PARIS, FRANCE — A unique imaging study has, for the first time, determined that the pathophysiology of STEMI is nearly identical in men and women—a finding that refutes the theory that the mechanisms of acute MI are different between the genders. What's more, women appear to respond just as well as men to primary PCI and stenting, despite their smaller vessels and higher risk profile, results of the Optical Coherence Tomography Assessment of Gender Diversity in Primary Angioplasty (OCTAVIA) study show.

Senior investigator Dr Giulio Guagliumi (Ospedali Riuniti di Bergamo, Italy) presented the OCTAVIA results during the opening late-breaking clinical-trial session here at EuroPCR 2014.

Speaking with heartwire, Guagliumi emphasized that previous studies show that women suffering from AMI tend to be older at the time of presentation than men, by about 10 years. They also tend to have more risk factors and face a higher mortality than men. "But the only data we have are from pathology series, which are very biased; they tend to [include] more young women. So there is a notion that ladies are different and that the mechanisms are different and that this can have a significant impact on the outcomes of ladies with STEMI. . . . There is a lot of speculation [about why women face worse outcomes], but no facts available."

One prevailing theory, he continued, is that female patients with STEMI are more likely to have so-called 'eroded' plaques, rather than 'ruptured' plaques—a theory derived from pathology studies, but never proven in vivo.

STEMI treatments have typically focused on plaque rupture, in which a thin fibrous cap ruptures, exposing the necrotic plaque core, which forms a clot that thromboses. In erosions, by contrast, the endothelium lining the vessel walls is hypothesized to erode, potentially secondary to vasospasm, leaving a raw surface that causes a thrombus to form in the lumen of the artery. Plaque erosion has been suggested as a potentially more serious cause of coronary thrombosis, and some research has proposed that a higher proportion of eroded plaques in women may explain why their STEMI outcomes tend to be worse.

Real-Time Answers

OCTAVIA was thus designed to look specifically at gender differences at the time of primary PCI, using optical coherence tomography (OCT) to assess the morphology of the culprit plaque, plus obtain histopathology/immunohistochemistry from aspirated plaque, as well as serum biomarkers. OCT measurements were taken immediately after thrombus aspiration just prior to stent implantation, then again poststenting, and a third time at nine months.

In all, OCTAVIA enrolled 140 STEMI patients at 14 Italian centers, matched by age and risk factors, undergoing primary PCI with stenting using an everolimus-eluting stent. At baseline, the only significant difference between groups was vessel size, which was significantly smaller in women. Women also were slower to reach the cath lab, although this difference just missed statistical significance.

Histopathology and immunohistochemistry showed no differences in plaque volume and makeup between groups and no differences in thrombus age, with roughly 30% of both men and women having "organized" thrombus as opposed to early thrombus (layers of platelets, fibrin, and acute inflammatory cells), seen in 70% of subjects. Serum biomarkers were also roughly similar between men and women.

For the OCT results, there were no differences by gender in the proportion of ruptured or eroded plaques, which were seen in roughly 50% and 25% of subjects, respectively. (The remainder were unclassifiable or, in two cases, spontaneous dissections.)
On repeat OCT at nine months, intended to assess stent healing, more than 90% of both men and women had fully covered stent struts. There were also no significant differences in any clinical end points (including death, reinfarction, stroke, stent thrombosis, or target vessel reintervention) at one year, although the authors caution that the study was not powered for clinical end points.

Other Practical Findings

The key message, said Guagliumi, is that we cannot find any sexual differences for patients coming in with a STEMI, and we can’t find any differences in their response to current-generation drug-eluting stents. The other important finding is that one-third of patients coming in with a STEMI do not have a ruptured plaque but have an eroded plaque as the cause of their MI. This was not very well known before.”

Guagliumi and colleagues are now investigating whether primary PCI with stenting is equally effective in eroded vs ruptured plaques.

Also of Note, in OCTAVIA

A number of other important practical findings also emerged from OCTAVIA, he added. One was the fact that OCT typically detected significant amounts of thrombus after thrombus aspiration. "That means we need much better tools for removing thrombus," Guagliumi said. Large thrombus-aspiration trials have typically failed to show a benefit of aspiration before stenting in AMI, he noted. One possibility for the failure of these studies is that even when aspiration is performed, “there is still a lot of thrombosis remaining,” he said.

Another point, he stressed, is that despite enrolling patients within six hours of their first symptoms, a full third of patients were found to have organized thrombus, suggesting the thrombus had actually been developing over days, not hours.

"That's a very important notion—it means this mechanism of building and washing away of thrombosis is not related to the last few hours only: this gives us the chance to identify a problem much earlier.”

Guagliumi points to previously published data showing that thrombus, in some cases, may start to develop much earlier than previously assumed. In some cases, he elaborated, if you press patients to remember whether they felt any kind of symptoms one or two days earlier, some may say they had a very fleeting period of chest pain that they dismissed at the time. This, said Guagliumi, may point to the opportunity to intervene earlier in the evolution of STEMI, potentially averting the acute event.

As for the important finding of a lack of gender differences, OCTAVIA provides some of the first conclusive proof that the mechanisms and time course of STEMI are no different in women from those in men. "CAD is a big problem for women today, which needs to be followed closely because it is usually underestimated," he stressed. When diagnosed, CAD is typically managed less invasively in women, yet OCTAVIA demonstrates that women respond just as well to primary PCI as men.

Women also tended to have longer symptom-to-balloon times, typically because they were slower to act on their own symptoms—a well-documented phenomenon in previous studies. "This is really something else we need to speed up," he said. In OCTAVIA, the delay from symptom onset to cath-lab admission was 2.3 hours for men and 2.5 hours for women, a difference that just missed statistical significance at 0.053.

Commenting on the study during a morning press conference, Dr Jean Fajadet (Clinique Pasteur, Toulouse, France) observed: “A major finding [of OCTAVIA] is certainly the delayed diagnosis of women, and this will impact on their prognosis. We will have to work on this.”

Also commenting, Dr William Wijns (Cardiovascular Center, Aalst, Belgium) pointed out that autopsy studies have suggested the proportion of “eroded” plaques in STEMI to be much lower, in the range of 3% to 5%. The rate of 25% seen in OCTAVIA indicates “that erosion is a much more frequent as a cause of STEMI: that's a very important finding.”
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