Morbidity and Mortality Following Endovascular Repair of Abdominal Aortic Aneurysms in the Elderly

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ABSTRACT: **Background:** Endovascular aneurysm repair (EVAR) of abdominal aortic aneurysms (AAA) is associated with decreased perioperative morbidity and mortality.

Objectives: To report the outcomes of EVAR among patients older than 80 years of age.

Methods: In this retrospective study, we reviewed patients older than 80 years of age who underwent elective EVAR at our institution between 2007 and 2017. The demographics, perioperative morbidity and mortality, and long-term results are reported.

Results: During the study period, 444 patients underwent elective EVAR for AAAs. Among them 128 patients (29%) were › 80 years of age. Mean age was 84 ± 3.4 (range 80–96) years, and 110 patients (86%) were male. The EVAR was technically successful in 127 patients (99%) and there were no intraoperative mortalities. Within 30 days of the surgery, nine patients (7%) died. Major and minor adverse events occurred in 26 (20%) and 59 (46%) patients, respectively. Factors associated with increased risk of perioperative morbidity and mortality included chronic kidney disease, peripheral artery disease, and the existence of three or more co-morbidities.

Conclusions: EVAR in the elderly can be performed with a high rate of success; however, it is associated with a substantial rate of morbidity and mortality, particularly when patients present with multiple co-morbidities. When performing EVAR in this population group, the risk of rupture must be considered opposed to the life expectancy of these patients and the risk of perioperative morbidity and mortality.

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KEY WORDS: elderly, endovascular aneurysm repair (EVAR), morbidity, mortality, overall survival

Life expectancy in the western world is gradually increasing. The population over 80 years old is also on the rise. The percentage of octogenarians and nonagenarians in the general population is currently 1.8%, and is expected to triple in size by 2050. People aged 80 years or older comprise the fastest growing age group in the world, increasing at 3.8% per year. By the middle of the century, one-fifth of the elderly will be 80 years or older [1]. As a result, the elderly population undergoing vascular interventions will increase in the years to come. As abdominal aortic aneurysm (AAA) is an age-related disease, the number of patients presenting to caregivers with AAAs is also expected to increase.

Open repair of AAAs is an acceptable method of treatment and carries a mortality rate of 5% in large randomized controlled studies [2,3]. Open repair in patients > 80 years old is often not performed since this population group is at risk of significant perioperative mortality and has multiple co-morbidities when compared to younger patients [4]. Advanced age is an independent risk factor for perioperative death and patients above the age of 80 years are associated with increased risk of 30-day and 1-year mortality after AAA repair [5-7].

Since the introduction of endovascular aneurysm repair (EVAR), there has been a significant shift in the treatment paradigm of AAAs. Mortality rates after EVAR were reported to be as low as 1.5% in the general population [2,3]. EVAR should be an alternative to open repair for the treatment of AAAs in the elderly; however, several studies have reported increased morbidity and mortality following EVAR in this population compared to the younger population [5, 8-10]. The purpose of this study is to report outcomes of EVAR in the elderly population and to report factors associated with poor outcome.

PATIENTS AND METHODS

This retrospective study was approved by the Sheba Medical Center internal review board and need for patient consent was waived.

This retrospective review comprised patients aged > 80 years who underwent EVAR at the Sheba Medical Center between 2007 and 2017. Inclusion criteria were patients aged > 80 years who underwent elective EVAR for infrarenal AAAs. The exclusion criteria were patients with a ruptured AAA, patients who required open repair or endovascular repair of complex aneurysms (fenestrated or branched endografts), and patients less than 80 years old.

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OUTCOME MEASURES

Our primary endpoints were technical success, perioperative morbidity and mortality, and long-term aneurysm-related mortality. The secondary endpoints included no re-intervention and overall survival.

Technical success was defined as successful intravascular access to the site of the aneurysm, successful deployment of the stent graft with secure fixation and patency of the stent graft, and absence of either type I or III endoleak at the completion of the procedure.

Major complications were defined as postoperative adverse events that required interventions (e.g., cardiac catheterization or reintubation) or events that required prolonged hospitalization (more than 3 days). Minor complications were defined as any adverse event that did not require re-intervention or did not extend length of hospital stay (more than 3 days).

All patients underwent a thorough cardiac evaluation prior to the procedure, which included clinical evaluation by a senior cardiologist and a transthoracic echocardiogram. In selected cases, additional non-invasive cardiac imaging (stress echo or myocardial perfusion imaging) was performed.

All patients were on statin therapy and at least one anti-platelet medication (unless there was an indication for dual anti-platelet therapy) prior to the surgery. Patients with a prior history of chronic obstructive pulmonary disease (COPD) or asthma underwent pulmonary evaluation, including pulmonary function tests and clinical evaluation, by a senior pulmonologist. Patients underwent routine preoperative computed tomography angiography (CTA) to determine the aortic dimensions. Patients with preexisting kidney disease (estimated glomerular filtration rate < 60) were treated with perioperative intravenous hydration.

All procedures were performed in a dedicated hybrid operating room. The surgery was performed routinely under general anesthesia. Intraoperatively, patients were monitored with a radial arterial line and urinary catheter. Femoral artery cutdowns were performed in all cases. A bifurcated stent graft was the device of choice and was used whenever thought to be feasible. An aorto-uni-iliac configuration was used in those cases where anatomy dictated the use of such devices. Following the intervention, patients were monitored in an intensive care unit for 24 hours, and then transferred to a regular hospital department for an additional 24–48 hours before discharge.

Following discharge, patients were evaluated at 1, 6, and 12 months, and annually thereafter, with a standardized follow-up protocol that included physical examination and duplex ultrasound of their abdominal aorta performed by a senior technologist in a dedicated vascular core lab. CTA was performed in those cases where a new or persistent endoleak was seen on duplex, or in cases of sac enlargement without an evident endoleak.

STATISTICAL ANALYSIS

Descriptive characteristics were reported as mean ± standard deviation or as a number of cases and percentages. Factors associated with mortality and morbidity were calculated using Chi-square tests for categorical data. A *P* value of < 0.05 was considered significant. Survival and freedom from re-intervention was estimated from the date of inclusion until death or loss to follow-up by the Kaplan–Meier method. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 23 (SPSS, IBM Corp, Armonk, NY, USA).

RESULTS

During the study period, 444 patients underwent EVAR for AAAs, with 128 patients (29%) older than 80 years of age. Mean age was 84 ± 3.4 (range 80–96), and 110 patients (86%) were male. The patient demographics and co-morbidities are presented in Table 1. Mean aneurysm size was 61 ± 12.6 mm (range 37–105 mm). Patients had an average of 4.8 co-morbidities, and 78% of the patients had at least three co-morbidities. Co-morbidities included coronary artery disease (CAD) (69 patients, 54%), chronic kidney disease (CKD) (54 patients 42%), and peripheral arterial disease (PAD) (42 patients 33%).

The most commonly used device was the Endurant stent graft (Medtronic Vascular, Santa Rosa, CA, USA), which was implanted in 79 of the patients. Other types of grafts used included Zenith (Cook, Bloomington, IN, USA) implanted in 28 patients, Excluder (W.L. Gore and associates, Flagstaff, AR, USA) implanted in 12, Incraft (Cordis Corp, Bridgewater, NJ, USA)

Table 1. Demographics and co-morbidities of patients

Characteristics	Number of patients	Percent
Mean age	84 ± 3.4	
80–89	117	91%
≥ 90	11	9%
Gender (male)	110	86%
Co-morbidities		
Hypertension	110	86%
Hyperlipidemia	99	77%
Smoking	77	60%
Coronary artery disease	69	54%
Chronic kidney disease	54	42%
Peripheral vascular disease	42	33%
Malignancy	31	24%
Cerebrovascular disease	28	22%
Chronic obstructive pulmonary disease	27	21%
Diabetes	23	18%
≥ 3 Risk factors	100	78%

implanted in 3 and Nellix (Endologix Inc, Irvine, CA, USA) implanted in 1 patient. The majority (77%) of the patients had a bifurcated stent graft implanted, 12% of the patients received an aorto-uni-iliac stent graft, a tube stent graft was implanted in 9% of the patients, and 2% underwent aortic sealing.

Technical success was achieved in 127 patients (99%) with no intraoperative mortality. Nine patients (7%) died within 30 days of the surgery. The causes of perioperative deaths are detailed in Table 2. The aorta of one patient ruptured during ballooning of the aortic neck at the end of the procedure resulting in massive bleeding. The patient did not recover and eventually died from multiorgan failure on postoperative day 4. Three patients required re-intubations due to pulmonary complications (pneumonia, aspiration, or COPD exacerbation) and eventually died. Two patients developed severe ischemic colitis. Both required emergency surgery and underwent colon resections and Hartman procedures; however, the patients continued to deteriorate following the surgery and eventually died. One patient presented with massive distal embolization into his lower extremities and internal iliac arteries, developed rhabdomyolysis, buttock necrosis and renal failure. Septic shock developed in one patient 5 days after the surgery, causing death, and one patient died from cardiac arrest due to a coronary event.

Major adverse events (48) occurred in 26 patients (20%). The details of the different complications, both major and minor, are outlined in Table 3. There were patients who had more than one (major, minor or both) complication.

Mean follow up was 19 months (1-81 months). During this period, 8 patients (6%) required re-interventions of the aneurysm due to different types of endoleak and aneurysmal sac expansion during the follow up period. The majority of interventions were performed using endovascular techniques, while two required a sacotomy. Based on Kaplan-Meier estimates, freedom from re-intervention at 60 months was 83% [Figure 1A].

Overall survival at 5 years was estimated at 38% [Figure 1B]. During the follow-up period 55 patients (43%) died. Known causes of death are reported in Table 2. The cause of death could not be determined in 26% of the patients, but only one of them died from aneurysm rupture. This patient underwent EVAR in 2012, required re-intervention 2 years later due to a type 3 endoleak and was re-admitted due to a ruptured aneurysm, most probably due to an undetected type 1B endoleak. Factors associated with increased risk of perioperative morbidity and mortality included: PAD, CKD, and the existence of 3 or more co-morbidities. Other factors (CAD, COPD, presence of malignancy, hyperlipidemia, and diabetes) were not associated with increased perioperative morbidity or mortality.

DISCUSSION

EVAR has gained widespread use over the past 2 decades for the treatment of AAAs and thoracic aortic aneurysms [11,12]. Large randomized trials comparing open repair to EVAR show that EVAR is associated with decreased perioperative mortality and mortality [2,3]. This technique appears to be particularly

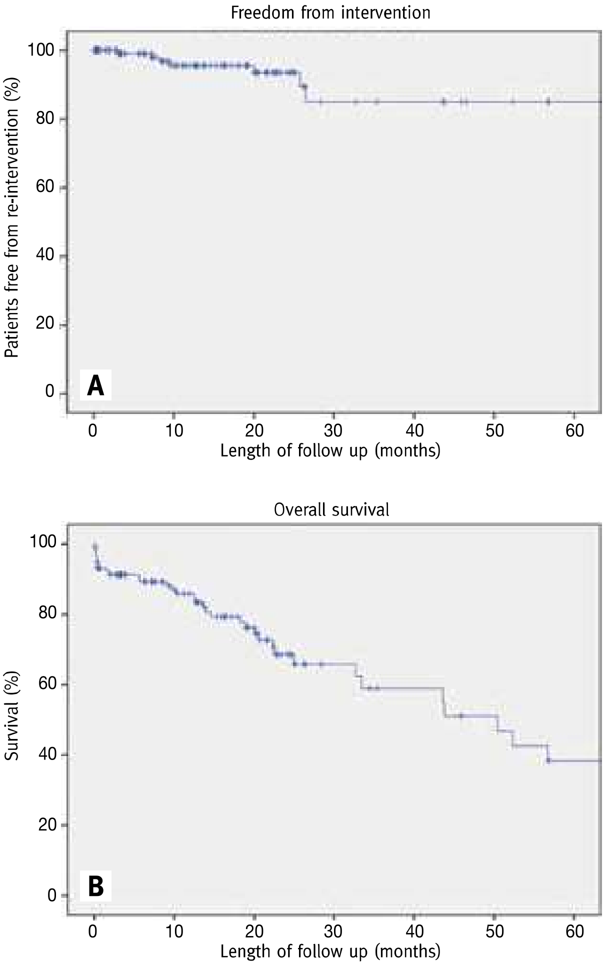
Table 2. Perioperative (30 day) and long term mortality

Cause of Death	N	Percent
Perioperative mortality		
Respiratory	3	2%
Gastrointestinal/ischemic colitis	2	2%
Bleeding	1	1%
Sepsis	1	1%
Massive distal embolization/rhabdomyolysis	1	1%
Cardiac	1	1%
Long-term mortality		
Unknown cause	33	26%
Sepsis	13	10%
Respiratory	4	3%
Bleeding	3	2%
Malignancy	3	2%
Cardiac	2	2%
Gastrointestinal	2	2%
Cerebrovascular accident	2	2%
Ruptured aneurysm	1	1%
Massive distal embolization/rhabdomyolysis	1	1%

Table 3. Perioperative (30 day) major and minor complications It was not uncommon that patients presented with more than one (major, minor, or both) complication

Major complications	N=48	Percent
Sepsis	11	9%
Cardiac	9	7%
Gastrointestinal	8	6%
Renal/urinary tract	7	5%
Respiratory	6	5%
Bleeding	3	2%
Distal embolization/limb occlusion	2	2%
Cerebrovascular accident	2	2%
Minor complications	**N=59**	**Percent**
Renal/urinary tract	26	20%
Surgical site	10	8%
Hematology	6	5%
Fever of unknown origin	6	5%
Respiratory	4	3%
Distal embolization/limb occlusion	4	3%
Gastrointestinal	3	2%

Figure 1. [A] Freedom from re-interventions **[B]** Overall survival



advantageous in the elderly, as this population typically presents with significant co-morbidities, compared to the younger population. EVAR 1 trial showed that perioperative mortality after EVAR was 1.8%; however, patients enrolled in this trial were classified as low risk, and all were suitable for open repair. Mean age was 74, 43% had a history of CAD, and renal function in the majority of the patients was normal [3]. In the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial, operative mortality among EVAR patients was 1.2% and moderate to severe complications occurred in 11% of the patients. In this trial, all patients were also suitable for open repair; mean age was 70 years, 40% presented with CAD, and 7% from renal disease. Of note, patients with PAD (ankle-brachial index less than 1) were excluded from these studies [2]. While these trials and others clearly demonstrated the benefit of EVAR over open repair, they do not represent outcomes in the elderly. Several studies have reported increased perioperative mortality and morbidity among octogenarians with perioperative mortality rates reported at 3.1–6% [9,13,14]. In a systematic review, Henebiens and colleagues [8] showed that pooled mortality rates following EVAR reached 4.6%. As the health of the elderly typically deteriorates with age, higher perioperative morbidity rates in this population is not surprising. In our cohort, 54% of the patients were diagnosed with CAD, 42% with CKD and the incidence of at least 3 major co-morbidities was 78%.

All of these factors account for a high rate of perioperative morbidity. Several studies have attempted to identify factors affecting survival after EVAR, including American Society of Anesthesiologists category, age of more than 75 years, congestive heart failure, renal impairment, and size of aneurysm [7,15,16]. Beck et al. [15] found that the predicted mortality was dependent on the number of risk factors present. Patients with no risk factors had a 1-year mortality of only 1.2% after open repair, while patients with three or four risk factors had predicted mortality rates ranging from 22% to 67% at 1 year.

In our study, PAD was associated with increased perioperative mortality and morbidity. Although it cannot directly explain the majority of the complications, it reflects a large atherosclerotic burden in the patients. PAD can explain why patients presented with distal embolization and possible kidney deterioration. The 5-year survival rate of 38% in our study is slightly lower than rates obtained in other recent studies [13,17]. De Blic and co-authors [13] reported a 5-year mortality rate of 53%, which is consistent with other studies. This difference could be explained by a slightly healthier population (18% with CKD vs. 42%, a higher percentage of patients with PAD in our study). Nevertheless, only one patient died due to an aneurysm related cause.

Elective surgical repair of an asymptomatic AAA is a prophylactic operation performed to gain life years at the cost of operative morbidity and mortality. This potential benefit of elective repair must be weighed against the natural course of an AAA. People with a heavy co-morbid burden have shorter life expectancies; whereas those with no co-morbid conditions, including very elderly persons, have favorable life expectancies relative to an average person of the same chronological age [18]. Since the morbidity rates in elderly is substantially higher than in younger patients, the conventional recommendations regarding indications for treatment of AAA might not be applicable. This is especially relevant since the 12-month rupture risk for an AAA with a diameter of 5–5.9 cm is 1–11% [19]. The decision to treat AAAs in the elderly must not rely solely on strict published criteria, which is based on size, but must also take into consideration the number and severities of co-morbidities of these patients.

CONCLUSIONS

EVAR can be performed in the elderly with a high rate of success; however, it is associated with a substantial rate of morbidity and mortality, particularly when patients experience multiple co-morbidities. When performing EVAR in the elderly, the risk of rupture must be taken into account considering the life expectancy of these patients and the risk of perioperative morbidity and mortality.

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References

1. World Population Aging: 1950–2050, 2005; [Available from http://www.un.org/esa/population/publications/worldageing19502050]. [Accessed July 2017].
2. 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 (16): 1607-18.
3. Greenhalgh RM, Brown LC, Kwong GP, et al. 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* 2004; 364 (9437): 843-8.
4. Scallan O, Novick T, Power AH, DeRose G, Duncan A, Dubois L. Long-term outcomes comparing endovascular and open abdominal aortic aneurysm repair in octogenarians. *J Vasc Surg* 2019; S0741-5214.
5. Hicks CW, Obeid T, Arhuidese I, Qazi U, Malas MB. Abdominal aortic aneurysm repair in octogenarians is associated with higher mortality compared with non-octogenarians. *J Vasc Surg* 2016; 64 (4): 956-65.
6. Brady AR, Fowkes FG, Greenhalgh RM, Powell JT, Ruckley CV, Thompson SG. Risk factors for postoperative death following elective surgical repair of abdominal aortic aneurysm: results from the UK Small Aneurysm Trial. On behalf of the UK Small Aneurysm Trial participants. *Br J Surg* 2000; 87 (6): 742-9.
7. Boult M, Maddern G, Barnes M,Fitridge R. Factors affecting survival after endovascular aneurysm repair: results from a population based audit. *Eur J Vasc Endovasc Surg* 2007; 34 (2): 156-62.
8. Henebiens M, Vahl A, Koelemay MJ. Elective surgery of abdominal aortic aneurysms in octogenarians: a systematic review. *J Vasc Surg* 2008; 47: 676-81.
9. Prenner SB, Turnbull IC, Serrao GW et al. Outcome of elective endovascular abdominal aortic aneurysm repair in nonagenarians. *J Vasc Surg* 2011; 54 (2): 287-94.
10. Geisbüsch P, Katzen BT, Tsoukas AI, Arango D, Peña CS, Benenati JF. Endovascular repair of infrarenal aortic aneurysms in octogenarians and nonagenarians. *J Vasc Surg* 2011; 54 (6): 1605-13.
11. Silverberg D, Glauber V, Rimon U, et al. Endovascular repair of complex aortic aneurysms. *IMAJ* 2014; 16 (1): 5-10.
12. Wolf Y, Rosen G. Towards endovascular treatment of the entire aorta. *IMAJ* 2014; 16 (1): 50-1.
13. De Blic R , Alsac JM , Julia P , et al. Elective treatment of abdominal aortic aneurysm is reasonable in patients >85 years of age. *Ann Vasc Surg* 2014; 28 (1): 209-16.
14. Saratzis A, Mohamed S. Endovascular abdominal aortic aneurysm repair in the geriatric population. *J Geriatr Cardiol* 2012; 9: 285-91.
15. Beck AW, Goodney PP, Nolan BW, et al. Predicting 1-year mortality after elective abdominal aortic aneurysm repair. *J Vasc Surg* 2009; 49 (4): 838-43.
16. Varkevisser RRB, O'Donnell TFX, Swerdlow NJ, et al. Factors associated with in-hospital complications and long-term implications of these complications in elderly patients undergoing endovascular aneurysm repair. *J Vasc Surg* 2019; pii: S0741-5214.
17. Ballotta E , Da Giau G, Bridda A, Gruppo M, Pauletto A, Martella B. Open abdominal aortic aneurysm repair in octogenarians before and after the adoption of endovascular grafting procedures. *J Vasc Surg* 2008; 47 (1): 23-30.
18. Cho H, Klabunde CN, Yabroff KR, et al. Comorbidity-adjusted life expectancy: a new tool to inform recommendations for optimal screening strategies. *Ann Intern Med* 2013; 159 (10): 667-76.
19. Cronenwett JL, Johnston KW. Rutherford's Vascular Surgery, 8th edn Philadelphia: Elsevier/Saunders. 2014.

Capsule

Spying on bacterial signals

Many bacteria produce small molecules for monitoring population density and thus regulating their collective behavior, a process termed quorum sensing. Pathogens like *Pseudomonas aeruginosa*, which complicates cystic fibrosis disease, produce different quorum-sensing ligands at different stages of infection. **Moura-Alves** and colleagues conducted experiments in human cells, zebrafish, and mice to show that a host organism can eavesdrop on these bacterial conversations. A host sensor responds differentially to bacterial quorum-sensing molecules to activate or repress different response pathways. The ability to "listen in" on bacterial signaling provides the host with the capacity to fine-tune physiologically costly immune responses.

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Capsule

VDACs are MOM's ruin

Mitochondrial DNA (mtDNA) is normally kept within the mitochondria. It can be released into the cytosol in response to stress and thus encounter cytosolic DNA sensors, triggering type I interferon responses. During apoptosis, mtDNA release is mediated by macropores in the mitochondrial outer membrane (MOM) created by oligomerization of the proteins BAX and BAK. **Kim** et al. found that during oxidative stress, mtDNA escapes instead through macropores formed by oligomerization of voltage-dependent anion channels (VDACs). In a mouse model of lupus, an inhibitor of VDAC oligomerization diminished mtDNA release and downstream signaling events. This treatment reduced lupus-like symptoms in the model, suggesting a potential therapeutic route for conditions mediated by mtDNA release.

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