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Conventional Abdominal Aortic Aneurysm Repair: Evidence-based Assessment

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Ruptured abdominal aortic aneurysm (AAA) is a frequent cause of death (9000 persons per year in the United States). Because open repair is highly effective in preventing rupture, surgeons advocate elective surgical treatment. With the trend toward evidence-based medicine, however, surgeons have come under strong pressure to justify their therapeutic decisions on the basis of objective data. The purpose of this study was to perform an evidence-based assessment of conventional surgical AAA repair.

For surgical treatment of cancer, it is relatively easy to evaluate the effectiveness of surgery, since the survival rate of unoperated cancer is well documented and thus can be used as a reference for measuring the outcome of surgery. A similar knowledge of the natural history of AAA is prerequisite for determining whether the operative risk associated with open AAA repair is offset by a reduction in the risk of fatal aortic rupture, which is the goal of surgical treatment. In addition to risk/ benefit analysis, this study will seek to answer two questions. The first is the extent to which it is possible to evaluate the risk of rupture and thus to select indications on the basis of clinical and laboratory findings. The second is the seldom-asked question of whether endovascular treatment and even conventional open repair really rule out subsequent occurrence of rupture. Only by providing clear answers to these questions can we know if AAA repair is an evidenced-based procedure.

NATURAL HISTORY OF AAA

In early reports such as those of Szilagyi et al.,[1] the natural history of AAA was extremely poor. This is probably because most cases diagnosed at that time involved advanced aneurysms with large diameters. In the more recent literature mortality rates for unoperated AAA diagnosed using modern technology have been less alarming than those given by Szilagyi. However, these clinical data have also been challenged.[2]

The best way to avoid the inherent bias in most clinical studies would be to use data from autopsy series from countries where postmortem studies are performed on a routine basis. One such study is available from the city of Malmo, Sweden, for the period between 1958 and 1986 (85% of deceased subjects).[3] As would be expected, this study showed that AAA is a predominantly male condition that becomes age-dependent after age 69 years, with a peak occurring during the eighth decade of life. The most interesting finding for the purpose of the present study is the number of ruptured AAA found during autopsy, i.e., 5.6 per year and per 100,000 inhabitants (8.4 for men and 3.0 for women). Peak incidence occurred between 80 and 89 years of age in men and over 90 years in women. In other countries such as England and Wales, the same age distribution has been observed, but with higher figures.[4]

This corresponds to the absolute incidence of fatal ruptured AAA, but what is the relative incidence of fatal rupture in relation to the total number of AAA discovered during autopsy? Only 14% of the total number of AAA discovered during autopsy in Malmo showed signs of rupture.[3] In other words, only one of seven aneurysms caused death. This would mean that for every seven AAA repairs performed only one patient is saved. It should be emphasized, however, that AAA in this Swedish study was defined simply as the presence of ectasia with no mention of diameter. As a result, many small AAA were probably counted, thus lowering the overall incidence of rupture.

In a series including 473 AAA discovered during autopsy, Darling et al.[5] reported a rupture rate of 24.9%. In addition to the number of ruptures, the authors also reported the diameter of the AAA and calculated the rupture rate as a function of AAA diameter. The rupture rate was 9.5% for small aneurysms <4 cm in diameter (42.5% of the total number of AAA) vs. 25% for aneurysms between 4 and 7 cm in diameter (31% of the total number of aneurysms). This study had two shortcomings, however. First, since autopsy was carried out on hospital patients rather than on a routine basis, there was probably a higher number of ruptures. Second, AAA diameter after death is necessarily smaller than during life because of the absence of mechanical dilatation from arterial

pressure.

Another question that must be answered involves mortality associated with elective AAA repair. Reported mortality rates vary among hospitals and among groups. Moreover, since groups with high mortality are unlikely to publish their results, it seems probable that the mean rates of 3.5% and 3.8% found in the medical literature[6,7] are unrealistic. A more objective assessment can be found in an American study conducted in 1994.[8] The authors compared the evolution of mortality associated with elective and emergency AAA repair in a single state based on official documents kept by each hospital. The advantage of this approach is that all centers practicing AAA repair in the state were included. The mortality rate associated with elective surgery in 1980 was 13.6%. Although this rate fell to 5.6% within a few years, these findings provide further proof of the discrepancy between what happens in everyday practice and what is reported in medical journals.

Even if it is assumed that all surgical centers practicing AAA repair can achieve a mortality rate of around 2% or even as low as the 1.4% reported by the Strasbourg group[9] and the 1.2% reported by the Cleveland group,[10] it would still not be fair to compare these rates directly with the 14% mortality rate spared by surgery. The main problem is that the incidence of fatal ruptured AAA is higher in the 80 to 89 age group.[3] Because of this age-related difference, a different picture is obtained when mortality is expressed in terms of years of life lost instead of individual lives lost. Indeed, the number of years of life lost is greater for a death occurring during elective AAA repair than for a death resulting from late rupture, e.g., at 86 years of age. The comparison would be much more favorable for surgery using the 25% mortality reported by Darling et al.[5] for ruptured AAA between 4 and 7 cm, which account for 31% of AAA-related deaths in hospital.

This shows that AAA size is an essential factor. This finding is not new and it is generally agreed that patients with large AAA must undergo surgery. The real controversy at the present time involves the definition of small aneurysms and their management. We define small AAA as lesions with a maximum diameter between 4 and 5.5 cm. Using the same definition, a British study[11] was carried out in which patients with small aneurysms were randomly assigned to two groups that underwent either early elective surgery or delayed repair when the diameter of the aneurysm reached or exceeded 5.5 cm. Results showed similar survival curves for patients who underwent immediate repair and patients who underwent repair after a period of active surveillance. A positive trend was noted in the immediate repair group after 10 years. A recent Veterans Administration study[12] led to similar findings despite a difference in operative mortality: 5.8% for the British vs. 2.7% for the Americans. The conclusions of these two studies were identical: delaying repair until AAA diameter reaches 5.5 cm does not result in significantly higher mortality provided that rigorous surveillance is performed. The benefits of delayed repair in terms of economic cost and patient comfort are obvious since needless expense and suffering are avoided for patients who die during the surveillance period from causes unrelated to ruptured AAA.

On the basis of these convincing findings, the recommendations of these studies seem quite reasonable. From an individual standpoint it must be pointed out, however, that 20 patients died during surveillance in the British study. It is difficult to explain why someone's father died because a known lesion was not treated. Thus, while AAA size and growth rate may provide a rational basis for selecting operative indications, there are exceptions to the rule and fatal rupture can occur in patients presenting aneurysms <5.5 cm in diameter. Thus it would be useful to define other variables to fine-tune selection of operative indications.

AAA HIGHER RISK OF RUPTURE

In my opinion, heredity is indubitably an added risk factor for ruptured AAA. In our experience we identified a group of patients with a strong family tendency to aneurysms in elders, children, and siblings. Since these patients have a higher risk of early rupture, immediate surgical repair is justified.[13]

Although studies over the past 20 years have provided evidence that the pathogenesis of AAA is not strictly "atherosclerotic," the fact remains that there is a link between atherosclerosis and development of AAA and consequently that failure to eliminate risk factors such as hypertension and smoking is extremely unfavorable. A British study demonstrated that smoking is a major risk factor for AAA expansion.[11] Cronenwett et al.[4] showed that the presence of hypertension and/or chronic obstructive lung disease was associated with a higher mortality rate due to rupture of AAA 5 cm in diameter.

In addition to risk factors for atherosclerosis, another parameter that should be taken into account is loss of elastin, which leads to AAA enlargement, and of collagen, which is a warning sign for rupture.[15] The reason that overall collagen content does not change as an AAA expands is that breakdown of normal collagen is accompanied by simultaneous synthesis of an altered form of collagen. Altered collagen is predominant in the

wall of ruptured AAA. Thus it can be thought that metabolic activity in the aortic wall is intense prior to rupture. Such an increase in metabolism has been documented by positron emission tomography (PET) in a few patients presenting symptomatic aneurysm or aneurysms on the verge of rupture. Further study is needed, however, to validate the utility of PET evaluation.[16]

LABORATORY MARKERS OF RUPTURE RISK

Are there any factors known to inhibit or stimulate proteases that might be assayed in serum? In other words, could laboratory markers be used to identify AAA that are expanding or at risk for rupture before they reach the breaking point?[7]

A possible candidate for use as a laboratory serum marker is MMP9, which has been directly implicated in the proteolytic degradation of the extracellular matrix of the aortic wall.[17] Plasma levels of MMP9 were measured in three groups of patients: patients with AAA, patients with stenosis of the abdominal aorta with or without claudication, and control patients with normal aorta. MMP9 levels were significantly higher in the AAA group than in the other two groups.[18] A significantly higher concentration of MMP9 was found around the site of rupture of an AAA. Further study will be necessary to determine if plasma MMP9 levels are also higher in cases involving ruptured AAA.[19]

Another factor that has been studied as a potential serum marker is α1-antitrypsin (α1-AT), since it is the most abundant serum inhibitor of proteases, α1-Antitrypsin deficiency is a predisposing factor for emphysema due to destruction of elastic fibers in the bronchi, and many investigators have reported a link between development of AAA and presence of chronic obstructive lung disease. However, current findings are so contradictory that it is now impossible to form any opinion as to the significance of this marker for the prognosis of AAA.[20]

LONG-TERM MORTALITY AFTER SURGICAL REPAIR

It has long been known that survival is shorter for patients who undergo AAA repair than for patients of the same age and gender without AAA. One study comparing life expectancy with and without AAA repair showed that median survival was 7.4 years after repair at 60 years vs. 14.5 years for the reference population and 4.7 years after AAA repair at 75 years vs. 9 years for the reference population.[22] The shorter survival of patients who undergo AAA repair has been attributed to the fatal complications of atherosclerosis, which is more severe in patients with AAA. While this is certainly true, it is still only fair to wonder first if any risk of rupture subsists after open repair, and second what the exact incidence of fatal iatrogenic complications is.

While development of a supraprosthetic AAA due to dilatation of the interrenal or suprarenal aorta is possible, the actual incidence of this complication is relatively low in correlation with the degree of elasticity of the aortic lesion rather than with any iatrogenic cause. Two complications with greater potential to cause failure of open AAA repair are rupture of false aneurysm involving the upper suture line and infection of the prosthetic graft. According to one study,[22] 2.5% of late mortality after AAA repair is related to surgical complications, especially aortoenteric fistula. The incidence of fatal rupture of a false aortic aneurysm is difficult to estimate. According to one study, the incidence of pseudo-AAA at 10 years was 4%.[23] The incidence of rupture involving false aneurysm has never been systematically studied, much less determined. Both of these complications should be included in any assessment of risk and potential benefit.

Until more data are available on long-term outcome, I will refrain from making any long commentary on the effectiveness of endovascular treatment. The recent conclusions of the Eurostar Study[24] indicate that the yearly combined complication/reoperation rate was approximately 10% and that it does not diminish with time. This would have to be subtracted from the theoretical benefit of preventing further enlargement of the AAA.

According to the most favorable study on the natural history of AAA, i.e., the prospective study of Nevitt et al.,[2] the incidence of rupture at 5 years for aneurysms >5 cm in diameter is 25%. To determine the effectiveness of open surgery in preventing this 25% rate of rupture at 5 years, we must take into account operative mortality (currently varying from 1 to 6% or higher) and late mortality, which is difficult to assess accurately but estimated to be around 2.5%.[22] Assuming that late mortality is stable and low, it seems reasonable to say that the benefit of open surgery is directly proportional to the natural risk of the group undergoing surgery and indirectly proportional to operative mortality.

On the basis of this quick assessment of the risks and benefits of surgical intervention versus no surgical intervention, it seems to me that the scale tips in favor of surgical intervention, at least insofar as open repair is

concerned. However, this conclusion remains shaky and subject to revision at any time. The opposite conclusion could easily be drawn if operative mortality were slightly higher in a group of patients with smaller lesions associated with a less unfavorable natural history.

The major lesson of the preceding discussion is the importance of our continuous efforts to reduce operative risks and optimize patient selection. The low mortality/morbidity rates recently reported by the most skilled groups[9,10] suggest that there is little to gain in that area. A more hopeful approach would be to improve patient selection based on aneurysm diameter by taking into account other risk factors such as atherosclerosis, family history, and, soon, appropriate plasma markers and PET findings.

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