REVIEWS

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Potential Indicators of the Degree of Abdominal Aortic Aneurysm Development in Rupture Risk Estimation*

Potencjalne wskaźniki stopnia rozwoju tętniaka aorty brzusznej w ocenie prawdopodobieństwa jego pęknięcia

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Abstract

Because of the increasing incidence of abdominal aortic aneurysm (AAA) this disease poses a serious epidemiological problem, particularly in the highly developed and developing countries in which the average age of the population is increasing. According to demographic forecasts, these trends will continue, with an incidence peak in the next two decades. With the current state of medical knowledge, it is impossible to prevent the formation and development of abdominal aortic aneurysms whereby the main treatment remains to be surgical intervention. Therefore, in the authors' opinion, besides continuing to explore the aetiopathogenesis of this disease, it is sensible to search for the potential indicators of the degree of AAA development. The present analysis of the indicators of the degree of AAA development currently recognized shows that their significance varies widely among researchers. This paper presents a review of information about the three main indicators of the degree of abdominal aortic aneurysm development: AAA maximum diameter, growth rate and mural thrombus presence. When searching for more objective indicators of AAA rupture probability and AAA development degree, researchers have become interested in indicators which might be the direct reflection of the structural changes taking place in the aortic wall. In the present authors' opinion, the evaluation of the mechanical properties of AAA walls holds the greatest promise for the reliable assessment of AAA wall rupture probability and the degree of AAA development (**Adv Clin Exp Med 2011, 20, 2, 221–225**).

Key words: abdominal aortic aneurysm, maximum diameter criterion, growth rate, mural thrombus.

Streszczenie

Zwiększenie zachorowań na tętniaka aorty brzusznej (AAA) czyni tę chorobę poważnym problemem epidemiologicznym, zwłaszcza w populacji krajów wysoko rozwiniętych i rozwijających się, gdzie rośnie średnia wieku społeczeństw. Prognozy demograficzne wskazują na dalsze pogłębianie tych tendencji, z apogeum zachorowań w okresie kolejnych dwu dekad. Przy obecnym stanie wiedzy medycznej zapobieganie powstawaniu i rozwojowi tętniaków aorty brzusznej jest niemożliwe, dlatego nadal zasadniczym leczeniem jest interwencja chirurgiczna. Zatem, w opinii autorów na obecnym poziomie wiedzy medycznej, poza dalszym wyjaśnianiem etiopatogenezy choroby, celowe jest poszukiwanie, sklasyfikowanie i określenie znaczenia potencjalnych wskaźników stopnia rozwoju tętniaków aorty brzusznej. Wniosłoby to nowe dane do badań nad etiopatogenezą choroby oraz pozwoliłoby na zobiektywizowanie wskazań do leczenia chirurgicznego w odniesieniu do oceny ryzyka pęknięcia ściany tętniaka. Przeprowadzona w niniejszej pracy analiza uznanych obecnie wskaźników stopnia rozwoju tętniaka aorty brzusznej wskazuje na zróżnicowane ich znaczenie, a nawet krańcowo odmienne poglądy poszczególnych badaczy co do znaczenia tych wskaźników. Zwolennicy powyższych wskaźników wskazują na łatwość użycia, a przeciwnicy na niedokładność, pośredni charakter oraz duże ryzyko popełnienia błędu związanego z ich oceną. W pracy dokonano przeglądu wiedzy na temat trzech podstawowych, stosowanych obecnie, wskaźników stopnia rozwoju

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tętniaka aorty brzusznej: kryterium maksymalnej średnicy, współczynnika wzrostu, a także znaczenia skrzepliny przyściennej. Poszukiwanie bardziej obiektywnych wskaźników prawdopodobieństwa pęknięcia tętniaka oraz stopnia jego rozwoju skłoniło badaczy do zainteresowania się wskaźnikami, które byłyby odzwierciedleniem przemian strukturalnych zachodzących w ścianie aorty. Autorzy sądzą, że największe szanse na wiarygodne prognozowanie prawdopodobieństwa pęknięcia ściany tętniaka oraz określenie stopnia jego rozwoju rokuje ocena właściwości mechanicznych ścian tętniaków aorty brzusznej (**Adv Clin Exp Med 2011, 20, 2, 221–225**).

Słowa kluczowe: tętniak aorty brzusznej, kryterium maksymalnej średnicy, współczynnik wzrostu, skrzeplina przyścienna.

Because of its incidence, the resultant high mortality rate, the difficult diagnosis and the lack of fully objective and reliable standards for the assessment of the degree of progression of the disease, abdominal aortic aneurysm (AAA) is a major problem from a medical (clinical), social and scientific point of view. The development of an AAA is long and gradual and usually an asymptomatic process [1]. This makes its diagnosis difficult and often the aneurysm is detected incidentally in the course of diagnosing other diseases. An untreated abdominal aortic aneurysm usually leads to death as the result of a rupture. AAA rupture is associated with a mortality rate of 80–90% [1, 2]. It is very hard to determine the probability of AAA rupture, mainly because the development of this disease is very complicated and its controlling mechanisms and their mutual interactions have not been fully explored. Therefore all kinds of parameters are being sought with a hope that they will make it possible to estimate most reliably the probability of AAA rupture. On the basis of the hitherto research, several indicators have been identified. The three most used indicators, i.e. AAA maximum diameter, AAA growth rate and the presence of mural thrombus, are described below.

Maximum Diameter

The maximum diameter criterion is currently used in clinical practice to evaluate indications for the surgical treatment of an abdominal aortic aneurysm since it is thought that the probability of AAA rupture increases with its diameter [1, 3]. Myers et al. [4] determined that AAA wall rupture will occur with a probability of: 2%, 3.2%, 25%, 35% and 75% when the aneurysm's diameter is respectively: below 40 mm, in the range of 40–49 mm, 50–59 mm, 60–69 mm and above 70 mm. An abdominal aortic aneurysm diameter of 50–55 mm is considered to be critical and when it is exceeded, the probability of AAA rupture increases exponentially [5]. On average, the probability of AAA rupture in the case of aneurysms 50 mm or more in diameter amounts to 7.6% [6]. However, Verloes et al. [7] showed that the probability of such a rupture is then much higher and can be as high as 22%. Also, in the case of small diameter (50–55 mm) aneurysms, the risk of AAA rupture is not definitely known. The research: *UK Small Aneurysm Trial* (*UKSAT*) [6] and *Aneurysm Detection and Management Trial* (*ADAM*) [8] showed that aneurysms with a diameter of 40–55 mm are characterized by a low probability of AAA rupture. This was corroborated by studies made in other research centers, which showed that the probability of rupture of an AAA with a diameter below 50 mm amounts to 0.5% [9] or 1% [6, 10]. A critically low probability (amounting to 0%) of rupture of an AAA with a diameter below 50 mm was obtained at the Mayo Clinic [11]. In contrast to the above reports, Cronenwett et al. [12] found that the probability of AAA rupture with a diameter below 50 mm is about 6%, but according to Nicholls et al. [13], it is as high as 10%. Many research centers report that the probability of rupture of an AAA with a diameter below 50 mm is around 12% [7, 14]. Whereas Fillinger et al. [15] estimated that the probability of rupture of an AAA with a diameter below 50 mm is as high as 23%. A similar result, i.e. 24%, was obtained by Brown and Powell [16]. It appears from the above reports that the maximum diameter criterion is highly imprecise.

Growth Rate

The growth rate is considered to be another important indicator of AAA rupture probability. Limet et al. [14] were the first to show that the risk of rupture may be associated not only with the aneurysm's diameter but also with the rate of its growth. This was confirmed by Lederle et al. [17] and Brown et al. [18]. Lederle et al. [17] found that the growth rate was significantly higher among patients with an AAA with rupture symptoms than among patients in whom the aneurysm rupture risk was negligible (respectively 7.5 mm/year relative to 4.1 mm/year). Studies by Brown et al. [18] showed that the growth of AAAs which later ruptured was much faster than that of AAAs which did not rupture (respectively 8.4 mm/year relative to 3.9 mm/year). In clinical practice, a growth rate of 5 mm/year or higher is associated with a high risk of AAA rupture [19]. Hallin et al. [20] estimated the probability of AAA rupture depending on the growth rate at 2% for aneurysms growing at a rate of 2–4 mm/year, at about 10% for aneurysms growing at a rate of 2–5 mm/year and at 22% for aneurysms growing at a rate of 3–7 mm/year. However, the view that the rate of growth is connected with the probability of AAA rupture is not commonly accepted. In 1985 Cronenwett et al. [12] found that there is no link between growth rate and AAA rupture risk and that the decisive parameter is the size of the aneurysm. This was confirmed by the studies made by Nevitt et al. [11]. Then Cronenwett et al. [21] demonstrated that the growth rate depends on the actual diameter of the aneurysm. In a paper published in 1996 [22], Cronenwett recapitulates that it is extremely difficult to assess the effect of growth rate on AAA rupture risk. This means that extensive and long-term non-surgical studies on patients with similar maximum AAA diameters but with different growth rates need to be carried out in order to determine whether growth rate is an independent indicator of AAA rupture. Moreover, it is difficult to precisely determine the rate of AAA growth in individual cases and the aneurysms themselves have periods of stabilization and rapid growth [23].

Mural Thrombus

The presence of mural thrombus in about 75% of AAA cases is the reason that it is considered to play a role in the pathogenesis of this disease [24]. However, the significance of mural thrombus in AAA rupture risk estimation is debatable [3]. Some researchers believe that mural thrombus constitutes a risk factor [25, 26] while others claim that it performs a protective function [24, 27]. There are also opinions that mural thrombus does not perform any significant role and that it cannot be used in AAA rupture risk probability assessment [28, 29]. The studies made by Vorp et al. [30] indicate that the presence of mural thrombus causes a reduction in AAA wall strength, amounting to 20% for a 4 mm thick mural thrombus relative a 1 mm thick mural thrombus. This is so because mural thrombus forms a barrier to oxygen, which cannot penetrate from the lumen of the vessel to its wall, causing local vascular wall anoxia and consequently, vascular wall degeneration. The cited authors suggest that by creating an oxygen deficient environment mural thrombus may lead to a compensatory inflammatory response, a local increase in proteolytic activity, a local wall weakening and consequently, to a break in the continuity of the AAA wall. Adolph et al. [31] claim that mural thrombus can play an active role in AAA pathogenesis since it contains inflammatory infiltration cells (macrophages and neutrophiles). Moreover, Stenbaek et al. [26] showed that an increase in mural thrombus surface area predisposes the aneurysm to rupture, particularly when the increase amounts to 15 mm^2 per year or more. Wolf et al. [25] found that an increase in mural thrombus volume is connected with an acceleration in the growth of the aneurysm. Thus they found that the larger the mural thrombus volume, the higher the probability of AAA rupture. Wang et al. [24] drew different conclusions as to the significance of mural thrombus volume. In their opinion, mural thrombus reduces stresses in the aneurysm wall by about 6–38% depending on the mural thrombus volume to total aneurysm volume ratio which they found to be in a range of 0.29–0.72. Vorp et al. [27] found that mural thrombus acts as a damper, reducing stress in the AAA wall. Analyzing computer tomography images, Pillari et al. [32] discovered that the growth of the aneurysm was associated with a synchronous increase in mural thrombus volume for aneurysms with a diameter of 50–70 mm, whereas in the case of aneurysms with a diameter larger than 70 mm, they did not find any significant changes in mural thrombus volume. Thus they found that mural thrombus performs a protective function in AAAs below 70 mm in diameter. But Schurink et al. [28] demonstrated that the presence of mural thrombus does not cause any reduction in the arterial blood pressure acting on the wall and so it does not play any significant role. On the basis of comparative studies of groups of ruptured and unruptured AAAs Hans et al. [3] did not find statistically significant differences in the mural thrombus to total aneurysm volume ratio between the studied groups. In their opinion, this finding disproves the usefulness of mural thrombus for the assessment of AAA rupture probability.

Discussion

In the second half of the 20th century, a dramatic (over sevenfold) increase in abdominal aortic aneurysm incidence occurred [33] and in the last 30 years just in the Eastern hemisphere the incidence has tripled [34]. The current number of persons with AAA is not precisely known. Sołtysiak [35] mentions that the occurrence of AAA in different parts of the world largely depends on the age structure and the criteria adopted for classifying pathological changes. Hence AAA incidence may range from 1.2% to 27%. Many authors report that abdominal aortic aneurysm affects about 2–4% of the world population [36, 37] and clinical observations indicate that its incidence is steadily increasing. Each year about 20–40 new cases per 100,000 persons are diagnosed [7, 36].

As a result of the rapid increase in the number of patients suffering from AAA, the constantly growing number of planned surgical excisions of AAA and the number of newly diagnosed cases, this disease has reached epidemic proportions in the ageing population of the highly developed and quickly developing countries. It is forecasted that the number of aneurysmal patients in most industrial countries will grow as the human lifespan and adverse environmental effects increase [1]. It is estimated that the number of aneurysmal patients will dramatically increase in the next two decades. Thus, the expenditures on healthcare for patients suffering from AAA will constantly grow.

With the current state of medical knowledge, the prevention of abdominal aortic aneurysms is impossible since the pathogenesis of this disease is unknown. The aetiology of AAA is probably multifactorial. A considerable number of potential etiological factors, e.g. genetic, anatomic, hemodynamic, biochemical and environmental (e.g. smoking) factors [38], and the effect of inflammatory processes and arteriosclerosis [39] are involved. In recent years many research centers around the world have focused their efforts on the explanation of the pathogenesis of abdominal aortic aneurysms and the description of the character of the changes taking place in the course of AAA development. Currently, various indicators, connected with the size of the aneurysm, the rate of its growth and the presence or absence of mural thrombus, are used to evaluate the degree of development of AAA and assess the probability of its rupture. The limitations and ambiguity of the conclusions emerging from the evaluation of the indicators have aroused interest in new criteria for evaluating the degree of development of AAA. The search for reliable indicators of the probability of AAA rupture and of the degree of its development has induced researchers to concentrate on the indicators which are the direct result of structural changes taking place in the connective tissue of the aorta. Therefore it is currently thought that the evaluation of the mechanical properties of the AAA walls holds the greatest promise for the reliable prediction of the probability of AAA wall rupture and for determining the degree of AAA development [15, 40]. However, the research into this is still in its early stages. In the authors' opinion, the above approach is reasonable since the breaking of AAA wall continuity can be considered as a classic case of material failure due to excessive loading of the vascular wall or to inadequate strength of the material or to a combination of the two factors.

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