Radial PCI in STEMI
Current Evidence, Unmet needs and Upcoming trials

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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.

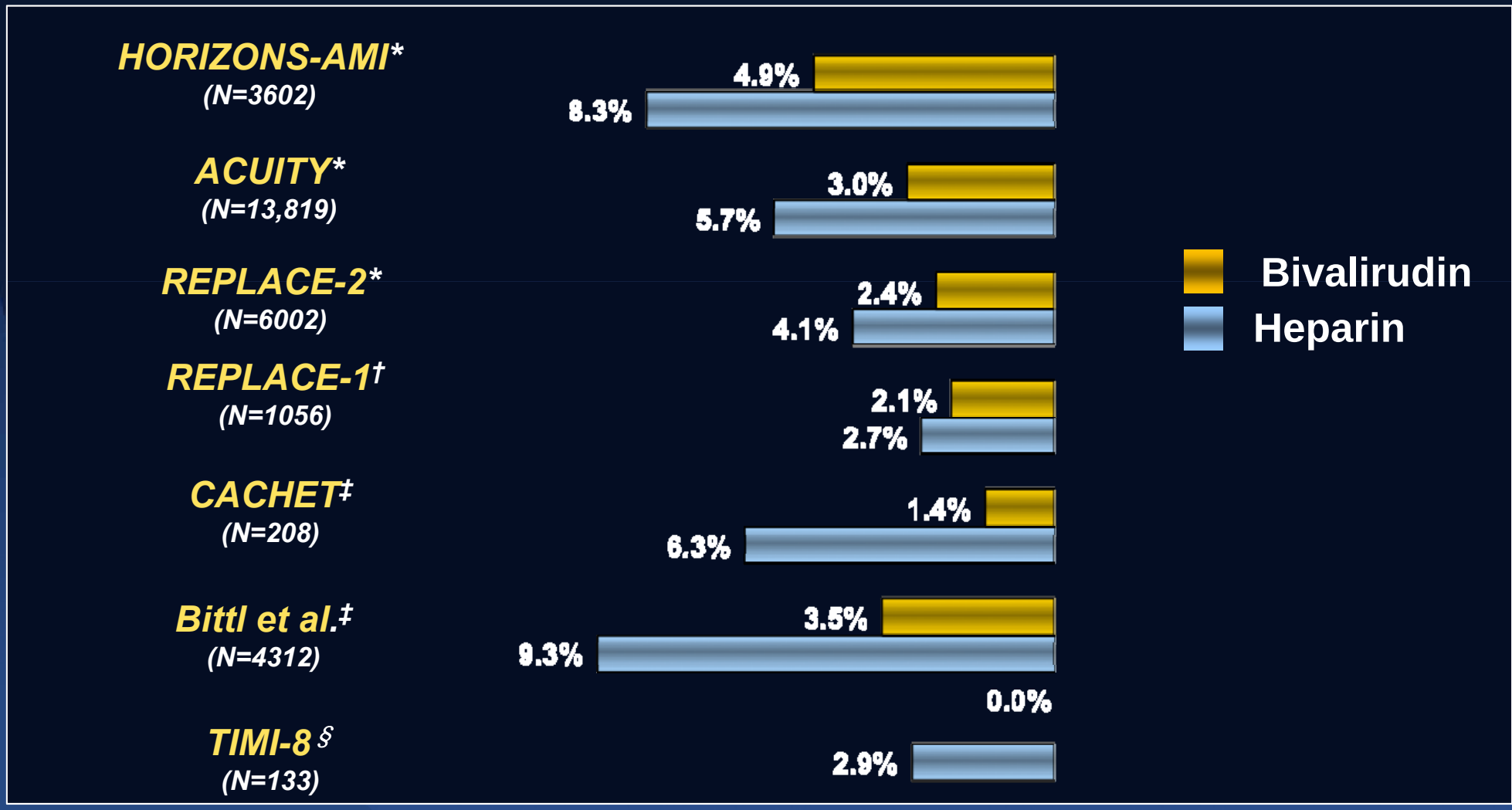
Affiliation/Financial Relationship	Company
• None	

Review of the current evidence

- Bleeding
- Evidence in STEMI Radial vs. Femoral
  - Rival
  - Rifle
  - STEMI-Radial
- Upcoming trials

1) Bleeding is frequent

Bivalirudin trials - Major Bleeding
Bleeding is the most common non cardiac complication

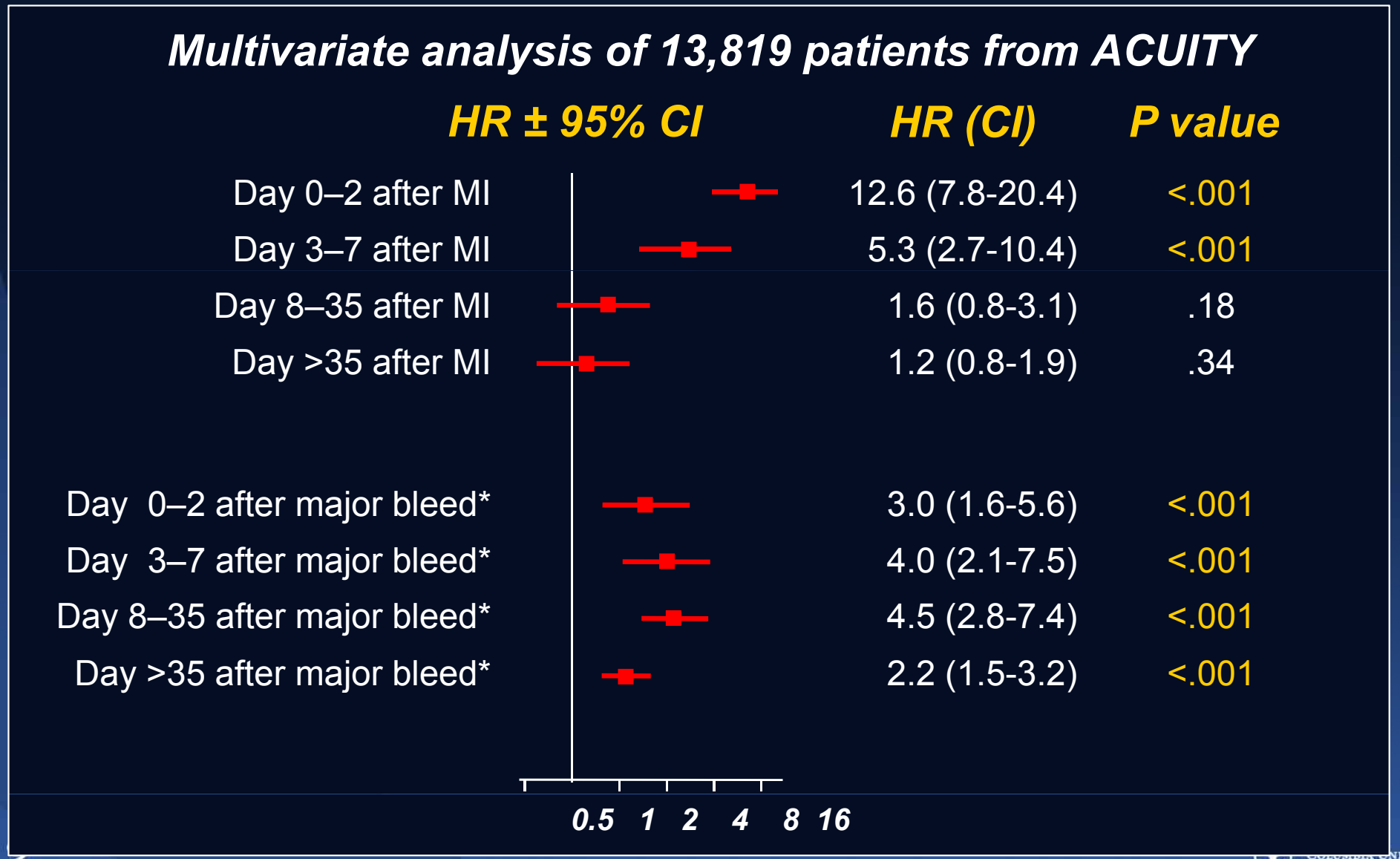


•30 days; †48 hours; ‡ 7 days; § 14 days

Antman et al AHJ 2002; Bittl et al AHJ 2001;Lincoff et al AJC 2004; Lincoff et al 2002; Stone et al NEJM 2006; Stone et al NEJM 2008

1) **Bleeding is frequent**
2) **Bleeding is bad**

Non-CABG Major Bleeding and Early MI Were Associated With Increased Rates of Mortality at 1 Year



1) **Bleeding is frequent**
2) **Bleeding is bad**
3) **Not all bleeding is equal**

Incidence, Prognostic Impact, and Influence of Antithrombotic Therapy on Access and Non-access Site Bleeding in PCI

17,393 pts from REPLACE-2, ACUITY, and HORIZONS-AMI randomized to Bivalirudin or Heparin plus a GPI.

TIMI Major/Minor Bleeding	Adjusted HR, 1-Year Mortality	*P* Value
Any Bleeding	3.17	< 0.0001
Access Site-Only	1.82	0.008
Nonaccess Site	3.94	0.0001

Conclusion: ***The mortality risk of nonaccess site bleeding is almost twice that of access site bleeding. Bivalirudin reduces both risks by about 40% compared with heparin and a GPI.***

Verheugt FWA, et al. J Am Coll Cardiol Intv. 2011;4:191-197.

1) **Bleeding is frequent**
2) **Bleeding is bad**
3) **Not all bleeding is equal**
4) **Bleeding costs money**

Independent Predictors of Initial Hospital Costs (NSTEMI) ACUITY

	Estimated Cost
Death	$9,061
MI	$3,388
Major bleed	$8,658
Minor bleed	$2,282
Unplanned PCI or CABG	$12,293
Initial management strategy	
PCI	$8,279
CABG	$29,461

1) **Bleeding is frequent**
2) **Bleeding is bad**
3) **Not all bleeding is equal**
4) **Bleeding costs money**

What can we do?

Radial?

Bivalirudin?

Closure devices?

What is the latest evidence in STEMI?

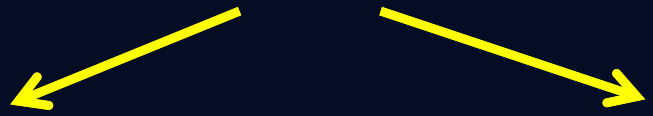
- RIVAL
- RIFLE
- STEMI-Radial

RIVAL Study Design

NSTE-ACS and STEMI
(n=7021)

Key Inclusion:
Intact dual circulation of hand required
Interventionalist experienced with both (minimum 50 radial procedures in last year)

Randomization



Radial Access	*Femoral Access*
(n=3507)	*(n=3514)*

Blinded Adjudication of Outcomes

Primary Outcome: Death, MI, stroke or non-CABG-related Major Bleeding at 30 days

Jolly SS et al. Am Heart J. 2011;161:254-60.

Definitions

Major Bleeding **(CURRENT/ OASIS 7)**	• Fatal • ≥ 2 units of Blood transfusion • Hypotension requiring inotropes • Leading to hemoglobin drop of ≥ 5 g/dl • Requiring surgical intervention • ICH or Intraocular bleeding leading to significant vision loss
Major Vascular Access Site Complications	• Large hematoma • Pseudoaneurysm requiring closure • AV fistula • Other vascular surgery related to the access site

Baseline Characteristics

	Radial (n =3507)	Femoral (n =3514)
Mean Age (years)	**62**	**62**
Male (%)	**74.1**	**72.9**
Diabetes (%)	**22.3**	**20.5**
Diagnosis at presentation		
UA (%)	**44.3**	**45.7**
NSTEMI (%)	**28.5**	**25.8**
STEMI (%)	***27.2***	***28.5***

Primary and Secondary Outcomes

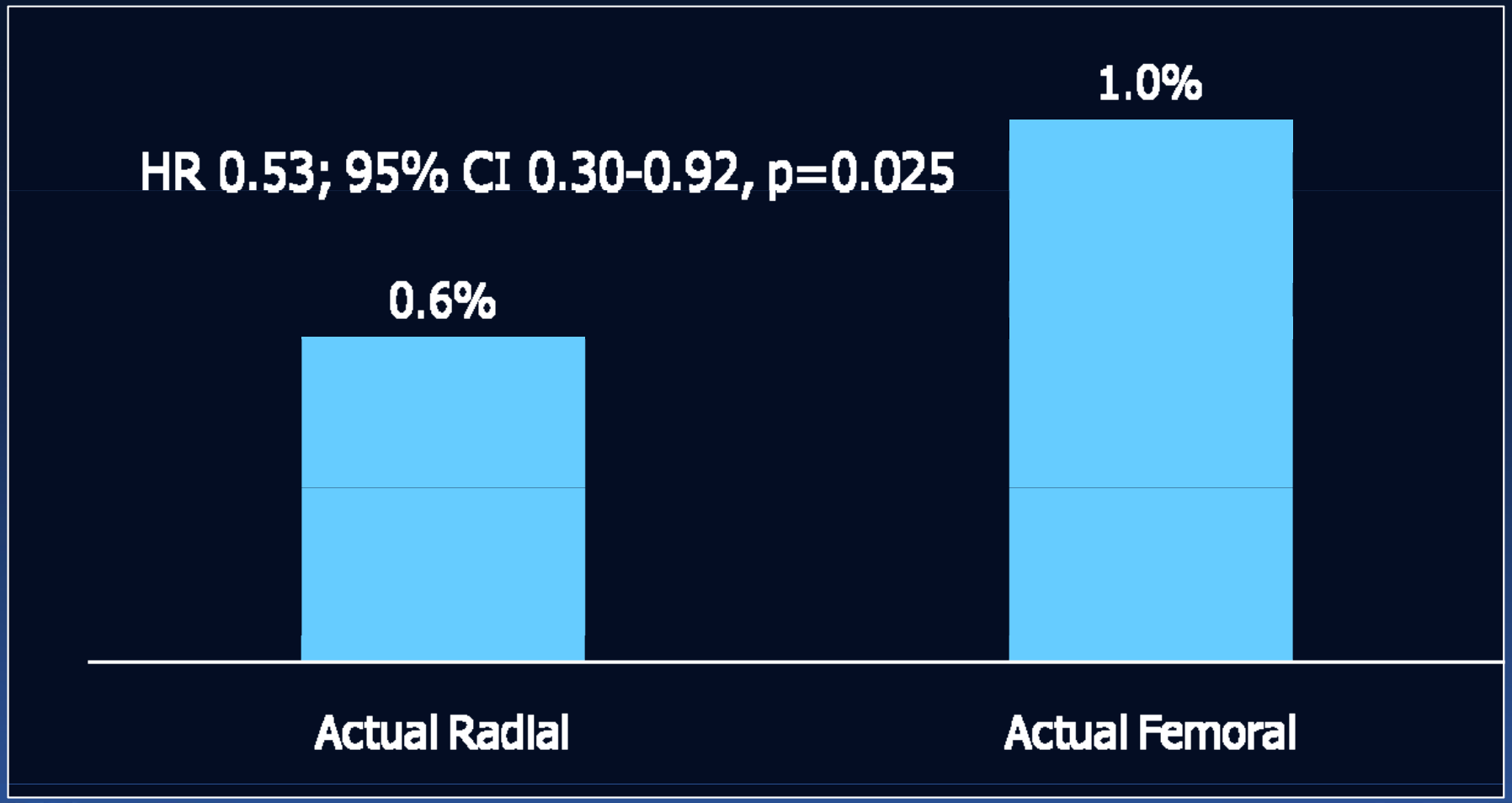
	Radial (n=3507) %	Femoral (n=3514) %	HR	95% CI	P
Primary Outcome					
Death, MI, Stroke, Non-CABG Major Bleed	**3.7**	**4.0**	0.92	0.72-1.17	0.50
Secondary Outcomes					
Death, MI, Stroke	**3.2**	**3.2**	0.98	0.77-1.28	0.90
Non-CABG Major Bleeding	**0.7**	**0.9**	0.73	0.43-1.23	0.23

Other Outcomes

	Radial (n=3507) %	Femoral (n=3514) %	HR	95% CI	P
Major Vascular Access Site Complications	**1.4**	**3.7**	0.37	0.27-0.52	*<0.0001*
Other Definitions of Major Bleeding					
TIMI Non-CABG Major Bleeding	**0.5**	**0.5**	1.00	0.53-1.89	1.00
ACUITY Non-CABG Major Bleeding*	**1.9**	**4.5**	0.43	0.32-0.57	*<0.0001*

** Post Hoc analysis*

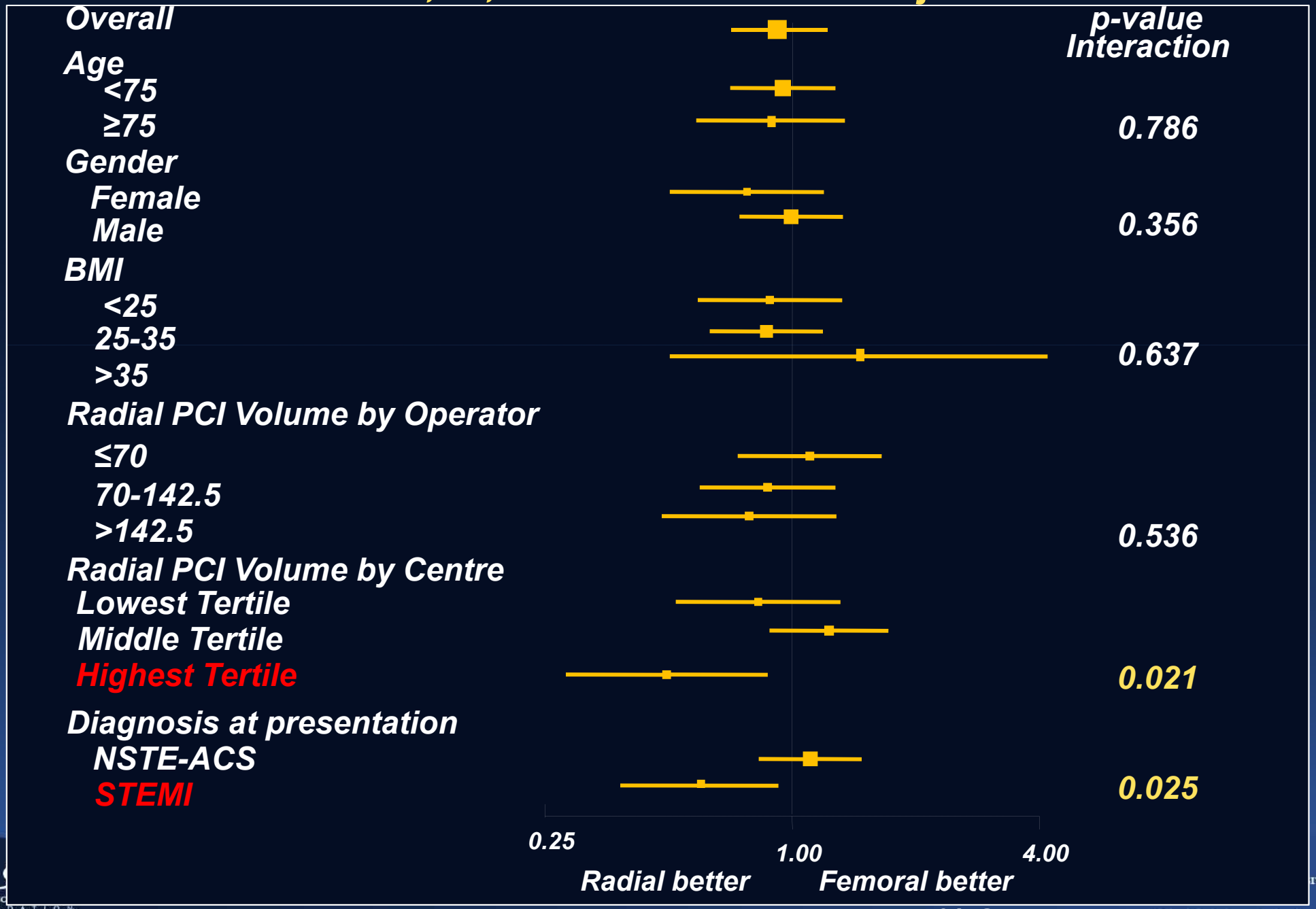
Non CABG major bleeding
by actual access site used to complete procedure (not intent to treat)*



**Post Hoc analysis*

Subgroups: Primary Outcome

Death, MI, Stroke or non-CABG major Bleed



Outcomes stratified by STEMI vs. NSTEACS

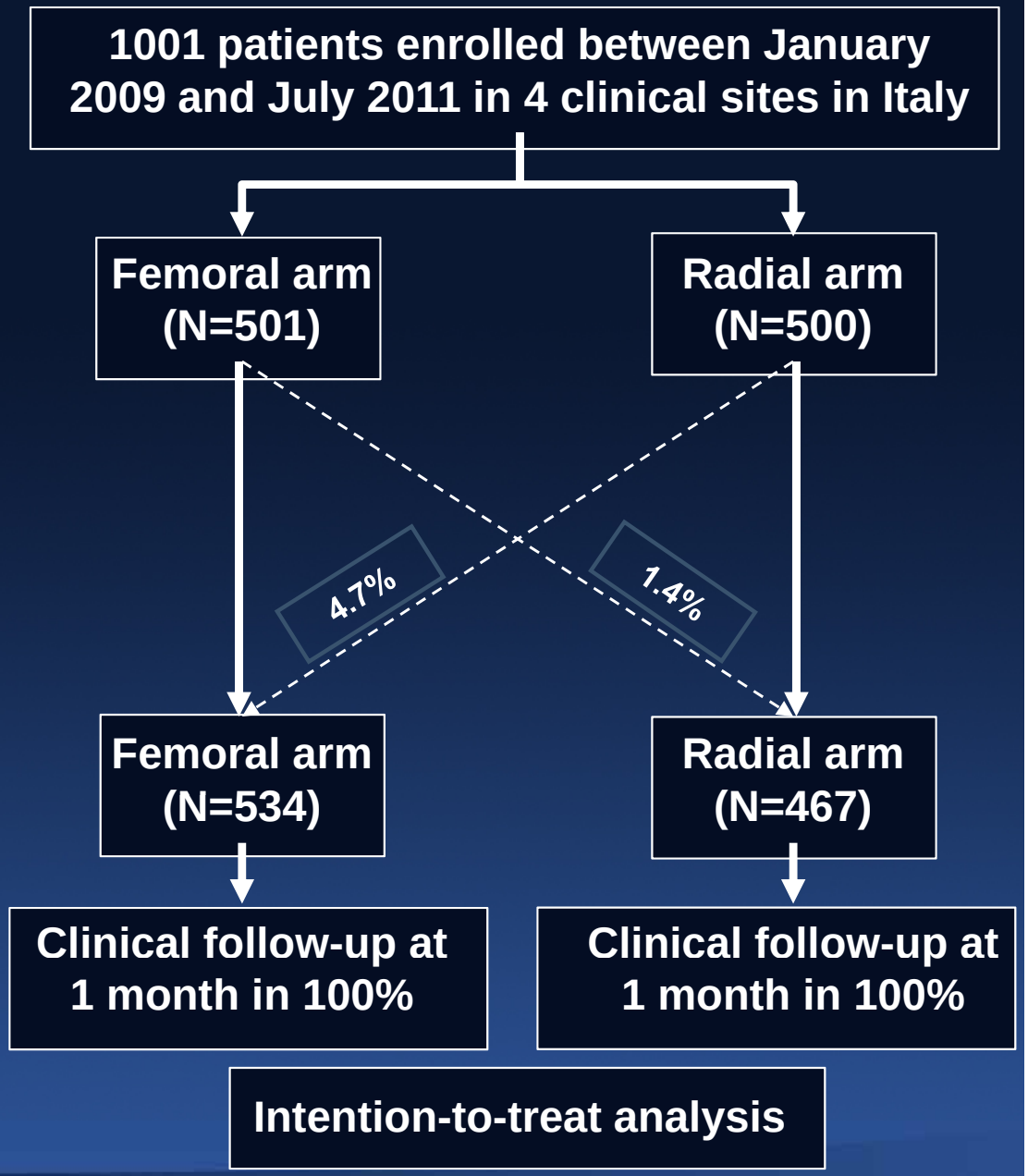
	2N	% Radial	% Femoral	Interaction p-value
Primary Outcome				
NSTE/ACS	5063	3.8	3.5	
STEMI	1958	3.1	5.2	0.025
Death, MI or stroke				
NSTE/ACS	5063	3.4	2.7	
STEMI	1958	2.7	4.6	0.011
Death				
NSTE/ACS	5063	1.2	0.8	
STEMI	1958	1.3	3.2	0.001
Non CABG Major Bleed				
NSTE/ACS	5063	0.6	1.0	
STEMI	1958	0.8	0.9	0.56
Major Vascular Complications				
NSTE/ACS	5063	1.4	3.8	
STEMI	1958	1.3	3.5	0.89

RIFLE STEACS - flow chart

Design

- **DESIGN:**
  Prospective, randomized (1:1), parallel group, multi-center trial.
- **INCLUSION CRITERIA:**
  all ST Elevation Myocardial infarction (STEMI) eligible for primary percutaneous coronary intervention.
- **ExCLUSION CRITERIA:**
  contraindication to any of both percutaneous arterial access.

  international normalized ratio (INR) > 2.0.



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ClinicalTrials.gov NCT01420614

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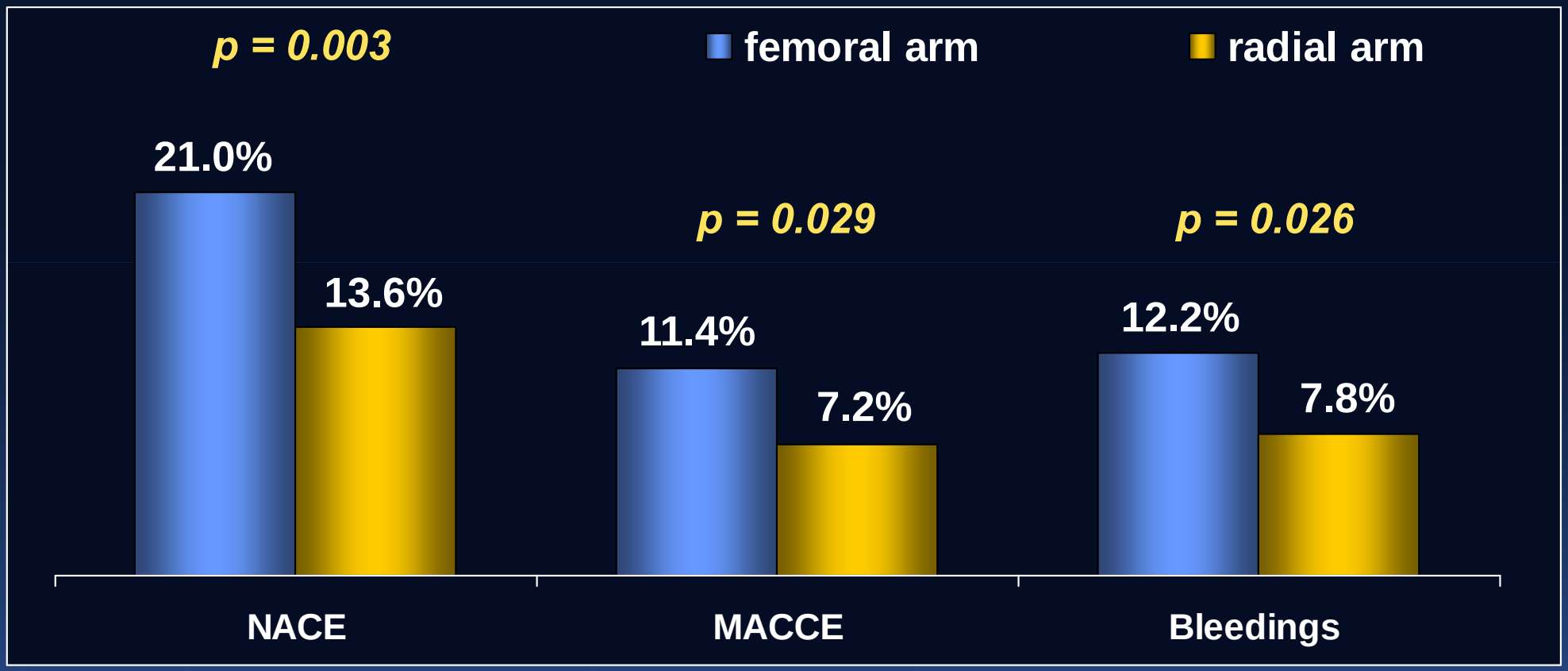
RIFLE STEACS – end-points

- Net adverse clinical events (NACE) at 30 days, defined as the composite of cardiac death, myocardial infarction (MI), target lesion revascularization, stroke, or non-coronary artery bypass graft (non-CABG)-related bleeding.
- Non CABG-related bleeding at 30 days (corresponding to type 2, type 3 and type 5 of BARC classification).

RIFLE STEACS – results

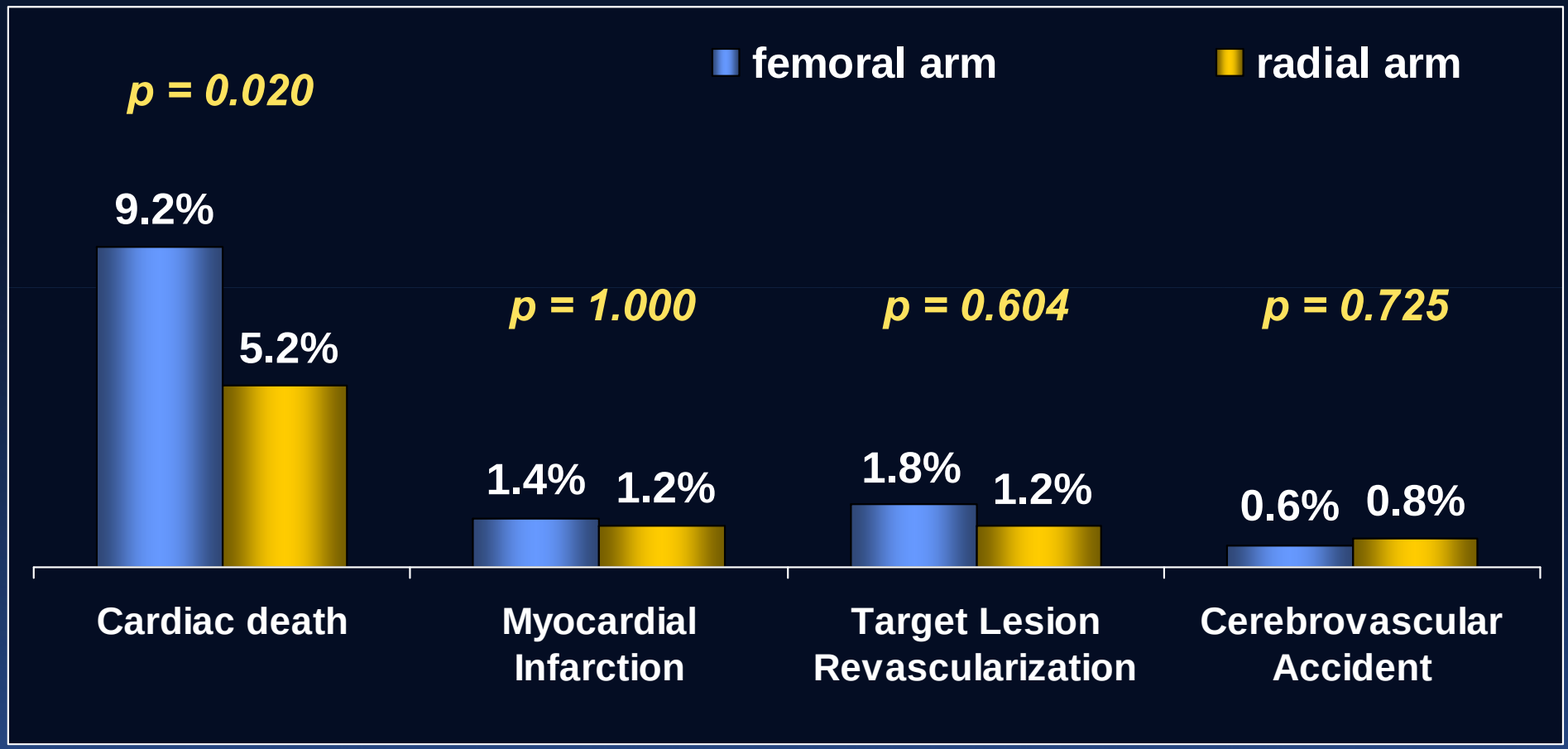
30-day NACE rate



Net Adverse Clinical Event (*NACE*) = MACCE + bleeding
Major Adverse Cardiac and Cerebrovascular event (*MACCE*) = composite of cardiac death, myocardial infarction, target lesion revascularization, stroke

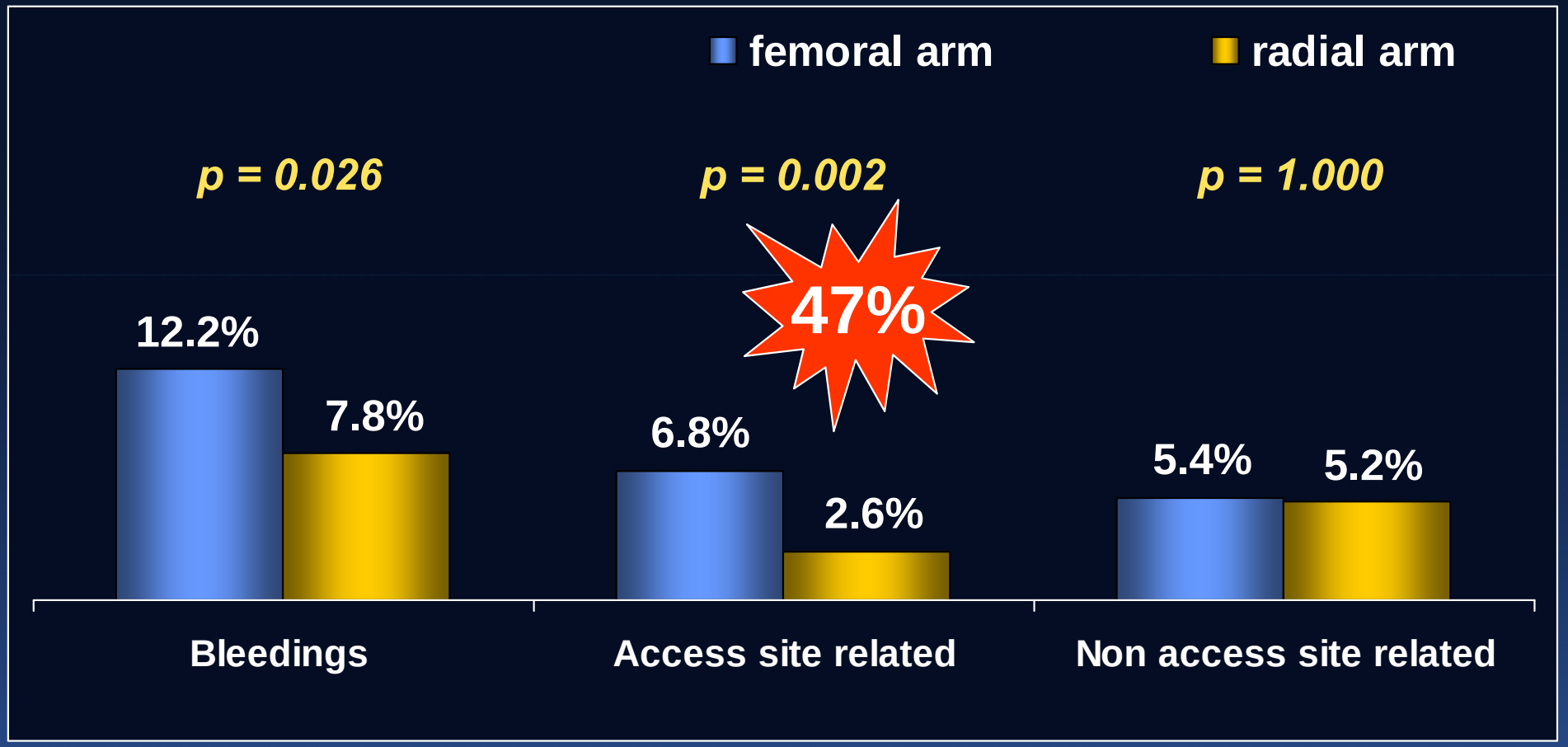
RIFLE STEACS – results

30-day MACCE rate



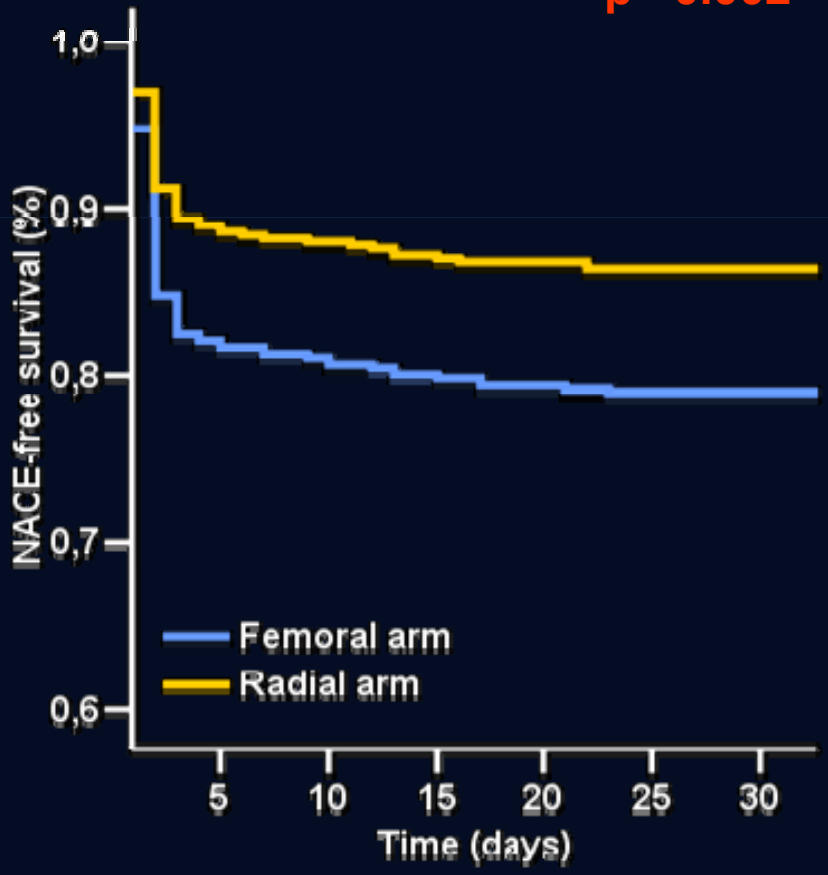
RIFLE STEACS – results

30-day bleeding rate



RIFLE STEACS – results

30-day NACE predictors



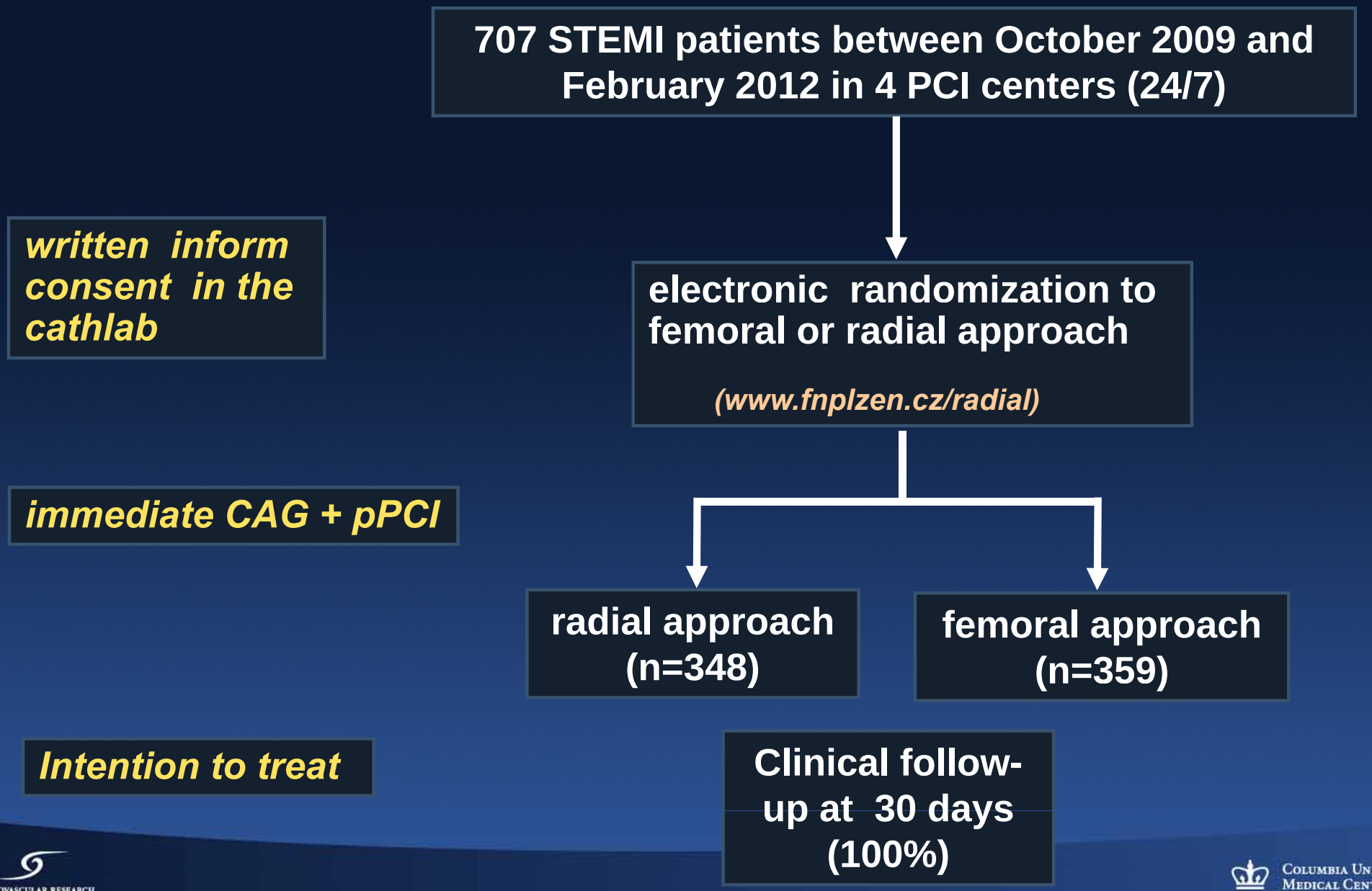
	OR	CI 95%	p value
Female gender	1.5	(1.1-2.3)	0.037
CKD	2.1	(1.4-3.1)	0.001
Radial access	0.6	(0.4-0.9)	0.012
Killip class	1.8	(1.5-2.2)	0.001
LAD culprit	1.7	(1.2-2.6)	0.006
TIMI 0 basal	1.4	(1.0-2.1)	0.073
LVEF <50%	1.6	(1.1-2.5)	0.025
TIMI 0-1 final	2.4	(1.1-5.1)	0.024

RIFLE STEACS - conclusions

- Radial access in patients with STEMI is associated with significant clinical benefit, in terms of both bleeding and cardiac mortality.

- Radial approach should thus no more be considered a valid alternative to femoral one, but become the recommended access site for STEMI (international guideline).

STEMI RADIAL - Study design:



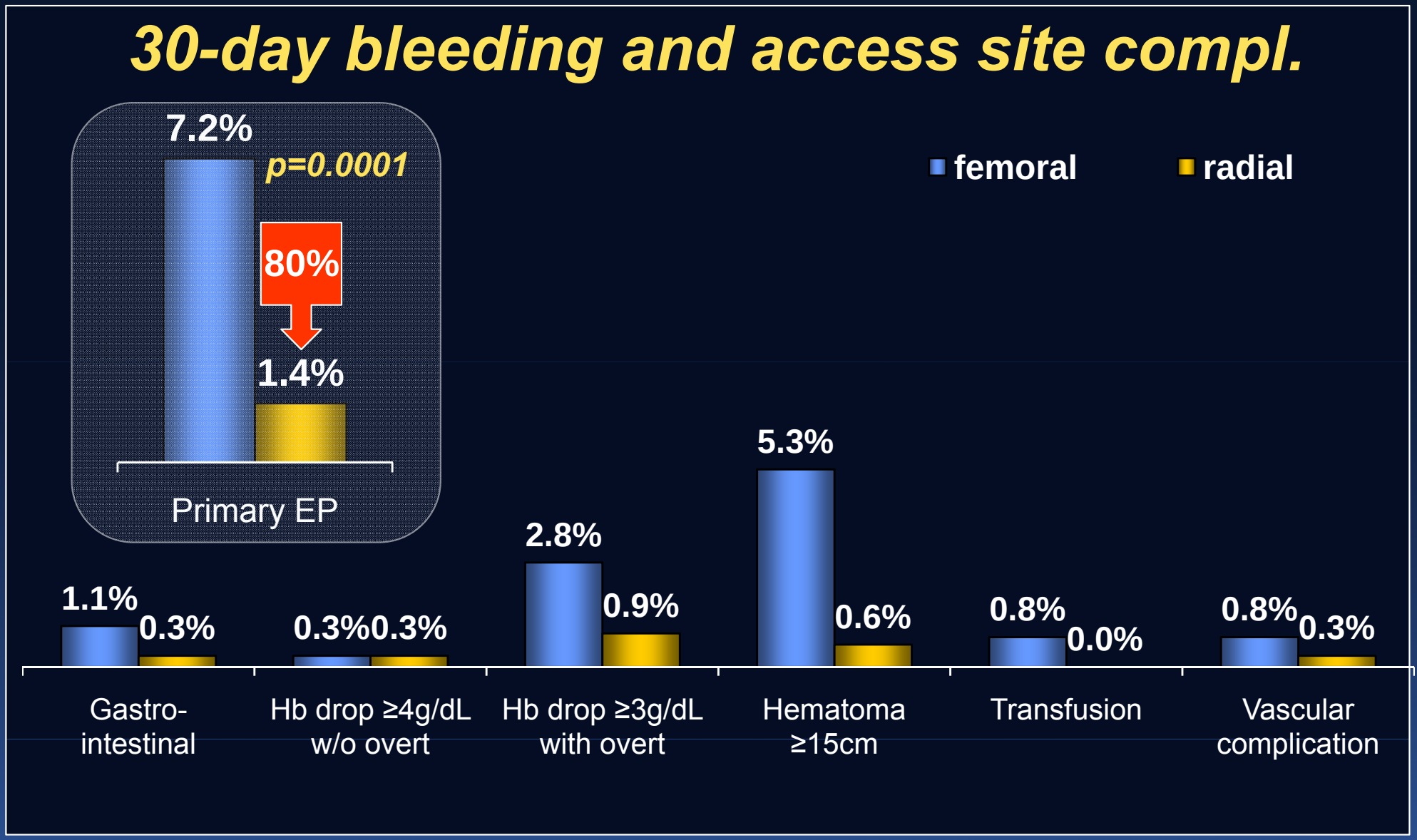
STEMI-RADIAL end-points

- **Primary** - **HORIZONS-AMI bleeding and access site complication ***
- **Secondary**
  - **MACE (death, MI, stroke)**
  - **NACE**
  - crossover
  - angiographic success
  - contrast volume
  - procedural and fluoroscopic times
  - ICU stay

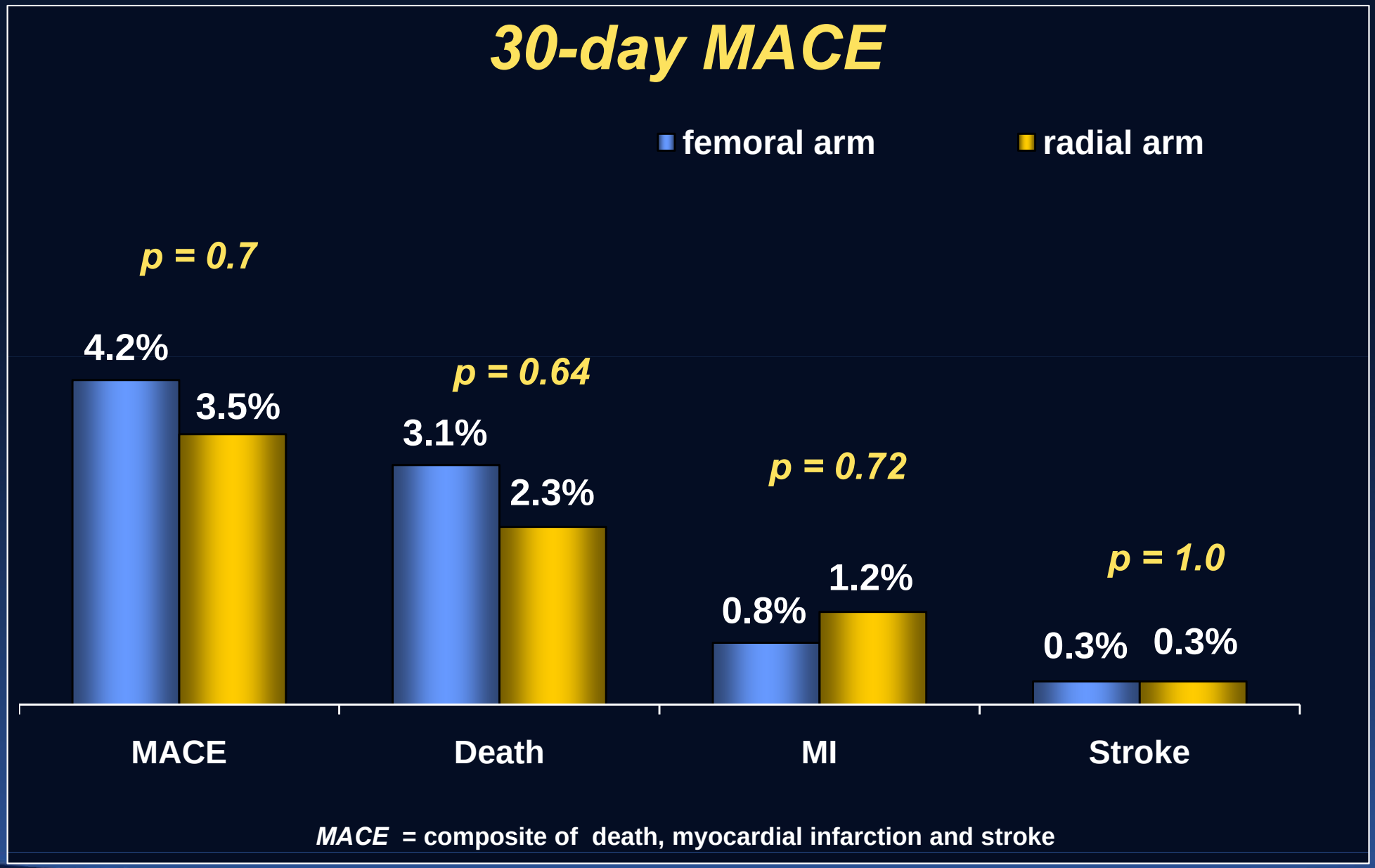
* Hematoma ≥15cm

STEMI RADIAL - results

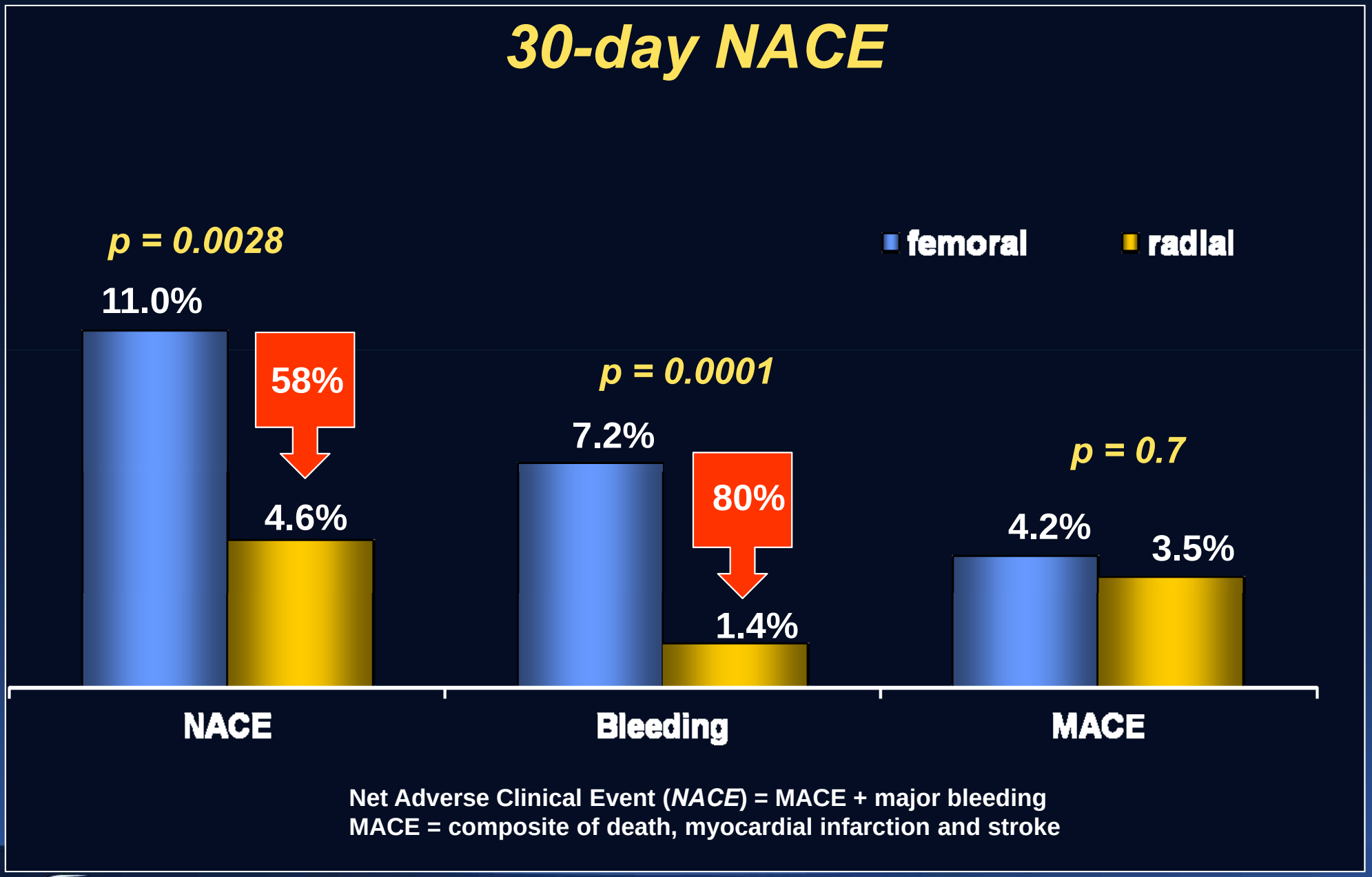
30-day bleeding and access site compl.



STEMI RADIAL - results



STEMI RADIAL - results



Net Adverse Clinical Event (*NACE*) = MACE + major bleeding
MACE = composite of death, myocardial infarction and stroke

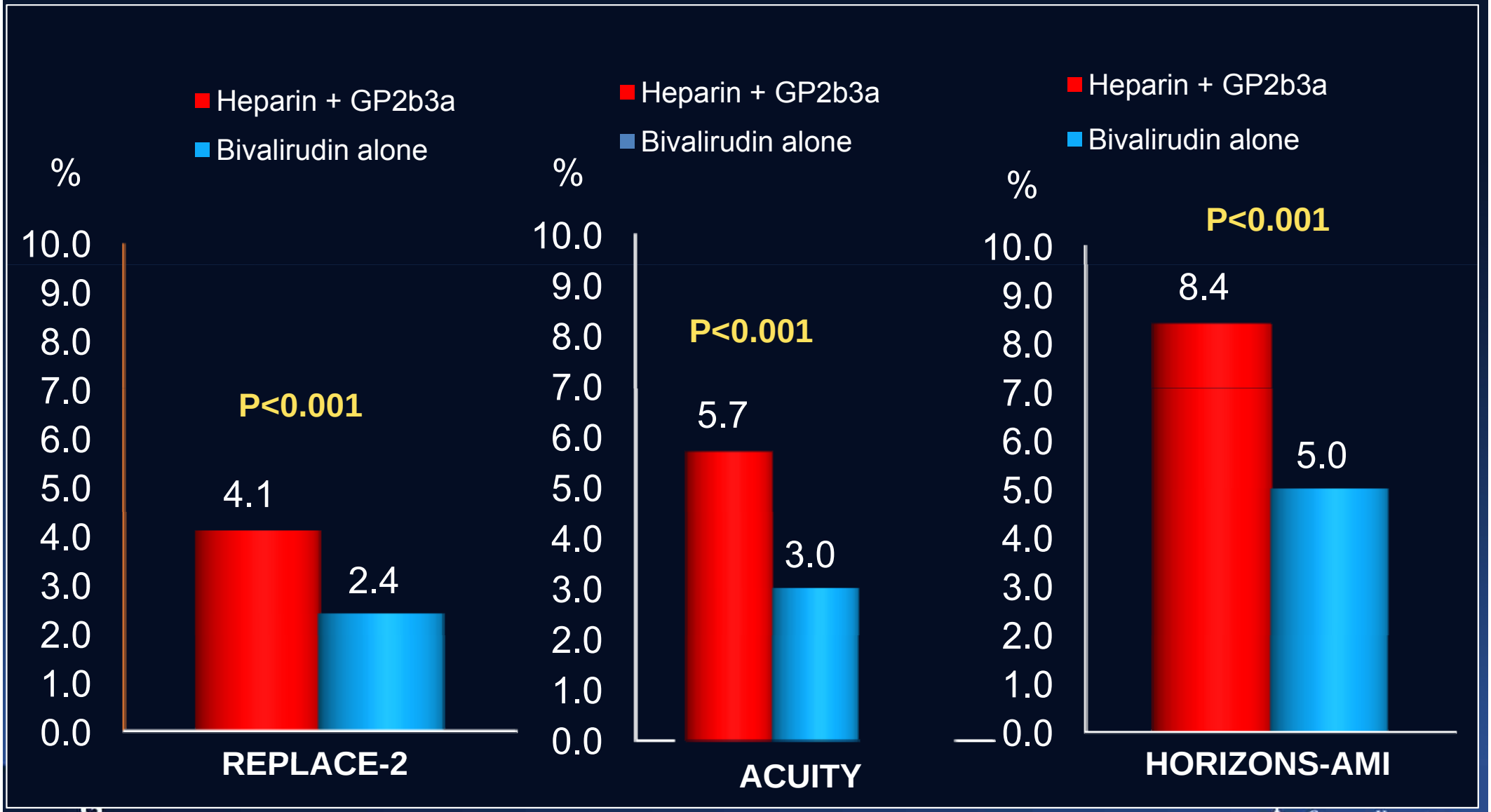
Unresolved questions in STEMI

Bivalirudin Radial

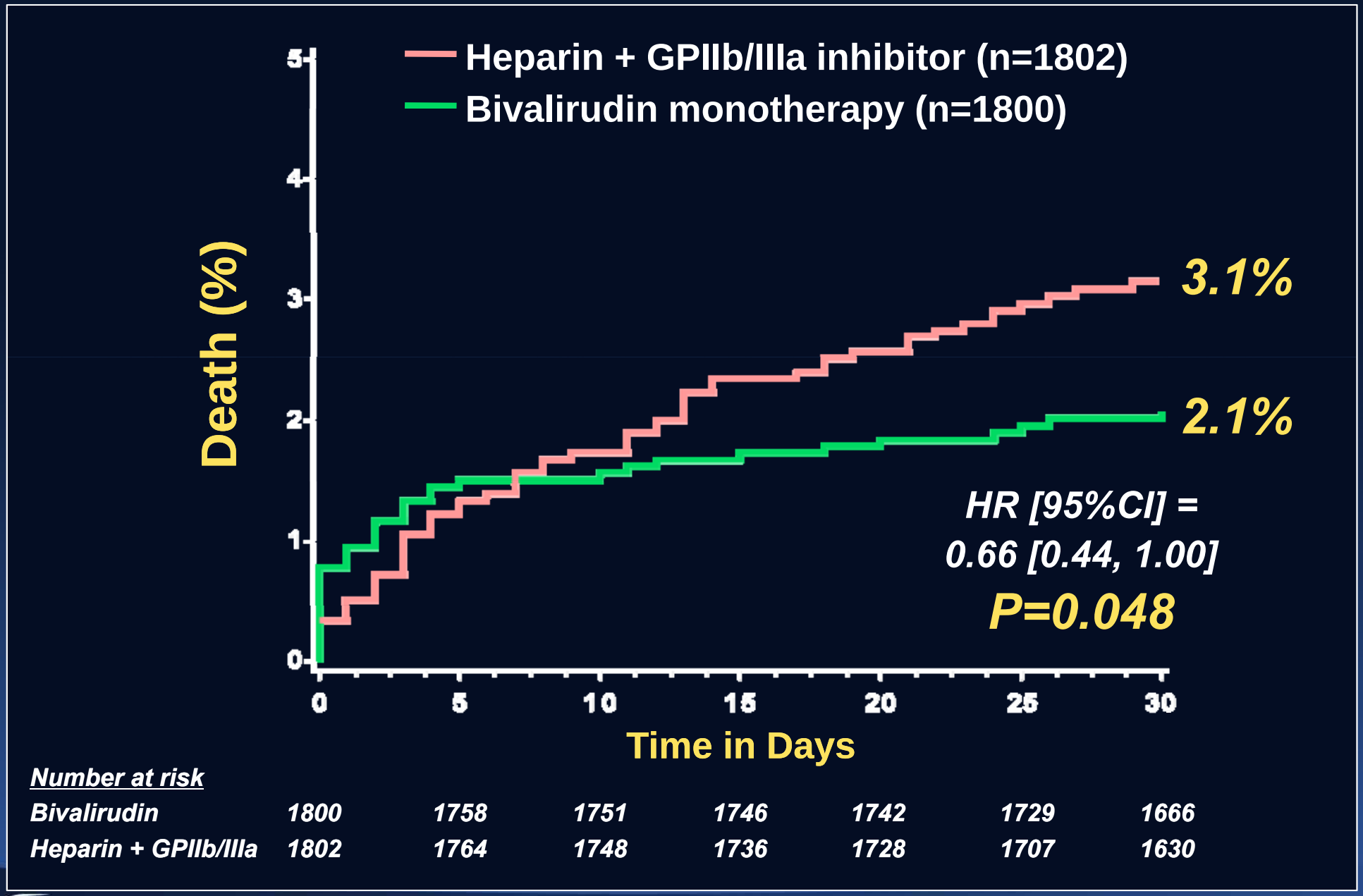
vs.

Bivalirudin Femoral + closure device

Less Bleeding with Bivalirudin: 17,393 patients



HORIZONS-AMI: 30-Day Mortality



Number at risk

Bivalirudin	***1800***	***1758***	***1751***	***1746***	***1742***	***1729***	***1666***
Heparin + GPIIb/IIIa	***1802***	***1764***	***1748***	***1736***	***1728***	***1707***	***1630***

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Stone, G et al. NEJM 2008;358:2218-2230

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RIFLE STEACS – population

Procedural characteristics

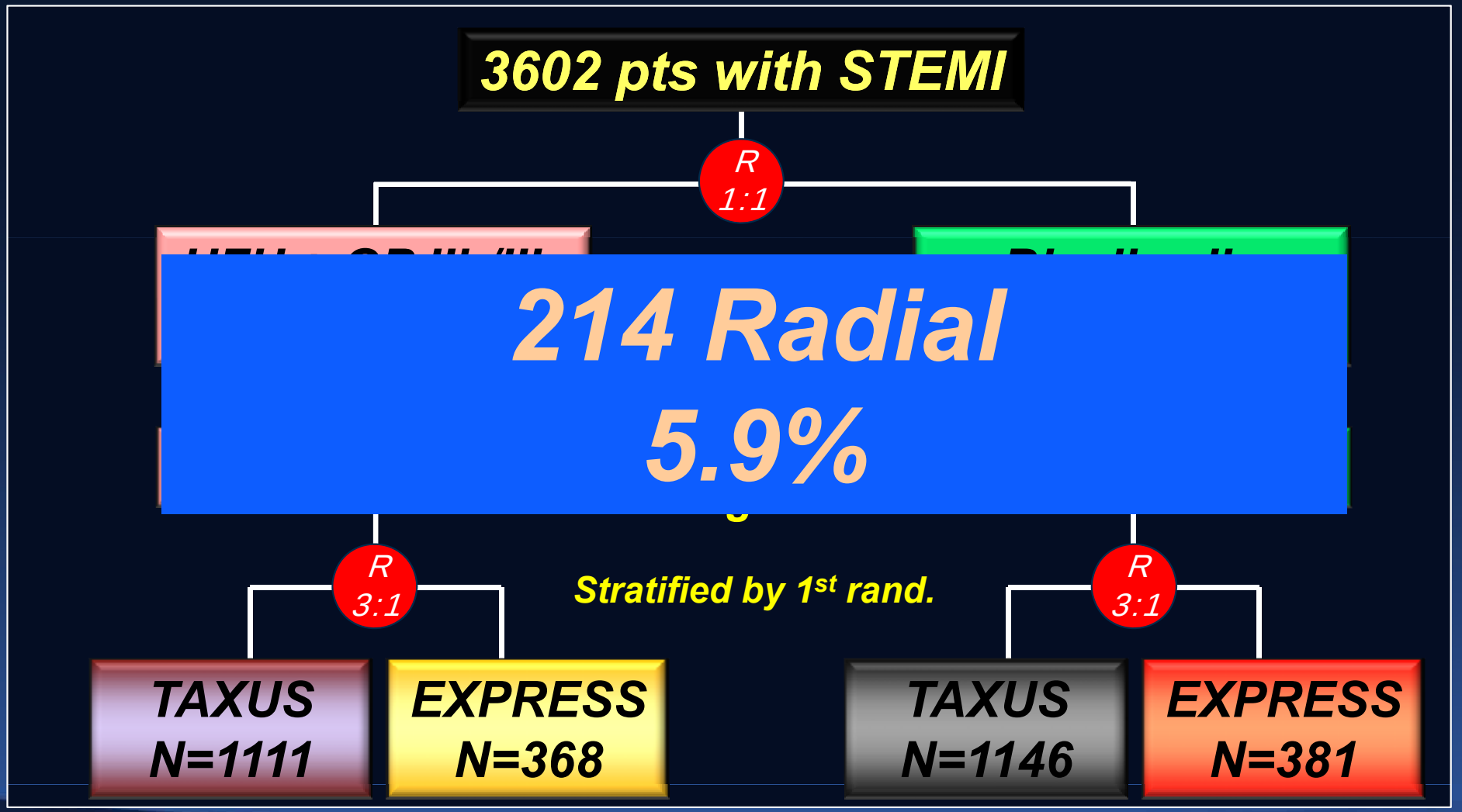
	overall (1001)	Femoral arm (n=501)	Radial arm (n=500)	p value
Symptom-balloon time (min)	313±277	322±292	328±301	0.752
SBP at admission (mmHg)	128±28	126±28	129±27	0.138
Prior failed thrombolysis	7.6%	7.0%	8.2%	0.477
Heparin dose (U/Kg)	75.6±21	75.2±20	76.0±22	0.548
GP IIb/IIIa inhibitors	68.6%	69.9%	67.4%	0.414
Bivalirudin	7.6%	7.2%	8.0%	0.635
Thrombectomy	40.7%	40.5%	40.8%	0.949
Intra aortic balloon pump	8.0%	8.4%	7.6%	0.727

RIVAL

	Radial (n=3507) %	Femoral (n=3514) %
ASA	99.2	99.3
Clopidogrel	96.0	95.6
LMWH	51.5	51.8
UFH	33.3	31.6
Fondaparinux	10.9	10.8
Bivalirudin	2.2	3.1
GP IIb IIIa inhibitors	25.3	24.0
PCI	65.9	66.8
CABG	8.8	8.3

HORIZONS AMI

Harmonizing Outcomes with Revascularization and Stents in AMI



Primary endpoint: NACE: Net Adverse Clinical Events and Major Bleeding (non CABG). NACE= Major Bleeding (non CABG) or Major adverse cardiovascular events (MACE, All-Cause death, Reinfarction, Ischemic TVR, Stroke)

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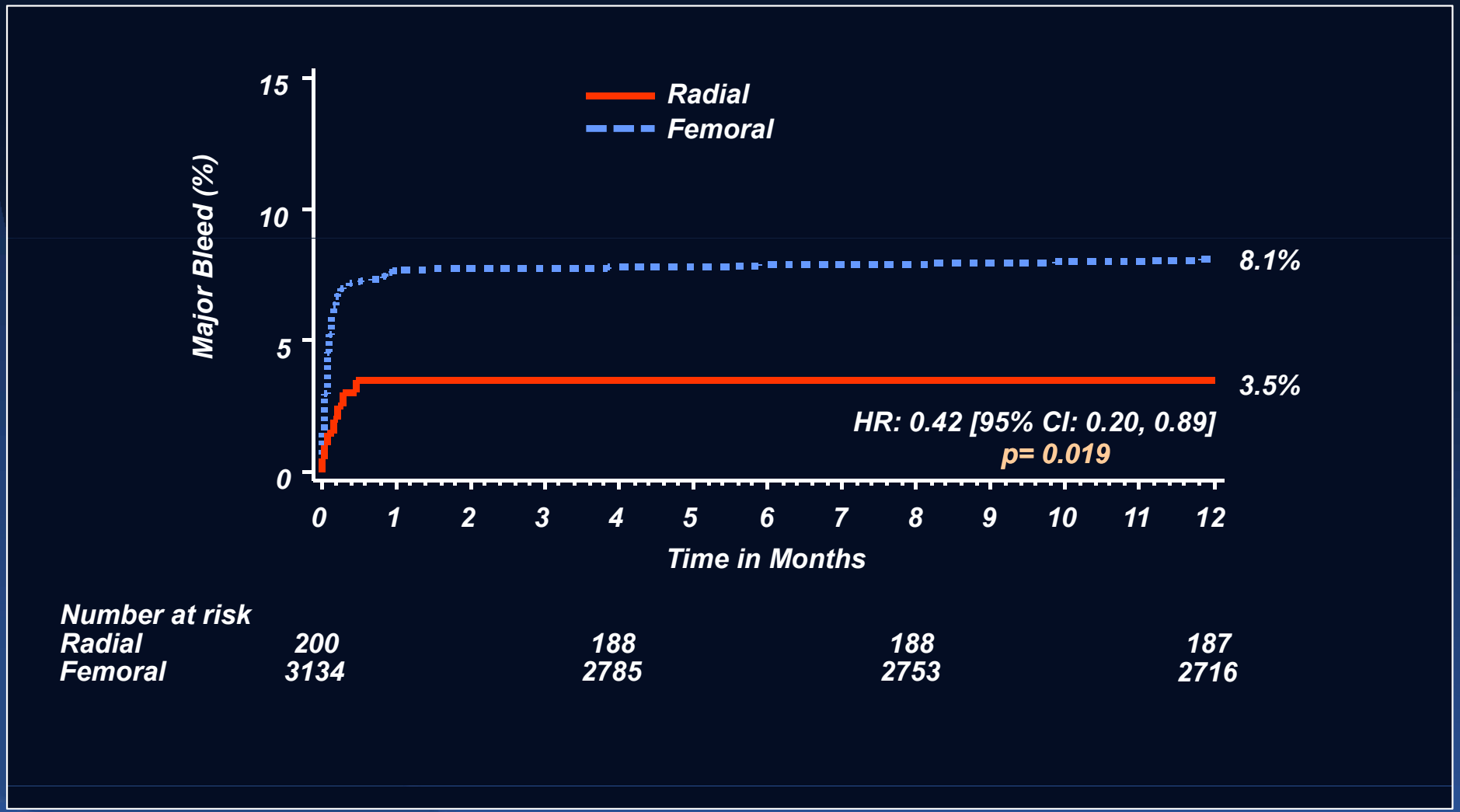
Kaplan-Meier Curves of 1-Year Cumulative Major Bleeding (non-CABG Related)



Généreux P. et al., Eurointervention;2011, 905-916

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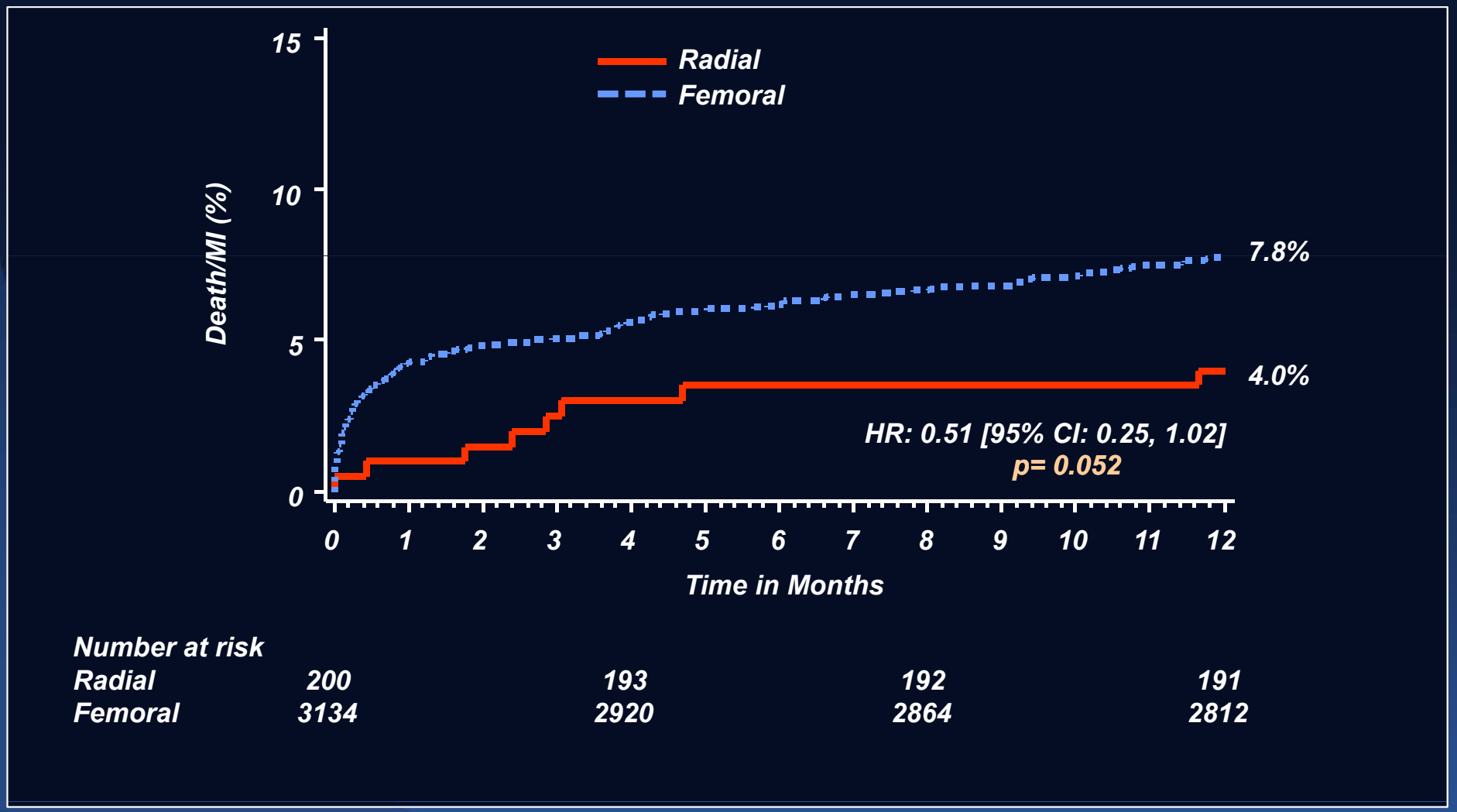
Kaplan-Meier Curves of 1-Year Cumulative Death/MI



Généreux P. et al., Eurointervention;2011, 905-916

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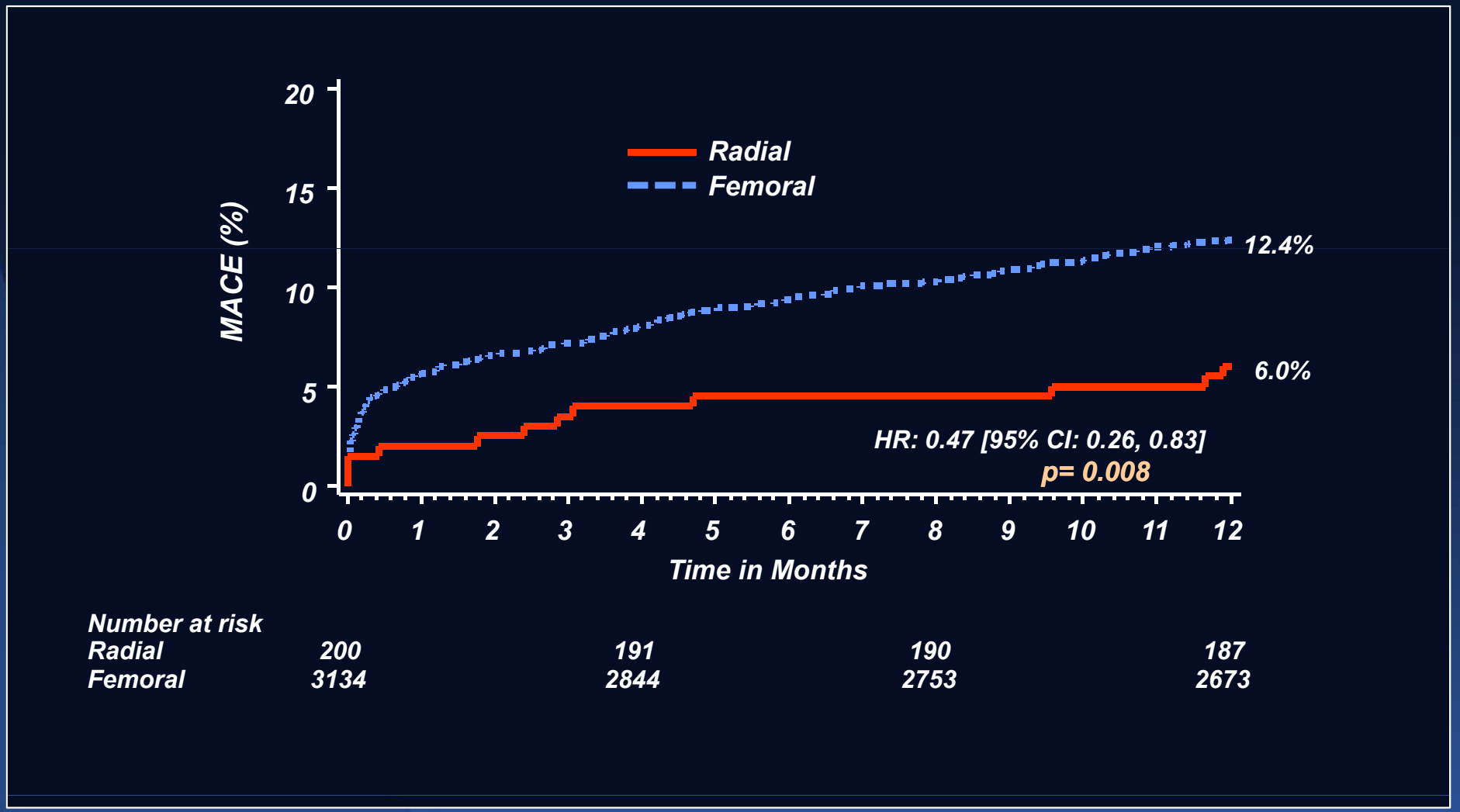
Kaplan-Meier Curves of 1-Year Cumulative *MACE*



Généreux P. et al., Eurointervention;2011, 905-916

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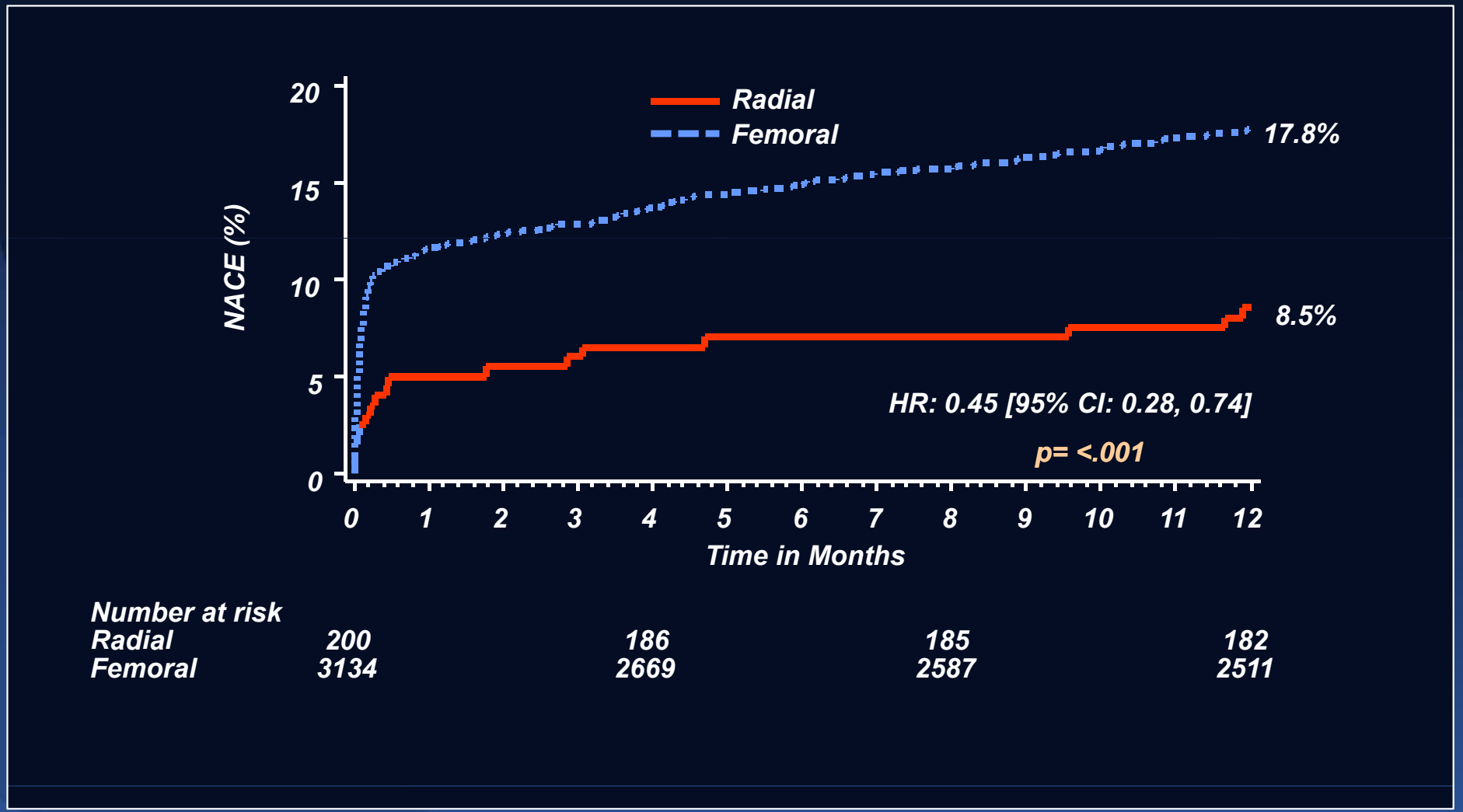
Kaplan-Meier Curves of 1-Year Cumulative NACE



Généreux P. et al., Eurointervention;2011, 905-916

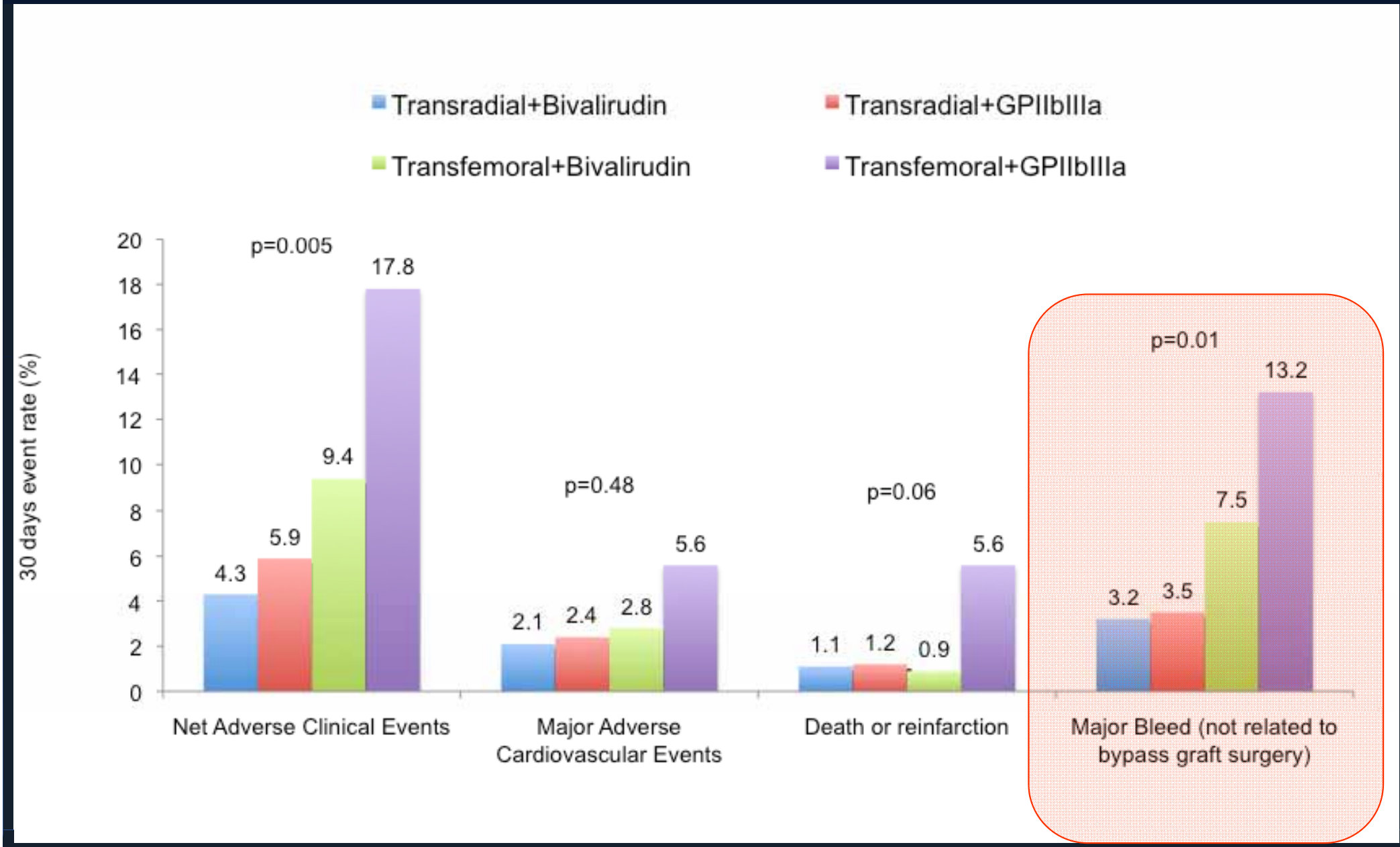
Multivariable Analysis
30 days and 1-year

30 days analysis		Hazard Ratio	p value
NACE	Radial (vs. Femoral)	0.31 [0.15, 0.66]	*<0.01*
MACE	Radial (vs. Femoral)	0.33 [0.10, 1.04]	0.058
Major Bleeding (non-CABG related)	Radial (vs. Femoral)	0.40 [0.18, 0.90]	*0.02*

1-year analysis		Hazard Ratio	p value
NACE	Radial (vs. Femoral)	0.40 [0.22, 0.74]	*<0.01*
MACE	Radial (vs. Femoral)	0.46 [0.23, 0.93]	*0.03*
Major Bleeding (non-CABG related)	Radial (vs. Femoral)	0.27 [0.07, 1.09]	0.06

The following potential covariates were included in the model : age, sex, race, BMI, Killip class, baseline anemia (defined as baseline hematocrit below 39% for men and 36% for women), platelet counts, creatinine clearance <60ml/min, white blood cell count, left ventricular ejection fraction, hypertension, hyperlipidemia, smoking, diabetes, insulino-dependent diabetes, previous MI, previous CABG, previous CAD (coronary artery disease), angina, heart failure, peripheral vascular disease, clopidogrel loading dose, pre-randomization heparin, baseline and discharge aspirin, baseline and discharge thienopyridines, randomization to bivalirudin vs. UFH+GP, symptom to first balloon time, LAD disease and access site (Radial vs. Femoral).

PG3



Généreux P. et al., Eurointervention;2011, 905-916

PG3 please review main horizon manuscript: exclusion: schock?

Also: do a slides with limitations for both study (ACUITY and HORIZON)
PHILIPPE GENEREUX, 2012-09-12

Access and Closure device used in HORIZONS

Access and closure	%
Radial	5.9%
Femoral without VCD	66%
Femoral with VCD	27%
AngioSeal	58.3%
StarClose	32.4%
PerClose	8.7%
Other	0.6%

30-day outcomes based on Access site and Closure device used in HORIZONS: Bivalirudin only

Outcome	Radial n=103	Femoral with VCD n=486	Femoral without VCD n=1196	p-value All Groups	P-value Radial vs. VCD	P-value Radial vs. no VCD	P-value Femoral VCD vs. Femoral no VCD
Major Bleeding (non-CABG related)	2.9% (3)	3.7% (18)	6.2% (73)	0.0680	0.6906	0.1811	0.0448
Retroperitoneal bleeding	0.0% (0)	0.0% (0)	0.5% (6)	0.2243	N/A	0.4704	0.1161
Access site hemorrhage	0.0% (0)	0.0% (0)	0.3% (3)	0.4755	N/A	0.6103	0.2680
Hematoma >=5cm at puncture site	0.0% (0)	1.2% (6)	1.3% (15)	0.5227	0.2591	0.2537	0.9624
Blood product transfusion	0.0% (0)	1.4% (7)	2.8% (33)	0.0702	0.2223	0.0887	0.1029

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Meta-Analysis 2004
30 Studies 37,066 patients

Limitations

Heterogeneity in Definition of bleeding
No Bivalirudin used
Old generation of closure devices (up to 20%faillure rate)
Lots of studies using 7-8Fr sheath…
Bias in selection of patients suitable for VCD

Favor VCD *Favor Manual compression*

Nikolsky et al. J Am Coll Cardiol 2004;44:1200 –9

Upcoming trials

SAFARI-STEMI Trial

The SAfety and efficacy of Femoral Access versus Radlal access for Primary PCI in STEMI

2770 pts with STEMI with symptom onset ≤12 hours

1:1

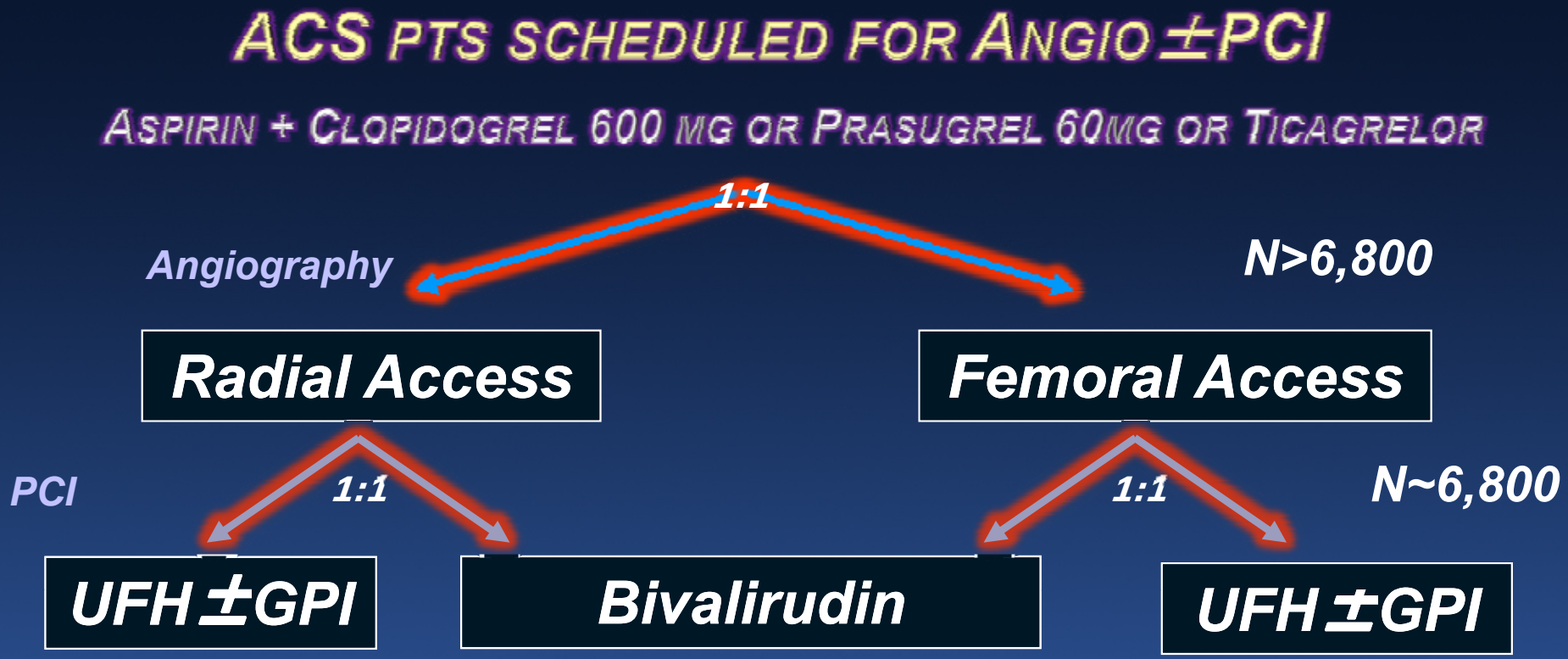
- Transradial Access (TRA) + Bivalirudin
- Transfemoral Access (TFA) + Bivalirudin

Primary Outcome
NACE: Death, reMI, stroke or TIMI bleed (major/minor)

PI: Michel Le May MD,
University of Ottawa Heart Institute,
Ottawa, Canada
ClinicalTrials.gov Identifier:
NCT01398254

MATRIX Trial

Minimizing Adverse hemorragic events by TRansradial access site and AngioX study



PI: Marco **Valgimigli**

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Key points

1) While both are associated with a bad prognosis, non-access site bleeding is associated with a worse outcome than access site bleeding
2) Bivalirudin is associated with the lowest rate of bleeding
3) Radial has been shown to be superior to femoral access according to bleeding outcomes in many studies but has never been compared head to head with closure devices in the bivalirudin era

Key points

5) **Current Data** comparing radial vs. femoral access with closure devices are retrospective/post-hoc analysis contaminated with selection bias

6) Randomized control trials are needed

MATRIX trial

SAFARI trial

My personal recommendations:

1) Use Bivalirudin in ACS and high risk bleeding patients
2) Radial access should be the default technique in all patients
3) If you don't know how to do radial and/or are not planning to learn it, at least use bivalirudin + vascular closure device in high risk patients…?

Thank you

Clinical History

72 yo F 160 cm 60 kg

HTN / Dyslipidemia / Active Smoker / Poor compliance

Severe PVD on Warfarin s/p FEM-FEM bypass

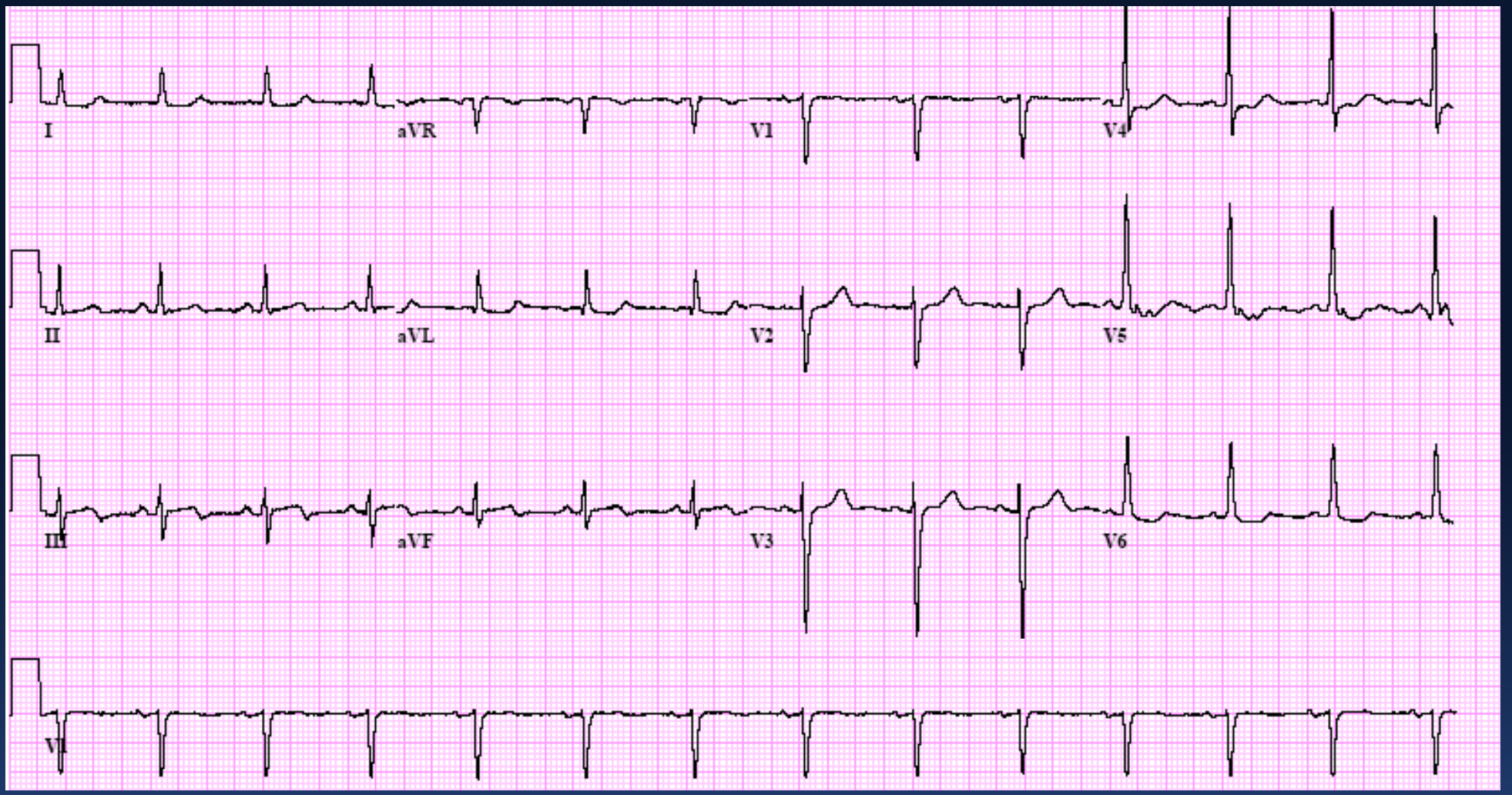
New onset of angina CCS 4/4 x 4 hours

"No active bleeding"

Hgb 6.6 / INR 1.5 / Cr-1.0

Troponine 5

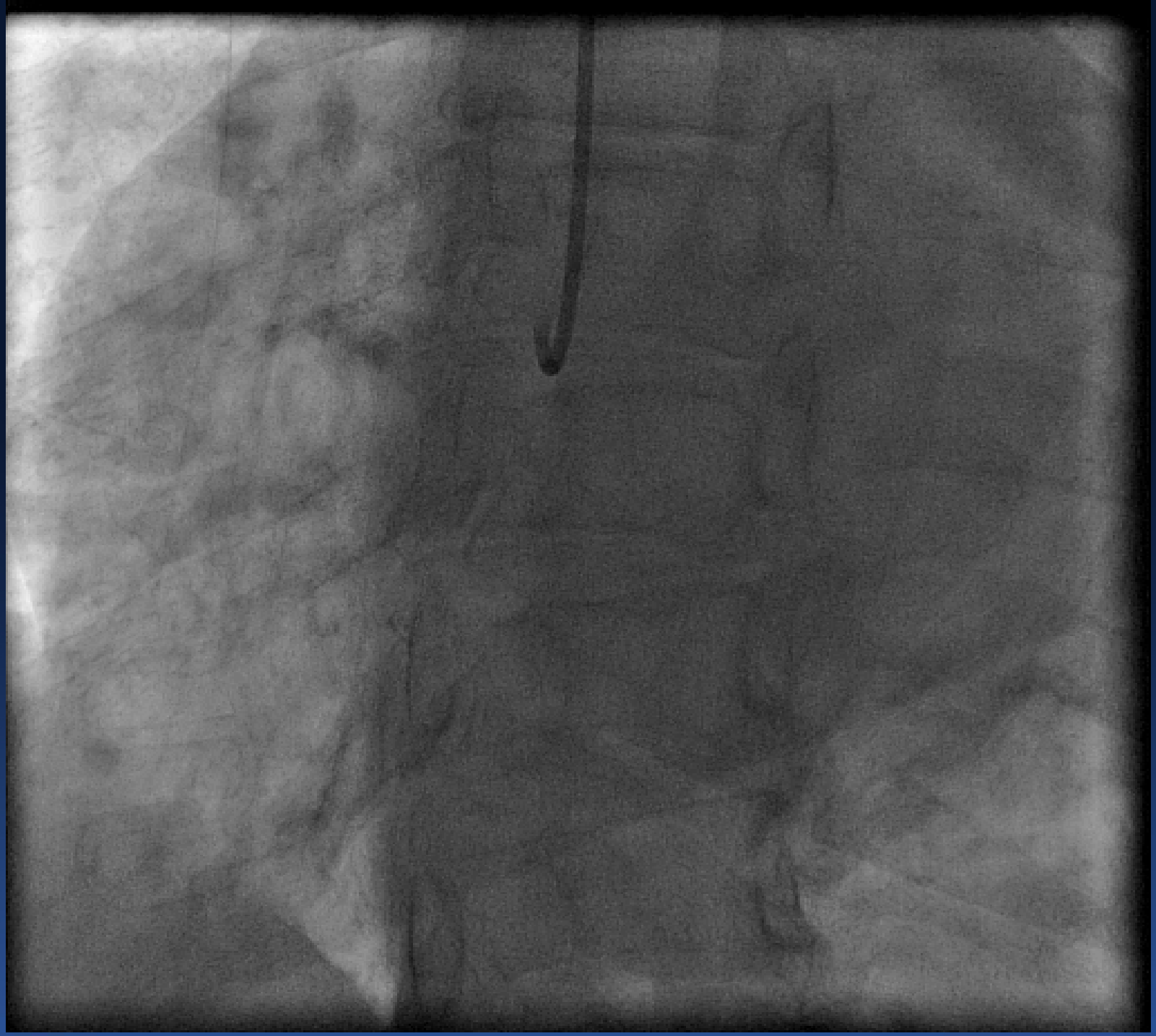
ASA 325 mg / 3 RBCU given



Ongoing chest pain post transfusion / Hgb 10.1

BP 95/60 HR 95/min

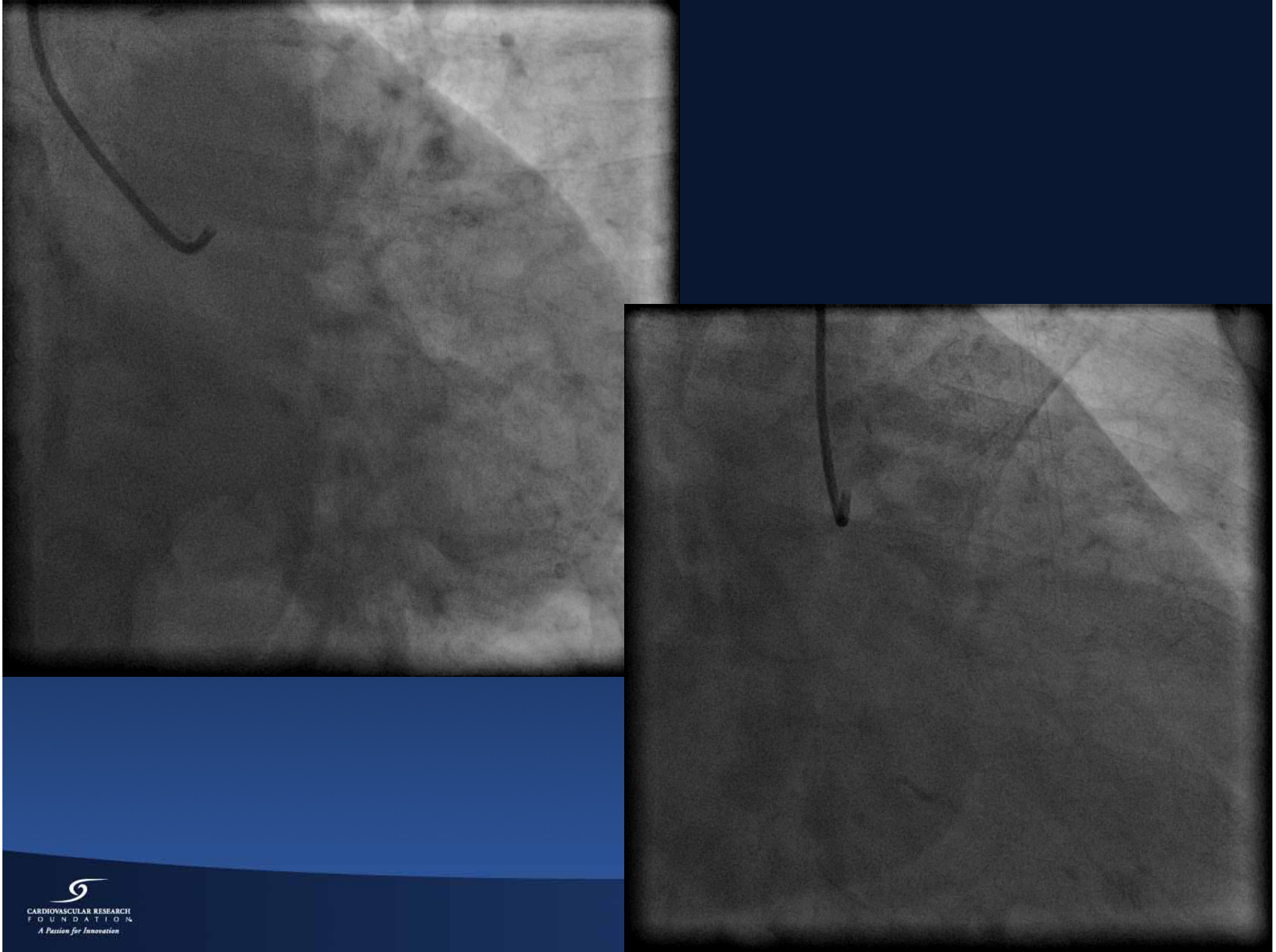
CT Chest-Abdo-Pelvis negative for Aortic dissection and bleeding



CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

RRA 6Fr / 4000 u heparine

COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian



CARDIOVASCULAR RESEARCH
FOUNDATION
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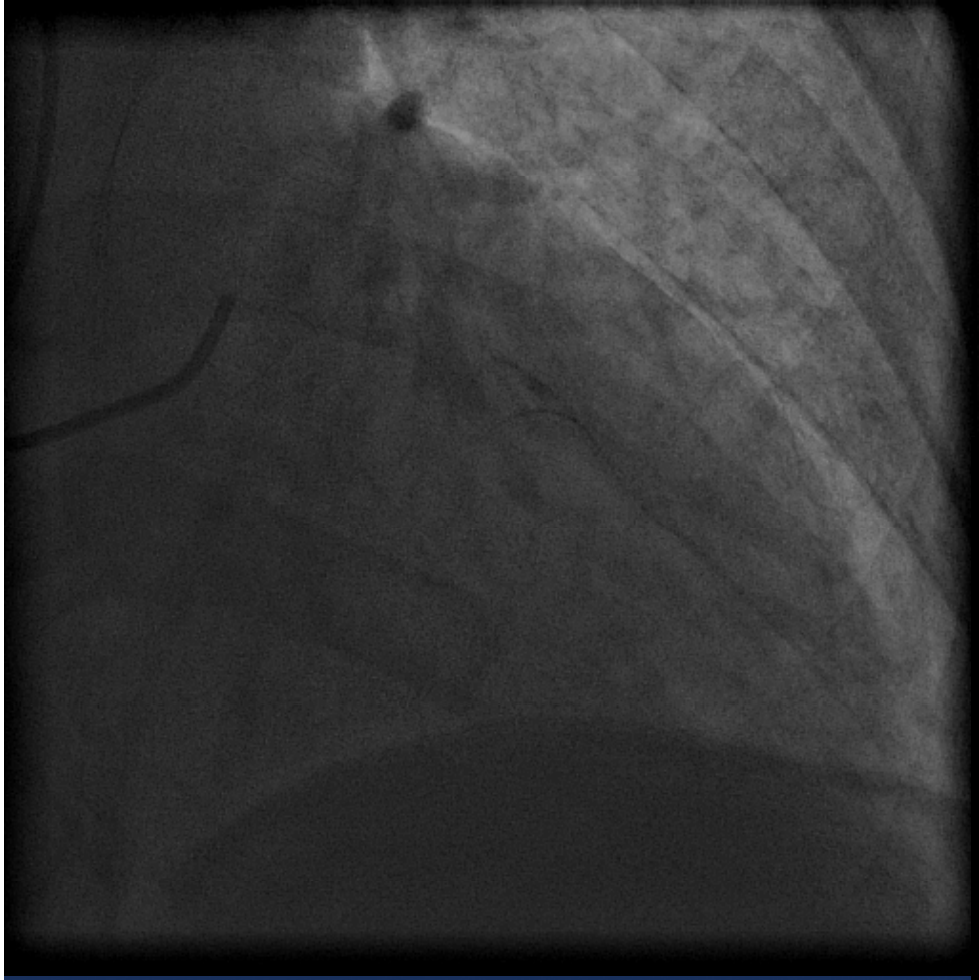

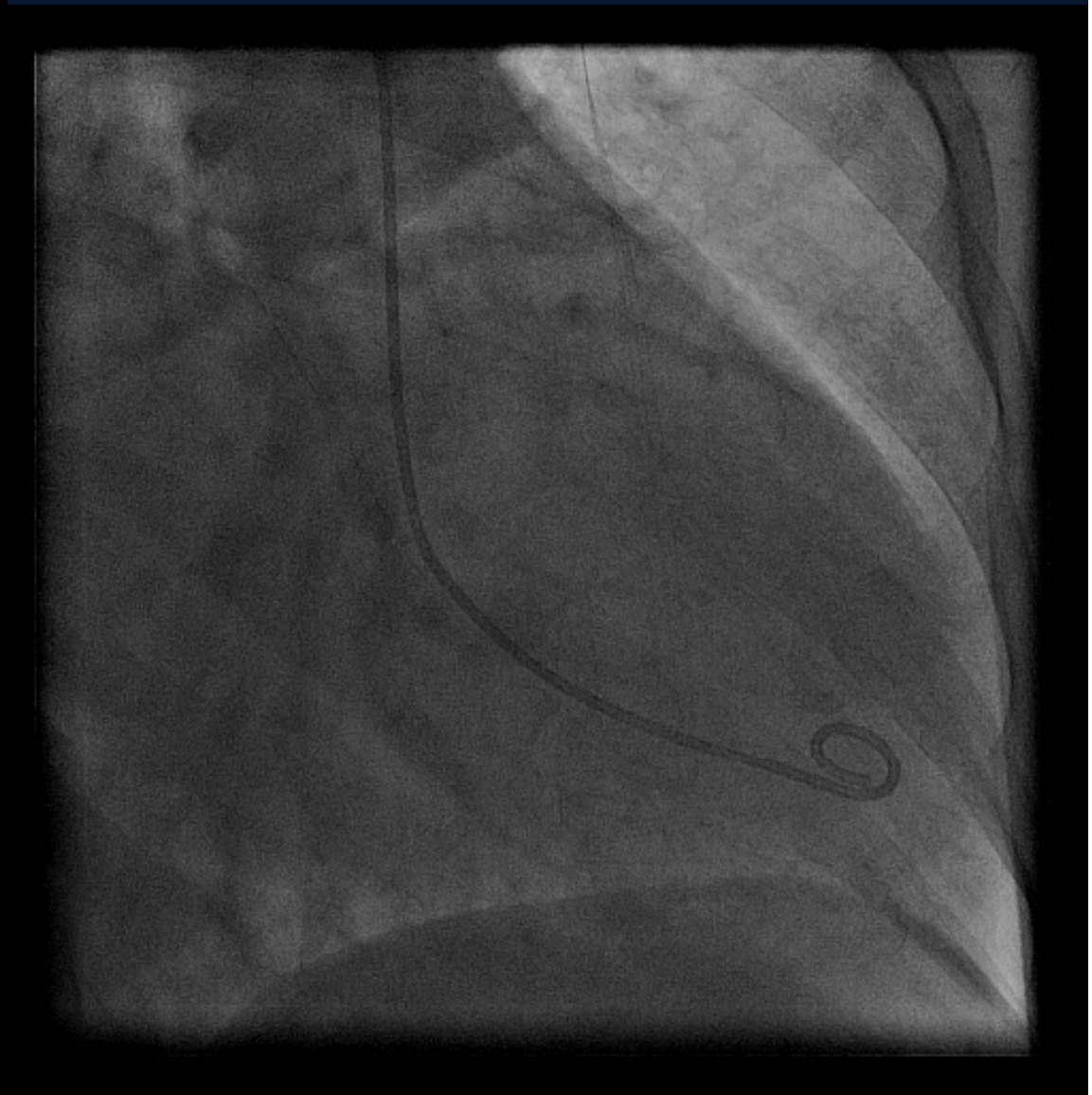

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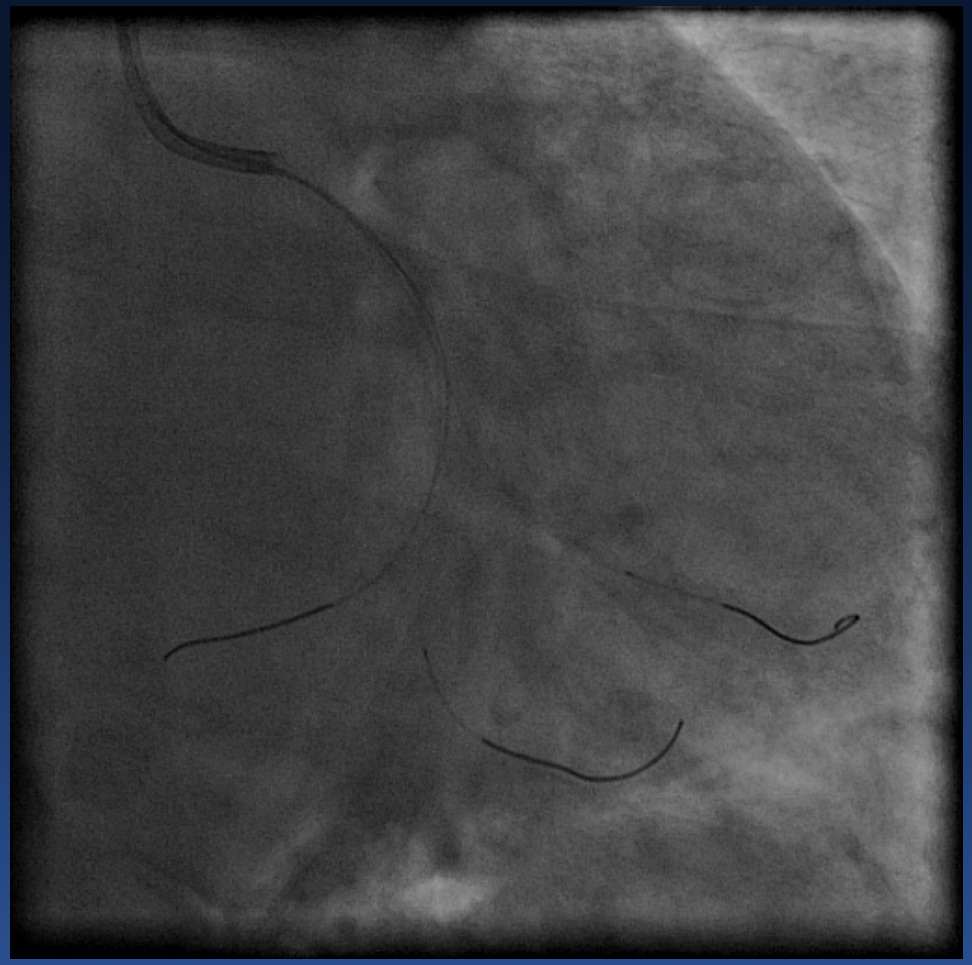
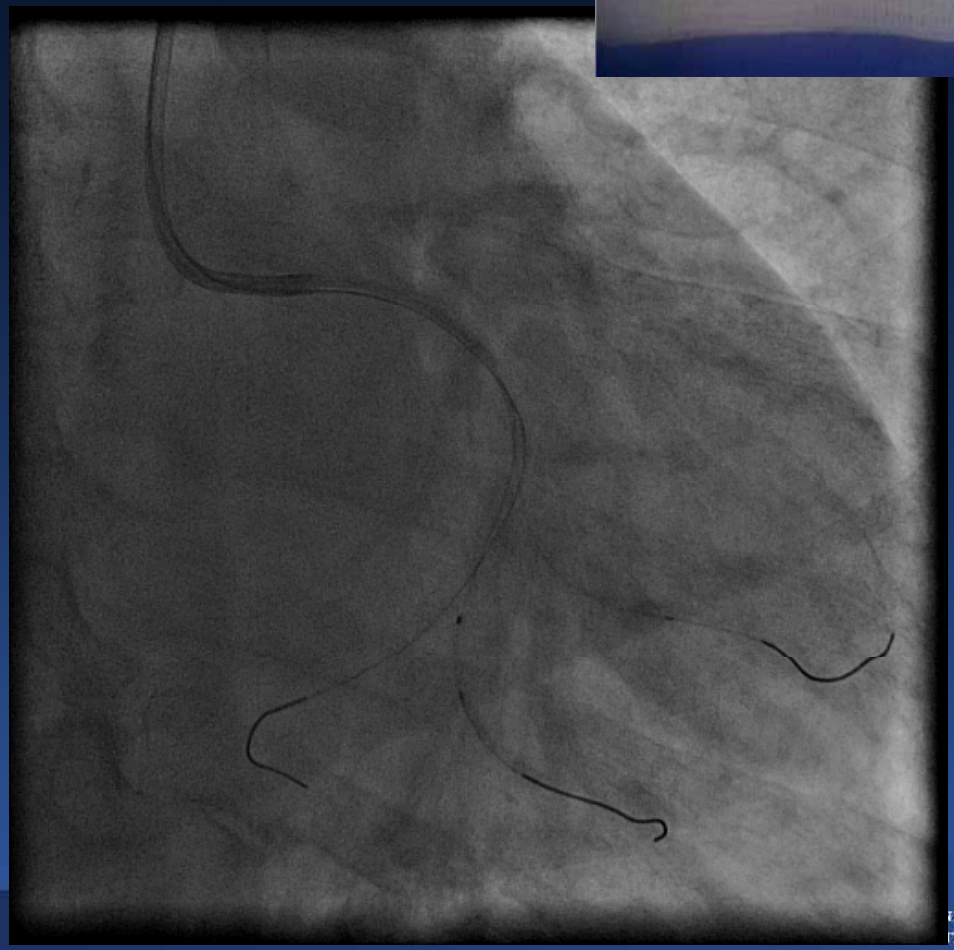
Strategy?

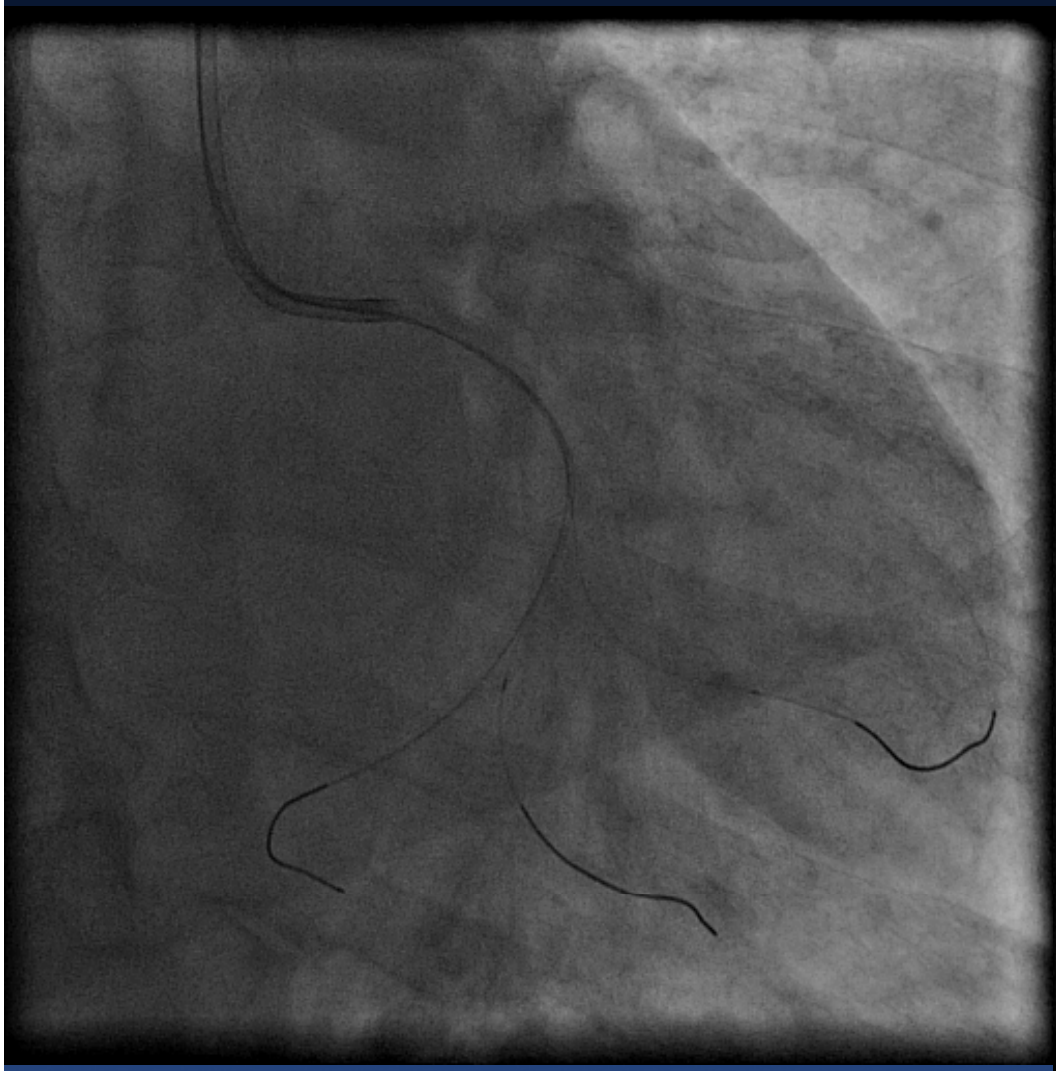
RRA / EBU 3.5 7 Fr/ Angiomax / Plavix 600mg loading

2 BMW and 1 Pilot 50 wires

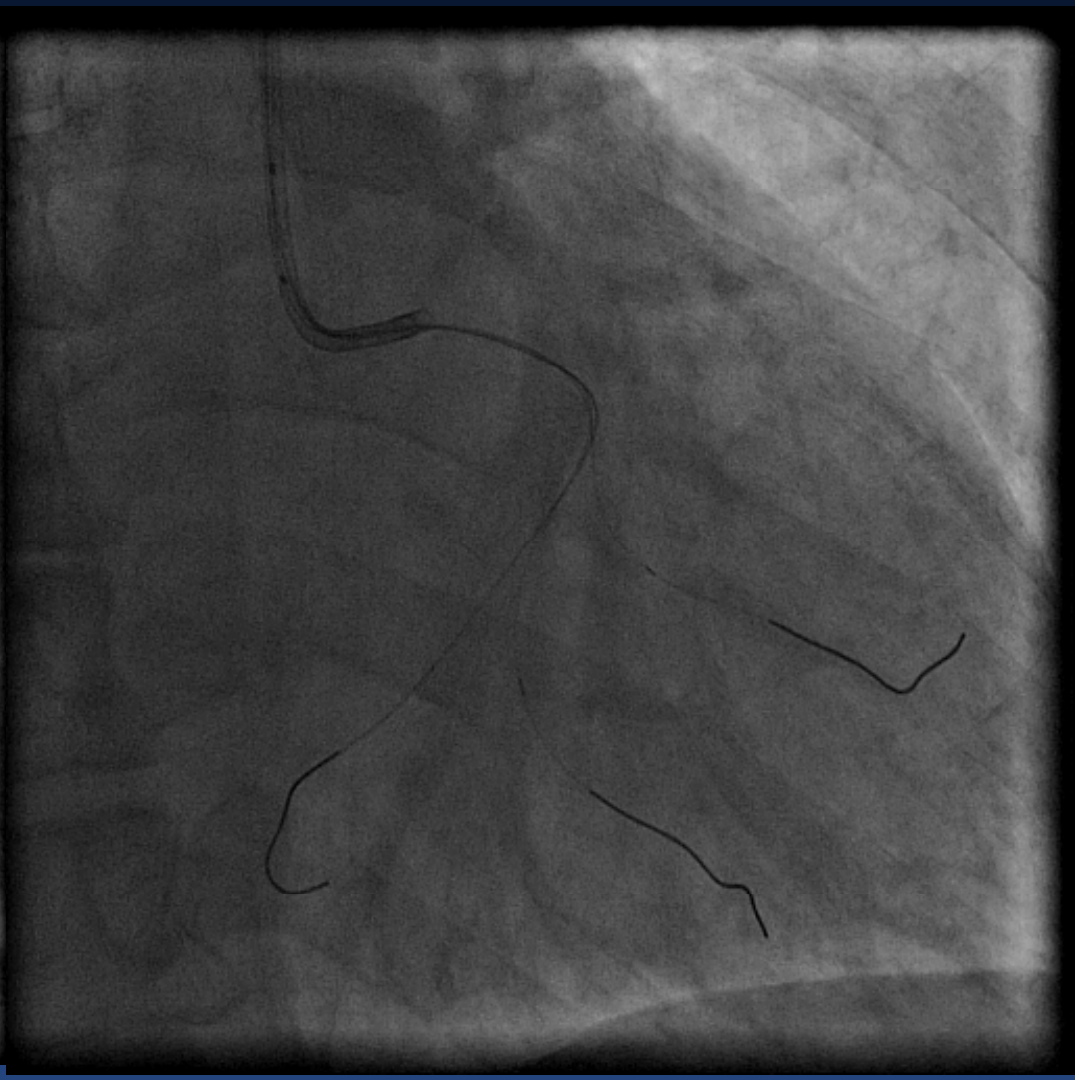
Thrombectomy x 3





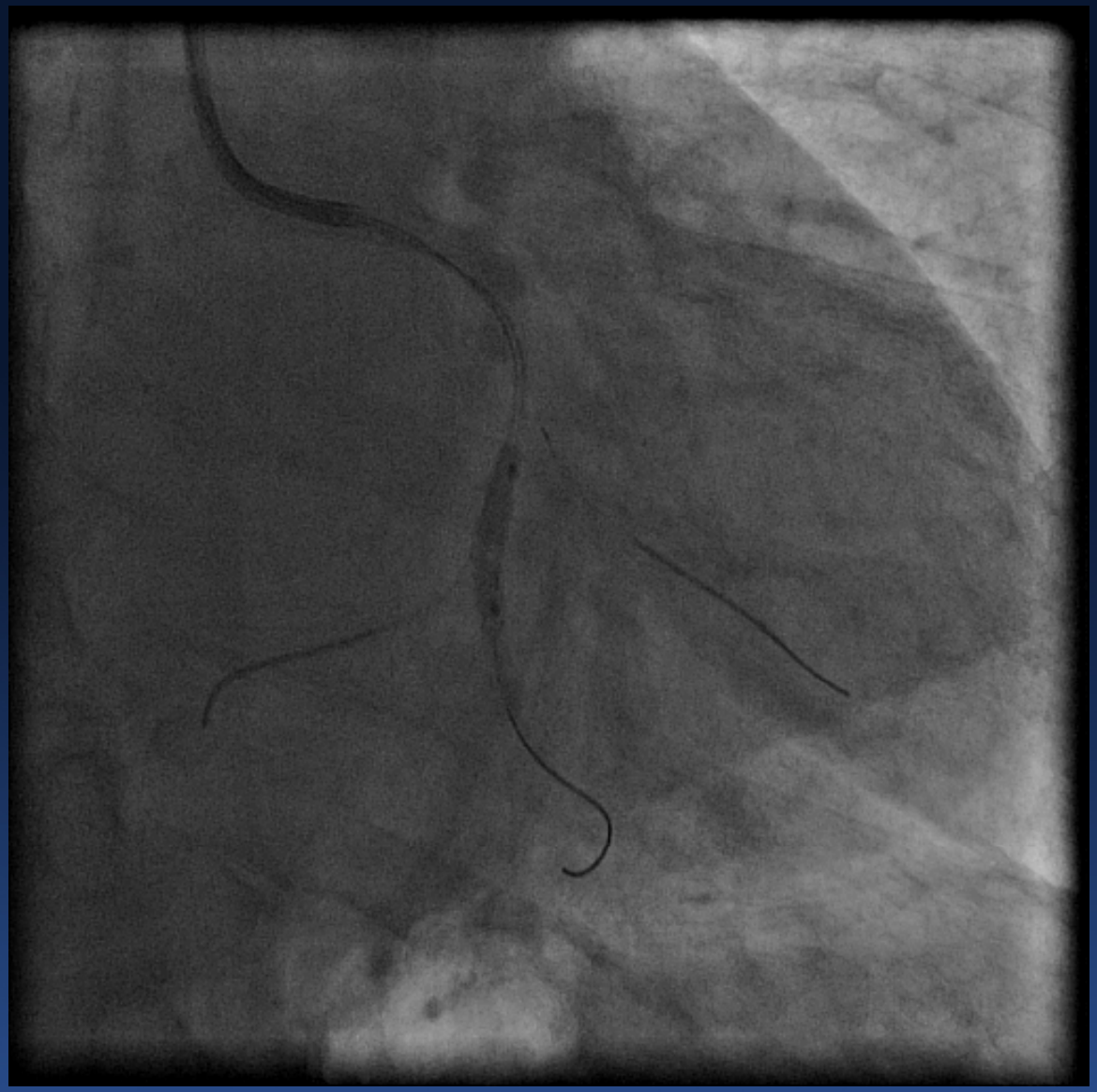


Post thrombo-aspiration



Post multiple inflations Maverick 2.5x15mm

OM2-OM3-dLcx

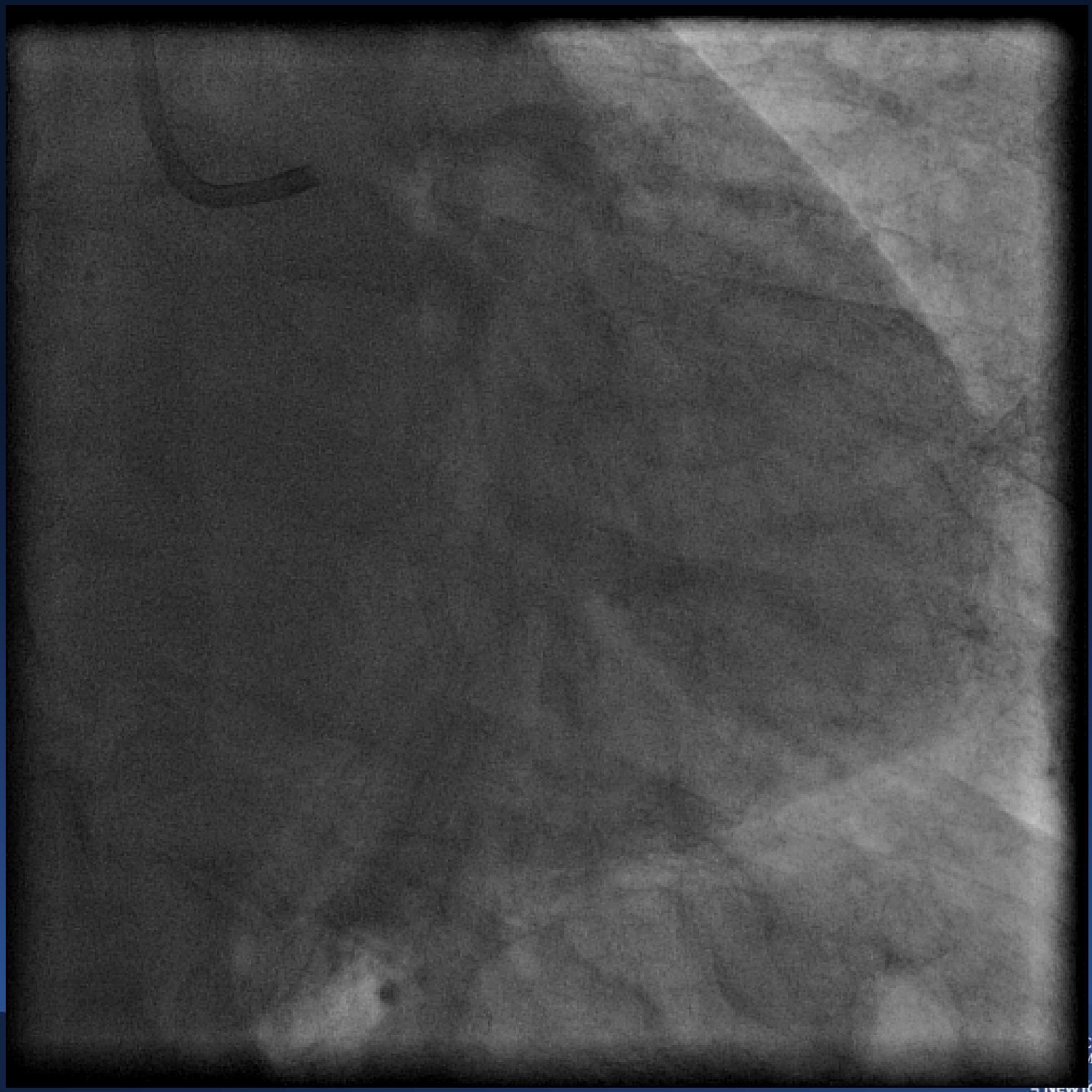


Mini-vision 2.75 x 24mm

Post dilatation Quantum 3.0

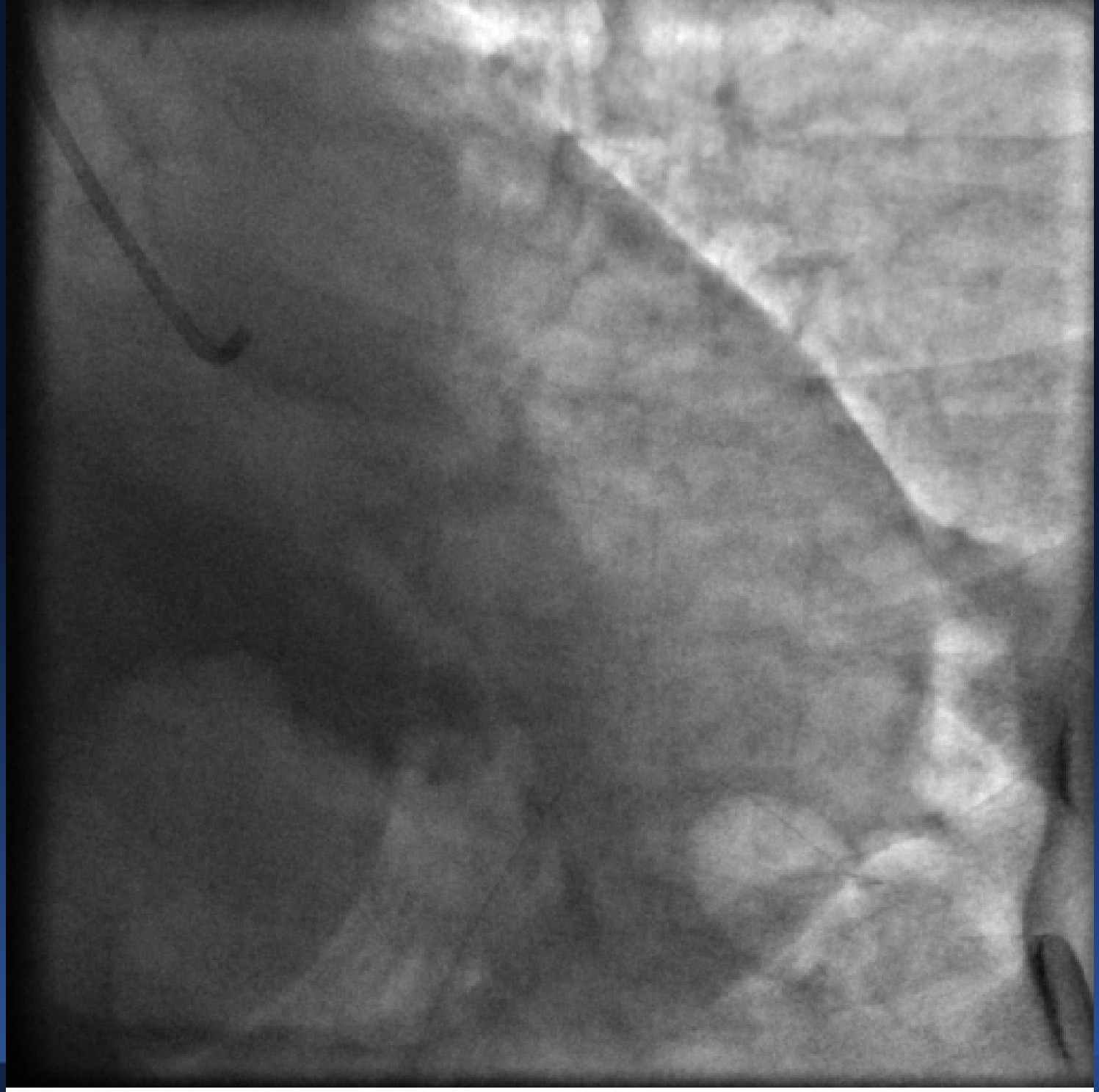
POBA distal Lcx and OM2

Maverick 2.5

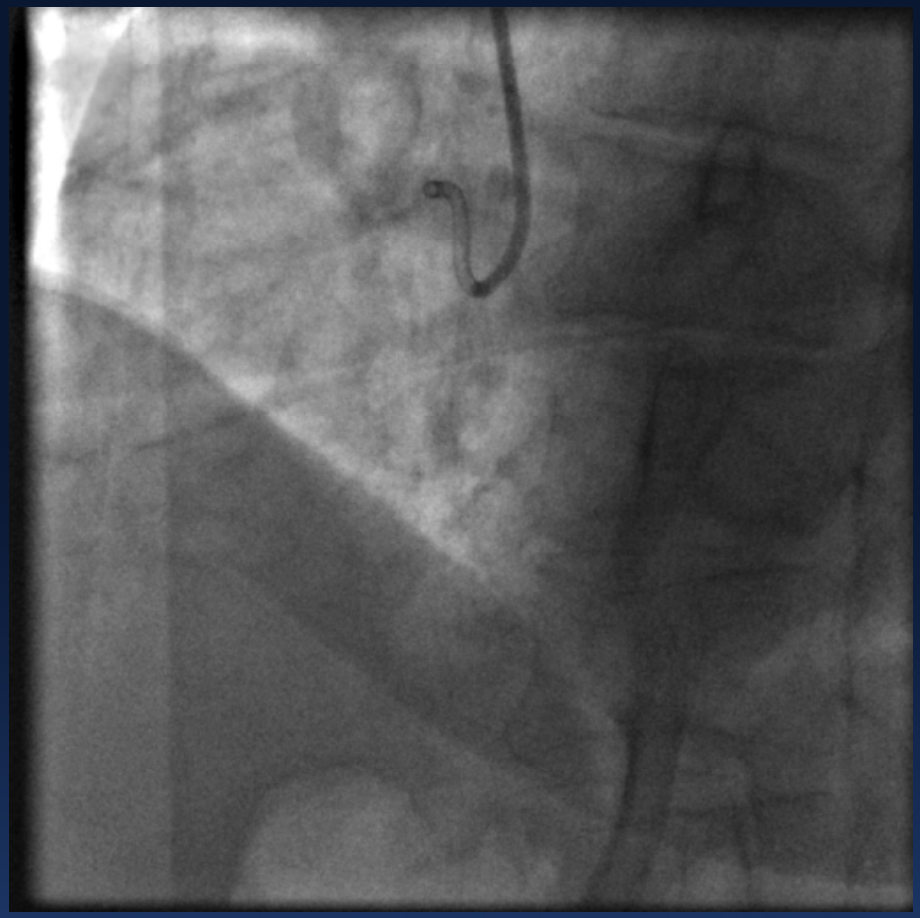


Follow-up

- 240 cc contrast
- 2700 mgy
- No chest pain
- EKG resolution of ST changes
- Ck max 200
- Tropo max 16
- Hgb stable post PCI
- Stage PCI of RCA 4 weeks later via RRA



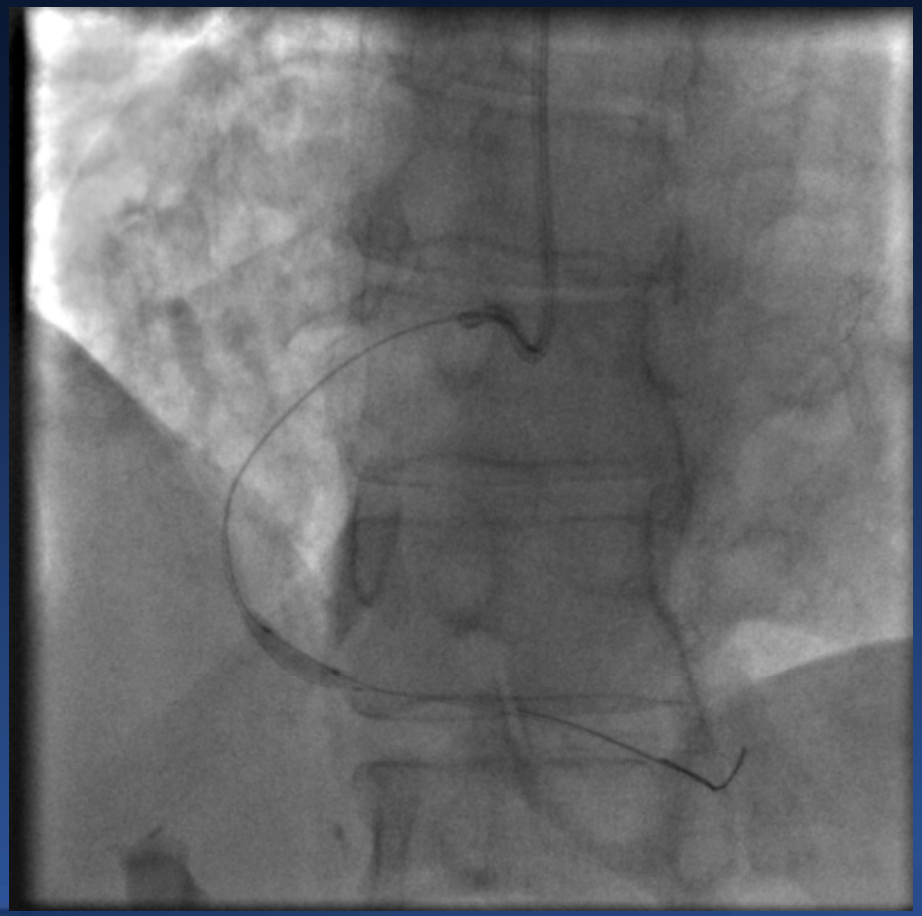
4 weeks later



RRA access

AL 0.75 6 Fr

Angiomax

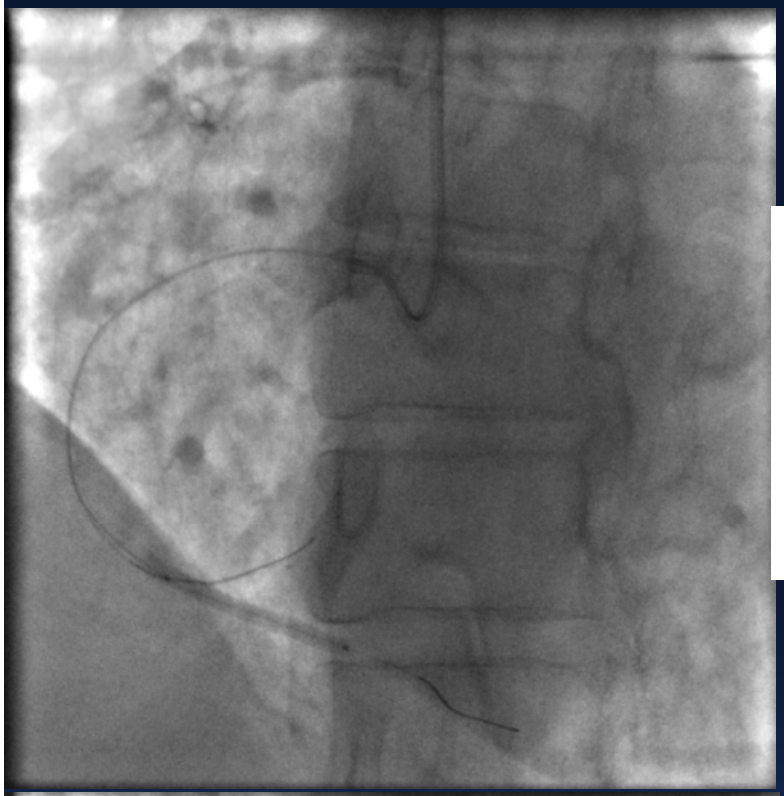


Whisper wire and BMW 0.0014

Fine cross

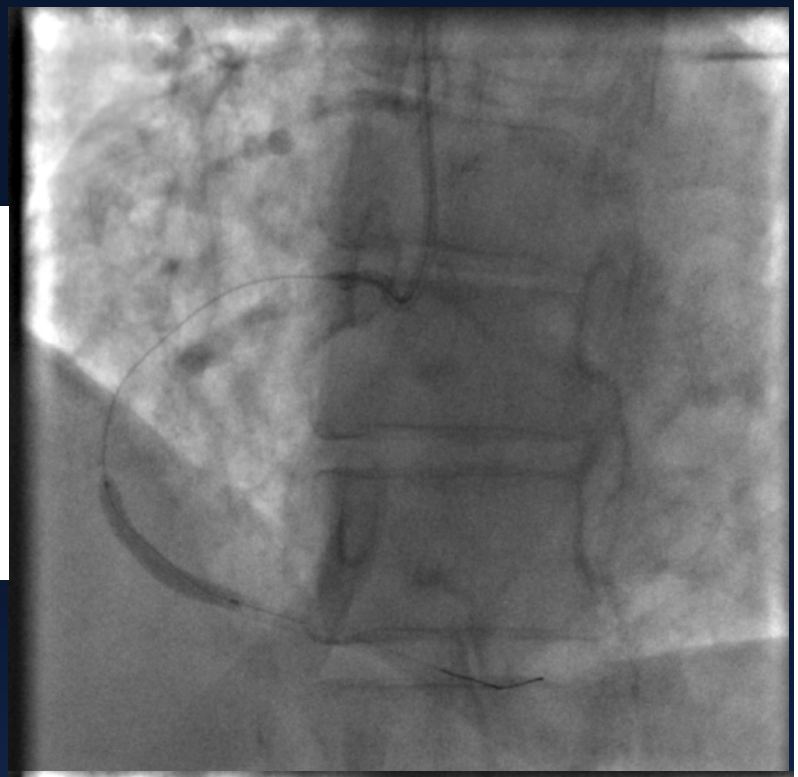
Wiggle wire RPDA (Whisper wire removed)

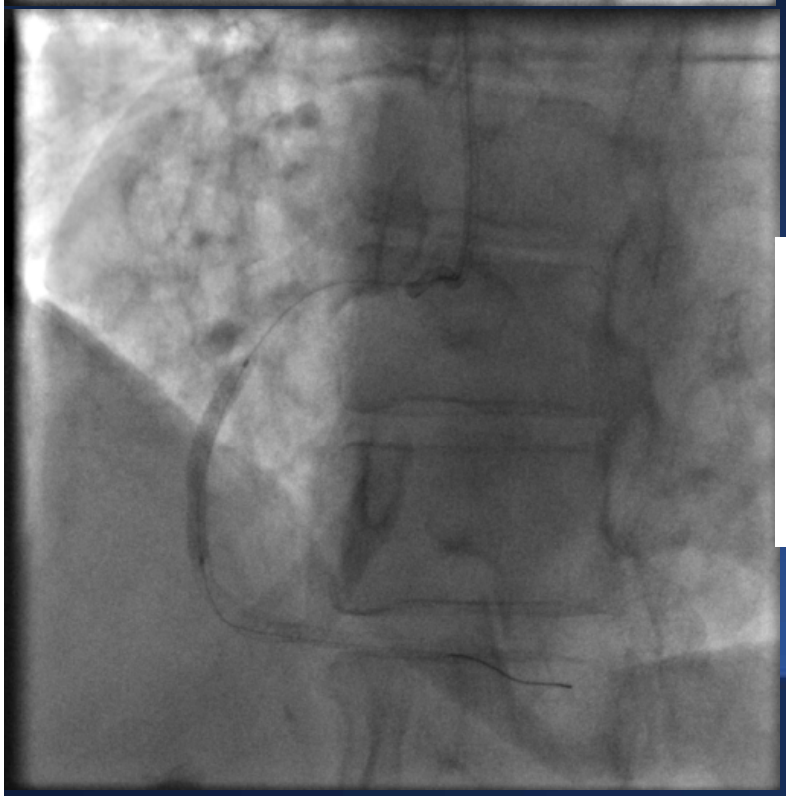
Pre-dilatation 2.5 x 15mm



Mini-vision 2.5x28mm
RPDA

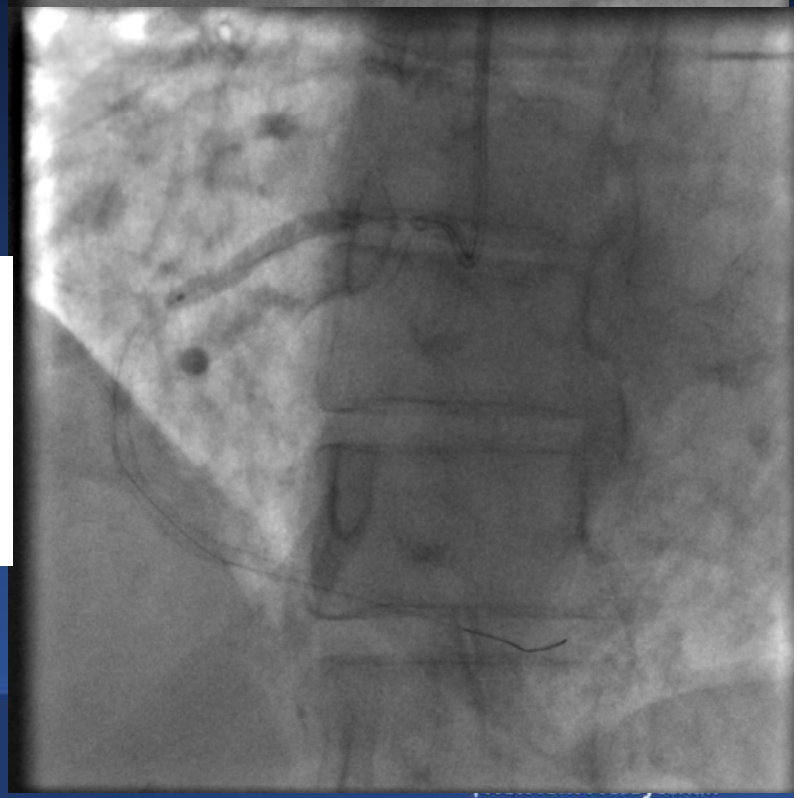
Veriflex 3x32mm
dRCA

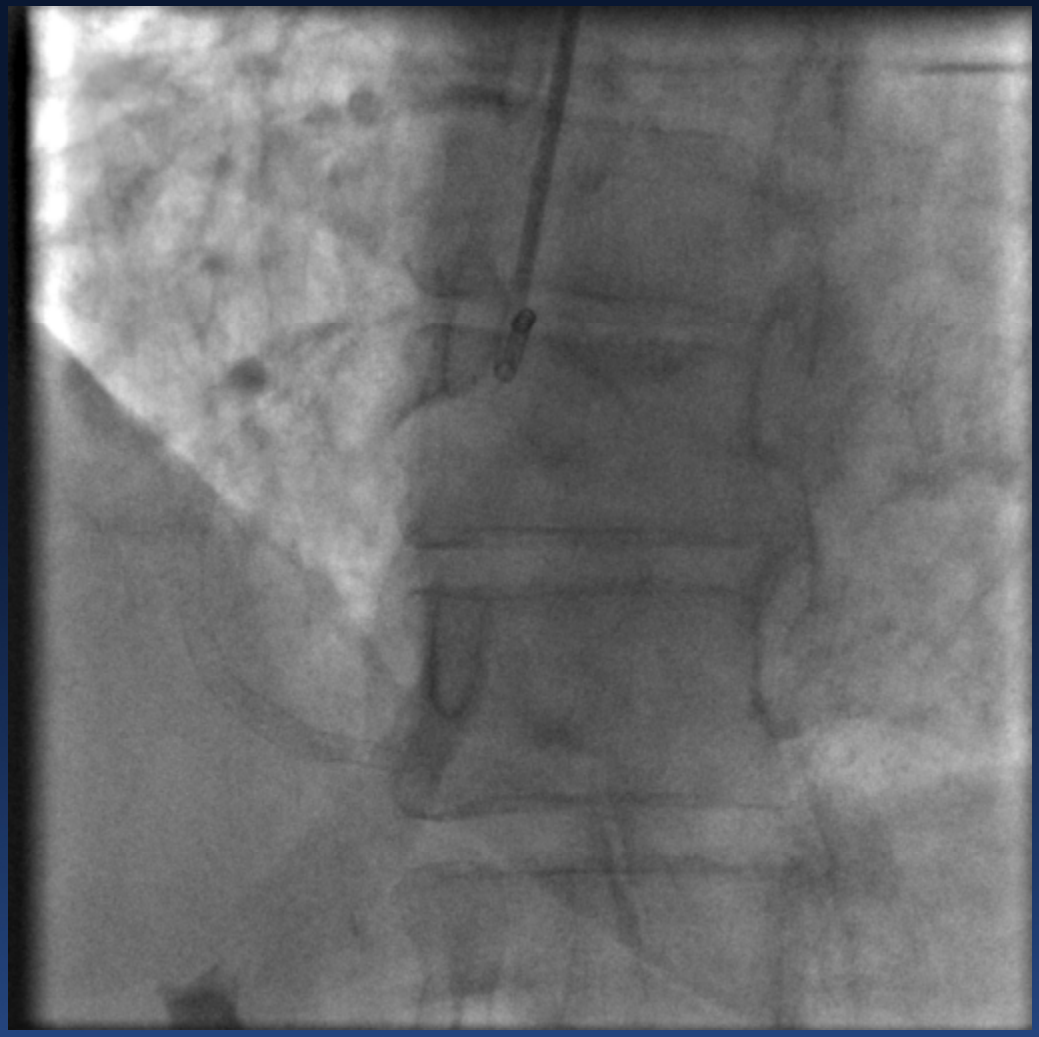


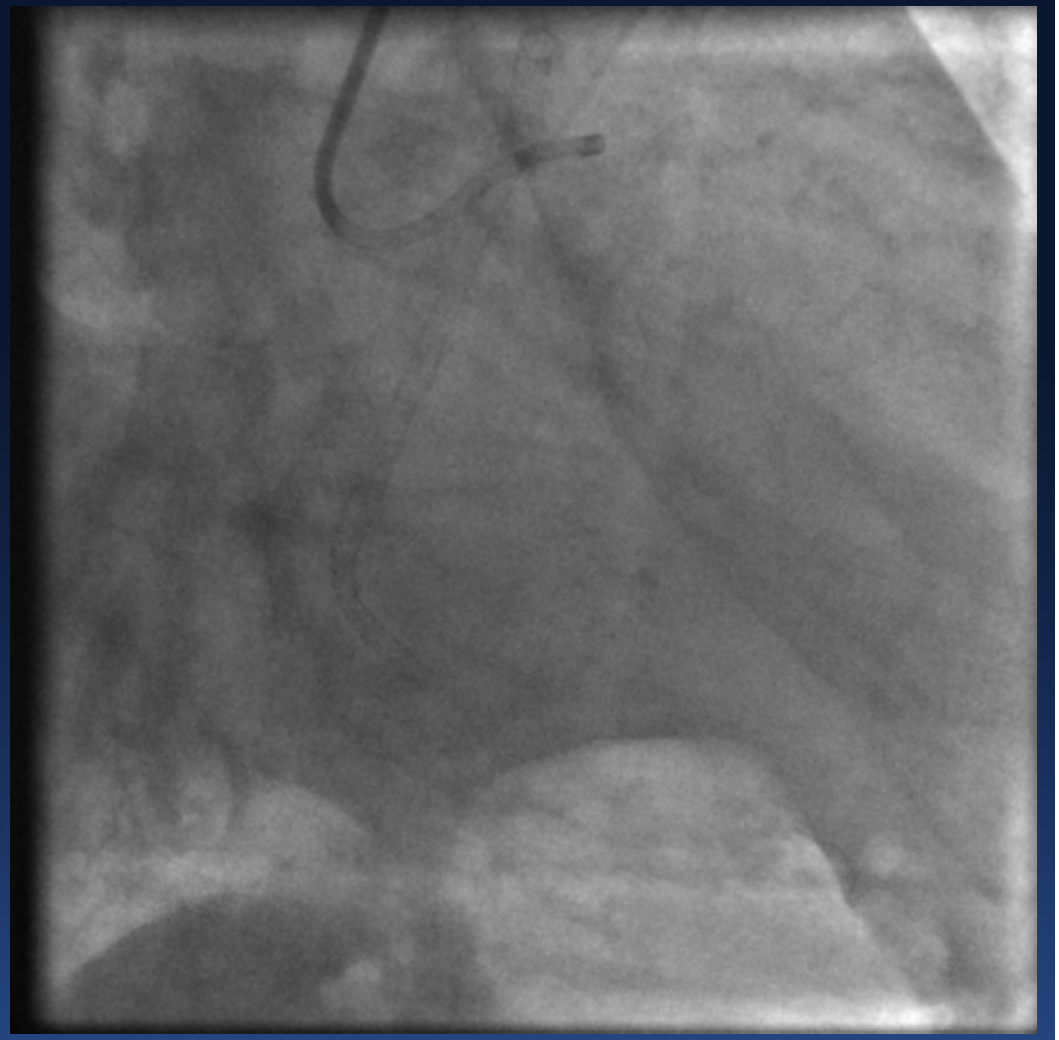


Veriflex 3 x 32mm
mRCA

Veriflex 3 x 32mm
pRCA







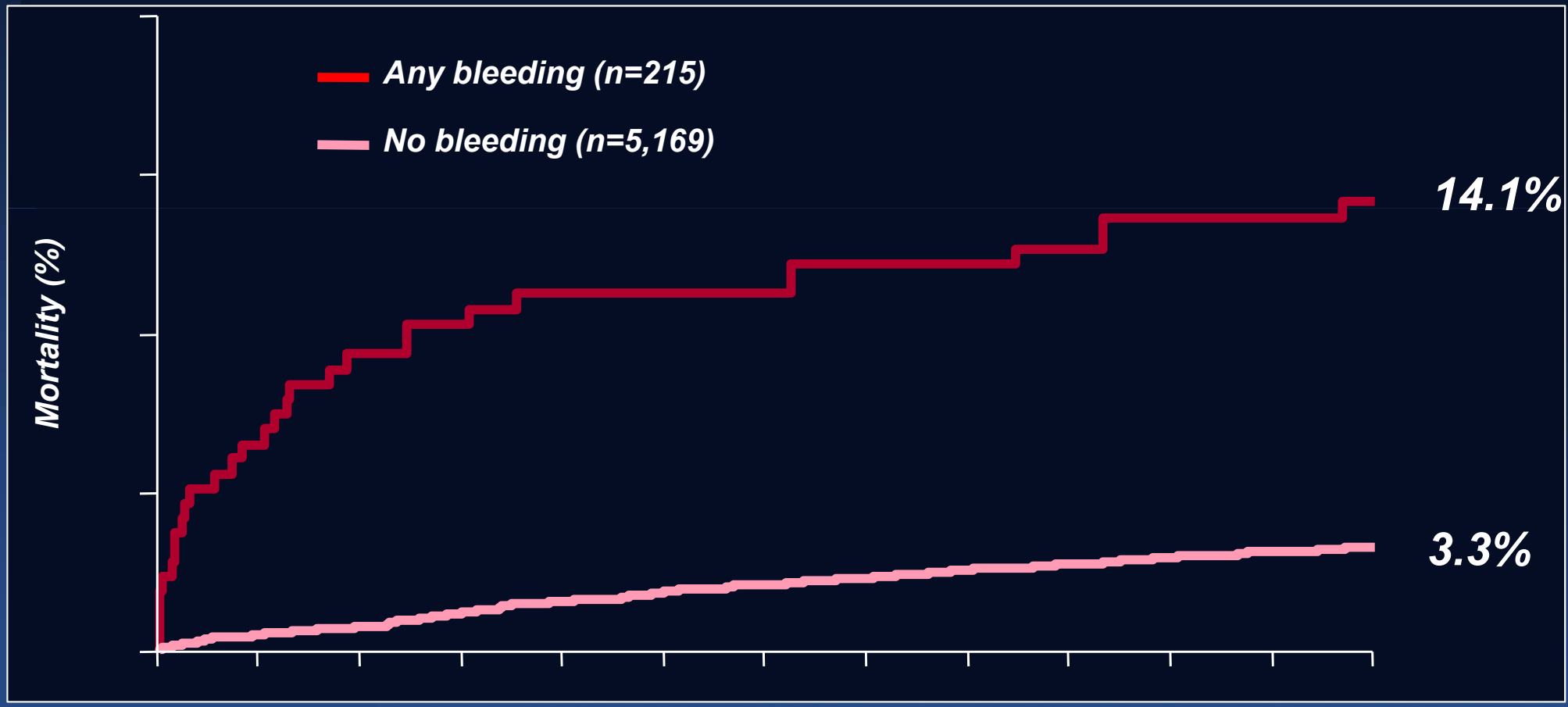
Final result

Follow-up

- 120 cc contrast
- 2 200 mgy
- No chest pain
- No Ck or troponin elevation
- Hgb stable post case
- P2Y12 INHIB POSTLOAD
  - 47%
- At follow up 3 months post PCI
  - No bleeding issues
  - No recurrent angina
  - Plavix discontinued 1 month post procedure

ISAR Meta-Analysis*: Significant Association of Any TIMI Bleeding Event With 1-Year Mortality

Meta-analysis of 5,384 patients undergoing PCI from 4 randomized trials to assess 1-year mortality



*ISAR-REACT, ISAR-SWEET, ISAR-SMART-2, and ISAR-REACT-2.
ISAR-REACT=Intracoronary Stenting and Antithrombotic Regimen: Rapid Early Action for Coronary Treatment; ISAR-SMART=Intracoronary Stenting or Angioplasty for Restenosis Reduction in Small Arteries-2; ISAR-SWEET=Intracoronary Stenting and Antithrombotic Regimen: Is Abciximab a Superior Way to Eliminate Elevated Thrombotic Risk in Diabetics