9

A Prospective Clinical Economic and Quality of Life Analysis of Open Repair, Endovascular Aortic Repair and Best Medical Treatment in High Risk Patients with AAA

Sherif Sultan and Niamh Hynes
Western Vascular Institute, University College Hospital Galway and Galway Clinic Ireland

1. Introduction

There is consensus that endovascular aneurysm repair (EVAR) offers several benefits when compared to open repair of abdominal aortic aneurysm (AAA). Although originally introduced for patients considered unfit for major surgery. (Parodi, 1991) EVAR has been used increasingly in patients judged fit for open repair (OR). Results of randomized trials demonstrated that the 30-day mortality in such patients is 2%. (EVAR trial 1 participants, 2005; Prinssen 2004)

The results of the EVAR-2 trial stunned the vascular community. The high mortality rates (9% at 30 days and 64% at 4 years) in the EVAR arm elicited trepidation that the minimally invasive approach may afford no benefit compared with the natural history of untreated AAAs in high-risk patients. (EVAR trial 2 participants, 2005) However, subsequent data from the Society for Vascular Surgery (SVS) Lifeline Registry (Sicard, 2006) and the Veterans Affairs National Surgical Quality Improvement Program (Bush, 2007) have shown that EVAR benefits many patients who fulfilled the EVAR-2 high-risk criteria by curtailing perioperative sequelae.

All of these published studies used objective endpoints of morbidity and mortality. However, in a high-risk cohort, the issue of quality of life in terms of years gained needs to be addressed, as well as the broader issue of the cost to society. There are also questions as to which patients are going to die from something else before they benefit from the aneurysm repair, which patients should not be treated, and what happens to patients who choose non-interventional management. These are complex issues, so it is necessary to approach optimizing AAA treatment of high-risk patients from a number of perspectives. Clinically, we need to verify the efficacy and safety of each treatment option and identify if a subgroup exists in which repair poses more of a risk than a benefit. Secondly, from the patient's viewpoint, what price is he/she willing to pay for quality of life? Finally, how much is the healthcare system keen to invest for optimal AAA treatment?

The aim of our study was to scrutinize EVAR as a feasible treatment option for high risk patients and elucidate whether it can enhance survival and quality of life in a cost-effective manner.

2. Methods

2.1 Study design

In 2002, a prospective study was designed to compare EVAR to open repair or best medical therapy (BMT) in high-risk AAA patients with aneurysms deemed suitable for EVAR. Patients with AAAs >4.5 cm on the initial duplex ultrasound had computed tomographic angiograms (CTA), which were scored for anatomical severity and EVAR suitability using guidelines from the Society for Vascular Surgery/American Association for Vascular Surgery (SVS/ AAVS). (Chaikof, 2002) Based on these recommendations, patients were assigned co-morbidity scores and classified as high risk if they were >60 years old and had at least one of the following co-morbidities:

- symptomatic congestive heart failure,
- valvular heart disease,
- cardiac arrhythmia,
- chronic obstructive pulmonary disease, or
- chronic kidney disease (kidney damage, a glomerular filtration rate,60 mL/min/1.73 m2 for 3 or more months regardless of the underlying etiology, or serum creatinine .200 mmol/L).

The decision on the management modality took into consideration life expectancy, operative risk, and risk of rupture, (Dorros, 1997; Sultan , 2001) but the ultimate decision was made by the patient after an adequate understanding of each procedure's risks and benefits had been discussed with the patient, the family, and the primary care physician.

Eligible patients electing BMT received a statin, a cardioselective beta-blocker, aspirin (300 mg/d), and clopidogrel (75 mg/d). Patients opting for intervention were also prescribed this pharmacological combination; however, clopidogrel was introduced only postoperatively. (Oaikhinan, 2004).

It is our policy that once a patient is deemed very high risk for elective AAA repair, the risk of survival following emergent repair does not warrant an attempt at surgery. Therefore, once a decision not to operate was taken, a red label was placed on the patient's hospital chart indicating that a decision not to operate had been made should the patient present to our Accident and Emergency Department with rupture. (Hynes, 2005)

2.2 Patient enrollment

Between January 2002 and January 2007, 1083 patients were referred to our tertiary care university center for evaluation of their aortic disease. Of these, 162 patients (119 men; mean age 76 years) were classified as high risk and had aneurysms anatomically suitable for EVAR. Fifty-two patients (36 men; mean age 74.6+/-7.3 years) had open repair, 66 (52 men; mean age 72.6+/-6.3 years) underwent EVAR, and 44 (31 men; mean age 80.9+/-6.7 years) were managed medically. All patients had the treatment that was originally decided upon.

All patients were classified as ASA (American Society of Anesthesiologists) III or IV; more than half (54%) of the OR group were ASA IV compared to 62% of the EVAR group and 80% of the non-operative group.

2.3 Follow-up protocols

EVAR patients had a plain abdominal radiograph (anteroposterior and lateral views) and color duplex ultrasound prior to discharge. They had a repeat color duplex ultrasound and

radiograph at 6 weeks, 3 months, 6 months, and 6-month intervals thereafter. CT scans were performed at 6 months and then yearly, unless there was evidence of sac expansion or substantial endoleak on duplex ultrasound or migration was noted on the radiograph.
Following open repair, patients were seen at 6 weeks, at 6-month intervals for 18 months, and yearly thereafter. OR patients had clinical examination and ankle-brachial index measurements at 6 weeks and clinical examination at subsequent visits. Duplex ultrasound or CT examination was performed if clinically indicated or the patient became symptomatic. BMT patients were followed at 6-month intervals with color duplex ultrasound at each visit.

2.4 Endpoints

The primary clinical endpoint was survival without aneurysm-related death. Cause of death was obtained from primary healthcare physicians if the death occurred outside our hospital or from medical records if the death occurred in hospital. All ruptures were confirmed by CT and/or autopsy. Secondary endpoints were freedom from all-cause mortality, secondary intervention, and major adverse clinical events (death, myocardial infarction, major amputation, cerebrovascular accident, respiratory morbidity requiring reintubation with/without tracheostomy, or renal failure requiring dialysis).
The two quality-of-life endpoints were cost per QALY (quality-adjusted life years) and TWIST (time spent without symptoms of disease and toxicity of treatment), a special QALY endpoint incorporating both length and quality of life. (Gelber, 1989) TWIST was useful for treatment comparison by compensating for situations when differences in aneurysm-related mortality were statistically significant but overall survival differences were not, since it acknowledges that extensions to disease-free time may be at the expense of treatment toxicity. To integrate quality and quantity of life, the quality-adjusted time with and without symptoms or toxicity (Q-TWIST) was used as a natural extension of the quality-of-life– oriented TWIST endpoint. QTWIST was an adaptation of the concept of QALYs; the methodology was extended so that periods spent with toxicity or relapses were included in the analysis but weighted to represent their quality value relative to TWIST. This allowed us to look at the intervention and the health effects persisting beyond the perioperative period.
In this study, the Q-TWIST was the sum of the quality-adjusted time (u) spent undergoing treatment and experiencing toxicity (TOX, i.e., hospital stay associated with the primary intervention including perioperative morbidity and mortality) plus the time spent free of disease in perfect health (TWIST), plus the time spent experiencing symptoms of disease relapse (REL, i.e., hospital stay associated with any secondary intervention including perioperative morbidity and mortality). In the formula for Q-TWIST (utTOX + TWIST + urREL), the utility values ut and ur associated with the periods of survival for both EVAR (ut50.7, ur50.7) and open repair (ut50.56, ur50.7) were based on sensitivity values from the Interim Report on the Cost-Effectiveness of Elective Endovascular Repair Compared to Open Surgical Repair of Abdominal Aortic Aneurysms prepared for the Ontario Ministry of Health and Long-term Care. (Bowen, 2005) The quality adjusted time utility for the BMT group in this study was u50.56.

2.5 Statistical analysis

The anatomical severity scores were correlated with technical success, endoleak rate, migration, conversion rate, and the need for secondary intervention. Prediction of

perioperative outcome was assessed using the Kertai customized probability model based on a combination of clinical predictors, type of vascular surgery, and concomitant medication use. (Kertai, 2005)

Cumulative rates for survival without aneurysm-related or all-cause death were estimated using Kaplan-Meier analysis; curves were compared using the log-rank test. Due to the risks of informative censoring and biased Kaplan-Meier estimates of the survival function, a partitioned survival analysis was performed.(Glasziou, 1998) Overall survival was partitioned into the time spent in each health state, i.e., time spent without symptoms or toxicity from treatment was separated from time spent with toxicity of treatment and with secondary intervention. The mean duration in each state for each group was combined as a weighted sum according to the Q-TWIST model. Weighting the time spent in each health state at the group level, rather that at the individual level, avoided the need to weigh censored survival times and thus overcame the problem of informative censoring. Kaplan-Meier survival curves corresponding to each transition time were overlaid on one graph to show the partitioning of overall survival. The upper time limit for the analysis, 48 months, was based on the follow-up time of the study cohort and was chosen to reduce censoring.

The influence of co-morbid factors on outcome was determined using Cox proportional hazards models. The risk of a complication after open repair was compared with that after EVAR; the results are presented as risk ratios (RR) with 95% confidence intervals (CI). Differences among treatment groups were evaluated with ANOVA and the Mann-Whitney U test for continuous variables or Fisher exact test for proportions. Differences among groups were taken as significant if $p<0.05$.

2.6 Cost analysis

The total costs per procedure, inclusive of follow-up, were calculated to estimate the cost per QALY and the incremental cost-effectiveness ratio of an EVAR program relative to the standard open repair program. The incremental cost effectiveness ratio was determined by measuring the incremental benefits (in life years) for the new intervention (EVAR) and dividing it by the incremental cost relative to current practice (cost of open repair).

A relative value unit (RVU) cost accounting system, which included both direct and indirect expenses, was used at our hospital. (Finkler, 1999; West, 1996) Individual charge items were assigned a weight or RVU. Expenses from revenue generating centers were allocated to each of the charge items within a department according to category, such as labor, supplies, equipment depreciation, and overhead. The cost per category was derived from each charge item on the basis of its RVU. Mean hospital costs and mean diagnostic-related group (DRG)–weighted payments were analyzed to determine net profit or loss for the hospital. The DRG codes for AAA repair were F08A (major reconstruct vascular procedures without cardiopulmonary bypass pump with catastrophic CC) and F08B (major reconstruct vascular procedures without cardiopulmonary bypass pump without catastrophic CC).

Data from our cost analysis were correlated with allocations to our hospital by the National Health Service Executive for the relevant DRG codes. The RVU used for a DRG was based on amalgamated data from the 9 main Irish National University Teaching Hospitals.

3. Results

Although patients in the BMT group were on average older (p<0.0001), there was no significant difference in the proportion of patients with major cardiac (p=0.104), pulmonary (p=0.170), or renal (p=0.108) diseases among the 3 groups (Table 1).

	OR	EVAR	BMT	p
Number	52	66	44	
Aneurysm Diameter, cm	6.2+/-1.6	5.4+/-1.1	6.2+/-1.7	**0.005***
Age, y	74.6+/-7.3	72.6+/-6.3	80.9+/-6.7	**<0.0001***
Cardiac	27 (51.9%)	38 (57.6%)	32 (72.3%)	0.104
Ischaemic Heart Disease	25 (48.1%)	39 (59.1%)	36 (68.2%)	0.137
Congestive Cardiac Failure	19 (36.5%)	34 (51.5%)	27 (61.4%)	**0.047***
Respiratory Disease	23 (44.3%)	40 (60.6%)	26 (59.1%)	0.170
Renal Impairment	18 (34.6%)	25 (37.9%)	24 (54.6%)	0.108
Hypertension	34 (65.4%)	45 (68.2%)	28 (63.6%)	0.881
Cerebrovascular Disease	12 (23.1%)	17 (25.8%)	8 (18.2%)	0.654
Mean SVS combined Co-morbidity Severity Score	7.75	9.89	11.1	0.057
Mean Kertai Customised Probability Index	28.0	34.4	35.6	0.070

Continuous data are presented as means ± standard deviation; categorical data are given as counts (percentages).
BMT: best medical treatment; EVAR: endovascular aneurysm repair; OR: open repair

Table 1. Demographics and Risk Factors for the 3 Treatment Groups

The mean aneurysm size was smaller in the EVAR group (mean 5.4±1.1cm; p=0.005) versus OR (mean 6.2±1.6cm) or BMT (mean 6.2±1.7cm). There were also no significant differences in the proportions of hypertensive patients (p=0.881).
All patients were anatomically suitable for EVAR, and the proportion of patients at moderate to severe risk of access failure, endograft limb obstruction, or embolisation was not statistically different among the groups (Table 2). However, using the strict SVS/AAVS scoring system, the proportion of patients at moderate to severe risk of endoleak was zero in the EVAR group (p=0.008), while the proportion of patients at moderate to severe risk of failed deployment was highest in the BMT group (p=0.015).

	OR	EVAR	BMT	
Global score for risk of major morbidity and mortality after endograft repair ≥2	39%	57%	65%	P=0.079
Anatomic score of risk of access failure or endograft limb obstruction ≥2	76%	57%	86%	***P=0.008****
Anatomic score of risk of embolization ≥2	85%	77%	95%	P=0.053
Anatomic score of risk of endoleak ≥2	30%	0%	56%	***P<0.0001****
Anatomic score of risk of failed deployed ≥2	39%	43%	79%	***P=0.0003****

BMT: best medical treatment; EVAR: endovascular aneurysm repair; OR: open repair

Table 2. Anatomical Severity Scores

3.1 Initial outcomes

In the EVAR group, all but 2 procedures were completed satisfactorily. An 82-year-old man with severely calcified iliac arteries was converted to open repair following right common iliac artery perforation and a 79 year-old woman implanted with a Quantum device that failed to deploy properly was treated with a silver-impregnated Dacron graft.

Insofar as operative details are concerned, the mean length of the operation was considerably reduced in the EVAR group (169 minutes) compared to the open repair group (193 minutes; p=0.04). The need for blood transfusions was also significantly lower in the EVAR group (mean 0.6 units) versus the open group (mean 1.8 units; p=0.015).

There was no significant difference in the mean rise in postoperative creatinine between the groups (p=0.845).

Mean lengths of hospital and intensive care unit (ICU) stay were reduced with EVAR (10.2 and 0.5 days, respectively) compared with OR (20.4 and 6.8 days, respectively; p<0.0001 for both). In the EVAR group, 11 type II endoleaks were noted on postoperative duplex and/or CT scans; all resolved spontaneously.

3.2 Clinical endpoints

Compared to open repair, the 30-day morbidity was significantly improved for EVAR patients (6% versus 23%; p=0.007), but 30-day mortality was not different between EVAR (3.0%) and OR (5.8%; p=0.653).

At 30 days, freedom from MACE was similar for EVAR (95.5%) and OR (88.5%; p=0.173, RR=0.39, 95% CI 0.10 to 1.46). At 4 years, freedom from MACE was significantly improved with EVAR (77.5%) compared with BMT (27.9%; p=0.001, RR=0.32, 95% CI 0.17 to 0.61) and similar to OR (75.4%; p=0.519, RR=0.76, 95% CI 0.33 to 1.73).

Mean follow-up was 22.7+/-16.1 months; no patient was lost to follow-up. There were 2 (3.0%) aneurysm-related deaths in the EVAR group, while in the BMT group, 11 (25%) ruptures occurred over the study period, 5 within 6 months of diagnosis. Nine of these BMT rupture patients presented to the hospital, and each had a CT scan that confirmed rupture; none of these patients was operated upon. The 2 remaining patients died in the community, and autopsy reports cited AAA rupture as the cause of death.

At 1 year, the chance of survival without aneurysm-related death was 12.2% higher in the EVAR group compared to the BMT group (p=0.049, RR=0.23, 95% CI 0.06 to 0.94). This survival benefit increased with time, and at 4 years, the survival without aneurysm-related death (Figure 1) was significantly greater in the EVAR group (96.7%) compared to BMT (66.8%; p=0.002, RR=0.08, 95% CI 0.02 to 0.26), but it was not statistically different from OR (93.9%; p=0.483, RR 0.53, 95% CI 0.09 to 3.09).

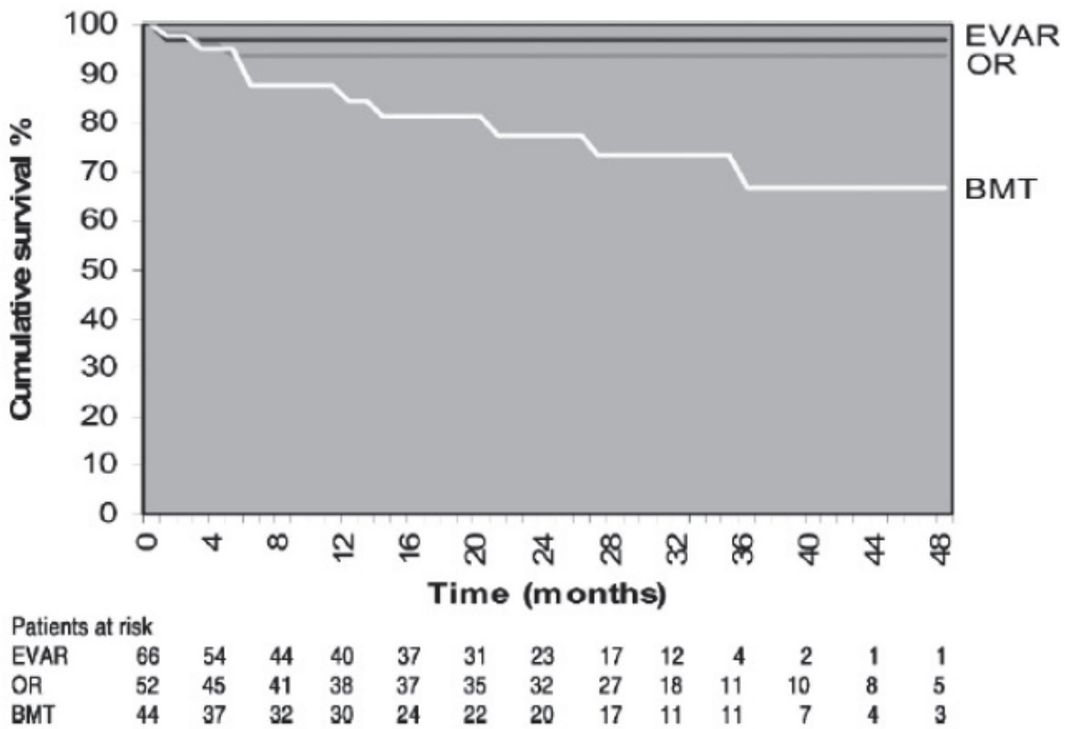
Only 2 factors were found to adversely influence survival without aneurysm-related death (Table 3): age (p=0.034, RR=1.09, 95% CI 1.01 to 1.18) and aneurysm size (p=0.004, RR=1.51, 95% CI 1.14 to 2.00).

Four-year cumulative survival without death from any cause (Figure. 2) following EVAR (78.8%) was not statistically different from OR (84.9%; p=0.590, RR=1.30, 95% CI 0.50 to 3.36), but was significantly improved compared to BMT (27.9%; p<0.001, RR=0.30, 95% CI 0.16 to 0.57). As with aneurysm-related mortality, only age (p=0.014, RR=1.06, 95% CI 1.01 to 1.10) and aneurysm size (p=0.001, RR=1.35, 95% CI 1.13 to 1.62) were found to influence freedom from all-cause mortality (Table 4).

Risk Factor	Risk Ratio	95% CI	p
Age	**1.0889**	**1.0066 to 1.1780**	**0.0337***
Male	1.8064	0.5052 to 6.4596	0.3630
Cardiac	1.9562	0.4893 to 7.8202	0.3426
Respiratory	2.0177	0.5885 to 6.9174	0.2641
Renal	1.9054	0.6416 to 5.6588	0.2457
Hypertension	1.1772	0.3613 to 3.8357	0.7866
Diabetes	1.2693	0.4514 to 3.5691	0.6512
Smoking	0.6712	0.2459 to 1.8323	0.4365
Aneurysm Diameter	**1.5098**	**1.1410 to 1.9977**	**0.0039***

CI: confidence interval.

Table 3. Results of the Cox Proportional Hazards Model for Aneurysm-Related Mortality



At 4 years, EVAR (96.7%) vs. OR (93.9%; p50.483, RR50.53, 95% CI 0.09 to 3.09) or vs. BMT (66.8%; p50.0021, RR50.08, 95% CI 0.02 to 0.26).
BMT: best medical treatment; EVAR: endovascular aneurysm repair; OR: open repair

Fig. 1. Aneurysm-related Kaplan-Meier survival curves.

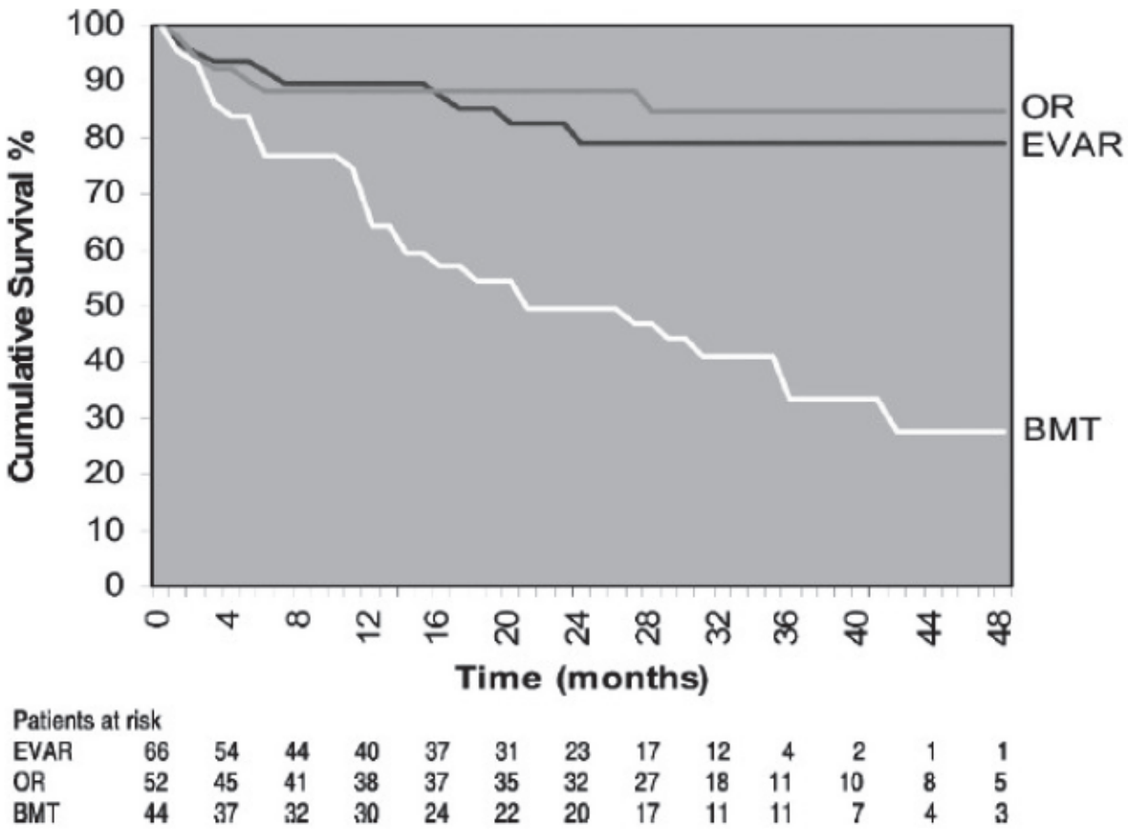


Fig. 2. All-cause Kaplan-Meier survival curves. At 4 years, EVAR (78.8%) vs. OR (84.9%; P=0.59, RR=1.3, 95% CI 0.50 to 3.36) or vs. BMT (27.9%; p=0.0005, RR=0.30, 95% CI 0.16 to 0.57).

Risk Factor	Risk Ratio	95% CI	p
Age	**1.0555**	**1.0109 to 1.1020**	**0.0141***
Male	1.7141	0.8223 to 3.5731	0.1505
Cardiac	1.3501	0.6614 to 2.7559	0.4097
Respiratory	1.3264	0.6781 to 2.5942	0.4093
Renal	1.3485	0.7273 to 2.5002	0.3426
Hypertension	1.2164	0.6265 to 2.3616	0.6605
Diabetes	1.3173	0.7217 to 2.4045	0.3693
Smoking	1.2317	0.6749 to 2.2479	0.4972
Aneurysm Diameter	**1.3495**	**1.1276 to 1.6151**	**0.0011***

CI: confidence interval.

Table 4. Results of the Cox Proportional Hazards Model for All-Cause Mortality

3.3 Secondary interventions

Over the observation period, there were 3 secondary interventions in the EVAR group versus 1 among the OR patients. Thus, at 4 years, the intervention-free survival rate for EVAR (94.5%) was similar to OR (98.1%, p=0.410, HR=2.51, 95% CI 0.35 to 18.0). In the OR group, an 80-year-old woman suffered distal embolization; femoral thromboembolectomy, endarterectomy, and femorofemoral bypass grafting were done 72 hours postoperatively.

Two EVAR patients had limb sequelae: a 76-year-old man had a kink develop in the contralateral limb due to aneurysm tortuosity and an 83-year-old man had a thrombosed left graft limb 1 year post EVAR. Both were treated with endovascular techniques and recovered. The third secondary procedure was done in an 82-year-old woman with a type III endoleak diagnosed on the postoperative duplex scan. An aortic cuff and iliac extension were placed 3 days after her primary procedure.

3.4 Quality of life assessment

Over a 4-year follow-up period, the QTWIST was 3.64 years for EVAR and 3.60 years for OR. The 28% 4-year freedom from all-cause mortality in the BMT group resulted in only a 2.22-year Q-TWIST for every 4 years of treatment. Sensitivity analysis showed that Q-TWIST was significantly improved with EVAR compared to OR over a full range of utility values between 0 and 1 ($p<0.003$; Table 5).

EVAR vs. Open Repair					
Utility for TOX					
Utility for Relapse	**0**	**0.25**	**0.50**	**0.75**	**1.0**
0	0.0029	0.0028	0.0027	0.0026	0.0025
0.25	0.0030	0.0028	0.0027	0.0027	0.0026
0.50	0.0030	0.0029	0.0028	0.0027	0.0026
0.75	0.0031	0.0029	0.0028	0.0027	0.0027
1.0	0.0031	0.0030	0.0029	0.0027	0.0027
EVAR vs. Best Medical Therapy					
Utility for TOX					
Utility for Relapse	**0**	**0.25**	**0.50**	**0.75**	**1.0**
0	0.039	0.044	0.05	0.057	0.064
0.25	0.040	0.045	0.05	0.057	0.064
0.50	0.040	0.045	0.05	0.059	0.066
0.75	0.041	0.046	0.05	0.059	0.066
1.0	0.041	0.046	0.05	0.060	0.067

Table 5. Threshold Utility Analyses

3.5 Cost analysis

In the analysis of costs (Table 6), 52 high-risk patients were treated with OR over a 5-year period (2002–2007) at a total inpatient cost of €1,257,457. The 66 patients treated with EVAR (14 patients more than OR) incurred a lower cost of €1,129,138. If the cost of follow-up over 4 years was included, the mean costs per patient were €18,476 for EVAR and €24,252 for OR, a savings of €5,776 per patient treated with EVAR. The in-hospital costs were €17,108 for EVAR and €24,182 for OR. For the F08A code, our hospital was assigned a RVU of 5.44 and was allocated €23,453 in our budget. For the F08B code, our hospital was assigned a RVU 2.44, providing a budgetary allocation of €10,625. Thus, for AAA repair, EVAR generated a net profit of € 6345 per case for the hospital, while OR was done at a net loss of €729 per case.

Costs		EVAR (n=66)	OR (n=52)	BMT (n=44)
Pre-op work-up				
CTAngiogram	€600	€39,600	€31,200	€26,400
Chest X-ray	€88	€5,779	€4,553	€3,853
Duplex Screening	€185	€12,210	€9,620	€8,140
Echocardiogram	€145	€9,570	€7,540	€6,380
Pulmonary function Tests	€125	€8,250	€6,500	€5,500
Pharmacy, transfusion and Laboratory costs	€305-€415	€27,390	€21,580	€13,420
Accomodation				
Hospital Bed *per diem*	€540	€348,300	€382,860	€23,760
ICU Bed *per diem*	€1,646	€51,018	€582,592	
Theatre				
Per diem Theatre Overheads (inc. Staffing, Radiology etc)	€6,402	€105,630	€166,447	
Equipment				
Graft (Intervascular)	€915	€1,830	€47,580	
Graft (Dynaflo)	€625	€11,250	€625	
Endograft	€7,000	€462,000		
Catheters/Wires/Balloons etc	€635	€41,941		
Embolisation				
Coils	€554	€1,659		
Catheters/Wires/Balloons etc	€359	€1,077		
Bed Stay	€545	€1,635		
Total-In-Patient Cost		**€1,129,138**	**€1,257,457**	**€87,453**
Follow-up				
Vascular Laboratory	€150	€33,150	€3,640	€23,350
PFA	€88	€19,351		
CTA	€300	€37,800		
Total Cost		**€1,219,439**	**€1,261,097**	**€110,803**
Mean Cost per Patient		€18,476	€24,252	€2,518
Q-TWiST		3.64years	3.60years	2.22years
QALY		0.91	0.90	0.56
Cost per QALY		**€5,076**	**€6,737**	**€1,134**

Table 6. Cost Analysis

Treatment with EVAR cost €5076 per QALY, which was €1661 less than OR, giving a negative incremental cost-effectiveness ratio (ICER) for EVAR versus OR of €144,388 per QALY gained. EVAR was €3,942 more expensive per QALY than BMT alone; the ICER was €45,595 per QALY gained with EVAR versus BMT.

4. Dicussion

At present, considerable controversy exists in the vascular community regarding optimum management of high-risk patients with large AAAs. There has been a remarkable convergence of data from randomized trials giving level-1 evidence that EVAR reduces operative mortality by two thirds compared with open repair; the survival benefit is sustained over intermediate-term follow-up in low- to intermediate risk patients.(EVAR trial-1 participants, 2005; Prinssen, 2004) However, the results of these trials cannot be generalized to patients who are at high risk for open repair. The patients in EVAR 2 (EVAR trial-2 participants, 2005) were older and had more cardiovascular co-morbidities; this was reflected in the high 9% 30-day mortality rate and a 4-year survival of only 36%. Moreover, there was considerable crossover between the trial groups and after randomization to the non-intervention group, 20% of patients subsequently underwent elective repair of their aneurysm. Furthermore, the trial was not limited to an objective list of high-risk criteria, which led to a lack of objectivity and uniformity in what is truly a high-risk patient. This biased the study against EVAR and weakened the investigators conclusions that prophylactic operations designed to improve survival cannot be effective in patients with short life expectancy. They concluded that EVAR is much more costly than no intervention, without a survival benefit in high-risk patients.

Our results show that EVAR can be safely performed in high-risk patients. Our 30-day perioperative mortality (3%) rate was considerably lower than the EVAR-2 trial. However, although we saw a clear advantage at 4 years with EVAR versus BMT, we did not see a clear benefit in terms of all-cause mortality for EVAR versus open repair. When interpreting these results, one has to question the merits of using all-cause mortality as a primary endpoint for a study on a specific treatment. All-cause mortality is an extremely important variable, but it is a metric of limited value when assessing a disease-specific treatment in a senior citizen population. This is best illustrated if you consider that 48 patients in EVAR 1 (EVAR trial-1 participants, 2005) died from cancer, representing about one third of the overall mortality over the study period. These cancer deaths diluted the overall survival benefit conferred by EVAR over open repair. It appeared more logical to us to use survival without aneurysm-related death as our primary endpoint, but here too, the difference between EVAR and OR was not significant, likely due to our high OR survival rate and low morbidity in the context of high-risk patients. This means that a large cohort is needed to show statistical significance without risk of a type II error. However, it confirms that high-risk patients can still experience low perioperative morbidity and high midterm survival if they are treated in centers with high-volume practice and appropriate preoperative patient assessment, optimal selection of operative strategy, careful intraoperative anesthetics management, meticulous attention to operative technical detail, and skilled postoperative management.

At 6 months, a significant 9.3% survival benefit was seen with EVAR compared to BMT. Fully half of the deaths in the non-operative group were due to rupture, and 50% of the ruptures occurred within the first 9 months, which helped to increase the benefit with EVAR to 30% at 4 years. The survival curves for EVAR and non-operative management continue to diverge after 4

years, which contrasts to the EVAR-2 trial, (EVAR trial-2 participants, 2005) in which a high operative mortality rate meant that no late difference in aneurysm related mortality and no difference in overall survival were seen despite more deaths occurring from aneurysm rupture in the non-intervention group. We are not alone in establishing that favorable outcomes are possible in high-risk patients. In an attempt to address some of the issues with EVAR 2, the SVS Outcomes Committee analyzed their Lifeline Registry (Sicard, 2006) and found that 565 of the ,3000 patients in the registry met the high-risk criteria set out in EVAR 2, far exceeding the number of patients in the EVAR 2 trial. Sicard et al. reported that there was a significant difference in 30-day mortality (2.9%) in the investigational device exemption (IDE) trial registries compared to 9% in EVAR 2. Moreover, the 4-year survival rate for the IDE group was 56% (based on all-cause mortality, not just aneurysm-related mortality), versus 36% in EVAR 2, so there was a difference of 20 percentage points between the 2 trials. One explanation for the large difference in both aneurysm-related and all-cause mortality rates between EVAR 2 and the US IDE data is that the EVAR-2 trial was dealing with sicker patients. Another possible explanation is that the actual medical care of these patients was different. The EVAR-2 trial participants explained the long delay between randomization and treatment because of the need to manage patient co-morbidities; they emphasized the need for optimization of the patient before the intervention. Despite a mean aneurysm diameter of 6.7 cm, EVAR was not done until a median of 57 days after randomization. During this time, 9 aneurysms ruptured, causing nearly half of the 20 aneurysm-related deaths in the EVAR group. Once the decision to intervene was taken in our study, the procedure was performed within 14 days, and despite 5 ruptures occurring in the non-operative group within the first 6 months, no ruptures occurred preoperatively in the EVAR or open repair groups. It could then be argued that if patients are anatomically suitable for EVAR, they should be treated without delay. However, it is extremely important to adequately assess and improve patient fitness before intervention, which is especially true in very high-risk patients. All our patients were given best medical treatment, (Oaikhinan, 2004) and every effort was made to optimize cardio-respiratory and renal function preoperatively, which our extended mean length of hospital stay reflects.

4.1 Benefit to the individual

The debate over the relative long- or intermediate- term risks and benefits associated with intervention versus observation is especially pertinent in the context of high-risk patients. The improvement in QALY in the immediate postoperative period for both EVAR and OR in most studies reflects the relief a patient must feel at overcoming intervention and escaping a potentially lethal disease. (Malina, 2007; UK Small Aneurysm Trial Participants, 1998) For some patients, the knowledge that they have a large or expanding aneurysm and the realization that outcomes following ruptured AAA repair are bleak may cause considerable psychological stress and impact significantly on their quality of life.

Most studies have shown that quality of life is improved in the perioperative period following EVAR compared to OR, which is a reflection of the shorter hospital stay, reduced blood loss, early improvements in physical mobility and pain, as well as a likelihood for a patient to be discharged to home rather than to an institution. (Geraghty, 2003; Lee, 2004) However, most studies demonstrated no difference in QALY when patients are surveyed at remote time points.(EVAR trial-2 participants, 2005; Lottman, 2004; Prinssen, 2004) On the other hand, Aljabri et al. (Aljabri, 2006) and the DREAM trial investigators (Prinssen, 2004) reported that EVAR patients had a lower QALY 6 months after surgery than in OR patients.

Much criticism has been directed toward EVAR because of the impression that the need for long-term surveillance and risk of secondary interventions will reduce future quality of life. The DREAM investigators (Blankensteijn, 2005) reported that the rate of reintervention after EVAR in the first 9 months after randomization was almost 3 times the rate after open repair. High reintervention rates were a problem in EVAR 1 (EVAR trial-1 participants, 2005) and are most certainly due to poor preoperative estimation of anatomical suitability. In EVAR 1, 54% of potentially eligible patients were found to be anatomically ''suitable'' for EVAR, but this proportion ranged from 6% to 100% across the 34 centers, illustrating the variation in assessing this important variable. In our study, the intervention-free survival rates at 4 years were similar for EVAR and OR.

Our low secondary reintervention rate most certainly impacted positively on our quality of life analysis. We had only 3 reinterventions in our EVAR patients, 2 for type III endoleak. None of the 11 type II endoleaks required treatment. In our experience, complete obliteration of all patent branches is not warranted. (Dias, 2004; van Marrewijk, 2004) Our policy is not to intervene either prophylactically or therapeutically for type II endoleaks unless there is a persistent increase in sac diameter .5 mm for 3 months; all of the type II endoleaks in this study resolved within 3 months, and there was no increase in sac diameter.

4.2 Benefit to society

The EVAR-1 investigators showed that aneurysm-related mortality stayed 3% lower with EVAR throughout the 4-year follow-up period. (EVAR trial-1 participants, 2005) However, obtaining this benefit required a 33% increase in hospital costs without a sustained benefit in quality of life. Rationing parameters for healthcare resources are admittedly controversial and generate ethical dilemmas. It has been suggested that perhaps EVAR should be restricted to those patients who are ''fit'' for surgery, by whatever definition deemed appropriate, as the procedure, the endovascular devices, the continuing need for surveillance imaging, and possible secondary re-interventions are costly.

To the contrary, we have shown that EVAR can be performed with clinical equivalence and enhances quality of life in high-risk patients. However, the benefit to the individual cannot be at the expense of the healthcare system. A report commissioned by the Belgian government and published in 2005 found that EVAR was not cost effective. (Bonneux, 2005) Multiple authors have reported that hospitals lose money on EVAR compared to earning significant profits from OR. In a comprehensive cost analysis, Bertges et al. (Bertges, 2003) analyzed the costs associated with EVAR in 221 Medicare patients and found that ''mean total hospital cost was $22,999, and mean reimbursement, weighted by case mix, was $20,837, resulting in a net loss of $2162'' per case. However, Patel et al. (Patel, 1999) in a hypothetical Markov model concluded that EVAR was cost effective, with a mean endograft cost of >$13,000 and overhead of an additional $1100. They used a baseline mortality rate of 4.8% for OR and concluded that if OR could be done with comparable morbidity and mortality to EVAR, the cost-effectiveness of EVAR ceased to exist. Similarly, the Belgian report recommended that long-term mortality and morbidity must be lower to make EVAR a cost-effective alternative to OR. (Bonneux, 2005) The Belgian report found that although the endograft contributed most to the cost disparity between OR and EVAR, CT follow-up was the second most important determinant, contributing more to cost than secondary interventions or procedure-related complications.

Contrary to the predictions of Patel et al. (Patel, 1999) and the Belgian report, (Bonneux, 2005) we found that despite no benefit in terms of freedom from MACE, EVAR was cost-effective compared to OR even in this high-risk cohort. We used a comprehensive analysis of the cost benefit ratio of EVAR on a real patient cohort in an attempt to validate the cost-effectiveness of EVAR. We found that the mean cost, including 4-year follow-up, was >€5,000 less with EVAR, giving a negative incremental cost-effectiveness ratio of €144,388 per QALY gained. This is in part due to a financial deal with our graft providers, reduced hospital stay, minimal need for ICU facilities, increasing use of duplex in follow-up, and a low secondary reintervention rate. However, to ensure cost-effectiveness and to guarantee maximum impact of this technology, we believe it must be performed in high-volume centers, which is in line with recommendations from the Belgian report. (Bonneux)

If we minimize perioperative problems, then the question that we really need to ask ourselves is which patients are going to die from something else before they benefit from the aneurysm repair? This question has not yet been answered by any trials or datasets and is fundamental to the treatment of aneurysm disease. From our data, the only factors that we identified as having a negative impact on both all-cause and aneurysm specific mortality were advanced age and large aneurysm diameter.

The physician and patient must decide on an individual basis whether any aneurysm repair should be undertaken, or as EVAR 2 might suggest, whether the patient is so ill that treating the aneurysm would not confer any survival benefit. We reported our results over 48 months, and although the 95% confidence intervals might suggest these to be simple speculative estimations, we strongly believe that our results reflect the reality that endovascular specialists face continually when dealing with high-risk patients. Our study may be underpowered due to the small sample size; however, the patient and family did take the lead in deciding which treatment best suited them.

4.3 Conclusion

We have shown that EVAR significantly reduces both long-term aneurysm-related and all-cause mortality, with minimal operative mortality risk and a low secondary intervention rate. High-risk patients ought to be managed in high-volume centers where they can benefit from specialized multidisciplinary care with low perioperative morbidity and mortality rates. EVAR and OR options are plausible and both can be tailored to the patient. In financial terms, our hospital has profited from our EVAR program. High patient turnover rates and low use of ICU facilities have certainly contributed to its profitability and overall benefit to the individual, health economy, and the community as a whole. We have shown EVAR to be a safe, durable, and feasible option for high-risk patients. It significantly improves quality of life compared to open repair or best medical therapy and can be performed with minimal risk of major complications or secondary intervention. The results of EVAR are exceptional and have positively influenced the choices available to the patients and their referring primary physicians.

5. References

Aljabri B, Al Wahaibi K, Abner D, et al. Patientreported quality of life after abdominal aortic aneurysm surgery: a prospective comparison of endovascular and open repair. J Vasc Surg. 2006;44:1182–1187.

Bertges DJ, Zwolak RM, Deaton DH, et al. Current hospital costs and Medicare reimbursement for endovascular abdominal aortic aneurysm repair. J Vasc Surg. 2003;37:272–279.

Blankensteijn JD, de Jong SE, Prinssen M, et al. Two-year outcomes after conventional or endovascular, repair of abdominal aortic aneurysms. N Engl J Med. 2005;352:2398–2405.

Bonneux L, Cleemput I, Vrijens F, et al. KCE report 23: Elective endovascular treatment of the abdominal aortic aneurysm (AAA). Brussels, Belgium: Belgium Health Care Knowledge Center; 2005.

Bowen J, De Rose G, Hopkins R, et al. Systematic review and cost-effectiveness analysis of elective endovascular repair compared to open surgical repair of abdominal aortic aneurysms. Interim Report for the Ontario Ministry of Health and Longterm Care. Hamilton, ON: Program for Assessment of Technology in Health, McMaster University; July 2005.

Bush RL, Johnson ML, Hedayati N, et al. Performance of endovascular aortic aneurysm repair in high-risk patients: results from the Veterans Affairs National Surgical Quality Improvement Program. J Vasc Surg. 2007;45:227–235.

Chaikof EL, Fillinger MF, Matsumura JS, et al. Identifying and grading factors that modify the outcome of endovascular aortic aneurysm repair. J Vasc Surg. 2002;35:1061–1066.

Dias NV, Ivancev K, Malina M, et al. Intraaneurysm sac pressure measurements after endovascular aneurysm repair: differences between shrinking, unchanged, and expanding aneurysms with and without endoleaks. J Vasc Surg. 2004;39:1229–1235.

Dorros G, Parodi J, Schonholz C, et al. Evaluation of endovascular abdominal aortic aneurysm repair: anatomical classification, procedural success, clinical assessment, and data collection. J Endovasc Surg. 1997;4:203–225.

EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. Lancet. 2005;365:2179–2186.

EVAR trial participants. Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial. Lancet. 2005;365:2187–2192.

Finkler SA, Ward DM. Cost Accounting for Health Care Organizations: Concepts and Applications, 2nd ed. Gaithersburg, MD: Aspen Publishers; 1999.

Gelber RD, Gelman RS, Goldhirsh A. A qualityof- life-orientated endpoint for comparing therapies. Biometrics. 1989;45:781–795.

Geraghty PJ, Sicard GA. Abdominal aortic aneurysm repair in high-risk and elderly patients. J Cardiovasc Surg (Torino). 2003;44:543–547.

Glasziou PP, Cole BF, Gelber RD, et al. Quality adjusted survival analysis with repeated quality of life measures. Stat Med. 1998;17:1215– 1229.

Hynes N, Koh N, Sultan S. Abdominal aortic aneurysm repair in octogenarians versus younger patients in a tertiary referral center. Vascular. 2005;13:1–11.

Kertai MD, Boersma E, Klein J, et al. Optimizing the prediction of perioperative mortality in vascular surgery by using a customized probability model. Arch Intern Med. 2005;165:898– 904.

Lee WA, Carter JW, Upchurch G, et al. Perioperative outcomes after open and m endovascular repair of intact abdominal aortic aneurysms in the United States during 2001. J Vasc Surg. 2004;39:491–496.

Lottman PE, Laheij RJ, Cuypers PW, et al. Health-related quality of life outcomes following elective open or endovascular AAA repair: a randomized controlled trial. J Endovasc Ther. 2004;11:323–329.

Malina M, Nilsson M, Brunkwall J, et al. Quality of life before and after endovascular and open repair of asymptomatic AAAs: a prospective study. J Endovasc Ther. 2000;7:372–379.

Oaikhinan K, Sultan S. An observational parallel group comparative study with and without the ''Magic Bullet'' (MB: Aspirin, cardio selective beta-blocker, Pravastatin and Clopidogrel) in the perioperative and postoperative period for abdominal aortic aneurysms surgery and femoral-popliteal segment revascularisation. Does the ''Magic Bullet'' improve the 30-day morbidity and mortality outcome? Br J Surg. 2004;91:113–114.

Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. Ann Vasc Surg. 1991;5:491–499.

Patel ST, Haser PB, Bush HL, et al. The costeffectiveness of endovascular repair versus open surgical repair of abdominal aortic aneurysms: a decision analysis model. J Vasc Surg. 1999;29:958–972.

Prinssen M, Verhoeven EL, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. N Engl J Med. 2004;351:1607–1618.

Prinssen M, Buskens E, Blankensteijn JD. On behalf of the DREAM trial participants. Quality of life after endovascular and open AAA repair. Results of a randomized trial. Eur J Vasc Endovasc Surg. 2004;27:121–127.

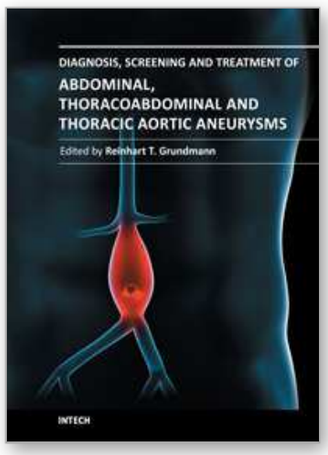
Sicard GA, Zwolak RM, Sidawy AN, et al. Endovascular abdominal aortic aneurysm repair: long-term outcome measures in patients at high-risk for open surgery. J Vasc Surg. 2006;44:229–236.

Sultan S, Moore D, Shanik G. Endoluminal stent grafts in the management of infrarenal abdominal aortic aneurysms: a realistic assessment. Eur J Vasc Endovasc Surg. 2001;21:70–74.

UK Small Aneurysm Trial Participants Health service costs and quality of life for early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms.. Lancet. 1998;352:1656–1660.

van Marrewijk CJ, Fransen G, Laheij RJ, et al. Is a type II endoleak after EVAR a harbinger of risk? Causes and outcome of open conversion and aneurysm rupture during follow-up. Eur J Vasc Endovasc Surg. 2004;27:128–137.

West TD, Balas EA, West DA. Contrasting RCC, RVU, and ABC for managed care decisions. A case study compares three widely used costing methods and finds one superior. Healthc Financ Manage. 1996;50:54–61.



Diagnosis, Screening and Treatment of Abdominal, Thoracoabdominal and Thoracic Aortic Aneurysms
Edited by Prof. Reinhart Grundmann

ISBN 978-953-307-466-5
Hard cover, 414 pages
Publisher InTech
Published online 12, September, 2011
Published in print edition September, 2011

This book considers mainly diagnosis, screening, surveillance and treatment of abdominal, thoracoabdominal and thoracic aortic aneurysms. It addresses vascular and cardiothoracic surgeons and interventional radiologists, but also anyone engaged in vascular medicine. The high mortality of ruptured aneurysms certainly favors the recommendation of prophylactic repair of asymptomatic aortic aneurysms (AA) and therewith a generous screening. However, the comorbidities of these patients and their age have to be kept in mind if the efficacy and cost effectiveness of screening and prophylactic surgery should not be overestimated. The treatment recommendations which will be outlined here, have to regard on the one hand the natural course of the disease, the risk of rupture, and the life expectancy of the patient, and on the other hand the morbidity and mortality of the prophylactic surgical intervention. The book describes perioperative mortality after endovascular and open repair of AA, long-term outcome after repair, and the cost-effectiveness of treatment.

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:

Sherif Sultan and Niamh Hynes (2011). A Prospective Clinical Economic and Quality of Life Analysis of Open Repair, Endovascular Aortic Repair and Best Medical Treatment in High Risk Patients with AAA, Diagnosis, Screening and Treatment of Abdominal, Thoracoabdominal and Thoracic Aortic Aneurysms, Prof. Reinhart Grundmann (Ed.), ISBN: 978-953-307-466-5, InTech, Available from: http://www.intechopen.com/books/diagnosis-screening-and-treatment-of-abdominal-thoracoabdominal-and-thoracic-aortic-aneurysms/a-prospective-clinical-economic-and-quality-of-life-analysis-of-open-repair-endovascular-aortic-repa

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen