Thoracic Aortic Aneurysm: Genetic and Image Evaluation for Elective Surgeries

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Abstract

Evidence shows that genetic variations in a single gene called gene mutations predispose individuals to aneurysms and dissections of the aorta and its branches. With the identification of these mutations, guidelines suggest that diagnosis management is the ideal time for surgical correction and the identification of individuals at high risk of rupture or dissection and their families. These mutations may be present in a syndromic way with simple phenotypic identification or family presentation. In individuals without phenotypic characteristics, familial occurrence of genetic mutation should be investigated through the family history, imaging scans and through genetic markers.

Keywords: Aortic aneurysm, thoracic; Aorta; Marfan syndrome; Loeys-Dietz syndrome

Introduction

In adult individuals, the diameter of the aorta does not exceed 40 mm and it gradually decreases as it sends its branches towards the abdomen. It can vary from individual to individual and it is influenced by body surface area, age, blood pressure and sex. Its expansion rate is approximately 0.9 mm in men and 0.7 mm in women per decade of life.

Approximately 10:100,000 individuals in the United States develop thoracic aortic aneurysms each year, of which 95.0% are asymptomatic or mildly symptomatic until an acute event occurs — rupture or dissection — thus changing the survival of individuals.

Rupture and dissection are more frequent in the ascending aorta when the vessel diameter >60 mm, affecting 31.0% of patients, while 43.0% when the descending aorta is >70 mm.

Echocardiography studies show that when the ascending aortic diameter is 60 mm there is a severe reduction of its distensibility, making it a “stiff pipe”, making the vessel to be highly susceptible to rupture.

Elective surgical treatment of the thoracic aorta is highly recommended to the detriment of emergency treatment, with five-year survival after elective surgery of 85.0%; in emergency operations, survival in the same period is 37.0%.

Evidence shows that genetic variations in a single gene predispose individuals to aneurysms and dissections of the aorta and its branches. With the identification of these simple genetic mutations, new guidelines suggest that diagnosis management is the ideal time for the surgery and the identification of individuals at high risk of rupture and their respective families.
Genetic mutations may be syndromic, with phenotypic identification, in which individuals have physical characteristics that suggest the diagnosis or they may be of a familial nature and, in such cases, the familial occurrence of genetic mutation must be deepened through family history, imaging scans and, recently, genetic markers.

The best known genetic mutation is the Marfan syndrome, of a dominant autosomal characteristic, a mutation of the FBN-1 gene. This gene is responsible for the production of fibrillin-1 protein, which is a component of the microfibrils that make up the fibrous skeleton of the heart and the elastic tissue of the tunica media of the thoracic aorta.

Individuals with this genetic mutation present ocular, skeletal and cardiovascular abnormalities. Among the connective tissue diseases, it seems that ectopia lentis is a remarkable characteristic of the Marfan syndrome. Cardiovascular complications are related to aneurysms and/or aortic dissections, specifically with involvement of the aortic root, which may or may not be associated with aortic insufficiency. Patients rarely present intracranial aneurysms.

Imaging diagnosis of aneurysms and their complications is done by transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE), computed tomography angiography (CTA) or magnetic resonance angiography (MRA) of the thoracic aorta. Sensitivity and specificity vary according to the anatomical location. TTE and TEE can also detect mitral insufficiency usually by expanding the fibrous skeleton of the heart.

Resection of the ascending segment of the aorta is recommended when the vessel diameter reaches 50 mm in uncomplicated cases and 45 mm in those who have severe aortic regurgitation, family history of sudden death or women wishing to become pregnant. In the descending aorta, surgical treatment is indicated when the diameter reaches 60 mm.

In 1995, the Loyes-Dietz syndrome was found. It is associated with the mutation of genes TGFBR1 and TGFBR2, of a dominant autosomal character, leading to the loss of function of the TGF-ß (transforming growth factor ß) signaling activity in the function of the smooth muscle cells. Especially when it comes the TGFBR2 mutation, some authors recommend surgery of the ascending aorta with minimal dilations — around 40-42 mm in adults — due to the high risk of dissection and rupture. The syndrome is characterized by craniosynostosis, bifid uvula, palate opening, hypertelorism, translucent skin, tortuosity of other vessels, however, aneurysms and dissections may affect the thoracic aorta and other vessels, including intracranial vessels.

Also in the category of family disease, mutation of the SMAD3 gene — called aneurysm-osteoarthritis syndrome of dominant autosomal character — was detected. It affects different vessels in addition to the thoracic aorta: the abdominal segment and iliac arteries in addition to the intracranial branches that may present aneurysms, having osteoarthritis as an early symptom. Until then, there is no definition of the diameter of the aorta to indicate surgical treatment. Patients with this syndrome should undergo imaging tests for the entire vascular bed, including the intracranial one.

Also recently, another mutation described involves the gene TGFBR2 in patients with the Marfan syndrome, associated with the thoracic aorta disease and intracranial aneurysm. The relatives of such patients should be investigated with imaging scans of the thoracic aorta and its branches.

Aside from patients with the Marfan syndrome, where there is an anomaly in the synthesis of the fibrillin-1 protein, mutations of TGFBR1, TGFBR2, TGFBR2 and SMAD seem to involve the TGF ß thus interfering with the decoding of the 8-2 transforming growth factor (TGF-ß2) involved in the proliferation and maintenance of the contractile function of smooth muscle cells of the tunica media of the aorta.

Mutation of the gene ACTA2 also has a family character and accounts for 10.0-14.0% of thoracic aortic aneurysms. It is also related to the contractile function of the smooth muscle cell. In this case, there is a variation of associations such as the presence of dissection of the descending aorta in young men, premature obstructive coronary artery disease, stroke (Moyamoya disease), patent ductus arteriosus and bicuspid aortic valve.

Mutations of the genes ACTA2 and MYH11 are associated with the function of contractile proteins of the smooth muscle cells existing in the tunica media of the aorta with a common pathway in the pathophysiological process involving the TGF ß.

The bicuspid aortic valve (BAV), a common congenital malformation, with a prevalence of 1.0-2.0% in the
general population, results in the fusion of the valve leaflets during embryonic valvulogenesis. It is associated with coarctation of the aorta, spontaneous dissection of the carotid arteries, aneurysms of the ascending aorta and aortic dissection. The fragility of the wall of the ascending aorta seems to be associated with morphological variation of the aortic valve and even individuals with normally functioning BAV may have involvement of the tubular portion of the ascending aorta. From the histopathological and molecular point of view, greater degeneration of the tunica media of the ascending aorta and the pulmonary artery has been demonstrated, involving fibrillin-1 deficiency.

Potential Conflicts of Interest
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Point of View
The opinions expressed in this manuscript are solely those of the authors. The International Journal of Cardiovascular Sciences welcomes different points of view in order to stimulate discussions to improve the diagnosis and treatment of patients.

References