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Review

Coronary Artery Ectasia – Is It Time for a Reappraisal?

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Summary: Coronary artery ectasia (CAE) is a well recognized clinical entity encountered during diagnostic cardiac catheterization. The etiopathogenesis of this condition is poorly understood. Due to the frequent presence of associated obstructive coronary artery disease it is considered to be a maladaptive process of atherosclerosis. Based on its association with aortic aneurysm, coronary ectasia is considered to be caused by genetic abnormalities. It is usually not a benign condition, as normal smooth laminar flow is disrupted with a potential of thrombus formation. The role of long-term anticoagulation in this condition has not been well established. It is speculated that with increasing use of newer, noninvasive modalities the incidence of ectasia may rise, therefore necessitating this review.

Key words: coronary artery ectasia, thrombosis, atherosclerosis, coronary artery disease

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Introduction

Coronary artery ectasia (CAE) is a well-recognized yet rare abnormality of the coronary anatomy. Since its discovery four decades ago, there have been several investigations highlighting the overall incidence, pathophysiology, and clinical significance.[1, 2–8] Despite an ongoing interest in establishing a treatment and a prognostic profile for patients affected with ectasia, there still remain several unclear and undefined areas. There is no consensus about the etiology, prognostic significance, and morbidity related to this pathologic entity. This uncertainty underlies the current dispute regarding the appropriate management and treatment of patients with CAE. This review is an effort to present available literature on CAE and to highlight areas that need further investigation.

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Definition and Incidence

Coronary artery ectasia is an abnormal, irregular, saccular dilatation[3, 8] of more than a third segment of the coronary artery to > 1.5 times the diameter of the normal segment.[1] There is an overlap of this condition with coronary artery aneurysm, which is more focal and probably a manifestation of the same pathologic process. The incidence of CAE ranges from 1.2–4.9%[1] (Table 1), with the highest reported at 4.9% in the Coronary Artery Surgery Study (CASS) registry.[9]

Etiology and Pathogenesis

It has been proposed that atherosclerosis contributes to development of CAE in up to 50% of the cases.[1, 3, 5, 7, 8 ,10] Other possible etiologies include congenital abnormalities and inflammatory and connective tissue diseases. The predominant histological feature of the wall of an ectatic artery reveals grossly thickened and fibrotic intima with extensive lipid deposition and marked thinning of the media. It is postulated that cytokine-induced tissue inflammation is an underlying contributor of vascular remodeling. In a study by Tokgozoglu *et al.*,[19] inflammatory markers such as the plasma interleukin-6 and C-reactive protein levels were found to be elevated in patients with CAE compared with those with normal coronaries.

Isolated CAE or "dilated coronaropathy," which excludes atherosclerosis, connective tissue diseases, and other cardiac defects, is very rare with an angiographic frequency of 0.1 to 0.32%.[1, 5] Genetic susceptibility is likely to explain why certain individuals are at risk to develop CAE.[11, 12] This is corroborated by the fact that there is an association between CAE and aortic aneurysm. The genetic abnormalities contributing to the development of aortic aneurysm have been studied extensively and several of these factors have overlapped in

TABLE 1 Comparative incidence of ectasia at coronary angiography

Author/study	Total no. of cases	Cases of ectasia	% with ectasia
Hartnell *et al.*	4,993	70	1.4
CASS	20,087	978	4.9
Markis *et al.*	2,457	30	1.2
Swanton *et al.*	1,000	12	1.2
Befeler *et al.*	1,246	16	1.3
Falsetti *et al.*	742	11	1.5
Alford *et al.*	1,654	37	2.2
Aintablian *et al.*	1,660	42	2.5
Pooled data	8,759	148	1.65

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patients with CAE.[13, 14] Angiotensin II plays an important role in abnormal vascular remodeling and has been implicated in CAE.[15] Daugherty *et al.*[16] showed that angiotensin II infusion in apolipoprotein E-deficient mice dramatically promoted vascular pathology, including an increase in the extent of atherosclerosis and formation of large aortic aneurysms. Another important contributor to vascular remodeling is matrix metalloproteinase 2 (MMP2), a principal enzyme that participates in extracellular matrix (ECM) degradation. A critical imbalance between MMPs and their endogenous tissue inhibitors has been demonstrated in patients with CAE.[17]

Clinical Significance of Coronary Artery Ectasia

Clinical Features

The clinical features of CAE are difficult to distinguish from those of associated coronary artery disease (CAD). There is a male preponderance, with a male to female ratio of 3:1.[5, 6, 8] Although it has been shown that >50% of patients with CAE have underlying coronary artery stenosis,[1, 3, 5, 7] the symptoms do not directly correlate with the degree of stenosis. Sayin *et al.*[21] postulated that CAE renders patients to higher risk of myocardial ischemia irrespective of extent of stenosis. Patients with CAE without stenosis had significantly abnormal treadmill stress tests compared with those with normal coronaries, suggesting decrease in coronary flow reserve and microvascular dysfunction as a possible contributing factor for myocardial ischemia. Angina is the most common presenting complaint in patients with CAE.[1, 4, 6] Although rare, ST-elevation myocardial infarction (MI),[22, 23] non-ST-elevation MI, arrhythmias, and sudden cardiac death[24, 25] have also been reported. Spontaneous dissection of an ectatic artery is a lethal complication and may result in arrhythmias and death.[26, 27]

An interesting observation is a negative correlation between diabetes and CAE. The prevalence of diabetes in patients with ectasia was found to be less frequent than that in patients with CAD.[20, 28] Williams *et al.*[29] found an impaired nitric oxide-mediated vasodilatation in non-insulin-dependent diabetics. Downregulation of MMP production in vascular smooth muscle cells in diabetics promotes negative arterial remodeling.[28] However, the largest study of ectasia to date, which included 978 subjects with aneurysmal CAD, contradicted the above result and did not confirm this negative correlation.[5]

The right coronary artery (RCA) is most commonly affected by ectasia, with an approximate 60% prevalence (Table 2). Involvement of the left anterior descending artery (LAD) and left circumflex (LCx) artery is variable. Based on the extent of coronary involvement, Markis *et al.*[6] proposed a classification of CAE which is used extensively (Table 3).

Pathophysiology of Myocardial Ischemia

The exact extent and pathophysiology of myocardial ischemia in patients with CAE is not clear. Various mechanisms including slow-flow and altered-flow dynamics have been implicated. In an objective study of Thrombolysis in Myocardial Infarction (TIMI) frame count, Papadakis *et al.*[32] demonstrated that presence of CAE was associated with higher TIMI frame count indicating slower coronary flow. It is interesting that a significantly lower myocardial blush grade was ob-

TABLE 2 Percentage involvement of various coronary arteries by ectasia

Authors	Year	No. of subjects	LM	LAD	LCx	RCA
Befeler *et al.*	1977	16	0	31	50	87
Swanton *et al.*	1978	11	0	9	54	45
Baron *et al.*	1979	23	0	57	75	96
Hartnell *et al.*	1985	70	7	29	24	40
Suzuki *et al.*	1994	74	4	10	13	73
Ilia *et al.*	1995	68	2	21	30	47
Demopoulos *et al.*	1997	203	5	16	26	51
Lahiri *et al.*	2002	84	8	51	28	63
Dogan *et al.*	2002	141	9	35	4	41
Bermudez *et al.*	2003	147	0	28	19	51
Lam *et al.*	2004	104	2	48	43	65

Abbreviations: LM = left main, LAD = left anterior descending, LCx = left circumflex, RCA = right coronary artery.

TABLE 3 Markis classification of coronary artery ectasia

Type 1	Diffuse ectasia of two or three vessels
Type 2	Diffuse ectasia in one vessel and localized in another
Type 3	Diffuse ectasia of a single vessel
Type 4	Localized or segmental ectasia

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TABLE 4 Optimal treatment of coronary artery ectasia

Medication	Dose	Mode of action
Warfarin	Keep INR ~ 2.0–2.5	Minimize thrombus formation
Aspirin	81–360 mg/day	Minimize platelet aggregation
Diltiazem	Variable	Minimize arterial spasm

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Abbreviation: INR = international Normalized Ratio.

served in patients with CAE despite brisk epicardial flow, thereby suggesting a disrupted microvascular network.[33] This was confirmed by Akyurek *et al.*,[4] where ectatic vessels had higher coronary blood flow with lower coronary flow reserve. Other possible mechanisms of myocardial ischemia are spasm of the ectatic arteries and dissection of the vessel wall.

Prognosis

Long-term prognosis and outcome in patients with CAE is unknown. The hypothesis that presence of ectasia renders patients to a higher risk of MI has not been confirmed in various studies.[1, 5, 8, 9, 34] In the CASS registry,[9] no difference in survival was observed between patients with or without CAE. Sadr-Ameli and Sharifi[31] divided patients into those with concomitant CAE and CAD and those with either CAD or CAE alone, and showed no difference in MI or death at 2 years between the groups with or without CAE. Reporting in 1976, Markis *et al.*[6] found a mortality rate of 15% at 2 years in patients with CAE, which at that time was similar to the mortality of medically treated patients with triple-vessel CAD. Several studies thereafter failed to show a mortality difference between CAE and CAD and concluded that CAE is a variant of atherosclerosis which confers no additional risk.[1, 5, 8]

Treatment

Role of Revascularization

The safety and success of coronary intervention in stenotic ectatic coronary segments is not well known. Ochiai *et al.*[35] compared the outcomes of angioplasty of stenoses adjacent to aneurysmal CAD in 270 patients and found no difference in outcomes, complications, or restenosis. Yip *et al.*[36] retrospectively analyzed patients with coronary artery aneurysms and demonstrated that the rate of successful reperfusion was higher, with an infarct-related artery diameter of < 4.0 mm compared with those with larger vessels. Studies comparing the incidence of bypass surgery in patients with ectasia found that surgical revascularization is more often recommended in patients with ectasia coexisting with stenosis, possibly because of physician preference.[30]

Role of Anticoagulation

Ectatic coronary arteries are prone to thrombus formation because of abnormal flow dynamics, spasm, and intimal damage. Several case reports have highlighted the clinical manifestation of CAE in the form of MI or unstable angina due to thrombosis in the involved segments.[37, 38] Prophylactic use of warfarin to reduce the sequelae of thrombosis has been suggested by many authors;[7, 39] however, there is no randomized study to demonstrate its influence on clinical outcome or mortality. Based on their experience, Sorrell *et al.*[2] have recommended an optimal therapeutic regimen (Table 4).

Conclusion

Coronary ectasia is not a benign condition due to its potential of causing ischemia as well as acute coronary events due to coronary spasm, slow flow, and thrombus formation. Optimal treatment guidelines have not been established. There are contradictory viewpoints about use of long-term anticoagulation in this condition. This is probably an optimal time to address the condition with a prospective larger trial, emphasizing the role of therapeutic strategies of anticoagulation and revascularization. It is speculated that with the increasing use of newer, less invasive modalities such as computed tomography angiograms, more cases of coronary ectasia will be identified. This may open the doors for well-designed prospective studies to understand the enigma of coronary ectasia better.

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