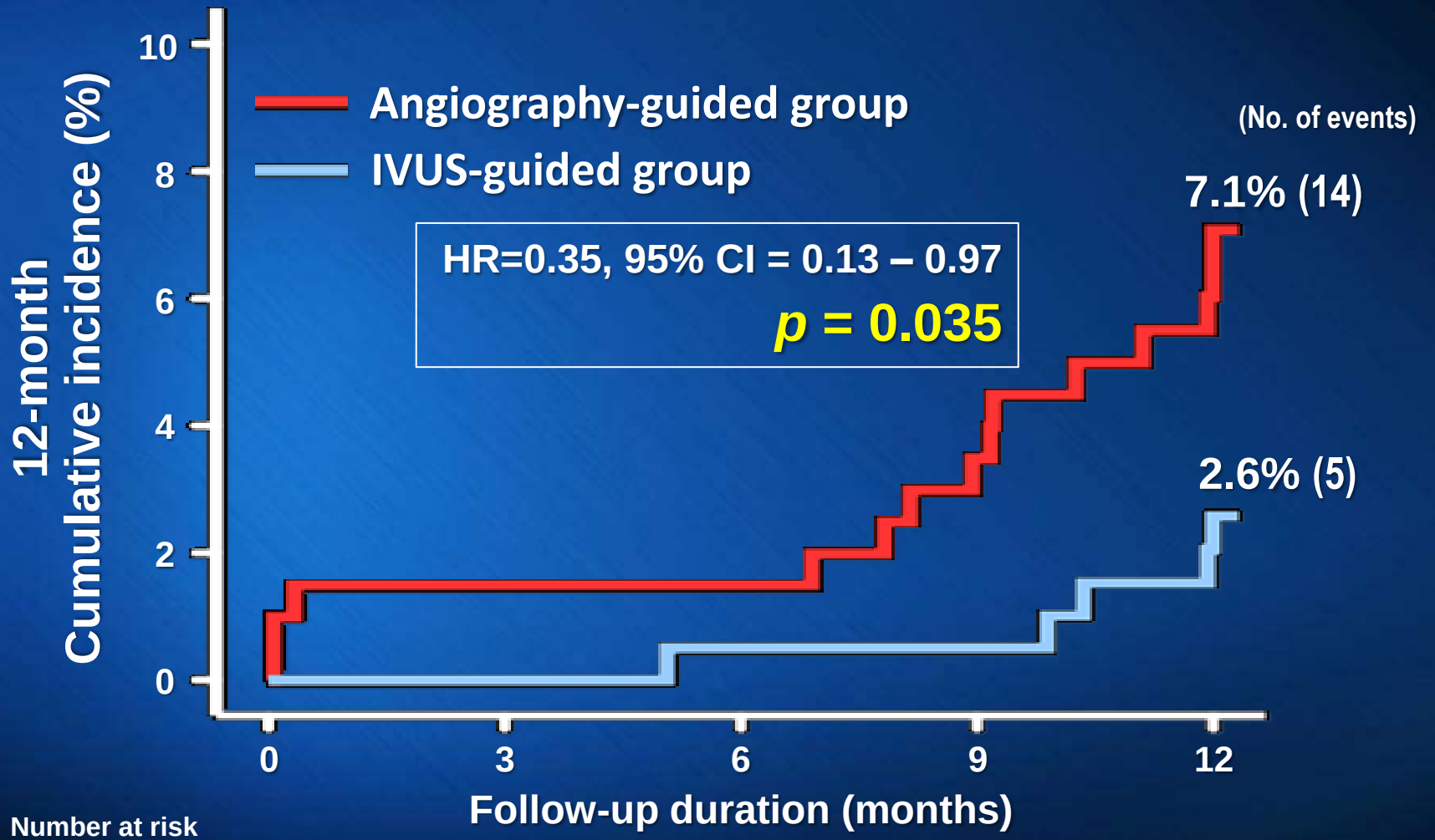
	IVUS-guided (n=201)	Angiography-guided (n=201)	p Value
Procedure success	199 (99.0%)	197 (98.0%)	0.411
Total number of stents, n	1.7 ± 0.8	1.6 ± 0.7	0.198
Mean stent diameter, mm	2.91 ± 0.52	2.85 ± 0.41	0.228
Total stented length, mm	43.6 ± 18.7	41.5 ± 17.6	0.245
High-pressure post-stent dilation	103 (51.2%)	83 (41.3%)	0.045
Maximum post-stent balloon pressure, atm	14.6 ± 3.7	13.8 ± 3.8	0.040
Post-procedure			
Reference vessel diameter, mm	2.92 ± 0.39	2.86 ± 0.45	0.144
Minimum luminal diameter, mm	2.64 ± 0.35	2.56 ± 0.41	0.025
Stent edge dissection	18 (9.0%)	27 (13.4%)	0.155

QCA at CTO segments

	IVUS-guided (n=201)	Angiography-guided (n=201)	p Value
Pre-procedure			
Reference vessel diameter, mm	2.69 ± 0.44	2.64 ± 0.55	0.346
Post-procedure			
Whole diseased segments			
Reference vessel diameter, mm	2.92 ± 0.39	2.86 ± 0.45	0.144
Minimum luminal diameter, mm	2.64 ± 0.35	2.56 ± 0.41	0.025
Percent diameter stenosis, %	9.0 ± 9.8	10.2 ± 10.9	0.272
CTO segments			
Minimum luminal diameter, mm	2.81 ± 0.37	2.69 ± 0.42	0.004
Percent diameter stenosis, %	3.3 ± 10.9	5.3 ± 12.5	0.095

CTO-IVUS study

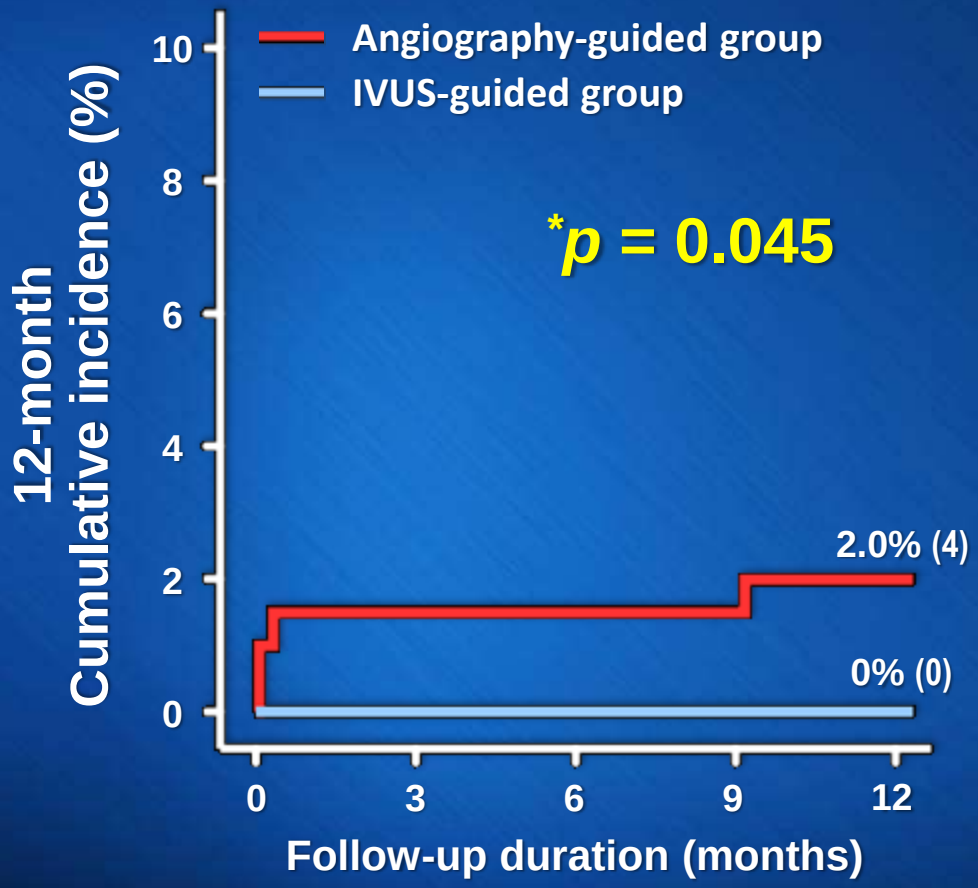
Primary endpoint (Cardiac death, MI, ST, or TVR)



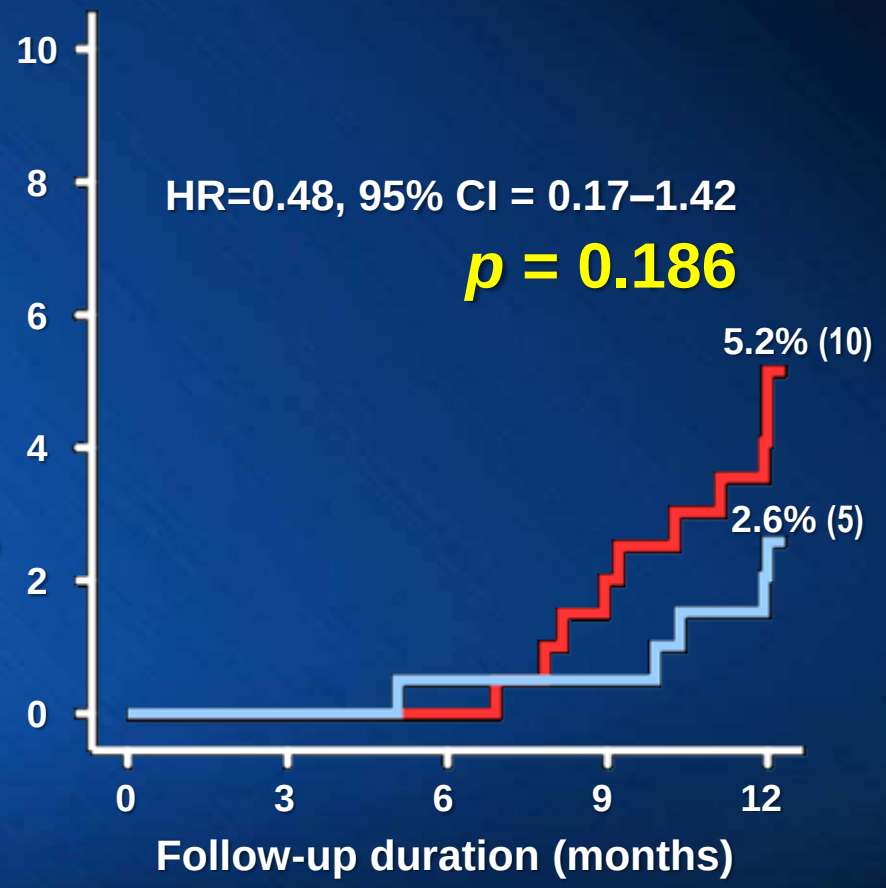
Number at risk			
Angiography-guided	201	198	179
IVUS-guided	201	198	186

Kim BK, et al. Circ Interv 2015

Cardiac death or MI



TVR



Number at risk						
Angiography-guided	201	198	187	201	199	180
IVUS-guided	201	199	190	201	198	186

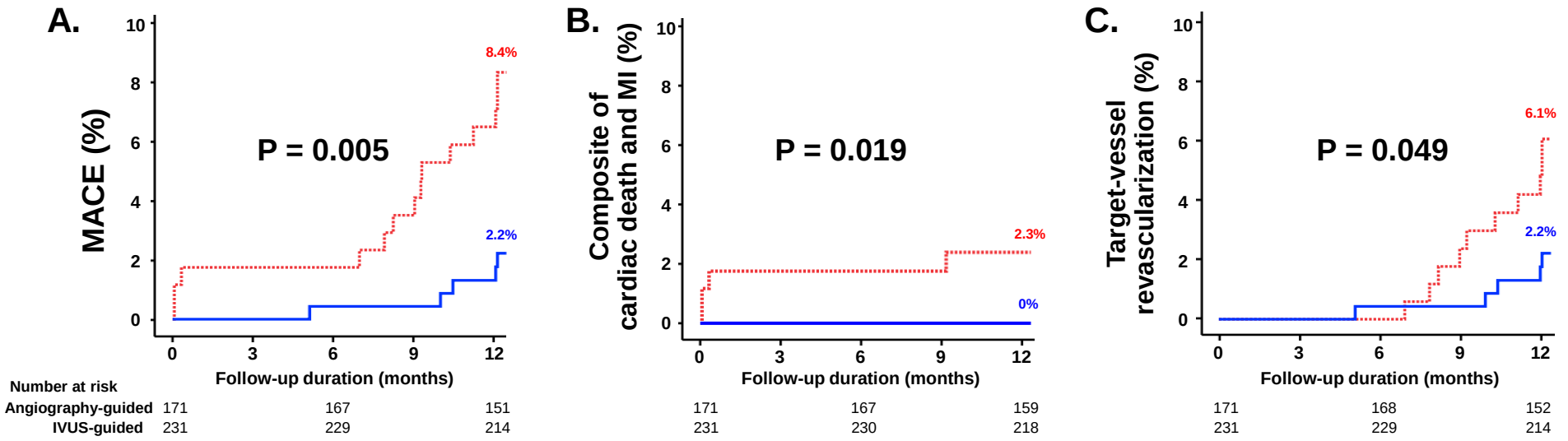
*Not calculable HR or CI because of no occurrence of the event

Kim BK, et al. Circ Interv 2015

Per-protocol Analysis of CTO-IVUS study

Angiography-guided group

IVUS-guided group



Number at risk					
Angiography-guided	171	167	151	171	167	159	171	168	152
IVUS-guided	231	229	214	231	230	218	231	229	214

Today's Talk

1. Outcome between successful vs. failed CTO ?

2. Comparison of clinical outcomes following CTO intervention?

3. Impact of risk factors on outcomes after successful CTO intervention & on-going K-CTO random trial

Comparison of 12-month clinical outcomes in diabetic and nondiabetic patients with chronic total occlusion lesions: a multicenter study

- Objectives
  - To investigate the impact of **DM on the prognosis** of the patients undergoing **DES-PCI for CTO**
- Study Population
  - K-CTO registry consisting of 26 Korean centers
  - From 2007 to 2009, a total of 2,865 Pts. undergoing PCI to CTO
  - Non-DM (n=1,888) vs. DM (n=977)

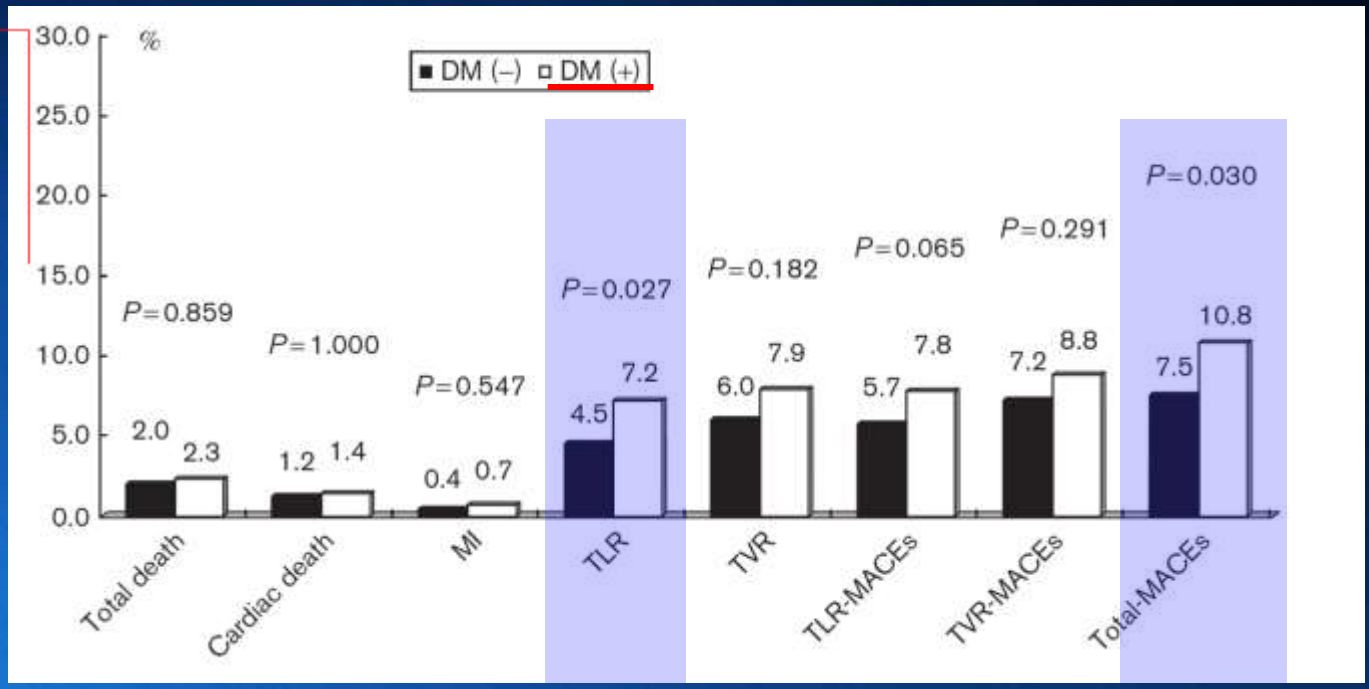
Independent Predictors of 12-month TLR & total MACEs

	TLR			Total MACEs		
	OR	95% CI	*P*	OR	95% CI	*P*
Age	0.992	0.970–1.015	0.477	0.993	0.977–1.009	0.364
Male	0.989	0.576–1.700	0.969	0.871	0.587–1.292	0.492
History of PCI	0.945	0.541–1.649	0.841	1.043	0.693–1.570	0.841
HTN	1.108	0.684–1.794	0.677	0.928	0.658–1.309	0.670
DM	2.201	1.407–3.442	0.001	1.677	1.207–2.330	0.002
History of MI	1.446	0.764–2.736	0.257	0.837	0.494–1.419	0.837
Current smoker	0.991	0.603–1.629	0.972	1.033	0.723–1.476	0.860
Dyslipidemia	1.111	0.688–1.797	0.285	0.785	0.551–1.120	0.182
HF	0.962	0.371–2.495	0.936	1.004	0.506–1.991	0.990
SES vs. PES	0.815	0.408–1.627	0.562	1.041	0.634–1.710	0.872
ZES sprinter vs. PES	1.394	0.841–2.311	0.198	1.413	0.952–2.097	0.087
ZES resolute vs. PES	1.021	0.572–1.823	0.944	1.021	0.572–1.823	0.944
EES vs. PES	1.128	0.377–3.370	0.829	1.144	0.493–2.656	0.755
Stent length	0.999	0.988–1.010	0.853	1.002	0.994–1.010	0.614

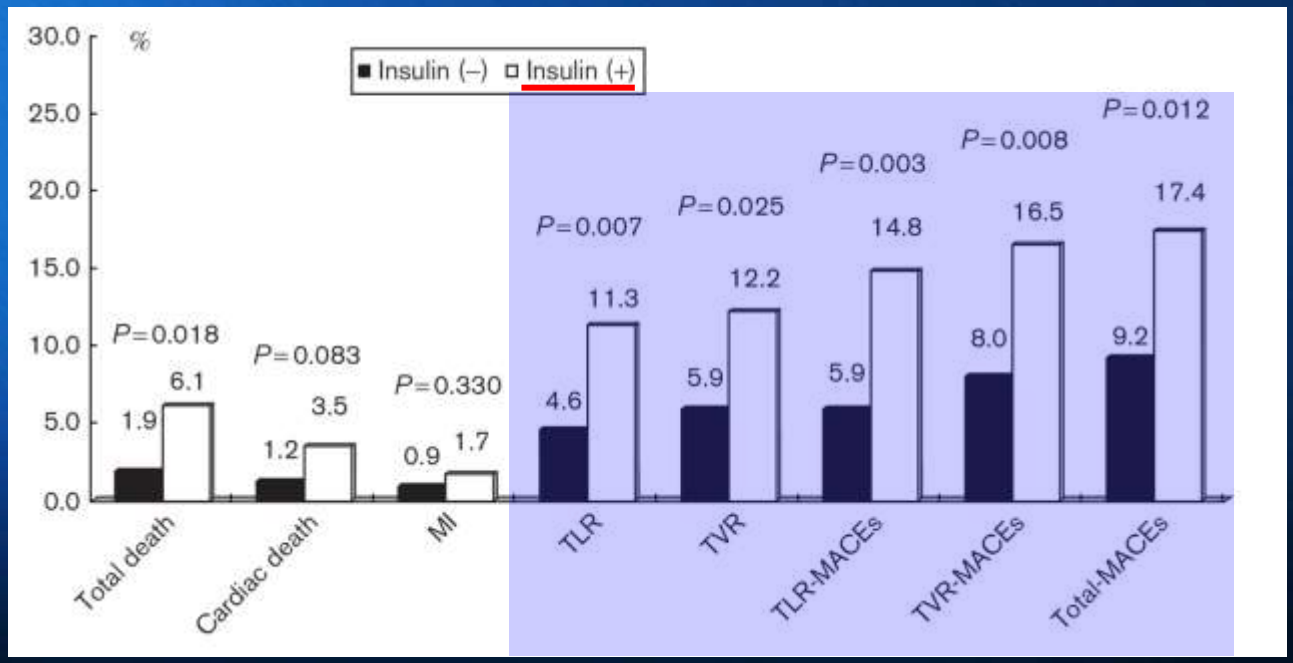
Rha SW et al., *Coron Artery Dis*, 2015

12mo. Outcomes in PS-matched population

DM vs. non-DM



Insulin vs. no insulin in DM Pts.



Rha SW et al., ***Coron Artery Dis***, 2015

Impact of Smoking Status on Clinical Outcomes After Successful Chronic Total Occlusion Intervention: Korean National Registry of CTO Intervention

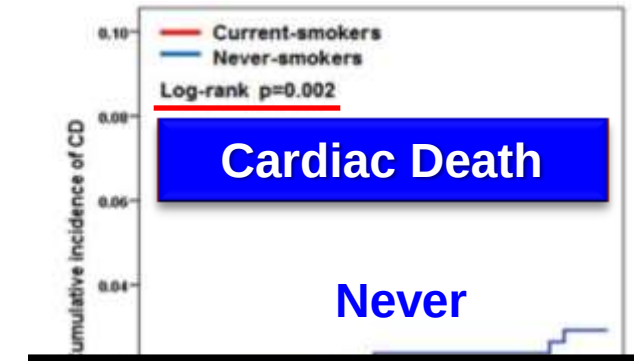
- **"Smoker's paradox"**
  - **Lower mortality** in **smokers** than in non-smokers **after AMI**
  - Smoking ass. with enhanced responsiveness to clopidogrel
  - Younger age, less comorbidities in smokers
- **Objectives**
  - To investigate the effects of **smoking on long-term outcomes** after successful PCI for CTO
- **Study Population**
  - Korean CTO (K-CTO) registry consisting of 26 Korean centers
  - From 2007 to 2009, a total of 1,527 Pts. undergoing PCI to CTO
  - **Current smokers, n=311, Never smokers n=903**

Yoon CH, Chae IH et al., *CCI*, 2015

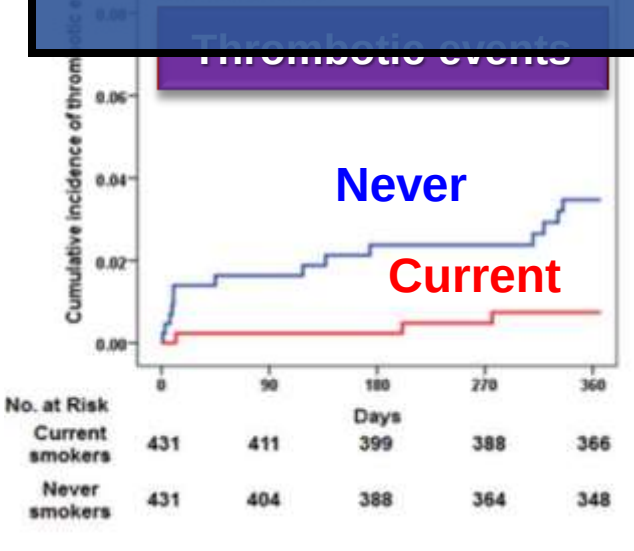
Baseline Characteristics

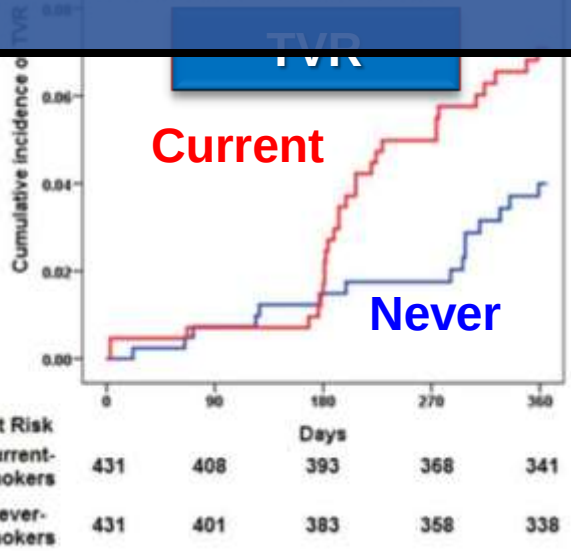
	Crude population				Propensity-score matched population		
	Overall ($n = 1527$)	Current-smokers ($n = 624$)	Never-smokers ($n = 903$)	P value	Current-smokers ($n = 431$)	Never-smokers ($n = 431$)	P value
Age (years)	62.3 ± 11.4	57.9 ± 11.2	65.4 ± 10.4	< 0.001	60.8 ± 10.3	61.8 ± 10.3	0.163
Male	1039 (68.0%)	568 (91.0%)	471 (52.2%)	< 0.001	380 (88.2%)	378 (87.7%)	0.917
Hypertension	970 (63.5%)	356 (57.2%)	614 (68.5%)	< 0.001	255 (59.2%)	261 (60.6%)	0.728
Diabetes mellitus	530 (34.7%)	199 (31.9%)	331 (36.9%)	0.049	150 (34.8%)	137 (31.8%)	0.386
Dyslipidemia	532 (34.8%)	209 (34.8%)	323 (37.6%)	0.294	156 (36.2%)	149 (34.6%)	0.669
History of IHD	395 (25.9%)	145 (23.2%)	250 (27.8%)	0.050	111 (25.8%)	110 (25.5%)	> 0.999
History of CHF	115 (7.5%)	42 (6.8%)	73 (8.2%)	0.375	28 (6.5%)	29 (6.7%)	> 0.999
Clinical indication of PCI				0.027			0.288
Stable angina	717 (47.0%)	284 (46.0%)	433 (48.4%)		204 (47.3%)	213 (49.4%)	
Unstable angina	581 (38.0%)	229 (37.1%)	352 (39.4%)		177 (41.1%)	154 (35.7%)	
NSTEMI	127 (8.3%)	57 (9.2%)	70 (7.8%)		32 (7.4%)	38 (8.8%)	
STEMI	87 (5.7%)	48 (7.8%)	39 (4.4%)		18 (4.2%)	26 (6.0%)	

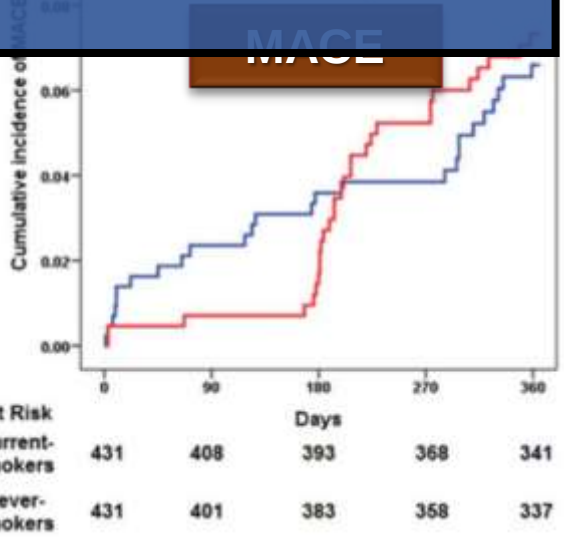
Yoon CH, Chae IH et al., *CCI*, 2015



- "**Smokers' paradox**" also applies to CTO patients after successful revascularization.
- **Smoking** is associated with **fewer thrombotic events** but with a **higher incidence of TVR.**







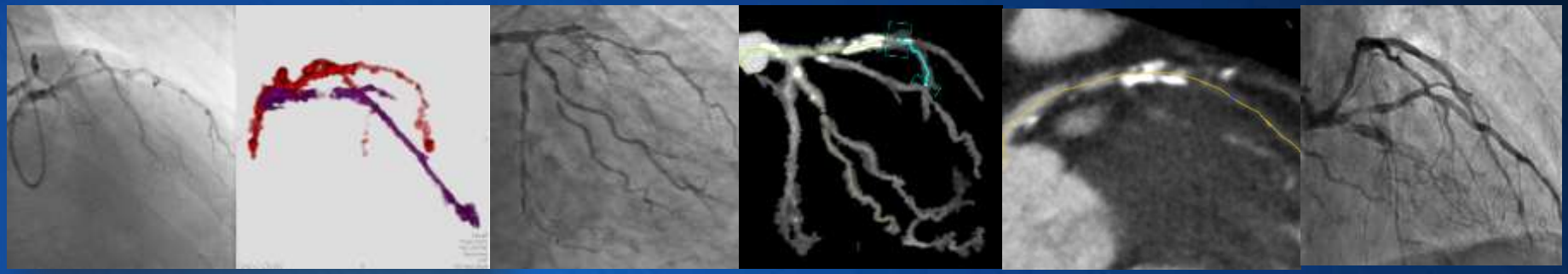
Question;

Could CT, improve the success rate of CTO intervention?

Role of CT scan for successful CTO intervention

1. Make the "at-a-glance CT image" matched with angiogram, "two different views

Identification of location of CTO, side branches & collateral channels



2. Qualitative and quantitative analyses of CTO segments

1) CTO length
2) Shape of proximal/distal entry of CTO; blunted or tapered
3) Morphology of CTO segment: No. of occlusion sites, bending at the entry or exit site or within CTO
4) Vessel remodeling in CTO segments, negative or positive
5) Calcification → "Geographic calcium mapping"
   - Maximal cross-sectional extent, <50% or >50%
   - Shape: concentric, <180°, >180°
   - Length & location

However,
these roles could not be proved by random trial…
Pre-procedural CT assessment before PCI, improve the success rate?

3. Analyses of the segments around CTO

– Vessel area and disease severity of reference segments

Randomized trial of K-CTO club

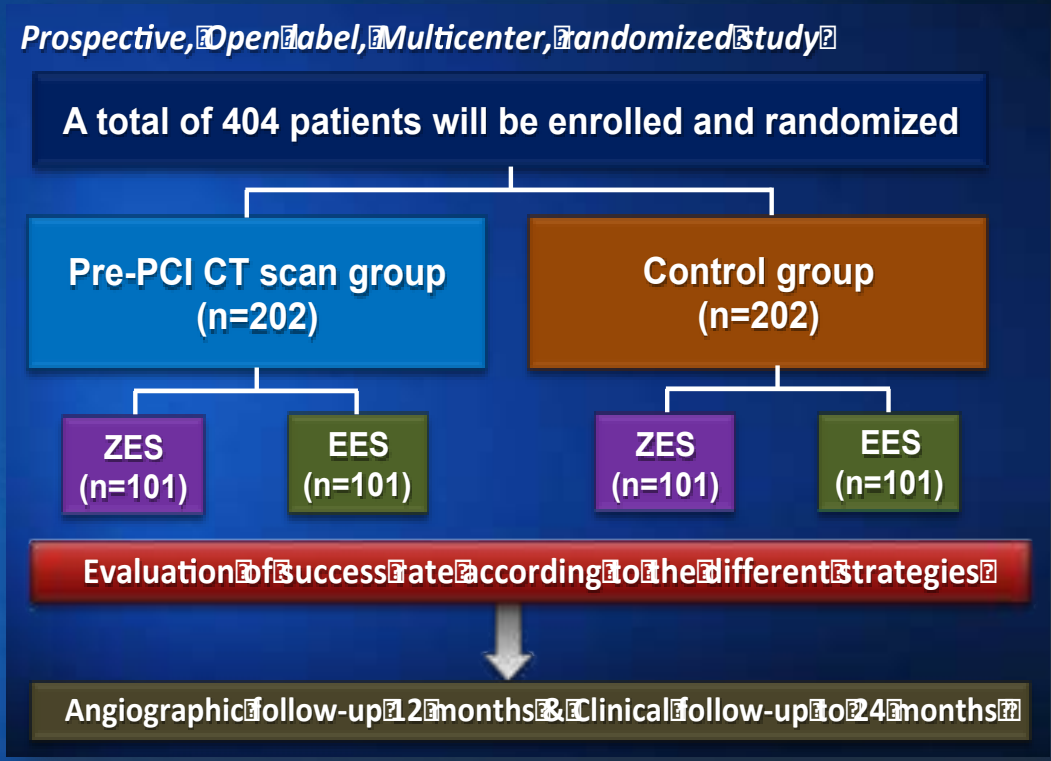
Role of CT scan for the successful CTO PCI; a randomized comparison between 3D CT-guided PCI vs. conventional treatment; CT-CTO trial

Objective

- To evaluate whether **pre-procedural 3D CT scan can improve the successful recanalization** in the treatment of CTO compared with conventional treatment

Primary end points

- Incidence of the successful CTO recanalization between pre-PCI CT scan group vs control group



Secondary end points

- **Comparison of MACE between ZES-R** (Endeavor Resolute Integrity) **and EES** (Xience)
- **Efficacy parameters for CTO PCI (Total procedural time / Total contrast amount)**

PI: Yangsoo Jang / **CT core lab:** Chang HJ / Kim BK (Yonsei University Severance Hospital)

Conclusion: Summary of K-CTO registry

- As compared to the failed CTO intervention, **the successful CTO intervention using DESs** showed …
  - ✓ **a lower occurrence of the composite of cardiac death and MI**
  - ✓ **a lower cardiac mortality rate and a need for bypass surgery**
  - ✓ **Clinical parameters (such as age, diabetes, and heart failure)** were independent predictors of fatal events.
- **IVUS-guided CTO intervention** showed the improved clinical outcomes after 2nd-generation DES, confirmed by K-CTO registry and the randomized CTO-IVUS study.
- The impacts of major risk CAD factors on clinical outcomes after CTO intervention could vary.
- The on-going K-CTO randomized trial, **CT-CTO trial** will show the role of pre-procedural CT scan for successful CTO.

Thank you for your attention