

CLINICAL PRACTICE

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Abdominal Aortic Aneurysms

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This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

A 76-year-old woman presents with a 2-day history of left-lower-quadrant pain. A computed tomographic (CT) scan reveals diverticulitis and an incidental 5.6-cm infrarenal abdominal aortic aneurysm. Her medical history is notable for hypertension, hypercholesterolemia, and obesity. She is a current smoker, with an 80 pack-year history. How should her case be managed?

THE CLINICAL PROBLEM

Abdominal aortic aneurysm is a segmental, full-thickness dilatation of the abdominal aorta exceeding the normal vessel diameter by 50%, although an aneurysm diameter of 3.0 cm is commonly regarded as the threshold. The natural history is characterized by progressive expansion; however, the growth rate for individual aneurysms can vary considerably, with some remaining stable for years and others growing rapidly. The best known predictor of rupture of abdominal aortic aneurysms is aneurysm size.^{1,2} Aneurysms are usually asymptomatic until they rupture. Rupture is often lethal; mortality is 85 to 90%. Of those persons who reach the hospital, only 50 to 70% survive.^{2,3} Thus, the goal is to identify and treat aneurysms before they rupture.

Abdominal aortic aneurysms are located between the diaphragm and the aortic bifurcation. An aneurysm is classified as suprarenal if it involves the origin of one or more visceral arteries, pararenal if it involves the origins of the renal arteries, and infrarenal if it begins beyond the renal arteries. The more cephalad the aneurysm, the more complex the repair. Approximately 85% of abdominal aortic aneurysms are infrarenal,⁴ and the common iliac arteries are often involved.

Although it was previously believed that aneurysms were a form of atherosclerosis, aortic aneurysmal disease is now recognized as a distinct degenerative process involving all layers of the vessel wall. The pathophysiology of aortic aneurysms is characterized by four events: infiltration of the vessel wall by lymphocytes and macrophages; destruction of elastin and collagen in the media and adventitia by proteases, including matrix metalloproteinases; loss of smooth-muscle cells with thinning of the media; and neovascularization.⁵ Dissection is a distinct process that most often involves the ascending, thoracic, or thoracoabdominal aorta and is rarely the source of aneurysms isolated to the infrarenal aorta.

Nonmodifiable risk factors for abdominal aortic aneurysm include older age, male sex, and a family history of the disorder.⁶ Starting at 50 years of age for men and 60 to 70 years of age for women, the incidence of aneurysms increases significantly with each decade.⁷ The risk of abdominal aortic aneurysm is approximately four times as high among men as among women and four times as high among people with a family history of the disorder as among those without a family history.⁶ Smoking is the strongest modifiable risk factor.^{6,8,9} Other, less prominent

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KEY CLINICAL POINTS

ABDOMINAL AORTIC ANEURYSMS

- Abdominal aortic aneurysms are usually asymptomatic until they rupture, with an ensuing mortality of 85 to 90%.
- Symptomatic patients require urgent repair.
- U.S. Preventive Services Task Force recommendations support screening in men 65 to 75 years of age with a history of smoking and selective screening in men 65 to 75 years of age without a smoking history, although the optimal cohort to be screened remains controversial.
- The usual threshold for elective repair is an aortic diameter of 5.5 cm in men and 5.0 cm in women.
- Endovascular repair results in lower perioperative morbidity and mortality than open repair, but the two methods are associated with similar mortality in the long term (8 to 10 years).
- Patients treated with endovascular repair require long-term surveillance owing to a small risk of aneurysm sac reperfusion and late rupture.
- Decisions regarding prophylactic repair — whether to pursue it and, if so, what type of repair to perform — must take into account anatomy (not all patients have anatomy amenable to endovascular repair), operative risk, and patient preference.

risk factors for abdominal aortic aneurysm include hypertension, an elevated cholesterol level, obesity, and preexisting atherosclerotic occlusive disease.⁶ Abdominal aortic aneurysms are more prevalent among whites than among blacks, Asians, and Hispanics.^{6,10} Lifestyle factors associated with a reduced risk include regular exercise and a favorable diet (i.e., adequate intake of fruit, vegetables, and nuts).⁶ Diabetes mellitus is also associated with a reduced risk.^{6,11}

The prevalence of abdominal aortic aneurysms appears to be declining. In a recent Swedish study involving ultrasonographic screening of 65-year-old men, the prevalence of abdominal aortic aneurysms was 2.2%,¹² whereas in earlier studies, the reported prevalence was 4 to 8% among men 65 to 80 years of age.^{6,13-15} This trend is probably the result of risk-factor modification — in particular, declining rates of smoking.^{6,16} Abdominal aortic aneurysms have been reported to result in approximately 13,000 deaths annually in the United States; however, this is probably an underestimation, given that unexplained sudden death can be related to aneurysm rupture.¹⁷⁻¹⁹

STRATEGIES AND EVIDENCE

SCREENING

Aneurysms can be discovered on abdominal examination; however, because of the retroperito-

neal location of the aorta, accuracy is low. Ultrasonography is the primary method used for screening and is highly sensitive (95%) and specific (100%).²⁰ CT scanning and magnetic resonance imaging (MRI) are expensive, incur risks (radiation exposure from CT and risks associated with intravenous contrast material), and should not be used for screening but rather reserved for preinterventional planning. A meta-analysis of four randomized trials of screening for abdominal aortic aneurysm in older men, with up to 15 years of follow-up, showed a significant and substantial reduction in the risk of death from abdominal aortic aneurysm and the need for emergency surgery, with an associated increase in elective intervention.²¹

Only a few countries have adopted national screening policies, and the targeted populations are inconsistent. In England, the recommendation is for a one-time screening of all men 65 years of age or older.²² The current recommendations of the U.S. Preventive Services Task Force are a one-time screening in men 65 to 75 years of age who have ever smoked (grade B recommendation) and selective screening in men 65 to 75 years of age who have never smoked (grade C recommendation).²³ Medicare also covers screening for patients with a family history of abdominal aortic aneurysm,²⁴ as recommended by some other professional guidelines.^{25,26} Data from nonrandomized

studies suggest that there may be subgroups of women who benefit from screening; however, this finding has not been prospectively validated.⁶ A scoring system inclusive of multiple recognized risk factors has been proposed to identify both men and women whose risk is sufficiently high to justify screening, but this has also not been prospectively validated.⁶ Even with the foregoing recommendations, screening is often not performed because patients and physicians may be unaware of the need.²⁷

ANEURYSM GROWTH AND SURVEILLANCE

Small abdominal aortic aneurysms (3.0 to 5.4 cm in diameter), when identified, should be monitored for expansion. In accordance with Laplace's law, the larger the aneurysm, the higher the rate of expansion. Current guidelines regarding the frequency of monitoring are as follows: for aneurysms with a diameter of 3.0 to 3.4 cm, every 3 years; 3.5 to 4.4 cm, yearly; and 4.5 to 5.4 cm, every 6 months.²⁵ A recent meta-analysis involving more than 15,000 patients, which assessed expansion and rupture rates as a function of aneurysm size, suggested that longer surveillance intervals (several years) may be safe, particularly for aneurysms smaller than 4.0 cm in diameter.²⁸

TREATMENT

Risk-Factor Modification

The prevalence and size of aneurysms are strongly associated with both the amount and duration of smoking; cessation of smoking can reverse this risk and is associated with a reduced rate of aneurysmal growth.^{6,8,9} The recognized association between either hypertension or hypercholesterolemia and the occurrence of abdominal aortic aneurysm suggests that control of these coexisting conditions with medications such as antihypertensive agents and statins may decrease the risk, although limited data are available to support this hypothesis (see below). In any case, many patients with abdominal aortic aneurysm have clinically significant cardiovascular disease; thus, medical management of coexisting conditions is recommended to reduce the incidence of cardiovascular events in these high-risk patients.²⁹

Medical Therapy

Several drugs have been evaluated for their potential to limit abdominal aortic aneurysm. Beta-blockers, antibiotics, and antiinflammatory agents

have been examined in randomized trials, and angiotensin-converting-enzyme inhibitors, angiotensin-receptor blockers, statins, and antiplatelet agents have been examined in nonrandomized studies. Unfortunately, none of these drugs have been shown to provide a benefit.^{30,31} Doxycycline inhibits matrix metalloproteinases, a finding that suggests that it might reduce the growth of aneurysms. However, in a placebo-controlled, randomized trial, doxycycline at a daily dose of 100 mg did not reduce the growth of small aneurysms over a follow-up period of 18 months.³² Several medication regimens, including a higher dose of doxycycline and drugs that inhibit the renin-angiotensin pathway, are currently being evaluated in randomized trials (ClinicalTrials.gov numbers NCT01756833, NCT01904981, and NCT01683084).

Indications for Aneurysm Repair

The goal of elective intervention is to prevent rupture. However, there are risks associated with surgery, and thus it is essential to select patients who are expected to have a long-term benefit from elective aneurysm repair. Although the diameter of an abdominal aortic aneurysm is the best known predictor of rupture, small aneurysms occasionally rupture, and some large aneurysms do not.

Two large, randomized trials, the U.K. Small Aneurysm Trial³³ and the Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study,³⁴ have compared elective open surgery with surveillance by means of ultrasonography or CT in patients with asymptomatic abdominal aortic aneurysms that were 4.0 to 5.5 cm in diameter. Elective open surgery did not improve survival in either trial. The annual risk of rupture for aneurysms that are less than 5.5 cm in diameter is 1% or lower,^{33,34} whereas the risk increases significantly for aneurysms above this threshold (Table 1).³⁵ Thus, under most circumstances, aneurysms should not be prophylactically repaired unless they are at least 5.5 cm in diameter. Results of a trial comparing endovascular repair with surveillance indicate that the 5.5-cm threshold also applies to patients treated with endovascular repair.³⁶

Nevertheless, there are occasions when repair of small aneurysms should be considered. Symptoms are a harbinger of rupture, and the time from the onset of symptoms to rupture and death can be brief and is unpredictable. Consequently,

Table 1. Annual Risk of Rupture of Abdominal Aortic Aneurysms.*

Aneurysm Size	1-yr Incidence of Rupture
	%
<5.5 cm	≤1.0
5.5–5.9 cm	9.4
6.0–6.9 cm	10.2
≥7.0 cm	32.5

* Data are from Powell et al.,³³ Lederle et al.,³⁴ and Lederle et al.³⁵ The overwhelming majority of study participants were men.

symptomatic aneurysms should be immediately repaired. Pain in the abdomen, back, or flank is the most common symptom, but aneurysms can produce many other symptoms or signs (e.g., hematuria or gastrointestinal hemorrhage); any symptom in a patient with a large aneurysm should be thoroughly evaluated. The rate of growth is another important predictor of rupture; aneurysms that expand by more than 0.5 cm in diameter over a period of 6 months should be considered for repair regardless of the absolute size.²⁶

The observations that aneurysms rupture at a smaller size in women than in men and that women have higher rupture-related mortality than men^{3,37-39} have led some experts to recommend a diameter of 5.0 cm as the threshold for elective intervention in women.²⁵ Because the operative mortality associated with aneurysm repair is also increased among women (who tend to be older than men at the time of presentation and have more complex anatomy), patient selection is important.^{37,39} Other factors that are associated with an increased risk of rupture and may prompt repair at a threshold of less than 5.5 cm include the presence of a saccular aneurysm (most aneurysms are fusiform) and a family history of abdominal aortic aneurysm.⁴⁰ The decision to pursue elective repair must take into account not only the risk of rupture but also the patient's operative risk and predicted longevity.⁴¹

Interventions for Aneurysm Repair

Two approaches to repairing aneurysms are currently available: open repair (performed since the 1950s) and endovascular repair (first performed in 1987).^{42,43} Open repair requires an abdominal or flank incision; vessels above and below the aneu-

rysm are controlled, and the aneurysm sac is opened with interposition of a synthetic graft (Fig. 1A). The 30-day mortality has remained on average between 4% and 5% for the past 20 years, although mortality as low as 2% has been reported; the hospital stay is on average 9 days, and full recovery takes weeks to months. Endovascular repair, a less invasive approach, involves the intraluminal introduction of a covered stent through the femoral and iliac arteries; the stent functions as a sleeve that passes through the aneurysm sac, anchoring in the normal aorta above the aneurysm and in the iliac arteries below the aneurysm (Fig. 1B). Endovascular repair can be performed percutaneously with the patient under local anesthesia; the 30-day mortality is approximately 1%, the hospital stay is on average 3 days, and full recovery usually occurs over a period of days to weeks. To be eligible for endovascular repair, a patient must have appropriate anatomy, including iliac vessels that are of sufficient size to allow introduction of the graft and an aortic neck above the aneurysm that allows anchorage of the proximal graft without covering the renal arteries (Fig. S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Thus, with existing techniques, there are some infrarenal aneurysms that are not amenable to endovascular repair because of anatomical constraints. Endovascular repair is performed by a variety of interventionalists.

The use of endovascular repair has grown steadily in the United States, and this procedure is currently performed in more than 75% of patients undergoing surgical intervention for abdominal aortic aneurysm (Fig. 2), with a portion of the remaining patients having unsuitable anatomy. Three major randomized trials have compared open repair with endovascular repair, each with a follow-up period of 7 to 10 years: the U.K. Endovascular Aneurysm Repair 1 (EVAR 1) trial,⁴⁴ the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial,⁴⁵ and the Open versus Endovascular Repair (OVER) Veterans Affairs Cooperative Study.⁴⁶ The findings of all three trials were similar (see Table S1 in the Supplementary Appendix). Endovascular repair confers an initial survival benefit; however, this benefit disappears over a period of 1 to 3 years. Endovascular repair and open repair are associated with similar mortality over the long term (8 to 10 years).

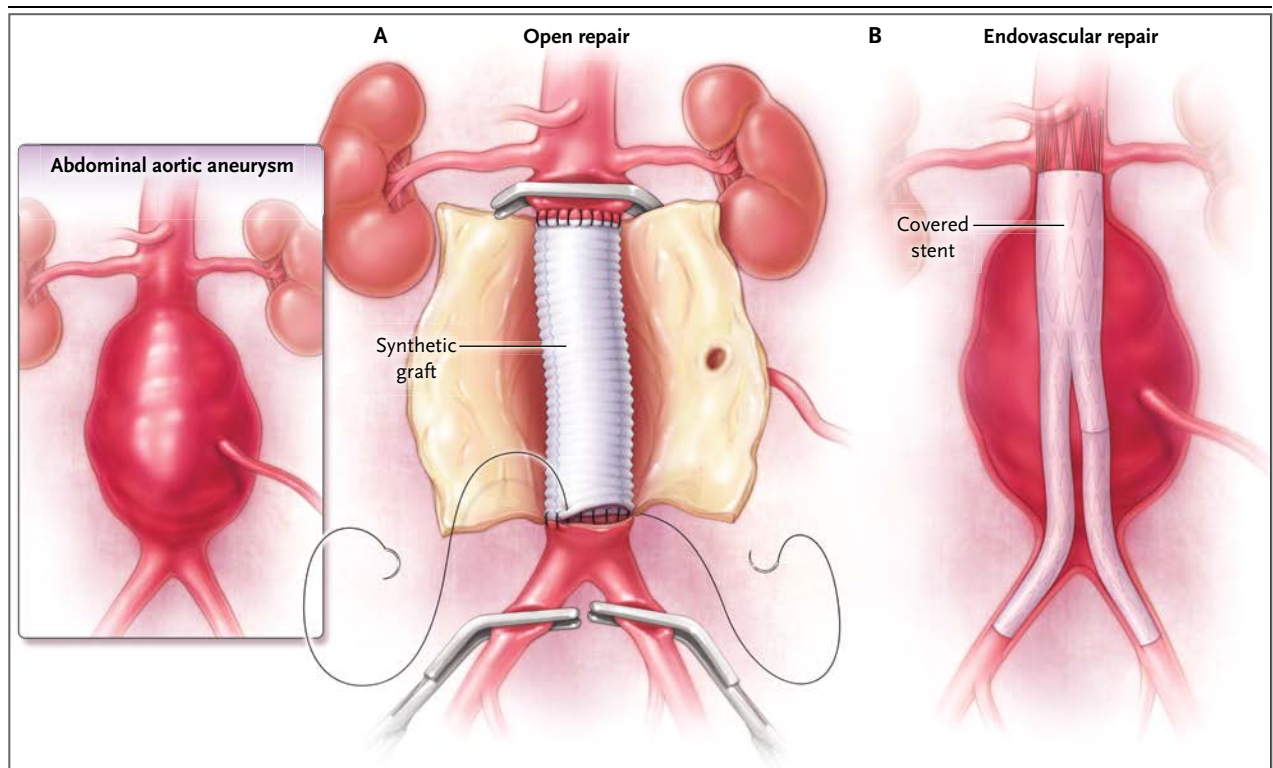


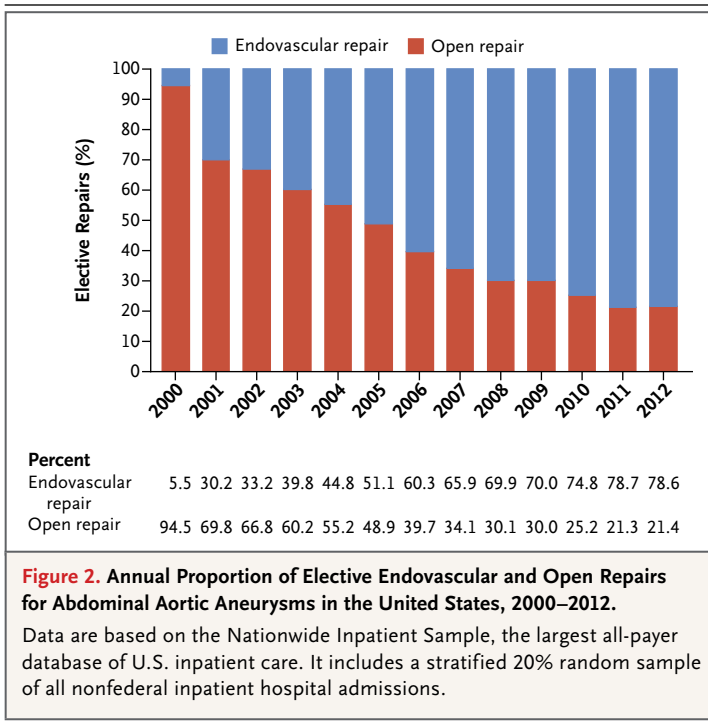
Figure 1. Techniques Available for Repair of Abdominal Aortic Aneurysms.

With open repair (Panel A), vessels above and below the aneurysm are controlled. The aneurysm sac is opened with interposition of a synthetic graft that is sutured proximally and distally to the normal aorta. With endovascular repair (Panel B), a covered stent is introduced intraluminally through the femoral and iliac arteries. The stent functions as a sleeve that bridges the aneurysm sac, anchoring in the normal aorta above the aneurysm and in the iliac arteries below.

Among patients who underwent endovascular repair in the three trials, approximately 20 to 30% required a secondary intervention during the next 6 years. Reintervention is often related to the development of endoleaks, which reperfuse the aneurysm and lead to continued aneurysm expansion. The vast majority of reinterventions for endovascular repair are percutaneous or require a groin incision; however, conversion to open repair is necessary in 2 to 4% of patients (Table S1 in the Supplementary Appendix). Late ruptures after endovascular repair were reported in each of the trials. The incidence was highest in the trial that began the earliest, the EVAR 1 trial (4.0%, vs. 0.6 and 1.4% in the more recent trials). Late ruptures typically occur in patients who have not undergone postoperative monitoring or those for whom a decision has been made not to reintervene. Because of the potential for reperfusion and the associated risk of aneurysm rupture,⁴⁷

patients who have undergone endovascular repair require long-term surveillance by means of CT or ultrasonography (at institutions with appropriate expertise), which is recommended at 1 month and 12 months after the intervention and yearly thereafter.²⁵

Patients who have undergone open surgery may also require other surgical interventions for complications related to the procedure, such as ventral hernia or adhesions. In the DREAM and OVER trials, which included assessment of these complications, approximately 20% of patients who underwent open repair required a second operation. In the DREAM trial, a secondary intervention was significantly less common after open repair than after endovascular repair (17% vs. 28%); however, in the OVER trial, there was no significant difference between groups (18% open vs. 22% endovascular). After open repair, CT monitoring for new or recurrent aneurysmal disease is recommended at 5-year intervals.²⁵



AREAS OF UNCERTAINTY

Recent technological advances in endovascular repair have made it an option for a larger proportion of patients; these advances include lower-profile grafts that can traverse diseased iliac arteries, fenestrated grafts (with holes to maintain renal blood flow) that can be used to treat aneurysms near the renal arteries (Fig. S2 in the Supplementary Appendix), and grafts with branches to the mesenteric and renal vessels for repair of suprarenal and thoracoabdominal aneurysms. Evaluation of long-term outcomes is necessary to determine the benefit of these newer strategies. More data are needed to improve the identification of patients most likely to benefit from screening and also from surgical intervention. Measures of wall stress by means of CT or MRI have been proposed to refine prediction of the risk of rupture, but further study is needed to determine whether these tests are warranted and if so, when they should be performed.⁴⁸ Randomized trials are in progress to determine whether doxycycline or other pharmacologic therapies can reduce or prevent the growth of aneurysms.

GUIDELINES

Guidelines have been published regarding screening, surveillance, and treatment of abdominal aortic aneurysms; however, there are inconsistencies, as described in this review. Recommendations that are consistent include screening at least once in men 65 to 75 years of age who have ever smoked and repair of aneurysms with an aortic diameter of 5.5 cm or larger in patients with an acceptable risk.^{20,25,26,49}

CONCLUSIONS AND RECOMMENDATIONS

The woman described in the vignette has lower abdominal pain and a 5.6-cm infrarenal aneurysm. It is essential to prove that the aneurysm is not the cause of her abdominal pain. The patient should be treated with antibiotics for diverticulitis and followed for pain resolution (which would provide support for this disorder as the cause of the pain). Once the diverticulitis has resolved, the aneurysm should be expeditiously repaired, because the risk of rupture for an aneurysm of this diameter is nearly 10% during the next year. The choice between endovascular repair and open repair should be individualized and made after a thorough evaluation with consideration of anatomy, patient age, preoperative risk, and patient preference. Given this patient's age and obesity, I would recommend endovascular repair over open surgery if her anatomy is appropriate. After endovascular repair, the graft should be monitored at 1 month and 12 months and on a yearly basis thereafter. The patient should be counseled to stop smoking and offered smoking-cessation treatment. Furthermore, she should be treated for hypertension and hypercholesterolemia, especially because patients with either or both of these conditions are at increased risk for other cardiovascular events.

Dr. Kent reports receiving consulting fees from Medtronic and holding a patent on methods for treating aneurysms. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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