ORIGINAL ARTICLE

Influence of coronary calcification patterns on hemodynamic outcome of coronary stenoses and remodeling

Koroner kalsifikasyonu şekillerinin koroner darlıklarının hemodinamik sonuçları ve yeniden şekillenme üzerindeki etkisi

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ABSTRACT

Objective: The histological characteristics of plaque may affect the hemodynamic outcome of a given coronary stenosis. In particular, the potential effect of volumetric calcium content and the topographical distribution in the lesion segment on physiological outcome has not yet been investigated. The aim of this study was to identify any potential correlation between patterns of calcification and the fractional flow reserve (FFR) and the coronary remodeling index (RMI).

Methods: A total of 26 stable angina pectoris and 34 acute coronary syndrome patients without persistent ST-segment elevation constituted the study population. FFR was used to assess 70 intermediate coronary stenosis lesions. After obtaining hemodynamic measurements, quantitative grayscale and virtual histology-intravascular ultrasound analyses were performed. The depth, length, and circumferential distribution of calcification of the lesions were also recorded.

Results: Within the analyzed segment (area of interest, lesion segment), FFR was correlated with maximal thickness of deep calcification (r=-0.285; p=0.021) and calcification angle (r=-0.396; p=0.001). In lesions with a calcification angle >180°, the mean FFR value was significantly lower compared with those <180° (0.64±0.17 *vs.* 0.78±0.08; p=0.024). RMI was correlated with maximal angle of superficial (r=-0.437; p<0.001) and deep (r=0.425; p<0.001) calcification. RMI was correlated with maximal thickness of superficial (r=-0.357; p=0.003) and deep (r=0.417; p<0.001) calcification. RMI was also correlated with FFR (r=-0.477; p<0.001).

Conclusion: This study demonstrated that the geometry, location, and amount of calcification of a plaque could affect hemodynamic and anatomical outcome measures in functionally significant stenoses by affecting vessel wall compliance.

ÖZET

Amaç: Histolojik plak özellikleri koroner darlıklarının yol açtığı hemodinamik sonuçları etkileyebilmektedir. Kalsiyumun topografik dağılımının koroner darlıklarının yol açtığı fizyolojik sonuçları nasıl etkilediği konusunda henüz bilimsel araştırma yapılmadı. Bu çalışma fraksiyonel akım rezervi (FAR) ile kalsifikasyon paternleri arasındaki olası ilişkiyi ortaya koymayı hedeflemektedir. Ayrıca, kalsifikasyon şekillerinin koroner yeniden şekillenmesi üzerindeki etkisi de araştırılmaktadır.

Yöntemler: Kararlı angina pektorisli 26 ve kalıcı ST yükselmesiz akut koroner sendromlu 34 hasta bu çalışmaya dahil edildi. Orta derece (gözle %50 ile %80 arası darlığa sahip olduğu değerlendirilen) 70 lezyon FAR ile değerlendirildi. Hemodinamik ölçümler alındıktan sonra damar içi ultrason ile gri skala ve gerçek histolojik parametreler en küçük lümen alanı ve tüm lezyon için değerlendirildi. Lezyonlar kalsifikasyonun derinliği, uzunluğu ve dairesel dağılımına göre sınıflandırıldı.

Bulgular: Analiz edilen segmentte, FAR ile en yüksek derin kalsifikasyon açısı (r=-0.396, p=0.001) ve kalınlığı (r=-0.285, p=0.021) arasında korelasyon saptandı. Kalsifikasyon açısı 180 dereceden geniş olanlarda ortalama FAR değerinin anlamlı derecede daha düşük olduğu tespit edildi (0.64±0.17 ve 0.78±0.08, p=0.024). Koroner yeniden şekillenmesi ile en yüksek yüzeysel (r=-0.437, p<0.001) ve derin (r=0.425, p<0.001) kalsifikasyon açısı arasında korelasyon vardı. Koroner yeniden şekillenmesi ile en yüksek yüzeysel (r=-0.357, p=0.003) ve derin (r=0.417, p<0.001) kalsifikasyon kalınlığı arasında korelasyon vardı, koroner yeniden şekillenmesi ile FAR arasında korelasyon saptandı (r=-0.477, p<0.001).

Sonuç: Bu çalışma, koroner arter plağındaki kalsifikasyonun geometrisi, yerleşim yeri ve dağılımının fonksiyonel olarak anlamlı darlıklarda hemodinamik sonuçları etkileyebildiğini gösterdi. Ayrıca koroner arter kalsifikasyon şekilleri ile koroner yeniden şekillenmesi arasında korelasyon olabileceği ortaya kondu.

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Fractional flow reserve (FFR) has been recognized as the gold standard modality to evaluate the ischemic potential of epicardial coronary stenosis and can substantially influence the decision-making process in clinical practice. This measurement, however, may be affected by hemodynamic irregularities caused by both vessel- and lesion-related factors, such as lesion eccentricity, surface geometry, and plaque composition. Determination of the potential factors that could affect the hemodynamic outcome produced as a result of any given coronary stenosis may provide further insight into understanding the interplay between the anatomical substrate and physiological consequences.

In the literature, there are only a limited number of studies that sought to examine the interaction between coronary lesion composition and FFR.[1–3] Earlier studies examining the effect of VH-IVUS reported that plaque composition in intermediate coronary lesions did not demonstrate any relationship to FFR. However, it has recently been demonstrated that for a given coronary stenosis geometry, plaque composition may influence hemodynamic outcome measures in functionally significant stenoses. In particular, necrotic core and calcium content were shown to be related to hemodynamic consequences of a given coronary stenosis. Furthermore, in this aforementioned study, the negative relationship between dense calcium (DC) content and FFR was also demonstrated to be associated with a calcium-induced decrease in arterial wall compliance. However, beyond the volumetric calcium content, the potential effects of its topographical distribution in the lesion segment on physiological outcome and anatomical vascular remodeling have not yet been clarified.

To this end, the present study aimed to examine the potential influence of patterns of calcification on both physiological (FFR) and anatomical (coronary remodeling) consequences of coronary stenosis.

METHODS

Patient population

Twenty-six patients seen between June 2012 and June 2013 with stable angina pectoris and 34 acute coronary syndrome patients without persistent ST-segment elevation treated between 2010 and 2012 for intermediate stenosis (50%–80%) detected in clinically indicated coronary angiography were included in this study. Patients underwent intravascular ultrasound (IVUS) and virtual histology (VH) IVUS imaging during routine diagnostic catheterization procedure. The hemodynamic severity of the stenoses was evaluated 36 to 48 hours after an acute event in patients who presented with non-ST elevation acute coronary syndrome. Patients with previous coronary artery by-pass surgery or severe valvular disease were excluded. The study was conducted in accordance with the Declaration of Helsinki, and the local ethical review board approved the study protocol. Written informed consent was obtained from all patients.

Abbreviations:

CSA	*Cross-sectional area*
DC	*Dense calcium*
EEM	*External elastic membrane*
FFR	*Fractional flow reserve*
IVUS	*Intravascular ultrasound*
MLA	*Minimal lumen area*
P&M	*Plaque plus media*
RMI	*Remodeling index*
VH	*Virtual histology*

Study protocol

Intracoronary hemodynamic measurements

For the assessment of hemodynamic significance of a given coronary stenosis, a pressure sensor equipped guidewire (PressureWire; St. Jude Medical Inc., MN, USA or ComboWire; Volcano Therapeutics, Rancho Cordova, CA, USA), was advanced across the lesion. Aortic pressure was obtained from the guiding catheter and distal intracoronary pressure was recorded from the pressure sensor. All hemodynamic signals were recorded at baseline and during maximum hyperemia induced by a bolus of intracoronary papaverine (20 mg for the left system and 15 mg for the right coronary artery and).

Pressure signals recorded on the device console (Radi Analyzer Xpress; St. Jude Medical Inc., St. Paul, MN, USA or ComboMap; Volcano Corp., San Diego, CA, USA) were extracted from the digital archive and analyzed offline after the procedure. FFR was calculated as the ratio of mean distal to mean aortic pressure during maximum hyperemia.

IVUS and VH-IVUS imaging

After obtaining the hemodynamic measurements, an IVUS catheter (Eagle Eye Gold; Volcano Corp., San Diego, CA, USA) was advanced over the pressure monitoring guidewire and automated pullback was performed at a speed of 0.5 mm per second. Quantitative grayscale and VH-IVUS analyses were performed and reported at the site of minimum lumen area (MLA) and across the entire lesion segment, ac-

cording to the recommendations of a consensus document on the interpretation and reporting of VH-IVUS parameters.[4] External elastic membrane (EEM) and lumen cross-sectional area (CSA) were measured. Plaque plus media (P&M) CSA was calculated as EEM minus lumen CSA, and plaque burden at MLA site was calculated as P&M divided by EEM CSA. Volume was calculated using Simpson's rule. Remodeling index (RMI) was expressed as the external elastic membrane CSA at the MLA site divided by the EEM CSA at the reference site. Lesion length was measured using the motorized pullback device (InVision Gold with the model R-l00 research pullback device; Volcano Corp., San Diego, CA, USA).

The 4 VH-IVUS plaque components (fibrous, fibro-fatty, DC, and necrotic core) were measured in every recorded frame in the entire diseased segment and expressed as absolute amounts and as a percentage of plaque area or plaque volume.

Statistical analysis

Statistical tests were performed with IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean+SD. Relationships between continuous variables were examined using the Pearson correlation or linear regression analysis. Relationships between hemodynamic parameters (FFR) and plaque components were examined, controlling for anatomical factors that may affect hemodynamic outcomes, including IVUS minimal luminal area (MLA), and lesion length by using partial correlation analysis. Significance was accepted as $p<0.05$.

RESULTS

Patient characteristics

Patient demographic details and angiographic findings are summarized in Table 1. Seventy culprit le-

Table 1. Patient characteristics

Clinical and demographical characteristics (n=60)	n	%	Mean±SD
Male/All patient	51	85	
Age (years)			58.8±10.5
Body mass index (kg/m²)			28.9±4.4
Diabetes Mellitus	30	50	
HbA1C (%)			6.7±1.5
Chronic renal disease	9	15	
Hypertension	44	73	
Dyslipidemia	29	48	
Smoking	35	58	
Stable angina	26	43	
Unstable angina and non-STEMI	34	57	
Previous myocardial infarction	5	8	
Ejection fraction (echocardiography), (%)			59.6±7.4
Percutaneous coronary intervention	49	70	
Stenoses (n=70)			
Left anterior descending artery	36	51	
Diagonal	1	1.4	
Coronary vessels			
Intermediate	4	5.7	
Circumflex	12	17.1	
Right coronary artery	17	24.3	
Stent length, mean (mm)			20.9±6.1

SD: Standard deviation.

Table 2. Intracoronary hemodynamic measurements

	Stable plaques (n=36)	Unstable plaques (n=34)	Total (n=70)
	Mean±SD	Mean±SD	Mean±SD
Mean aortic pressure baseline (mmHg)	102.3±17.6	106.5±15.1	102.3±17.6
Mean aortic pressure hyperemic (mmHg)	93.0±19.0	98.6±15.5	95.4±19.1
Mean distal intracoronary pressure baseline (mmHg)	89.0±23.6	81.8±25.4	86.6±24.2
Mean distal intracoronary pressure hyperemic (mmHg)	68.3±20.2	64.3±20.6	67.3±20.3
Fractional flow reserve	0.72±0.14	0.64±0.14	0.70±0.14

SD: Standard deviation.

sions from 34 patients with acute coronary syndrome without persistent ST-segment elevation and 26 stable angina pectoris patients were studied. All acute coronary syndrome patients had a single culprit lesion, whereas 36 lesions were assessed in the 26 stable angina pectoris patients. A total of 49 lesions (70%) were treated with percutaneous coronary intervention after hemodynamic and morphological evaluation. Half of the stenoses (51%) evaluated in this study were located in the left anterior descending artery.

Hemodynamic and morphological findings

a. Effect of calcification pattern on hemodynamic consequence of coronary stenoses

The mean intracoronary hemodynamic measurements are listed in Table 2. The mean FFR value was 0.70±0.14. Functionally significant coronary stenosis, defined as FFR <0.80, was observed in 50 lesions. Grayscale and VH-IVUS characteristics are provided in Table 3. The mean MLA was 2.62±0.8 mm^2, the mean EEM cross-sectional area was 12.8±4.2 mm^2, and the mean plaque burden was 78.1±7.7%. The parameters for calcification patterns were determined as the maximal angle of superficial and deep calcification and maximal length and thickness of superficial and deep calcium within the analyzed segment (entire lesion segment and MLA).

The maximal deep calcification angle within the analyzed segment (area of interest, lesion segment) was correlated with FFR (r=-0.396; p=0.001) (Figure

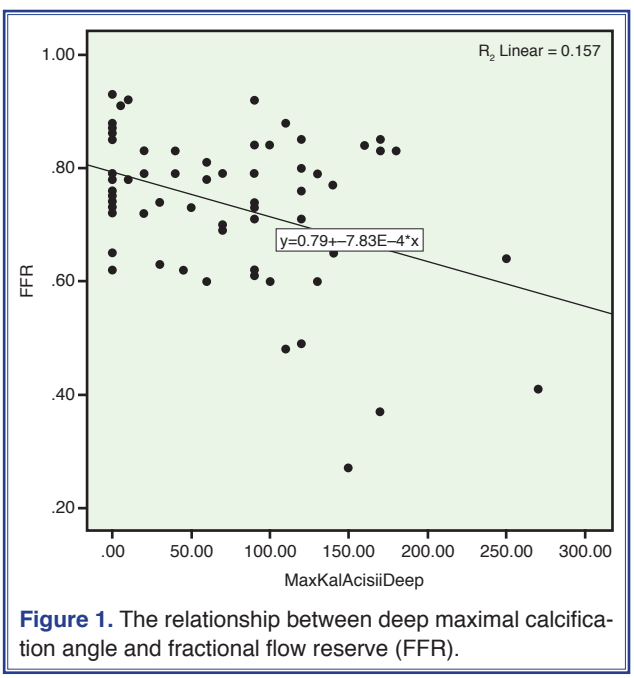

Figure 1. The relationship between deep maximal calcification angle and fractional flow reserve (FFR).

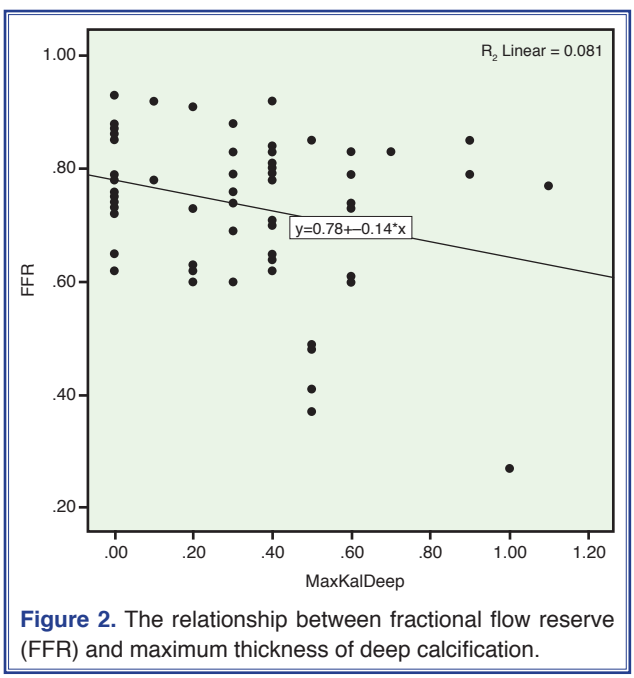

Figure 2. The relationship between fractional flow reserve (FFR) and maximum thickness of deep calcification.

Table 3. Intracoronary ultrasonographic characteristics (n=70)

Gray scale measurements		
At the minimum luminal cross sectional area		
EEM (mm^2)	12.8±4.2	
Plaque + media (mm^2)	10.2±3.2	
Plaque burden (%)	78.1±7.7	
Minimal luminal area (mm^2)	2.62±0.8	
Volumetric analysis		
EEM volume (mm^3)	188.5±25.9	
Luminal volume (mm^3)	54.9±24.5	
Plaque + media volume (mm^3)	129.2±83.5	
Other gray scale IVUS data		
Lesion length (mm)	14.9±8.4	
Attenuated plaque, n (%)	17 (24)	
Reference EEM cross sectional area (mm^2)	12.14±4.04	
Remodelling index	1.1±0.3	
EEM compliance (mean) ($mm^2mmHg^{-1}x10^3$)	1.9±1.3	
Virtual histology measurements		
At the minimum luminal cross sectional area	%	mm^2
Fibrous area	55.2±14.1	4.3±2.3
Fibro-fatty area	13.5±11.7	1.1±1.1
Necrotic core area	21.2±9.0	1.7±1.1
Dense calcium area	9.0±10.5	0.6±0.5
Necrotic core/dense calcium areas	4.7±4.3	
Volumetric analysis	%	mm^3
Fibrous volume	54.2±10.6	48.8±35.5
Fibro-fatty volume	14.3±10.8	11.8±10.7
Necrotic core volume	21.4±7.7	21.3±18.8
Dense calcium volume	9.9±9.1	8.9±10.4
Necrotic core/dense calcium volumes	3.5±2.4	

EEM: External elastic membrane; IVUS: Intravascular ultrasonography.

1). This correlation remained significant even after controlling for MLA using partial correlation analysis (r=-0.373; p=0.002). Maximal thickness of deep calcification in the area of interest was correlated with FFR (r=-0.285; p=0.021) (Figure 2). This correlation also remained significant after controlling for MLA by partial correlation (r=-0.268, p=0.031). Lesions were then grouped based on the angle of calcification (>180°<). In lesions with a calcification angle of >180°, the mean FFR value was significantly lower compared with those of <180° (0.64+0.17 *vs.* 0.78+0.08; p=0.024) (Figure 3).

b) Effect of vascular remodeling pattern on hemodynamic consequence of coronary stenoses

RMI was correlated with maximal angle of superficial (r=-0.437; p<0.001) (Figure 4a) and deep (r=0.425; p<0.001) calcification (Figure 4b). RMI was also correlated with % DC volume in the entire analyzed lesion segment (r=-0.330; p=0.007) and with maximal thickness of superficial (r=-0.357; p=0.003) (Figure 5a) and deep (r= 0.417; p<0.001) calcification (Figure 5b). There was a negative correlation between RMI and the length of a calcific segment with >180° angle of calcification (r=-0.277;

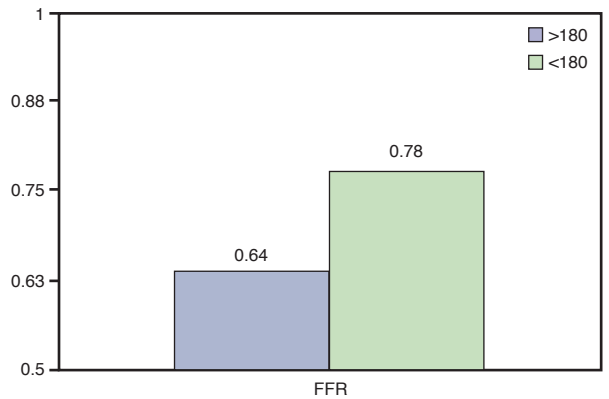

Figure 3. The mean fractional flow reserve (FFR) value was significantly lower in lesions with calcification angle >180° with compared to those with <180° (0.64±0.17 vs. 0.78±0.08, p=0.024).

p=0.024). RMI was also correlated with FFR (r=-0.477; p<0.001 (Figure 6).

DISCUSSION

The findings of this study suggest that patterns of lesion calcification may substantially contribute to hemodynamic effects produced by individual coronary stenoses and vascular remodeling in the diseased segment.

Although 3 previous studies have shown that the composition of a given coronary stenosis may not have a significant impact on its hemodynamic effect,[1–3] we recently demonstrated that a necrotic core component and calcium content in a diseased segment may influence the hemodynamic effect generated by physiologically significant coronary stenoses.[5] In particular, in that study, we showed that the FFR value decreases with an increase in volumetric calcium content in the area of interest. However, the potential effect of patterns of calcification (length, angle, and thickness) in the diseased vascular segment on translesional pressure drop has not yet been determined.

In addition to the classic physical determinants of pressure drop across stenosis, such as MLA and lesion length, factors that are potentially related to frictional energy loss caused by surface characteristics may have a considerable effect on the pressure drop across a stenosis. An individual plaque component can contribute to the generation of micro-turbulences at the plaque level that lead to loss of kinetic energy in the blood flow and an increase in translesional pressure gradient via increasing surface irregularities,

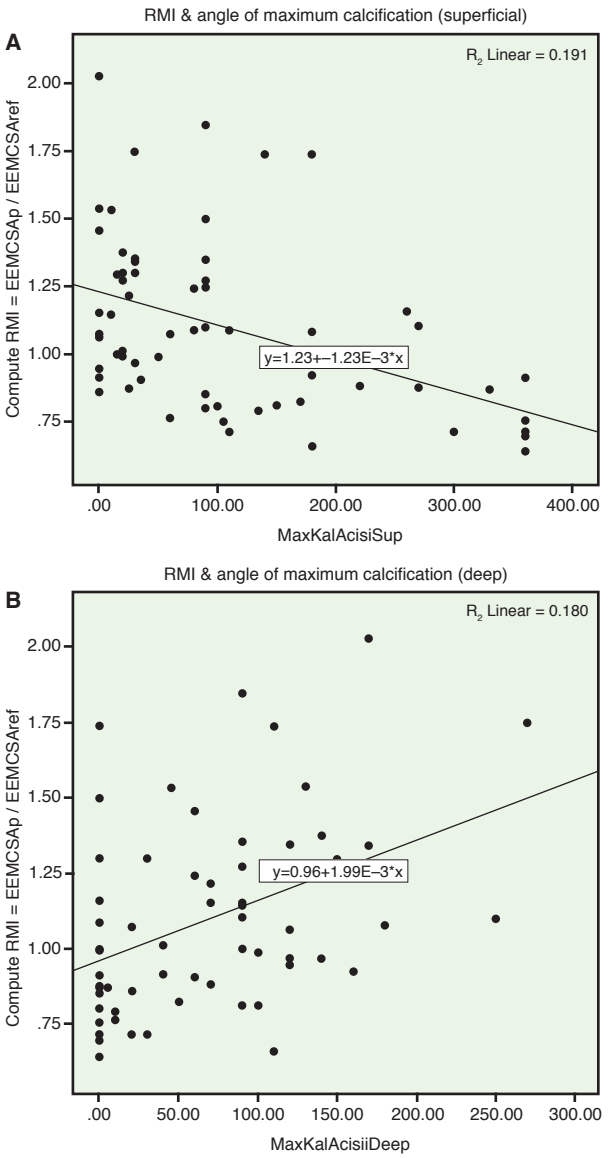

Figure 4. Relationship between remodelling index (RMI) and angle of maximal calcification.

EEM: External elastic membrane; CSA: Cross sectional area; Ref: Reference site.

and therefore, to stenosis resistance. Accordingly, the presence of ruptured plaques has been shown to influence the hemodynamic significance of a given coronary stenosis. In addition, the calcium content of the diseased segment may influence the magnitude of the translesional pressure drop via decreasing arterial wall compliance. It is understood that compliance of the coronary arteries can exert a remarkable effect on hemodynamic endpoints, especially in the physiologically significant lesion subset. In our earlier study, an inverse correlation found between DC volume and arterial wall compliance supported the concept that

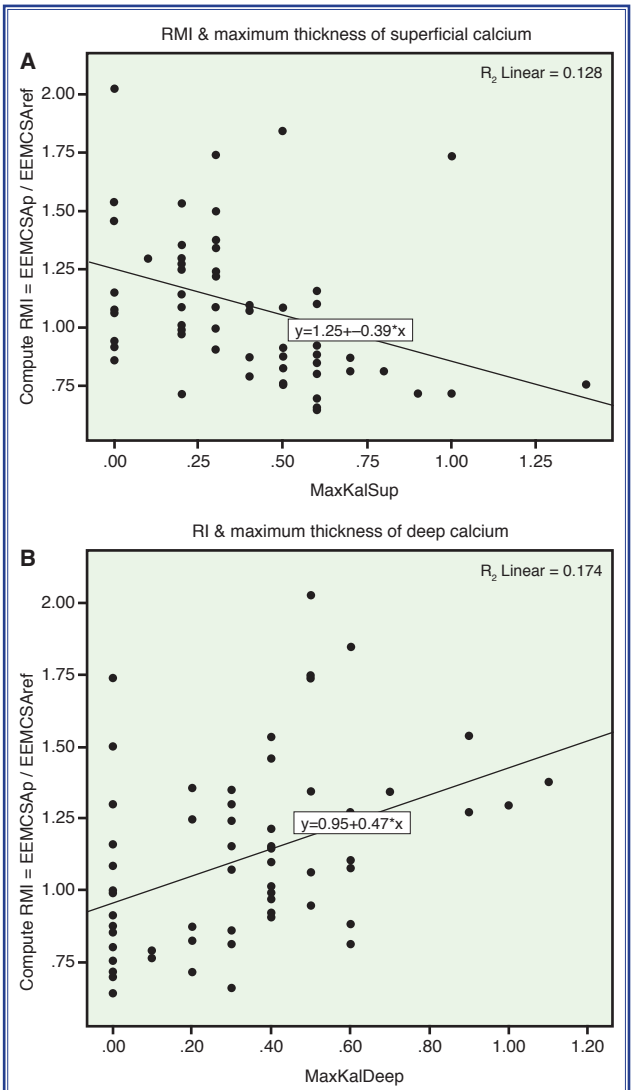

Figure 5. Relationship between remodelling index (RMI) and maximal thickness of calcium.

EEM: External elastic membrane; CSA : Cross sectional area; Ref: Reference site.

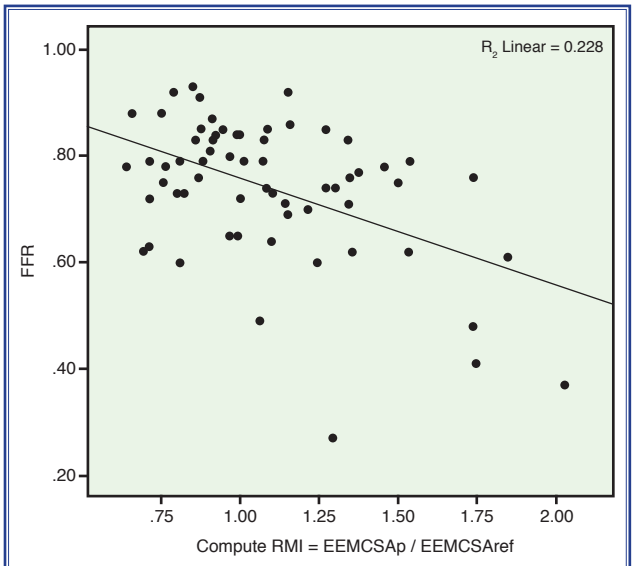

Figure 6. The relationship between remodelling index(RMI) and fractional flow reserve (FFR).

EEM: External elastic membrane; CSA : Cross sectional area; Ref: Reference site.

the amount of calcification may influence hemodynamic outcomes by reducing vessel compliance.[5] In line with this finding, it was previously reported that there was a negative correlation between EEM compliance and magnitude of calcification.[6,7] Therefore, the correlation demonstrated between calcium content and the magnitude of ischemia generated by the stenosis may partly be explained by the calcium-induced decrease in arterial compliance. However, beyond its volumetric magnitude, the topographical distribution of calcification may also influence the ischemia generated by a given coronary stenosis. In the current study, the geographical and geometrical distribution of calcification within the diseased coronary segment was assessed in detail using VH-IVUS analysis. After controlling for physical determinants of the trans-stenotic pressure drop, the angle and thickness of deep calcification were found to be negatively associated with FFR. In particular, lesions with a calcification angle greater than 180° had a significantly lower FFR value compared with those with a calcification angle less than 180°. These findings confirm and expand on the substantial impact of lesion calcification on the hemodynamic effect generated by coronary stenoses. In addition to volumetric calcium content, its geometrical features also affect the magnitude of the ischemia produced by any given coronary stenosis.

Clinical studies have shown that positive remodeling in the diseased segment is associated with more biological activation and unstable clinical presentation compared with their intermediate and negatively remodeled counterparts.[8–10] The current study included mostly unstable plaques in the positively remodeled coronary segments and demonstrated a surprisingly negative correlation between FFR and the remodeling index. This unexpected finding can be explained by the complex nature of the unstable plaques with surface irregularities, fissures, and micro-ruptures, which may cause a disproportionally high frictional energy loss and pressure drop across the stenosis. In particular, RMI values decrease with an increase in angle and thickness of superficially located calcium. On the contrary, RMI

values increase with an increase in angle and thickness of the deep/adventitial calcium. These findings imply that a greater magnitude of calcification at a superficial level is linked with negative/constrictive remodeling, but an greater degree of calcification at an adventitial level is associated with positive remodeling, which is a hallmark of the vascular wall features of unstable plaques. These findings may appear to be contradictory. However, in a large study involving patients who underwent computed tomography coronary angiography, lesion calcification was found to be an independent predictor of poor prognosis.[11] This result was also thought to be surprising, as the conventional paradigm was that soft plaques were thought to be more vulnerable.[12] In the current study, the relationship between the degree of adventitial calcification and positive remodeling suggests that calcium-induced decrease in compliance at the site of coronary lesions may lead to a pathogenic rheological state that may predispose to plaque rupture and cardiac events in the future.

Conclusion

This study demonstrated that for a given stenosis geometry, the thickness and circumferential distribution of calcification may influence the hemodynamic relevance of a certain coronary stenosis and vascular remodeling in diseased coronary segments.

Limitations

This is a single-center study and included a relatively small number of patients.

Different plaque characteristics between patients with stable and unstable angina pectoris may affect hemodynamic outcome and interpretation of study results. Circumferential regional differences in compliance were not considered in the present study. To clarify the difference between superficial and deep calcium correlation with the remodeling index, we need further studies that include more patients.

Conflict-of-interest: None declared.

REFERENCES

1. Brugaletta S, Garcia-Garcia HM, Shen ZJ, Gomez-Lara J, Diletti R, Sarno G, et al. Morphology of coronary artery lesions assessed by virtual histology intravascular ultrasound tissue characterization and fractional flow reserve. Int J Cardiovasc Imaging 2012;28:221–8. [CrossRef]
2. Waksman R, Legutko J, Singh J, Orlando Q, Marso S, Schloss T, et al. FIRST: Fractional Flow Reserve and Intravascular Ultrasound Relationship Study. J Am Coll Cardiol 2013;61:917–23.
3. Rogers JH, Wegelin J, Harder K, Valente R, Low R. Assessment of FFR-negative intermediate coronary artery stenoses by spectral analysis of the radiofrequency intravascular ultrasound signal. J Invasive Cardiol 2006;18:448–53.
4. García-García HM, Mintz GS, Lerman A, Vince DG, Margolis MP, van Es GA, et al. Tissue characterisation using intravascular radiofrequency data analysis: recommendations for acquisition, analysis, interpretation and reporting. EuroIntervention 2009;5:177–89. [CrossRef]
5. Hüseyinova G, Aslanger E, Çakır O, Atıcı A, Panç C, Demirkıran A, et al. Potential contribution of virtual histology plaque composition to hemodynamic-morphologic dissociation in patients with non-ST elevation acute coronary syndrome. Int J Cardiol 2015;187:33–8. [CrossRef]
6. Ishihara Y, Kawasaki M, Hattori A, Imai H, Takahashi S, Sato H, et al. Relationship among coronary plaque compliance, coronary risk factors and tissue characteristics evaluated by integrated backscatter intravascular ultrasound. Cardiovasc Ultrasound 2012;10:32. [CrossRef]
7. Alfonso F, Macaya C, Goicolea J, Hernandez R, Segovia J, Zamorano J, et al. Determinants of coronary compliance in patients with coronary artery disease: an intravascular ultrasound study. J Am Coll Cardiol 1994;23:879–84. [CrossRef]
8. Schoenhagen P, Ziada KM, Kapadia SR, Crowe TD, Nissen SE, Tuzcu EM. Extent and direction of arterial remodeling in stable versus unstable coronary syndromes: an intravascular ultrasound study. Circulation 2000;101:598–603. [CrossRef]
9. Pasterkamp G, Schoneveld AH, van der Wal AC, Haudenschild CC, Clarijs RJ, Becker AE, et al. Relation of arterial geometry to luminal narrowing and histologic markers for plaque vulnerability: the remodeling paradox. J Am Coll Cardiol 1998;32:655–62. [CrossRef]
10. Varnava AM, Mills PG, Davies MJ. Relationship between coronary artery remodeling and plaque vulnerability. Circulation 2002;105:939–43. [CrossRef]
11. Hadamitzky M, Achenbach S, Al-Mallah M, Berman D, Budoff M, Cademartiri F, et al; CONFIRM Investigators. Optimized prognostic score for coronary computed tomographic angiography: results from the CONFIRM registry (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter Registry). J Am Coll Cardiol 2013;62:468–76. [CrossRef]
12. Ahmadi N, Ruiz-Garcia J, Hajsadeghi F, Azen S, Mack W, Hodis H, et al. Impaired coronary artery distensibility is an endothelium-dependent process and is associated with vulnerable plaque composition. Clin Physiol Funct Imaging 2016;36:261–8.

Keywords: Coronary calcification; coronary remodeling; fractional flow reserve; intravascular ultrasound.

Anahtar sözcükler: Koroner arter kalsifikasyonu; koroner yeniden şekillenme; fraksiyonel akım rezervi; intravasküler ultrason.