Coronary Artery Ectasia: From Diagnosis to Treatment

SOPHIE MAVROGENI
Onassis Cardiac Surgery Center, Athens, Greece

Coronary artery ectasia (CAE) represents a form of atherosclerotic coronary artery disease seen in 3-8% of patients undergoing coronary angiography. The presence of ectatic segments produces sluggish blood flow, with exercise-induced angina and myocardial infarction, regardless of the severity of coexisting stenotic coronary disease. The introduction of new non-invasive modalities, such as coronary artery computed tomography and magnetic resonance angiography, and the systematic testing of modern antiplatelet and vasoreactive medication, look promising for the better treatment and prognosis of these patients.

Etiology and prevalence

CAE, or aneurismal coronary artery disease, is defined as dilatation of an arterial segment to a diameter at least 1.5 times that of the adjacent normal coronary artery.\(^1\)\(^,\)\(^,\)\(^3\) CAE can be found in up to 5% of angiographic and in 0.22% to 1.4% of autopsy series.\(^4\)\(^,\)\(^7\) It can be either diffuse, affecting the entire length of a coronary artery, or localized. When the dilatation involves the entire vessel the word “ectasia” is used instead of aneurismatic disease. Coronary artery ectasia or aneurysm is attributed to atherosclerosis in 50% of cases, whereas 20-30% have been considered to be congenital in origin. In the great majority of these patients ectasia coexists with coronary artery disease. Only 10% to 20% of cases of CAE have been described in association with inflammatory or connective tissue diseases.\(^2\)\(^,\)\(^8\) Coronary dilatation has been described as isolated ectasia,\(^9\) in association with connective tissue disorders such as scleroderma,\(^10\)\(^,\)\(^11\) in Ehlers-Danlos syndrome,\(^12\) different types of antineutrophil cytoplasmic antibody (ANCA)-related vasculitis,\(^13\) and also in syphilitic aortitis\(^14\) and in Kawasaki disease.\(^15\) In a small percentage of patients CAE can be congenital in origin.\(^16\) The differentiation between congenital and acquired coronary aneurysms may often be difficult, despite the exclusion of other associated diseases. Acquired CAE should also be differentiated from coronary aneurysms following coronary interventions. These include true or pseudo-aneurysms during coronary balloon angioplasty, but more importantly following coronary stent placement, atherectomy and brachytherapy.\(^17\) Occasionally, large ulcerated coronary plaques can be misinterpreted angiographically as coronary aneurysms. Their true cause can be revealed by intravascular ultrasound (IVUS).\(^18\)\(^-\)\(^20\)

Recent studies have documented the association of CAE with the presence of aneurysms in other vascular beds as well, probably owing to a common underlying pathogenetic mechanism. CAE has been seen more frequently in patients with aneurysms of the abdominal and ascending aorta, the popliteal arteries, veins, and
the pulmonary artery. In a retrospective study by Stajduhar et al, 8% of patients operated for abdominal aortic aneurysm had CAE, compared with 2.9% of patients who were operated for occlusive peripheral vascular disease.

**Pathophysiology and classification**

The presence of aneurismal segments produces sluggish or turbulent blood flow, with increased incidence of typical exercise-induced angina pectoris and myocardial infarction, regardless of the severity of coexisting stenotic coronary disease. This is due to the repeated dissemination of microemboli to segments distal to the ectasia, or to thrombotic occlusion of the dilated vessel. Slow blood flow in the coronary artery may also be a causative factor. Patients with pure ectasia (15% of the total population with CAE) have a more benign course, but 39% of them still present signs of previous myocardial infarction. There is a higher incidence of adverse events in this population compared to people with normal coronary arteries.

As a first attempt to clarify anatomical variations, Markis proposed a classification of CAE based on the extent of ectatic involvement. In decreasing order of severity, diffuse ectasia of two or three vessels was classified as Type I, diffuse disease in one vessel and localized disease in another vessel as Type II, diffuse ectasia of one vessel only as Type III and localized or segmental ectasia as Type IV. In addition, CAE has been classified, according to the anatomical shape of the ectatic segment, into fusiform or saccular types. Older studies preferred the term ‘coronary aneurysm’ for the more discrete and saccular-type ectatic segments, reserving the term ‘ectasia’ for the fusiform diffuse vessel involvement. All three coronary vessels can be affected by CAE, but in almost 75% of patients an isolated artery is ectatic. In patients with concomitant coronary artery disease, the proximal and mid segments of the right coronary artery (RCA) are the most frequently involved, followed by the left anterior descending artery and the left circumflex. The reason for the higher RCA predisposition to CAE is not well understood. In a small percentage of patients, CAE does not coexist with coronary stenoses. In this subgroup, the condition more frequently involves part or the whole length of the artery in a diffuse form (‘dilated coronaropathy’).

In terms of pathophysiology, it is well known that atheromatous plaques do not project into the lumen but lie in a depression in the media that may bulge outwards. In this way, the triad of atheroma, thrombosis and aneurysm becomes linked in one continuous pathological process, and both expansion and shrinkage of coronary vessels is an important process in coronary artery disease (CAD). This process of “arterial remodeling” is fundamental to the pathophysiology of CAD in native coronary lesions and after interventional procedures. However, the clinical significance of these complex changes of vessel and plaque size is incompletely understood. In vivo experience with IVUS has confirmed that arterial expansion and shrinkage can both be a manifestation of coronary atherosclerosis. Positive remodeling (arterial expansion) is frequently associated with unstable coronary syndromes, whereas negative remodeling (arterial shrinkage) is associated with stable coronary syndromes. These changes of vessel size are clearly related to atherosclerotic disease progression and regression. Therefore, the observation of remodeling is important in the assessment of plaque vulnerability and stabilization. A better understanding of the remodeling response may have important implications in the diagnosis, prevention and treatment of CAD.

**Diagnostic assessment**

X-ray coronary angiography is the main diagnostic technique for the identification of coronary artery ectasia. IVUS is an excellent tool for assessing luminal size and characterizing arterial wall changes. Ge et al observed a significant atheromatous burden in the majority of CAE cases, with plaque areas evenly distributed between proximal and distal reference segments, as well as within the aneurismal segment. Percentage stenosis, however, was significantly lower within the CAE, due to the larger vessel area, highlighting the difficulty in assessing the degree of stenosis when it appears within an ectatic segment. Importantly, IVUS correctly differentiates true from false aneurysms caused by plaque rupture. Emptied plaque cavities may appear angiographically as CAE and the distinction is of clinical importance, as false aneurysms may lead to acute coronary syndromes.

Disturbances in blood flow filling and washout are common in CAE, and are clearly associated with the severity of ectasia. Angiographic signs of turbulent and stagnant flow include delayed antegrade dye filling, a segmental back flow phenomenon, and local deposition of dye in the dilated coronary segment. Akyurek et al used the Doppler wire to measure blood flow velocity and coronary flow reserve in patients with isolated CAE and in a control group.
They reported a trend for lower resting blood flow velocity within the CAE group compared to controls. Following intracoronary administration of papaverine, a potent hyperemic stimulus, the coronary flow reserve was 1.51 in the CAE compared with 2.67 in the control arteries (p < 0.001), suggesting a combination of epicardial flow disturbances and microvascular dysfunction as the cause of myocardial ischemia. A point of interest was that the estimated resting absolute volumetric flow within the CAE was found to be 3 times higher than in control patients. This finding contradicts previous data documenting myocardial ischemia in areas supplied by ectatic arteries, using coronary sinus lactates and exercise stress test.

The correct follow up of ectatic vessels is hampered by the need for repeated angiograms. Three-dimensional, non contrast-enhanced, free-breathing coronary magnetic resonance angiography (MRA) facilitates visualization of the vast majority of the proximal and middle segments of the left main, left anterior descending and right coronary arteries. Coronary MRA has already proved to be of clinical value for the assessment of anomalous coronary artery disease, and it is in some cases superior to X-ray coronary angiography in delineating the course of an anomalous vessel, but it is still considered an investigational technique for the assessment of stenotic native vessel. However, it has been proposed as a valuable tool for patients who present with severe left ventricular systolic dysfunction, where the underlying disease is either severe multi-vessel coronary artery disease or non-ischemic cardiomyopathy. Our group proved that coronary MRA is equal to quantitative coronary angiography, with the additional advantage of being a noninvasive technique. Compared with CT, MRA has the advantage of requiring no exposure to ionizing radiation or injection of a contrast agent. Coronary MRA may offer further valuable information, when complemented with coronary flow data, about the possibility of thrombotic occlusion of the aneurysmal vessels. Additionally, MRA, being a noninvasive, non-radiating technique, can be easily used for the efficient follow up of these patients. Our group has also applied MRA alone or in combination with inflammation or viability study in the evaluation of Kawasaki and other autoimmune diseases (Figure 1).

Recently, coronary artery computed tomography (CACT) has been used in the evaluation of ectatic vessels. The prevalence of coronary artery ectasia in a population who underwent CACT was 8%. The right coronary artery was most commonly affected and most participants had single-vessel involvement. Coronary artery ectasia was usually associated with atheromatous changes, but not with significant coronary artery disease, and thrombosis was a rare complication. In another study using CACT the prevalence of CAE in the population was around 3%. Contrast attenuation measurements with CT coronary angiography correlate well with the flow alterations assessed with classic X-ray coronary angiography. However, CACT can not be suggested as a technique of choice for the follow up of patients because of its high radiation dose. Further improvements in terms of radiation dose are awaited with interest in the near future.
Therapeutic approach

In contrary to atherosclerotic coronary artery disease, the medical management of patients with CAE has not been adequately addressed. Previous studies based on the significant flow disturbances within the ectatic segments suggested chronic anticoagulation as main therapy. However, this treatment has not been tested prospectively, and could not be recommended unless supported by further studies. Heparin infusion, as well as fibrinolysis, have been successfully used for re-canalization in isolated cases of acute thrombotic occlusions, occasionally revealing an absence of flow-limiting stenoses. When coexisting with CAD, the prognosis and treatment of CAE are the same as for CAD alone. In isolated CAE, the prognosis is better and anti-platelet drugs are the mainstay of treatment. For better patient management, it is important to clarify the mechanism underlying CAE, using additional clinical, histopathological and pathophysiological investigations. In fact, every patient with CAE should be evaluated systematically for pathological changes in other vascular territories, in both the arterial and venous systems, which might occur as part of the disease process.

The coexistence of CAE with obstructive coronary lesions in the great majority of patients and the observed incidence of myocardial infarction, even in patients with isolated coronary ectasia, suggested the generalized administration of aspirin in all patients with CAE. The role of combined antiplatelet therapy, with the addition of adenosine diphosphate inhibitors, has not yet been evaluated in prospective randomized studies. However, Yasar et al have recently reported that patients with isolated CAE have elevated plasma levels of P-selectin, beta-thromboglobulin and platelet factor 4 compared with control participants who have angiographically normal coronary arteries, suggesting increased platelet activation in patients with CAE. Medications with vasodilating properties against coronary spasm have also been proposed. It is of interest that nitrates, by causing further coronary epicardial dilation, have been shown to exacerbate myocardial ischemia and are discouraged in patients with isolated CAE. At present, there are no vasoactive medications that have already been tested and can be widely recommended to patients with CAE. As CAE represents a form of atherosclerotic heart disease, intense risk factor modification for primary and secondary prevention is obviously necessary. Sudhir et al reported that CAE is 6 times more frequent among patients with familial hypercholesterolemia than in a control group, suggesting a link between abnormal lipoprotein metabolism and aneurysmal coronary artery disease.

For patients with coexisting obstructive lesions and symptoms or signs of significant ischemia despite medical therapy, percutaneous and/or surgical coronary vascularization can safely and effectively restore normal myocardial perfusion. Ochiai et al reported the excellent acute and long-term results of balloon angioplasty in lesions adjacent to coronary aneurysms; these findings also agree with our own clinical observations. Special attention should be paid to the need for adequate stent expansion and wall stabilization in these vessels. The implantation of covered versus bare metal stents offers a superior acute angiographic result, excluding the ectatic segment, but the long-term benefit has not been adequately proven.

Coronary artery bypass grafting has been used for the treatment of significant coronary artery disease coexisting with ectatic coronary segments. The presence of thrombus within the CAE and the question of the necessity to remove large aneurysms have led to the introduction of a variety of operative procedures, including proximal and distal ligation and aneurysm resection. The postoperative outcome, however, was uniformly good.

Prognosis

Recently, some indexes have been suggested as prognostic factors in CAE. Dagli et al found low plasma adiponectin levels in acquired CAE, attributed to atherosclerosis, and suggested that adiponectin might be playing a role in the etiopathogenesis and progression of CAE. This in turn may indicate that hypo-adiponectinemia may reveal an increased risk for CAE development. Ozbay et al proposed that levels of high-sensitivity C-reactive protein may be a good prognostic index in CAE patients, as in those with stenosis. Additionally, Kozar et al suggested that TIMI frame count measurement depends on the ectasia size or ectasia ratio; thus an increased ectasia ratio is markedly associated with decreased TIMI frame counts and worse prognosis in patients with CEA. Further studies are needed to clarify the importance of these findings in clinical practice.

Conclusions

CAE represents a form of atherosclerotic coronary
artery disease seen in 3-8% of patients undergoing coronary angiography. The introduction of new non-invasive modalities and the systematic testing of modern antiplatelet and/or vasoactive medication look promising for the better treatment and prognosis of these patients.

References