‘Higher Risk, Higher Benefit’ Strategy with Evolocumab in Post-MI Patients

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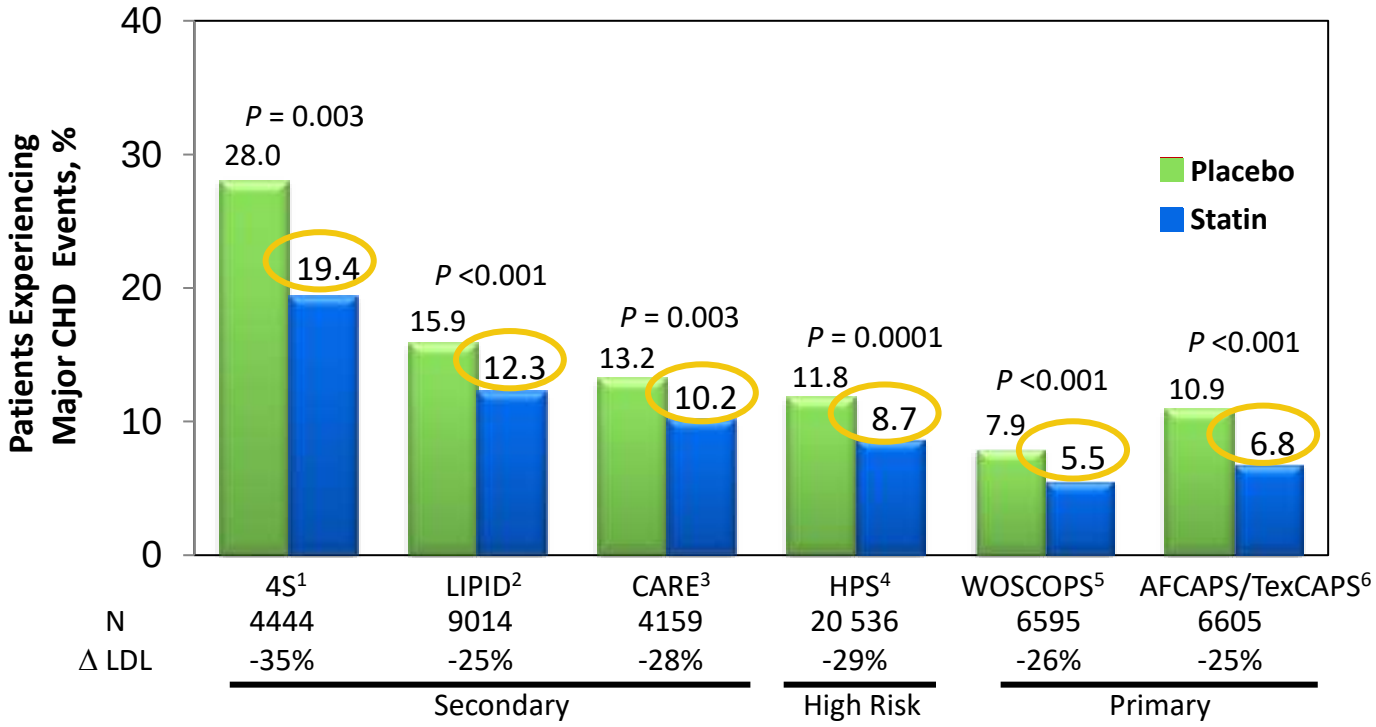
Michael Jordan and Six Championships

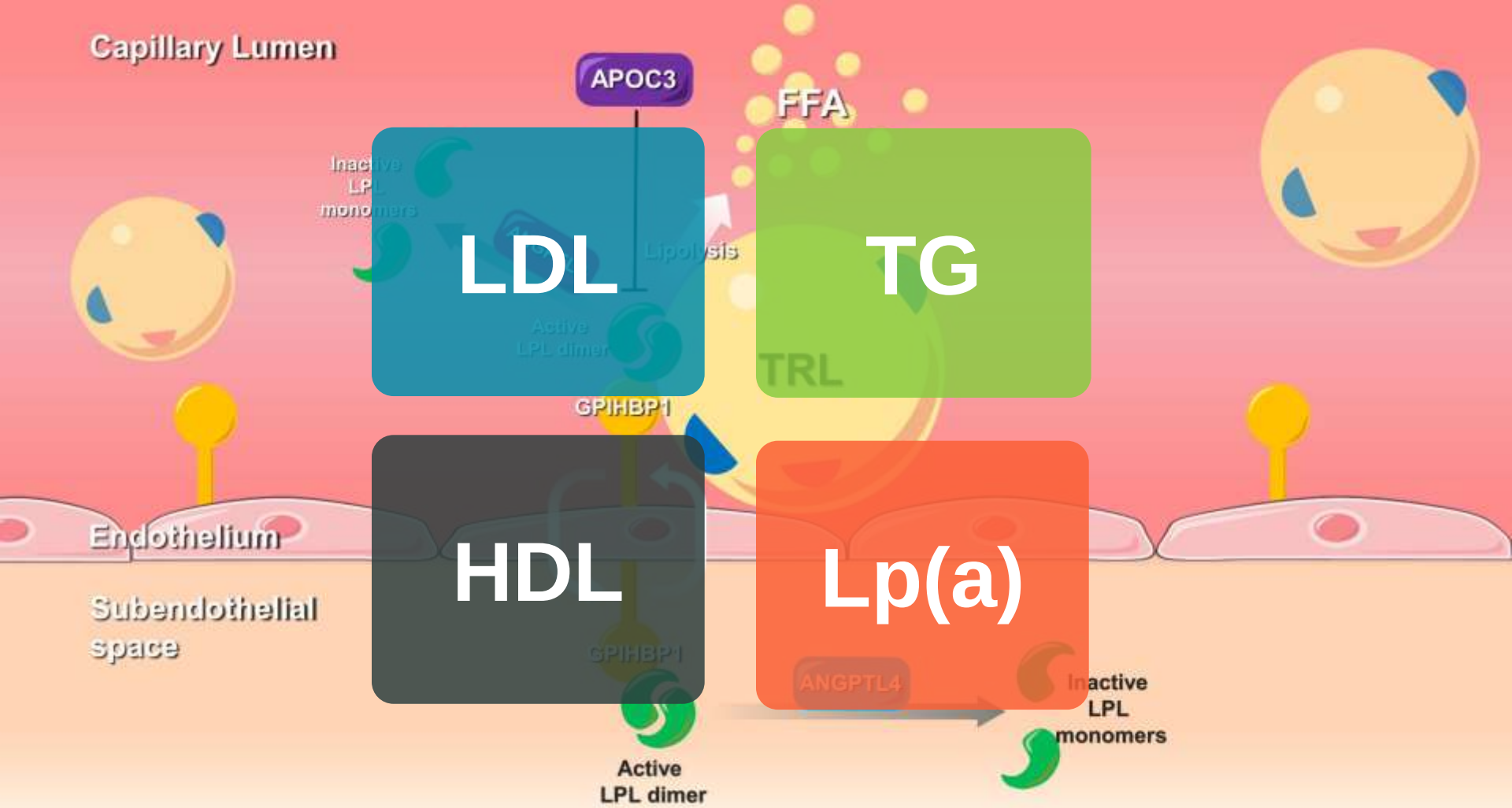

Jerry Krause:
Management build great teams. Let's rebuild.
Michael Jordan:
Rebuild? I'm retiring.
BULLS
23

0 final appearances since 1998

Residual CVD Risk with LDL-C Lowering



Ref) 1. 4S Group. *Lancet.* 1994;344:1383-1389.
2. LIPID Study Group. *N Engl J Med.* 1998;339:1349-1357.
3. Sacks FM et al. *N Engl J Med.* 1996;335:1001-1009.
4. HPS Collaborative Group. *Lancet*. 2002;360:7-22.
5. Shepherd J et al. *N Engl J Med.* 1995;333:1301-1307.
6. Downs JR et al. *JAMA.* 1998;279:1615-1622.

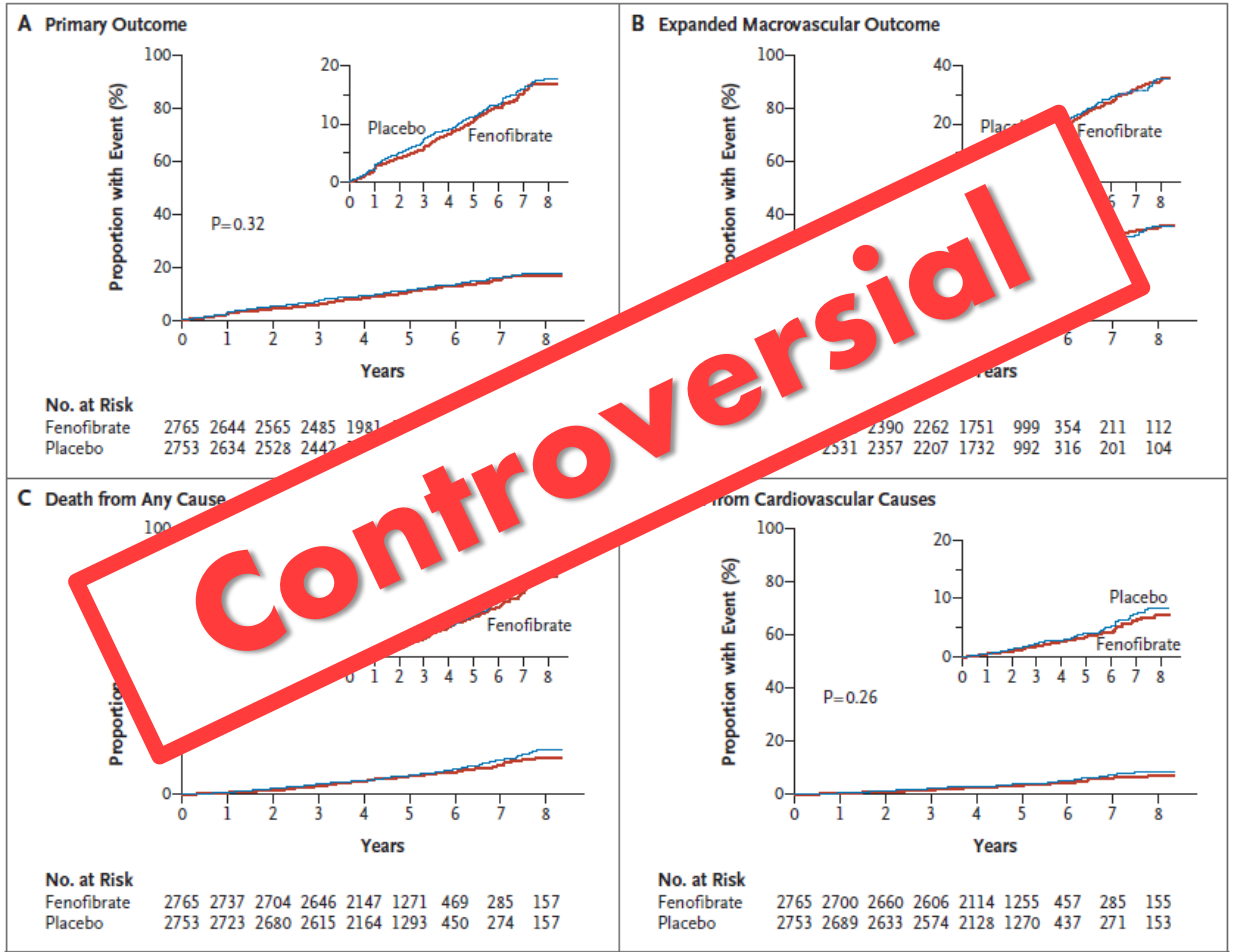


Jang AY and Koh KK et al. New Trends in Dyslipidemia Treatment. *Circulation Journal*. 2020.


LDL
TG
HDL
Lp(a)

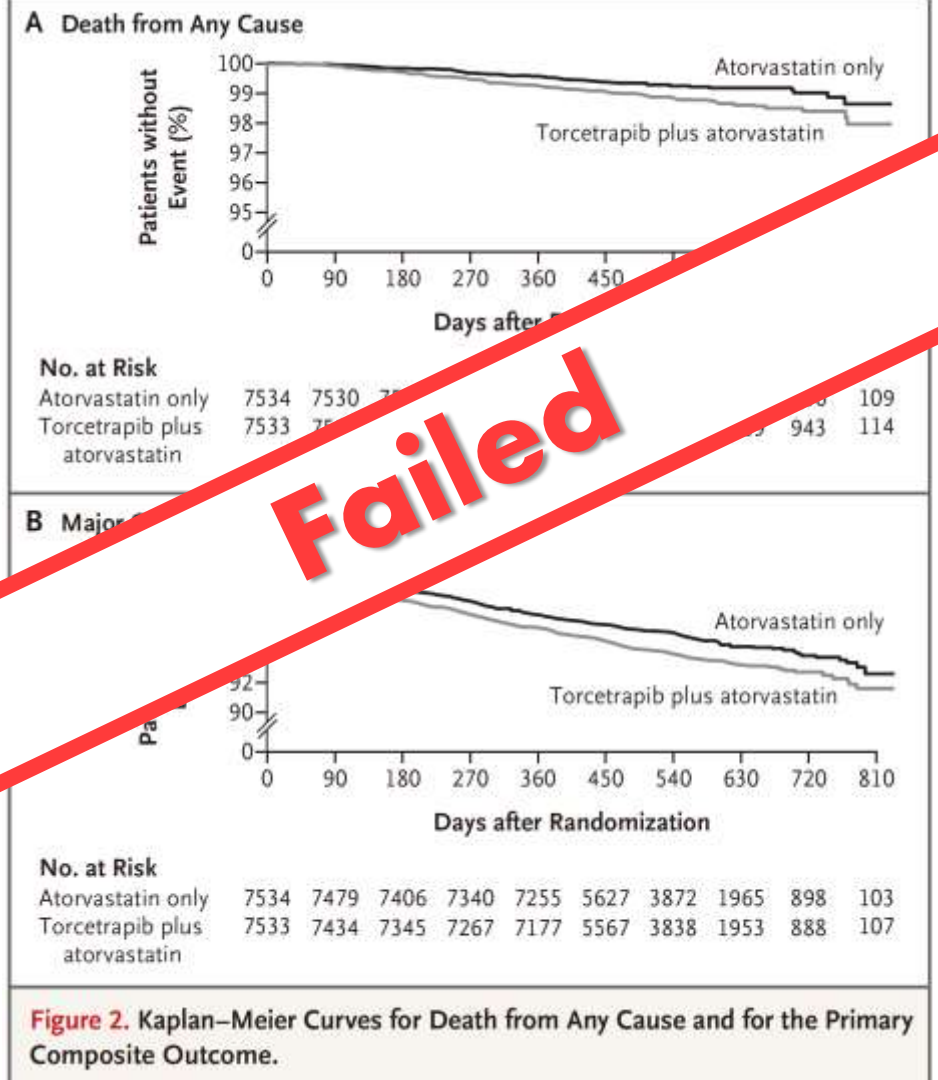
Statin + Fenofibrate combination: No CV benefit

TG



Controversial

HDL

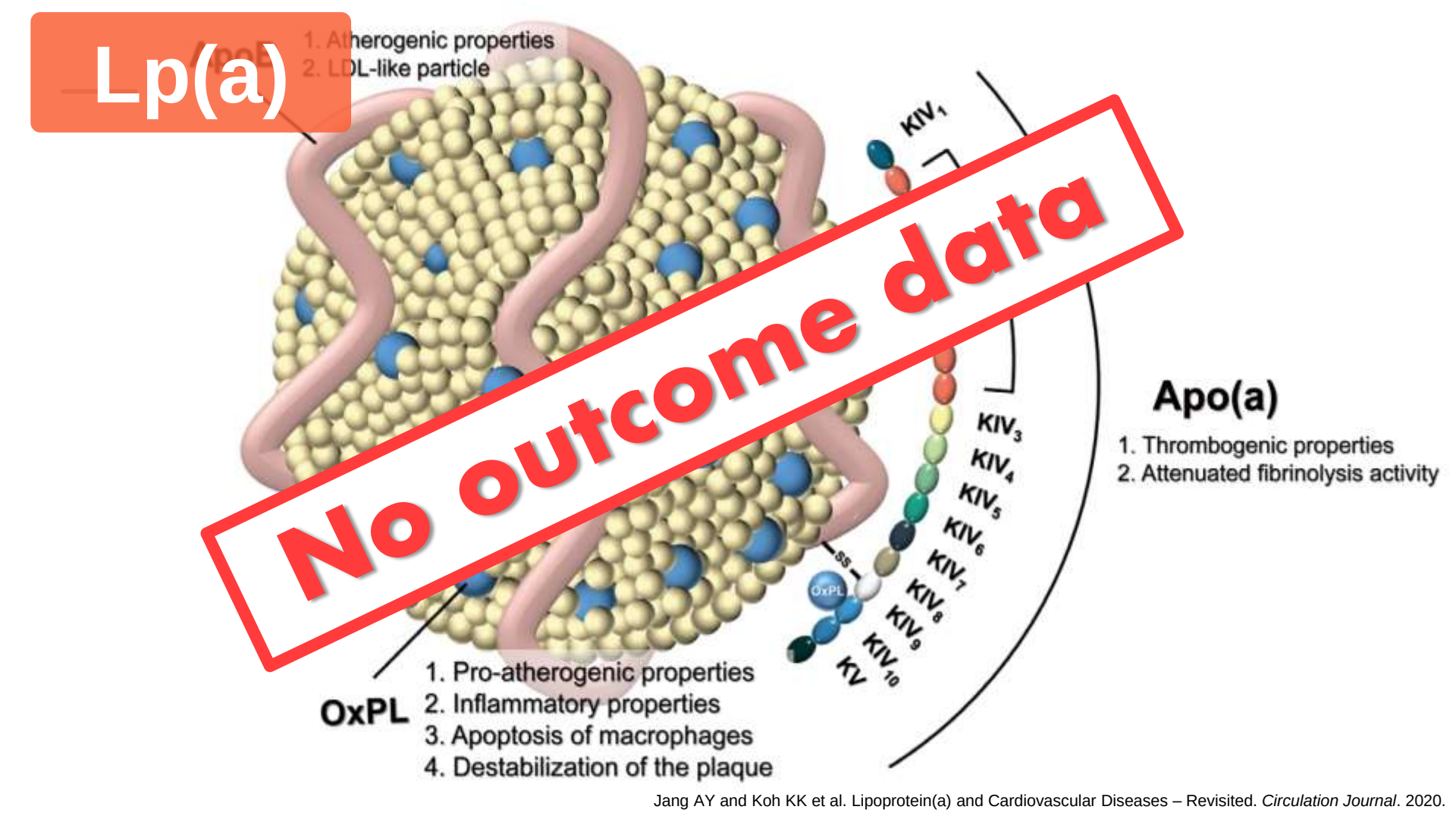


Failed

Figure 2. Kaplan–Meier Curves for Death from Any Cause and for the Primary Composite Outcome.

N Engl J Med 2007;357:2109-22

Lp(a)



No outcome data

Jang AY and Koh KK et al. Lipoprotein(a) and Cardiovascular Diseases – Revisited. *Circulation Journal*. 2020.

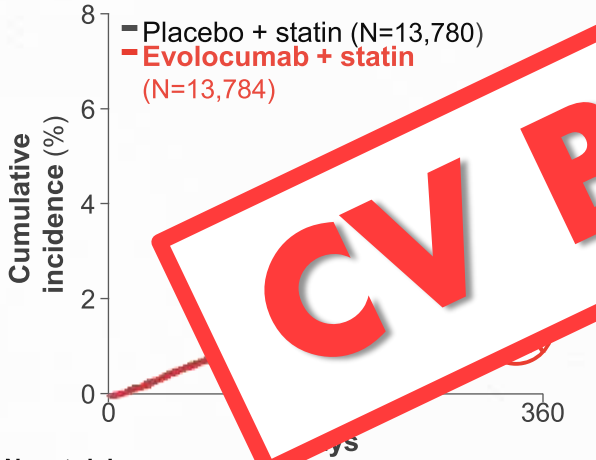
The Longer, The Better!
Evolocumab Showed a Greater Risk Reduction Over Time

LDL-C

Composite of CV death, MI, or st

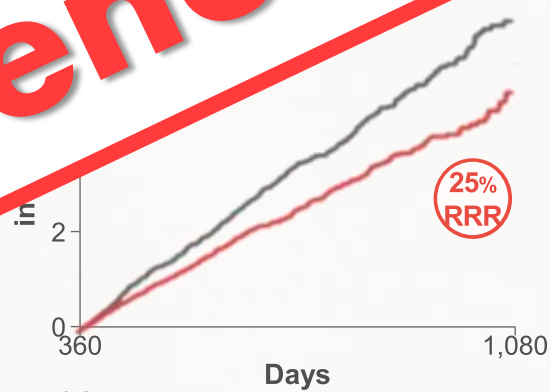
CV Benefit!

Months 0-12



No. at risk

13,780	Placebo+Statin	13,148
13,784	Evolocumab+Statin	13,248



No. at risk

13,524	Placebo+Statin	925
13,548	Evolocumab+Statin	911

Risk of MI or stroke

35% RRR
MI

24% RRR
STROKE

For this analysis the relative risk reduction for the composite endpoint from months 13-36 was driven by a reduction in the risk of MI HR:0.65 (0.55-0.77) and stroke HR: 0.76 (0.60-0.97). Observed HR for CV death: 1.12 (0.88-1.42)[1]

RRR=relative risk reduction; **HR**=hazard ratio; **MI**=myocardial infarction; **CV**=cardiovascular

1. Sabatine MS, *et al. N Engl J Med.* 2017;376:1713-1722.

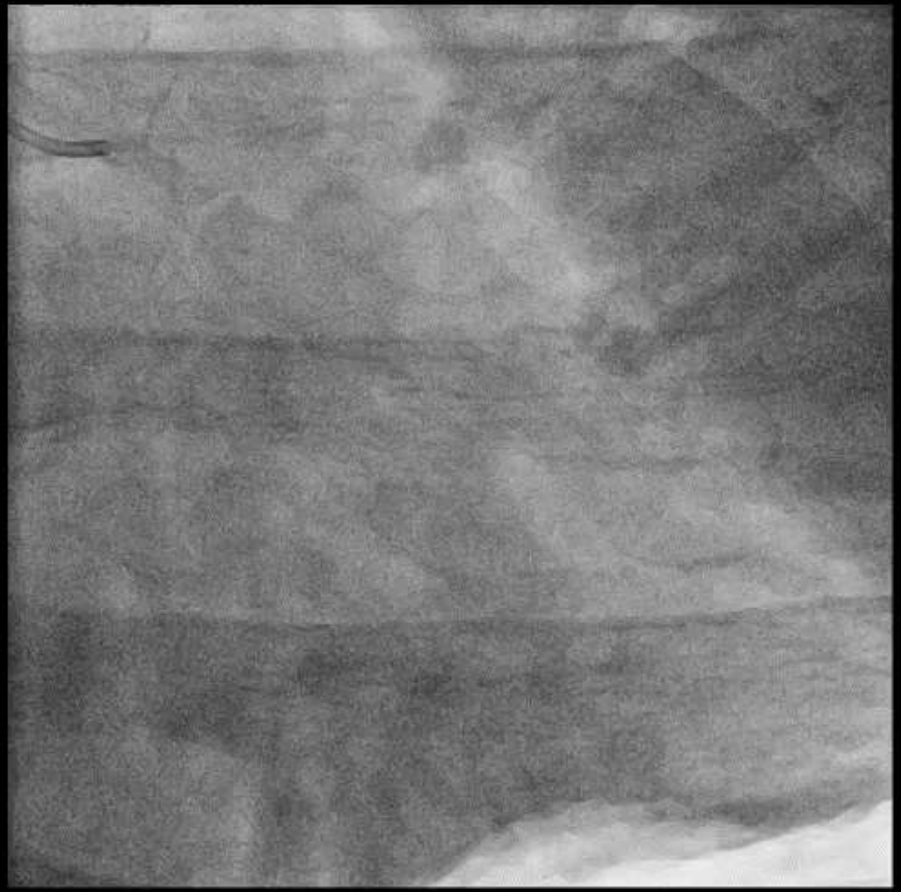
Case #1

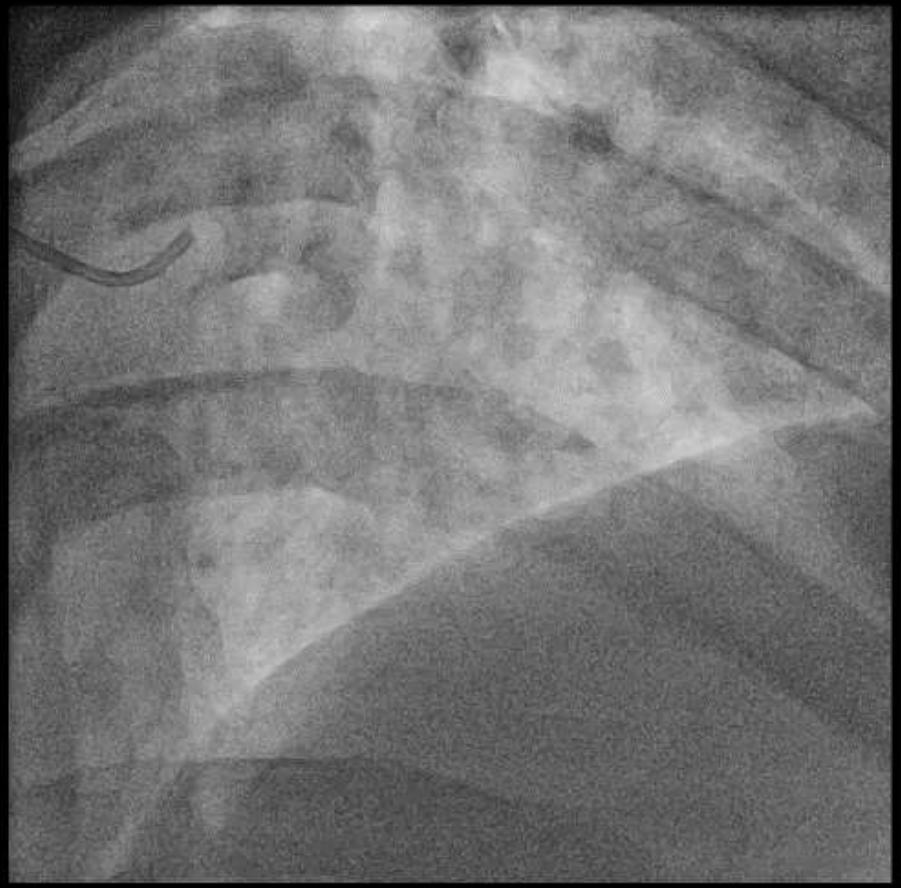
CASE: 34 M, Chest pain

< PHx >

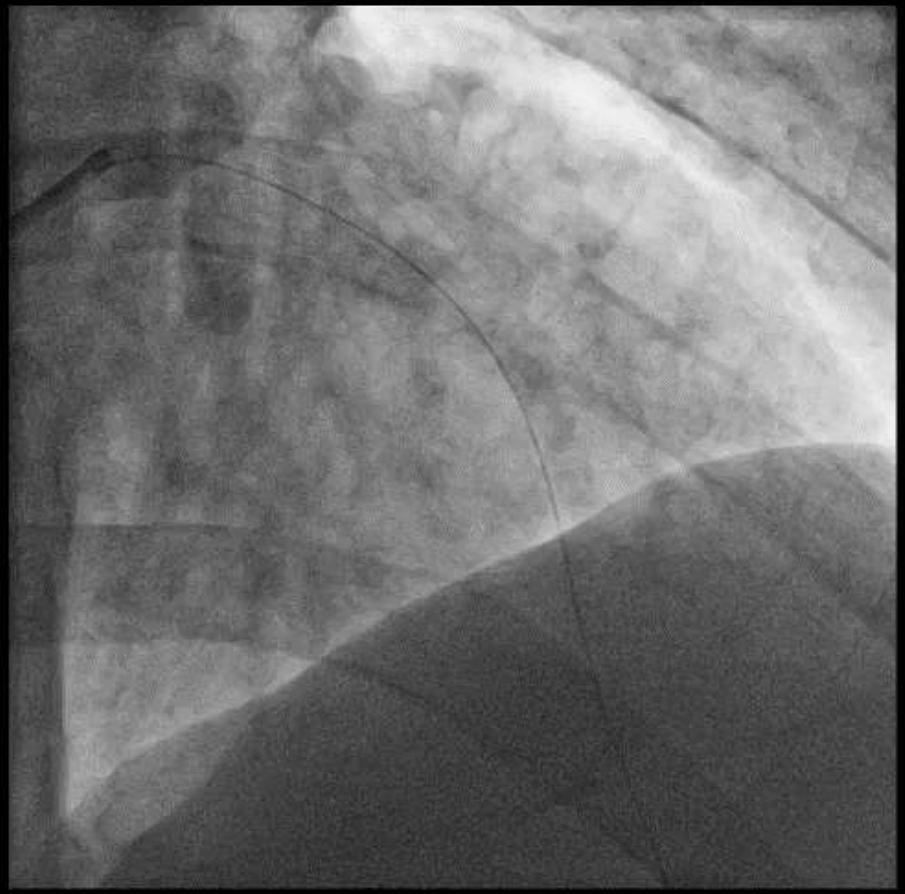
- Hypertension
- Newly diagnosed diabetes
- Heavy smoker
- Fast food diet
- 175cm 95.3kg (BMI: 31.1)
- FHx: Mother: CAD (+)
- Father: CAD (+)

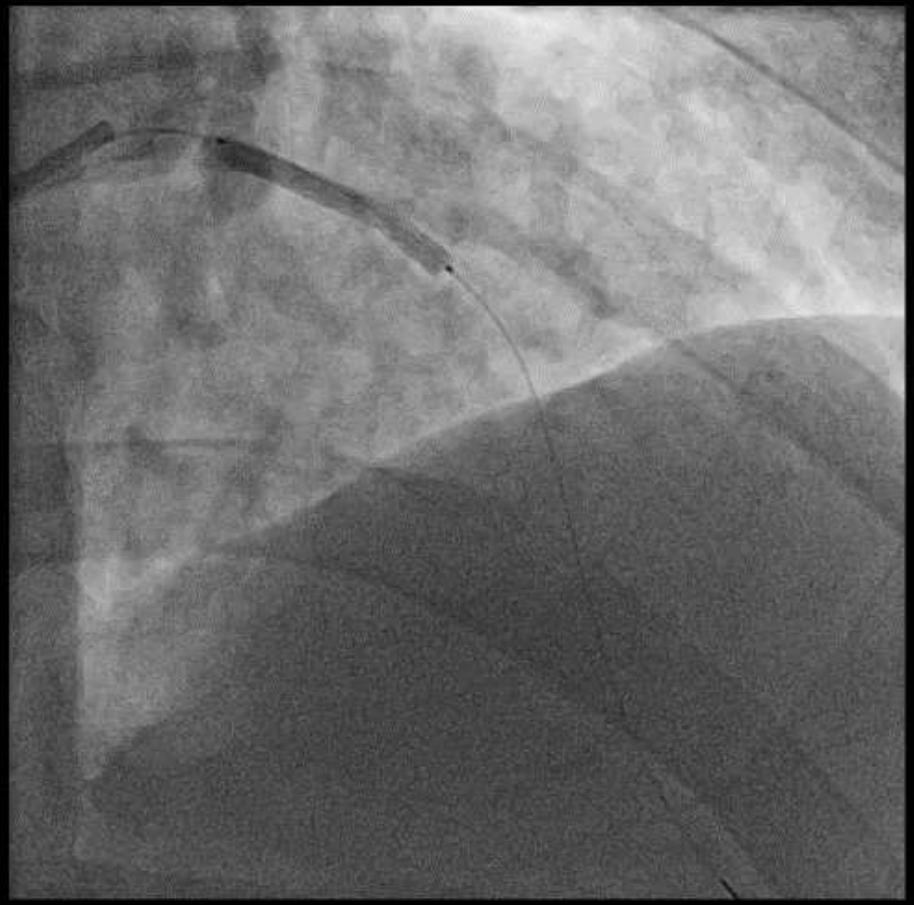
CASE: 34 M, Chest pain



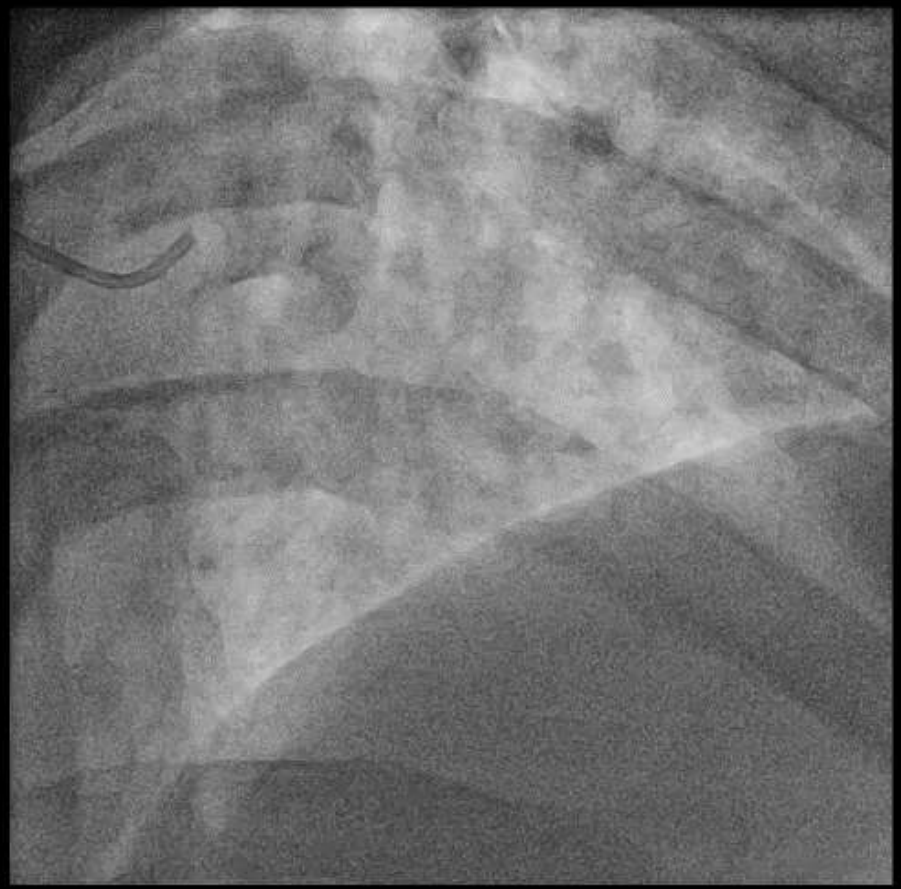


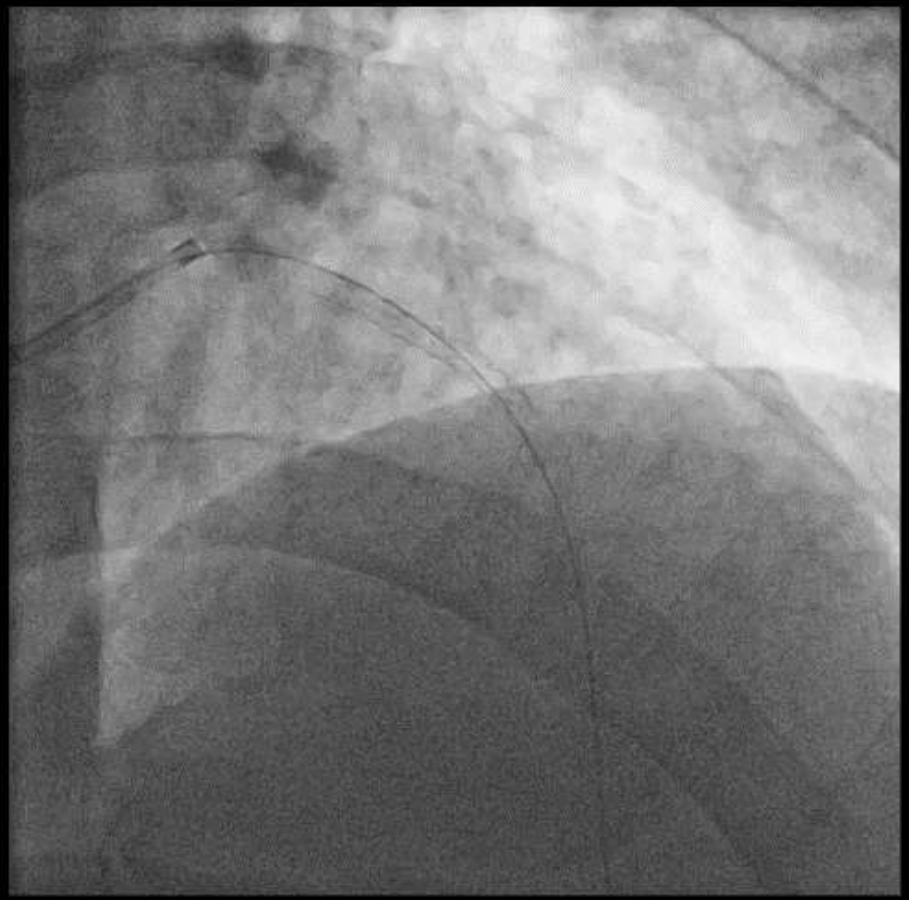
CASE: Thrombectomy and Stent Insertion





CASE: Final Angiography





CASE: 34 M, Genetic test for FH

Identified variation(s)

Gene	DNA change	Predicted AA change	Zygosity	Disease	Inherit	Class
LDLR	c.20[illegible]54C>T	p.Pro685Leu	Het	FH	AD	PV

Heterozygous FH

Reference sequence: NM_000527.5(LDLR)

OMIM disease: FH, Familial hypercholesterolemia

Abbreviation: AD, Autosomal dominant; Het, Heterozygous; PV, Pathogenic Variant

◇ INTERPRETATION

유전성 이상지질혈증 유전자 패널 분석 결과, LDLR 유전자에서 Pathogenic Variant (PV)가 발견되었습니다.

CASE: 34 M, Genetic test for FH

- **<FH Reimbursment Guidelines >**
- FH genetic test (+)
  - LDL-C > 190 When (treatment naïve)
  - LDL-C > 100 mg/dL (after maximal statin)
- FH genetic test (-)
  - LDL-C > 190 When (treatment naïve)
  - Tendon xathoma (>6 mm on X-ray)

CASE: 34 M, Genetic test for FH

- **<FH Reimbursment Guidelines >**
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- FH genetic test (-)
  - LDL-C > 190 When (treatment naïve)
  - Tendon xathoma (>6 mm on X-ray)

Case: Lab

- **TC:** 337 mg/dL
- **TG:** 155 mg/dL
- **HDL-C:** 48 mg/dL
- **LDL-C:** 260 mg/dL
- Lp(a): 32.5 nmol/L

Ezetimibe 10mg /Rosuvastatin 20mg

Evolocumab 140mg q2wks

- **TC:** 250 mg/dL
- **TG:** 90 mg/dL
- **HDL-C:** 68 mg/dL
- **LDL-C:** 170 mg/dL

레파타 급여기준

☐ ① 초고위험군: 주요 ASCVD 2개이상* 또는 주요 ASCVD 1개+고위험요인 2개이상

주요 ASCVD

- ☐ 1년 이내 Acute Coronary Syndrome
- ☑ Myocardial Infarction
- ☐ Ischemic Stroke
- ☐ Symptomatic PAD (ABI <0.85인 파행의 과거력 또는 이전의 혈관재생술이나 절단)

*동일한 주요 ASCVD를 두 번 경험한 경우도 해당

고위험 요인

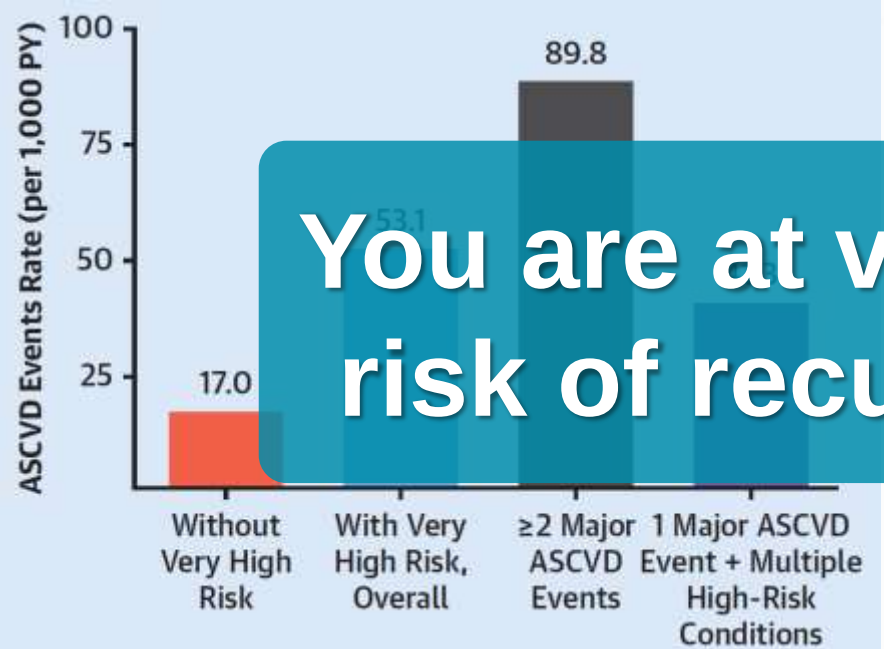
- ☐ 65세 이상
- ☑ 고혈압
- ☑ 현재 흡연
- ☐ 당뇨병
- ☐ 울혈성 심부전 과거력
- ☐ LDL-C ≥100 mg/dL (최대내약용량의 스타틴+에제티미브 치료 이후)
- ☐ CABG 또는 PCI 과거력 (주요 ASCVD 제외)
- ☐ 만성신장질환 (eGFR 15-59 mL/min/1.73 m²)
- ☑ HeFH

☑ ② 최대내약용량 스타틴+에제티미브 복용
단, 환자가 고강도 스타틴에 불내성을 보이는 경우에는 내약성을 보이는 용량으로 가능

☑ ③ LDL-C ≥70 mg/dL

Follow up loss

Patients With VHR ASCVD Risk* Have 3 Times Higher Rate of Experiencing Another Event Than Patients Without VHR ASCVD Risk



You are at very high risk of recurrence.

Among patients with very high ASCVD risk, the ASCVD event rate was higher for those with multiple major ASCVD events compared to those with one major event and multiple high-risk conditions

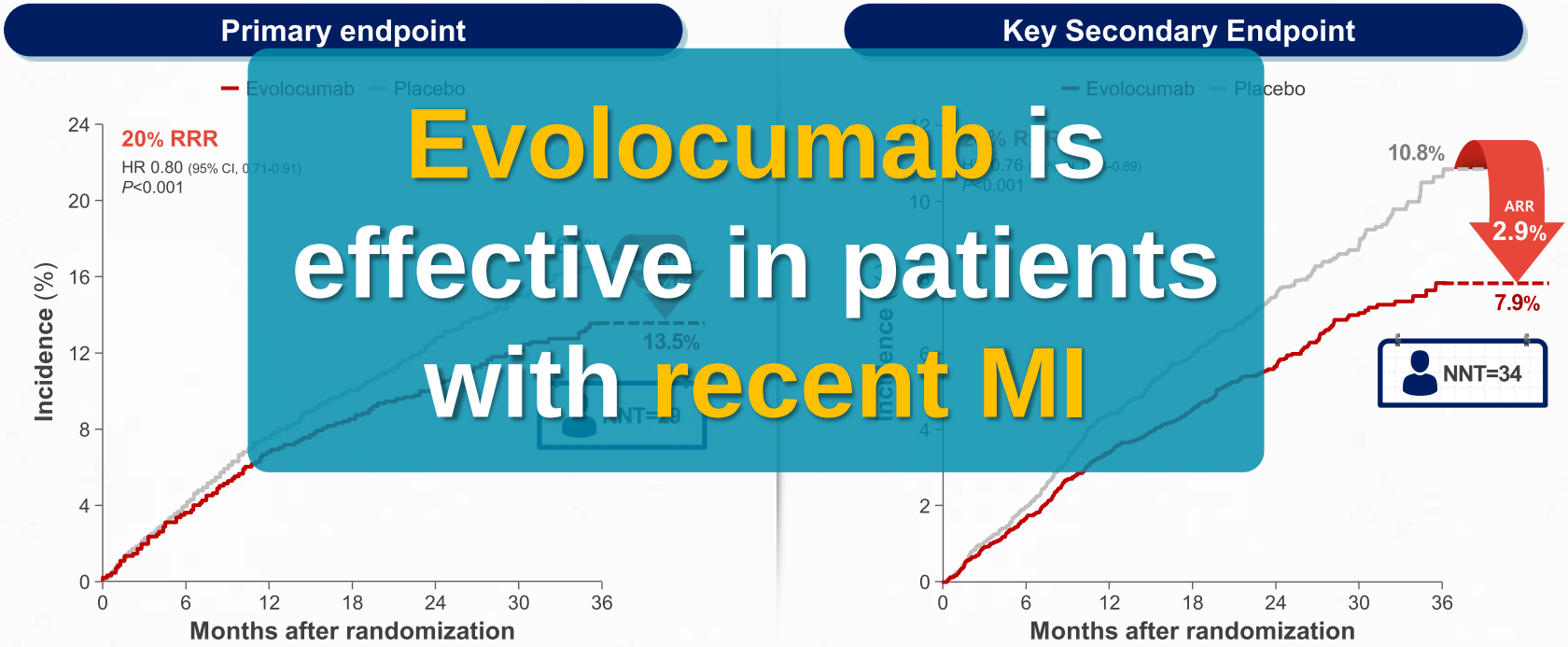
* Patients who met the definition of very high risk in the 2018 AHA/ACC blood cholesterol guideline

Very high risk ASCVD patients require intensive lipid-lowering therapy to receive substantial ASCVD risk reduction

Colantonio, L.D. et al. J Am Coll Cardiol. 2019;74(20):2496–507.

Analysis From the FOURIER: Clinical Benefit of Evolocumab in Patients with Recent MI (<2 Years)

Evolocumab is effective in patients with recent MI



Primary endpoint: Cardiovascular death, MI, stroke, hospitalization for unstable angina, or coronary revascularization;
Key secondary endpoint: Cardiovascular death, MI, or stroke.

1. Sabatine MS, *et al. Circulation.* 2018;138:756-766.

Case: Lab

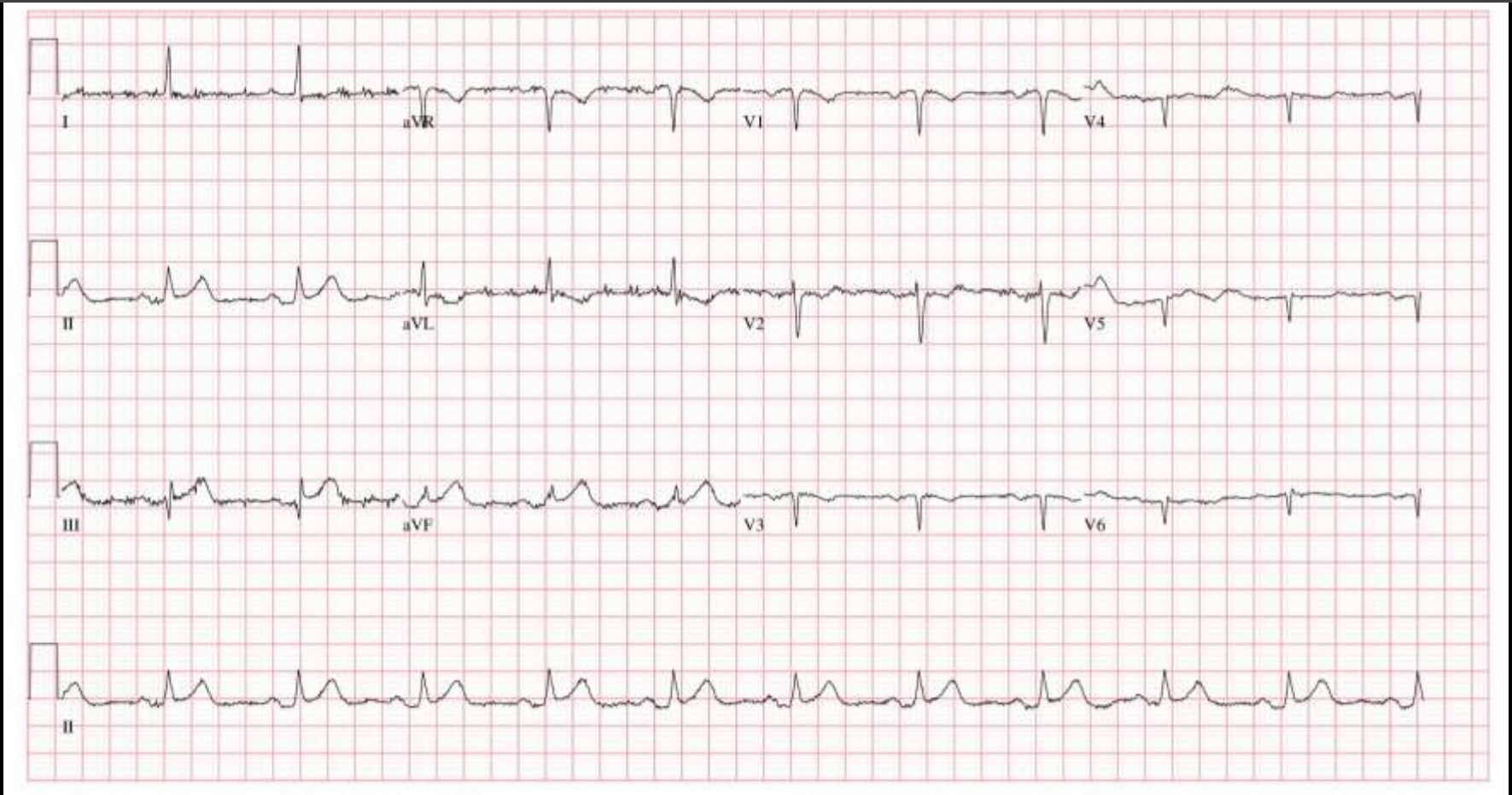
LDL-C 170 to 35 mg/dL

Case #2

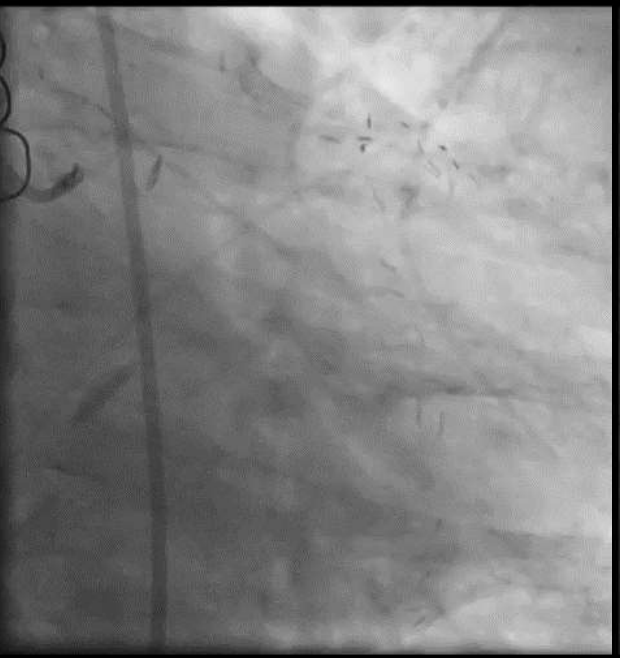
CASE: 74 M, Chest pain

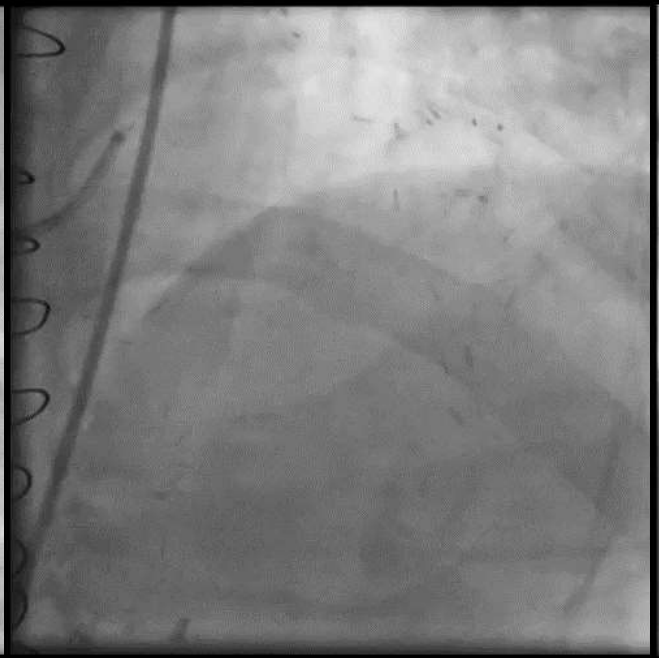
- V/S: 80/50-90
- Multiple previous ASCVD
  - Prior MI (s/p 2005 CABG)
  - Prior Stroke (1998)
  - Prior PAD (Rt. CIA CTO + s/p 2005 Rt. CIA stenting)
- HTN
- Smoker
- Dyslipidemia

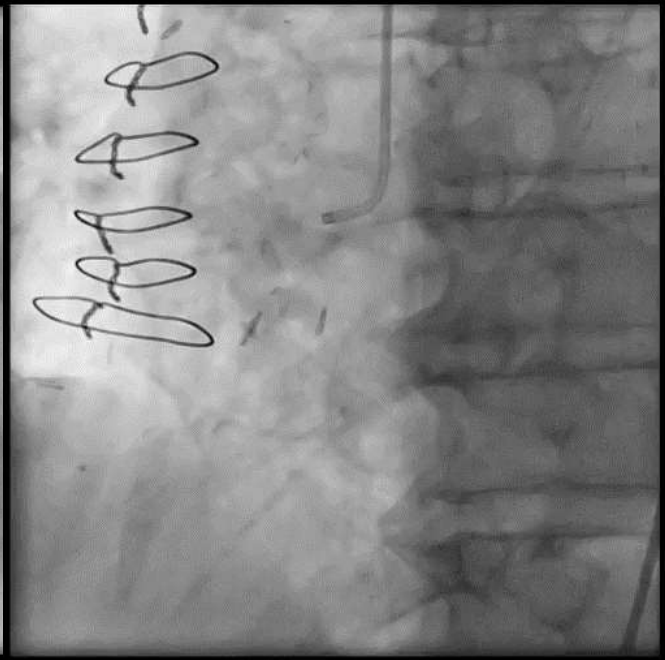
CASE: 79 M, Chest pain



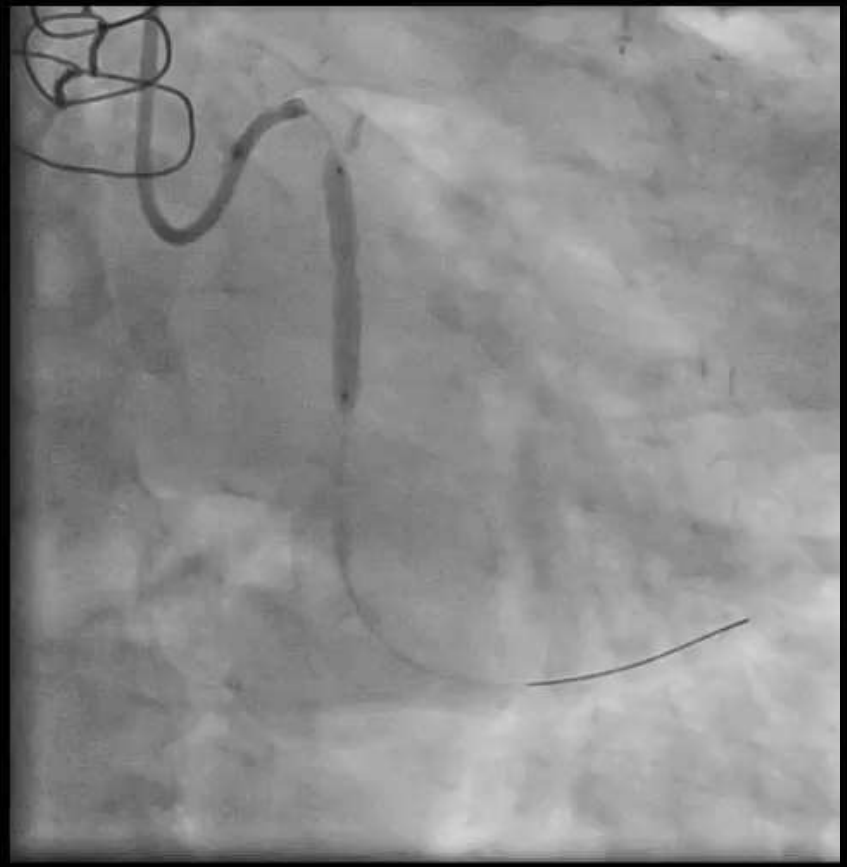
Past history: MI 2012

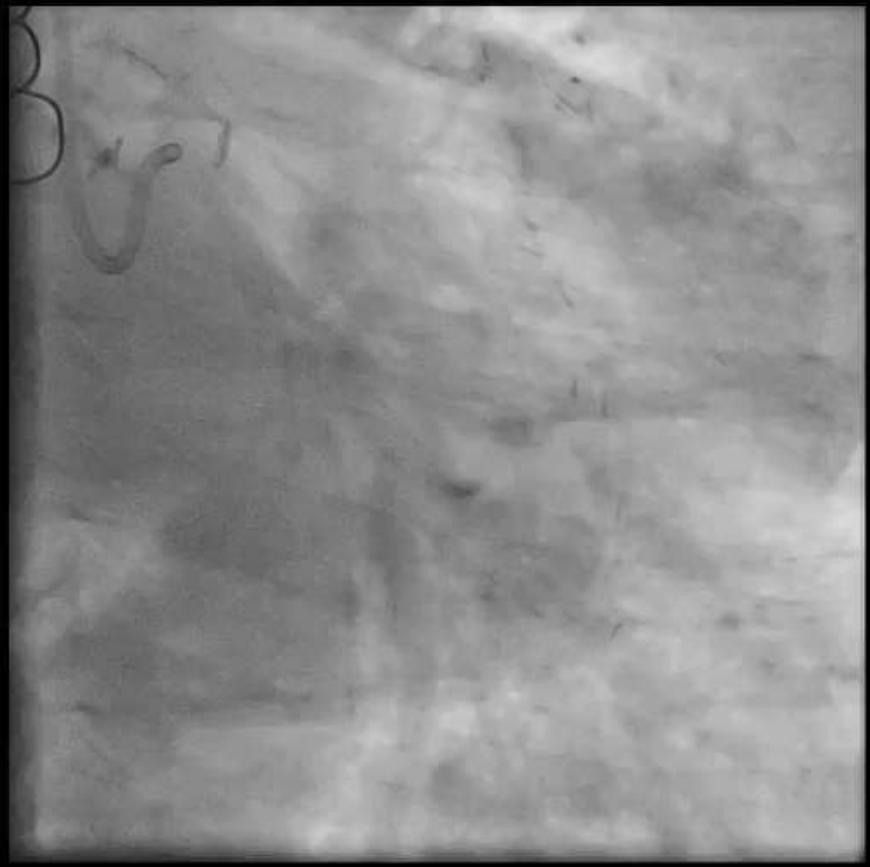




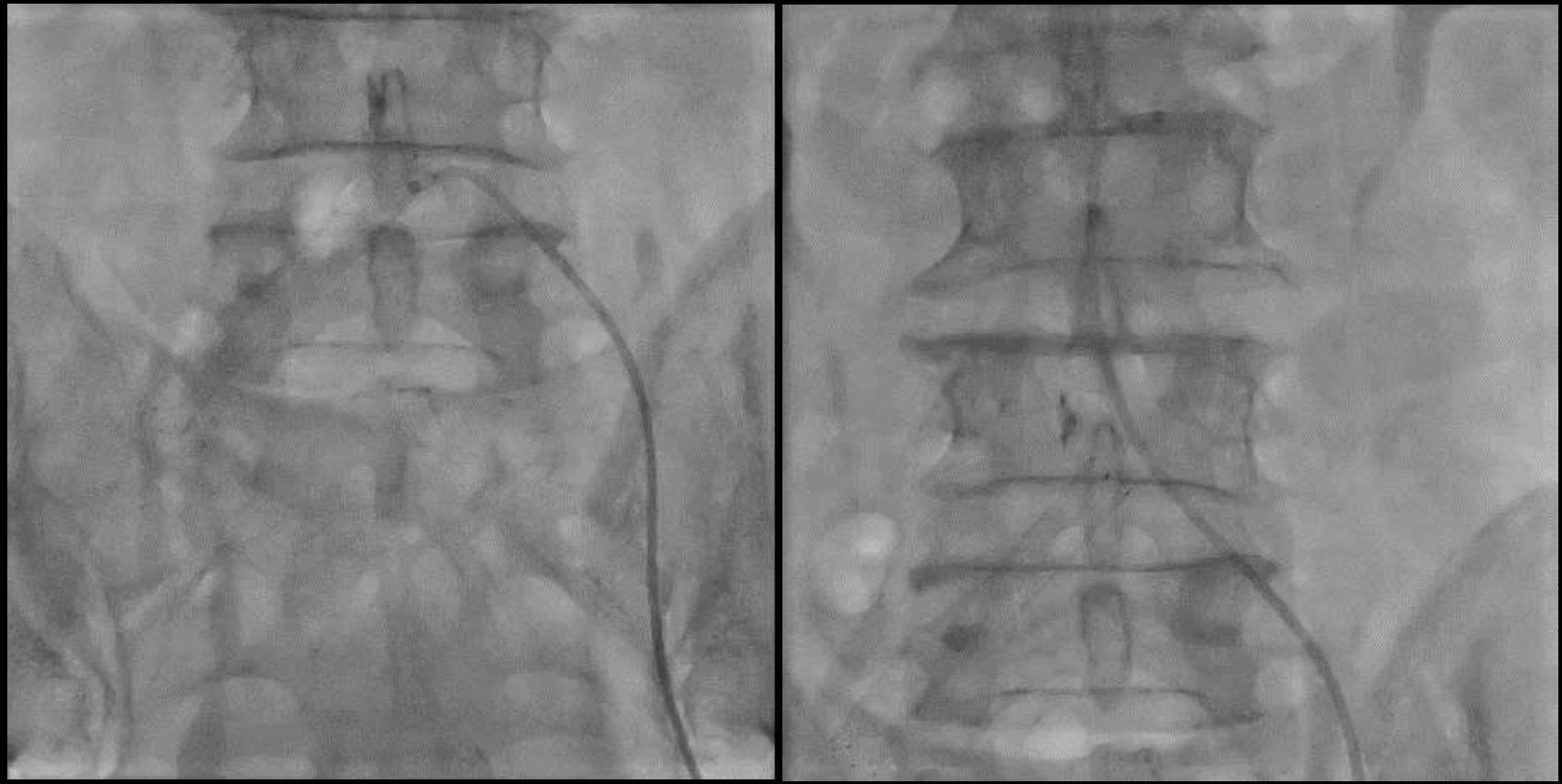


Past history: MI (2012)

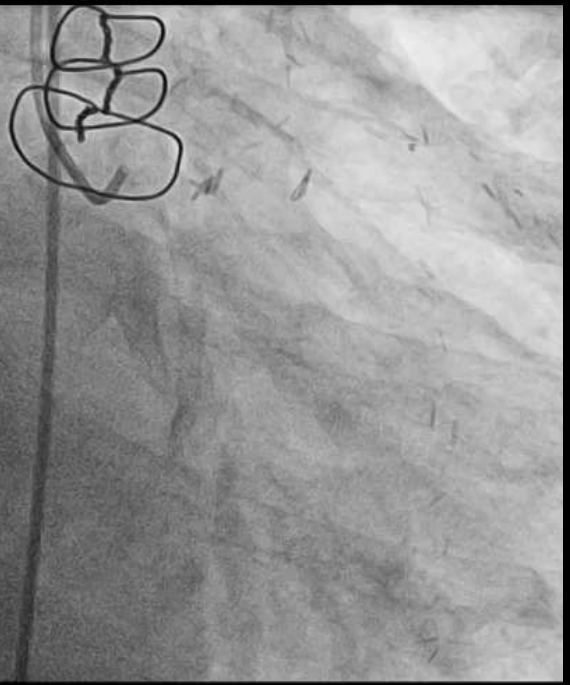


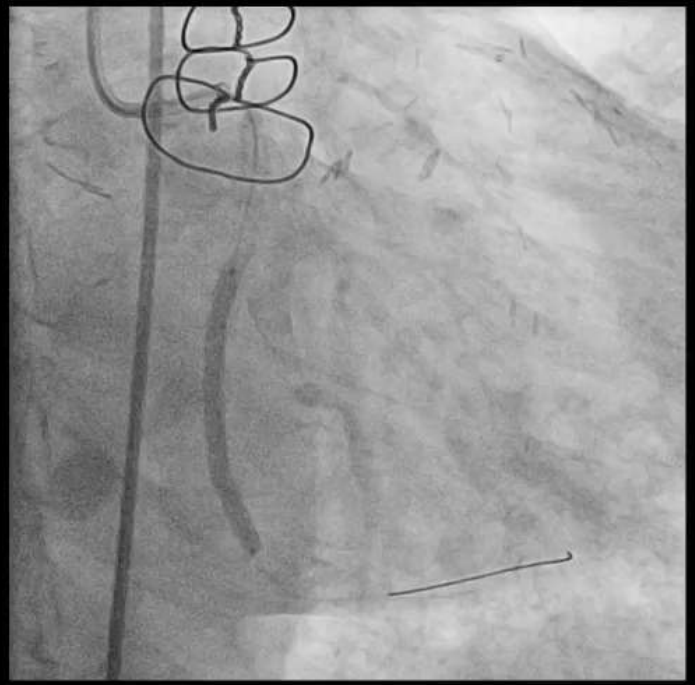


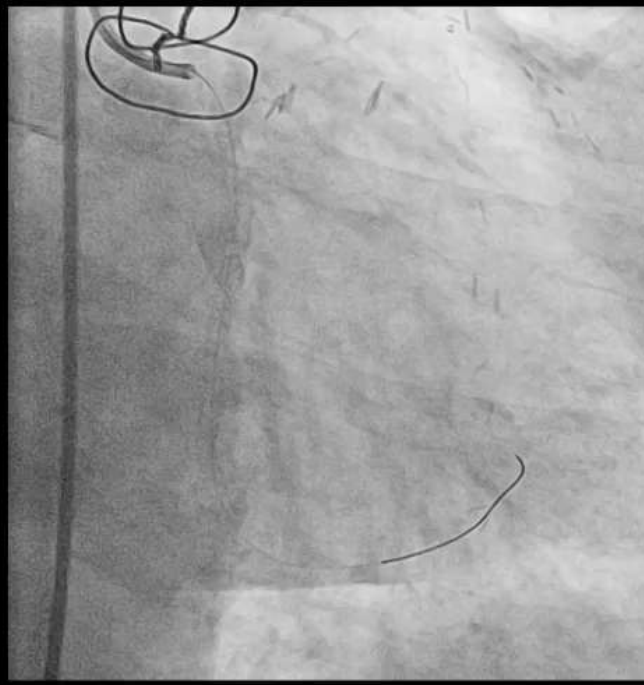
Past history: PAD s/p 2005 Rt. CIA Stenting



Emergent PCI to dLCX







dLCX Xience 3.0 x 36 mm

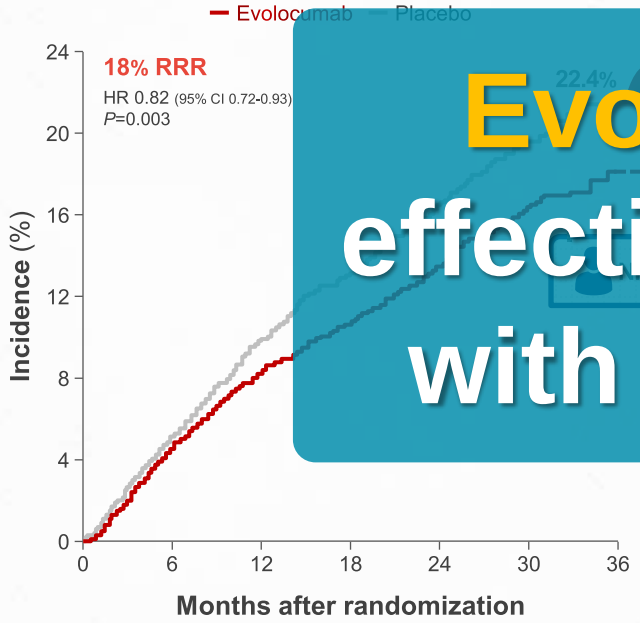
CASE #1: 74 M Summary

- Multiple previous ASCVD
  - Prior STEMI x 2 (s/p 2005 CABG, s/p 2021 PCI)
  - Prior Stroke (1998)
  - Prior PAD (Rt. CIA CTO + s/p 2005 Rt. CIA stenting)
- HTN
- Smoker
- **Lp(a): 150.1 nmol/L**
- Dyslipidemia **(LDL-C 81, on ezetimine 10 + atorvastatin 40mg)**

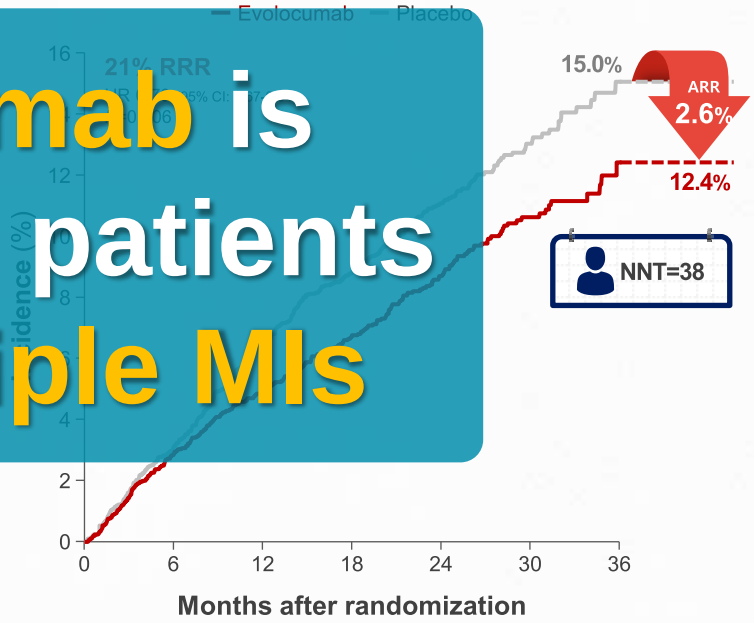
Analysis From the FOURIER: Clinical Benefit of Evolocumab in Patients with Multiple MIs (≥2)

Evolocumab is effective in patients with multiple MIs

Primary endpoint



Key Secondary Endpoint



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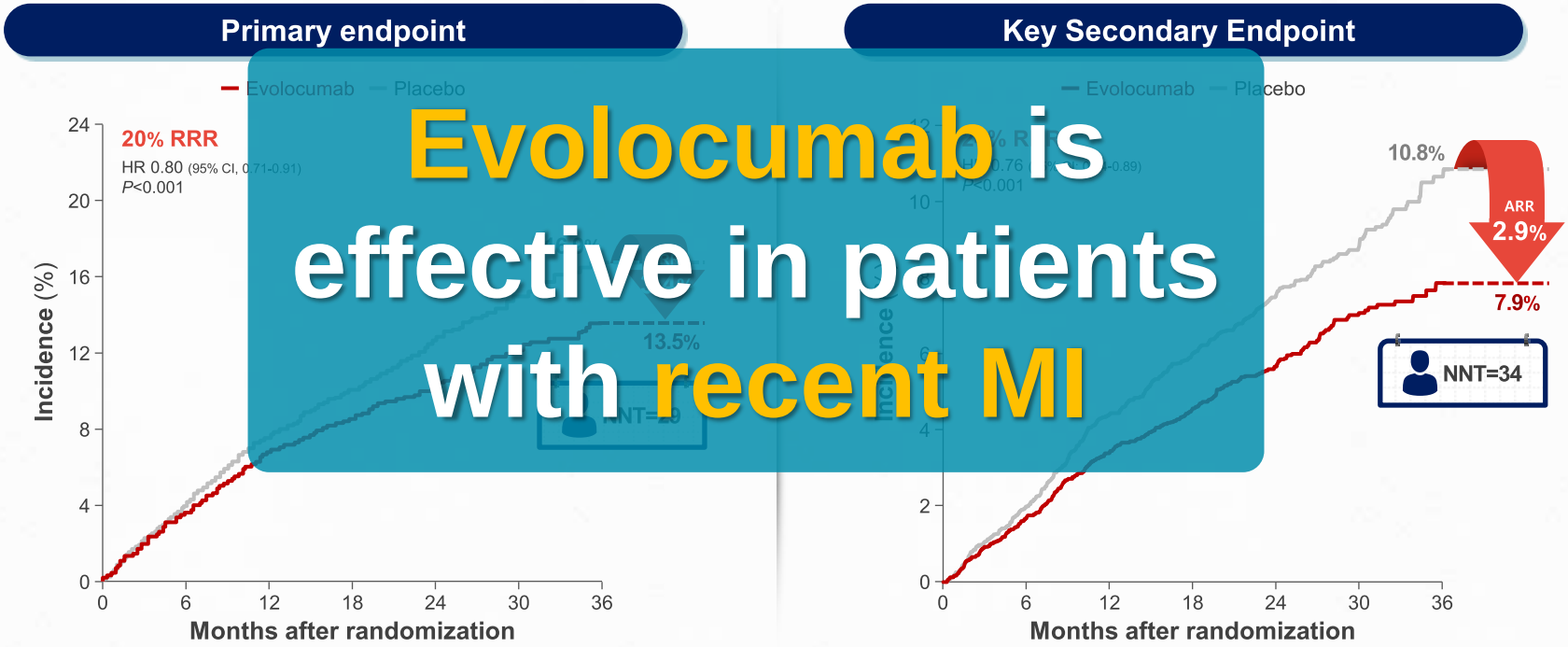
1. Sabatine MS, *et al. Circulation.* 2018;138:756-766.

Analysis From the FOURIER: Clinical Benefit of Evolocumab in Patients with Recent MI (<2 Years)

Evolocumab is effective in patients with recent MI



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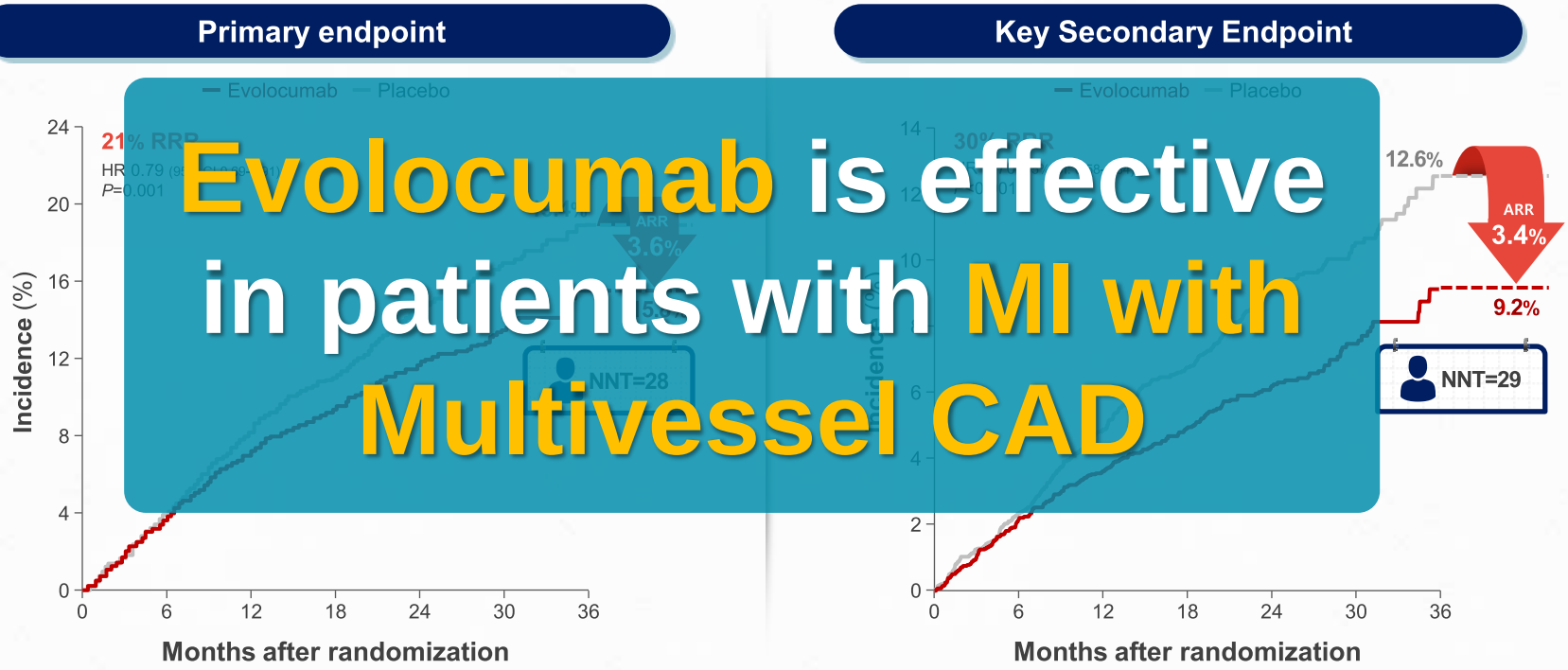
Analysis From the FOURIER: Clinical Benefit of Evolocumab in MI Patients with Multivessel CAD

Evolocumab is effective in patients with MI with Multivessel CAD



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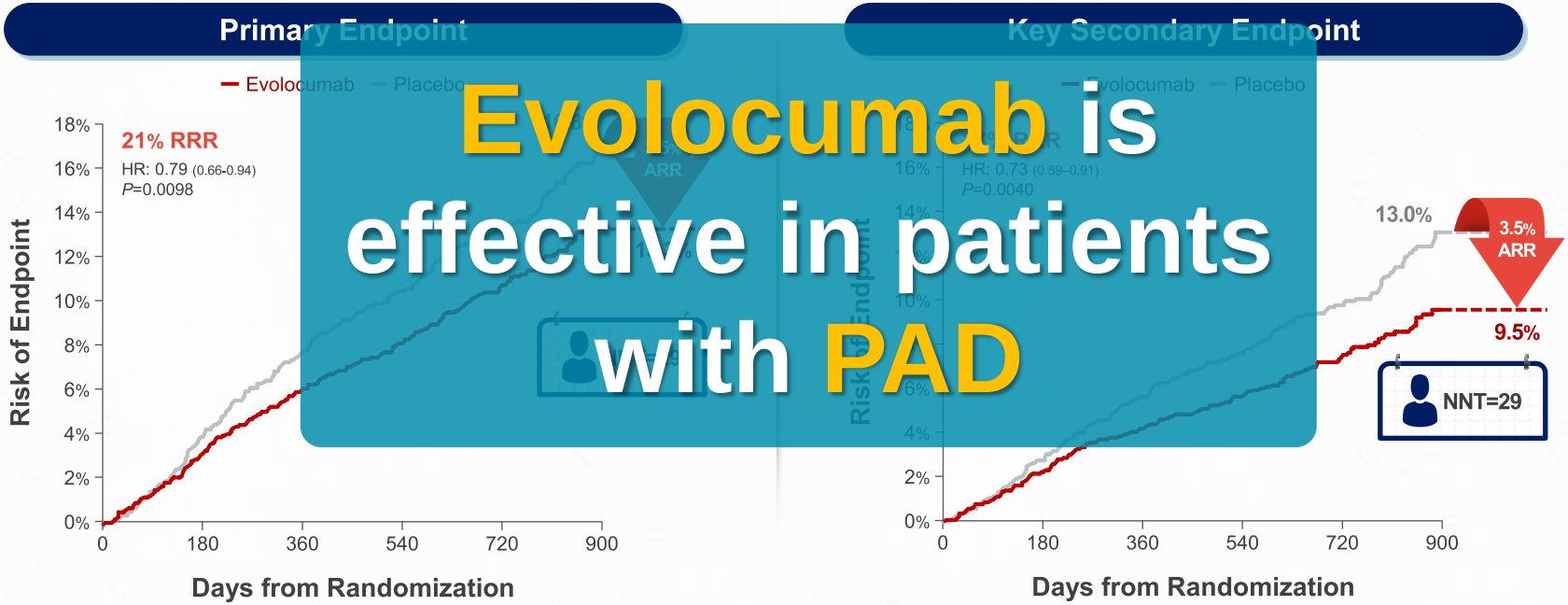
Evolocumab Significantly Reduced the Primary Endpoint and Key Secondary Endpoint in Patients with Peripheral Artery Disease



Evolocumab is effective in patients with PAD

*Composite of CV death, MI, stroke, hospital admission for unstable angina, or coronary revascularization

CV, cardiovascular; **PAD**, peripheral artery disease; **MI**, myocardial infarction; **ARR**, absolute risk reduction; **CI**, confidence interval; **HR**, hazard ratio; **NNT**, number needed to treat.

1. Bonaca MP, et al. *Circulation.* 2018;137:338-350.

레파타 급여기준

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주요 ASCVD

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- ☑ Myocardial Infarction
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  (ABI <0.85인 파행의 과거력 또는 이전의 혈관재생술이나 절단)

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- ☐ 65세 이상
- ☑ 고혈압
- ☑ 현재 흡연
- ☐ 당뇨병
- ☐ 울혈성 심부전 과거력
- ☐ LDL-C ≥100 mg/dL
  (최대내약용량의 스타틴+에제티미브 치료 이후)
- ☑ CABG 또는 PCI 과거력 (주요 ASCVD 제외)
- ☐ 만성신장질환 (eGFR 15-59 mL/min/1.73 m²)
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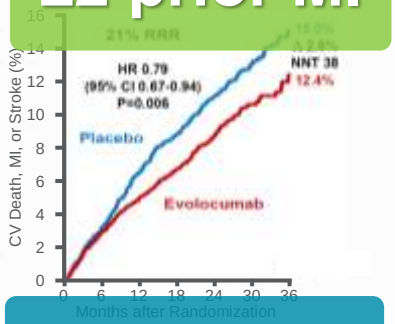
☑ ③ LDL-C ≥70 mg/dL

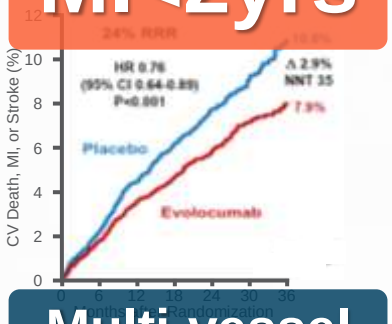
Higher Risk, Higher Benefit!

FOURIER: Evolocumab Effective in Multiple High-Risk Patient Subgroups

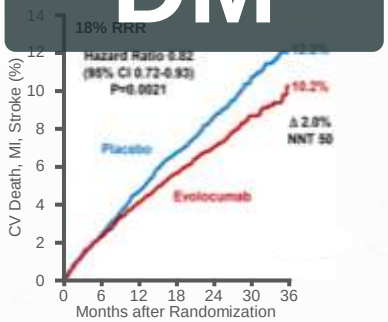
≥2 prior MI



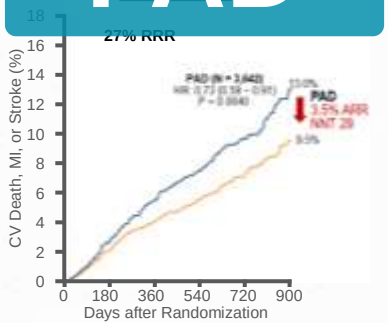
MI<2yrs



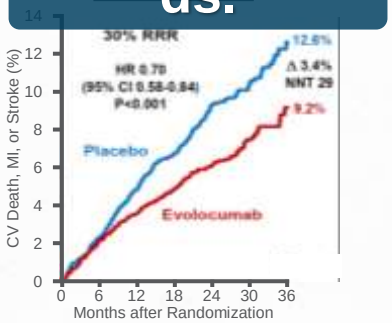
DM



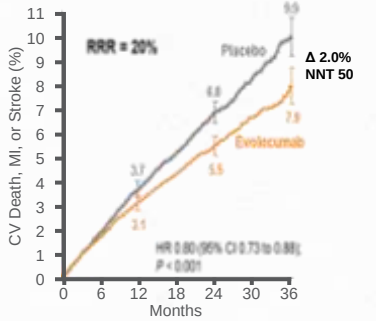
PAD



Multi-vessel ds.



All FOURIER Patients[4]



ARR, absolute risk reduction; CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction; NNT, number needed to treat; PAD, peripheral artery disease; RRR, relative risk reduction.

1. Sabatine MS, et al. Circulation. 2018;138:756-766. 2. Sabatine MS, et al. Lancet Diabetes Endocrinol. 2017;5:941-950. 3. Bonaca MP, et al. Circulation. 2017;137:338-550.
4. Sabatine MS, et al. N Engl J Med. 2017;376:1713-1722.

Summary

- **Evolocumab** is effective in **reducing CV risk in high risk** patients
- **Early Evolocumab** is better for Post-MI patients


LDL
TG
HDL
Lp(a)

CASE#4: 60 M, High calcium score (320) and Hyperlipidemia

CC:

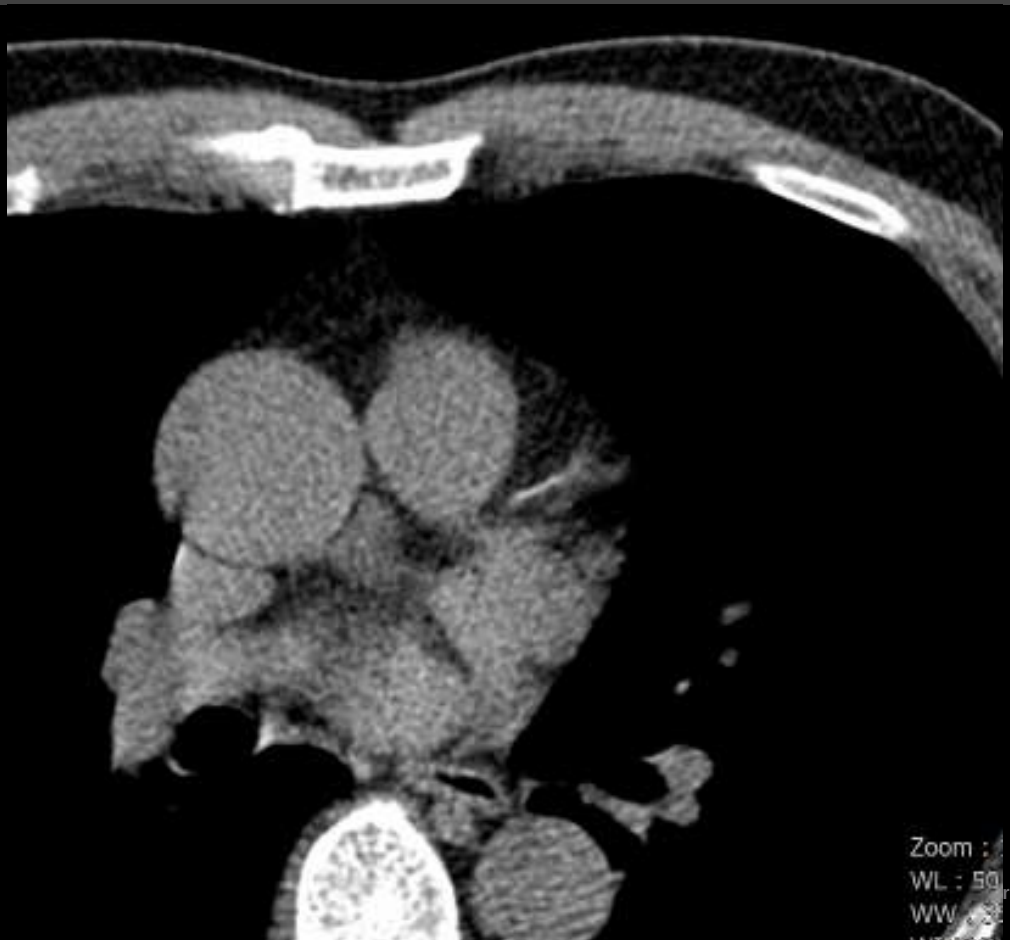
1) Hyperlipidemia:

-TC 291, TG 157, LDL-C 249 mg/dL

- On rosuvastatin 10mg + ezetimibe 10mg + fenofibrate 150mg

2)Coronary calcium score: 320

CASE: 60 M, High calcium score (320) and Hyperlipidemia



AMGEN

CASE: 60 M, High calcium score (320) and Hyperlipidemia

< PHx >

- Diabetes, Hb A1c: 6.6% on medication
- Smoker 40 pack years
- 175cm 95.3kg (BMI: 31.1)
- FHx: Father: CAD (+) → CABG (+)