



# Morphology of the human aorta and age-related changes: anatomical facts

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**Abstract:** Aorta is the largest artery in the human body. Its starting point is the aortic orifice of the aortic valve and it terminates at the level of the fourth lumbar vertebra. The main function of the aorta is to transport oxygenated blood to supply all the organs and cells. With advancing age, the structure and hence the function show progressive changes. Various changes in the aortic morphology include the luminal diameter of aorta, whole length of the aorta, thickness, the microstructural components also change, and these include collagen, elastin and smooth muscle cells. In addition, the dimensions of all segments of the aorta increase with age in both sexes. Since age is a major risk factor for degenerative change and diseases affecting the aorta, understanding the detailed anatomy of the aorta may provide essential information concerning the age-associated process of the aorta. Knowledge of the morphological changes in the aorta is also important for future clinical therapies pertaining to aortic disease. Additionally, the information regarding the structural changes with age may be applied for age determination. This review describes the overview of the anatomy of the aorta, age related changes in the morphology of the aorta and aortic diseases.

**Key words:** Aorta, Thoracic aorta, Abdominal aorta, Age change

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## Introduction

Aging is a complicated process which influences general functions and structure of an organ, resulting in progressive changes in organ dysfunction [1, 2]. Age is a well-known major risk factor for various disorders, especially in cardiovascular diseases (CVD). CVD are increasing worldwide [1, 3]. The prevalence of CVD increases with age and usually affects the older age group [4]. Consequently, it implies that these age-associated changes contribute to the cardiovascular dysfunction and lead to clinical disorders. In the cardiovascular

system, the main age-related change structures are within the heart, heart valves, and the vascular system. In vascular system of the human body, the aorta is the largest artery and it is a type of elastic artery. It originates from the left ventricle at the level of the aortic valve of the heart and ends at the level of bifurcation of the common iliac arteries. The main function of the aorta is to conduct oxygenated blood from the heart throughout the whole of body. Generally, the aorta is divided into three main sections defined by their location i.e., the ascending aorta, arch of the aorta, and the descending aorta. The descending aorta is divided into the thoracic aorta and abdominal aorta. At microscopic level, the arterial wall composes of three distinct layers which named the tunica intima, tunica media, and tunica adventitia from the inner surface to an outer layer. The changes of the human aorta with age usually occur involving the structural and function properties of the wall. Many studies into age-dependent changes in the

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aorta have been done and it was found that the impact can be on the diameter, length, and thickness including the tissue composition within the aortic wall. These studies found that the lumen diameters enlarged progressively with age [5, 6]. As regards the thickness of the aortic wall, there are age-associated structural changes in the tunica intima and media. Studies have shown that these two layers had gradually increased with age [7-10]. Histology of the aortic wall also changed with aging. Collagen, elastin, and smooth muscle cells are the major tissues in the arterial wall. The composition of these tissues had changed in both quantity and their organization in each tunica of the aortic wall [11]. The enlargement and elongation and stiffness of the arterial wall cause increased blood pressure [12]. In this review, we describe the anatomy of the aorta, age-associated changes in the aorta including diseases affecting the human aorta.

## The Anatomy of the Aorta

The aorta is the largest vessel in the body. The main function is to transport the oxygen-rich blood from the heart to the various organs in the body. The aorta arises from the left ventricle of the heart extending upwards into the chest becoming the arch of the aorta and then downwards into the abdomen and it branches into the common iliac arteries superior to the pelvis. The aortic root is the part of the aorta which is attached to the heart. The aortic valve is the major portion of the aortic root that allows blood to flow from the heart to the whole body when it is open. In addition, the aortic valve prevents back flow of blood into the heart when it is closed. The blood supply to the cardiac tissue which makes up the majority of the heart itself, the left and right coronary artery, are branches off the aortic root providing oxygenated blood to the tissue. The length of the ascending aorta is approximately 5 cm. It begins at the upper part of the base of the left ventricle that is on a level of the inferior border of the 3rd costal cartilage behind the left side of the sternum. The ascending aorta passes obliquely upward, forward, and to the direction of the heart axis that is the same level of the second right costal cartilage. It is located behind the posterior surface of the sternum until it becomes the aortic arch. The aortic arch begins at the level of the upper border of the second sternocostal articulation on the right side. At first, it runs upwards, backwards, and to the left passing in front of the trachea. Then, it is directed backwards on the left side of the trachea and passes downwards on the left side of the body to

the T4 vertebra at the lower border when it becomes continuous with the descending aorta. The upper border of the aortic arch is approximately 2.5 cm below the manubrium [13, 14]. There are several branches arising from the aortic arch. They are the left carotid artery, the left subclavian artery, and the brachiocephalic artery. The left carotid artery supplies blood flow to the brain at left side and the left subclavian artery supplies blood to the upper extremity at left side. The blood supply to the right upper extremity including the right side of the brain comes from the brachiocephalic artery. The aortic arch continues to descend into the thorax and becomes the descending aorta. This vessel is divided to two parts which are thoracic and abdominal aorta. The first is the thoracic aorta, it is situated in the posterior mediastinal region that begins on the left side of inferior border of the T4 vertebra and then descends on the left side of the T5-T12 vertebra in the thorax. Finally, it terminates at the level of aortic hiatus in the diaphragm which is the point of separation between the chest cavity and the abdominal cavity. At this point, it is located on the left side of the vertebral column and supply blood flow to muscles of the thoracic wall and the spinal cord. The continuation of the thoracic aorta is the abdominal aorta which enters into the abdominal region through the aortic hiatus which is in front of the inferior border of the T12 vertebral body. Then, it descends anterior to the vertebral column and terminates at the level of the L4 vertebral body. Finally, the abdominal aorta separates into the right and left common iliac arteries which situate superior to the pelvis. There are paired visceral branches: suprarenal arteries, renal arteries, and gonadal arteries (ovarian or testicular). Then, there are arteries that are unpaired parietal branches from this aorta which include the median sacral artery and the paired parietal which are subcostal arteries, inferior phrenic arteries, and lumbar arteries. The termination of the abdominal aorta then bifurcates to form the common iliac arteries which carry blood to supply the lower extremities and the various pelvic structures [13, 14].

There are three main types of arterial vascular system. The first type is elastic arteries which include the aorta, common carotid artery, brachiocephalic trunk, pulmonary arteries, and subclavian artery. The second type is the distributing branch known as the muscular arteries as radial, femoral, coronary, and cerebral arteries, etc. The third type are the arterioles which are the terminal branches of the vessels [15]. The aorta is a type of elastic artery and the largest vessel in the body. The arterial walls of the circulatory system generally

are composed of three layers but the layers vary depending on the type of artery. There are three layers to the aortic wall, the tunica intima, tunica media, and tunica adventitia. First, the tunica adventitia is located on the outermost of the aortic wall includes collagen fibres, some elastic fibres, fibroblasts and mast cells. The connective tissue contains vasa vasorum which are small vessels which supply blood to the aortic wall. In the middle layer, the tunica media, there are many elastic fibres, and this is the thickest layer. This layer composes of smooth muscle cells, collagen fibres type I and III, and many elastic fibres. The elastic fibres are arranged in concentric layers called elastic lamellae. There is also an external elastic lamina which separates layers of tunica media and tunica adventitia. And the innermost layer is the tunica intima. This layer is thin and is composed of a single layer of endothelial cells. The subendothelial cells contain loose connective tissue and a few fibroblasts. In addition, there are other cells which have features similar to smooth muscle cells. These are known as myointimal cells. The myointimal cells accumulate lipids and increase the thickness of the layer when age increases. There is an internal elastic lamina which divides the tunica intima and tunica media layers [15-17].

### Age-Associated Changes in the Morphology of the Human Aorta

Vascular aging changes gradually from infancy but changes become more significant in middle age then deteriorate with aging [18]. These changes affect the thickness of each layer of wall and the lumen size of the aorta. Da Silva et al. [19] studied the infrarenal aorta in 645 cadavers. They suggested that infrarenal aortic diameter was related to age. There was a direct relation between the level of sclerosis of the wall and diameter of the aortic lumen. Sawabe et al. [20] studied 833 autopsies with an age range of 2–94 years. They measured the internal circumference of each part of the aorta by using a hard scale and they carried out an assessment of atherosclerosis. They found a correlation between aortic circumference and age which was highest in the descending aorta and an increase in the diameter of the descending aorta which was related to an increase in the severity of atherosclerosis. The aortic wall components consist of collagen fibres, elastic fibres, and smooth muscle cells. Calcification was found in the wall and those physical changes in the aortic wall are the result of various pathological conditions including CVD such as atherosclerosis which is a common disease associated

with age [10, 21]. Movat et al. [22] studied 92 human aortas by necropsy. They investigated the qualitative structure and development of the intimal thickening of the human aorta. They found that the differences of the thickness in the tunica intima were associated with age and location within the aorta. Thickness of the tunica intima and the composition of the atrial wall gradually changed from the fetus to old age. In the first to fourth decades, differences were found in the thickness in the tunica intima between the proximal and distal part of the aorta. The intima of the distal part was thicker than the proximal part of the aorta. Schlatmann and Becker [23] studied qualitative histological changes in relation to age in the tunica media of 100 normal aortas. They described histological features such as elastin fragmentation and fibrosis. It was found that these changes showed a correlation with age. Elastin fragmentation decreased with aging and fibrosis increased with increasing age. In the middle-aged and aged cadavers, the degeneration of the elastic fibres was in the media, internal and external elastic laminae. Maurel et al. [24] studied the distribution of morphological appearance related-to age changes in different segments of the aorta in cadavers aged less than 50 years (20–48) and aged more than 50 years. The results showed that the aorta in those aged less than 50 years had a number of elastic fibres with less ground substance. There were decreased numbers of elastic fibres and the space between the elastic lamella was wider. With advancement of age, the tunica intima was found to be thickened with what was damage of internal elastic fibres. Degradation of elastic lamellae was found in the tunica media and elastic fibres were irregularly arranged and fragmented. Yamada et al. (2015) [25] studied the normal human ascending aorta from autopsy of people 56 and 86 years old. It was found that the collagen content tends to increase with age ( $r=0.72$ ,  $P=0.020$ ). Moreover, Alex and Amma [26] studied 55 human ascending aorta by autopsy in the fetus to 80 years of age. They investigated the tunica media thickening and grades of elastic fragmentation. They found that the percentage thickness of the tunica media was highest in the age range 30–40 years ( $72.4\pm 22\%$ ) and decreased after 40 years. It was found that the elastic lamina in the tunica media increased up to the age of 20 years and remained the same until 50 years. This study review provides the morphometric measurement of the aorta with a view from above in Fig. 1.

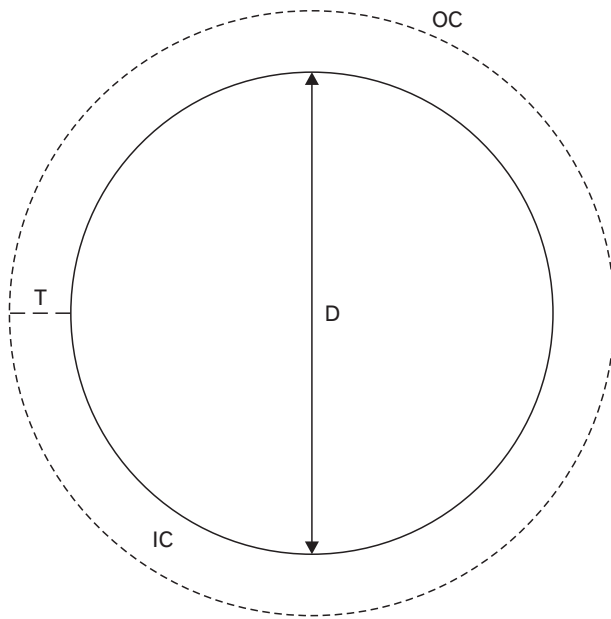


Fig. 1. Sketch demonstrating the morphometric measurement of the aorta in view from above. T, thickness; D, diameter; OC, outer circumference (dashed line); IC, inner circumference.

## Atherosclerosis

Atherosclerosis is the most common cause of mortality worldwide and it is usually related to other CVD such as coronary heart disease [27]. The pathological process of atherosclerosis in arteries is characterized by an accumulation of plaque in the intima layer. The plaque consists of fats, cholesterol, matrix fibres, cells, and tissue debris. The clinical outcomes of this process lead to thrombosis, lumen obstruction, haemorrhage, and embolization [28, 29]. The various theories regarding the process of atherosclerosis have been widely reported and the most accepted to date is that it is a response to injury of the endothelium or is an inflammatory response [30]. Hypertension, smoking, mechanical forces and immune reactions may cause changes in the endothelial cells resulting in cell dysfunction [28, 29]. Features of atherosclerosis can be observed using various methods such as gross examination, histological examination, chemical analysis, radiological examination, etc. This study focuses on gross and histological changes.

### Gross morphological changes in atherosclerosis

- Stage 1: A fatty streak is defined as yellow area.
- Stage 2: Fibrous plaque is increasing the thickness of tunica intima and obvious lipid accumulation. The plaque pres-

ents as a white to yellow area.

- Stage 3: Complicated lesion form, i.e., lesions which have additional changes such as haemorrhage, thrombosis, ulceration, and calcification [27, 31].

### Histological classification of atherosclerosis

According to The American Heart Association, observation of atherosclerosis plaque is classified into the following 8 types, mainly using composition of the plaque [31, 32]:

- Type I composed of isolated foam cells and macrophages (initial lesion).
- Type II composed of multiple layers of foam cells (fatty streaks).
- Type III composed of isolated extracellular lipid pools without a core of lipid (intermediate lesion/preatheroma).
- Type IV or atheroma lesion contains a large core of extracellular lipid occupying an extensive area. The deposition of extracellular lipid in this type is known as the lipid core and there is no lesion on the surface as seen in a thrombosis.
- Type V composed of a lipid core and thick layers of fibrous tissue in the intima or around it. There is a formation of new fibrous connective tissue which consists of collagen and smooth muscle cells. Sometimes there is calcification in the other parts of the lesion (fibroatheroma).
- Type VI the surface of the plaque has defects like hematoma or haemorrhage, and thrombosis (complicated lesion). It may have occurred as the only lesion or on the surface of all lesions.
- Type VII is prominent calcification.
- Type VIII is prominent fibrous tissue changes.

### Future Direction

Changes in the aorta both macroscopically and microscopically as a result of age are well documented. Nevertheless, there are few studies describing the changes in both gross morphology and histological composition particularly in the normal human aorta. Unfortunately, there are no studies about age-associated changes in the aorta in the Thai population. Hence, we aim to examine the changes in the general morphology and microstructural compositions in the normal human aorta related to aging in our future studies. Recently, there is wide use of computer software such as image analysis tools and artificial intelligence. This is because this software is convenient and is cost-effective and also a non-invasive approach. It may be interesting to measure the morphometric

parameters of the aorta using image analysis software and investigate the relationship between the aortic morphology and age. The difference in aortic diameter, circumference, and the average thickness of the aorta may be measured by using image analyser. As regards histological studies, it will be better to investigate the thickness of the tunica intima and tunica media and also quantify the main components in the aortic wall, specifically collagen, and elastin, including glycosaminoglycans using image analysis and artificial intelligence. The information on the morphology of the human aorta may also be important in the future for the manufacture of prosthetic vessels. In addition, the correlation between age and aortic morphology may be used in age determination from the aorta in Thai or any other population.

## Conclusion

Manifestation of the aging process affecting the aortic structures can be found in the pattern of aortic diameter, aortic circumference, thickness, and the total length of the aorta. The luminal diameters and whole length of the aorta progressively increase with age in both sexes. The thickness of the tunica intima and tunica media in the aortic wall also increase with the advancement of age. This aortic wall thickening may reduce the elasticity of the vessel and is also related to the synthesis of many components within the arterial wall. There is a decrease in the number of elastic fibres and smooth muscle cells in the tunica media and an increase in the amount of collagen fibres as the age increases. Consequently, analysis of the morphology of the aorta and the microstructural composition of the human aorta related to age changes has crucial implications for future clinical treatment in aortic pathology and as an age indicator.

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