Intracoronary imaging assessment of atherosclerosis in vasomotor dysfunction and phenotypes of non-obstructive coronary artery disease

D. Pellegrini[1], R. Konst[2], S. Elias-Smale[2], R.J. Van Geuns[2], N. Van Royen[2], P. Damman[2]

[1]*Papa Giovanni XXIII Hospital, Bergamo, Italy;* [2]*University Medical Center St Radboud (UMCN), Nijmegen, Netherlands (The)*

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Background: A consistent portion of patients with stable angina is affected by coronary vasomotor dysfunction, in the form of epicardial vasospasm (VSA) or coronary microvascular dysfunction (CMD). Although available data suggest a worse prognosis compared to normal population, anatomical background and associations with atherosclerosis are still uncertain.

Purpose: To define specific morphological features in patients with stable angina and coronary vasomotor dysfunction.

Methods: We enrolled all patients referred to our laboratory in the first half of 2019 for coronary reactivity testing (CRT) for stable angina and suspected vasomotor dysfunction. After confirming non-obstructive coronary artery disease by angiography, CRT consisted of acetylcholine test and physiology assessment with resting and hyperemic indexes. In addition, optical coherence tomography (OCT) was performed. All tests were performed in the left anterior descending artery. Patients were divided in 3 groups: VSA, CMD and control group (no CMD/VSA), according to international COVADIS consensus documents. Two independent reviewers assessed the OCTs to identify markers of atherosclerosis.

Results: We enrolled 48 patients. Mean age was 55.19±7.71 years. 46 (96%) were females. 3 patients were removed due to mixed VSA and CMD, resulting in 45 subjects eligible for analysis: 17 had VSA, 22 CMD and 6 were controls. Baseline characteristics, resting and hyperemic indexes were similar in the groups, except for the index of microvascular resistance (IMR), being higher in CMD group. Moving from control group, to CMD, to VSA, OCT suggested a trend of increasing prevalence of fibroatheromas (0% in controls, 36% in CMD, 47% in VSA, p 0.12), thin-cap fibroatheromas (0% vs 18% vs 29%, respectively, p 0.29) and neovascularisation (17% vs 23% vs 47%, p 0.19). On the other hand, macrophage infiltration was higher in CMD group (55% in CMD, vs 47% in VSA, vs 33% in controls, p 0.64). Plaques covered 43% of the vessel in VSA group (34% being lipid-rich), 35% in CMD (lipid: 36%) and 30% in controls (p 0.69; 17% lipid). Lipid pools showed a different distribution across the groups. Control group had small pools (mean/max lipid arc 56/65°, length: 5.5 mm), CMD showed intermediate width (arc 82/106°), but long extension (11.5 mm), while VSA had large pools (94/127°, p 0.05/0.08), with intermediate length (7 mm, p 0.58). Lipid index (mean arc x lipid length) was similar in VSA (632) and CMD (642), but lower in control group (203, p 0.35).

Conclusions: This study hints at atherosclerosis as an underlying pathophysiology in VSA and CMD. A trend to increasing burden, both in terms of extension and vulnerability, was observed across patients with normal arteries, CMD and VSA. Peculiar patterns of atherosclerosis may be associated with specific phenotypes of vasomotor dysfunction, with larger lipid pools and neovascularization being associated with VSA and macrophage infiltration being more common in CMD.