All You Need to Know About Vulnerable Plaque

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AT EUROPCR 2026, the session 'All We Need to Know About Vulnerable Plaque', chaired by Salvatore Brugaletta, Hospital Clínic de Barcelona, Spain, explored one of the most important unresolved questions in contemporary interventional cardiology: can identifying vulnerable plaque help prevent future myocardial infarction, and if so, should these lesions be treated?

The session brought together experts in intracoronary imaging, preventive intervention, and vascular biology to explore three key issues: why vulnerable plaque matters, how it should be identified, and whether intervention offers benefit beyond intensive medical therapy. Throughout the discussion, a recurring theme emerged: although clinicians are becoming increasingly adept at identifying high-risk plaques, uncertainty remains regarding which lesions warrant treatment and how best to manage them.

IDENTIFYING THE VULNERABLE PLAQUE

Opening the session, Hector Garcia-Garcia, MedStar Washington Hospital Center, Washington, D.C., USA, focused on the characteristics that define vulnerable plaque and their relationship with future adverse cardiovascular events.

According to Garcia-Garcia, the most common pathway leading to acute coronary syndromes remains plaque rupture arising from a native plaque with high-risk morphological features. He argued that three characteristics are central to the identification of vulnerable plaque: large plaque burden, lipid-rich composition, and thin fibrous cap thickness.[1]

Among these features, plaque burden emerged as the strongest predictor of major adverse cardiovascular events.[1] Typically measured by delineating both the vessel wall and lumen and expressing the proportion occupied by plaque as a percentage, a plaque burden exceeding 70% was highlighted as a key marker of vulnerability.[1] Garcia-Garcia described intravascular ultrasound (IVUS) as the preferred technique for characterising these vulnerable, non-obstructive plaques.[1]

Lipid content was identified as the second most important predictor of future events, and can be assessed using near-infrared spectroscopy (NIRS) and optical coherence tomography (OCT). Findings from the Lipid-Rich Plaque study and PROSPECT II demonstrated that plaques with high lipid content identified by NIRS-IVUS are associated with increased rates of future coronary events.[2,3]

Thin fibrous cap thickness, primarily assessed using OCT, remains a more controversial marker. While studies have linked thin fibrous caps and lipid arcs exceeding 180° with adverse outcomes,

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associations have not been entirely consistent across datasets.[4,5]

Small lumen area, typically below 4 mm², has also been associated with increased risk and can be assessed using IVUS, OCT, and coronary CT angiography.[1] As Garcia-Garcia noted, the field continues to debate which plaque characteristics provide the greatest prognostic value and how best to combine them for risk prediction.

BEYOND A SINGLE MARKER OF VULNERABILITY

Francesco Prati, San Giovanni Addolorata Hospital, Rome, Italy, expanded on this discussion by reviewing evidence from OCT-based studies, including CLIMA, COMBINE, and PECTUS, alongside NIRS-IVUS investigations such as PROSPECT II and Lipid-Rich Plaque.

While Garcia-Garcia emphasised plaque burden as the strongest predictor of future events, Prati argued that fibrous cap thickness may be the most important marker of plaque vulnerability. Drawing on long-term follow-up from the COMBINE OCT-FFR study, he highlighted evidence that patients with OCT-defined thin-cap fibroatheroma experience substantially higher rates of death and myocardial infarction than those without these features.[6]

Similarly, findings from the CLIMA registry demonstrated worse outcomes among patients with a combination of adverse OCT characteristics, including thin fibrous cap, large lipid arc, macrophage infiltration, and small minimal lumen area.[7]

Prati proposed a hierarchy of risk markers, placing fibrous cap thickness first, followed by lipid-rich plaque, minimal lumen area, and inflammatory cell infiltration. However, rather than relying on any single feature, he advocated for combining multiple imaging markers, as explored in the CLIMA and INTERCLIMA programmes.[7]

Despite growing evidence linking vulnerable plaque characteristics to future events, Prati acknowledged that no universal consensus currently exists regarding the morphological criteria that should define vulnerability. Whether individual features or combined phenotypes provide the most clinically useful approach remains an area of active investigation.

SHOULD VULNERABLE PLAQUES BE TREATED?

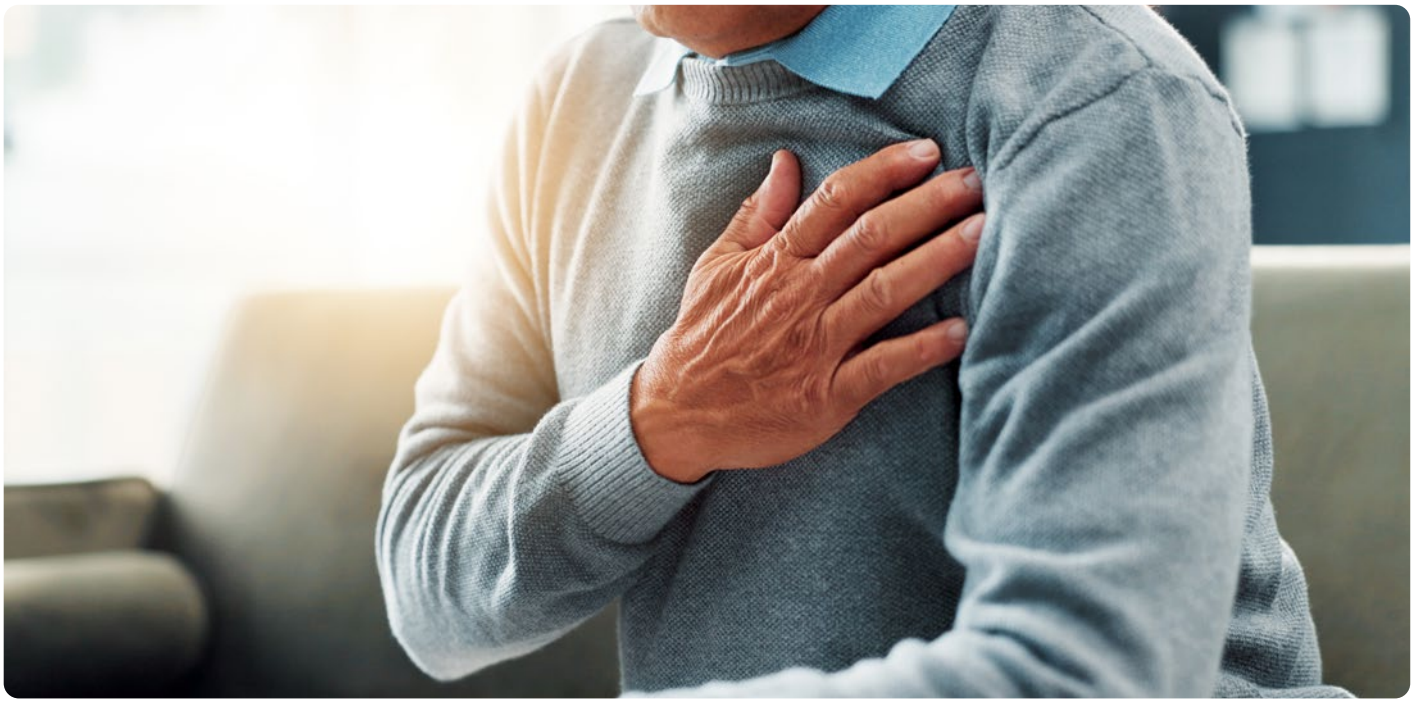
If identifying vulnerable plaque remains challenging, determining how to manage it may be even more controversial.

Elvin Kedhi, Royal Victoria Hospital, Montreal, Canada, argued that current physiology-guided strategies fail to identify many future myocardial infarctions because they focus primarily on ischaemia-producing lesions. He described vulnerable plaque as the true substrate of future coronary events, noting that thin-cap fibroatheroma has been associated with a five-fold increase in major adverse cardiovascular events despite the absence of demonstrable ischaemia.[8]

Referencing studies such as FAME II and ISCHEMIA, Kedhi argued that although ischaemia-guided revascularisation reduces myocardial infarction rates, many subsequent events continue to arise from intermediate, non-ischaemic lesions that would not typically be selected for intervention. In his view, using physiology alone to predict future infarction is akin to using "a butter knife as a screwdriver." For Kedhi, vulnerable plaque itself should become the primary target of preventive treatment.

This debate was illustrated by a clinical case presented by Josep Gomez-Lara, Bellvitge University Hospital, Barcelona, Spain. A 69-year-old man underwent successful primary percutaneous coronary intervention for an inferior ST-elevation myocardial infarction. Subsequent evaluation identified intermediate,

> **Absence of ischaemia does not necessarily equate to absence of future risk**



non-culprit lesions in the left circumflex and left anterior descending arteries. Despite negative physiological assessment, OCT revealed vulnerable plaque characteristics, including plaque burden approaching 80%, minimal lumen area below 2.1 mm², and fibrous cap thickness of 70 µm. Two years later, the patient was readmitted with a non-ST-elevation acute coronary syndrome caused by progression and rupture of one of these previously identified lesions.

Importantly, Gomez-Lara stressed that such cases remain the exception rather than the rule, with the majority of vulnerable plaques never progressing to clinical events. The case nevertheless highlighted a key message repeated throughout the session: absence of ischaemia does not necessarily equate to absence of future risk.

Kedhi reviewed several potential treatment approaches, including contemporary drug-eluting stents, drug-coated balloons, bioresorbable scaffolds, and emerging bioadaptor technologies. While modern drug-eluting stents remain the benchmark for procedural safety and efficacy, he argued that long-term outcomes may be improved by bioadaptor devices.

However, the discussion that followed highlighted the uncertainty that continues to surround preventive treatment of vulnerable plaque. Audience members raised concerns regarding permanent implants, including restenosis, neoatherosclerosis, and device-related events, with drug-coated balloons being discussed as a potential alternative that avoids leaving material behind in the vessel.

Not all panellists shared the same enthusiasm for preventive intervention. During the discussion, Peter Libby, Mass General Brigham Hospital, Massachusetts, USA, argued that advances in medical therapy may ultimately prove as important as advances in device technology, cautioning against committing patients to permanent implants before stronger evidence becomes available.

> **Inflammation remains one of the field's major blind spots and an important driver of plaque progression**

THE FUTURE OF VULNERABLE PLAQUE

Looking ahead, Libby suggested that the next major advance in the field may come from better characterisation of plaque biology rather than plaque morphology

> **Vulnerable plaque is no longer simply a pathological concept; it is now visible in everyday clinical practice**

alone. While advances in imaging have improved the identification of high-risk plaque features, he argued that inflammation remains one of the field's major blind spots and an important driver of plaque progression.

In particular, Libby highlighted photon-counting CT as a potentially transformative technology, offering significantly improved tissue characterisation compared with current CT systems. Combined with emerging measures such as perivascular fat attenuation, these approaches may enable more precise assessment of coronary inflammation and plaque biology.

Gomez-Lara also highlighted the ongoing VULNERABLE trial, which aims to determine whether preventive treatment of high-risk, non-culprit plaques can reduce future cardiovascular events.[9] Designed to evaluate whether prophylactic intervention can improve outcomes in lesions identified as vulnerable despite lacking functional significance, the study may provide some of the strongest evidence yet on whether identifying vulnerable plaque should alter clinical management. As evidence continues to emerge, clinicians may soon have greater clarity regarding which plaques should be treated and which are best managed conservatively.

CONCLUSION

The session demonstrated that vulnerable plaque is no longer simply a pathological concept; it is now visible in everyday clinical practice. Imaging modalities, including IVUS, OCT, and NIRS, have enabled increasingly sophisticated identification of high-risk plaque features, while emerging technologies, such as photon-counting CT, promise further advances.

Yet visibility has outpaced certainty. Although vulnerable plaque characteristics are clearly associated with future adverse events, uncertainty remains regarding which features matter most and whether intervention should follow identification.

As summarised in the session's closing learning points, the presence of a thin fibrous cap, wide lipid arc, narrow lumen, and inflammation should prompt clinicians to stop and think. What remains unclear is whether the optimal response is to treat, monitor, or leave the lesion alone. The answer will likely depend on the results of the next generation of vulnerable plaque trials.

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