INVITED COMMENTS

The United Kingdom Small Aneurysm Trial: Implications for surgical treatment of abdominal aortic aneurysms

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The optimal management of small abdominal aortic aneurysms (AAAs) is controversial. Some recommend early surgery, and others recommend ultrasound scan surveillance unless a larger threshold size is reached or rapid expansion occurs. For this reason, the recent publication of the results of the United Kingdom Small Aneurysm Trial (UK Trial) has been eagerly awaited.[1] Initially, some vascular surgeons may find its results disquieting. No survival rate advantage could be shown for early surgery in patients with nontender 4.0-cm to 5.5-cm diameter AAAs in comparison with patients who were followed with serial ultrasound scan surveillance until the aneurysm enlarged to greater than 5.5 cm or was considered to be symptomatic. After the randomization of 1090 patients aged 60 to 76 years with a mean aneurysm diameter of 4.6 cm, the 6-year life-table survival rate was remarkably equivalent at 64% in both groups. This was caused, in part, by a higher than expected elective operative mortality rate of 5.8%, which offset a small reduction in rupture risk and late mortality rates in the surgical group. As expected, a large number of patients (61%) who were initially in the surveillance group underwent AAA repair during the follow-up period because of AAA expansion or symptoms.

By all standards, this is a well-conducted study for which the UK Trialists deserve congratulations. As with any large multi-centered study involving the care of real patients, some problems are expected. In this trial, 8% of the patients inappropriately crossed over into the other treatment group, but an analysis of the treatment that was actually received did not alter the conclusions. A more difficult issue is that 20% of the patients in the surveillance group underwent surgery because of "tenderness" of the aneurysm. This is a subjective evaluation that could have introduced a bias by surgeons who had a concern for individual patients. However, aneurysm tenderness, especially if new, is a legitimate indication that could not be avoided. Finally, it is unfortunate that the cause of death was determined with autopsy in only 29% of the deaths because AAA rupture may masquerade as a cardiac event and be undercounted.

The safety of ultrasound scan surveillance was, in part, a result of meticulous follow-up: ultrasound scan studies were performed every 6 months for 4.0-cm to 4.9-cm AAAs and every 3 months for 5.0-cm to 5.5-cm AAAs. Compliance with follow-up in the UK Trial approached 100%, an enviable result that is not likely to be achieved in routine practice unless a computerized follow-up program is instituted and combined with appropriate clinical follow-up to detect the onset of symptoms or a tender aneurysm.

The UK Trial concluded that ultrasound scan surveillance is safe and that open surgical repair for 4.0-cm to 5.5-cm AAAs is not necessary for the average patient in this study. How should these results influence our management of a small AAA? Decision analysis has shown that the proper selection of patients for AAA repair is primarily influenced by the following factors: (1) elective operative risk, (2) aneurysm rupture risk, and (3) life expectancy, in combination with patient preference.[2] Thus, rather than reach a global conclusion concerning the UK Trial, an appropriate response is to consider the application of each of these selection factors to the individual patient.

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J Vasc Surg 1999;29:191-4.

0741-5214/99/$8.00 + 0 **24/39/96141**

1. The elective operative mortality rate of 5.8% in this trial was disappointing and higher than the 2% mortality rate projected in the initial study design.[3] This mortality rate is similar to the overall results of other multi-centered studies, such as the Canadian Aneurysm Study (4.7%),[4] or other population experiences, such as in Michigan (5.6%, in 1990).[5] However, the mortality rate of elective AAA repair has been improving over the past decade: 3.8% in the province of Ontario in 1988 to 1992,[6] and 3% for ages 65 to 69 years and 4% for ages 70 to 74 years in United States Medicare patients in 1995.[7] Had the UK Trial achieved an elective operative mortality rate of 2% to 3%, it is likely that early surgery would have shown a significant benefit. Is it possible to select patients who will have a low operative risk? Multiple algorithms have been suggested to predict cardiac events,[8,9] and a large meta-analysis identified seven prognostic factors that are independently predictive of operative mortality rate after elective AAA repair.[10] The absence of the most important risk factors (renal dysfunction, congestive heart failure, cardiac ischemia, and chronic pulmonary disease) can accurately identify a low-risk group with a predicted operative mortality rate of 2% or less. The operative mortality rate associated with elective AAA repair also is dependent on surgeon and hospital experience and volume. Thus, to predict the mortality risk for individual patients, the surgeon must consider the patient risk factors and have knowledge of the operative results.
2. The rupture risk of 4.0-cm to 5.5-cm diameter AAAs under surveillance in the UK Trial was low—1% per year. Other investigators previously have reported the safety of careful surveillance of small AAAs, with subsequent repair when expansion occurs. With such a strategy in an Ontario population, Brown et al[11] recommended a threshold diameter of 5.0 cm with computed tomographic scan for elective AAA repair because AAA rupture occurred between 5.0 and 5.6 cm during surveillance. Although not statistically significant because of sample size, there was also a trend in the UK Trial to suggest that early surgery was relatively more beneficial in the subgroup of patients with 4.9-cm to 5.5-cm diameter AAAs. It is important to emphasize that AAA rupture was avoided in both of these studies by means of elective repair in approximately 50% of the patients after 3 years. Usually, this resulted from AAA expansion, which averaged 3.3 mm/y in the UK Trial but was 7.0 mm/y in the Ontario trial for 4.5-cm to 5.0-cm AAAs. These results suggest that, for patients with good life expectancy, the issue of small AAA repair is only a question of "when", not "if". In this scenario, patient preferences should be a guiding factor. It is unfortunate that rupture risk of individual AAAs cannot be determined with more precision. Although AAA size and documented expansion are the dominant predictors of rupture, other factors, such as hypertension, chronic pulmonary disease, smoking, family history, and aneurysm morphology, appear to influence outcome and can assist individual patient decision making.[12-15]
3. Elective AAA repair is a prophylactic operation intended to prolong life. Thus, it is ideally applied to patients who have a long life expectancy. Unfortunately, AAAs primarily affect older patients with other comorbidites that shorten life expectancy to approximately 60% after 5 years, as confirmed in the UK Trial. Thus, the optimal selection of patients for AAA repair necessitates an accurate assessment of life expectancy in addition to perioperative risk. On a population basis, age is the best predictor of life expectancy and was a significant predictor in the UK Trial. For an individual patient of a specific age, however, specific comorbidities are equally important. After successful AAA repair, long-term survival is reduced if the patient has coronary artery disease, renal insufficiency, pulmonary insufficiency, hypertension, or peripheral atherosclerosis.[16] The UK Trial found that reduced long-term survival was associated with a lower forced expiratory volume at 1 second and a lower ankle brachial index. Although survival rates are difficult to predict with precision, by evaluating these risk factors in combination with age, it is possible to select a subgroup of patients with small AAAs who have good long term survival and are more likely to benefit from surgery.

In a companion article, the UK Trial analyzed the cost of early surgery versus ultrasound scan surveillance and the associated health-related quality of life.[17] Not surprisingly, the average cost of early surgery was higher, although the cost of ultrasound scan surveillance was ultimately increased by the 60%

of patients who underwent surgery in the surveillance group. Thus, the final cost difference between the two strategies was reduced to approximately $2000. Interestingly, the patients who underwent early surgery reported a positive improvement in current health perception and a less negative change in bodily pain than the patients who underwent surveillance. The impact of these results will necessitate a more formal cost-effectiveness analysis, particularly in the subgroups of patients who might benefit from early AAA repair. Similarly, the potential impact of endovascular AAA repair will depend on the ultimate effectiveness and operative mortality rate of this technique. If the low operative mortality rate (2%) reported in the United States multi-centered trials continues, it is possible that endovascular repair could have a major impact on the conclusions of the UK Trial.[18,19]

Clearly, arbitrarily setting a single threshold diameter for elective AAA repair in all patients is naive. In the subgroup of patients who are younger and healthier or who have additional risk factors for AAA rupture, elective repair at a smaller size (eg, 4.0 to 5.0 cm) is likely to be beneficial if a low operative risk can be ensured. To accomplish this, a careful evaluation of operative risk factors is necessary, which may include a comprehensive analysis of cardiac risk and treatment when indicated. When surveillance is selected as the optimal strategy, follow-up must be meticulous to achieve the admirable results of the UK Trial because half of the patients will likely require elective repair within 3 years.

Despite the results of the UK Trial, the optimal timing of elective AAA repair for individual patients will remain a challenging surgical problem. On the basis of this study, however, the burden of proof is clearly shifted onto the surgeon who recommends early repair, who must assure a low operative mortality rate in these selected patients. Like other previous studies, the UK Trial has established that careful surveillance with timely elective intervention is safe for small AAAs. Because the rupture risk is relatively low for these small AAAs, the operative results must be outstanding to recommend early repair. Vascular surgeons have long realized that surgical decision making for patients with small AAAs is complex and must consider elective operative risk, aneurysm rupture risk, and life expectancy, in addition to patient preferences. The UK Trial has provided additional important data to inform these decisions.

REFERENCES

1. Mortality results for randomised controlled trial of early elective surgery or ultrasonongraphic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial participants. Lancet 1998;352:1649-55.
2. Katz DA, Littenberg B, Cronenwett JL. Management of small abdominal aortic aneurysms. Early surgery vs watchful waiting. JAMA 1992;268:2678-86.
3. The U.K. Small Aneurysm Trial: design, methods and progress. The UK Small Aneurysm Trial participants. Eur J Vasc Endovasc Surg 1995;9:42-8.
4. Johnston KW, Scobie TK. Multicenter prospective study of nonruptured abdominal aortic aneurysms. I. Population and operative management. J Vasc Surg 1988;7:69-81.
5. Katz DJ, Stanley JC, Zelenock GB. Operative mortality rates for intact and ruptured abdominal aortic aneurysms in Michigan: an eleven-year statewide experience. J Vasc Surg 1994;19:804-17.
6. Wen S, Simunovic M, Williams J, Johnston K, Naylor C. Hospital volume, calendar age, and short term outcomes in patients undergoing repair of abdominal aortic aneurysms: the Ontario experience, 1988-92. J Epidemiol Community Health 1996;50:207-13.
7. Finlayson S, Birkmeyer J, Fillinger M, Cronenwett J. Should endovascular surgery lower the threshold for repair of abdominal aortic aneurysms? J Vasc Surg 1999. In press.
8. Eagle KA, Brundage BH, Chaitman BR, et al. Guidelines for perioperative cardiovascular evaluation for noncardiac surgery. Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). J Am Coll Cardiol 1996;27:910-48.
9. Palda VA, Detsky AS. Guidelines for assessing and managing the perioperative risk from coronary artery disease associated with major noncardiac surgery. American College of Physicians. Ann Intern Med 1997;127:309-12.
10. Steyerberg EW, Kievit J, de Mol Van Otterloo JC, et al. Perioperative mortality of elective abdominal aortic aneurysm surgery. A clinical prediction rule based on literature and individual patient data. Arch Intern Med 1995;155:1998-2004.
11. Brown PM, Pattenden R, Vernooy C, Zelt DR, Gutelius JR. Selective management of abdominal aortic aneurysms in a prospective measurement program. J Vasc Surg 1996;23:213-22.
12. Cronenwett JL, Murphy TF, Zelenock GB, et al. Actuarial analysis of variables associated with rupture of small abdominal aortic aneurysms. Surgery 1985;98:472-83.
13. Verloes A, Sakalihasan N, Koulischer L, Limet R. Aneurysms of the abdominal aorta: familial and genetic aspects in three hundred thirteen pedigrees. J Vasc Surg 1995;21:646-55.
14. Strachan DP. Predictors of death from aortic aneurysm among middle-aged men: the Whitehall study. Br J Surg 1991;78:401-4.
15. Vorp DA, Raghavan ML, Webster MW. Mechanical wall stress in abdominal aortic aneurysm: influence of diameter and asymmetry. J Vasc Surg 1998;27:632-9.
16. Cronenwett JL. Factors influencing the long-term results of aortic aneurysm surgery. In: Yao J, Pearce W, editors. Vascular surgery: long term results. East Norwalk, CT: Appleton and Lange; 1993. p. 171-9.

17. Health service costs and quality of life for early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial participants. Lancet 1998;352:1656-60.
18. Goldstone J, Brewster D, Chaikof E, Katzen B, Moore W, Pearce W. Endoluminal repair versus standard open repair of abdominal aortic aneurysm: early results of a prospective clinical comparison trial. Proceedings of the 46th Scientific Meeting of the International Society for Cardiovascular Surgery, North American Chapter; 1998 Jun 7–8; San Diego, Calif.
19. Zarins C, White R, Schwarten D, et al. Medtronic AneuRx stent graft system versus open surgical repair of AAA: multicenter clinical trial. J Vasc Surg 1999. In press.

Submitted Dec 2, 1998; accepted Dec 2, 1998.