The pathogenesis of plaque rupture and ACS

DR CHARANJIT RIHAL: Hi, this is Dr Chet Rihal. Today my guest is Dr Amir Lerman, who's a vice chair for cardiovascular research in our division of cardiology. Among Amir’s many interests has been the pathogenesis of acute coronary syndromes. Amir, good morning.

DR AMIR LERMAN: Good morning, Chet. Thank you for having me.

DR CHARANJIT RIHAL: You're very welcome. Listen, Amir, tell us about the pathogenesis of ACS, particularly this concept of a vulnerable plaque.

DR AMIR LERMAN: The concept of vulnerable plaque came from an observation that we have—not only us but other people, that most patients that present with acute coronary syndrome actually do not have significant obstructive coronary disease. They draw our attention more to the structure of the plaque rather than the amount of the plaque. We learn a lot from pathology—from the studies by Renu Virmani who taught us a lot from autopsies—that apparently acute coronary syndrome is actually a result of abnormalities in the plaque structure and the constituents of the plaque in mainly the large necrotic core, the thin-cap fibroatheroma, and a lot of constituents of the plaque from inflammation [and] blood vessel neovascularization that at some point [causes] a plaque eruption, creating a thrombus leading to the acute coronary syndrome.

DR CHARANJIT RIHAL: What you’re saying is that mild plaques can be so-called "vulnerable" under certain conditions. Can these vulnerable plaques be detected in vivo or is this just an autopsy phenomenon?

DR AMIR LERMAN: No. That's a very good question. The plaque can be detected in vivo with more sophisticated novel imaging modalities such as intravascular ultrasound, with an additional virtual histology component. With new images such as optical coherence tomography [OCT] and lipid scans, we can essentially detect the histology—close to the histology of the plaque—and determine if this plaque has a lot of necrotic core [and] a lot of lipid volume. We can measure the thickness of the fibroatheroma—or the shoulders that are covering the plaque—and in the future we'll probably be able also to look at the amount of neovascularization that may lead to plaque hemorrhage in the acute coronary syndrome.

DR CHARANJIT RIHAL: You were heavily involved in the PROSPECT study. Can you give us a brief synopsis of that and tell us how it should change our practice, if so?

DR AMIR LERMAN: The PROSPECT study—just briefly—was a prospective study in about 700 patients in which we looked at (with the direction of Gregg Stone who was the principal investigator) the natural history of vulnerable plaque
as detected with virtual histology over three years. And we found that about 20% of the patients had an event. The interesting part is [that] half of them—[a total of] almost 11% to 12% [of those enrolled] had an event not in the culprit lesion that underwent a PCI—indicating again that (when they look at that meta-analysis), the presence of [a] necrotic core was one of the major components that leads to a cardiovascular event.

However, in the study—which was relatively small—if you're looking at events, the majority of the events were not actually acute coronary syndromes or sudden cardiac deaths. The majority of the events were actually leading to progression of disease over time at the site where you have necrotic core and more plaque volume and less lumen.

I think that this has taught us a lot, that the coronary artery has heterogeneous components. It's a dynamic process. Some necrotic cores can undergo healing. Some areas without healing can undergo rupture. We are still in the phase of learning, [which has] taught us that we need to look not only at the lumen and the degree of stenosis but rather [at the] depth of disease, atherosclerosis [in] the disease of the vascular wall, not of the lumen, and learn how to look at the pathogenesis of the disease that's leading to acute coronary syndrome.

DR CHARANJIT RIHAL: Amir, can these vulnerable plaques be detected in vivo or are these just autopsy phenomena?

DR AMIR LERMAN: An excellent question. We have now currently more advanced and sophisticated intravascular imaging modality that allows us to look at the structure of the plaque, including ultrasound with virtual histology, including OCT, that can tell us [exactly] not only the constitution of the plaque but can allow us to accurately measure the thickness of the cap. And our new modalities using spectroscopy [allow us] to look at the lipid content of the plaque.

DR CHARANJIT RIHAL: One of the neat things you've done, Amir, is you have developed a movie that illustrates really nicely this concept of the vulnerable plaque and the events that lead to plaque rupture and then the occlusion of the vessel. We're going to make this video available to our audience members. It can be downloaded right underneath this video segment. Tell us what this movie shows.

DR AMIR LERMAN: This movie was done by putting together multiple histology slides from autopsies, creating the concept of the plaque that is growing, creating a positive remodeling and not obstructing the lumen, creating a mild obstruction of the lumen (about 40%). The necrotic core is increasing, the cap becomes thinner, and at some point in the shoulder of the plaque there is rupture, exposing the circulation to thrombogenic surface and creating an occlusive thrombus.
DR CHARANJIT RIHAL: Why does the shoulder rupture? Why does it occur at the shoulder?

DR AMIR LERMAN: The shoulders rupture first of all [because of] physical instability there, but also they found out that there was a lot of inflammation, macrophages, that created a lot of weakness of the tissue, mainly in the shoulder.

DR CHARANJIT RIHAL: My guest today has been Dr Amir Lerman, who's the vice chair for cardiovascular research here at Mayo Clinic. He talked to us today about the pathogenesis of acute coronary syndrome, specifically as it relates to the role of the vulnerable plaque, and he has put together a wonderful movie that I'm sure you will find interesting. You are free to download it and use it in your presentations if it'll be useful. Thank you for joining us today. Thank you, Amir.

DR AMIR LERMAN: Thank you for having me.