Coronary artery ectasia: current concepts and interventions

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1. ABSTRACT

Coronary artery ectasia (CAE) is a well-recognized angiographic finding, characterized by abnormal dilatation of the coronary arteries. We reviewed the current concepts of the condition including etiology, pathogenesis, flow alterations, clinical implications, prognosis and treatment. CAE is often viewed as a variant of obstructive coronary atherosclerosis. Exaggerated positive vascular remodeling due to inflammation, and chronic overstimulation of the endothelium by nitric oxide are potential causative mechanisms. The condition is associated with cardiovascular risk factors such as smoking and hypertension, while it appears to be inversely associated with age and diabetes mellitus. Patients with CAE typically present with angina, and are at risk for myocardial infarctions and sudden cardiac death due to slow flow, coronary vasospasm, dissection, and/or intracoronary thrombosis. CAE may be a diffuse disease associated with dilatation in other parts of the vasculature. As the incidence of this not so benign condition is expected to rise, the optimal treatment options remain undefined. Medical therapy with anticoagulants, nitrates and calcium channel blockers has been proposed and seems rational; however prospective studies with proof of efficacy are needed.

2. INTRODUCTION

Abnormal epicardial dilatation of the coronary arteries has been recognized for decades. The most widely used term for this condition now is "coronary artery ectasia". Coronary artery ectasia (CAE) is defined as an abnormal segmental or diffuse dilatation exceeding more than a third of the coronary artery length with the diameter of the ectatic segment measuring more than 1.5 times the diameter of a normal adjacent segment (1-3). This definition may underestimate the true incidence of the disease, because the distribution of CAE is quite variable and not always focal, and the normal reference segments may not be easily identified (4). However, the incidence of CAE reported in the literature may overestimate the true frequency in the general population, since the current gold standard for diagnosis is coronary angiography, and patients referred to coronary angiography are pre-selected (5). The incidence of CAE ranges from 1.2%-4.9% (1). In the largest series from the CASS registry, Swaye *et al* (2) found CAE in 4.9% of more than 20000 coronary angiograms they reviewed. In an Indian cohort with ischemic heart disease, the incidence of CAE has been reported to exceed 10% (6). CAE may overlap with coronary artery aneurysm, which is more focal and probably a manifestation of the similar pathologic process

Table 1. Etiology of CAE

Congenital (10-20% of cases associated with)	Acquired
Bicuspid aortic valve	Atherosclerosis (more than 50% of cases)
Aortic root dilatation	Collagen vascular disease (Ehler-Danlos syndrome, scleroderma, systemic lupus erythematosus, Kawasaki disease, Polyarteritis nodosa)
Ventricular septal defect	Infections
Pulmonary stenosis	Cardiac lymphomas
Cyanotic heart disease	Iatrogenic following angioplasty
Congenital	10-20% of cases associated with
	Bicuspid AV
	Aortic root dilatation
	VSD
	Pulmonary stenosis
	Cyanotic heart disease
Acquired	1. Atherosclerosis - more than 50% of cases
	2. Collagen vascular disease
	Ehler-Danlos syndrome
	Scleroderma
	Systemic lupus
	Kawasaki disease
	Polyarteritis nodosa
	3.Infections
	4.Cardiac lymphomas

7). It is expected that with the increasing use of computed tomography angiograms more cases of coronary ectasia will be diagnosed in the future (7). Although this abnormality has long been recognized, its etiology, clinical significance and prognosis are still poorly understood. Clinical presentations including ischemia and acute coronary events due to coronary spasm, dissection, slow flow, and thrombus formation are reported. The ideal treatment of this condition has not been established.

3. ETIOLOGY

The origin of CAE is considered to be congenital in about 10% - 20% of the cases with the remainder being acquired (8) (Table 1). Congenital CAE is frequently associated with other cardiac abnormalities such as bicuspid aortic valve, aortic root dilatation, ventricular septal defect or pulmonary stenosis (9, 10). Additionally, association with cyanotic congenital heart disease has been recognized (9).

Acquired CAE accounts for the majority of the cases and is most commonly attributed to atherosclerosis (11), with less frequent etiologies being inflammatory and connective tissue diseases such as scleroderma (12), Ehler-Danlos syndrome (13), systemic lupus erythematosus (14), Kawasaki disease (15), polyarteritis nodosa (16), bacterial infections (17), and cardiac lymphomas (18). Iatrogenic ectasia may result with interventional coronary procedures. Localized ectasia has been reported after angioplasty in about 5% of cases and particularly after extensive dissection (19, 20). It has also been described following directional coronary atheroctomy (21, 22), and pulsed laser angioplasty (23). In a large study that included 792 lesions, the prevalence of coronary artery aneurysm following directional coronary atherectomy was low (2.7%) with a favorable long-term clinical outcome (24).

4. HISTOPATHOLOGY

The histopathologic examination of an atherosclerotic ectatic artery reveals thickened fibrotic intima with lipid deposition with foam cells and fibrous caps. There is a marked destruction and reduction of the medial elastic fibers with disruption of the internal elastic lamina, usually out of proportion to the degree of intimal involvement (8, 25-27). The loss of musculoelastic arterial wall components of the coronary artery media in CAE is unrelated to the local atheromatous burden (27, 28). The functional loss of these components is the predominant pathology in CAE (8, 26, 28) and possibly results from chronic vascular inflammation. Markis *et al.* (26) have reported that if the media is intact and uninvolved, there was no evidence of ectasia. In the non-atherosclerotic forms of CAE, there is an intact vessel intima, but with extensive media degeneration (smooth muscle replacement by hyalinized collagen) (29, 30).

5. PATHOGENESIS AND CAUSATIVE MECHANISMS

The causative mechanisms of abnormal luminal dilation in CAE are unknown. Patients with CAE have decreased nitrate-mediated response of brachial artery compared to patients with coronary artery disease (CAD) alone, suggesting more severe dysfunction, or possibly greater destruction of the media layer in CAE than in CAD (31). Considering the similar histological findings, CAE is often viewed as a maladaptive process of atherosclerosis (11, 32). In fact, 'aneurysmal' and 'stenotic' coronary atherosclerosis may represent the extremes of a continuous pathological process (32).

Arterial remodeling reflects the dynamic changes of the external elastic membrane (EEM) over time (32). "Positive remodeling" describes an expansion in EEM area (33) that allows considerable plaque accumulation without luminal loss (32), and is observed in proliferative lesions in early CAD. Thus CAE can be regarded as a consequence of extensive positive remodeling (5). The major precursor of vascular remodeling is probably tissue inflammation. This hypothesis is supported by several studies linking the presence of CAE with elevated inflammatory markers such as plasma interleukin-6 (34), plasma soluble adhesion molecules: V-CAM, I-CAM, and E-selectin (35), and C-reactive protein (CRP) (36, 37). Inflammation forms an important component of vascular aneurysm formation with extensive medial and adventitial inflammatory cell infiltration (38). Plasma neopterin, a marker of immune activation and macrophage activity (39, 40) is significantly higher in patients with isolated CAE. Kocaman and colleagues (41) found that patients with isolated CAE had increased total and differential leukocytic counts, supporting the view that increased inflammation and leukocytosis can lead to the coronary ectatic process without visible atherosclerosis, and that leucocytes may play a critical role in this condition.
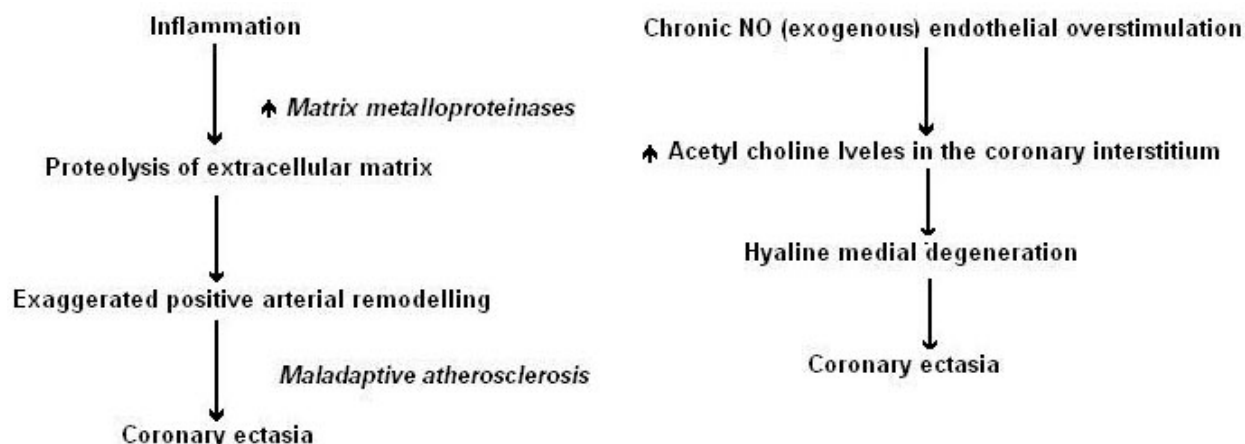
Figure 1. Pathogenetic mechanisms of coronary ectasia.

Hemodynamic conditions (flow, wall stretch, shear stress) may also act as signals or triggers for vascular remodeling (42-44) resulting in the synthesis or activation of mediators for cell growth, apoptosis, migration and changes in extracellular matrix (45). The composition of extracellular matrix is regulated by matrix-metalloproteinase (MMP) activity, which selectively degrades the extracellular matrix components and may play an important role in the remodeling response (46-48). Patients with CAE were found to have a higher percentage of the 5A/5A polymorphism of the metalloproteinase-3 (MMP-3), compared to patients with obstructive coronary lesions (49). Over-expression of MMP-3 may lead to enhanced proteolysis of various matrix proteins, such as proteoglycans, laminin, fibronectin and collagen types III, IV, V, and IX resulting in excessive vessel wall dilatation. The evidence suggests that the presence of higher MMP-3 levels and a critical imbalance between MMPs and their endogenous tissue inhibitors in patients with generalized CAE (50). Similar association between MMP-3 levels and CAE is observed in patients with Kawasaki disease (51).

Another mechanism involves chronic over stimulation of the endothelium with excessive nitric oxide (NO) and NO donors leading to abnormal coronary dilatation (52). Inflammatory cell mediated NO production by iNOS results in high NO levels and toxic products that degrade elastin and disrupt the extracellular matrix (53). Enhanced NO production has also been documented, via the iNOS pathway, following an increase in the local interstitial concentration of acetylcholine (54). 'Clustering' of CAE has been observed in Vietnam veterans exposed to herbicidal Agent Orange (55). The compound inhibits acetyl-cholinesterase, resulting in higher levels of acetylcholine and enhanced NO production. This suggests a possible link between NO over stimulation and medial thinning leading to CAE. Johanning *et al.* (56) have experimentally shown that NO production plays a

major role in inflammation and aneurysm pathogenesis, and inhibition of NO limits aneurysmal dilatation of the aorta.

Manginas *et al.* (4) speculated that CAE occurs due to two different mechanisms in two distinct patient groups: 1. commonly in patients with concomitant CAD due to severe and chronic arterial inflammation and 2. subjects without coronary atherosclerosis as a result of exogenous interstitial NO vascular over stimulation (Figure 1).

6. CORONARY ARTERY ECTASIA AS A GENERALIZED VASCULAR DISEASE

Coronary ectasia being a diffuse abnormality of the vessel wall rather than a localized disease of a single arterial segment has been proposed (57). This view is consistent with studies describing a diffuse form of disease involving multiple vessels (8, 26, 28). Associations have been reported with peripheral, aortic and pulmonary ectasia or aneurysms (28, 58-61). In a retrospective cohort of patients undergoing vascular surgery, coronary ectasia were found in 20.8% with abdominal aortic aneurysm (AAA) and 2.9% with occlusive peripheral vascular disease (60). An incidence of CAE up to 26% was found in patients with aneurysm of ascending aorta compared to 5% in age-matched control group (62). The association of CAE with venous abnormalities suggested the possibility of a generalized defect of the entire vascular wall. CAE has been reported in association with varicosities of the coronary sinus and its tributaries (28), varicose veins (63), and varicocele (64). The overexpression of iNOS has been shown in varicose veins (65), supporting the possible role of NO in the pathogenesis of CAE.

7. CARDIOVASCULAR RISK FACTORS

CAE has a strong male predominance (male: female=3:1) which may represent the higher incidence of AD in men (1, 8, 26, 66). The role of systemic hypertension in the pathogenesis of CAE is akin to its association in patients with aneurysmal disease (2, 26). Age has been shown to be inversely associated with incidence of CAE (66). Similarly,

Table 2. CAE classification

Class	Types I to IV are in order of decreasing frequency (26).
Type I	Diffuse ectasia involving two or more vessels
Type II	Diffuse ectasia involving one vessel and localized ectasia involving another
Type III	Diffuse ectasia involving one vessel only
Type IV	Localized or segmental ectasia only

diabetes mellitus does not appear to be a significant risk factor in the pathogenesis of CAE. Diabetic subjects have down regulation of MMP production in vascular smooth muscle cells and monocytes (67, 68) with negative arterial wall remodeling in response to atherosclerosis (69, 70). These observations coupled with low prevalence of diabetes noticed in patients with CAE (8, 27) are consistent with reported inverse association between CAE and diabetes mellitus (71, 72). Likewise, increased prevalence of AAA has been reported in patients without diabetes mellitus (73, 74). Diabetes is positively-associated with atherosclerosis and negatively-associated with CAE, a contradiction which suggests that CAE is not simply a variant of coronary atherosclerosis (5), but other factors are important in the pathogenesis. The association of dyslipidemia and smoking with CAE is less clear. Swaye *et al.* (2) found no clear difference in the incidence of smoking, lipid abnormalities, or a family history of CAD in patients with and without ectasia. Conversely, CAE was reported to be 6 times more frequent among patients with familial hypercholesterolemia than in control group, suggesting a link between abnormal lipoprotein metabolism and aneurysmal CAD (75). Saglam and colleagues (37) also found that 27 of 51 patients with isolated CAE had plasma lipid abnormalities. The frequency of hyperlipidemia in patients with isolated CAE was similar to those with significant coronary stenosis. Pinar *et al.* (72) found smoking to be more common in patients with CAE than in those with CAD. Cocaine use was also found to be an independent predictor of CAE irrespective of smoking (76).

8. CLINICAL AND IMAGING FEATURES

Angina is the most common presenting complaint in patients with CAE (1, 26, 77). The incidence of angina pectoris in patients with isolated CAE is similar to those with significant coronary artery stenosis with or without accompanying ectasia (3). Patients with CAE without stenosis had positive results during myocardial perfusion scintigraphic evaluation and treadmill exercise tests (37, 78). In patients with isolated CAE, the extent of the ectasia, diffuse ectasia and backflow-phenomenon in an ectatic left anterior descending artery were identified as the most important angiographic predictors of ischemia on exercise testing (79).

Rare cases of ST-elevation myocardial infarction (MI) (80, 81), non-ST elevation MI (82), ventricular arrhythmias, and sudden cardiac death (83) have been reported with CAE. In a retrospective study that included 3870 patients, Valente *et al.* (84) described the angiographic characteristics of patients with CAE, in relation to its clinical expression. Among 109 patients with ST elevation MI or acute coronary syndrome, one third had

ectatic vessel related culprit lesions most commonly involving the right coronary artery. Two thirds had culprit lesions in a stenotic artery, with CAE presenting as an incidental finding in other vessels.

Coronary angiography is the gold standard for the assessment of CAE and concomitant CAD (4). CAE has been classified according to the anatomical shape of the ectatic segment into fusiform or saccular types (28). The term "coronary aneurysm" was used to describe more focal and saccular ectatic segments, while the term "ectasia" was reserved for the more diffuse fusiform vessel disease (26, 85). The most widely used classification is based on the extent of involvement of coronary arteries (26). 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 (Table 2).

Any of the major epicardial vessels can be affected by CAE (3); the right coronary artery being the most commonly affected artery by ectasia, with an approximate prevalence of 60% (7). In patients with concomitant CAD, the proximal and mid segments of the right coronary artery are the most frequently involved (Figure 2), followed by the left anterior descending artery and the circumflex artery (2, 3). About one-third of the stenotic lesions are located in the vessels affected by the ectatic process, while in two-thirds being in the non-ectatic vessels (3). The right coronary artery is also the most commonly involved coronary artery in patients with isolated CAE ranging from 45% to 75% (2, 3, 28, 49, 86) (Figure 3). The angiographic distinction between CAE and emptied plaque cavities or pseudo-aneurysms is of clinical importance as the latter may lead to acute coronary syndromes (87). Intravascular ultrasound (IVUS) can correctly differentiate true from false aneurysms caused by plaque rupture (88). Recently, non–invasive documentation of CAE has been demonstrated using multidetector computed tomographic angiography (89) and magnetic resonance imaging (90).

9. FLOW ALTERATIONS AND MYOCARDIAL ISCHEMIA

Angiographic signs of an impaired coronary blood flow in isolated CAE include delayed antegrade dye filling, a segmental back flow phenomenon (milking phenomenon) and local deposition of dye (stasis) in the dilated coronary segment (11, 26). A significantly lower myocardial blush grade on coronary angiograms is observed in patients with CAE suggesting a disturbed microvascular network (91).
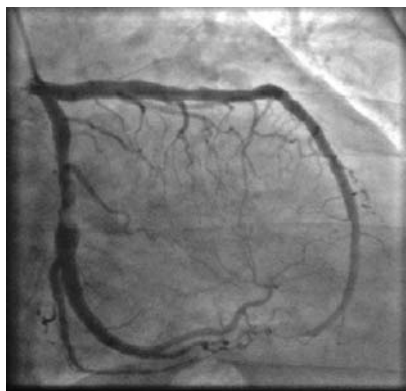
Figure 2. Right anterior oblique view of left coronary angiogram showing ectasia of the left anterior descending and left circumflex arteries. Note the luminal irregularities suggestive of non-obstructive atherosclerosis.

Figure 3. Left anterior oblique view of right coronary angiogram showing ectatic right coronary artery. Note the right atrial and ventricular pacemaker leads.

Slow flow has been demonstrated in CAE in several studies. A higher Thrombolysis In Myocardial Infarction (TIMI) frame count (TFC), which is an angiographic index of coronary flow velocity along the entire epicardial coronary artery is seen in both ectatic and non-ectatic arteries in patients with CAE indicating slower coronary flow rate (92,93). The slow flow phenomenon observed in apparently normal coronary arteries in patients with isolated CAE of the right coronary artery might be related to high microvascular resistance preceding the development of CAE in these arteries (93). Patients with CAE had a trend to a lower resting blood flow velocity, compared to a control group using a doppler wire (Flow-wire) (77). Following intracoronary administration of papaverine, a potent hyperemic stimulant, the coronary flow reserve is significantly lower (1.51) in the CAE compared with the control arteries (2.67), suggesting a combination of epicardial flow disturbances and microvascular dysfunction as the cause of myocardial ischemia. The presence of coexisting stenosis and the severity of ectasia did not alter the TFC in patients with CAE (94). However, a positive correlation between ectasia size and ectasia ratio (the diameter of the ectatic segment/the diameter of an adjacent normal segment) with the TFC of the ectatic right coronary arteries is reported. Observing a slow blood flow rate in an ectatic vessel may be due to the conversion from a laminar to turbulent coronary flow in the ectatic segments (95).

Spasm of the ectatic arteries may be another possible mechanism for myocardial ischemia (7). Contrary to the notion, ectatic coronary segments have been shown to undergo intense coronary spasm in response to exogenous administration to vasoactive medications such as ergonovine and acetylcholine. Spasm may occur within the ectatic or adjacent segments (96, 97).

Spontaneous dissection and intracoronary thrombosis have been reported in patients with CAE (82, 98-100). Intracoronary thrombosis within the ectatic segment and distal embolization of this thrombotic material is a plausible mechanism of myocardial ischemia/infarction in patients with isolated CAE (30, 100, 101). Patients with isolated CAE have elevated levels of plasma P-selectin, transforming growth factor-β and platelet factor-4 compared to controls with angiographically normal coronary arteries, suggesting increased platelet activation in patients with CAE (102). Decreased coronary blood flow velocity and alteration of laminar to turbulent coronary flow in the dilated segment may increase platelet activity in patients with isolated CAE. Increased platelet activity contributes to the development of intracoronary thrombus within the ectatic segment and distal micro embolization (102).

10. PROGNOSIS

Large prospective studies are needed to accurately assess the outcome and long-term prognosis in patients with CAE. However, the current body of knowledge suggests that the long-term outcome of patients with CAE is directly related to the severity of the coexisting obstructive coronary lesions. CAE may not confer a significant additional risk than the coexisting coronary stenosis (1-3, 26). In the CASS registry, the presence of CAE has no effect on the adjusted 5-year survival of patients with CAD, and the mortality is reported to be approximately 2% per year (2). MI is present in one third of patients with isolated CAE (with no or non-significant coronary stenosis) in the corresponding myocardial territory. The overall cardiac event rate in this group is low with comparable 2-year survival in patients with and without CAE (96.7% vs. 94.8% (3).

11. TREATMENT

The medical management of patients with CAE is not well established. No randomized controlled trial has been performed to assess the efficacy of any particular therapy. As the outcome is determined by coexistent obstructive CAD, risk factor modification for primary and secondary prevention is necessary in all patients with CAE (4).

11.1. Medical therapy

Most patients with CAE have associated obstructive coronary lesions or the risk factors for CAD. Patients with isolated coronary ectasia have a risk of myocardial infarction due to micro emboli and thrombotic occlusion (30). As a consequence, aspirin should be administered to all patients with CAE (2,101). The role of combined antiplatelet therapy, with the addition of thieopyridine is uncertain (4). Perlman and Ridgeway (103) propose long-term warfarin therapy in patients with CAE. Prophylactic warfarin is proposed as a therapeutic strategy in reducing the thrombosis resulting from flow alterations within the ectatic segments (8, 104,105). However, there is no randomized study to demonstrate its impact on clinical outcome. Statins and angiotensin-converting enzyme inhibitors decrease the plasma hs-CRP levels in patients with CAE (106). Combination treatment with angiotensin-converting enzyme inhibitors and statins may be effective for isolated CAE and should be considered with the aim to suppress inflammation and prevent thrombosis (41).

Nitrates may exacerbate myocardial ischemia by causing additional coronary epicardial dilatation, and are routinely not recommended in patients with isolated CAE (11). Whenever nitrates are used, it is advised to provide nitrate-free "holiday" to prevent chronic exposure (52). It is also thought that the beta-blockers may augment vasospasm via unopposed alpha receptor stimulation. On the contrary, other authors suggested that the use of beta-blockers in patients with CAE may be theoretically beneficial due to their negative chronotropic effect and reduction in myocardial oxygen consumption (11, 107). Sorrell *et al.* (52) proposed optimal therapeutic regimen including: (1) warfarin anticoagulation with target INR approx. 2.0 – 2.5, (2) antiplatelet therapy with aspirin, (3) antispasm therapy with calcium-channel blockers.

11.2 Role of revascularization

Percutaneous and surgical coronary revascularization has been successful in patients with coexisting obstructive lesions and symptoms or signs of significant ischemia despite maximal medical therapy (4). Proximal and distal ligation, aneurysmectomy and aneurysm resection have good post-operative outcome (108,109). There is no difference in the procedural success, complications or restenosis following angioplasty of stenotic lesions with or without adjacent aneurysmal CAD (110). Autologous venous graft-covered stent is a valuable approach in selected cases to seal the coronary artery aneurysm (111). Biliary, sirulimus-eluting, and recently carotid stents have been used to intervene on the stenotic ectatic coronary arteries (112-114). However, there are no evidence-based guidelines for the management of stenotic lesions associated with CAE. In the presence of CAE, special attention should be paid for adequate stent expansion and wall apposition which at times can be accomplished only with IVUS. In addition, extra care is important during introduction and withdrawal of the device, in order to avoid stent dislocation (4).

12. CONCLUSION

CAE is seen in about 5% of cases undergoing coronary angiography. It is usually associated with obstructive CAD, and may be considered as an expression of atherosclerosis. Pathologic mechanisms include inflammation with exaggerated positive vascular remodeling and over stimulation of the endothelium by NO. The inappropriate coronary dilatation leads to flow disturbance. The most frequent presentation of patients with CAE is angina with the attendant risk for cardiovascular events including myocardial infarction and even sudden death. Slow flow, micro embolism, thrombosis, spasm, spontaneous dissection and increased platelet activation are potential causes for development of myocardial ischemia in CAE. CAE may be a diffuse systemic disease involving arteries as well as veins. The prognosis is determined mainly by the severity of the coexisting obstructive CAD. Currently, there are no guidelines for treatment of CAE. The use of anticoagulants, nitrates and beta blockers is controversial. Surgical and percutaneous revascularization techniques have been demonstrated to be feasible alternatives for revascularization. Large prospective studies are needed to evaluate the efficacy, risks and benefits of the different treatment modalities.

13. REFERENCES

1. G. G. Hartnell, B. M. Parnell and R. B. Pridie: Coronary artery ectasia. Its prevalence and clinical significance in 4993 patients, *Br Heart J* 54, 392-395 (1985)

2. P. S. Swaye, L. D. Fisher, P. Litwin, P. A. Vignola, M. P. Judkins, H. G. Kemp, J. G. Mudd and A. J. Gosselin: Aneurysmal coronary artery disease, *Circulation* 67, 134-138 (1983)

3. V. P. Demopoulos, C. D. Olympios, C. N. Fakiolas, E. G. Pissimissis, N. M. Economides, E. Adamopoulou, S. G. Foussas and D. V. Cokkinos: The natural history of aneurysmal coronary artery disease, *Heart* 78, 136-141 (1997)

4. A. Manginas and D. V. Cokkinos: Coronary artery ectasias: imaging, functional assessment and clinical implications, *Eur Heart J* 27, 1026-1031 (2006)

5. E. Yetkin, S. Kilic, N. Acikgoz, H. Ergin, Y. Aksoy, I. Sincer, E. Akturk, A. Beytur, N. Sivri and H. Turhan: Increased prevalence of varicocele in patients with coronary artery ectasia, *Coron Artery Dis* 16, 261-264 (2005)

6. S. N. Sharma, U. Kaul, S. Sharma, H. S. Wasir, S. C. Manchanda, V. K. Bahl, K. K. Talwar, M. Rajani and M. L. Bhatia: Coronary arteriographic profile in young and old Indian patients with ischaemic heart disease: a comparative study, *Indian Heart J* 42, 365-369 (1990)

7. P. Ramappa, A. Kottam, H. Kuivanemi and D. Thatai: Coronary artery ectasia--is it time for a reappraisal? *Clin Cardiol* 30, 214-217 (2007)

8. R. H. Swanton, M. L. Thomas, D. J. Coltart, B. S. Jenkins, M. M. Webb-Peploe and B. T. Williams: Coronary artery ectasia--a variant of occlusive coronary arteriosclerosis, *Br Heart J* 40, 393-400 (1978)

9. R. Chugh, J. K. Perloff, M. Fishbein and J. S. Child: Extramural coronary arteries in adults with cyanotic congenital heart disease, *Am J Cardiol* 94, 1355-1357 (2004)

10. T. Ucar, S. Atalay, M. Tekin and E. Tutar: Bilateral coronary artery dilatation and supravalvular pulmonary stenosis in a child with noonan syndrome, *Pediatr Cardiol* 26, 848-850 (2005)

11. D. Kruger, U. Stierle, G. Herrmann, R. Simon and A. Sheikhzadeh: Exercise-induced myocardial ischemia in isolated coronary artery ectasias and aneurysms ("dilated coronopathy"), *J Am Coll Cardiol* 34, 1461-1470 (1999)

12. S. Chaithiraphan, E. Goldberg, M. O'Reilly and P. Jootar: Multiple aneurysms of coronary artery in sclerodermal heart disease, *Angiology* 24, 86-93 (1973)

13. S. Imahori, R. M. Bannerman, C. J. Graf and J. C. Brennan: Ehlers-Danlos syndrome with multiple arterial lesions, *Am J Med* 47, 967-977 (1969)

14. A. H. Matayoshi, M. R. Dhond and L. J. Laslett: Multiple coronary aneurysms in a case of systemic lupus erythematosus, *Chest* 116, 1116-1118 (1999)

15. S. Hiraishi, K. Yashiro, K. Oguchi, S. Kusano, K. Ishii and K. Nakazawa: Clinical course of cardiovascular involvement in the mucocutaneous lymph node syndrome. Relation between clinical signs of carditis and development of coronary arterial aneurysm, *Am J Cardiol* 47, 323-330 (1981)

16. P. H. Tang and A. J. Segal: Polyarteritis nodosa of infancy. Fatal late complication, *JAMA* 217, 1666-1670 (1971)

17. A. Davidson, E. Eshaghpour, N. Young and G. S. Mintz: Late thrombosis of a coronary artery mycotic aneurysm, *Am Heart J* 121, 1549-1550 (1991)

18. D. S. Gardiner and G. B. Lindop: Coronary artery aneurysm due to primary cardiac lymphoma, *Histopathology* 15, 537-540 (1989)

19. C. Vassanelli, M. Turri, G. Morando, G. Menegatti and P. Zardini: Coronary arterial aneurysms after percutaneous transluminal coronary angioplasty--a not uncommon finding at elective follow-up angiography, *Int J Cardiol* 22, 151-156 (1989)

20. E. T. Bal, H. W. Thijs Plokker, E. M. van den Berg, S. M. Ernst, E. Gijs Mast, R. M. Gin and C. A. Ascoop: Predictability and prognosis of PTCA-induced coronary artery aneurysms, *Cathet Cardiovasc Diagn* 22, 85-88 (1991)

21. M. A. Krolick, W. J. Bugni and J. W. Walsh: Coronary artery aneurysm formation following directional coronary atherectomy, *Cathet Cardiovasc Diagn* 27, 117-121 (1992)

22. N. B. De Cesare, J. J. Popma, D. R. Holmes Jr, R. J. Dick, P. L. Whitlow, S. B. King, C. A. Pinkerton, D. J. Kereiakes, E. J. Topol and C. C. Haudenschild: Clinical angiographic and histologic correlates of ectasia after directional coronary atherectomy, *Am J Cardiol* 69, 314-319 (1992)

23. M. B. Preisack, W. Voelker, K. K. Haase and K. R. Karsch: Case report: formation of vessel aneurysm after stand alone coronary excimer laser angioplasty, *Cathet Cardiovasc Diagn* 27, 122-124 (1992)

24. Y. Oikawa, J. Yajima, D. J. Angiolillo, M. Akabane, R. Funada, S. Matsuno, T. Inaba, Y. Nakagawa, M. Nakamura, H. Sawada and T. Aizawa: Short- or long-term outcomes of coronary artery aneurysms occurring after directional coronary atherectomy, *J Invasive Cardiol* 20, 159-160 (2008)

25. A. S. Daoud, D. Pankin, H. Tulgan and R. A. Florentin: Aneurysms of the coronary artery. Report of ten cases and review of literature, *Am J Cardiol* 11, 228-237 (1963)

26. J. E. Markis, C. D. Joffe, P. F. Cohn, D. J. Feen, M. V. Herman and R. Gorlin: Clinical significance of coronary arterial ectasia, *Am J Cardiol* 37, 217-222 (1976)

27. R. Virmani, M. Robinowitz, J. B. Atkinson, M. B. Forman, M. D. Silver and H. A. McAllister: Acquired coronary arterial aneurysms: an autopsy study of 52 patients, *Hum Pathol* 17, 575-583 (1986)

28. B. Befeler, M. J. Aranda, A. Embi, F. L. Mullin, N. El-Sherif and R. Lazzara: Coronary artery aneurysms: study of the etiology, clinical course and effect on left ventricular function and prognosis, *Am J Med* 62, 597-607 (1977)

29. A. L. Mattern, W. P. Baker, J. J. McHale and D. E. Lee: Congenital coronary aneurysms with angina pectoris and myocardial infarction treated with saphenous vein bypass graft, *Am J Cardiol* 30, 906-909 (1972)

30. S. Rath, Y. Har-Zahav, A. Battler, O. Agranat, Z. Rotstein, B. Rabinowitz and H. N. Neufeld: Fate of nonobstructive aneurysmatic coronary artery disease: angiographic and clinical follow-up report, *Am Heart J* 109, 785-791 (1985)

31. Y. Aksoy, N. Acikgoz, N. Sivri, E. Bariskaner, E. Akturk, H. Turhan and E. Yetkin: Decreased nitrate-mediated dilatation in patients with coronary artery ectasia: an ultrasonographic evaluation of brachial artery, *Coron Artery Dis* 17, 365-369 (2006)

32. P. Schoenhagen, K. M. Ziada, D. G. Vince, S. E. Nissen and E. M. Tuzcu: Arterial remodeling and coronary artery disease: the concept of "dilated" versus "obstructive"

coronary atherosclerosis, *J Am Coll Cardiol* 38, 297-306 (2001)

33. S. Glagov, E. Weisenberg, C. K. Zarins, R. Stankunavicius and G. J. Kolettis: Compensatory enlargement of human atherosclerotic coronary arteries, *N Engl J Med* 316, 1371-1375 (1987)

34. L. Tokgozoglu, O. Ergene, O. Kinay, C. Nazli, G. Hascelik and Y. Hoscan: Plasma interleukin-6 levels are increased in coronary artery ectasia, *Acta Cardiol* 59, 515-519 (2004)

35. H. Turhan, A. R. Erbay, A. S. Yasar, Y. Aksoy, A. Bicer, G. Yetkin and E. Yetkin: Plasma soluble adhesion molecules; intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin levels in patients with isolated coronary artery ectasia, *Coron Artery Dis* 16, 45-50 (2005)

36. A. K. Adiloglu, R. Can, C. Nazli, A. Ocal, O. Ergene, G. Tinaz and N. Kisioglu: Ectasia and severe atherosclerosis: relationships with chlamydia pneumoniae, helicobacterpylori, and inflammatory markers, *Tex Heart Inst J* 32, 21-27 (2005)

37. M. Saglam, O. Karakaya, I. Barutcu, A. M. Esen, M. Turkmen, R. Kargin, O. Esen, N. Ozdemir and C. Kaymaz: Identifying cardiovascular risk factors in a patient population with coronary artery ectasia, *Angiology* 58, 698-703 (2007)

38. A. E. Koch, G. K. Haines, R. J. Rizzo, J. A. Radosevich, R. M. Pope, P. G. Robinson and W. H. Pearce: Human abdominal aortic aneurysms. Immunophenotypic analysis suggesting an immune-mediated response, *Am J Pathol* 137, 1199-1213 (1990)

39. C. Huber, J. R. Batchelor, D. Fuchs, A. Hausen, A. Lang, D. Niederwieser, G. Reibnegger, P. Swetly, J. Troppmair and H. Wachter: Immune response-associated production of neopterin. Release from macrophages primarily under control of interferon-gamma, *J Exp Med* 160, 310-316 (1984)

40. M. Sahin, E. Varol, M. Ozaydin, A. Altinbas, O. Aydin, S. M. Aslan, A. Dogan and S. Kaya: Comparison of neopterin levels in patients with coronary artery ectasia versus patients with obstructive coronary artery disease, *South Med J* 101, 476-479 (2008)

41. S. A. Kocaman, G. Tacoy, A. Sahinarslan and A. Cengel: Relationship between total and differential leukocyte counts and isolated coronary artery ectasia, *Coron Artery Dis* 19, 307-310 (2008)

42. G. H. Gibbons and V. J. Dzau: The emerging concept of vascular remodeling, *N Engl J Med* 330, 1431-1438 (1994)

43. V. J. Dzau and G. H. Gibbons: Vascular remodeling: mechanisms and implications, *J Cardiovasc Pharmacol* 21 Suppl 1, S1-5 (1993)

44. B. L. Langille, Arterial remodeling: relation to hemodynamics, *Can J Physiol Pharmacol* 74, 834-841 (1996)

45. D. B. Cowan and B. L. Langille: Cellular and molecular biology of vascular remodeling, *Curr Opin Lipidol* 7, 94-100 (1996)

46. H. Nagase and J. F. Woessner Jr: Matrix metalloproteinases, *J Biol Chem* 274, 21491-21494 (1999)

47. S. Ye, S. Humphries and A. Henney: Matrix metalloproteinases: implication in vascular matrix remodelling during atherogenesis, *Clin Sci (Lond)* 94, 103-110 (1998)

48. C. M. Dollery, J. R. McEwan and A. M. Henney: Matrix metalloproteinases and cardiovascular disease, *Circ Res* 77, 863-868 (1995)

49. N. Lamblin, C. Bauters, X. Hermant, J. M. Lablanche, N. Helbecque and P. Amouyel: Polymorphisms in the promoter regions of MMP-2, MMP-3, MMP-9 and MMP-12 genes as determinants of aneurysmal coronary artery disease, *J Am Coll Cardiol* 40, 43-48 (2002)

50. A. Finkelstein, Y. Michowitz, A. Abashidze, H. Miller, G. Keren and J. George: Temporal association between circulating proteolytic, inflammatory and neurohormonal markers in patients with coronary ectasia, *Atherosclerosis* 179, 353-359 (2005)

51. H. Senzaki, S. Masutani, J. Kobayashi, T. Kobayashi, H. Nakano, H. Nagasaka, N. Sasaki, H. Asano, S. Kyo and Y. Yokote: Circulating matrix metalloproteinases and their inhibitors in patients with Kawasaki disease, *Circulation* 104, 860-863 (2001)

52. V. L. Sorrell, M. J. Davis and A. A. Bove: Current knowledge and significance of coronary artery ectasia: a chronologic review of the literature, recommendations for treatment, possible etiologies, and future considerations, *Clin Cardiol* 21, 157-160 (1998)

53. J. S. Beckman and W. H. Koppenol: Nitric oxide, superoxide, and peroxynitrite: the good, the bad, and ugly, *Am J Physiol* 271, C1424-37 (1996)

54. P. M. Vanhoutte, Endothelium and control of vascular function. State of the Art lecture, *Hypertension* 13, 658-667 (1989)

55. J. F. England, Herbicides and coronary ectasia, *Med J Aust* 2, 260 (1981)

56. J. M. Johanning, D. P. Franklin, D. C. Han, D. J. Carey and J. R. Elmore: Inhibition of inducible nitric oxide synthase limits nitric oxide production and experimental aneurysm expansion, *J Vasc Surg* 33, 579-586 (2001)

57. M. J. Williams and R. A. Stewart: Coronary artery ectasia: local pathology or diffuse disease? *Cathet Cardiovasc Diagn* 33, 116-119 (1994)

58. C. L. LaMendola, A. T. Culliford, L. J. Harris and M. T. Amendo: Multiple aneurysms of the coronary arteries in a patient with systemic aneurysmal disease, *Ann Thorac Surg* 49, 1009-1010 (1990)

59. M. Ruttimann, J. P. Perez, R. Richard, L. Brinquin and J. P. Bonsignour: Intracranial aneurysm and coronary ectasia), *Presse Med* 26, 1141-1143 (1997)

60. K. C. Stajduhar, J. R. Laird, K. M. Rogan and D. C. Wortham: Coronary arterial ectasia: increased prevalence in patients with abdominal aortic aneurysm as compared to occlusive atherosclerotic peripheral vascular disease, *Am Heart J* 125, 86-92 (1993)

61. H. Triantafillidi, I. Rizos, A. Androulakis, K. Stratos, C. Arvaniti and P. Toutouzas: Coronary artery ectasia, aneurysm of the basilar artery and varicose veins: common presentation or generalized defect of the vessel wall? A case report, *Angiology* 52, 287-291 (2001)

62. M. C. Papadakis, A. Manginas, P. Cotileas, V. Demopoulos, V. Voudris, G. Pavlides, S. G. Foussas and D. V. Cokkinos: Documentation of slow coronary flow by the TIMI frame count in patients with coronary ectasia, *Am J Cardiol* 88, 1030-1032 (2001)

63. A. E. Androulakis, G. K. Andrikopoulos, A. N. Kartalis, P. N. Stougiannos, A. A. Katsaros, D. N. Syrogiannidis, E. N. Tapanlis, C. Stefanadis and I. E. Kallikazaros: Relation of coronary artery ectasia to diabetes mellitus, *Am J Cardiol* 93, 1165-1167 (2004)

64. E. Yetkin and J. Waltenberger: Novel insights into an old controversy: is coronary artery ectasia a variant of coronary atherosclerosis? *Clin Res Cardiol* 96, 331-339 (2007)

65. T. Jacob, A. Hingorani and E. Ascher: Overexpression of transforming growth factor-beta1 correlates with increased synthesis of nitric oxide synthase in varicose veins, *J Vasc Surg* 41, 523-530 (2005)

66. G. D. Giannoglou, A. P. Antoniadis, Y. S. Chatzizisis, E. Damvopoulou, G. E. Parcharidis and G. E. Louridas: Prevalence of ectasia in human coronary arteries in patients in northern Greece referred for coronary angiography, *Am J Cardiol* 98, 314-318 (2006)

67. M. Kuzuya, T. Asai, S. Kanda, K. Maeda, X. W. Cheng and A. Iguchi: Glycation cross-links inhibit matrix metalloproteinase-2 activation in vascular smooth muscle cells cultured on collagen lattice, *Diabetologia* 44, 433-436 (2001)

68. M. D. Baugh, J. Gavrilovic, I. R. Davies, D. A. Hughes and M. J. Sampson: Monocyte matrix metalloproteinase production in Type 2 diabetes and controls--a cross sectional study, *Cardiovasc Diabetol* 2, 3 (2003)

69. M. Vavuranakis, C. Stefanadis, K. Toutouzas, C. Pitsavos, V. Spanos and P. Toutouzas: Impaired compensatory coronary artery enlargement in atherosclerosis contributes to the development of coronary artery stenosis in diabetic patients. An *in vivo* intravascular ultrasound study, *Eur Heart J* 18, 1090-1094 (1997)

70. R. Kornowski, G. S. Mintz, A. J. Lansky, M. K. Hong, K. M. Kent, A. D. Pichard, L. F. Satler, J. J. Popma, T. A. Bucher and M. B. Leon: Paradoxic decreases in atherosclerotic plaque mass in insulin-treated diabetic patients, *Am J Cardiol* 81, 1298-1304 (1998)

71. A. E. Androulakis, A. A. Katsaros, A. N. Kartalis, P. N. Stougiannos, G. K. Andrikopoulos, E. I. Triantafyllidi, A. A. Pantazis, C. I. Stefanadis and I. E. Kallikazaros: Varicose veins are common in patients with coronary artery ectasia. Just a coincidence or a systemic deficit of the vascular wall? *Eur J Vasc Endovasc Surg* 27, 519-524 (2004)

72. E. Pinar Bermudez, R. Lopez Palop, I. Lozano Martinez-Luengas, R. Cortes Sanchez, P. Carrillo Saez, R. Rodriguez Carreras, F. Pico Aracil and M. Valdes Chavarri: Coronary ectasia: prevalence, and clinical and angiographic characteristics), *Rev Esp Cardiol* 56, 473-479 (2003)

73. J. F. Blanchard, H. K. Armenian and P. P. Friesen: Risk factors for abdominal aortic aneurysm: results of a case-control study, *Am J Epidemiol* 151, 575-583 (2000)

74. S. S. Kang, F. N. Littooy, S. R. Gupta, G. R. Johnson, S. G. Fisher, W. L. Cote, G. F. Steffen, M. A. Mansour, N. Labropoulos and J. C. Maggio: Higher prevalence of abdominal aortic aneurysms in patients with carotid stenosis but without diabetes, *Surgery* 126, 687-91; discussion 691-2 (1999)

75. K. Sudhir, T. A. Ports, T. M. Amidon, J. J. Goldberger, V. Bhushan, J. P. Kane, P. Yock and M. J. Malloy: Increased prevalence of coronary ectasia in heterozygous familial hypercholesterolemia, *Circulation* 91, 1375-1380 (1995)

76. A. Satran, B. A. Bart, C. R. Henry, M. B. Murad, S. Talukdar, D. Satran and T. D. Henry: Increased prevalence of coronary artery aneurysms among cocaine users, *Circulation* 111, 2424-2429 (2005)

77. O. Akyurek, B. Berkalp, T. Sayin, D. Kumbasar, C. Kervancioglu and D. Oral: Altered coronary flow properties in diffuse coronary artery ectasia, *Am Heart J* 145, 66-72 (2003)

78. T. Sayin, O. Doven, B. Berkalp, O. Akyurek, S. Gulec and D. Oral: Exercise-induced myocardial ischemia in patients with coronary artery ectasia without obstructive coronary artery disease, *Int J Cardiol* 78, 143-149 (2001)

79. A. Altinbas, C. Nazli, O. Kinay, O. Ergene, O. Gedikli, M. Ozaydin, A. Dogan and G. Gunay: Predictors of exercise induced myocardial ischemia in patients with isolated coronary artery ectasia, *Int J Cardiovasc Imaging* 20, 3-17 (2004)

80. S. Sanyal and N. Caccavo: Is nitroglycerin detrimental in patients with coronary artery ectasia? A case report, *Tex Heart Inst J* 25, 140-144 (1998)

81. I. Mrdovic, T. Jozic, M. Asanin, J. Perunicic and M. Ostojic: Myocardial reinfarction in a patient with coronary ectasia, *Cardiology* 102, 32-34 (2004)

82. M. Kuhl and C. Varma: A case of acute coronary thrombosis in diffuse coronary artery ectasia, *J Invasive Cardiol* 20, E23-5 (2008)

83. V. D. Rosenberg and L. M. Nepomnyashchikh: Pathomorphological peculiarities of coronary artery ectasias and their role in the pathogenesis of sudden cardiac death, *Bull Exp Biol Med* 138, 515-521 (2004)

84. S. Valente, C. Lazzeri, C. Giglioli, F. Sani, S. M. Romano, M. Margheri, M. Comeglio and G. F. Gensini: Clinical expression of coronary artery ectasia, *J Cardiovasc Med (Hagerstown)* 8, 815-820 (2007)

85. P. A. Tunick, J. Slater, I. Kronzon and E. Glassman: Discrete atherosclerotic coronary artery aneurysms: a study of 20 patients, *J Am Coll Cardiol* 15, 279-282 (1990)

86. S. Celik, T. Erdogan, H. Kasap, S. Kaplan, I. Durmus, O. Gedik and A. Kiris: Carotid intima-media thickness in patients with isolated coronary artery ectasia, *Atherosclerosis* 190, 385-387 (2007)

87. V. Fuster, B. Stein, J. A. Ambrose, L. Badimon, J. J. Badimon and J. H. Chesebro: Atherosclerotic plaque rupture and thrombosis. Evolving concepts, *Circulation* 82, II47-59 (1990)

88. T. J. Garrand, G. S. Mintz, J. J. Popma, S. A. Lewis, N. A. Vaughn and M. B. Leon: Intravascular ultrasound diagnosis of a coronary artery pseudoaneurysm following percutaneous transluminal coronary angioplasty, *Am Heart J* 125, 880-882 (1993)

89. A. R. Zeina, D. Sharif, J. Blinder, U. Rosenschein and E. Barmeir: Noninvasive assessment of coronary artery ectasia using multidetector computed tomography, *Coron Artery Dis* 18, 175-180 (2007)

90. S. I. Mavrogeni, A. Manginas, E. Papadakis, S. Foussas, M. Douskou, P. Baras, I. Seimenis and D. V. Cokkinos: Correlation between magnetic resonance angiography (MRA) and quantitative coronary angiography (QCA) in ectatic coronary vessels, *J Cardiovasc Magn Reson* 6, 17-23 (2004)

91. S. Gulec, Y. Atmaca, M. Kilickap, O. Akyurek, O. Aras and D. Oral: Angiographic assessment of myocardial perfusion in patients with isolated coronary artery ectasia, *Am J Cardiol* 91, 996-9, A7 (2003)

92. M. C. Papadakis, E. Leontiadis, A. Manginas, V. Voudris, G. Pavlides, G. Karatasakis, S. G. Foussas, A. S. Mihalis and D. V. Cokkinos: Frequency of coronary artery ectasia in patients undergoing surgery for ascending aortic aneurysms, *Am J Cardiol* 94, 1433-1435 (2004)

93. K. Senen, E. Yetkin, H. Turhan, R. Atak, N. Sivri, B. Battaloglu, I. Tandogan, M. Ileri, F. Kosar, R. Ozdemir and S. Cehreli: Increased thrombolysis in myocardial infarction frame counts in patients with isolated coronary artery ectasia, *Heart Vessels* 19, 23-26 (2004)

94. F. Kosar, N. Acikgoz, I. Sahin, E. Topal, H. Gunen, N. Ermis and S. Cehreli: Effects of co-existence of coronary stenosis and the extent of coronary ectasia on the TIMI frame count in patients with coronary artery ectasia, *Int Heart J* 46, 211-218 (2005)

95. F. Kosar, N. Acikgoz, I. Sahin, E. Topal, Y. Aksoy and S. Cehreli: Effect of ectasia size or the ectasia ratio on the thrombosis in myocardial infarction frame count in patients with isolated coronary artery ectasia, *Heart Vessels* 20, 199-202 (2005)

96. A. A. Bove and R. E. Vlietstra: Spasm in ectatic coronary arteries, *Mayo Clin Proc* 60, 822-826 (1985)

97. H. Suzuki, Y. Takeyama, Y. Hamazaki, A. Namiki, S. Koba, H. Matsubara, J. Hiroshige, M. Murakami and T. Katagiri: Coronary spasm in patients with coronary ectasia, *Cathet Cardiovasc Diagn* 32, 1-7 (1994)

98. H. V. Huikuri, S. M. Mallon and R. J. Myerburg: Cardiac arrest due to spontaneous coronary artery dissection in a patient with coronary ectasia--a case report, *Angiology* 42, 148-151 (1991)

99. Y. Tanabe, E. Itoh, I. Nakagawa and K. Suzuki: Pulse-spray thrombolysis in acute myocardial infarction caused by thrombotic occlusion of an ectatic coronary artery, *Circ J* 66, 207-210 (2002)

100. S. T. Rab, D. W. Smith, B. N. Alimurung, R. Rab and S. B. King 3rd: Thrombolytic therapy in coronary ectasia and acute myocardial infarction, *Am Heart J* 119, 955-957 (1990)

101. S. S. al-Harthi, M. S. Nouh, M. Arafa and M. al-Nozha: Aneurysmal dilatation of the coronary arteries: diagnostic patterns and clinical significance, *Int J Cardiol* 30, 191-194 (1991)

102. A. S. Yasar, A. R. Erbay, S. Ayaz, H. Turhan, F. Metin, E. Ilkay and I. Sabah: Increased platelet activity in patients with isolated coronary artery ectasia, *Coron Artery Dis* 18, 451-454 (2007)

103. P. E. Perlman and N. A. Ridgeway: Thrombosis and anticoagulation therapy in coronary ectasia, *Clin Cardiol* 12, 541-542 (1989)

104. J. J. Hart and C. G. Joslin: Coronary artery ectasia, *Kans Med* 98, 6-9 (1998)

105. V. L. Sorrell, M. J. Davis and A. A. Bove: Origins of coronary artery ectasia, *Lancet* 347, 136-137 (1996)

106. Y. Ozbay, M. Akbulut, M. Balin, H. Kayancicek, A. Baydas and H. Korkmaz: The level of hs-CRP in coronary artery ectasia and its response to statin and angiotensin-converting enzyme inhibitor treatment, *Mediators Inflamm* 2007, 89649 (2007)

107. G. Jackson, L. Atkinson and S. Oram: Improvement of myocardial metabolism in coronary arterial disease by beta-blockade, *Br Heart J* 39, 829-833 (1977)

108. R. Vijayanagar, E. Shafii, M. DeSantis, R. S. Waters and A. Desai: Surgical treatment of coronary aneurysms with and without rupture, *J Thorac Cardiovasc Surg* 107, 1532-1535 (1994)

109. S. Harandi, S. B. Johnston, R. E. Wood and W. C. Roberts: Operative therapy of coronary arterial aneurysm, *Am J Cardiol* 83, 1290-1293 (1999)

110. M. Ochiai, T. Yamaguchi, J. Taguchi, M. Ohno, H. Yoshimura, M. Kashida, K. Kuwako, T. Isshiki and K. Kurokawa: Angioplasty of stenoses adjacent to aneurysmal coronary artery disease, *Jpn Heart J* 31, 749-757 (1990)

111. C. Stefanadis, K. Toutouzas, E. Tsiamis and P. Toutouzas: New stent design for autologous venous graft-covered stent preparation: first human application for sealing of a coronary aneurysm, *Catheter Cardiovasc Interv* 55, 222-227 (2002)

112. M. Agirbasli, D. C. Morris and J. J. Marshall: The use of intrastent peripheral stent in large coronary arteries: report of three cases, *Catheter Cardiovasc Interv* 50, 498-501 (2000)

113. S. W. Rha, S. P. Wani and D. J. Oh: Parallel stenting using two sirolimus-eluting stents in an ectatic coronary artery stenosis, *Heart* 93, 976 (2007)

114. V. Le, M. Abu-Fadel and T. A. Hennebry: The use of tapered self-expanding stents and embolic protection devices in the treatment of stenotic ectatic coronary arteries: a report of two cases, *Catheter Cardiovasc Interv* 72, 643-646 (2008)

Abbreviations: CAE: coronary artery ectasia; CAD: coronary artery disease; EEM: external elastic membrane; CRP: C-reactive protein; MMP: matrix-metalloproteinase; MMP-3: matrix-metalloproteinase-3; NO: nitric oxide; AAA: abdominal aortic aneurysm; IVUS: intravascular ultrasound; TFC: TIMI frame count.

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