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The ascending aortic aneurysm: When to intervene?

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ABSTRACT

Background: Thoracic ascending aorta aneurysms (TAA) are an important cause of mortality in adults but are a relatively less studied subject compared to abdominal aortic aneurysms (AAA). The purpose of this review is to explain the main aspects (etiology, pathophysiology, diagnosis) of this disease and to summarize the most recent developments in its management.
Methodology: Literature was obtained through online health related search engines (PubMed, MEDLINE) by including the following keywords: ascending aorta aneurysm, thoracic aneurysms, Marfan syndrome, bicuspid aortic valve, familial thoracic syndrome, aortic dissection, aorta imaging and aortic aneurysm guidelines. We included articles dating from 1980 to 2014.
Findings: Literature revealed how lethal this disease can be and how simple steps such as follow-up and prophylactic surgery can significantly reduce morbidity and mortality. This review also allowed us to realize the many developments that have been made in recent years in the understanding of pathologic mechanisms of this disease.
Conclusion: TAA is a silent disease that needs to be recognized early in its course and followed closely in order to recommend appropriate preventive and prophylactic therapy in a timely manner.

1. Introduction

The dilation of the ascending aorta is a common incidental finding on transthoracic echocardiography performed for unrelated indications. While the potential complications of aortic rupture and dissection are well recognized, most physicians are trained for the treatment of heart and coronary artery diseases, with limited knowledge and experience in the optimal management of patients with a dilated ascending aorta. The purpose of this article is to review the current understanding of the etiology, diagnosis, medical management and timing of surgical intervention in the patient with a dilated ascending aorta or ascending thoracic aortic aneurysm (TAA).

1.1. Anatomy

The aorta is divided into two main segments: thoracic and abdominal. The thoracic aorta is further divided into 3 parts: ascending, arch and descending. The ascending aorta originates beyond the aortic valve and ends right before the innominate artery (brachiocephalic trunc). It is approximately 5 cm long and is composed of two distinct segments. The lower segment, known as the aortic root, encompasses the sinuses of Valsalva and sinotubular junction (STJ). The upper segment, known as the tubular ascending aorta, begins at the STJ and extends to the aortic arch (innominate artery). More than 50% of TAA are localized to the ascending aorta, which may affect either the aortic root or tubular aortic segment [1].

1.2. Definition of aortic aneurysm

Published data on arteries diameter in healthy population are often scant or variable because of different imaging modalities used for measurement. Nevertheless, by common convention, aortic dilatation refers to a dimension that is greater than the 95th percentile for the normal person age, sex and body size. In contrast, an aneurysm is defined as a localized dilation of the aorta that is more than 50% of predicted (ratio of observed to expected diameter ≥ 1.5). Aneurysm should be distinguished from ectasia, which represents a diffuse dilation of the aorta less than 50% of normal aorta diameter.

An official cutoff for the definition of aortic dilatation has not been determined because of the variability of this measure, but most experts agree that ascending aorta size should be correlated to size and gender. In addition, some authors suggest using the aortic size index [2] which takes into account the body surface area, thus

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minimizing classification of normal aorta as pathologically dilated and vice versa.

1.3. Epidemiology

Thoracic aortic aneurysms (TAA) and its associated complications are life threatening clinical entities that rank in the top 20 leading causes of mortality in the United States (15th leading cause of death in people over 65 years old) (*CDC*, http://webapp.cdc.gov/cgi-bin/broker.exe). Unfortunately, the mortality rate of patients presenting with complications of TAA has remained relatively stable in the last two decades, in contrast to the improved survival observed in patients presenting with complications of coronary artery disease (CAD). As Clouse et al. pointed out, the prognosis of patients with TAA is indeed improved if they are treated before complications occur [3].

The incidence of TAA has been reported to be only 5.9 cases per 100,000 person-years in the early 1980s, however recent advances in imaging modalities, aging of the population, increased use of transthoracic echocardiography and routine screening have resulted in a twofold increase in the incidence [4]. According to the CDC, the incidence of ascending TAA is estimated to be around 10 per 100,000 person-years. Women and men have similar incidences of thoracic aortic aneurysm but the age at diagnosis is a decade higher in women (70s) than in men (60s).

1.4. Pathophysiology

The aorta is an elastic vessel composed of three main layers: the tunica intima, the tunica media and the tunica adventitia. The internal elastic lamina separates the intima from the media.

Elastic fiber in the medial layer of the aorta allows continuous forward flow during the whole cardiac cycle. During systole, expansion of the aorta allows kinetic energy from left ventricular contraction to be stored as potential energy in the aortic wall. In diastole, recoil of the aorta transforms the stored potential energy back to kinetic energy, propelling the blood distally into the arterial bed. With aging, there is fragmentation of elastic fiber, smooth muscle dropout and replacement by amorphous material (known as cystic medial degeneration), which leads to increased stiffness and weakening of the aortic wall which predisposes to dilatation of the ascending aorta. In addition, according to Laplace's law, the dilation of the aorta increases wall tension, triggering vascular wall remodeling and even further aortic dilatation.

Recent developments have helped better explain the cellular changes that lead to aneurysmal ascending aortas. The different conditions that cause TAAs either affect structural components of the aortic wall or alter the intracellular signaling cascade that maintains vascular wall integrity. The main culprit in this disease seems to be the *TGF-B1* signaling mechanism that is responsible for activating matrix degradation through increased production of plasminogen activators and release of matrix metalloproteinases [5].

For example, mutations in ACTA2 alter the function of smooth muscle cell actin and are responsible for 14% of inherited TAAs [6]. In addition, the MYH11 gene affects the C-terminal coiled-coil region of the smooth muscle myosin heavy chain, a specific contractile protein of smooth muscle cells [7] and increases TAA formation.

Other mutations can affect both the structure and the metabolic homeostasis of the vascular wall. For instance, the mutation of fibrillin 1 in Marfan syndrome weakens the vascular wall given that it is a reinforcing structure [8] and it also alters the regulation of the bioavailability of TGFB1 [9].

Other mutations affect the TGF-B signaling pathway directly by affecting the TGF-B receptors such as in Loeys–Dietz syndrome [10]. Other mutations alter the regulatory mechanisms that inhibit the activity of the TGF-B pathway such as the mutation of GLUT10, a glucose transporter whose deficiency is associated with arterial tortuosity syndrome [11] or the mutation of the SMAD3 gene that encodes a protein necessary for the signaling downstream of the TGF-B pathway [12].

Many other structural anomalies and metabolic alterations have also been implicated in the pathogenesis of TAAs but will not be extensively reviewed in this article.

1.5. Etiologies

The process of cystic medial degeneration can be either due to an innate defect or an acquired one. As can be seen in Table 1, ascending TAA is frequently seen with connective tissue diseases such as Marfan syndrome, Ehlers–Danlos syndrome, or familial aneurysms syndrome [13]. Data suggests that this process can also occur in congenital disease such as tetralogy of Fallot [14] and bicuspid aortic valve (BAV). Hypertension and smoking appear to accelerate the process by increasing elastolytic enzymes in the aortic medial layer [13]. Atherosclerosis has long been considered as a second cause of aortic aneurysm formation, with atheromatous plaques destroying small muscle cells and elastic fiber architectures, resulting in weakening of the aortic wall. However, this concept has recently been challenged; and it is now thought that atherosclerosis is not a primary cause, but a concomitant process in the diseased medial layer of the aortic wall [13].

Other less common etiologies can contribute to TAA formation. These include post-traumatic aortic transection, aortic cannulation post-CABG surgery, chronic aortic dissection, bacterial or syphilitic infection and vasculitic aortitis. These uncommon etiologies are not discussed in this review.

1.6. Risk factors

Different studies have shown that the ascending aorta diameter significantly correlates with age, waist circumference, smoking history and hypertension; the latter being the most prevalent risk factor for acute aortic dissection [15]. In a recent study, mean carotid intimal media thickness as well as epicardial adipose tissue were associated with ascending aorta dilatation [16]. In a study examining 833 autopsy cases, six risk factors (age, sex, body height, smoking history, hypertension and severe atherosclerosis) have been associated with ascending aorta dilations with age being the most important predictor of dilatation [17].

2. Diagnosis

2.1. Presentation

Dilatation of the ascending aorta is a very indolent process as it takes many years to develop and it is asymptomatic initially. In patients who develop an ascending aortic aneurysm secondarily to a systemic disorder, signs of the primary disease are the ones who lead the clinician to look for the dilatation such as in Marfan syndrome. Otherwise, this pathology remains quiet until its catastrophic complications occur or when it is incidentally seen on cardiovascular imaging related to other causes. We can prevent these complications by screening asymptomatic patients. Feared events include aortic dissection or rupture, pericardial hemorrhage, cardiac tamponade and occlusion of aortic branches. In addition, some patients, in a lesser proportion, can also develop intramural hematomas or penetrating aortic ulcers.

As shown in Tables 2.1 and 2.2, these complications do not manifest at the same age or at the same ascending aortic size. They are greatly dependent on the predisposing condition and, as discussed later, on the management of this disease.