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Risk of Recurrence in ACS: Why they happen and how to stop them?

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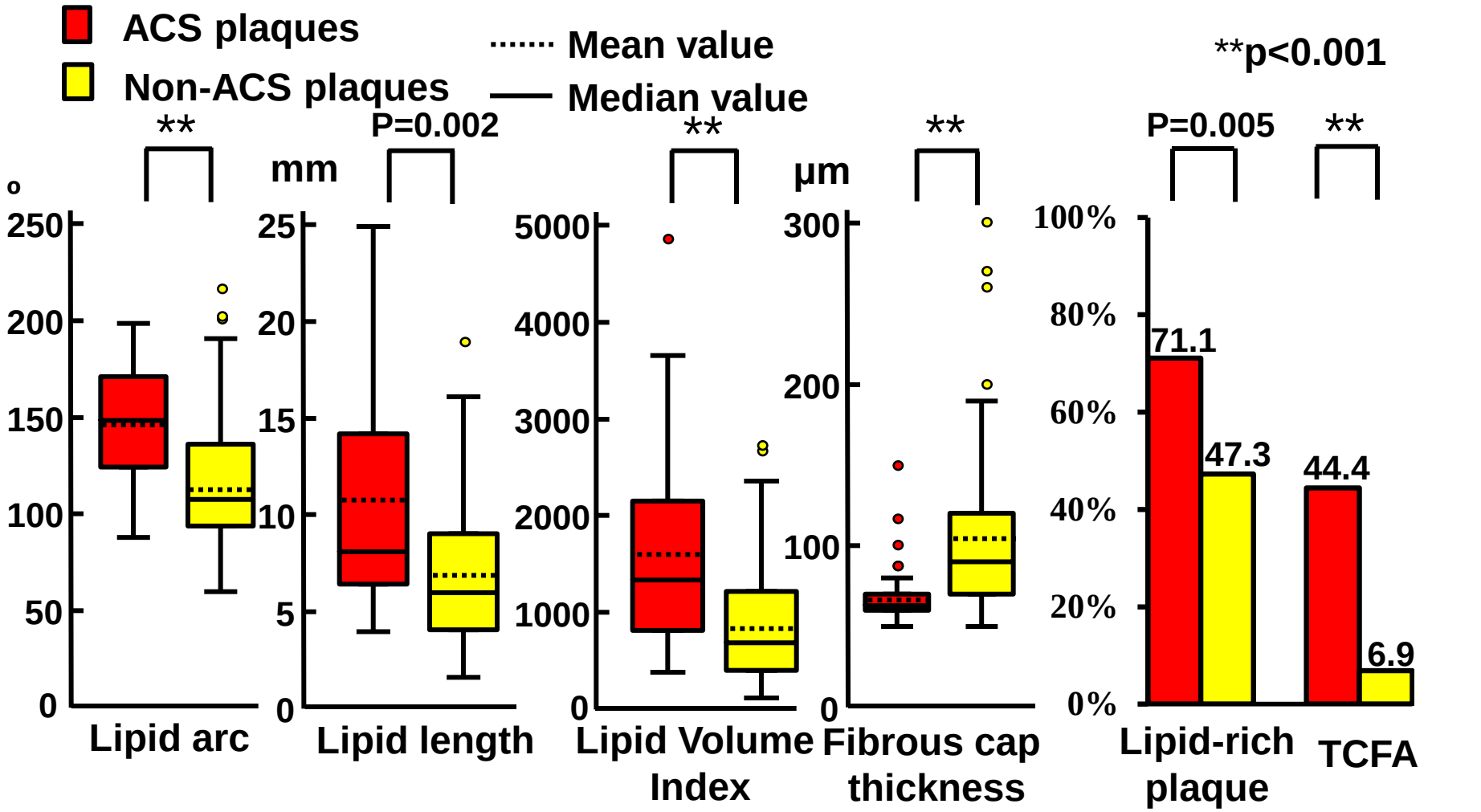
- Panvascular inflammation
- Fibrous cap
- Plaque burden
- Contemporary medical therapy

Background

- Patients with ACS have a higher incidence of recurrent ischemic events.
- Pan-vascular plaque instability may be the underlying mechanism.

Plaque-based comparison



Kato et al. Circulation CV Img 2012

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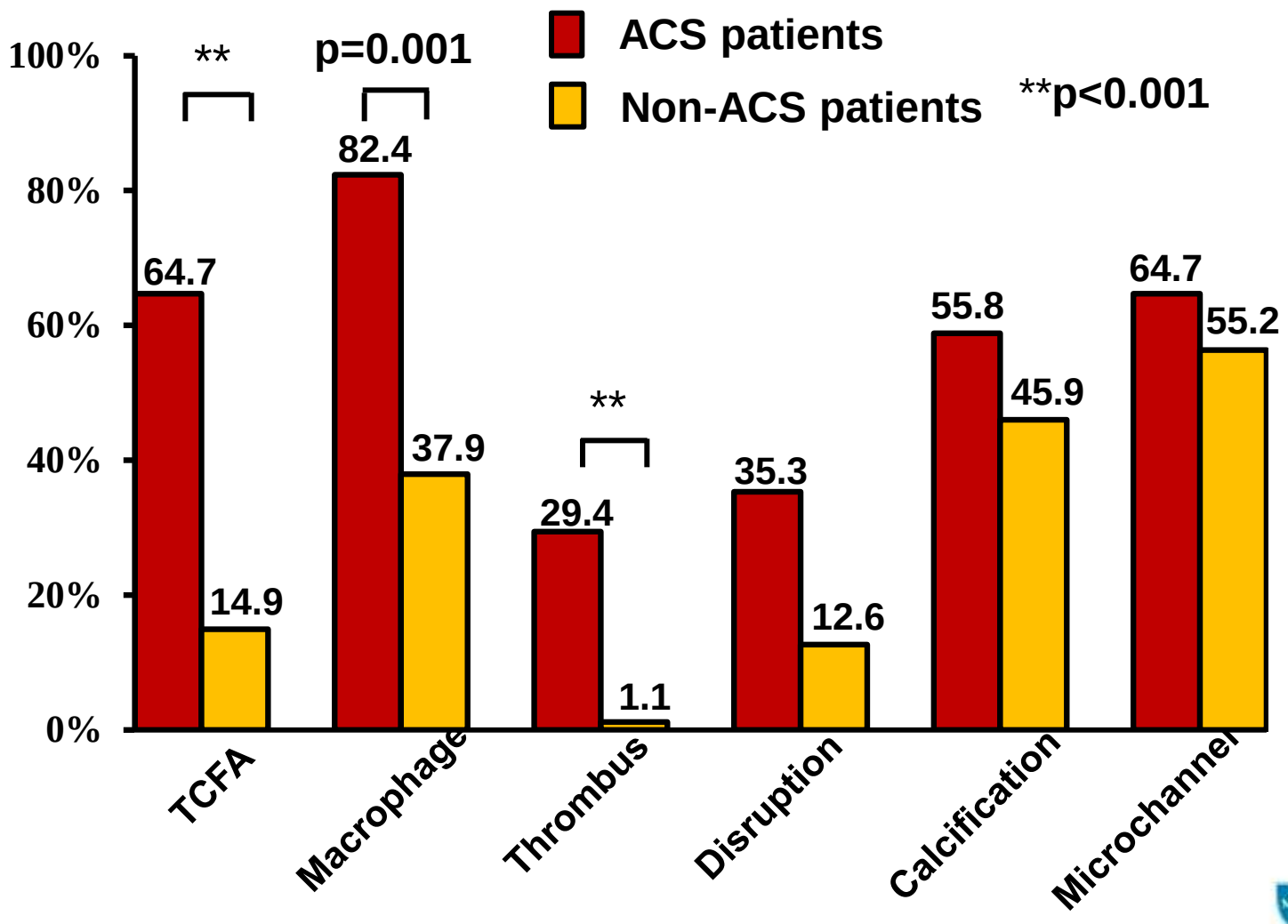
Patient-based comparison



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Conclusions

1. Compared to non-ACS plaques, ACS plaques in the non-culprit lesion had a larger lipid volume index and a thinner fibrous cap.

2. TCFA, macrophage, and thrombus in the non-culprit plaques were more frequent in ACS patients.

→ Panvascular Inflammaiton

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Aim

To analyze OCT and IVUS images of all 3 major epicardial arteries in ACS patients, and compare the morphological characteristics between the 3 groups.

- ruptured culprit plaque (RCP)
- ruptured non-culprit plaque (RNCP): silent rupture
- non-ruptured TCFA

Tian et al. JACC 2014

OCT findings: Rupture vs Non-rupture

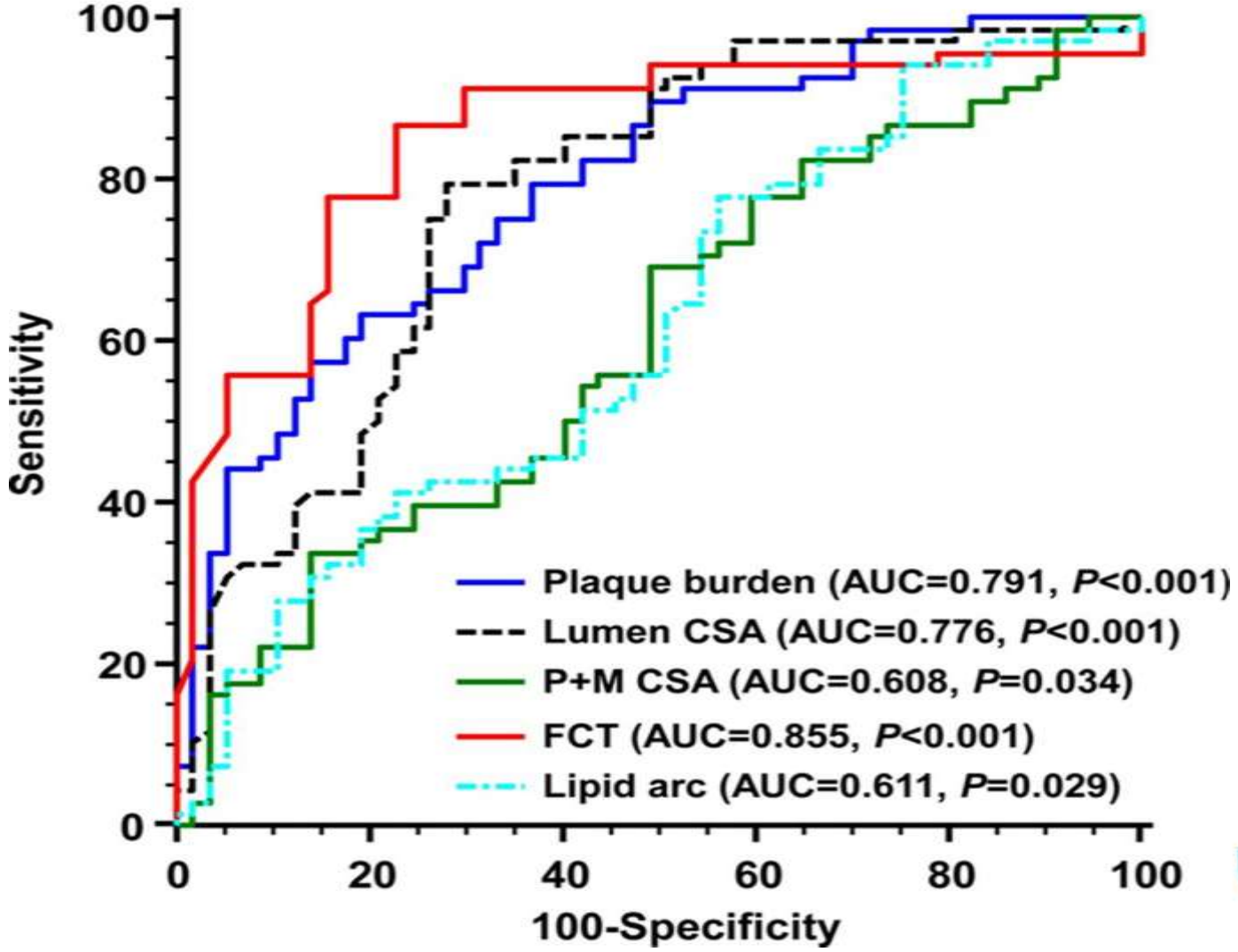
	RCP (n=49)	RNCP (n=19)	TCFA (n=58)	*P* value		
				RCP *vs.* RNCP	RCP *vs.* TCFA	RNCP *vs.* TCFA
FCT, μm	**43±11**	**41±10**	**56±9**	0.276	**<0.001**	**<0.001**
Lipid arc, °	241±64	214±54	207±63	0.023	0.005	0.581
Lipid length, mm	11.5±5.5	10.5±2.8	10.5±4.9	0.409	0.238	0.778
Microvessel	24(49)	7(37)	21(36)	0.174	0.193	0.986
Macrophage	40(82)	14(74)	49(85)	0.468	0.684	0.258
Calcification	24(49)	6(32)	27(47)	0.098	0.805	0.273
Cholesterol crystal	19(39)	5(26)	14(24)	0.355	0.122	0.877
Thrombus	38(78)	12(63)	0(0)	0.279	<0.001	<0.001

IVUS findings: Clinical vs Silent

	RCP (n=49)	RNCP (n=19)	TCFA (n=58)	*P* value		
				RCP *vs.* RNCP	RCP *vs.* TCFA	RNCP *vs.* TCFA
Proximal reference segment						
EEM CSA, mm^2	13.0±4.2	12.3±4.4	13.7±5.4	0.537	0.432	0.167
Lumen CSA, mm^2	6.5±2.3	7.2±3.3	8.8±4.0	0.419	<0.001	0.069
Distal reference segment						
EEM CSA, mm^2	9.1±3.2	9.2±4.1	10.6±3.4	0.959	0.039	0.027
Lumen CSA, mm^2	5.5±2.0	6.0±3.5	7.8±3.2	0.550	<0.001	0.190
Lesion segment						
EEM CSA, mm^2	12.8±3.5	12.6±4.6	13.9±5.2	0.829	0.154	0.219
Lumen CSA, mm^2	**2.1±0.9**	**4.6±2.3**	**5.1±2.7**	**0.001**	**<0.001**	0.423
P+M CSA, mm^2	10.8±3.3	8.0±2.8	8.9±3.6	0.001	0.005	0.233
Plaque burden, %	**82±7.2**	**64±7.2**	**62±12.5**	**<0.001**	**<0.001**	0.795
Remodeling index	1.18±0.12	1.18±0.13	1.15±0.14	0.897	0.310	0.528

Ruptured vs Non-rupture

Figure 3



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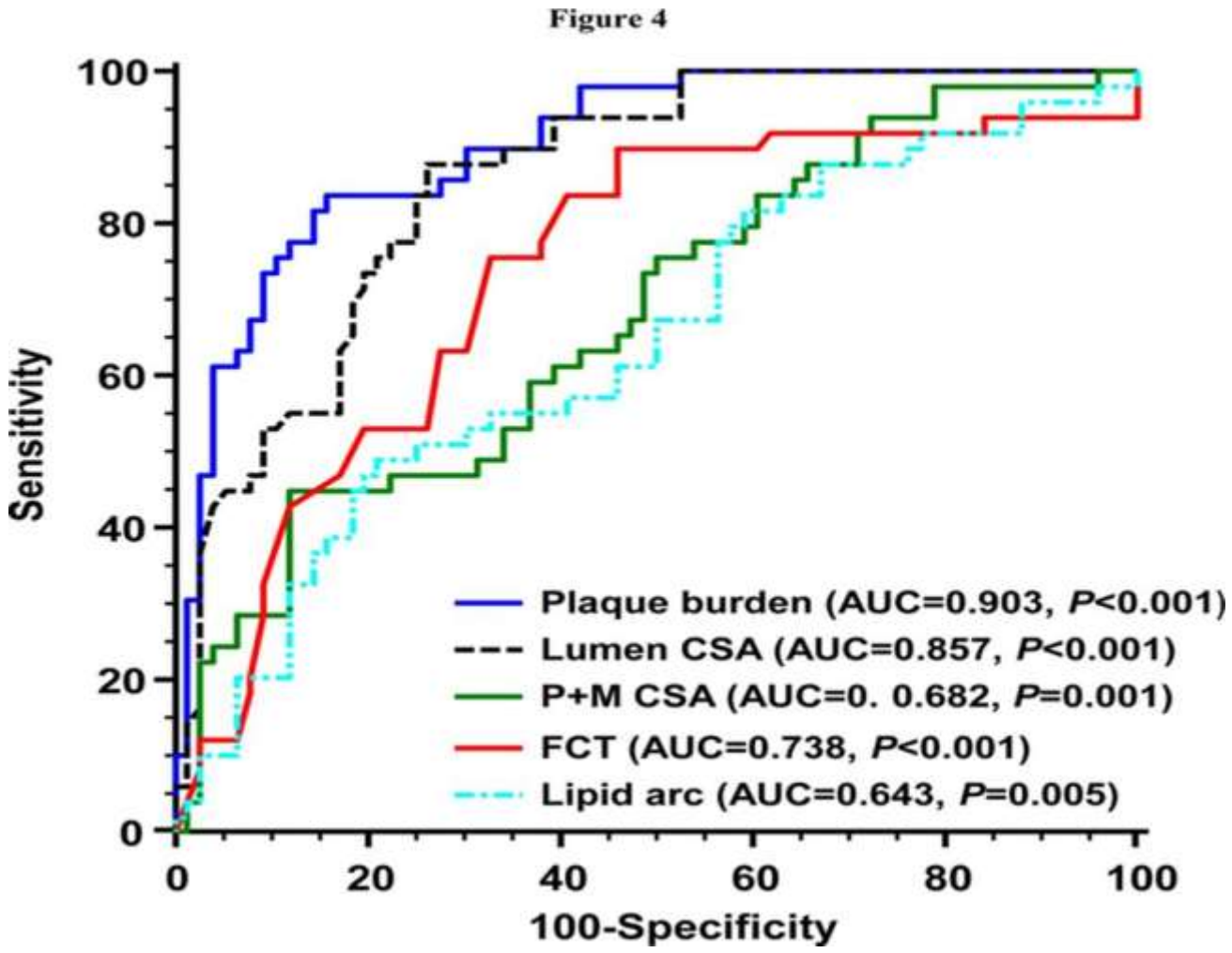
Clinical event vs Silent



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Conclusions

1. Fibrous cap thickness is a critical morphological discriminator between ruptured plaques and non-ruptured TCFA.
2. Plaque burden and lumen area are important morphological features of RCP.

- Panvascular inflammation
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Background

1. It was generally believed that ACS most frequently occurred at the site of mild to moderate coronary stenosis.

2. However, recent studies have shown that most ACS occur at the site of severe coronary stenosis.

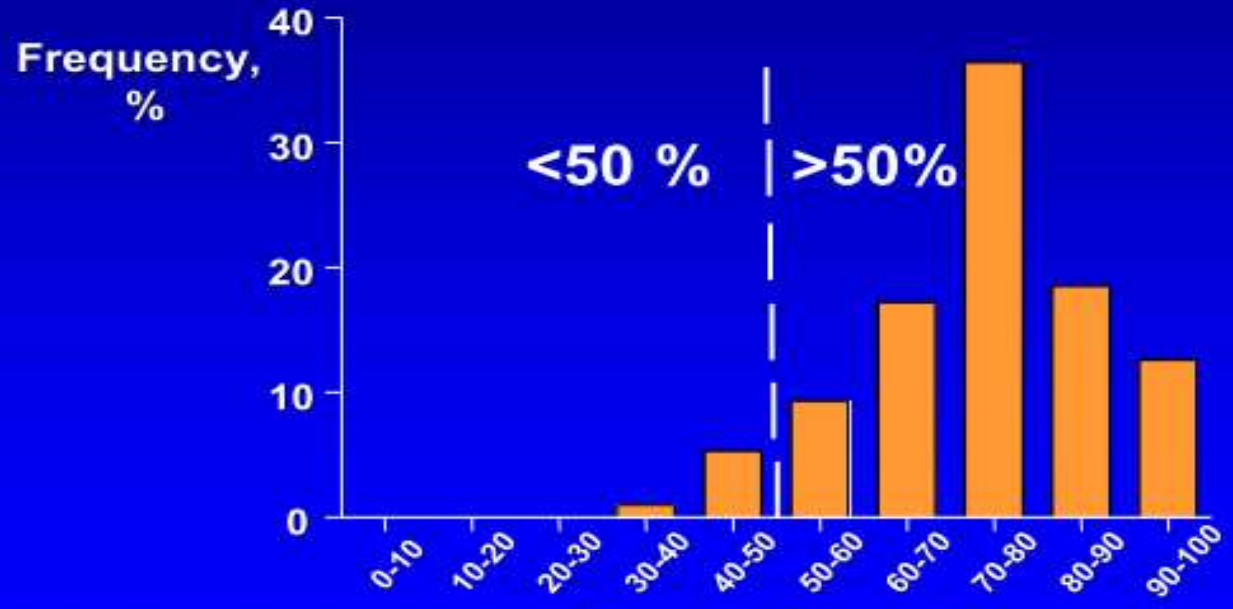
Old studies supporting mild stenosis

	Number of Patients	Delay Angio-MI
Ambrose et al *JACC* 1988	23	1 month to 7 years
Little et al. *Circulation* 1988	42	4 days to 6.3 years
Giroud et al. *AJC* 1992	92	1 month to 11 years
Moise et al. AJC 1984	116	39 months
Webster et al JACC 1990	30	55 months
Hackett et al AJC 1989	10	21 months
Total	**313**	**Average 3.9 yrs!**

Recent study supporting severe stenosis

Stenosis Severity at Primary PCI in AMI

- 156 stenoses with distal flow enabling accurate QCA out of 250 consecutive Acute MI's
- In 92 %, underlying stenosis was > 50%
- In 71 %, underlying stenosis was > 70%



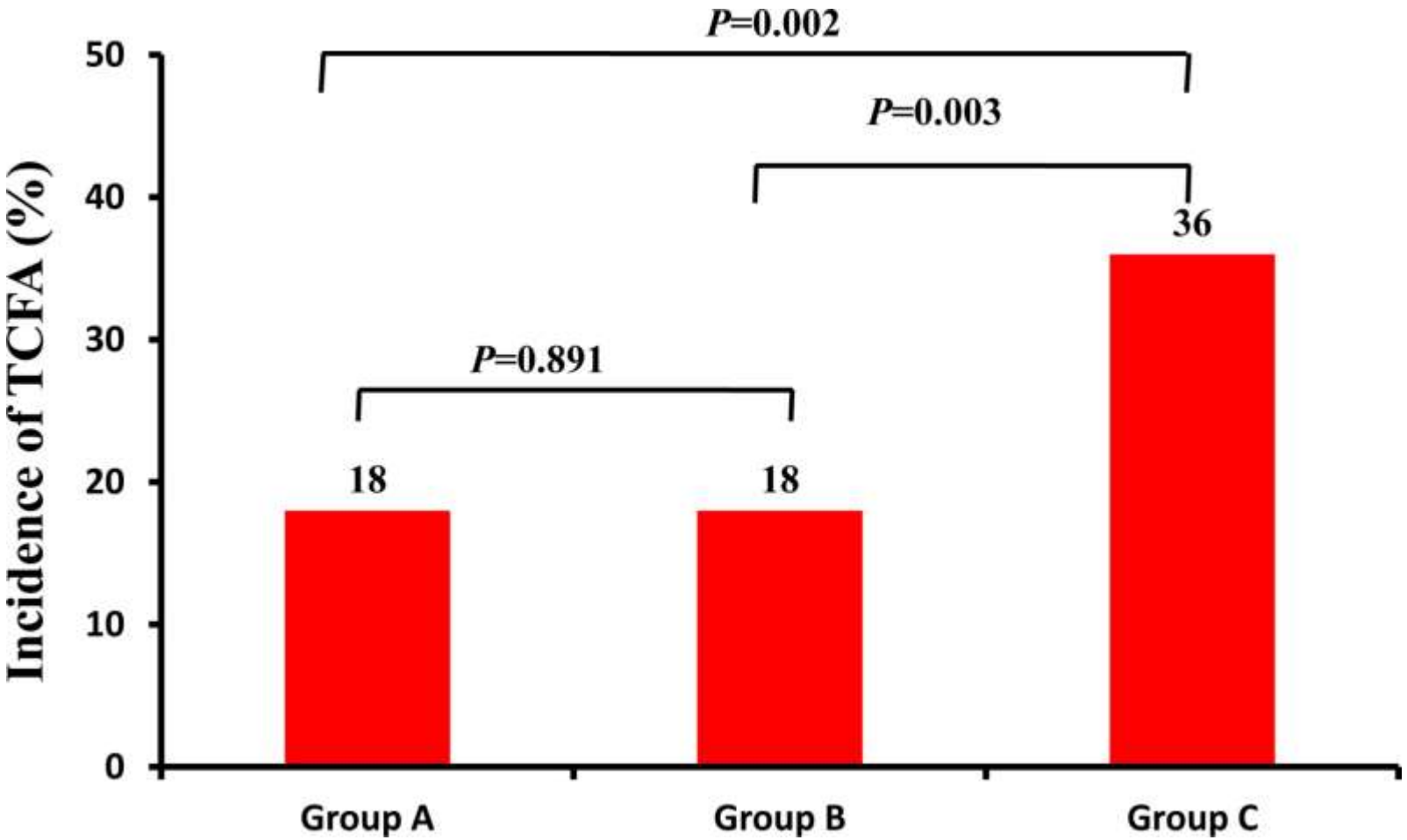
Frobert et al CCI, 2007, 70: 958-965

Method

- 643 plaques with >30% angiographic diameter stenosis were detected from 255 subjects.
- Of 643 lesions,
  - Group A (30-49%DS)
  - Group B (50-69%DS)
  - Group C (>70%DS)

Tian et al. JACC 2014

Prevalence of TCFA



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OCT findings

	Group A (n=58)	Group B (n=40)	Group C (n=33)	*P* A vs. B	*P* A vs. C	*P* B vs. C
FCT , μm	57±6.6	56±7.5	**49±9.2**	0.762	<0.001	0.001
Lipid arc, °	214±56	209±55	204±59	0.669	0.837	0.766
Lipid length, mm	9.4±4.6	10.5±5.5	9.6±4.5	0.218	0.846	0.393
Microvessel	13(22)	15(38)	**19(58)**	0.141	<0.001	0.082
Cholesterol crystal	8(14)	10(25)	**13(40)**	0.048	0.002	0.429
Macrophage	44(76)	29(73)	28(85)	0.749	0.215	0.234
Calcification	25(43)	18(45)	14(42)	0.793	0.958	0.880

Conclusions

1. The relative prevalence of TCFA is twice as high in severely stenotic lesions compared to less severe lesions.

1. Furthermore, severely stenotic TCFA has more features of plaque vulnerability.

2. These findings suggest that severely stenotic TCFA lesions may lead to clinical events in the near future, while greater number of mild to moderate lesions may lead to adverse events during long-term follow-up.

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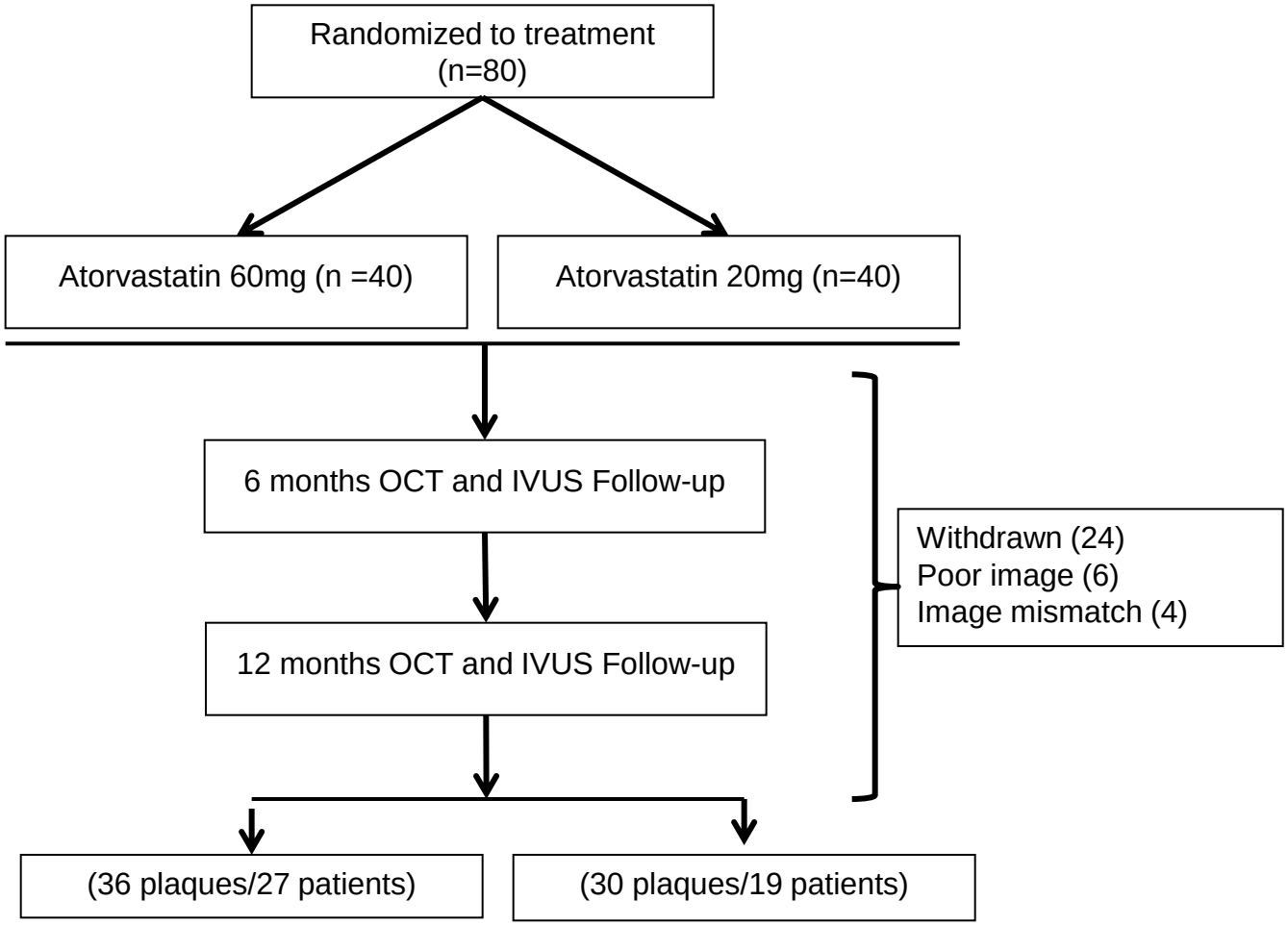
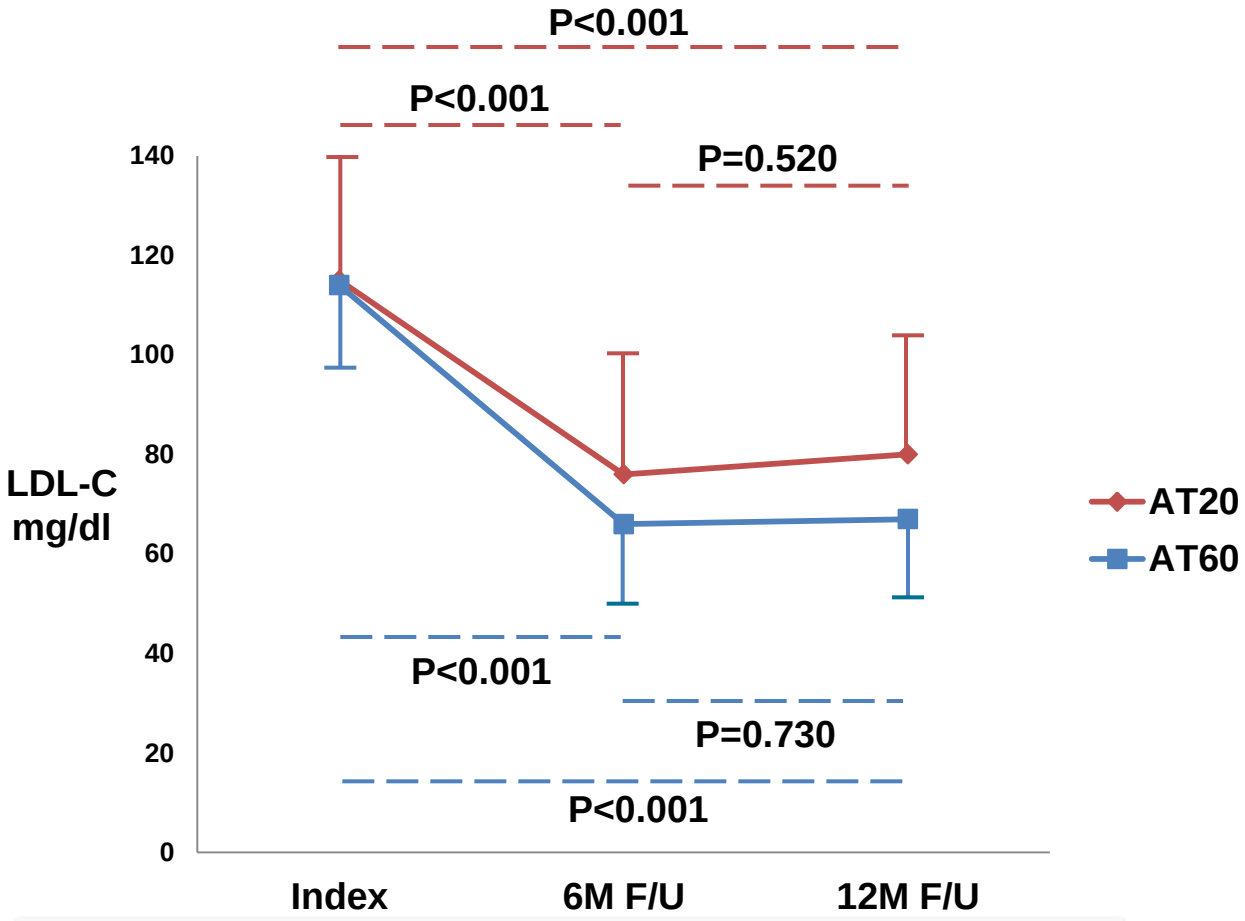
Study Design



LDL-C Levels



	Index	6M F/U	12M F/U
AT 20 mg (n = 19)	115±28	76±28	80±32
AT 60 mg (n = 27)	114±23	66±22	67±21

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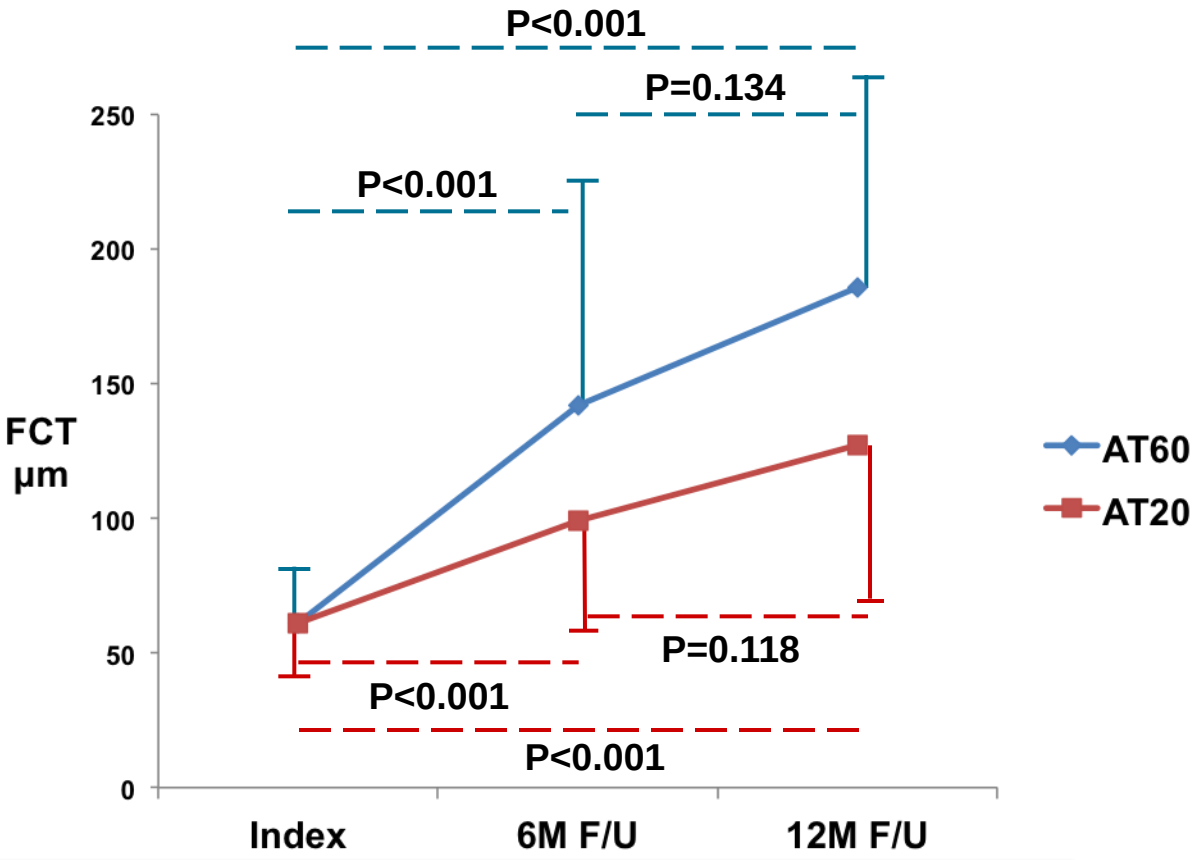
Fibrous Cap Thickness (FCT)



AT 60 mg (n = 36)	61±21	142±91	186±85
AT 20 mg (n = 30)	61±18	99±49	127±68
P AT60 vs. AT20	0.963	0.022	0.004

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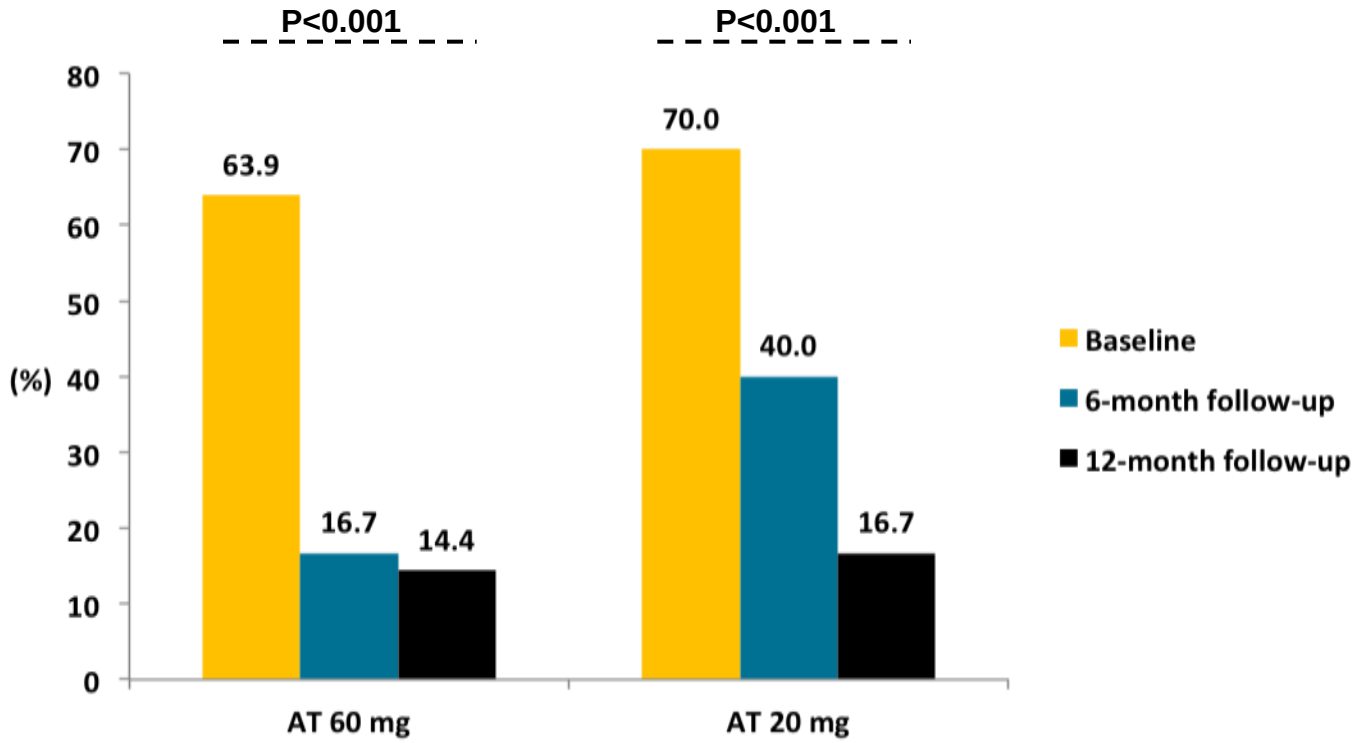
TCFA

- The prevalence of TCFA continuously decreased from baseline to 6 months and to 12 months in both groups (p<0.001).



Hou et al. AJC 2016

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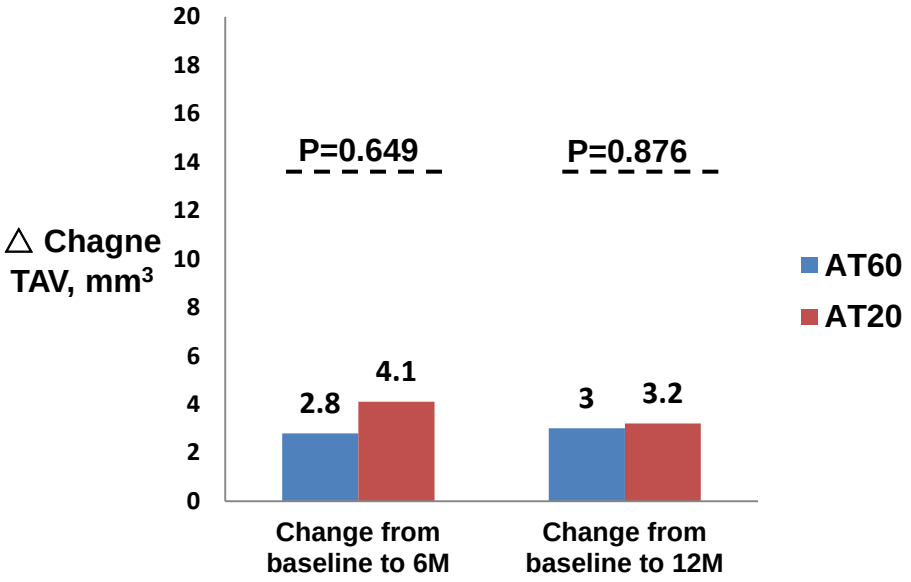
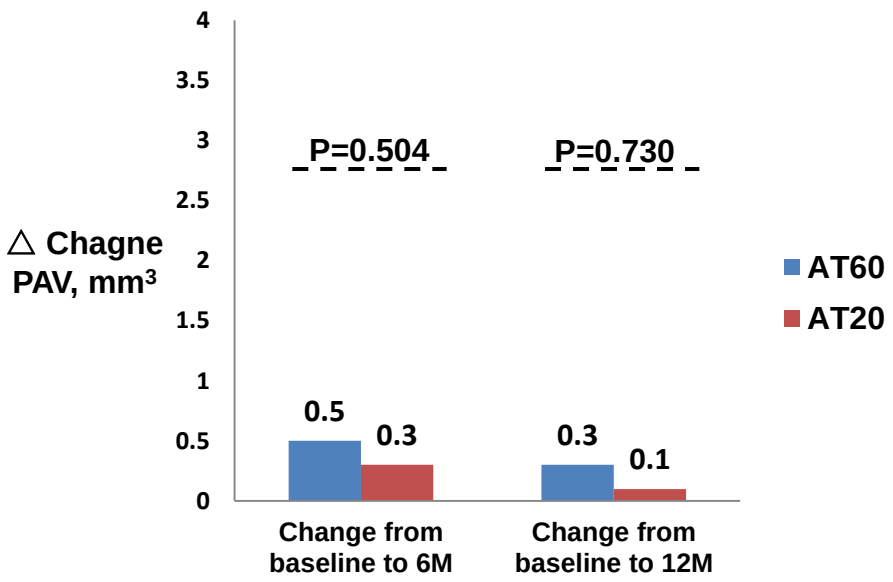
IVUS findings

Absolute change in TAV



Absolute change in PAV



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Conclusions

1. Both intensive and moderate statin therapy stabilized coronary plaques.

2. Intensive statin therapy induced more rapid and effective stabilization of lipid plaques.

3. No significant changes in plaque volume were observed over time regardless of intensity of statin therapy.

Summary (1/2)

- Non-culprit lesions in ACS patients have higher vulnerability.
- FCT is a critical morphological discriminator for plaque rupture, while plaque burden and lumen area are important morphological features of clinical events.

Summary (2/2)

- The relative prevalence of TCFA is twice as high in severely stenotic lesions compared to less severe lesions and severely stenotic TCFA has more features of plaque vulnerability.

- Intensive statin therapy induced more rapid and effective stabilization of lipid plaques.

Collaborators

Registry
21 sites

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Thank You

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