

Factors influencing the risk of abdominal aortic aneurysm rupture

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Abstract

Abdominal aortic aneurysm is a relatively common vascular pathology and its rupture is an underestimated cause of death from cardiovascular causes. Determining the risk of rupture is the key clinical problem, translating directly into the choice of proper therapeutic strategy and constitutes an indication for surgical management. In most cases, aneurysm diameter is considered the decisive predictive factor. In light of current research data, it seems necessary to also consider such factors, as demography, medical history and morphology (geometry, the presence of mural thrombus) of the aneurysm. A multitude of factors, both biological and biophysical, poses a great challenge for the researchers. This publication constitutes a concise summary of current literature data on the topic.

Key words: abdominal aortic aneurysm, intraluminal thrombus, aneurysm rupture

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Introduction

Abdominal aortic aneurysm (AAA) is most often defined as dilatation of the aorta up to 3 cm in diameter or more. Apart from its diameter, location of the aneurysm in relation to renal and celiac arteries, as well as to aortic bifurcation is another key aspect of AAA anatomy. Most often, in 80% of cases, AAA is located in the infrarenal part of the aorta [1]. Common iliac artery aneurysms coexist with AAA in about 25% of cases and rarely occur as isolated lesions [2, 3].

The incidence of abdominal aortic aneurysms is estimated at 2–8% among males over 65 years of age, while in a female population it is about four times lower. According to the results of the Aneurysm Detection and Management (ADAM) study, the risk of rupture

in each subsequent year amounts to 9% for aneurysms with a diameter 55–59 mm, 10% for aneurysms with a diameter 60–69 mm, and 33% for aneurysms ≥ 70 mm in diameter. It should be noted that despite less frequent occurrence, the risk of aneurysm rupture is four times larger in females, which is important while qualifying for surgery. In the event of aneurysm rupture, mortality reaches 85–90% [4–6].

Known risk factors for abdominal aortic aneurysm formation include age, sex, smoking, and comorbidities: atherosclerosis, coronary artery disease, hyperlipidemia, hypertension, and chronic obstructive pulmonary disease. Abdominal aortic aneurysms are four times more common in men and their incidence grows with age. Smoking is a powerful risk factor for the development of both atherosclerosis and the aneurysm itself,

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as it sustains the inflammatory reaction and proteolysis, resulting in subsequent weakening of aortic walls. Development of aneurysms is also facilitated by genetic collagen defects in the course of such disorders as Marfan or Ehlers-Danlos syndrome.

Biomechanics

Aneurysm ruptures when tension on the aortic wall exceeds its strength. Maximal diameter of the aneurysm is the main prognostic factor influencing the assessment of rupture risk. It happens sometimes that even small aneurysms rupture while large aneurysms remain stable. Obviously, there are other factors destabilizing vascular wall and influencing the risk of rupture apart from aneurysm diameter.

According to the laws of hydrodynamics and Bernoulli equation, the faster a fluid flows through a pipe, the lower the pressure it exerts on its walls. In a vessel with a variable diameter, in sections of larger diameter, fluid flow slows down and exerts higher pressures on the walls. Such reasoning seems counterintuitive and was referred to as the “hemodynamic paradox”. This phenomenon is crucial to understanding the forces exerted on vascular vessel walls in the course of some diseases. It influences the assessment of vascular wall tension and explains, among other things, the phenomenon of post-stenotic vascular dilatation.

In case of AAA, increase in vessel diameter causes a sudden rise in pressure exerted on its wall compared to the non-dilated region. There is an enormous number of factors potentially influencing aortic wall strength and, besides aortic diameter, encompasses shape, wall thickness, the extent of atherosclerosis, intraluminal thrombus thickness, blood pressure, and many others. Aneurysm geometry, symmetry, tortuous course, or angular bends are of high prognostic value. As demonstrated by 3-D computer analysis of vascular wall stress using a finite element method, aneurysms that are asymmetrical with regard to the long axis of the vessel, vascular stress is significantly higher compared to aneurysms of the same diameter, but symmetrical. Protrusion of the aortic wall on one side causes a significant increase in tension on the opposite wall [7, 8]. Aneurysms of the same diameter may differ significantly with respect to wall stress and resulting risk of rupture depending on the anatomy. Peak aortic wall stress described by mathematical modeling is a good predictor of aneurysm rupture and may be used in case of doubts concerning qualification to intervention [9, 10].

Among patients with an AAA over 55 mm in diameter and in good general condition, qualification to the procedure usually does not rise any doubts. More

problematic are patients with aneurysms that are small in diameter, but with unfavorable anatomy, or elderly patients with multiple comorbidities, for whom vascular surgery poses a particularly high periprocedural risk. In such cases, using mathematical modeling to evaluate aortic wall stress might enable better assessment of indications to intervention and choice of most appropriate treatment.

Development of endovascular techniques revolutionized the approach to the treatment of abdominal aortic aneurysms. Currently, stentgraft implantation is the treatment of choice in the majority of patients. The complex anatomy of an aneurysm encompassing renal and celiac arteries requires the use of elaborate systems that are associated with significant risk of late complications. Another possibility is to use multilayer flow modulators. Instead of directly excluding the aneurysm from circulation, they direct the blood flow to physiological direction. Reduced flow through the aneurysmal sac attenuates aortic wall tension and allows the thrombus to form while preserving patency of the aorta and collaterals. However, it should be noted that multilayer flow modulators are not currently considered a standard technique with proven efficacy and safety profile. Further studies are necessary before they become recognized by scientific societies and included in the guidelines.

Thrombus formation within aneurysmal sac is a natural process and occurs in 70–80% of cases [11]. The role of thrombus in aneurysm progression remains unclear. Available data indicate both positive, as well as, negative effects of thrombi on aneurysm’s stability. Accumulation of morphotic elements of blood, including neutrophils and macrophages, at the site of the thrombus, is associated with the release of inflammatory mediators. It creates an environment favorable to the development of oxidative stress and proteolysis by metalloproteinases with subsequent elastic fiber and smooth muscle cell degradation. It gradually weakens the aortic wall and facilitates aneurysmal progression. Moreover, a thick thrombus causes local hypoxia of the aortic wall, which in turn leads to increased angiogenesis and propagation of inflammatory processes from the outside as well [12–14].

Based on examination of 356 thrombi samples collected from 19 patients at the time of AAA surgery, O’Leary *et al.* [15] demonstrated significant differences in morphology of thrombi and, consequently, their biomechanical properties. They distinguished three types of thrombi: type 1 — multilayer thrombus with thick outer layer, whose strength decreases gradually toward the aortic wall, type 2 — multilayer thrombus with thin outer layer, whose mechanical strength drops abruptly toward the aortic wall, and type 3 —

a homogeneous thrombus of semi-liquid consistency and poor mechanical strength [15].

There were also studies evaluating the effects of intensity of inflammatory reaction on thrombus development and aneurysm progression using positron emission tomography. Sites of increased fludeoxyglucose (18F-FDG) uptake in the aortic wall, indicating augmented inflammatory processes, were observed in regions where thrombus was thick and wall stress was high. These results suggest that the inflammatory process is stimulated by mechanical stress on the vascular wall and correlates with local thrombus thickness [16].

In 2006, a team led by JP Vande Geest developed a statistical model for the assessment of the risk of aneurysm rupture (RPI, rupture potential index). This index compares vascular wall strength against its tension. Wall strength is determined based on thrombus thickness, the diameter of the aneurysm, sex, and family history of aneurysms. Wall tension is evaluated with mathematical modeling using the finite element method [17]. This concept was recently developed by Joldes et al., who created computer software (BioPARR) that allows for individual evaluation of the risk of aneurysm rupture by clinicians. Based on their results it was demonstrated that the presence of thrombus is associated with significantly reduced aortic wall tension. This finding is also corroborated by other publications [18, 19]. The large diameter of the aneurysm is associated with increased wall tension, although it is not a linear dependence and dispersion of the results is quite significant [20].

In their study, Haller et al. [21] showed that larger diameter of the aneurysm correlates with higher vascular wall tension while the presence of a thrombus reduces both peak and mean aortic wall tension, but is associated with higher rupture risk, especially of small aneurysms. These results suggest that the effect of thrombus on aortic wall weakening exceeds the benefit of reduced wall tension and that effect facilitates rupture [21].

Speelman et al. [22] reached the same conclusion in their research. Based on the analysis of computed tomography images of 30 patients, they demonstrated that larger thrombus attenuates aortic wall tension, but remains associated with a quicker progression of aneurysm diameter. In 2005 Sachinder et al. [23] performed a comparison of ruptured and unruptured aneurysms with regard to the size and location of the thrombus. In ruptured aneurysms, the diameter of an aneurysm, as well as thrombus volume, were both larger. There were no significant differences with regard to the ratio of thrombus volume to aneurysm volume between the two groups. Similar findings were reported by Khosla et al. [24], who examined thrombi from 28 patients with ruptured abdominal aortic aneurysms and 56 patients

with a stable aneurysm. There was no association between thrombus volume and aneurysm rupture.

Summary

Based on the available scientific data, it is difficult to draw definite conclusions and formulate guidelines regarding factors influencing the risk of abdominal aortic aneurysm rupture. Complexity of the problem, especially biological and biomechanical aspects of an aneurysm, do not allow for simplification and declaring a clear dependence of the risk of rupture on aneurysm diameter or thrombus size. Although the larger size of an aneurysm is associated with increased vascular wall stress, geometry and shape of the lesion are even more important than the maximal diameter. On one hand, the presence of a thrombus and its thickness exert protective effects by reducing wall stress, but on the other hand, it promotes local inflammation and contributes to vascular wall weakening. The thrombus itself is a heterogeneous structure; thus, its composition and resultant mechanical properties may differ significantly between patients. Current research is aimed at creating systems that allow for individual evaluation of each patient. It seems that only such an approach will enable future optimal qualification of patients to interventional treatment taking into account the potential benefit-risk balance.

Conflict of interest

None.

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