Plaque Rupture in Coronary Atherosclerosis Is Associated With Increased Plaque Structural Stress

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ABSTRACT

OBJECTIVES The aim of this study was to identify the determinants of plaque structural stress (PSS) and the relationship between PSS and plaques with rupture.

BACKGROUND Plaque rupture is the most common cause of myocardial infarction, occurring particularly in higher risk lesions such as fibroatheromas. However, prospective intravascular ultrasound–virtual histology studies indicate that <10% higher risk plaques cause clinical events over 3 years, indicating that other factors also determine plaque rupture. Plaque rupture occurs when PSS exceeds its mechanical strength; however, the determinants of PSS and its association with plaques with proven rupture are not known.

METHODS We analyzed plaque structure and composition in 4,053 virtual histology intravascular ultrasound frames from 32 fibroatheromas with rupture from the intravascular ultrasound–virtual histology in Vulnerable Atherosclerosis study and 32 fibroatheromas without rupture on optical coherence tomography from a stable angina cohort. Mechanical loading in the periluminal region was estimated by calculating maximum principal PSS by finite element analysis.

RESULTS PSS increased with increasing lumen area (r = 0.46; p = 0.001), lumen eccentricity (r = 0.32; p = 0.001), and necrotic core ≥10% (r = 0.12; p = 0.001), but reduced when dense calcium was ≥10% (r = −0.12; p = 0.001). Ruptured fibroatheromas showed higher PSS (133 kPa [quartiles 1-3: 90 to 191 kPa] vs. 104 kPa [quartiles 1-3: 75 to 142 kPa]; p = 0.002) and variation in PSS (55 kPa [quartiles 1-3: 37 to 75 kPa] vs. 43 kPa [quartiles 1-3: 34 to 59 kPa]; p = 0.002) than nonruptured fibroatheromas, with rupture primarily occurring either proximal or immediately adjacent to the minimal luminal area (87.5% vs. 12.5%; p = 0.001). PSS was higher in segments proximal to the rupture site (143 kPa [quartiles 1-3: 101 to 200 kPa] vs. 120 kPa [quartiles 1-3: 78 to 180 kPa]; p = 0.001) versus distal segments, associated with increased necrotic core (19.1% [quartiles 1-3: 11% to 29%] vs. 14.3% [quartiles 1-3: 8% to 23%]; p = 0.001) but reduced fibrous/fibrofatty tissue (63.6% [quartiles 1-3: 46% to 78%] vs. 72.7% [quartiles 1-3: 54% to 86%]; p = 0.001). PSS >135 kPa was a good predictor of rupture in higher risk regions.

CONCLUSIONS PSS is determined by plaque composition, plaque architecture, and lumen geometry. PSS and PSS variability are increased in plaques with rupture, particularly at proximal segments. Incorporating PSS into plaque assessment may improve identification of rupture-prone plaques. (J Am Coll Cardiol Img 2017;■:■-■) © 2017 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Rupture of a coronary plaque is the precipitating event in the majority of myocardial infarctions (MI) (1). Postmortem (2) and in vivo intravascular studies (3,4) identify fibroatheromas (FAs), and in particular thin-cap fibroatheromas (TCFAs), as the most common predisposing lesion. TCFAs are widespread in human coronary artery disease, including asymptomatic individuals and those with stable and unstable syndromes (3). However, the incidence of major adverse cardiovascular events (MACEs) associated with TCFAs identified by intravascular ultrasound–virtual histology (IVUS-VH) is <10% over ~3 years of follow-up (3,4), suggesting that factors other than plaque and lumen size or plaque phenotype are important in determining plaque rupture.

Plaque rupture occurs when intraplaque stress exceeds the material strength of the overlying fibrous cap; increased plaque structural stress (PSS) is therefore a potential mechanism that determines rupture of a higher risk lesion. PSS can be calculated through an engineering technique known as finite element analysis (FEA), which approximates a solution to the equations of mechanical equilibrium by considering tissue material properties, plaque geometry, and local hemodynamic forces. Histological and IVUS-VH studies have identified necrotic core size, fibrous cap thickness, and the presence of microcalcification as important determinants of PSS (5-7). PSS has also been shown to be increased in patients presenting with acute coronary syndromes (ACS) versus stable symptoms (8). However, the determinants of PSS and its relationship to plaques that demonstrate rupture in vivo in human coronary arteries are not known. We sought to identify the parameters that determine PSS and variations in PSS across ruptured and non-ruptured FAs identified using IVUS-VH to determine whether plaque stress is increased in plaques that have experienced rupture, and whether incorporating PSS into plaque assessment improves identification of rupture-prone plaques.

METHODS

STUDY DESIGN. All plaques from the VIVA (VH-IVUS in Vulnerable Atherosclerosis) study with evidence of rupture (n = 32) on gray-scale (GS) IVUS were included in the study (3). The presence of rupture was verified by the Krakow Cardiovascular Research Institute core laboratory. To compare ruptured versus nonruptured plaques, we performed optical coherence tomography (OCT) before IVUS imaging on a separately recruited cohort of 40 patients with stable angina admitted for elective percutaneous coronary intervention (PCI) (Ethics committee approval ref 11/EE/0277). OCT imaging ensured that only plaques with no evidence of rupture or erosion were included in the nonruptured control group. Because spontaneous rupture occurred only in FAs in VIVA, only IVUS-VH–identified FAs (VH-FAs) were included in the nonruptured group, yielding 32 plaques from 32 patients (Figure 1, Online Appendix).

IVUS-VH AND OCT ANALYSIS. IVUS-VH data were acquired with 20-MHz Eagle-Eye catheters (Volcano Corporation, Rancho, Cordova) using motorized pullback at 0.5 mm/s. OCT data were acquired with Dragonfly C7 catheters (St. Jude Medical, St. Paul, Minnesota) using an automated pullback at 20 mm/s. Plaque classification, identification of rupture (Figure 2) and characterization of rupture location along the plaque length (Online Figure 1) were performed as previously described (Online Appendix). IVUS-VH plaque frames that demonstrated ruptures were not included in the final analysis for ruptured plaques, unless otherwise stated, because the extreme luminal eccentricity resulting from rupture at these frames would make PSS calculations unreliable.

BIOMECHANICAL ANALYSIS. Plaques underwent dynamic 2-dimensional FEA simulations as previously described (8) (Online Appendix). Maximum principal stress was used to indicate the critical mechanical conditions within the structure, referred as PSS. Variation in PSS refers to the difference in PSS between systole and diastole. A 65-μm layer of fibrous tissue was introduced during mesh generation to account for the limited axial resolution of IVUS-VH to detect a fibrous cap between lumen and necrotic core/dense calcium. Examples of PSS band plots with their corresponding IVUS-VH images are shown in Figure 3. Because PSS varies between frames, analysis was also performed after dividing plaques into 2-mm segments and averaging PSS across the IVUS-VH frames composing each segment. To estimate PSS at the exact site of rupture, the luminal boundary of frames demonstrating rupture was reconfigured with necrotic core present beneath this. PSS derived from these frames was compared with PSS from frames from the control cohort that demonstrated rupture after balloon inflation (Online Figure 2).

STATISTICAL ANALYSIS. Data were assessed for normality using the Shapiro-Wilk test. Normally