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Endovascular repair of mycotic aortic aneurysms confers good medium-term outcomes and aneurysmal sac resolution

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ABSTRACT

Introduction: Mycotic aortic aneurysm (MAA) is a life-threatening condition. Endovascular repair (EVAR) of aortic aneurysms has been found to be a safe and effective alternative to open repair. We aimed to present the short- to medium-term outcomes for EVAR of MAA in our cohort.

Methods: We conducted a retrospective study of 23 consecutive patients with MAA who underwent EVAR in our hospital from January 2008 to July 2017.

Results: The mean age of our study population was 62 years. The mean aneurysmal size was 3.2 cm. Abdominal MAA (n = 16, 70%) were the most common, followed by thoracic MAA (n = 4, 17%). There was no 30-day mortality in our cohort. Endoleak (Types 1, 3, 4) was detected in 3 (13%) cases. At the one-month surveillance computed tomography aortogram, all patients had a reduction in aneurysmal size and 5 (22%) had complete aneurysmal sac resolution. 7 (30%) patients had sac resolution at six months and 8 (35%) patients at 12 months. Overall survival was 91%, 80% and 61% at one, 12 and 60 months, respectively.

Conclusion: EVAR is a feasible and durable method for the repair of MAA, with a five-year overall survival of 61%. All patients in our study had a reduction in aneurysmal size at one month, with 65% having complete aneurysmal sac resolution by 12 months.

Keywords: endovascular aortic repair, mycotic aortic aneurysms

INTRODUCTION

Mycotic aortic aneurysm (MAA) is a life-threatening condition that represents 0.5%–2.6% of all aortic pathologies.[1] Patients who develop these aneurysms commonly have multiple risk factors for an immunocompromised state. In addition, they tend to present with concomitant sepsis, which puts them at high surgical risk.[2] Classically, the standard approach consists of aggressive intravenous (IV) antibiotic therapy with open surgical debridement of the aneurysm and surrounding infected tissue, as well as extra-anatomic or *in situ* bypass.[3,4] However, outcomes are poor, especially in the elderly, with mortality and morbidity rates of up to 43%.[5]

Endovascular repair (EVAR) of aortic aneurysms provides a safe and effective alternative to a largely invasive approach,[6,7] with multiple benefits, including reduction of massive blood loss, lower incidence of early mortality/morbidity, and avoidance of aortic cross-clamping, which predisposes to prolonged distal ischaemia.[8,9] This is especially so in high-risk surgical patients. However, EVAR has various limitations – the infected material and debris are left inside the patient, which predisposes to the risk of the prosthesis being infected, as well as persistent or recurrent sepsis. Other challenges include rupture of the aorta above or below the graft due to continued infection,[5] and other conventional EVAR risks such as endoleak, contrast-induced nephropathy and embolic or thrombotic events. In this study, we aimed to present the short- to medium-term outcomes for EVAR of MAA, especially in terms of sac resolution, as well as a review of the current available literature.

METHODS

We conducted a single-institution retrospective review of 23 patients who underwent EVAR of MAA in our hospital from January 2008 to July 2017. The diagnosis of MAA was based on a combination of the following criteria: (a) clinical presentation (fever, pain, sepsis); (b)

biochemical results (leucocytosis, elevated inflammatory markers like C-reactive protein); and (c) radiological findings (large aneurysms that were ruptured/contained, peri-aortic gas).

A common study protocol was applied, with collected data consisting of patient demographics, comorbidities, biochemistry upon presentation, aneurysm characteristics (size and morphology), duration of antibiotic therapy, operative data, postoperative complications and radiological surveillance results. Devices used to repair the aneurysms consisted of stents-grafts from Medtronic (Minneapolis, MN, USA), Cook Medical (Bloomington, IN, USA) and Endologix (Irvine, CA, USA).

All patients received broad-spectrum empirical IV antibiotics 1–90 days preoperatively in consultation with the infectious diseases (ID) physician. Patients with positive blood cultures were switched to organism-specific antibiotics once the results were out, while the remaining patients continued with broad-spectrum antibiotics. 11 patients were considered stable and underwent early stenting after control of systemic sepsis with antibiotics, while the other 12 underwent emergency repairs. Postoperatively, the patients completed six weeks of targeted IV antibiotics followed by targeted lifelong suppressive antibiotics upon consultation with the ID physician. They also received regular reviews: clinical examination, biochemical testing and follow-up computed tomography (CT) at one, six and 12 months. All patients with negative blood cultures were prescribed Bactrim (trimethoprim and sulfamethoxazole).

Investigated factors were analysed using descriptive statistics. Percentages were used for categorical data and means with standard deviations for continuous data. A Kaplan-Meier survival analysis was performed to ascertain the survival rates at pre-determined intervals. All data analysis was performed using IBM SPSS Statistics version 21.0 for Windows (IBM Corp, Armonk, NY, USA).

RESULTS

During the nine-year study period, 23 patients (21 male and 2 female) with MAA were identified (Table I). The mean age of the study population was 62 (range 42–80) years. The median clinical follow-up duration was 19 (range 2–143) months. 17 (74%) patients had at least one risk factor for an immunocompromised state, the most common being diabetes mellitus (48%), followed by human immunodeficiency virus (22%), chronic steroid use (17%) and chronic kidney disease (17%). 16 (70%) patients had positive blood cultures, with *Salmonella* Enteritidis being the most common organism identified (n = 11, 48%).

Table I. Patient characteristics (n = 23).

Characteristic	**No. (%)**
Age* (yr)	61.6 ± 10 (42–80)
Male gender	21 (91)
Risk factor for immunocompromised state	
Diabetes mellitus	11 (48)
Human immunodeficiency virus	5 (22)
Chronic steroid use	4 (17)
Chronic kidney disease	4 (17)
Fever	12 (52)
White blood cell (> 10 × 10^9/L)	14 (61)
C-reactive protein (> 5 mg/L)	17 (74)
Haemoglobin (male < 12 g/dL, female < 10 g/dL)	12 (52)
Creatinine (> 100 U)	8 (35)
Albumin (< 35 g/L)	21 (91)
Positive blood cultures	
Salmonella Enteritidis	11 (48)
Others†	5 (22)
Concurrent infection	
Intra-abdominal collection	3 (13)
Bacteraemia	14 (61)
Aorto-enteric fistula	1 (4)
Aneurysm morphology	
Size* (cm)	3.21 ± 1.55 (1.1–6.8)
Rupture	6 (26)
Multiple aneurysms	1 (4)
Aorto-enteric fistula	1 (4)
Aneurysm location	
Abdominal	16 (70)
Thoracic	4 (17)
Common iliac	3 (13)

**Data presented as mean ± standard deviation (range). †Includes Escherichia coli, Klebsiella, Mycobacterium tuberculosis, Streptococcus pneumoniae and Burkholderia pseudomallei*

Upon presentation, 12 (52.2%) patients had fever, 14 (60.9%) had leukocytosis (> 10 × 109/L), 12 (52.2%) had anaemia (male < 12 g/dL, female < 10 g/dL), 17 (73.9%) had elevated C-reactive protein (> 5 mg/L) and 21 (91.3%) had hypoalbuminaemia (< 35 g/L). The mean preoperative antibiotic duration at the time of operative repair was 15 (range 1–90) days. Postoperatively, all patients received lifelong antibiotics.

Abdominal MAA (n = 16, 70%) were the most common, followed by thoracic MAA (n = 4, 17%) and common iliac aneurysms (n = 3, 13%). 6 (26%) patients presented with a ruptured aneurysm and 1 (4%) patient had an aorto-enteric fistula. The mean aneurysmal size was 3.2 (range 1.1–6.8) cm. The mean operation time was 132 (range 64–310) minutes. The mean amount of blood loss was 112 (range 50–300) mL and the average duration of stay in the intensive care unit or high dependency unit was 2.25 (range 1–10) days. There was no 30-day mortality, and the mean length of hospital stay was 31 (range 5–84) days (Table II). Post-repair, 9 (39.1%) patients contracted nosocomial infections, 8 (34.8%) required a second operation, 7 (30.4%) had acute kidney injury and 5 (21.7%) had cardiac complications. One patient had thrombosis of the left common iliac artery.

Table II. Operative data and outcomes (n = 23).

Parameter	**No. (%)**
Primary operative data*	
Duration of operation (min)	132 (64–310)
Blood loss (mL)	112 (50–300)
ICU/HDU stay (day)	2.25 (1–10)
Complication	
Nosocomial infection	9 (40)
Cardiac	5 (22)
Respiratory	1 (4)
Acute kidney injury	7 (30)
Limb occlusion	1 (4)
Secondary operation	
Endoleak (Type 1, 3, 4)	4 (17)
Image-guided drainage of peri-aortic abscess	3 (13)
Others	1 (4)
Outcomes	
30-day mortality	0

Duration of hospital stay† (day)	30.9 ± 20.5
Duration of follow-up‡ (mth)	31.4 ± 34.4 (2–143)
Surveillance	
Recurrent sepsis	4 (17)
Aneurysmal sac resolution at 1 mth on CT	5 (22)
Aneurysmal sac resolution at 6 mth on CT	7 (30)
Aneurysmal sac resolution at 12 mth on CT	8 (35)
Overall survival¶	
1 mth	91
6 mth	86
12 mth	80
24 mth	80
36 mth	71
48 mth	61
60 mth	61

*Data presented as *mean (range); †mean ± SD; ‡mean ± SD (range); and ¶percent. CT: computed tomography; HDU: high dependency unit; ICU: intensive care unit; SD: standard deviation*

Endoleak (Types 1, 3, 4) was detected in 4 (17%) patients, for which they underwent stent re-lining after detection on surveillance imaging. 3 (13%) patients required image-guided drainage of peri-aortic abscesses and 1 (4%) patient required a laparotomy and excision of an aorto-esophageal fistula with duodenal-jejunal anastomosis. 2 (9%) patients suffered from recurrent aneurysm-related sepsis and there was one aneurysm-related mortality (secondary to aorto-esophageal fistula). Other causes of mortality included pneumonia secondary to systemic lupus erythematosus, metastatic lung cancer, malignant pleural effusion secondary to esophageal carcinoma, enterococcemia secondary to psoas abscess, and ischaemic heart disease. Of the other five cases of mortality, only one patient underwent an emergency repair.

At one-month surveillance CT aortogram, all patients had a reduction in the size of the aneurysm; of these, 5 (22%) patients had complete aneurysmal sac resolution. 7 (30%) had sac resolution at six months, and 8 (35%) had sac resolution at 12 months. Overall survival was 91%, 86%, 80% and 61% at one, six, 12 and 60 months, respectively (Table II, Fig. 1). There was no difference in survival between those who underwent elective and emergency repair, as the causes of mortality in this series were largely unrelated to the aneurysm, with the exception of the one case of aorto-esophageal fistula.

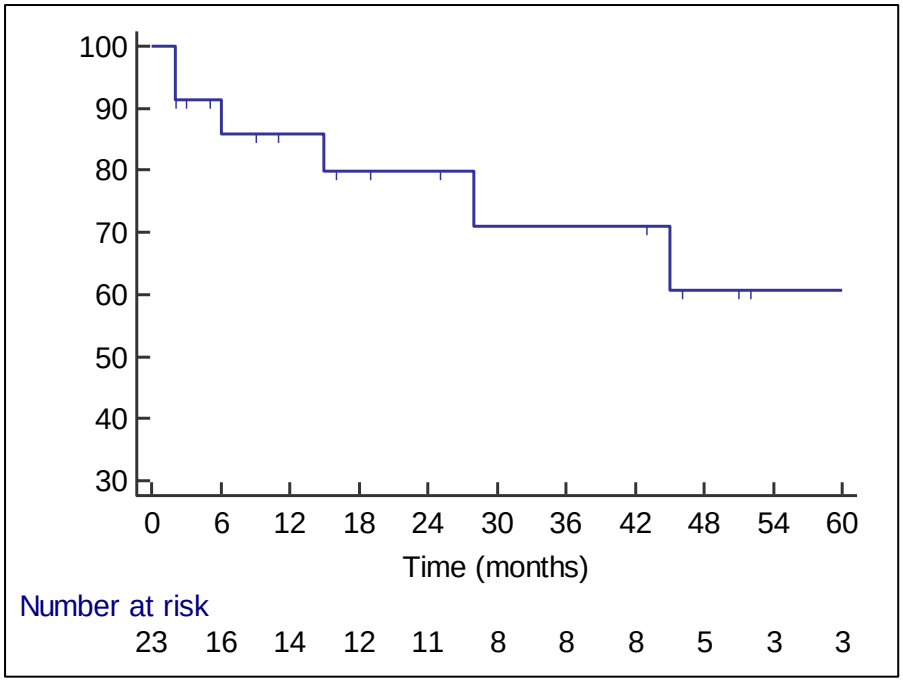

Fig. 1 Kaplan-Meier survival curve shows overall survival of 91%, 80% and 61% at 1, 12 and 60 months, respectively.

DISCUSSION

Despite advances in perioperative optimisation and antimicrobial regimes, an optimal treatment strategy for MAA has yet to be agreed upon. Although EVAR is now widely used and generally acceptable, the decision to rely solely on EVAR as the therapeutic gold standard is uncertain. Kim et al reported good short- and medium-term outcomes in their series with open repair of MAA despite their patients being at high risk for open surgery.[10] Hybrid therapy (combination of EVAR and open surgery) remains an option, especially for those with recurrent sepsis. However, for some physicians, placing a prosthetic material in an infected field is counter-intuitive, even controversial.

In the Asian population, studies have shown that *Salmonella* infections are more common compared to their Western counterparts.[11] A review of the existing literature (Table III) found that out of seven studies conducted in the East, six reported *Salmonella* as the most common organism identified in blood cultures.[12-17] This corresponds to our finding – 70% of

our patients who had positive blood cultures were positive for *Salmonella*. *Salmonella*-related aneurysms are also known to have rapid disease progression and a risk of early rupture. This is because *Salmonella* tends to adhere to vascular endothelium, especially if it is diseased by atherosclerosis.[12]

Kritpracha et al reported that EVAR had a poor outcome in patients with fistula complication.[16] This is also noted in our study, as the only aneurysm-related death was secondary to an aorto-esophageal fistula. It is likely because these patients tend to present with overwhelming sepsis and shock, and are unable to recover due to their advanced age and comorbidities. Our centre had overall higher rates of nosocomial infections as well as cardiac and kidney complications compared to those reported in the current literature. This could be due to the advanced age of our patient population and their various comorbidities, which precluded them to a difficult postoperative recovery. Our centre's endoleak rate of 17% is comparable to that of other studies (range 0%–34%).[2,12,17] Of note, the Type 3 and 4 endoleaks that occurred in this series were from the older-generation stent grafts, and such leaks are exceedingly rare with the advent of modern devices.

Our five-year survival rate of 61% was similar to that of other studies,[18,19] while our in-hospital mortality rate was also comparable to that reported in other studies,[12,13,20,21] with a mean rate of 10% (range 0%–25%). Compared with open surgery, which showed in-hospital mortality rates of 12%–27%,[3,9,11] our in-hospital mortality rate for EVAR was much lower, at 0%. Thus, EVAR as the first-line treatment in patients with MAA is a reasonable approach due to its low in-hospital mortality rate. Notably, most of the identified studies did not report the five-year survival rates due to the lack of follow-up.

In our study, the reported sac resolution rates of 22%, 30% and 35% at one, six and 12 months, respectively, are one of the first few reported and should be a documented follow-up marker for future studies. We noted that five studies in the current literature had published their

CT surveillance results (Table IV). Of these, three studies reported complete resolution of the aneurysmal sac in their surviving patient population[6,18,22] and two studies reported a significant reduction in aneurysmal size after seven and 12 months, respectively.[23,24] However, as these papers had only a small sample population of 1–8 patients, it is difficult to draw any statistically meaningful conclusions from them.

Table IV. Studies documenting MAA sac resolution after EVAR.

Study, yr	Sample size	Resolution on surveillance CT
Semba et al, 1998[22]	3	Complete thrombosis of MMA achieved in all patients; no re-infection or recurrence at median follow-up of 24 mth in 2 survivors.
Heikkinen et al, 2005[24]	2	Patient 1 had new aneurysms at 2-mth follow-up, which were excised and replaced with vein grafts; patient was well on follow-up after 7 yr, with no recurrence. Patient 2 did well at 7-mth follow-up, and aneurysm had shrunk by 1.1 cm.
Ting et al, 2006[23]	7	Significant reduction in the diameter of pseudoaneurysm (> 5 mm) after 12 mth.
Clough et al, 2009[6]	1	Complete sac resolution upon procedure; patient was well on imaging follow-up after 4 yr.
Lee et al, 2014[18]	8	5 survivors had complete resolution of infected aneurysms; no stent-graft infection was observed during follow-up up to 8 yr.

CT: computed tomography; EVAR: endovascular repair; MAA: mycotic aortic aneurysm

Compliance to antibiotic therapy is of utmost importance. As recurrent infection cannot be excluded, lifelong antibiotic therapy and radiological surveillance are mandatory. This is especially so in our patient population, most of whom are frail and immunosuppressed and hence might not be able to mount an early response to recurrent infection. However, there is no universal agreement on the mandatory use of lifelong antibiotic therapy; in some centres, antibiotic therapy may be discontinued if there is no clinical or radiological evidence of ongoing sepsis.[1,9,25]

The main limitation of the current study is its small sample size due to the rarity of the disease, resulting in the inability to reach statistically meaningful conclusions. Other

limitations include the retrospective nature of the study and the existence of patient selection bias. Furthermore, the median follow-up duration of 19 months is not long enough to identify all cases of late aneurysm-related mortality, especially in patients who underwent EVAR. Therefore, an extended, multi-institutional study that compares the outcomes of open repair and EVAR would be recommended.

In conclusion, EVAR was a feasible and durable method for repairing MAA in our patients who were on lifelong antibiotics. Although the aortic interventions performed were successful, immunocompromised patients had difficult postoperative recoveries. All our patients saw a reduction in aneurysmal size at one month, with 65% having complete aneurysmal sac resolution by 12 months. The recurrence rate for aneurysm-related sepsis was low at 9% and the five-year overall survival rate was acceptable at 61%.

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Table III. Endovascular repair for mycotic aortic aneurysms in the literature.

Study, year	Male (%)	Mean age (yr)	Immuno-compromise (%)	Thoracic (%)	Abdominal (%)	Rupture (%)	Positive blood culture (%)	Commonest organism (%)	Endo-leak (%)	Mean LOS (day)	Postop complication (%)	In-hospital mortality (%)	Median follow-up (day)	30-day survival (%)	1-year survival (%)	5-year survival (%)
Stanley et al, 2003[26]	50	71	25	75	25	25	100	*Streptococcus* (50)	0	Nil	Nil	25	Nil	75	75	Nil
Jones et al, 2005[27]	44	64	Nil	89	11	0	Nil	Nil	11	Nil	44	11	36	89	78	Nil
Tisenhausen et al, 2008[20]	100	75	50	17	83	Nil	67	*S. aureus* (50)	17	11	50	0	Nil	100	50	33
Lew et al, 2008[28]	78	72	33	78	22	89	56	*S. aureus* (100)	11	Nil	56	Nil	Nil	78	67	Nil
Clough et al, 2009[6]	37	Nil	37	70	30	32	79	S. aureus (36)	27	Nil	53	Nil	20	89	73	29
Zhou et al, 2009[12]	100	56	71	29	71	14	29	*Salmonella* (28)	14	22	0	0	Nil	100	100	Nil
Silverberg et al, 2010[21]	100	74	Nil	50	50	Nil	100	*Salmonella* (50)	25	Nil	Nil	0	Nil	100	Nil	Nil
Patel et al, 2010[29]	73	Nil	20	100	0	Nil	55	S. aureus (55)	15	Nil	30	15	29	85	55	25
Heath et al, 2011[8]	75	72	Nil	100	0	Nil	50	*Streptococcus* (75)	Nil	Nil	Nil	Nil	Nil	100	50	0
Kritpracha et al, 2011[16]	86	66	57	19	81	Nil	48	*Salmonella* (80)	0	Nil	10	Nil	22	81	Nil	Nil
Yu et al, 2012[13]	71	70	14	29	71	14	100	*Salmonella* (86)	Nil	Nil	14	0	Nil	100	57	Nil
Kan et al, 2012[14]	67	Nil	50	42	58	50	100	*Salmonella* (83)	0	Nil	33	19	24	100	92	Nil
Sedivy et al, 2012[17]	78	Nil	19	34	66	16	69	*Salmonella* (41)	13	23	31	Nil	45	81	50	Nil
Stellmes et al, 2013[30]	17	69	17	100	0	67	67	*S. aureus* (50)	34	Nil	0	17	43	83	Nil	Nil
Jia et al, 2013[31]	83	73	58	17	83	83	67	*S. aureus* (25)	0	Nil	19	Nil	30	100	67	Nil
Johnstone et al, 2013[2]	57	68	71	100	0	29	100	*S. aureus* (43)	14	Nil	29	14	25	86	71	14
Huang et al, 2014[15]	75	Nil	100	42	58	67	83	*Salmonella* (67)	0	48	58	Nil	24	100	83	Nil
Lee et al, 2014[18]	63	57	25	13	38	Nil	75	*S. aureus* (50)	Nil	Nil	50	Nil	Nil	75	62	62

Sorelius et al, 2014[19]	71	69	47	31	63	38	62	*S. aureus* (20)	11	Nil	25	Nil	Nil	91	75	55

LOS: length of stay; postop: postoperative; S. aureas: Staphylococcus aureus