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The Abdominal Aortic Aneurysm – Prognosis, Treatment, Screening and Cost-Effectiveness

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1. Introduction

Mass screening is claimed for finding a disease in which symptoms are not yet occurred. The indication for such an examination is given if the early detection of the disease allows treatment with lower morbidity and mortality than treatment at an advanced stage. In addition, the long-term prognosis of the patients must be considered. Screening makes only sense if the overall mortality of a specific population can be diminished by the diagnostic and therapeutic measures. In assessing the screening for an asymptomatic abdominal aortic aneurysm (AAA) that has to be treated surgically to avoid the rupture of the AAA with its associated high fatality rate, the expected extension of life should be weighed against the risk of surgery. It must be ensured that the untreated disease would progress to rupture of the AAA with fatal outcome. The benefits of screening and subsequent prophylactic operation must be contrasted its risk and cost. It is the objective of the following remarks to outline the value of screening for AAA on the basis of studies on the prevalence of AAA, risk of rupture, and the results of surgical treatment. Meanwhile, two different approaches are available for the treatment of AAA, open repair and endovascular aneurysm repair (EVAR). The considerations for prophylactic repair of AAA must therefore also include morbidity and mortality of the two interventions and the evaluation of cost-benefit ratio. This will be shown in the following.

2. Prevalence of abdominal aortic aneurysm and mortality rate

Generally, an AAA is considered to be present when the minimum anterioposterior diameter of the aorta reaches 3.0 cm (Hirsch et al., 2006). The prevalence of AAA depends on various risk factors, as advancing age, family history, male gender, and tobacco use. According to the ACC/AHA guidelines (Hirsch et al., 2006) the prevalence of AAA 2.9 to 4.9 cm in diameter ranges from 1.3 % for men aged 45 to 54 years up to 12.5 % for men 75 to 84 years of age. Comparable prevalence figures for women are 0% and 5.2 %, respectively. Scott et al., 1995 reported in men and women aged 65-80 years a prevalence rate of 4 % overall and 7.6 % of men. Vardulaki et al., 1999 observed in two different areas the prevalence of AAA ranging between 5.3 % and 8% and between 6.18% and 9.88 %, respectively, in men aged between 65 and 79 years. In the Multicentre Aneurysm Screening Study (MASS) the prevalence in men aged 65-74 years was 4.9% (Ashton et al., 2002). In these studies the AAA was defined as an aortic diameter ≥ 3cm. If clinically important aneurysms are only taken into account (AAA

measuring ≥ 4 cm in diameter) the indicated prevalence would be lower. Van Walraven et al., 2010 identified the prevalence of incidental AAA during imaging for other reasons. In 79,121 abdominal images 812 incidental AAA with a mean diameter of 4.0 cm (1% of all studies) were detected in patients with a mean age of 74 years. Lederle et al., 1997 reported the results of ultrasonography screening for AAA in 73,451 US veterans who were 50 to 79 years of age and had no history of AAA. The infrarenal aortic diameter was at least 4 cm in 1031 patients (1.4%), 368 patients (0.5%) had an AAA of 5 cm or larger. Smoking was the factor most closely associated with AAA in this study. In men who never smoked the prevalence of AAA 4 cm or larger was 0 % (patient age 50 to 59 years) and 0.8% (patient age > 75 years), respectively. The corresponding figures for men who smoked were 0.9 % and 2.7 %, respectively. A second cohort study of the Department of Veterans Affairs medical centers (Lederle et al., 2000) including 52,745 subjects aged 50 to 79 years confirmed the findings previously reported and supported the hypothesis that AAA is primarily a smoking-related disease. In this study AAA of 4.0 cm or larger were detected in 613 participants (1.2%). The excess prevalence associated with smoking accounted for approximately 75% of all AAA of 4.0 cm or larger. Smoking as a very strong risk factor for AAA was also proven by the Tromsø study (Forsdahl et al., 2009). When subjects who reported to have never been a daily smoker were compared with those who currently were smoking 20 cigarettes or more, the latter group had a > 13 times increased risk of an incident AAA during follow-up. In the women`s health initiative, an observational study involving 161,808 postmenopausal women, too, a strong positive association between smoking and clinically important AAA was found (Lederle et al., 2008). The prevalence defines the number of AAA present in a specific population during a particular point in time. This does not mean that these subjects will die of a ruptured aneurysm. Vardulaki et al., 1999 estimated the prevalence of AAA reaching around 10 % of the population at an age of 74 years, nevertheless in the year 1997 ruptured AAA caused not more than approximately 2.1 % of all deaths in men and 0.75 % of all deaths in women over the age of 65 in England and Wales. These data have not changed in the last 10 years; on the contrary, the mortality rate might be even decreasing. In the year 2009, 2415 men, 72.4 % of them being ≥ 75 years old, and 1239 women, 71.8 % of them being ≥ 80 years old, died of ruptured AAA in England and Wales (Office for National Statistics, 2011). In addition, 402 men and 184 women died of AAA without mention of rupture. With reference to 238,062 deaths in men and 253,286 in women, in 2009 therefore merely 1% of all deaths in men and 0.49 % in women were caused by ruptured AAA in England and Wales. Including the insufficiently defined cases, AAA caused 1.18% of all deaths in men and 0.56 % in women. In men 65 years of age or older, ruptured AAA caused 1.24 % of deaths and 1.45%, respectively, including the insufficiently defined cases. For the USA, 2,423,712 deaths are reported in the year 2007, including 12,986 deaths caused by all kinds of aortic aneurysms and dissections, not only AAA. 58.7 % of these patients were 75 years of age or older. These were 0.53% of all deaths, and 0.58% of the deaths in men and women over the age of 64 years, respectively (Xu et al., 2010). The small percentage of deaths due to AAA and the relatively old age of the population dying of ruptured AAA demonstrate the impossibility to increase significantly the median life expectancy of the total population by an untargeted mass screening for AAA (Dimick & Upchurch, 2003) and call for more sophisticated strategies, also for financial reasons.

3. Risk of rupture

The statements about the natural course of the disease and the risk of rupture are mainly based on the results of the randomized studies that compared immediate repair with

surveillance for small AAA (Lederle et al., 2002; UK Small Aneurysm Trial Participants, 1998, 2002). The evidence report prepared for the Agency for Healthcare Research and Quality (AHRQ) analyzed these and further observational studies (Wilt et al., 2006). They came to the conclusion that the annual risk of rupture is 1% or lower for AAA less than 5.5 cm. The 1-year risk of rupture increases with aneurysm size and may exceed 10% in individuals with AAA > 6cm. For AAA that attain a size of > 8 cm, the risk may exceed 25 % at 6 months. Female sex, higher mean arterial blood pressure, current smoking, and poor lung function increase the risk of aneurysm rupture in addition to the size of initial AAA diameter (UK Small Aneurysm Trial Participants, 1999, 2002). A systematic review of the literature concluded that the rupture rate of small AAA with a diameter range 3.0-5.5 cm amounts to 0 to 1.61 ruptures per 100 person-years (Powell et al., 2011). These authors criticized that most studies have been poorly reported and did not have clear ascertainment and diagnostic criteria for aneurysm rupture. The inaccurate assessments of the risk of rupture might be due in part to the bimodal growth pattern of AAA observed by A.R. Thompson et al., 2010. They found nearly 50% of all aneurysms never progressing to surgery and rupture. Conversely, adjusted annual growth rates of at least 2 mm significantly predicted AAA-related events. In addition, medical treatment may influence the growth rate of AAA. Schlösser et al., 2008 reported for small AAA (initial AAA diameter between 3.0 and 5.5 cm) a rupture rate of 0.9 % per patient-year corresponding to the data mentioned above. The mean expansion rate of AAA was 2.5 mm / year in this study. Patients using lipid-lowering drugs had a 1.2 mm/ year lower AAA growth rate compared to non-users.

4. Treatment recommendations

In the absence of symptoms related to an aneurysm, the threat that the aneurysm will rupture is the major consideration. The treatment recommendations 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 ACC/AHA guidelines give the following treatment recommendations (Hirsch et al., 2006): - Patients with AAA measuring 4.0 to 5.4 cm in diameter should be monitored by ultrasound or CT scans. - Patients with AAA measuring 5.5 cm or larger should undergo repair to eliminate the risk of rupture. - Intervention is not recommended for asymptomatic AAA measuring less than 5.0 cm in men or less than 4.5 cm in women. - Repair can be beneficial in patients with AAA measuring 5.0 to 5.4 cm in diameter. This latter recommendation is not based on the results of the trials that were cited (Lederle et al., 2002; UK Small Aneurysm Trial Participants, 2002). Both trials reported no benefit from repair of AAA less than 5.5 cm in diameter or in any subgroup of patients defined by aneurysm diameter at entry, a finding that directly refutes the ACC-AHA recommendation, for which no alternative justification is presented (Lederle et al., 2006). Survival was not improved by elective repair of AAA smaller than 5.5 cm compared with surveillance, even when operative mortality was low (Lederle et al., 2002; UK Small Aneurysm Trial Participants, 1998, 2002). In the UK Small Aneurysm Trial, even after 12 years of follow-up mortality in the surgery and surveillance groups actually did not differ (63.9% and 67.3 %, respectively) (Powell et al., 2007). A Cochrane review also found no overall benefit for early surgery of small AAA (4.0 to 5.5 cm) (Ballard et al., 2008). Here are the indications for endovascular aneurysm repair (EVAR) currently the same as for open repair. Under the hypothesis that the perioperative risk might be lower with EVAR compared to open repair,

the PIVOTAL study has sought to determine whether EVAR for AAA measuring 4 to 5 cm in diameter compared to surveillance might be of benefit (Ouriel et al., 2010). Among patients randomized to treatment, 89% underwent aneurysm repair. Among patients randomized to surveillance, 31 % underwent aneurysm repair during the course of the study. Significant differences with respect to aneurysm rupture or aneurysm-related death could not be detected between both groups after a mean follow-up of 20 ± 12 months. EVAR and rigorous surveillance appeared to be equally safe alternatives for patients with small aneurysms, at least in the short-term run.

5. Perioperative mortality after endovascular and open repair of AAA

The evidence report prepared for the AHRQ (Wilt et al., 2006) compared EVAR with open repair in patients who were medically fit for open repair. The pooled 30-day mortality was 1.6 % for EVAR vs. 4.7 % for open repair of AAA. This may lead to the conclusion that endovascular repair is preferable to open repair with respect to the 30-day operative mortality. The conclusion is based mainly on the results of the EVAR 1 trial (Greenhalgh et al., 2004) and the DREAM study (Prinssen et al., 2004), which found a perioperative mortality for EVAR vs. open repair of 1.6% vs. 4.6%, and 1.2% vs. 4.6%, respectively. Later on, an additional 170 patients were enrolled in the EVAR 1 trial, with mortality at 30 days after surgery of 1.8% in the endovascular repair group and 4.3 % in the open repair group (United Kingdom EVAR Trial Investigators, 2010a). Also in the Veterans Affairs Cooperative Study, EVAR resulted in fewer perioperative deaths than open repair (0.5 % vs. 3.0%) (Lederle et al., 2009). In patients 67 years of age or older, a study with 22,830 matched patients in each cohort described a perioperative mortality after EVAR of 1.2 % vs. 4.8 % after open repair. The reduction in mortality with EVAR increased with patient age (2.1% difference for patients 67 to 69 years old to 8.5% for those 85 years of age or older) (Schermerhorn et al., 2008). Additional information provides a systematic review and meta-analysis of the literature including 28,862 patients. In this review, the pooled estimate for operative mortality with EVAR was 3.3% (95% confidence interval 2.9 to 3.6%) (Franks et al., 2007). In reverse, a meta-analysis considering 115,273 elective open AAA repairs mentioned a mean mortality rate of 5.56 %, with a significant relationship between higher surgeon caseload and lower mortality (E.L.Young et al., 2007). After all, the German national registry comprising 10,163 elective open repairs of AAA performed in 131 hospitals reported an overall perioperative mortality rate of 3.2% (Eckstein et al., 2007).

5.1 Long-term outcome after endovascular and open repair of AAA

Long-term outcome after aneurysm repair depends on the patient`s age, his risk factors and comorbidities. In the UK Small Aneurysm Trial, the death rate in these patients was about twice that in the general population matched for age and sex (Powell et al., 2007). Others found the long-term survival after elective AAA open repair similar to that in the general population, with a survival rate of 50.7 % and 31.5 % at 10 and 15 years after surgery. The main cause of death was cardiovascular disease (18.2%), followed by cancer (14.5%) (Vega de Céniga et al., 2010). In the Swedish Vascular Registry, crude long-term survival at 10 years after elective AAA repair was 33.8% for women and 40.4 % for men (Mani et al., 2009). Excluding AAA repair-related mortality, defined as death within 90 days after surgery, relative survival at 10 years after repair was 53.6 % for women and 72.2 % for men. Two

randomized trials compared the long-term outcome after endovascular vs. open repair of AAA. In the UK EVAR 1 trial, after a median follow-up of 6.0 years 260/626 (41.5 %) patients had died in the EVAR group compared with 264/626 (42.2%) in the open repair group (United Kingdom EVAR Trial Investigators, 2010a). 76 of these 524 deaths were aneurysm related, 5.8% in the EVAR and 6.4% in the open repair group. This means that the early benefit of lower operative mortality in the EVAR group was completely lost in the longer term, with substantially higher aneurysm-related mortality in the EVAR group than in the open repair group during follow-up. In the DREAM study, too, no differences were seen between both procedures in total mortality or aneurysm-related mortality in the long-term run. Six years after randomization, the cumulative overall survival rates were 69.9% for open repair and 68.9 % for endovascular repair (De Bruin et al., 2010). In patients considered to be physically ineligible for open repair of AAA the survival rates are distinctly lower. In the EVAR 2 trial those patients were randomly assigned to undergo EVAR or to have no intervention (United Kingdom EVAR Trial Investigators, 2010b).The mean age of the patients was 76.8 ± 6.5 years, the mean aneurysm diameter was 6.7± 1.0 cm. After a median follow-up of 3.1 years, death from any cause was seen in 145/197 (73.6%) patients of the EVAR group and in 160/207 (77.3%) of the no repair group. Thus, EVAR as compared with no intervention did not lead to an improvement in overall survival, although the aneurysm-related mortality was significantly reduced by the intervention. (The overall aneurysm-related deaths were 25/197 (12.7%) in the EVAR group and 53/207 (25.6%) in the no repair group).

5.2 Reinterventions and readmissions after endovascular and open repair of AAA

Graft-related complications and reinterventions constitute an argument against endovascular repair. In the EVAR1 trial, the overall rates of graft-related complications and reinterventions were higher by a factor of three to four in the EVAR group than in the open repair group (United Kingdom EVAR Trial Investigators, 2010a). The rate of complications for all patients was 12.6 per 100 person-years in the endovascular repair group and 2.5 per 100 person-years in the open repair group. The DREAM study (De Bruin et al., 2010) reported six years after randomization cumulative rates of freedom from secondary interventions of 81.9% for open repair and 70.4 % for EVAR. After open repair, the most frequent reintervention was correction of an abdominal incision hernia, whereas EVAR reinterventions were most often performed because of endograft-related complications, such as endoleak and endograft migration. The French ACE trial compared EVAR and open repair in patients with AAA anatomically suitable for EVAR and at low-risk or intermediate-risk for open surgery (Becquemin et al., 2011). At 3 years of follow-up, there was no difference in in-hospital mortality or survival, however, the crude percentage of reinterventions was higher in the EVAR group than after open surgery (16% vs. 2.4%) with a trend toward a higher aneurysm-related mortality (4% vs. 0.7%). In this study, open repair of AAA proved to be as safe as EVAR in patients with low to intermediate risk factors, but remained a more durable option. In the two cohorts of Medicare beneficiaries described by Schermerhorn et al., 2008 late survival was similar after open repair as compared with EVAR, but late reinterventions related to AAA were more common after EVAR vs. open repair (9.0% vs. 1.7%). This higher reintervention rate was balanced by an increase in laparotomy-related reinterventions and hospitalizations after open repair (overall, at 4 years these interventions occurred in 4.1% of patients in the EVAR group and 9.7 % in the open

repair group). This research team reported subsequently long-term results without any change in the conclusion (Giles et al., 2011). Through 6 years of follow-up, overall reinterventions or readmissions were slightly more common after EVAR vs. open repair (7.6 vs. 7.0/100 person-years). Reinterventions or readmissions accounted for 9.6% of all EVAR deaths and 7.6% of all open repair deaths in the follow-up period. The difference likely contributed to the erosion of the perioperative survival benefit of EVAR over time.

5.3 Cost-effectiveness of endovascular and open repair of AAA

A detailed cost analysis of EVAR and open repair was provided in the EVAR 1 trial (United Kingdom EVAR Trial Investigators, 2010a). The mean cost of the primary aneurysm repair was £13,019 in the EVAR group and £11,842 in the open repair group. During 8 years of follow-up, the mean cost of aneurysm-related readmissions was £2,283 in the EVAR group and £442 in the open repair group. The total average cost of aneurysm-related procedures in the EVAR group was £3,019 more than in the open repair group. A Health Technology Assessment (HTA) report analyzed the cost-effectiveness of endovascular repair of AAA in patients at varying levels of risk on the basis of six published decision models (Chambers et al., 2009). Both models considered relevant for the decision in the UK concluded that EVAR was not cost-effective on average compared with open repair at a threshold of £20,000 per quality adjusted life-year (QALY). Based on the results of this assessment of clinical effectiveness and cost-effectiveness, open repair should be the treatment of choice for patients with AAA who have good or moderate fitness. In subgroup analysis, EVAR was likely to be cost-effective in patients with a poor risk of operative mortality. In patients considered of very poor fitness or unfit of open repair, EVAR may be cost-effective at a threshold of £20,000 per QALY up to 77 years in patients with an 8 cm aneurysm, up to 74 years in patients with a 6 cm aneurysm, and up to 71.5 years in patients with a 5 cm aneurysm. Increasing the threshold to £30,000 per QALY increases the age at which EVAR is cost-effective by about 2 years. The HTA report (Chambers et al., 2009) besides concluded that EVAR cannot currently be recommended for the treatment of ruptured aneurysms. Hayes et al., 2010 came to the opposed argumentation. In their health economic model EVAR dominated open repair in the base case analysis, with a mean cumulative cost/patient of £17,422 for EVAR and £18,930 for open repair of acute (ruptured or symptomatic) AAA. In the emergency setting, EVAR was cost-effective compared with open repair at a threshold value of £20,000 to 30,000 per QALY.

5.3.1 Cost-effectiveness of surgery vs. surveillance in small aneurysms

Cost was analyzed in the UK Small Aneurysm Trial (Powell et al., 2007). After 12 years of follow-up, three-quarters of the surveillance group eventually had aneurysm repair. Estimates suggested that the cost of treatment was 17% higher in the early surgery group compared with the surveillance group, with a mean difference of £1326. In this trial, most of the patients underwent open aneurysm repair. Whether EVAR would be more cost effective in small aneurysms compared with surveillance was analyzed by K.C. Young et al., 2010 in a Markov model. The model demonstrated that early EVAR for 4.0 cm-5.4 cm AAA led to fewer QALYs at greater costs when compared with observational management and elective repair at 5.5 cm. From this data it must be concluded that in patients with small aneurysms surveillance is more cost effective than early surgery independently of the kind of surgical procedure.

6. Mortality of ruptured AAA (rAAA)

Heikkinen et al., 2002 assessed the mortality of rAAA in a defined geographic area. The mean annual incidence of rAAA was 6.3/100,000 inhabitants. Out of 221 patients presenting with rAAA, 82 (37%) died before arriving at hospital. 79.8 % of the admitted patients underwent emergency surgery. The overall hospital mortality was 63.3 %, including the nonadmitted cases the cumulative mortality of rAAA was 76.9 %. Similar ratios were observed by Qureshi et al., 2007. In this study, 48% (225/468) of patients with rAAA died before surgical repair (including the patients dying in the community). The 30-day perioperative mortality of rAAA was 43 % (105/243 patients), while overall mortality was 70% (330/468), including the deaths in the community. Filipovic et al., 2007 analyzed treatment and outcome after emergency hospital admission for rAAA in England. A total of 2463 women and 7615 men were admitted with a primary diagnosis of rAAA (mean age 79.8 and 74.9 years, respectively). Only 60% of patients underwent surgical repair (39.6 % of women and 66.4% of men). Overall, 75.6 % of women and 61.7 % of men died within 30 days of admission. McPhee et al., 2007 used the Nationwide Inpatient Sample of the USA to identify 37,016 patients presenting with rAAA between the years 2001 and 2004. In this analysis, too, women were less likely to undergo surgical intervention compared to men (59% vs. 70%). For those that underwent repair, women had higher in-hospital mortality rates than men (43% vs. 36%). A metaanalysis of 116 studies published between 1991 and 2006 and comprising 60,822 patients suggested that overall mortality of open repair for rAAA was 48.5 % and did not change significantly over the years (Hoornweg et al., 2008).

6.1 Endovascular vs. open repair of ruptured AAA

The question arises whether EVAR might be superior to open surgery for treatment of rAAA. No randomized trials could be identified so far by a Cochrane review to answer this issue (Dillon et al., 2007). There was no high quality evidence to support the use of emergency EVAR in the treatment of rAAA. Nevertheless, these authors assumed that in selected cases EVAR may be associated with a trend towards reduction in blood loss, duration of intensive care treatment, and mortality. This assumption is confirmed by a series of 104 consecutive patients with rAAA, of whom 25 underwent endovascular repair, and 79 open surgery (Ten Bosch et al., 2010). In this study the intraoperative, 30-day, and 6-month mortality was 4%, 20%, and 28% after EVAR compared with 6.1%, 45.5%, and 54.5% after open surgery. Davenport et al., 2010 examined the National Surgical Quality Improvement Program database from the years 2005 to 2007 to compare 30-day multicenter outcomes for endovascular vs. open repair of rAAA. After adjustment for preoperative mortality risk factors, the mortality risk was higher for open repair vs. EVAR but did not reach significance. However, composite 30-day morbidity risk was significantly lower after EVAR vs. open repair of rAAA. Open repair was associated with increased transfusion requirements. Veith et al., 2009 argued that EVAR has a lower procedural mortality at 30 days than open repair at least in selected cases and that EVAR is better than open repair for treating patients with rAAA provided they have favorable anatomy. In this collected experience with use of endovascular repair in 1037 patients with rAAA overall 30-day mortality after EVAR was 21.2%. Centers performing EVAR for rAAA whenever possible, did so in 28% to 79% of their patients, and had a 30-day mortality of 19.7% for 680 EVAR patients and 36.3 % for 763 open repair patients. In addition, outcome following endovascular and open repair of rAAA was evaluated by Giles et al., 2009 interrogating the

Nationwide Inpatient Sample database to identify all repairs between 2000 and 2005 for rAAA. In the study period, 2323 patients (1794 men; median age 75 years) with rAAA had endovascular repair, while 26,106 patients (20,311 men; median age 73 years) had an open procedure. Overall mortality after rAAA repair was 40.8%, 32.6% for endovascular and 41.5% for open repair. Mortality after EVAR was significantly lower than after open surgery for patients ≥70 years (36% vs. 47%), but not for those <70 years (24% vs. 30%). McPhee et al., 2009 used the same database for the years 2001- 2006. They as well demonstrated lower overall in-hospital mortality for EVAR than open repair of rAAA (31.7% vs. 40.7%). The survival benefit of EVAR over open repair was amplified by institutional volume. Higher elective open repair as well as rAAA volume increased the mortality advantage for EVAR.

6.2 Long-term outcome after repair of ruptured AAA

In the Swedish Vascular Registry (Mani et al., 2009) the 10-year crude survival after rAAA repair was 13.2 % in women and 24.9 % in men; the relative survival, excluding AAA repair-related mortality, was 46% and 68.4%, respectively. Schlösser et al., 2010 have quantified the age-and gender-specific mortality risks for 1,463 patients hospitalized for rAAA. Mean age was 79 years in women and 72 years in men. Mortality risks at 28-day, 1-year, and 5-year increased significantly with age (28-day: from 36 to 91 % in men, and 59 to 92% in women; 5-year: from 51 to 97% in men and 79 to 96 % in women). In patients aged <80 years, mortality risks were significantly higher in women than in men. Cerebrovascular disease and previous hospitalization for congestive heart failure were significant predictors of short- and long-term mortality. It must remain an open question whether a prophylactic aneurysm repair before rupture would have had a major influence on the life expectancy of these patients.

7. Screening for AAA

The essential findings regarding screening are subsumed in a Cochrane review on the basis of four completed randomized controlled studies (Cosford & Leng, 2007). These were conducted in Chichester, UK (Scott et al., 1995), in the UK (Multicentre Aneurysm Screening Study) (MASS) (Ashton et al., 2002), in Perth, Western Australia (Norman et al., 2004), and in Viborg, Denmark (Lindholt et al., 2005). In these trials, 15,775 men and women aged 65 to 80 years (Chichester), 67,800 men aged 65 to 74 years (MASS), 41,000 men aged 65 to 83 years (Western Australia), and 12,639 men aged 64 to 73 (Viborg) were randomly allocated to ultrasound screening for AAA or no intervention. The Cochrane review concluded that, in summary of the results, there was a significant reduction in mortality from AAA in men aged 65 to 79 years who undergo ultrasound screening (odds ratio (OR) 0.60; 95% Confidence Interval (CI) 0.47 to 0.78). There was insufficient evidence to demonstrate benefit in women (Cosford & Leng, 2007). All-cause mortality was not significantly different between screened and unscreened groups three to five years after screening (men, OR 0.95; 95% CI 0.85 to 1.07); women, OR 1.06; 95% CI 0.93 to 1.21). This had been expected given the relative infrequency of AAA as a cause of death. Meanwhile the final results of the Chichester study have been reported (Ashton et al., 2007) with respect to 6040 men randomized to ultrasound screening or to the control group. Screening detected an AAA in 170 patients. In the group of men invited for screening, AAA-related mortality was reduced over a median 15-year follow-up period from 1.8 to 1.6 %, although the results were not significant for this population size. A mortality benefit from screening men aged 65 to 74

years for AAA was seen in MASS over 10 years of follow-up (S.G. Thompson et al., 2009). In this trial 33,883 men were invited to screening and 27,204 (80%) attended. 1334 aneurysms ≥ 3.0 cm were detected at initial scan. Patients were referred to a hospital for possible elective surgery when the aneurysm reached 5.5 cm, the aneurysm had expanded by 1cm or more in one year, or symptoms attributable to the AAA were reported. Surveillance involved rescanning: annually for those with AAA diameters of 3.0 - 4.4 cm and every three months for those with diameters of 4.5 to 5.4 cm. Over the 10 years of the trial 552 elective operations took place in the invited group and 226 in the control group. Overall, 155 deaths related to AAA (absolute risk 0.46 %) occurred in the invited group and 296 (0.87%) in the control group. Total mortality, however, did not differ significantly between both groups (30.3 % in the invited group and 30.9% in the control group, respectively), because deaths from AAA comprised only about 2% of all deaths. A comparable long-term benefit was observed in the Viborg trial. The relative risk reduction of the screening program in AAA-related mortality was 66%, but the risk reduction in all-cause mortality amounted merely 2% (Lindholt et al., 2010). The number needed to screen to save one life was 352 (Lindholt et al., 2005). Pooled mid-term and long-term effects of screening on AAA-related and total mortality were examined by Lindholt & Norman, 2008 in a meta-analysis including new data not considered in the Cochrane review (Cosford & Leng, 2007). Screening offered a significant mid-term reduction in AAA-related mortality. In addition, all-cause mortality was reduced after 3 to 5 years, but not significantly. The long-term results showed a significant reduction in AAA-related mortality and overall mortality. A significantly greater number of elective operations, and significantly fewer emergency operations were also noticed in the invited group compared to the controls. An updated meta-analysis of randomized controlled trials of AAA screening in men aged ≥ 65 years revealed also a strong trend toward a significant benefit provided by screening. Screening for AAA showed a reduction in all-cause long-term mortality by 5 per 1000 compared with controls (number needed to screen to save one life was 217) (Takagi et al., 2010a). The recommendations of the U.S. Preventive Services Task Force (USPSTF) are consistent with the results of the studies mentioned. One-time screening for AAA by ultrasonography in men aged 65 to 75 years who have ever smoked is recommended (grade B recommendation). No recommendation is made for or against screening for AAA in men age 65 to 75 years who have never smoked (grade C recommendation). The USPSTF recommends against routine screening for AAA in women (grade D recommendation) (U.S. Preventive Services Task Force, 2005). The Society for Vascular Surgery (SVS) greatly expanded these recommendations (Chaikof et al., 2009) in contrast to the USPSTF. The SVS recommends one time ultrasound screening for AAA for all men at or older than age 65, or as early as age 55 years for those with a family history of AAA (Level of recommendation: strong. Quality of evidence: high). One-time ultrasound screening for AAA is recommended for all women at or older than 65 years with a family history of AAA or who have smoked (Level of recommendation: strong. Quality of evidence: moderate). As a direct consequence of these recommendations the Screen Abdominal Aortic Aneurysms Very Efficiently (SAAAVE) Act is effective in the USA since January 2007. Medicare beneficiaries have access to a free, one-time ultrasound screening to check for AAA. The screening will be available for men who have smoked at least 100 cigarettes during their life, and men and women with a family history of AAA. On this basis, a total of 2918 veteran males 65 to 75 years of age (average age, 71 +/- 6 years) were screened for AAA over a 1-year period (Lee et al., 2009). An AAA was diagnosed in 5.1% (148/2918) of patients. The majority of aneurysms (83%)

were small (3.0 - 4.4 cm). A clear-cut indication for prophylactic repair (aneurysm diameter > 5.5 cm) was given in 4.1 % (6/148) of aneurysms and 0.2 % of patients, respectively. The NHS in the UK also announced an AAA screening program being introduced gradually across England from spring 2009. Once fully implemented, the program will invite all men for screening during the year that they turn 65. Depending on the results from the scan surveillance imaging (follow-up scan) will be offered in a year for patients with an AAA of 3 to 4.4 cm, and in three months for patients with an aortic diameter of 4.5 to 5.4 cm. Men with a large aneurysm of over 5.5 cm are referred to a consultant vascular surgeon to discuss treatment (NHS Abdominal Aortic Aneurysm Screening Programme, 2011).

7.1 Aneurysm surveillance/ rescreening

The optimal frequency of aneurysm surveillance has not been defined by randomized clinical studies. The SVS (Chaikof et al., 2009) recommends the following procedure. Re-screening patients for AAA is not recommended if an initial ultrasound scan performed on patients 65 years of age or older demonstrates an aortic diameter of < 2.6 cm (Level of recommendation: strong. Quality of evidence: moderate). Follow-up imaging at 5-year intervals is recommended for patients with a maximum aortic diameter between 2.6 and 2.9 cm (Level of recommendation: weak. Quality of evidence: low). Follow-up imaging at 3 years is recommended for patients with an AAA between 3.0 and 3.4 cm (Level of recommendation: strong. Quality of evidence: low). Surveillance imaging at 12-month intervals is recommended for patients with an AAA of 3.5 to 4.4 cm (Level of recommendation: strong. Quality of evidence: low). Surveillance imaging at 6-month intervals is recommended for patients with an AAA of 4.5 to 5.4 cm (Level of recommendation: strong. Quality of evidence: low).

7.2 Cost effectiveness of screening for AAA

The high mortality of rAAA, particularly when the patients who die before surgical repair are considered and not exclusively the procedure related mortality, certainly favors the recommendation of prophylactic repair of asymptomatic AAA 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 cost effectiveness of ultrasound screening for AAA has been assessed in several studies. In MASS, the adjusted mean additional cost per patient screened was £ 63.4 at 4 years follow-up (Multicentre Aneurysm Screening Study Group, 2002). 47 fewer deaths related to AAA were observed in the screening group than in the control group at total additional costs of £ 2.2m. Over 4 years the estimated mean incremental cost effectiveness ratio for screening was £ 28,400 per life year gained. Because the main costs of the program (initial screening and elective surgery for those with aneurysm diameter > 5.5 cm) occur early on, whereas the benefit in terms of life years increases over time, the cost per life year gained was estimated to fall around £ 8000 after 10 years. This estimation was confirmed later on. The extent of reduction in number of deaths related to AAA in the invited group led to an estimated incremental cost effectiveness ratio of £ 7600 per life year gained over the 10 years of the trial (S.G. Thompson et al., 2009). The cost effectiveness of screening for AAA was also estimated in the Viborg trial. The costs per life year saved were Euro 9057 after 5 years (Lindholt et al., 2006). In the long-term run screening was found to be even more cost effective, at a probability above 0.97 for a willingness to pay threshold of

Euro 5000 (Lindholt et al., 2010). In contrast, the cost effectiveness of screening Danish men aged 65 for AAA was rejected by Ehlers et al., 2009a. They developed a decision tree and Markov model to simulate the short-term and long-term effects of screening for AAA. In this analysis, the incremental cost effectiveness ratio varied from £32,640 to £ 66,001 per QALY with a mean cost of £43 485. At a willingness to pay threshold of £30,000 the probability of screening being cost effective was less than 30%. Their study contradicted the widespread conception that screening for AAA is cheap. A possible reason for the discrepancy between this study and that by S.G. Thompson et al., 2009 might be that the MASS results (S.G. Thompson et al., 2009) reflect a sample group screened at age 65-74. Ehlers et al., 2009a, however, have directly modeled the effects of the current policy of inviting men aged 65 to participate in a screening program, what is fundamentally different from a one-time screening of all elderly men (Buxton, 2009; Ehlers et al. 2009b). This latter approach will benefit from a higher prevalence of AAA and thus show a better cost effectiveness (Ehlers et al. 2009b). Ehlers et al., 2009a emphasized that ultrasonography may be cheap on a per person basis, but screening is not just a test but a program. If screening is to be effective then overall administration of the program, operational planning, a communication strategy, a quality assurance system, and more are needed. Hoffmann et al., 2009 assessed routine screening for asymptomatic AAA in high-risk patients in an emergency department. The sonographers were able to completely visualize and correctly measure the abdominal aortas of only 71% of patients. AAA ultrasonography performance varied markedly among sonographers, depending on training and experience (Hoffmann et al., 2010). Even in a special aortic screening program, out of 2918 patients 9.9 % were inappropriately screened (Lee et al., 2009). How the quality of ultrasonography influences the cost effectiveness of screening programs has to be carefully monitored. In all published decision analytic models of AAA screening, patients with an AAA ≥ 5.5 cm were assumed to face a constant probability of rupture no matter how many years they have had a large AAA (Ehlers et al., 2008). If all men are screened in the year that they turn 65 the calculated number of gained life years due to screening could be overestimated as the age of males dying of ruptured AAA is well over 65 years (72.4 % of men who died in 2009 of ruptured AAA in England and Wales were ≥ 75 years old, see above). In MASS, the mean age of the men who died at 10-year follow-up was 74.7 years in both, invited group and control group, respectively. These findings did not suggest any major general differences in health care between the groups as a result of screening (S.G. Thompson et al., 2009). In addition, economic evaluations did not incorporate evidence that the lives of tobacco smokers are generally shorter than those of the general population (> 90% of patients with AAA have a history of smoking) (Ehlers et al., 2008). MASS found an association between AAA death and participation in the AAA screening program, but life-style issues were not controlled. The gained life years could be due to other things than surgery such as smoking cessation and further life-style changes (Ehlers et al., 2009b). In this context it should be noted that statin therapy was not analyzed in the cost effectiveness studies. The use of statins seems to slow the growth of small aneurysms and to improve freedom from aneurysm repair and rupture (Schouten et al., 2006; Mosorin et al., 2008; Takagi et al., 2010b). If these results should be confirmed in randomized studies, the recommendations for small aneurysm repair would have to be modified and the cost effectiveness of screening would be diminished. Moreover, the introduction of EVAR could have a negative impact on cost effectiveness of screening what must be evaluated in the future. Provided that screening

and/or repair are employed on a much wider scale than occurred in the trials, the ratio of benefit to harm would be reduced or even reversed. EVAR is assumed to be a moderately risky procedure, if screening leads to a large increase in elective EVAR in patients whose AAA would never have ruptured, the expected benefit of screening on AAA-related mortality may never be realized (Lederle, 2008). Instead screening all men during the year that they turn 65, a selective screening might be more cost effective. Mani et al., 2010 evaluated the long-term outcome and the cost effectiveness of selective AAA screening among patients referred to the vascular laboratory for arterial examination. An AAA was detected in 181 of 5924 (3%) patients (mean age 72.8 years), of whom 21.5% underwent elective repair (perioperative mortality 5.1%) after 7.5 years of follow-up. In this analysis, screening was cost effective (11,084 Euro/life year gained) which suggests that screening patients with atherosclerotic disease, rather than the whole population, might be more cost effective (Greenhalgh, 2004).

8. Conclusion

The available data have proven the benefit of screening with respect to a reduction of AAA-related mortality. One-time screening for AAA by ultrasonography in men aged 65 to 75 years who have ever smoked is therefore recommended (U.S. Preventive Services Task Force, 2005). Whether these recommendations should be further extended as suggested by the Society for Vascular Surgery (Chaikof et al., 2009) is debatable. So far, the risk reduction in all-cause mortality by screening is small. Changes in the management of ruptured and non-ruptured aneurysms such as EVAR might have a significant impact on efficiency and cost effectiveness of screening programs that is not elucidated. Some doubts remain with respect to the NHS screening program (Johnson, 2008) inviting all men for screening during the year that they turn 65. At least for smaller aneurysms the risk of rupture is difficult to estimate. Statins and other new treatments are expected to decelerate the growth of small aneurysms found by screening. The mortality of prophylactic AAA repair can be greater than the likelihood of rupture. Operative results of hospitals are central to whether screening saves or looses lives (Greenhalgh & Powell, 2007). Operative mortality may be lower with EVAR compared with open repair; however, EVAR comprises frequent follow-up examinations. In addition, reinterventions which impair patient's quality of life are more common after EVAR than after open repair. People who have been screened and found to have an aorta that is dilated less than 5.5 cm, will be condemned to six monthly or annual ultrasound examinations to estimate the size of the aneurysm. These people have felt comfortable as long as they were not informed about the diagnosis; the impact of the knowledge of the diagnosis on quality of life is scarcely investigated. The demand for national screening programs concerns not only patients with a possible indication for operation but also the much greater group of persons in whom the size of the aneurysm is small and constitutes no indication for treatment (and will never be so). Johnson, 2008 claims rightly, that persons taking the test will need intensive counseling about the possible consequences that screening might have for their future lives and psychological wellbeing. The psychological consequences of screening were described by Lindholt et al., 2000. Quality of life was lower among men with a small AAA compared to the controls and declined further below control values during the period of conservative treatment. Diagnosis of an AAA impaired quality of life permanently and progressively in conservatively treated patients, anything but surprising, since a cohort of patients find it

intolerable to have what they often describe as a "time bomb inside" them (Johnson, 2008). As far as cost effectiveness of screening for AAA is concerned, the society in question has to decide whether £ 7600 up to more than £ 44,000 per life year gained is adequate. In the case of limited resources it is justified to ask whether the funds should be used for search of an asymptomatic disease or whether it would be better to invest in prophylactic measures like smoking cessation. The lack of attention that smoking cessation receives in some primary and specialist settings is a concern; > 90% of patients with AAA have a history of smoking. Nicotine replacement therapy and brief counseling by physicians costs around US $ 2000 to 6000 per life year saved compared with no treatment (Lancet, 2009). These caveats emphasize that costs and outcomes of screening for AAA need to be carefully monitored.

9. References

Ashton HA, Buxton MJ, Day NE, Kim LG, Marteau TM, Scott RA, Thompson SG & Walker NM; Multicentre Aneurysm Screening Study Group. (2002). The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet* 360(9345):1531-1539

Ashton HA, Gao L, Kim LG, Druce PS, Thompson SG & Scott RA. (2007). Fifteen-year follow-up of a randomized clinical trial of ultrasonographic screening for abdominal aortic aneurysms. *Br J Surg* 94(6): 696-701

Ballard DJ, Filardo G, Fowkes G & Powell JT. (2008). Surgery for small asymptomatic abdominal aortic aneurysms. *Cochrane Database Syst Rev* 8; (4): CD001835

Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, Steinmetz E & Marzelle J; ACE trialists.(2011). A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. *J Vasc Surg* 53(5): 1167-1173

Buxton MJ. (2009). Screening for abdominal aortic aneurysm. *BMJ* 338:b2185

Chaikof EL, Brewster DC, Dalman RL, Makaroun MS, Illig KA, Sicard GA, Timaran CH, Upchurch GR Jr & Veith FJ; Society for Vascular Surgery.(2009). The care of patients with an abdominal aortic aneurysm: the Society for Vascular Surgery practice guidelines. J Vasc Surg 50 (4 Suppl): S2-49

Chambers D, Epstein D, Walker S, Fayter D, Paton F, Wright K, Michaels J, Thomas S, Sculpher M & Woolacott N. (2009). Endovascular stents for abdominal aortic aneurysms: a systematic review and economic model. *Health Technol Assess* 13(48): 1-189, 215-318, iii

Cosford PA & Leng GC. (2007). Screening for abdominal aortic aneurysm. *Cochrane Database Syst Rev* (2): CD002945

Davenport DL, O'Keeffe SD, Minion DJ, Sorial EE, Endean ED & Xenos ES. (2010). Thirty-day NSQIP database outcomes of open versus endoluminal repair of ruptured abdominal aortic aneurysms. *J Vasc Surg* 51(2): 305-309.e1

De Bruin JL, Baas AF, Buth J, Prinssen M, Verhoeven EL, Cuypers PW, van Sambeek MR, Balm R, Grobbee DE & Blankensteijn JD; DREAM Study Group.(2010). Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 362(20): 1881-1889

Dillon M, Cardwell C, Blair PH, Ellis P, Kee F & Harkin DW. (2007). Endovascular treatment for ruptured abdominal aortic aneurysm. *Cochrane Database Syst Rev* (1): CD005261

Dimick JB, Upchurch GR Jr. (2003). The quality of care for patients with abdominal aortic aneurysms. *Cardiovasc Surg* 11(5): 331-336

Eckstein HH, Bruckner T, Heider P, Wolf O, Hanke M, Niedermeier HP, Noppeney T, Umscheid T & Wenk H. (2007). The relationship between volume and outcome following elective open repair of abdominal aortic aneurysms (AAA) in 131 German hospitals. *Eur J Vasc Endovasc Surg* 34(3): 260-266

Ehlers L, Sørensen J, Jensen LG, Bech M & Kjølby M. (2008). Is population screening for abdominal aortic aneurysm cost-effective? *BMC Cardiovasc Disord* 8: 32

Ehlers L, Overvad K, Sørensen J, Christensen S, Bech M & Kjølby M. (2009a). Analysis of cost effectiveness of screening Danish men aged 65 for abdominal aortic aneurysm. *BMJ* 338: b2243

Ehlers L, Kjølby M, Christensen S, Bech M, Overvad K & Sørensen J. (2009b). The Danish health economic modelling study on AAA screening is not flawed. Rapid response to: Analysis of cost effectiveness of screening Danish men aged 65 for abdominal aortic aneurysm. *BMJ* 338: b2243

Filipovic M, Seagroatt V & Goldacre MJ. (2007). Differences between women and men in surgical treatment and case fatality rates for ruptured aortic abdominal aneurysm in England. *Br J Surg* 94(9): 1096-1099

Forsdahl SH, Singh K, Solberg S & Jacobsen BK. (2009). Risk factors for abdominal aortic aneurysms: a 7-year prospective study: the Tromsø Study, 1994-2001. *Circulation* 119(16): 2202-2208

Franks SC, Sutton AJ, Bown MJ & Sayers RD. (2007). Systematic review and meta-analysis of 12 years of endovascular abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg* 33(2): 154-171

Giles KA, Hamdan AD, Pomposelli FB, Wyers MC, Dahlberg SE & Schermerhorn ML. (2009). Population-based outcomes following endovascular and open repair of ruptured abdominal aortic aneurysms. *J Endovasc Ther* 16(5): 554-564

Giles KA, Landon BE, Cotterill P, O'Malley AJ, Pomposelli FB & Schermerhorn ML. (2011). Thirty-day mortality and late survival with reinterventions and readmissions after open and endovascular aortic aneurysm repair in Medicare beneficiaries. *J Vasc Surg* 53(1): 6-12,13.e1

Greenhalgh RM. (2004). National screening programme for aortic aneurysm. *BMJ* 328(7448): 1087-1088

Greenhalgh RM, Brown LC, Kwong GP, Powell JT & Thompson SG; EVAR trial participants. (2004). Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet* 364(9437): 843-848

Greenhalgh R, Powell J. (2007). Screening for abdominal aortic aneurysm. *BMJ* 335(7623): 732-733

Hayes PD, Sadat U, Walsh SR, Noorani A, Tang TY, Bowden DJ, Gillard JH & Boyle JR. (2010). Cost-effectiveness analysis of endovascular versus open surgical repair of acute abdominal aortic aneurysms based on worldwide experience. *J Endovasc Ther* 17(2): 174-182

Heikkinen M, Salenius JP & Auvinen O.(2002). Ruptured abdominal aortic aneurysm in a well-defined geographic area. *J Vasc Surg* 36(2): 291-296

Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, Hiratzka LF, Murphy WR, Olin JW, Puschett JB, Rosenfield KA, Sacks D, Stanley JC, Taylor LM Jr, White CJ, White J, White RA, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK,

Nishimura R, Ornato JP, Page RL & Riegel B. (2006). ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease) endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *J Am Coll Cardiol* 47(6): 1239-1312

Hoffmann B, Um P, Bessman ES, Ding R, Kelen GD & McCarthy ML. (2009). Routine screening for asymptomatic abdominal aortic aneurysm in high-risk patients is not recommended in emergency departments that are frequently crowded. *Acad Emerg Med* 16(11): 1242-1250

Hoffmann B, Bessman ES, Um P, Ding R & McCarthy ML. (2011). Successful sonographic visualisation of the abdominal aorta differs significantly among a diverse group of credentialed emergency department providers. *Emerg Med J* 28(6): 472 - 476

Hoornweg LL, Storm-Versloot MN, Ubbink DT, Koelemay MJ, Legemate DA & Balm R.(2008). Meta analysis on mortality of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 35(5): 558-570

Johnson JN.(2008). Should we screen for aortic aneurysm? No. *BMJ* 336(7649): 863

Lancet. (2009). Editorial: Cardiologists should be less passive about smoking cessation *Lancet* 373(9667): 867

Lederle FA, Johnson GR, Wilson SE, Chute EP, Littooy FN, Bandyk D, Krupski WC, Barone GW, Acher CW & Ballard DJ. (1997). Prevalence and associations of abdominal aortic aneurysm detected through screening. Aneurysm Detection and Management (ADAM) Veterans Affairs Cooperative Study Group. *Ann Intern Med* 126(6): 441-449

Lederle FA, Johnson GR, Wilson SE, Chute EP, Hye RJ, Makaroun MS, Barone GW, Bandyk D, Moneta GL & Makhoul RG. (2000). The aneurysm detection and management study screening program: validation cohort and final results. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. *Arch Intern Med* 160(10): 1425-1430

Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, Ballard DJ, Messina LM, Gordon IL, Chute EP, Krupski WC, Busuttil SJ, Barone GW, Sparks S, Graham LM, Rapp JH, Makaroun MS, Moneta GL, Cambria RA, Makhoul RG, Eton D, Ansel HJ, Freischlag JA & Bandyk D; Aneurysm Detection and Management Veterans Affairs Cooperative Study Group. (2002). Immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 346(19): 1437-1444

Lederle FA, Powell JT & Greenhalgh RM. (2006). Repair of small abdominal aortic aneurysms. *N Engl J Med* 354(14): 1537-1538

Lederle FA. (2008). Screening for AAA in the USA. *Scand J Surg* 97(2): 139-141

Lederle FA, Larson JC, Margolis KL, Allison MA, Freiberg MS, Cochrane BB, Graettinger WF & Curb JD; Women's Health Initiative Cohort Study. (2008). Abdominal aortic aneurysm events in the women's health initiative: cohort study. *BMJ* 337: a1724

Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT Jr, Matsumura JS, Kohler TR, Lin PH, Jean-Claude JM, Cikrit DF, Swanson KM & Peduzzi PN; Open Versus Endovascular Repair (OVER) Veterans Affairs Cooperative Study Group. (2009). Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. *JAMA* 302(14): 1535-1542

Lee ES, Pickett E, Hedayati N, Dawson DL & Pevec WC. (2009). Implementation of an aortic screening program in clinical practice: implications for the Screen For Abdominal Aortic Aneurysms Very Efficiently (SAAAVE) Act. *J Vasc Surg* 49(5): 1107-1111

Lindholt JS, Vammen S, Fasting H, Henneberg EW. (2000). Psychological consequences of screening for abdominal aortic aneurysm and conservative treatment of small abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 20(1): 79-83

Lindholt JS, Juul S, Fasting H & Henneberg EW. (2005). Screening for abdominal aortic aneurysms: single centre randomised controlled trial. *BMJ* 330(7494): 750

Lindholt JS, Juul S, Fasting H & Henneberg EW. (2006). Cost-effectiveness analysis of screening for abdominal aortic aneurysms based on five year results from a randomised hospital based mass screening trial. *Eur J Vasc Endovasc Surg* 32(1): 9-15

Lindholt JS & Norman P. (2008). Screening for abdominal aortic aneurysm reduces overall mortality in men. A meta-analysis of the mid- and long-term effects of screening for abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 36(2): 167-171

Lindholt JS, Sørensen J, Søgaard R & Henneberg EW. (2010). Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. *Br J Surg* 97(6): 826-834

Mani K, Björck M, Lundkvist J & Wanhainen A. (2009). Improved long-term survival after abdominal aortic aneurysm repair. *Circulation* 120(3): 201-211

Mani K, Alund M, Björck M, Lundkvist J, Wanhainen A. (2010). Screening for abdominal aortic aneurysm among patients referred to the vascular laboratory is cost-effective. *Eur J Vasc Endovasc Surg* 39(2): 208-216

McPhee JT, Hill JS & Eslami MH. (2007). The impact of gender on presentation, therapy, and mortality of abdominal aortic aneurysm in the United States, 2001-2004. *J Vasc Surg* 45(5): 891-899

McPhee J, Eslami MH, Arous EJ, Messina LM & Schanzer A. (2009). Endovascular treatment of ruptured abdominal aortic aneurysms in the United States (2001-2006): a significant survival benefit over open repair is independently associated with increased institutional volume. *J Vasc Surg* 49(4): 817-826

Mosorin M, Niemelä E, Heikkinen J, Lahtinen J, Tiozzo V, Satta J, Juvonen T & Biancari F. (2008). The use of statins and fate of small abdominal aortic aneurysms. *Interact Cardiovasc Thorac Surg* 7(4): 578-581

Multicentre Aneurysm Screening Study Group. (2002). Multicentre aneurysm screening study (MASS): cost effectiveness analysis of screening for abdominal aortic aneurysms based on four year results from randomised controlled trial. *BMJ* 325(7373): 1135

NHS Abdominal Aortic Aneurysm Screening Programme. February 2011. Available from http://aaa.screening.nhs.uk/cms.php?folder=2436

Norman PE, Jamrozik K, Lawrence-Brown MM, Le MT, Spencer CA, Tuohy RJ, Parsons RW & Dickinson JA. (2004). Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. *BMJ* 329(7477): 1259

Office for National Statistics. Mortality statistics. Review of the national statistician on deaths in England and Wales, 2009. February 2011. Available from www.statistics.gov.uk/downloads/theme_health/dr2009/dr-09.pdf

Ouriel K, Clair DG, Kent KC & Zarins CK; Positive Impact of Endovascular Options for treating Aneurysms Early (PIVOTAL) Investigators. (2010). Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms. *J Vasc Surg* 51(5): 1081-1087

Powell JT, Brown LC, Forbes JF, Fowkes FG, Greenhalgh RM, Ruckley CV & Thompson SG. (2007). Final 12-year follow-up of surgery versus surveillance in the UK Small Aneurysm Trial. *Br J Surg* 94(6): 702-708

Powell JT, Gotensparre SM, Sweeting MJ, Brown LC, Fowkes FG & Thompson SG.(2011). Rupture rates of small abdominal aortic aneurysms: a systematic review of the literature. *Eur J Vasc Endovasc Surg* 41(1): 2-10

Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R, Buskens E, Grobbee DE & Blankensteijn JD; Dutch Randomized Endovascular Aneurysm Management (DREAM)Trial Group. (2004). A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 351(16): 1607-1618

Qureshi NA, Rehman A, Slater N, Moss E, Shiralkar S, Patel RT, Grimley RP & Jayatunga AP. (2007). Abdominal aortic aneurysm surgery in a district general hospital: a 15-years experience. *Ann Vasc Surg* 21(6): 749-753

Schermerhorn ML, O'Malley AJ, Jhaveri A, Cotterill P, Pomposelli F& Landon BE. (2008). Endovascular vs. open repair of abdominal aortic aneurysms in the Medicare population. *N Engl J Med* 358(5):464-474

Schlösser FJ, Tangelder MJ, Verhagen HJ, van der Heijden GJ, Muhs BE, van der Graaf Y & Moll FL; SMART study group. (2008). Growth predictors and prognosis of small abdominal aortic aneurysms. *J Vasc Surg* 47 (6): 1127-1133

Schlösser FJ, Vaartjes I, van der Heijden GJ, Moll FL, Verhagen HJ, Muhs BE, de Borst GJ, Tiel Groenestege AT, Kardaun JW, Reitsma JB, van der Graaf Y & Bots ML. (2010). Mortality after hospital admission for ruptured abdominal aortic aneurysm. *Ann Vasc Surg* 24(8): 1125-1132

Schouten O, van Laanen JH, Boersma E, Vidakovic R, Feringa HH, Dunkelgrün M, Bax JJ, Koning J, van Urk H & Poldermans D. (2006). Statins are associated with a reduced infrarenal abdominal aortic aneurysm growth. *Eur J Vasc Endovasc Surg* 32(1): 21-26

Scott RA, Wilson NM, Ashton HA & Kay DN. (1995). Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. *Br J Surg* 82(8): 1066-1070

Takagi H, Goto SN, Matsui M, Manabe H & Umemoto T. (2010a). A further meta-analysis of population-based screening for abdominal aortic aneurysm. *J Vasc Surg* 52(4): 1103-1108

Takagi H, Matsui M & Umemoto T. (2010b). A meta-analysis of clinical studies of statins for prevention of abdominal aortic aneurysm expansion. *J Vasc Surg* 52(6): 1675-1681

Ten Bosch JA, Teijink JA, Willigendael EM & Prins MH. (2010). Endovascular aneurysm repair is superior to open surgery for ruptured abdominal aortic aneurysms in EVAR-suitable patients. *J Vasc Surg* 52(1): 13-18

Thompson AR, Cooper JA, Ashton HA & Hafez H .(2010). Growth rates of small abdominal aortic aneurysms correlate with clinical events. *Br J Surg* 97(1): 37-44

Thompson SG, Ashton HA, Gao L & Scott RA; Multicentre Aneurysm Screening Study Group. (2009). Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomised Multicentre Aneurysm Screening Study. *BMJ* 338: b2307

United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D & Sculpher MJ. (2010a). Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med* 362(20): 1863-1871

United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG & Epstein D. (2010b). Endovascular repair of aortic aneurysm in patients physically ineligible for open repair. *N Engl J Med* 362(20): 1872-1880

UK Small Aneurysm Trial Participants. (1998). Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. *Lancet* 352 (9141): 1649-1655

U.K. Small Aneurysm Trial Participants. (1999). Risk factors for aneurysm rupture in patients kept under ultrasound surveillance. *Ann Surg* 230(3): 289-297

UK Small Aneurysm Trial Participants. (2002). Long-term outcomes of immediate repair compared with surveillance of small abdominal aortic aneurysms. *N Engl J Med* 346(19): 1445-1452

U.S. Preventive Services Task Force. (2005). Screening for abdominal aortic aneurysm: recommendation statement. *Ann Intern Med* 142(3): 198-202

van Walraven C, Wong J, Morant K, Jennings A, Jetty P & Forster AJ. (2010). Incidence, follow-up, and outcomes of incidental abdominal aortic aneurysms. *J Vasc Surg* 52(2): 282-289

Vardulaki KA, Prevost TC, Walker NM, Day NE, Wilmink AB, Quick CR, Ashton HA & Scott RA. (1999). Incidence among men of asymptomatic abdominal aortic aneurysms: estimates from 500 screen detected cases. *J Med Screen* 6(1): 50-54

Vega de Céniga M, Estallo L, Barba A, de la Fuente N, Viviens B & Gómez R. (2010). Long-term cardiovascular outcome after elective abdominal aortic aneurysm open repair. *Ann Vasc Surg* 24(5): 655-662

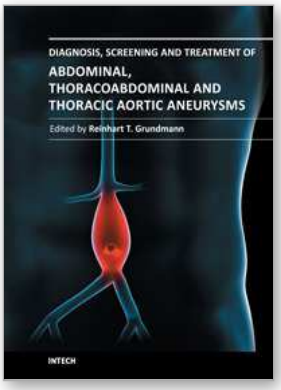
Veith FJ, Lachat M, Mayer D, Malina M, Holst J, Mehta M, Verhoeven EL, Larzon T, Gennai S, Coppi G, Lipsitz EC, Gargiulo NJ, van der Vliet JA, Blankensteijn J, Buth J, Lee WA, Biasi G, Deleo G, Kasirajan K, Moore R, Soong CV, Cayne NS, Farber MA, Raithel D, Greenberg RK, van Sambeek MR, Brunkwall JS, Rockman CB & Hinchliffe RJ; RAAA Investigators. (2009). Collected world and single center experience with endovascular treatment of ruptured abdominal aortic aneurysms. *Ann Surg* 250(5): 818-824

Wilt TJ, Lederle FA, Macdonald R, Jonk YC, Rector TS & Kane RL. (2006). Comparison of endovascular and open surgical repairs for abdominal aortic aneurysm. *Evid Rep Technol Assess (Full Rep)* 144: 1-113. Rockville (MD): Agency for Healthcare Research and Quality (US)

Xu J, Kochanek KD, Murphy SL & Tejada-Vera B. (2010). Deaths: Final Data for 2007. *National Vital Statistics Reports* 58, Number 19. Available from www.cdc.gov/NCHS/data/nvsr/nvsr58/nvsr58_19.pdf

Young EL, Holt PJ, Poloniecki JD, Loftus IM & Thompson MM. (2007). Meta-analysis and systematic review of the relationship between surgeon annual caseload and mortality for elective open abdominal aortic aneurysm repairs. *J Vasc Surg* 46(6): 1287-1294

Young KC, Awad NA, Johansson M, Gillespie D, Singh MJ & Illig KA. (2010). Cost-effectiveness of abdominal aortic aneurysm repair based on aneurysm size. *J Vasc Surg* 51(1): 27-32



Diagnosis, Screening and Treatment of Abdominal, Thoracoabdominal and Thoracic Aortic Aneurysms
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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.

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