REVIEW ARTICLE

Coronary aneurysms

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KEY WORDS

coronary aneurysm, location of aneurysms in the coronary tree, percutaneous treatment, thromboembolic complications

ABSTRACT

Coronary aneurysms represent anomalies identified in 0.15–4.9% of patients undergoing coronary angiography. At present there is no uniform definition of this pathology. According to current definitions, the term "aneurysm" refers to both diffuse over 150% dilation of the largest diameter of a coronary artery, and limited spherical or saccular dilation. Aneurysms are observed most commonly in the right coronary artery, and least frequently in the left main coronary artery. It has been demonstrated that atherosclerosis is the main cause of these anomalies in adults, and Kawasaki disease in children and adolescents. However, regardless of the pathogenesis of the aneurysm, pathology of the media of the blood vessel plays a major role in its formation. The most prevalent consequence of aneurysms in the coronary arteries is formation of a thrombus with distal embolization, vasospasm or vessel disruption at the site of wall injury. Therefore, therapeutic management in this anomaly involves both the prevention of thromboembolic complications and percutaneous or surgical closure of the aneurysm entry.

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INTRODUCTION The first case of the coronary artery anomaly described as an aneurysm lesion was reported in 1761 by Morgagni, whereas Munker et al. in 1958 reported a coronary aneurysm diagnosed with coronary angiography. This anomaly of the coronary arteries is observed in 0.15–4.9% of patients undergoing coronary angiography.[1]

Despite many years of studies on pathology of coronary aneurysms, the mere creation of a definition and classification attempts brought many problems to researchers. At present this vascular pathology is described as dilation of blood vessel lumen, exceeding the diameter of the adjacent normal segment, or more precisely – dilation exceeding the largest diameter of a coronary vessel of a given patient more than 1.5-fold.[2-7] On the other hand, Markies et al.[8] used a term "ectasia" to describe this type of anomaly, and in addition, according to the morphological picture and the number of affected arteries, they proposed a classification of aneurysms. As type 1 they described dilations in all 3 epicardial coronary arteries, type 2 as dilation in 1 blood vessel only with accompanying stenosis in another coronary artery, and type 3 as dilation limited only to 1 artery. Tunick et al.[9] in their work described aneurysms as limited, unusual dilation of the coronary artery with spherical or saccular shape (FIGURE 1 and FIGURE 2AB), including spindle-like changes, which they termed "ectasia" (FIGURE 3). Likewise Syed and Lesh[3] limited the term "aneurysms" to unusual, limited saccular or spindle-like dilation of the coronary artery, and reserved the term "ectasia" for diffuse dilation that refers to 50% of the blood vessel length (FIGURE 4).

Most commonly coronary aneurysms are located in the right coronary artery (FIGURE 1), and then in decreasing order in the left descending artery, the left circumflex artery (FIGURE 2AB), and only exceptionally in the left main coronary artery.[10]

Etiology Lack of a uniform definition of aneurysms is associated with differences in descriptions of their incidence in coronary angiograms. Daound et al.[10] in their autopsy studies reported their incidence at the level of 1.4%, whereas in the Coronary Artery Surgery Study (CASS) presence of coronary aneurysms was identified in 4.9% of patients.

Even though coronary aneurysms can be diagnosed at any age, it is atherosclerosis that is considered their main cause.[1,3-7,9] The remaining factors significantly contributing to coronary

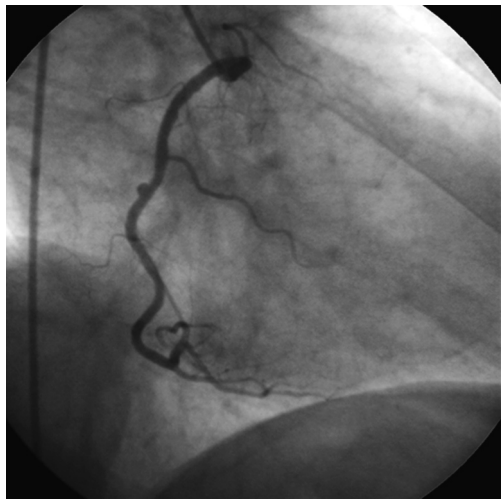

FIGURE 1 Coronary aneurysms located in the right coronary artery

aneurysm formation include: Kawasaki disease, coronary artery revascularisation procedures (balloon angioplasty, laser, atherectomy), inflammatory arterial diseases (polyarteritis nodosa, syphilis, systemic lupus erythematosus, Takayasu disease), candidosis, chest traumas, connective tissue disorders (Marfan's syndrome, Ehlers-Danlos syndrome, scleroderma) and primary hyperaldosteronism.

It has been observed that atherosclerotic and so-called inflammatory aneurysms are mostly multiple, and are not limited to 1 artery (FIGURE 4), in contrast to congenital and posttraumatic aneurysms, and these formed after revascularisation procedures.

It is not surprising that there are ongoing studies aimed at establishing the pathogenesis, in order to develop the so-called targeted therapy. In 50–52% of cases, the underlying cause of coronary aneurysms is atherosclerosis. Microscopic examinations of the walls of aneurysmal coronary vessels demonstrated typical components of atherosclerotic plaques, i.e. lipid and hyalin deposits in the intima, focal calcifications and fibrosis, cholesterol crystals, thrombi, inflammatory cells and destructive changes in the intima and media.[8]

Dauod et al.[10] have acknowledged that aneurysms are formed as a result of poststenotic transformation of kinetic energy to potential energy, and pressure abnormalities in the vessel. However, Berkoff and Rowe[11] believed that aneurysms are formed when an atherosclerotic plaque borders with a degenerated, thin media, and this site is a potential focus of plaque disruption. As a result of thrombus formation at this site, its elements can migrate with bloodstream to peripheral segments of the coronary vessel, causing microcirculation impairment and clinical symptoms of ischemia. Probably, the atherosclerotic material located at the membrane injury side is eluted. This "hollow" site presumably is a point of aneurysm formation. Studies of Befeler et al. followed the same concept.[1] On the contrary, a theory of Markis et al.[8] suggested that the formation of the atherosclerotic aneurysm takes place as a result of imbalance between intravascular pressure and elasticity of the vascular wall. In this case, the decreased tone of the wall facilitates destruction of the media. Moreover, Siouffi et al.[12] explained that the elevated velocity of blood flow at the stenotic site, in the result of increased shear stress, leads to the endothelial injury and in consequence to poststenotic vasodilation.

Formation of aneurysms after percutaneous revascularisation procedures provoked the search for mechanisms of their formation.[13-20] During the 1st month after angioplasty mainly a positive hypertrophy is observed, that is adaptive enlargement of the vessel, whereas within 1–6 months the vessel begins to "shrink", i.e. to reduce its volume. Only in a fraction of patients does the late pathologic remodelling appear, which seems a continuation of the early, positive hypertrophy. Daoud et al.[10] suggested that aneurysm formation is the consequence of transformation of kinetic energy to potential energy under the influence of enlarging atherosclerotic changes in the vascular wall, and changes in the wall structure triggered by the procedure. On the other hand, Holmes et al.,[21] followed by Berkoff and Rowe,[12] concluded that a thin, degenerated media, adjacent to the atherosclerotic plaque located in the intima, is responsible for the lesions, because under the influence of tone and pressure changes during the procedure it may lead to plaque rupture and formation of erosion at this site. This damaged atherosclerotic plaque becomes a potential site of aneurysm formation (locus minoris resistentiae). The concept of pathological media and damaged intima of the blood vessel in the neighbourhood of the lumen-decreasing in atherosclerotic plaque, complicated by ulcerations and thrombotic lesions, and increasing the risk of aneurysm formation, was confirmed by Befeler et al.[1] This observation was supported by Walford et al.[22], who in addition linked the development of aneurysms after angioplasty with blood vessel dissections formed during the procedure. When analysing available data, it has been concluded that the disproportionately matched (too large) balloon catheter is a factor predisposing to aneurysm formation at the revascularisation site.[3] This correlation was also recorded by Bal et al.[23], who confirmed the presence of aneurysms in 9% of patients that had had dissection, in comparison with 2.9% of patients with uncomplicated revascularisation procedure. Stent implantation at the dissection site maintains the vessel patency, but does not cover the whole length of wall dissection, and predisposes to aneurysm formation at the stent ends. Moreover, the very structure of the stent may the intima and the muscular layer leading to their atrophic changes, and thereby decreasing the elasticity (strength) of the blood vessel, which becomes more susceptible to further lumen expansion under the influence of pressures in the vessel. Introduction of drug eluting stents (DES) to prevent endothelial hyperplasia, entailed a potential risk of concomitant, negative influence of the remaining vascular

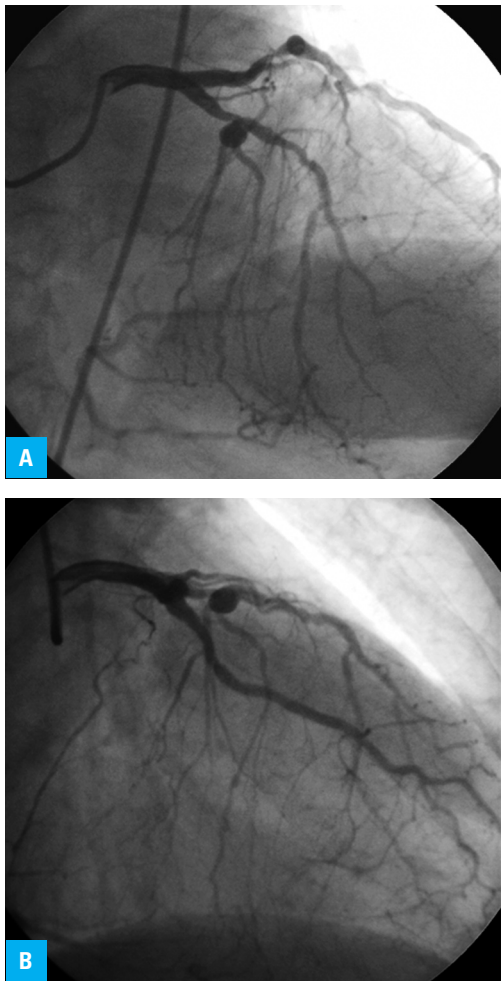

FIGURE 2 Coronary aneurysms located in the left coronary artery
A View RAO 5°, CRAN 35°
B View RAO 25°, CRAN 30°

structures.[24,25] However, the tests carried out, especially the result of intracoronary ultrasonography, dissipated this concern – in the study by Degertekin et al.[25] aneurysmal artery dilation was observed only in one patient at the site of DES implantation. It was expected that the introduction of the most modern percutaneous treatments of stenotic coronary arteries, i.e. atherectomy, cutting balloons, brachytherapy, and laser procedures, would limit the incidence of aneurysms as post-procedural complications. However, these techniques are not complication-free, because early and late formations of aneurysms at the revascularization site have been observed.[3,26-31] Their incidence following directional atherectomy is 10%[3,27], and in the case of laser-based procedures – 0.3%[30]. Aneurysm formation is likely related, as in the remainder, to periprocedural injury to the intima.

However, mechanisms of their formation differ, namely, early aneurysms after atherectomy develop due to formation of "pseudoaneurysms", whereas late formation of aneurysms results from injury to the intima and media of the blood vessel.[20]

Of note, all authors agree that pathology of the media of a blood vessel, which may be secondary to its extension by the atherosclerotic process and by percutaneous revascularization procedure, plays an important role in aneurysm development, regardless of its pathogenesis.

Clinical symptoms All investigators who study coronary aneurysms fail to identify typical clinical symptoms that could be associated with their occurrence.[1,3-8,32] Zoneraich et al.[33] were the only that observed a diastolic murmur associated with a large left circumflex artery aneurysm.

Because over 50% of patients have advanced coronary atherosclerosis, the predominant symptom in their clinical presentation is stenocardia associated with ischemic heart disease of various severity (from stable angina to myocardial infarction).

While analyzing the results of the CASS study, the investigators sought to identify the factors that predisposed to development of coronary aneurysms. In effect, they found a correlation with abdominal aorta aneurysms and arterial hypertension, and excluded a significant influence of coronary risk factors or left ventricular dysfunction. Importantly, Barcley et al.[34] emphasized common coexistence of abdominal aorta and coronary aneurysms. Therefore, in patients undergoing surgery due to aortic aneurysm, especially while reporting chest pain, urgent cardiac examinations should be performed. In contrast, Aintablian and Hamby[35] concluded that neither arterial hypertension, nor diabetes mellitus, dyslipidemia and a positive family history are associated with an increased risk of aneurysm formation.

Certainly, coexistence of Kawasaki disease, or connective tissue disorders with chest pain, even in young subjects, should direct further investigation.

It should be remembered that coronary aneurysm can result in thrombus formation within the aneurysms and peripheral embolization, vasospasm sometimes leading even to myocardial infarction, and also rupture of a weakened wall. Daoud et al.[10] during autopsy discovered thrombi in 70% of the examined aneurysms. Myler et al.[32] reported a coronary angiographic case, where in addition to aneurysm they observed thrombus formation within the aneurysm. An interesting analysis of the group of patients was presented by Rath et al.[36], who distinguished patients with aneurysms, but without obstructive lesions within the coronary arteries, who had a follow-up angiography because of aggravating symptoms of coronary heart disease. In all patients a total artery occlusion distal from the aneurysm was demonstrated. A similar observation was made by Anabtawi et al.[37], who discovered thrombi within the aneurysms during coronary by-pass surgery.

Subsequent investigators – Befeler et al.[1], observed segmental left ventricular contractility disorders, even though during coronary angiography no coronary artery stenosis was demonstrated. This was accounted by a potential for distal embolization with the material originating from a thrombus inside the aneurysm. It should be emphasised that the very presence of an aneurysm causes disorders in laminar blood flow

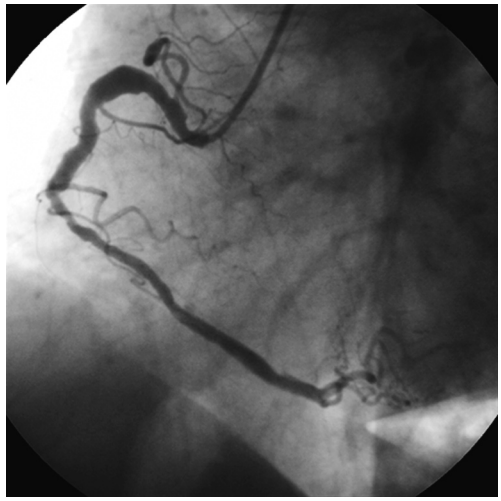

FIGURE 3 Coronary aneurysms located in the left descending artery and dilation of blood vessel lumen of the left circumflex artery

within the vessel, impairing its filling and decreasing perfusion of peripheral segments of the vessel, as documented by Swanton et al.[38]

Diagnosis A "gold standard" in diagnosis of a coronary aneurysm still remains coronary angiography, which apart from establishing this diagnosis provides additional information about size, shape, location and the number of existing anomalies, and moreover provides an image of the coronary artery status. Non-invasive tests that can be helpful in establishing a diagnosis of an aneurysm include the bidimensional transthoracic echocardiography and transesophageal echocardiography. Unfortunately, these methods allow to investigate solely proximal segments of the coronary arteries.

Out of advanced imaging techniques Pucillo et al.[39] employed the magnetic resonance to visualize this vascular pathology. Undoubtedly, it is also possible to use the remaining diagnostic methods such as the multi-slice computed tomography, or the electron beam computed tomography. However, because of the relatively high price of these devices, they are not yet used in the everyday practice.

Treatment Despite an increasing recent interest in the issue of coronary aneurysms, there are still no uniform guidelines for therapeutic management.[3,4,32] Little chance of gathering an adequately large group of patients and a wide range of their clinical characteristics constitutes a significant obstacle in performing objective clinical studies. The results published recently have been based mostly on personal experience of the investigators, and not on controlled studies. However, management in patients with diagnosed most frequent atherosclerotic aneurysms comes down to a choice of management options, depending on morphological conditions of the coronary arteries.

Undoubtedly, because of an increased thrombotic risk in patients with aneurysmal arteries, anticoagulant treatment should be definitely used. Because neither class of drugs (antiplatelet or coumarin derivatives) has been shown superior so far, they are recommended on an individual basis, depending on morphology of the coronary arteries and concomitant diseases. It should be however remembered that nitrates, commonly used in ischemic heart disease, can produce the so-called steal syndrome, and exacerbate stenocardia.

Because pharmacotherapy may prevent only potential complications of the aneurysm, researchers focused on search for methods of the aneurysm removal. At present, a method of choice is angioplasty with implantation of a special stent-graft type stent, or coronary artery by-pass graft (CABG) with concomitant aneurysm resection.

A question certainly ensues which of these methods is more favorable. Reports emphasize unquestionable benefits of the CABG treatment in Kawasaki disease. Nevertheless it seems that, since the results of clinical observation of patients with coronary aneurysms after cardiosurgical treatment do not differ from results of conservative treatment, this therapeutic approach should be reserved for patients at risk of this vascular pathology rupture. In the remaining patients, indications for surgical treatment are identical to these in the case of coronary heart disease.[32] However, taking into account the great burden associated with cardiac surgery, less invasive methods of treatment of this pathology have been sought.

Invasive cardiology undoubtedly provides such possibilities. It seems that the stents with a polytetrafluoroethylene membrane, so-called stent-grafts, have found a greatest range of applications.[40] These stents consist of 2 parts and a synthetic membrane mounted between them, which not only close aneurysm entry, but also reduce the likelihood of microembolism with morphotic elements of the thrombus from its cavity. Some centres also use implantation of a venous graft mounted on a stent, a so-called spring coil. The latter methods are more complicated, and their effect to a significant degree depends on the very extensive experience of the operator. Nevertheless, regardless of the invasive treatment method used, in every patient it is necessary to use a prolonged (a minimum of 6 months) antiplatelet therapy.

CONCLUSIONS Atherosclerosis is the most common basis of formation of coronary aneurysm. Unfortunately, the lack of specific prodromal symptoms or factors predisposing to their formation significantly limits the diagnostic possibilities, and in consequence therapeutic modalities. The majority of patients reporting for coronary angiography suffer from advanced coronary atherosclerosis, with the resultant need for the revascularization procedure. Unfortunately, in some cases the procedure aimed at dilating the stenotic coronary artery and freeing the patient from their complaints, stimulates the formation of a new

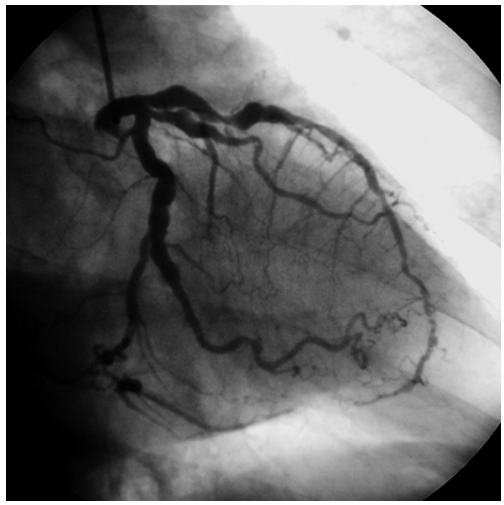

FIGURE 4 Angiogram showing aneurysmal segments separated by lumen stenoses in the left anterior descending artery

vascular pathology. At the same time, one should remember about the specificity of this group of patients – thrombus forming within the aneurysm increases the likelihood of embolization in the coronary microcirculation, and therefore these patients require more aggressive anticoagulant therapy once the diagnosis has been made.

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