INVITED COMMENTARY

Invited Commentary for “From Innumeracy to Insight: The Uncertainty of Help versus Harm in Treatment of Asymptomatic Aortic Aneurysms” by Legemate and Bossuyt

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In the current issue of European Journal of Vascular and Endovascular Surgery, Legemate and Bossuyt claim there is insufficient evidence to support elective repair of asymptomatic AAA 5.5–6.5 cm. Introducing a model is intellectually stimulating and forces analytical thinking. Based on the outcome of their model they conclude that patients may “expect little on longevity while they are at risk of dying from surgery or suffering from serious morbidity”. Consequently, they propose a randomised controlled trial (RCT) to be carried out. Furthermore, they suggest that it is innumeracy, inability to think in numbers, that explains why many surgeons consider that they are offering benefit to their patients by operating them. Although it is important to challenge established concepts and current practice, these are rather provocative statements, and we are grateful for having this opportunity to comment on the paper.

To analyse the uncertainty of help versus harm due to treatment of aneurysms, the authors created natural frequency trees based on assumptions. A model addressing this issue would, however, need to be far more complex. It is our experience, from studying the cost-effectiveness of different models for AAA-screening men1 and women,2 that difference in outcome between simple calculations and a decision analysis model may be significant, affecting conclusions in an unexpected way. A decisional analysis model, such as a Markov model, allows long time periods to be modelled, in which risk and events are continuous. This is particularly important when the timing of an event is uncertain, which is the case of a rupture of an AAA.

Due to the simplicity of the model in the paper by Legemate and Bossuyt, several important variables were not included. For instance, no attempts were made to evaluate the risk of rupture nor the risk of surgery for symptoms or expansion in the surveillance group, nor to extract data on major complication-rates from the literature. One of the main criticisms against the well performed RCTs, comparing watchful waiting with early surgery among patients with small AAAs (4–5.5 cm), was the fact that a large proportion of the patients in the conservative group were operated on.3,4 In the UK Small Aneurysm Trial (UKSAT) 321 of the 527 (61%) randomised to ultrasonographic surveillance had undergone surgery, after a mean follow-up of 4.6 years.3 In the elective surgery group 517 of 563 (92%) underwent elective surgery. Outcome was measured by intention to treat, thus comparing patients operating on in 61% or 92%, respectively. After 6.5 years 74% versus 93% had been operated on, and long-term all cause mortality was better in the early surgery group, 48% vs 43%, \( p = 0.03 \).5 The proportion of patients being operated on is likely to be even higher among patients with AAAs >5.5 cm.

Another important factor not contemplated by Legemate and Bossuyt is that of life expectancy (LE). To restrict the analysis to 5-years survival exaggerates the impact of the perioperative mortality and morbidity, and introduces a bias against surgery. Long-term survival and life-years gained (LYG), that can be negative when lost, are more appropriate outcome measures, preferably using quality-adjusted life-years (QALY). Calculating LYG and QALY balance the

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negative impact of perioperative mortality, especially when young patients with long LE die during this prophylactic operation, against the benefit of decreasing long-term mortality.

LE in Europe is dynamic. Among Swedish men 65 year old, LE increased from 14.65 in 1983 to 18.49 years in 2004. An increase of LE of 3.84 years during 22 years means a gain in LE of 64 days/year. Thus, the 65 year old man reduces his LE with less than 10 months when he becomes 66, and 65 year old women can be expected to become 86. Although survival of patients with AAA is somewhat decreased (≈0.9), they too benefit from this development. The specific LE of patients with AAAs, depending on their gender and age, is not sufficiently studied.

A factor of great importance when evaluating the possible benefit of AAA-surgery is the autopsy-rate. We know that with a low autopsy-rate many patients dying from ruptured AAA will be misclassified as cardiac events. In 2003 only 14% of those who died in Sweden were examined post-mortem, and only 6% in women above 75 years. Any RCT comparing surgery with watchful waiting must include post-mortem examination in a majority of patients, and certainly in the cases where premortal diagnosis is unclear. This issue has not been sufficiently addressed in previous trials.

The natural course of AAA is difficult to study. Information obtained from studies of patients with small AAAs or patients unfit for surgery provide incomplete information, due to differences in the studied populations. In a large cohort of carefully monitored patients from the UKSAT and an associated study, the rupture risk increased sharply for AAAs >5.9 cm. In a study of 198 AAAs >5.5 cm in patients refusing or unfit for elective repair, the annual rupture risk was 10% for AAAs 5.5–6.9 cm and 32% for AAAs >7 cm. In another follow-up study of patients with untreated AAAs >5 cm, the cumulative risk of rupture was 13% at one and 24% at two years. In the classical study by Darling, 50% of all ruptured AAAs found at autopsy were less than 7 cm, but the diameter of AAAs are difficult to estimate at autopsy. Of all ruptured AAAs in the Huntington district, 7.4% were less than 6 cm. The expansion and change in rupture risk over time affect the results substantially, emphasizing the importance of including these factors in a model.

No attempt was done to extract data from the literature in a systematic way. In fact, the assumptions made seem so biased that they only serve to prove the authors hypothesis that surgical treatment is unlikely to have a major effect on survival in patients with AAA. The authors consider 5% mortality and 10% major complication rates associated with asymptomatic AAA surgery. Many centers report mortality-rates <3% after elective surgery. In Sweden 690 elective AAA repairs were performed during 2005 with a mortality of 2.8%, 266 (39%) were EVAR. With the observed low morbidity- and mortality rates achieved by endovascular AAA repair, the assumptions included in the paper are even less realistic and applicable. We do agree with the authors, of course, that patients should be treated in hospitals with very low surgical mortality and major morbidity rates.

The gender aspect is completely missing in the paper by Legemate and Bossuyt. We know from the UKSAT that women in the surveillance group had a three-fold rupture-risk. In the Swedish cause of death registry 30% dying from ruptured AAA are women, but only 15% of those operated on for AAA in Sweden are women, indicating a too low operative activity on women with AAA. Would it really be ethically possible to randomise women to watchful waiting with an AAA above 5.5 cm, when this increased rupture-risk has already been shown? Surgical decision-making in asymptomatic cases is complex. Three key variables have to be considered: elective operative risk, the risk of AAA rupture and life expectancy. In selected cases an AAA diameter of 5–5.5 cm generally justifies elective repair. However, an individual approach is recommended. For older patients and patients with important co-morbidities, the threshold diameter is greater, and up till 25% of the patients are considered unfit for surgery.

The crucial issue when contemplating a RCT is that of equipoise. Given the patient has an AAA of 5.5–6.5 cm, how many vascular surgeons would accept themselves, or would be prepared to counsel their relatives, to be randomised into the trial proposed by Legemate and Bossuyt?

In conclusion, we believe there is enough data to support that elective repair of AAA >5.5 cm is effective in reducing AAA-related death in most patients. We consider a randomised trial unethical in the light of current knowledge. Studies on specific surgical indications on particular subgroups of patients in whom surgical indications are controversial would be more appropriate.

References


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