ESA-RANDOMIZED CONTROLLED TRIAL

Endovascular Repair of Abdominal Aortic Aneurysm in Patients Physically Ineligible for Open Repair

Very Long-term Follow-up in the EVAR-2 Randomized Controlled Trial

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Objective: The aim of the study was to compare long-term total and aneurysm-related mortality in physically frail patients with abdominal aortic aneurysm (AAA) randomized to either early endovascular aneurysm repair (EVAR) or no-intervention.

Summary Background Data: EVAR-2 remains the sole randomized trial to identify whether EVAR reduces mortality in patients physically ineligible for open repair.

Methods: Between September 1999 and August 2004, 404 patients from 33 centers in the United Kingdom aged ≥ 60 years with AAA > 5.5 cm in diameter were randomized 1:1 using computer-generated sequences of randomly permuted blocks stratified by center to receive either EVAR (197) or no-intervention (207). The primary analysis compared total and aneurysm-related deaths in groups until June 30, 2015 (mean, 12.0 yrs; maximum 14.1 yrs).

Results: Mean follow-up until death or censoring was 4.2 years. There were 187 deaths (22.6 per 100 person-yrs) in the EVAR group and 194 (22.1 per 100 person-yrs) in the no-intervention group. By 12 years of follow-up the estimated survival was 5.3% [95% confidence interval (CI), 2.6–9.2] in the EVAR group and 8.5% (95% CI, 5.2–12.9) in the no-intervention group; there was no significant difference in life expectancy between the groups (both 4.2 yrs; $P = 0.97$). However, overall aneurysm-related mortality was significantly lower in the EVAR group [3.3 deaths per 100 person-yrs compared with 6.5 deaths per 100 person-yrs in the no-intervention group, adjusted hazard ratio 0.55 (95% CI, 0.34–0.91; $P = 0.019$)]. Patients surviving beyond 8 years were younger, with higher body mass index, estimated glomerular filtration rate, and forced expiratory volume in 1 second.

Conclusions: EVAR does not increase overall life expectancy in patients ineligible for open repair, but can reduce aneurysm-related mortality.

Keywords: elective abdominal aortic aneurysm repair, patients physically ineligible for open abdominal aortic repair, the use of endovascular aneurysm repair (EVAR) in unfit patients

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In the 1990s endovascular aneurysm repair (EVAR) was introduced and was originally developed for patients who were considered to be physically ineligible for open surgical repair of abdominal aortic aneurysm (AAA). EVAR-1,¹ the first multicenter randomized trial of EVAR versus open repair, began in 1999 in the United Kingdom. This was soon followed by the DREAM² and ACE³ multicentre trials in Europe, and the OVER trial⁴ in the USA. These randomized, controlled trials enrolled physically fit patients able to undergo either EVAR or open repair. EVAR-2 patients were too high risk for open repair, so randomized to EVAR or no-intervention. EVAR-2 remains unique in this regard.

Results up to 4 years of follow-up, reported in 2005,⁵ showed no benefit of endovascular repair on total or aneurysm-related mortality. This was from the higher than expected operative mortality after endovascular repair of 8.7% which was considerably higher than that reported among patients in the EVAR-1 trial (1.8%). Overall mortality was 68% at 4 years. Longer-term results up to 10 years of follow-up, reported in 2010, showed that EVAR was associated with a significantly lower rate of aneurysm-related mortality than no-intervention.⁶ However, EVAR was not associated with a reduction in the rate of death from any cause. The rates of graft-related complications and reinterventions were also higher with endovascular repair.

After 5 and 10 year results of EVAR-2 were known,^{5,6} it has become increasingly recognized that there is a cohort of patients who either have such a limited life expectancy or such extensive comorbidities that repair of an AAA should not be considered.^{7,8} However, concern of rupture remains. In a review of 1514 patients from 11 studies experiencing 347 ruptures, Parkinson et al⁹ reported a cumulative yearly rupture rate of 3.5% (AAA 5.0–6.0 cm), 4.1% (AAA 6.1–7.0 cm), and 6.3% (AAA > 7.0 cm).

De Martino et al¹⁰ have reported on 309 of 1653 patients with AAA < 6.5 cm deemed unfit for open repair and questioned how to determine whether patients unfit for open repair should undergo any repair at all. Even those who favor EVAR agree that EVAR does not benefit all high-risk patients.¹¹ In the EVAR-2 trial, the participating clinicians seemed to have had good judgment in selecting patients for this trial: by 4 years $< 40\%$ of patients remained alive and by 8 years this had reduced to $< 20\%$.⁶ Nevertheless, approximately 20% of patients who remain alive after 8 years were perhaps physically the fittest of all the patients enrolled in the EVAR-2 trial and it is of interest to compare their very long-term survival both by intention-to-treat and per-protocol analysis. This starts to enable description of the patients who, although physically frail and ineligible for open repair, may have many life years ahead and might benefit from EVAR, particularly if conducted under local anesthesia. Such information could be important for updating the guidelines for the management of physically frail patients with large aneurysms.

METHODS

Between September 1, 1999 and August 31, 2004, 404 patients were recruited from 33 hospitals in the United Kingdom to participate in EVAR trial 2. Patients of both sexes who were at least 60 years of age with large aneurysms (≥ 5.5 cm in diameter) and deemed physically ineligible for open repair, according to specified criteria,¹² were randomly assigned (1:1) to undergo either endovascular repair or no-intervention. Randomization was conducted using computer-generated sequences of randomly permuted blocks stratified by center at the trial hub (Charing Cross Hospital). There was no blinding, and patients and treating clinicians were aware of group assignment. A total of 197 patients were assigned to the endovascular group, and 207 were assigned to the no-intervention group.

Ethical approval was obtained for the extended patient follow-up after September 1, 2009, from the UK North West Multicentre Research Ethics Committee, which did not require patients to provide consent again for the ongoing follow-up of the EVAR trial 2 between September 2009 and June 2015, up to 15 years after first randomization. Patients were followed for mortality until June 30, 2015 by record-linkage, with regular reports from NHS Digital (<https://www.digital.nhs.uk/>).

The procedures used have been previously described including how fitness for open repair was defined.^{6,12} The “traffic light” system was defined. Cardiac, respiratory, and renal function questions helped classify into RED—failure to be considered suitable for any procedure at that time based on cardiac factors; AMBER—failure to satisfy criteria for open repair but possibly suitable for EVAR trial 2; GREEN—suitable for open or EVAR repair. Participating trial centers were reminded that all patients should continue in regular follow-up (the protocol specified annual follow-up) and all patients, including those with lapsed follow-up, should be recalled for a final clinical and imaging follow-up in 2014. The maximum aortic or sac diameter and the presence of complications were recorded at each patient follow-up. The trial protocol specified annual follow-up for clinical and imaging assessment and serum creatinine concentrations. The management of aneurysm-related complications was left to the discretion of the trial center. The Trial Endpoint Committee adjudicated the cause of death, aneurysm-related mortality, and other events based on International Classification of Diseases (version 10) causes listed and dates of aneurysm-related reinterventions: this committee was unaware of study group assignment.

The primary outcomes for this trial were total and aneurysm-related mortality. Aneurysm-related mortality was defined as all deaths from aneurysm rupture before repair, within 30 days of the primary procedure, within 30 days of any reintervention attributable to the aneurysm, from other aneurysm-related causes (including graft infection or fistula), or from secondary aneurysm rupture after repair. Secondary outcomes included rate of reintervention in each group. Patients were followed up for graft-related complications and reinterventions from September 1, 1999 to December 31, 2014. Graft-related reinterventions between September 1, 2009 and December 31, 2014 were directly obtained from the trial centers.

Statistical Methods

As of September 1, 2009, there were 96 patients with an average age of 82 reported alive and under follow-up in the EVAR trial 2 (50 and 46 in the EVAR and no-intervention groups, respectively). This gave 80% power at the 5% significance level to detect a hazard ratio of 1.83 during the extended follow-up period in EVAR-2, assuming 10% to be still alive at the end of June 2015.

All analyses were performed according to a predefined statistical analysis plan and were based primarily on the intention-to-treat

principle, with outcomes assessed from the time of randomization. The criteria used to censor individuals are provided in the appendix. Cox-regression modeling was used to compare total mortality, aneurysm-related mortality, and graft-related reinterventions, the latter analyzed using a repeated-measures Cox model.¹³ Crude regression estimates were presented as well as ones adjusted for 2 sets of baseline covariates: primary adjustment for age, sex, aneurysm diameter, forced expiratory volume in 1 second (FEV₁), log(creatinine), and statin use; secondary adjustment for the primary covariates as well as body mass index (BMI), smoking status (current, past, and never), systolic blood pressure, and serum cholesterol. For the graft-related reintervention analysis, additional secondary adjustment was made for top neck aortic diameter at the level of the lowest renal artery, neck length (distance between the lowest renal artery and the start of the aneurysm), and common iliac diameter (largest of both legs). The primary and secondary adjustment results were very similar, and the latter are reported. Baseline data were almost complete with 92% of patients in EVAR-2, having a complete set of covariates for the adjusted analyses. Hazard ratios were presented as the EVAR group relative to no intervention. Owing to nonproportional hazards during the first 8 years of follow-up⁶ data were analyzed by splitting follow-up into 4 time periods: Randomization to 6 months, 6 months to 4 years, 4 to 8 years, beyond 8 years. Deviations from the proportional hazards assumption were assessed overall and within these periods by regressing scaled Schoenfeld residuals against log of time. Regression estimates are presented both unadjusted and adjusted for baseline covariates. Kaplan–Meier estimates were used to show survival probabilities up to 15 years in each group. Tests of interaction were performed for total and aneurysm-related mortality between randomized group and prespecified subgroups sex, age, and aneurysm diameter. Further exploratory analyses also assessed any effect modification associated with BMI, percent predicted FEV₁ (FEV₁% predicted), and estimated glomerular filtration rate (eGFR). Age, aneurysm diameter, BMI, % predicted FEV₁ and eGFR were kept as continuous variables for testing for an interaction effect.

As a reasonable proportion of individuals in the no intervention group received EVAR during the course of follow-up, 2 additional analyses were conducted: (1) a per-protocol analysis whereby individuals were censored at the time that they deviated from protocol; (2) a causal estimate^{14,15} of the efficacy of EVAR versus no-intervention that avoids potential selection biases seen in a per-protocol analysis (see supplementary material for further details of these analyses, <http://links.lww.com/SLA/B289>). In particular, it was previously found that patients in the no-intervention group who switched to EVAR were significantly more fit at baseline than patients assigned to EVAR who underwent repair,⁶ hence potentially favoring EVAR in a per-protocol analysis.

All analyses were carried out in Stata version 13 (StataCorp, TX). The Data Monitoring and Ethical Committee approved the statistical analysis plan.

RESULTS

Between September 1, 1999 and August 31, 2004, 404 patients were recruited to participate in EVAR trial 2. A total of 197 patients were randomly assigned to the endovascular group, and 207 were assigned to the no-intervention group. There were no significant differences between the 2 groups with respect to baseline characteristics, mean age 76.8 years, 347 (86%) were men (Table S1 supplement, <http://links.lww.com/SLA/B289>). At September 1, 2009, 51 of 197 patients were known to be alive in the EVAR group and 46 of 207 patients in the no-intervention group and 1 patients had been lost to follow-up for mortality. By December 31, 2014, 53 patients (31 of 50

FIGURE 1. CONSORT diagram for survival and clinical follow-up in EVAR trial 2 (per protocol patients marked with an asterisk*).

in the EVAR group and 22 of 46 in the no-intervention group) had no further clinical follow-up. By June 30, 2015, no further patients had been lost to follow-up for mortality. A total of 179 patients in the EVAR group and 71 patients in the no-intervention group underwent repair during follow-up. The mean (max) time to repair was 2.2 (14.6) months in the EVAR group and 15.7 (66.5) months in the no-intervention group. The CONSORT diagram is shown in Figure 1.

Total Mortality and Aneurysm-related Mortality

Patients were followed for mortality until June 30, 2015 (mean 12.0 yrs, median 12.2 yrs); mean follow-up to either death or censoring was 4.2 years. During 1707 person-years of follow-up 381 deaths occurred, 84 of which were aneurysm-related.

For total mortality, there were 22.6 deaths per 100 person-years in the EVAR group and 22.1 deaths per 100 person-years in the no-intervention group (Table 1). Beyond 8 years the number of

TABLE 1. Deaths from Any Cause and Aneurysm-related Causes, According to Time Since Randomization

	Endovascular Repair (N = 197)	No Repair (N = 207)	Hazard Ratio (95% CI)		P*
	No./Total No. (Rate/100 Person-yrs)	No./Total No. (Rate/100 Person-yrs)	Unadjusted	Adjusted†	
Any death					
All patients	187/197 (22.6)	194/207 (22.1)	1.03 (0.84–1.26)	1.07 (0.86–1.34)	0.52
Time since randomization					
0–6 mo	24/197 (26.0)	19/207 (19.0)	1.38 (0.76–2.52)	1.32 (0.68–2.54)	0.41
>6 mo–4 yrs	92/173 (21.4)	108/188 (23.6)	0.90 (0.69–1.20)	1.02 (0.75–1.37)	0.92
>4–8 yrs	49/81 (21.7)	42/80 (19.7)	1.11 (0.73–1.67)	0.96 (0.61–1.51)	0.85
>8 yrs	22/31 (27.5)	25/38 (23.2)	1.20 (0.67–2.12)	1.15 (0.60–2.21)	0.68
Aneurysm-related death					
All patients	27/197 (3.3)	57/207 (6.5)	0.50 (0.32–0.80)	0.55 (0.34–0.91)	0.019
Time since randomization					
0–6 mo	15/197 (16.3)	9/207 (9.0)	1.82 (0.80–4.16)	1.78 (0.75–4.21)	0.19
>6 mo–4 yrs	10/173 (2.3)	35/188 (7.6)	0.31 (0.15–0.62)	0.34 (0.16–0.72)	0.0050
>4 yrs	2/81 (0.7)	13/80 (4.0)	0.16 (0.03–0.69)	0.17 (0.04–0.84)	0.030

*P value adjusted for covariates.

†Hazard ratios adjusted for age, sex, maximum aneurysm diameter, FEV₁, log creatinine, statin use, BMI, smoking status, systolic blood pressure, and total cholesterol (34 individuals excluded due to missing data).

deaths and mortality rate was similar between the 2 randomized groups. By 12 years of follow-up, the estimated survival was 5.3% [95% confidence interval (CI), 2.6–9.2] in the EVAR group and 8.5% (95% CI, 5.2–12.9) in the no-intervention group (Fig. 2). There was no significant difference in life expectancy (restricted to 12 yrs of follow-up) between the groups (4.2 yrs in both the EVAR and the no-intervention groups; $P = 0.97$).

Overall, the rate of aneurysm-related mortality was 3.3 deaths per 100 person-years in the EVAR group and 6.5 deaths per 100 person-years in the no-intervention group, adjusted hazard ratio 0.55 (95% CI, 0.34–0.91; $P = 0.019$) (Table 1). Beyond 8 years of follow-up, there were few aneurysm-related deaths, 2 in the EVAR group (at 8.0 and 13.2 yrs after

randomization) and 1 in the no-intervention group (at 9.3 yrs after randomization) with survival curves remaining parallel (Fig. 2). However, at 8 years only 9 of 38 patients in the no-intervention group remained with an intact unrepaired aneurysm versus 0 of 31 in the EVAR group.

Deaths according to time since randomization and cause of death are shown in Table 2. Overall, there were 16 deaths from aneurysm rupture in the EVAR group (13 primary and 3 secondary ruptures) and 54 in the no-intervention group (53 primary and 1 secondary rupture). Respiratory deaths in the EVAR group were more than double those in the no-intervention group (47 vs 18), and were higher in every period of follow-up (Table S2 supplement, <http://links.lww.com/SLA/B289>).

FIGURE 2. Kaplan–Meier estimates for total survival and aneurysm-related survival up to 12 years of follow-up. Twelve-year survival probabilities are reported.

TABLE 2. Deaths According to Time Since Randomization

	EVAR	No Repair
Any death	187 (94.9%)	194 (93.7%)
Time of death		
Randomization to 6 mo	24 (13%)	19 (10%)
6 mo–4 yrs	92 (49%)	108 (56%)
4–8 yrs	49 (26%)	42 (22%)
Beyond 8 yrs	22 (12%)	25 (13%)
Cause of death		
AAA related	27 (14%)	57 (29%)
Procedure-related AAA	11 (6%)	3 (2%)
AAA rupture	13 (7%)	53 (27%)
Secondary AAA rupture	3 (2%)	1 (1%)
Coronary heart disease	45 (24%)	60 (31%)
Stroke	4 (2%)	5 (3%)
Other (incl. PAD)	3 (2%)	3 (2%)
Cancer, lung	13 (7%)	8 (4%)
Cancer, other	27 (14%)	20 (10%)
Respiratory	47 (25%)	18 (9%)
Renal	3 (2%)	4 (2%)
Other	18 (10%)	15 (8%)
Unknown	0 (0%)	4 (2%)

Further analysis was carried out to compare baseline characteristics between those who did not survive >8 years and the 69 (17%) who did (Table 3). The patients who survived >8 years were younger, with higher BMI, higher eGFR, and better lung function than patients who survived <8 years. There was also a small difference in aneurysm diameter, with slightly smaller aneurysms in the long-term survivors, but this effect diminished once adjusted for the other predictors in a multivariate model.

There was no evidence of any significant interactions with randomized group for either total or aneurysm-related mortality,

except for a weak suggestion (not significant after Bonferroni correction) that patients with higher eGFR benefitted more from EVAR than no intervention, although this benefit was not seen for total mortality (Table S3 supplement, <http://links.lww.com/SLA/B289>).

The hazard ratios for total and aneurysm-related mortality reduced (in favor of EVAR) when considering a per-protocol analysis. However, the causal analysis gave results similar to an intention-to-treat analysis, suggesting that EVAR is effective at reducing the rate of aneurysm-related deaths, but not the rate of deaths from any cause (Table S4 supplement, <http://links.lww.com/SLA/B289>).

Aneurysm-related Reinterventions

During 1485 person-years of follow-up 54 graft-related reinterventions were performed in 38 patients in the EVAR group and 21 graft-related reinterventions performed in 15 patients in the no-intervention group (Table S5 supplement, <http://links.lww.com/SLA/B289>). There was a significantly higher rate of reinterventions in the EVAR group in the 6 months following randomization (Table S6 supplement, <http://links.lww.com/SLA/B289>). Beyond 4 years the rate of reintervention was similar between the 2 groups, although after 8 years a substantial number of patients were lost to further clinical follow-up.

DISCUSSION

Very long-term follow-up of EVAR-2 patients indicates that although some patients (<10%) survive to 12 years, either with or without aneurysm repair, the majority of EVAR-2 patients had a limited life expectancy and hence at no time does aneurysm repair confer an overall survival benefit. Interpretation from the earlier results of this trial that for these patients it is better to take time to optimize patient fitness before considering EVAR continues to hold up. This is supported by recent work from Scott et al,¹⁶ showing that

TABLE 3. Comparison of Baseline Characteristics for those Individuals who Survived ≥8 Years after Randomization Versus those who did not in EVAR Trial 2

Baseline Characteristic*	Did Not Survive >8 yrs (N = 334)	Survived >8 yrs (N = 69)	P	
			Univariate†	Multivariate‡
Age (yrs)	77.2 (6.6) [0]	74.9 (6.1) [0]	0.0049	0.013
No. of males (%)	287 (86) [0]	60 (87) [0]	0.82	–
AAA diameter (cm)	6.7 (1.0) [0]	6.6 (1.2) [0]	0.028	0.12
Body Mass Index (kg/m ²)	26.2 (4.7) [2]	27.8 (4.8) [0]	0.010	0.017
Diabetes (%)	47 (14) [3]	12 (18) [1]	0.47	–
Smoking status (%)	[0]	[0]	0.96	–
Current	58 (17)	12 (17)		
Past	255 (76)	52 (75)		
Never	21 (6)	5 (7)		
History of cardiac disease§ (%)	233 (70) [0]	52 (75) [0]	0.35	–
Systolic blood pressure (mm Hg)	139 (21) [0]	139 (24) [0]	0.91	–
Diastolic blood pressure (mm Hg)	79 (12) [3]	80 (12) [0]	0.41	–
Ankle-brachial pressure index (mean of both legs)	0.98 (0.20) [24]	1.01 (0.21) [1]	0.52	–
FEV ₁ (% predicted)	63.6 (26.1) [12]	70.1 (24.1) [1]	0.06	0.0038
eGFR¶	57 (21) [1]	63 (17) [1]	0.0084	0.0043
Serum cholesterol (mmol/L)	4.8 (1.1) [19]	4.8 (1.3) [1]	0.99	–
Statin use (%)	138 (41) [1]	30 (43) [0]	0.76	–
Aspirin use (%)	186 (56) [1]	41 (59) [0]	0.59	–

*Continuous variables presented as mean (SD). Categorical variables presented as number (%). Data in squared brackets indicate number of patients with missing data.

†P value calculated from a Wilcoxon rank-sum nonparametric test for continuous variables and a χ^2 test for categorical variables.

‡P value calculated from a multivariate logistic regression model including predictors significant at $P < 0.10$ in univariate analyses.

§Cardiac disease defined as previous history of any of the following: myocardial infarction, angina, cardiac revascularization, cardiac valve disease, significant arrhythmia, or uncontrolled congestive cardiac failure.

¶eGFR calculated by the abbreviated MDRD equation: $186 \times (\text{Creat}/88.4) - 1.154 \times (\text{Age}) - 0.203 \times (0.742 \text{ if female})$. Units mL/min/1.73 m².

patients with aneurysms between 5.5 and 7.0 cm, who were not recommended for immediate repair had a low rate of aneurysm rupture, leaving sufficient time for the optimization of patient fitness before delayed repair. By the end of patient follow-up, 71 of 207 (34%) patients assigned to no-intervention had undergone aneurysm repair, some many years after randomization. Over 12 years of follow-up there was no difference in either survival or average life years between the randomized groups.

Comparison of baseline characteristics for patients, intervention or not, who survived >8 years, shows they were younger, with higher BMI, higher eGFR, and better lung function.

By intention-to-treat, causal and per-protocol analysis, aneurysm-related mortality was lower for EVAR, especially in the per-protocol analysis. However, it has already been reported that cross-over patients who received EVAR were fitter at that time than those who had EVAR at baseline.⁶

There are several limitations to this very long-term follow-up. First, the trial has been criticized for the considerable number of the no-intervention group who did eventually undergo aneurysm repair, even very late after randomization (crossovers), potentially diluting any effect of EVAR when comparing groups as randomized. However, a causal analysis (which only considers patients who complied with their treatment allocation) estimates that there was no benefit of EVAR in reducing the total mortality rate. Second, the proportion of patients still alive after 8 years was small, and although there was no evidence of a benefit of EVAR in these surviving patients, the small sample and considerable crossover by this time means that this evidence is less robust. Third, today's practice includes improved devices and epidural anaesthesia is performed in most cases, not a minority (47%). Indication for reintervention for various endoleaks, kinking, and migration has altered substantially over the EVAR trial years. If patients had been randomized today, they might have had different aneurysm-related outcomes. Fourth, in the very long-term follow-up a significant proportion of patients were lost to clinical follow-up at the original trial centers, which could have led to the under-reporting of both late complications, reinterventions, and aneurysm-related mortality, particularly in those who had undergone aneurysm repair. Moreover, in those patients who underwent endovascular repair (including those in the no-intervention group), it is probable that reinterventions may not have been performed due to physical frailty. In contrast, the strengths of this study include the complete long-term follow-up of the cohort for total mortality covering the full life span of the majority of patients and new insights from a supporting causal analysis. The trial highlights the fact that the patient population had high comorbidities and all-cause mortality is the dominant driver in the patient population.

In summary, in very long-term follow-up of patients ineligible for open repair in the EVAR-2 trial, EVAR did not increase overall life expectancy but did reduce aneurysm-related mortality.

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DISCUSSANTS

First Discussant: Anders Wanhainen (Uppsala, Sweden):

I would like to congratulate Professor Greenhalgh and the UK EVAR trial investigators for their pioneering work. The introduction of EVAR has revolutionized aortic surgery. The RCT EVAR-1 and its followers, comparing standard open repair with EVAR, from the basis of today's knowledge and have had a fundamental impact on current practice.

The EVAR-2 trial has been less influential, but is unique in that it is the only RCT evaluating the patients for whom EVAR originally was designed, that is, the frail patients not suitable for open surgery. Why do you think the EVAR-2 trial has not been as influential on clinical practice as other RCTs in this field?

During 15 years that have passed, procedure- and device-related factors have evolved substantially. Some examples include the increasing use of local anesthesia for EVAR, less reinterventions for type II endoleaks, and availability to conformable stent graft system with active fixation, as well as more advanced imaging systems for preplanning and EVAR performance. I wonder, how should we interpret the long-term results from the EVAR-2 trial in view of on today's practice?

I would like to thank the society for providing me with the manuscript and the privilege of discussing this article.

Response From Roger Greenhalgh (London, United Kingdom):

First of all, let me congratulate you Professor Wanhainen on your membership of this distinguished European Surgical Association. Thank you for your generous comments.

Very late follow-up of the EVAR-1 trial has underlined the strengths and weaknesses of endovascular repair against open repair and has sparked great interest. However, 5-year-follow-up results of EVAR-2 in the Lancet (2005) reported that all-cause mortality was not improved by EVAR, confirmed after 10 and 15 years. Almost overnight endovascular repair was no longer performed for EVAR-2 patients. So, from that point of view, the EVAR-2 saved a lot of unnecessary operations and I regard that as very influential. I would add that, at 15 years, aneurysm-related mortality is improved by EVAR very clearly and it will be interesting to see if this encourages EVAR use for EVAR-2 type patients.

You are right. With today's practice, there could be different results. There are newer devices but no evidence that they will

themselves change outcomes but they may. I do not think it is a matter of just expecting the manufacturers to make a better device. It is also the responsibility of the surgeons working with radiologists or having the skills to select the right device for the right aorta. Therefore as you say the imaging is improving and that could give better results but the main reason for failure in EVAR-1 was the failure to follow-up. The surgeons backed off and did not follow the patients and reinterventions were not performed. That could apply for EVAR-2 although we do not have the data. Therefore you are perfectly right, in my view, that endovascular repair is an evolving technique and it could have different results in the future.