Clinical, Microbiologic, and Outcome Analysis of Mycotic Aortic Aneurysm: The Role of Endovascular Repair

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Abstract

Background: Mycotic aortic aneurysm (MAA) is an infrequent but devastating form of vascular disease.

Methods: We conducted a retrospective cohort study at a major medical center to identify independent risk factors for MAA and to provide opinions about treating it. The study population consisted of 43 patients who had had 44 MAAs over a period of 15 y.

Results: All of the patients had positive blood cultures, radiologic findings typical of MAA, and clinical signs of infection (leukocytosis, fever, and elevated C-reactive protein). The mean age of the patients was 63.8 ± 10.6 y and the mean period of their follow up was 35.7 ± 39.3 mo. Twenty-nine patients with MAAs underwent traditional open surgery, 11 others received endovascular stent grafts, and four MAAs were managed conservatively. The most frequent causative pathogens were *Salmonella* (36/44 patients [81.8%]), in whom organisms of *Salmonella* serogroup C (consisting mainly of *S. choleraesuis*) were identified in 14 patients, organisms of *Salmonella* serogroup D were identified in 13 patients, and species without serogroup information were identified in nine patients. The overall mortality in the study population was 43.2% (with an aneurysm-related mortality of 18.2%, surgically related mortality of 13.6%, and in-hospital mortality of 22.7%).

Conclusions: Shock is a risk factor for operative mortality. Misdiagnosis and treatment of MAA as low back pain, co-existing connective-tissue disease such as systemic lupus erythematosus and rheumatoid arthritis, and *Salmonella* serogroup C-associated bacteremia are risk factors for aneurysm-related death. Endovascular repair should be considered as an alternative option to the open repair of MAA.

MYCOTIC AORTIC ANEURYSM (MAA) is a rare but life-threatening disease with an incidence of 0.7–3% among all aortic aneurysms [1–3]. Despite advances in the peri-operative management and anti-microbial therapy for MAA, the mortality in open surgery for it remains high, at 22%–36% [4,5]. Recently, the literature has carried an increasing number of successful reports of endovascular repair of MAA [6–8]. Most reports of MAA have focused on the results of its surgical treatment, with less discussion of the roles of pathogens and factors prognostic for its outcome. The study described here was undertaken to analyze the clinical and microbiologic features of MAA and

risk factors for its having a poor outcome, with the goal of providing better therapeutic opinions for patients with this condition.

Patients and Methods

Patients

The Institutional Review Board of Chang Gung Memorial Hospital approved the study. Information was collected retrospectively on all patients with a diagnosis of MAA between June 1997 and June 2012. The population in the study consisted of 43 patients with 44 diagnosed MAAs.

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All of these patients had positive blood cultures, clinical signs of infection (leukocytosis, fever, an elevated C-reactive protein [CRP] concentration), and radiologic findings typical of MAA. Characteristic radiologic features of MAAs included a lobulated vascular mass, an indistinct and irregular aortic wall, peri-aneurysmal edema, a peri-aneurysmal soft-tissue mass, and peri-aneurysmal gas.

In-hospital mortality was defined as death in the hospital after a diagnosis of MAA. Aneurysm-related death included death from bleeding, prosthetic infection, free rupture, local abscess, and other conditions directly attributed to MAA. Surgical mortality was defined as death related to surgical intervention, such as from post-operative pneumonia, peri-operative myocardial infarction, and extended bowel ischemia. Hospital-stay was defined as the period beginning on the date of a definitive diagnosis of MAA and extending to the date of discharge or death. Overall mortality was defined as death from any cause during the study period.

Pre-operative management

Intravenous antibiotic therapy was given to patients in the study when bacteria were found in a blood culture. Emergent surgical or endovascular intervention was undertaken for uncontrolled infection (persistent fever and septic shock), uncontrolled bleeding, or evidence of impending aneurysmal rupture (severe pain, shock, and pseudo-aneurysm formation on imaging studies). An elective surgical procedure was recommended for patients who were afebrile or had a good response to antibiotic therapy. A good response to antibiotic therapy was defined as regression of a febrile episode, a declining white blood cell count (WBC) and serum CRP concentration, and hemodynamic stabilization.

Open surgical technique

Surgical management consisted of debridement of necrotic tissue, copious saline irrigation, and repair of an aneurysm with an in situ prosthetic graft or through reconstruction with an extra-anatomic bypass. For patients who underwent vascular reconstruction with an in situ prosthetic graft, aortic anastomosis was done with the simple interposition of a Dacron graft through a midline laparotomy or thoracotomy. No cadaveric grafts were available at our institution, and woven graft material was used in all in situ reconstructions. In patients who underwent extra-anatomic bypass, an 8-mm expanded polytetrafluoroethylene (ePTFE) prosthetic graft was implanted for axillo-femoral bypass and a 6-mm ePTFE graft was used for femoro-femoral bypass. The ends of the proximal and distal aorta were ligated with nylon tape and the stumps were sutured with running polypropylene sutures. Some of the in situ prosthetic grafts or aortic stumps in patients who had extra-anatomic bypass procedures were covered with a vascularized omental flap.

Endovascular intervention

All patients underwent pre-operative imaging consisting of contrast-enhanced computed tomographic (CT) angiography of the chest, abdomen, and pelvis. Evaluation for suitability for endovascular repair of an MAA included examination of the morphology of the aneurysm, investigation of visceral artery involvement, determination of the size of the thoracic/abdominal aorta, and assessment of the iliac arteries (Fig. 1). All procedures were performed in the operating room, typically through open femoral arteries. Adjunctive surgical procedures, including celiac and superior mesenteric artery bypass, renal artery bypass, and thoracic aortic debranching

FIG. 1. A mycotic aortic aneurysm (MAA) presenting as hydronephrosis with urosepsis. (A) Pre-operative image of MAA. Black arrow indicates hydronephrosis with double J tube in the ureter. Black asterisk indicates MAA with content rupture and retroperitoneal hematoma. (B) Endovascular repair of MAA. White arrow indicates stent-graft in aorta. White asterisk indicates successful exclusion of the MAA.

of the innominate, carotid, or subclavian arteries, with 8-mm Gore-Tex grafts (Gore Medical, Flagstaff, AZ), were performed at the time of the endovascular procedures.

Antibiotic treatment

If blood-culture results were available pre-operatively, the antibiotic chosen for use was preferably organism-specific, or was otherwise a drug with a broad spectrum. Parenteral antibiotic therapy was administered for 4–6 wk before the endovascular repair of an MAA, except in the case of emergent operations. An additional 4-wk of parenteral antibiotic therapy was given if there was fever, pain, and elevation of the CRP and/or WBC. Only one patient in the endovascular-repair group completed the full 6 wk of antibiotic therapy before intervention. Most patients with MAAs received 1–2 wk of antibiotic therapy because of fever of unknown origin. This was not part of the pre-interventional antibiotic treatment regimen.

Statistical analysis

Continuous variables were compared through the use of unpaired two-tailed Student *t*-tests. Discrete variables were compared through the use of two-tailed Fisher exact tests. The relevance of the clinical variables examined in the study was further assessed with Cox proportional hazards models. The actuarial survival curve was generated with the Kaplan–Meier method and a log-rank test. All statistical analyses were done with Stata data analysis software version 8.0 (Stata Corporation, College Station, TX). The results are presented as mean values $\pm$ SD. Statistical significance was defined as a value of $p < 0.05$.

Results

Patients

The study population consisted of 43 patients with a mean age of 63.5 ± 10.4 y (range, 41–81 y) and 44 independent MAAs. The mean follow-up period in the study was 35.55 ± 39.74 mo (range, 0–120 mo). The clinical data collected in the study are shown in Table 1. The most frequent presenting symptoms were fever and pain. Twelve patients (27.3%) presented with unstable hemodynamics because of hemorrhage or sepsis. Five patients presented with low back pain that was mistreated as spinal stenosis.

Medical co-morbidities in the study patients included hypertension (in 86.4%), diabetes mellitus (in 54.6%), chronic obstructive pulmonary disease (in 27.3%), a history of stroke (in 30.5%), peripheral arterial disease (in 11.4%), infective endocarditis (in 11.4%), cirrhosis of the liver (in 9.1%), connective-tissue disease (in 6.8%), osteomyelitis of the lumbar spine (in 13.6%), chronic renal insufficiency (in 18.2%), and end-stage renal disease requiring hemodialysis (in 4.6%).

The microbiologic distribution of the MAAs in the study is summarized in Table 2. The most frequent pathogens were *Salmonella* species (36/44 MAAs [81.8%]), with *Salmonella* serogroup C (*S. choleraesuis*) identified in 14 MAAs, *Salmonella* serogroup D (mainly *S. enteritidis*) in 13 MAAs, and *Salmonella* species without serogroup information in nine MAAs. The mean hospital stay in the study was 46.7 ± 29.6 d. The mean follow-up period, including that of patients who died, was 35.55 ± 39.74 mo (range, 0–120 mo).

TABLE 1. DEMOGRAPHIC CHARACTERISTICS OF 44 MYCOTIC AORTIC ANEURYSMS IN 43 PATIENTS

Clinical characteristics	No. of patients (%)	
Male gender	35	(79.5)
Age (years) mean $\pm$ SD	63.45 $\pm$	10.44
Clinical presentation		
Pulsatile mass	5	(11.4)
Fever	37	(84.1)
Watery diarrhea	4	(9.1)
Bloody stool	2	(4.6)
Pain	33	(75.0)
Chest	2	(4.6)
Abdomen	26	(59.1)
Back	5	(11.4)
Hydronephrosis	4	(9.1)
Shock	12	(27.3)
Treated as spinal disease	5	(11.4)
Medical comorbidities		
Hypertension	38	(86.4)
Chronic obstructive pulmonary disease	12	(27.3)
Diabetes mellitus	24	(54.6)
Peripheral arterial occlusive disease	5	(11.4)
History of stroke	9	(20.5)
Chronic kidney disease	8	(18.2)
End-stage renal disease	2	(4.6)
Connective-tissue disease	3	(6.8)
Liver cirrhosis	4	(9.1)
Lumbar osteomyelitis	6	(13.6)
Hospital stay (d) mean $\pm$ SD	46.7 $\pm$	29.6
Follow up (d) mean $\pm$ SD	1066.5 $\pm$	1192.1
Aneurysm-related mortality	8	(18.2)
Surgical mortality	6	(13.6)
Hospital mortality	10	(22.7)
Overall mortality	19	(43.2)

Types of treatment used

Twenty-nine of the 44 MAAs in the study population were repaired surgically, of which 11 were managed with endovascular stent grafts. Four MAAs were managed with conservative medical treatment. Table 2 summarizes the treatments used for the MAAs in the study. The ages, gender distributions, and clinical presentations of the patients in the three treatment groups in the study were similar. Patients selected for endovascular repair had more pre-procedural comorbidities (except for connective tissue disease) than did those selected for open repair. With regard to the surgical anatomic location of the aortic lesions in the study population, the highest percentage of lesions in the group of patients undergoing endovascular repair was in the thoracic aorta (36.4%), whereas the highest percentage of lesions in the group undergoing open repair was in the abdominal aorta (51.7%). Most of the organisms of *Salmonella* serogroup C found in the patients undergoing surgical repair were common serovariants, with *S. enterica* serovar Choleraesuis the predominant pathogen, although *Salmonellae* of serogroup D were the most frequent causative pathogens of MAA in the endovascular-treatment group. There was obvious selection bias based on the characteristics of the MAAs in the study population. Thus, for example, thoracic aortic aneurysms required thoracotomy and extracorporeal cardiopulmonary circulatory support for open surgery. The high risk entailed

TABLE 2. DESCRIPTIVE STATISTICS ACCORDING TO TREATMENT GROUPS FOR 44 MYCOTIC AORTIC ANEURYSMS IN 43 PATIENTS

Clinical characteristics	Medical treatment only (n=4)	Surgical treatment (n=29)	Endovascular repair (n=11)	p value
Age (years) mean $\pm$ SD	68.0 $\pm$ 14.2	63.4 $\pm$ 9.1	62.0 $\pm$ 12.8	0.63
Male sex	2(50.0%)	24(82.8%)	9(81.8%)	0.34
Presenting symptoms and signs				
Pulsatile mass	1	3(10.3%)	1(9.1%)	0.57
Fever	4	22(75.9%)	11(100%)	0.16
Watery diarrhea	0	4(13.8%)	0	0.7
Bloody stool	0	2(6.9%)	0	1
Pain				0.84
Chest	0	2(6.9%)	0	
Abdomen	4(100%)	15(51.7%)	7(63.6%)	
Back	0	4(13.8%)	1(9.1%)	
Hydronephrosis	0	3(10.3%)	1(9.1%)	1
Shock	1(25.0%)	7(24.1%)	4(36.4%)	0.76
Mistreatment as spinal disease	1(25.0%)	2(6.9%)	2(18.2%)	0.23
Medical comorbidities				
Hypertension	3(75.0%)	24(82.8%)	11(100%)	0.28
Smoke	0	5(17.2%)	5(45.5%)	0.13
Chronic onstructive pulmonary disease	1(25.0%)	7(24.1%)	4(36.4%)	0.76
Diabetes mellitus	2(50.0%)	15(51.7%)	7(63.6%)	0.89
Peripheral arterial occlusive disease	0	0	5(45.5%)	0.004
Cerebrovascular accident	0	3(10.3%)	5(45.5%)	0.01
Chronic renal insufficiency	0	5(17.2%)	3(27.3%)	0.58
End stage renal disease	1(25.0%)	0	1(9.1%)	0.05
Connective tissue disease	2(50.0%)	1(3.5%)	0	0.03
Liver cirrhosis	2(50.0%)	1(3.5%)	1(9.1%)	0.03
Lumbar osteomyelitis	0	3(10.3%)	3(27.3%)	0.37
Lab				
Hb (g/dL)	8.43 $\pm$ 1.20	11.21 $\pm$ 2.06	12.67 $\pm$ 2.99	0.01
HCT (%)	26.40 $\pm$ 3.31	35.63 $\pm$ 6.34	37.46 $\pm$ 7.08	0.01
PLT (per uL)	171.75 $\pm$ 85.14	251.0 $\pm$ 134.81	222.91 $\pm$ 109.50	0.58
WBC (per uL)	9.13 $\pm$ 1.45	14.21 $\pm$ 18.27	12.38 $\pm$ 6.47	0.7
BUN (mg/dL)	29.50 $\pm$ 17.75	28.21 $\pm$ 20.46	19.82 $\pm$ 17.22	0.21
Cr (mg/dL)	2.63 $\pm$ 3.59	1.68 $\pm$ 1.21	1.16 $\pm$ 1.13	0.09
AST (U/L)	36.50 $\pm$ 29.99	26.31 $\pm$ 14.78	37.91 $\pm$ 15.83	0.15
Anatomic position on CT				0.83
Thoracic	1(25.0%)	5(17.2%)	4(36.4%)	
Thoracoabdominal	1(25.0%)	4(13.8%)	1(9.1%)	
Abdominal	2(50.0%)	15(51.7%)	4(36.4%)	
Distal AAA-bifurcation	0	5(17.2%)	2(18.2%)	
Responsible pathogen on blood culture				0.21
<i>Salmonella</i> serogroup C	1(25.0%)	11(37.9%)	2(18.2%)	
<i>Salmonella</i> serogroup D	1(25.0%)	7(24.1%)	5(45.5%)	
<i>Salmonella</i> without serotype information	1(25.0%)	8(27.6%)	0	
Other	1(25.0%)	3(10.3%)	4(36.3%)	
Follow-up data				
Hospital stay (days)	20.3 $\pm$ 16.9	47.2 $\pm$ 25.2	54.8 $\pm$ 39.4	0.13
Follow-up (days)	20.3 $\pm$ 16.9	1,363.6 $\pm$ 1,334.1	663.9 $\pm$ 506.1	0.01
Aneurysm-related mortality	3(75.0%)	5(17.2%)	0	0.01
Surgical mortality	0	5(17.2%)	1(9.1%)	1
Hospital mortality	3(75.0%)	6(20.7%)	1(9.1%)	0.04
Overall mortality	4(100%)	13(44.8%)	2(18.2%)	0.02

AAA=abdominal aortic aneurysm; AST=aspartate aminotransferase; BUN=blood urea nitrogen; Cr=creatinine; CT=computed tomography; Hb=hemoglobin; HCT=hematocrit; PLT=platelets; WBC=white blood cells.

by open surgery for thoracic aortic aneurysms prompted more frequent endovascular repair in patients with these lesions.

Antibiotic therapy alone for MAAs resulted in three in-hospital deaths, all of which were related to the patients' MAAs. Two of the three patients died suddenly after refusing surgery and one died of massive hemoptysis. En-

dovascular repair was associated with less aneurysm-related and surgical death than was surgical repair (zero vs. 17.2% and 9.1% vs. 17.2%, respectively.). Because we began doing endovascular repair only in 2005, the endovascular repair group had a shorter follow up than did the surgical repair group.

Open surgical repair

Twenty-nine MAAs (29/44, 65.9%), the details of which are summarized in Table 3, were treated surgically without adjuvant endovascular intervention. Surgical management was divided into the two groups of in situ reconstruction with prosthetic graft interposition and extra-anatomic bypass, according to the revascularization procedure that was used. The surgical mortalities for in situ reconstruction and extra-anatomic bypass were 17.7% and 25%, respectively. Most extra-anatomic bypass procedures (91.7%) were done for infra-renal MAAs; more thoracic and thoraco-abdominal MAAs were treated with in situ reconstruction. Four cases of thoracic MAA required extra-corporeal cardiopulmonary bypass with deep hypothermic circulatory arrest (DHCA) to facilitate in situ reconstruction. Nine patients who had extra-anatomic bypass procedures survived to discharge, of whom four (44.4%) later developed limb ischemia or disabling claudication.

Endovascular repair

Eleven MAAs (11/44, 25.0%), the details of which are summarized in Table 4, were treated through endovascular repair. These MAAs were located in the thoracic aorta in four patients, thoracoabdominally in two patients, in the infra-renal abdominal aorta in three patients, and in the distal abdominal aorta in two patients. The only death among patients undergoing endovascular repair was attributed to post-operative pneumonia. No mortality was attributed to the progression of an aneurysm or a complication of treatment. A single infection of a prosthesis that had been revised by removal of an endovascular stent and interposition of a Dacron graft occurred 3 months after this. The mortality among patients undergoing open surgery for MAA has been 40% since 2005, when the endovascular stent graft became available at our institution.

Risk factor and survival analysis

In-hospital death occurred in 10 of the patients and late death in nine of the patients in the study population. Eight patients died of aneurysm-related causes (rupture, recurrent infection, and re-bleeding) and six patients died of complications related to surgery. The aneurysm-related mortality was 18.2%, the surgical mortality was 13.6%, and the in-hospital mortality was 22.7%, with the overall mortality being 43.2% (Table 1). Four patients managed with medical treatment died during follow up, with three of these deaths being related to complications of MAAs. The Kaplan–Meier cumulative survival curves for patients undergoing surgical and those undergoing endovascular repair are shown in Figure 2. The overall rates of survival with surgical and endovascular repair did not differ significantly from one another ($p = 0.5112$). Cox proportional-hazards models used for investigating potential risk factors for surgical, aneurysm-related, and in hospital death, and for overall survival, are shown in Table 5.

Discussion

Mycotic aortic aneurysm is a clinically challenging condition. The challenge begins with establishing the diagnosis [7,9,10]. In the study described here, the most common

presenting symptoms were fever (84.1%) and pain (75.0%), followed by shock (27.3%). However, fever, dull pain, and leukocytosis are often nonspecific symptoms and lead to delayed or incorrect diagnoses. In our series, some patients had been treated as having acute pyelonephritis (fever plus flank pain and positive hydronephrosis on kidney echography) or spinal osteomyelitis (fever, malaise, and back pain in bed-ridden patients) before a final diagnosis was made of MAA.

Mycotic aortic aneurysm is less common in Western countries, where it comprises only 0.5%–1.3% of aortic aneurysms, than in reports of Asian populations, in which such aneurysm constitutes as many as 13.3% of aortic aneurysms, with an increasing incidence in the Chinese population [7,11]. Current widespread use of CT has allowed the identification of MAAs before they lead to complications, specifically in patients evaluated for abdominal pain or unexplained sepsis [3,12]. Without appropriate treatment, MAA may progress to rupture and death. In the present study, 75% of the patients who had neither surgical nor endovascular repair of their MAAs died from aneurysm-related complications. Open repair has been regarded as the gold standard in treating MAAs [13–16]. Endovascular repair of degenerative thoracic and abdominal aortic aneurysms is well established; however, the insertion of an endovascular graft in an infected field remains a controversial measure.

The standard treatment for infra-renal MAAs consists of surgical resection of the aneurysm, extensive debridement of the surrounding soft tissue, and revascularization, followed by long-term antibiotic therapy [1,5,15,17]. Options for revascularization in infra-renal MAAs include in situ reconstruction and use of a prosthetic graft or extra-anatomic bypass. In situ reconstruction with use of a prosthetic graft is attended by a greater risk of graft infection than extra-anatomic bypass procedure. Previous studies have shown that 20% of patients who survive in situ graft reconstruction require a subsequent extra-anatomic bypass as the result of infection of the initial graft [4,16]. The revascularization in extra-anatomic bypass procedures is done remotely from the site of infection, which decreases the rate of graft infection but is attended by a greater frequency of late vascular-related complications. Reports of open repair of MAAs indicate a mortality of >20%, with significant short-term and long-term morbidity related to the operation [4,7,16]. In our series, 29 patients underwent open repairs, of which 17 consisted of reconstruction of the aorta with in situ repair and 12 consisted of open repair with an extra-anatomic bypass. The surgical mortalities in the groups that had in situ repair and extra-anatomic bypass were 17.7% and 25%, respectively. Extra-anatomic bypass was possible for 91.7% of the infra-renal MAAs in the study population, whereas most thoracic MAAs were reconstructed with the interpositioning of in situ grafts.

The roles of endovascular stent-grafts for the management of MAAs have not been extensively discussed in the literature [6,18–20]. Evolving endovascular technology has in recent years provided viable, less invasive alternatives for the management of aortic diseases [21]. However, the consensus of expert opinion does not favor the endovascular repair of MAAs, and it is usually reserved for patients with prohibitively high risks for open surgical repair [21]. This is because the endovascular repair of MAAs challenges the surgical principle of wide debridement of infected tissues and the

TABLE 3. SURGICAL REPAIR PROCEDURES FOR MYCOTIC AORTIC ANEURYSM IN 29 PATIENTS

	Age (y)	Hospital mortality	Overall mortality	Infrarenal position	Surgical subtype	Case number	Adjuvant procedures (n)	Complication (n)
In situ reconstruction (n = 17)	62.0 ± 10.1	3 (17.7%)	7 (41.2%)	9 (52.9%)	Tube graft interposition or autologous graft	7	Splenectomy (2), pulmonary lobectomy (1) visceral artery implantation (2)	Ischemic bowel (1)
					Y graft interposition	6	Cholecystectomy (1) closure of IVC fistula (1) left internal iliac artery ligation (1)	Acute kidney injury (1) Arrested bleeding (1)
					Graft interposition with cardiopulmonary by- pass and DHCA	4	Branch graft interposi- tion with visceral arterial revasculariza- tion (1)	Arrested bleeding (1) CVA (1) Vocal cord palsy (1) Post-operative prosthetic infec- tion by ORSA (1)
Extra-anatomic bypass (n = 12)	65.3 ± 7.5	3 (25.0%)	6 (50.0%)	11 (91.7%)	Axillo-bifemoral by- pass with ligation of aneurysm	10	Omental flap (1) Excision of necrotic esophagus(1)	Claudication (4) Tracheostomy creation (2) Renal failure (1) Ischemic bowel (1) Persistent sepsis (2) Nil
					Femoro-femoral bypass with ligation of ab- dominal aortic aneu- rysm	2		

CVA = cardiovascular accident; ORSA = oxiticillin-resistant *Staphylococcus aureus*; DHCA = deep hypothermic circulatory arrest.

TABLE 4. DETAILS OF ENDOVASCULAR REPAIR OF MYCOTIC AORTIC ANEURYSM IN 11 PATIENTS

Location of MAA	Patient number	Hospital mortality	Overall mortality	Endovascular procedure	Case number	Adjuvant procedure (n)	Complication (n)
Thoracic aorta	4	0	1	Endovascular exclusion with Cook Zenith TX2 graft	4	Intentional subclavian artery coverage (3), axillo-axillary bypass (1), decortication for empyema thoracis (1)	CVA (1), ischemic hand (2)
Thoraco-abdominal aorta	2	0	0	Endovascular exclusion with Cook Zenith TX2 graft	1	Nil	Nil
				Endovascular exclusion with Cook Zenith AAA graft	1	Visceral revascularization of SMA, renal artery, and celiac artery	Re-intubation (1)
Infra-renal abdominal aorta	3	0	0	Endovascular exclusion with Cook Zenith AAA graft	3	Nil	Nil
Distal AAA-bifurcation	2	0	0	Fluency (Bard) stent/Viabahn (Gore) endoprosthesis	2	Double J insertion for hydronephrosis (1), CT-guided drainage of peri-graft hematoma (1)	Prosthesis infection, graft revision at 3 mo (1)

AAA=abdominal aortic aneurysm; CT=computed tomography; CVA=cerebrovascular accident; MAA=mycotic aortic aneurysm; SMA=superior mesenteric artery.

effective drainage of suppuration that is paramount to the successful open repair of these lesions.

In our series, 11 patients, beginning in 2005, had endovascular surgery for MAAs. Approximately half (5/11, 45.5%) of these patients' aneurysms were located in the thoracic or thoraco-abdominal aorta. We have treated thoracic and suprarenal MAAs more aggressively than in previous reports of the endovascular management of MAAs, using a hybrid technique with visceral debranching and video-assisted thoracoscopic surgery (VATS) to facilitate

endovascular repair and eliminate foci of infection, respectively. Our early (30-d) mortality with the endovascular repair of MAAs was zero (0/11), and the rate of survival for at least one year was 81.8% (9/11 patients). This result is comparable to that in a recent systematic review [18].

The known causative organisms of MAA in western countries are *S. aureus* (28%), *Salmonella* spp. (15%), and *Pseudomonas aeruginosa* (10%) [22,23]. However, *Salmonella* has been consistently reported as the most common pathogen in Asian patients with MAAs. *Salmonella* is a genus of bacterium

FIG. 2. Kaplan-Meier curves of actuarial overall survival of study patients. The open boxes represent patients undergoing endovascular repair and the black triangles represent patients undergoing open surgical repair. The probability of survival is plotted on the vertical axis and the survival period in days is plotted on the horizontal axis.

TABLE 5. COX PROPORTIONAL HAZARDS MODELS FOR POTENTIAL RISK FACTORS AFFECTING ANEURYSM-RELATED, SURGICAL, AND IN-HOSPITAL DEATH AND OVERALL SURVIVAL

Variance	Hazard ratio	Standard error	Z	p > z	95% Confidence interval
Hazard model for surgical death according to model selection					
Shock	5.50	0.9	3.58	0.05	(0.94–32.17)
<i>Salmonella</i> serotype C	3.07	0.91	1.53	0.21	(0.52–18.14)
Endovascular repair of MAA	0.48	1.13	0.42	0.51	(0.05–4.37)
Hazard model of aneurysm-related death according to model selection					
Hematocrit	0.80	0.09	5.43	0.02	(0.67–0.97)
Treated as spinal disease before MAA was diagnosed.	13.04	0.91	7.96	0.004	(2.19–77.57)
Connective-tissue disease	7.18	0.97	4.07	0.04	(1.06–48.86)
<i>Salmonella</i> serogroup C	6.31	0.83	4.88	0.03	(1.23–32.37)
Hazard model of in-hospital death according to model selection					
Treated as spinal disease before MAA was diagnosed.	8.88	0.78	7.93	0.005	(1.94–40.60)
Connective-tissue disease	6.97	0.85	5.23	0.02	(1.32–36.80)
Endovascular repair of MAA	0.21	1.1	2.01	0.16	(0.02–1.82)
Hazard model of overall mortality according to model selection					
Shock	4.00	0.48	8.29	0.004	(1.56–10.28)
Treated as spinal disease before MAA was diagnosed.	7.22	0.76	6.67	0.01	(1.63–32.10)
Endovascular repair of MAA	0.19	0.86	3.64	0.06	(0.04–1.05)

MAA = mycotic aortic aneurysm.

in the family Enterobacteriaceae, and the species *Salmonella enterica* comprises more than 2,500 serotypes, of which large numbers are important medically to human beings and animals. The serotypes of *S. enterica* commonly associated with MAAs are Typhimurium (serogroup B), Enteritidis (serogroup D), and Choleraesuis (serogroup C) [24, 25].

Most *Salmonella* infections are limited to uncomplicated gastroenteritis that seldom requires an antimicrobial treatment. The development of MAA is the most serious complication of *Salmonella* infection in adults. *Salmonella* usually reside in the phagosomes of host macrophages and other antigen-presenting cells, such as dendritic cells. *Salmonella* pathogenicity islands (SPIs) on the genome contribute to the invasiveness of the organism. However, the exact mechanisms involved in the pathogenesis of aortic aneurysms remain unknown [26,27].

Our study also found some interesting links between public health policy and the epidemic distribution of MAAs. *Salmonella* of serotype Choleraesuis, or literally, “the *Salmonella* of swine,” and MAAs associated with infection by *Salmonella* of this serotype are found mainly in Taiwan [28, 29]. *Salmonella* of serotype Choleraesuis, in contrast to *Salmonella* of other serotypes, usually induces a systemic inflammatory response with a high incidence of bacteremia and mortality in swine and humans [30]. The emergence of fluoroquinolone-resistant *S. choleraesuis* in humans, attributed to the use of antibiotics of this type in animals, complicates the management of MAAs [30].

Shock was strongly associated with surgical mortality (hazard ratio [HR] 5.5, $p=0.05$). Mistreatment of MAA as spinal disease was strongly associated with aneurysm-related mortality (HR 13.04; $p=0.004$), with the next strongest associations being connective-tissue disease (HR 7.18; $p=0.04$) and *Salmonella* serogroup C bacteremia (HR 6.31; $p=0.03$). Inappropriate management of MAA as spinal disease was identified as a factor strongly correlated with in-hospital mortality (HR 8.88; $p=0.005$), with the next strongest correlation being with connective-tissue disease (HR 6.97; $p=0.02$). Although the endovascular approach is not a factor

in mortality in MAA, it has a trend toward a protective effect against surgical death (HR 0.48; $p=0.51$), in-hospital death (HR 0.21; $p=0.16$) and overall mortality (HR 0.19; $p=0.06$). The Kaplan–Meier cumulative survival curves for open surgical repair and endovascular repair demonstrated no significant difference between these two procedures in terms of overall survival ($p=0.511$).

Major limitations of the present study were its retrospective design and small patient population. With such limitations, we thoroughly examined our 14-y experience in the treatment of MAA, attempting to identify variables that influenced adversely the treatment outcome and to obtain information about the use of endovascular techniques in this patient population. In this effort, one of our greatest limitations has been the recent implementation of endovascular techniques, resulting in comparatively short follow-up periods for patients having endovascular repairs as compared with those having open repairs. However, the present study may be the first study to include an analysis of risk factors for mortality in the open surgical repair and endovascular repair of MAAs.

The present study improves upon previous research by detailing the roles of different therapeutic options, effects of bacteriologic analysis, and prognostic factors in MAA. Shock is a risk factor for surgical mortality in the treatment of MAA. Risk factors for aneurysm-related death are the mistreatment of MAA as spinal disease, connective-tissue disease, or *Salmonella* serogroup C bacteremia. Although it is still early in our experience with the endovascular treatment of MAA, and we intend to conduct a longer follow-up study of patients who undergo such treatment, which will be critically important, we currently consider its endovascular treatment to be a valuable option for this complex condition.

Author Disclosure Statement

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References

- Reddy DJ, Shepard AD, Evans JR, et al. Management of infected aortoiliac aneurysms. *Arch Surg* 1991;126:873–878.
- Baird RN. Mycotic aortic aneurysms. *Eur J Vasc Surg* 1989;3:95–96.
- Lopes RJ, Almeida J, Dias PJ, et al. Infectious thoracic aortitis: A literature review. *Clin Cardiol* 2009;32:488–490.
- Fichelle JM, Tabet G, Cormier P, et al. Infected infrarenal aortic aneurysms: When is in situ reconstruction safe? *J Vasc Surg* 1993;17:635–645.
- Hsu RB, Tsay YG, Wang SS, Chu SH. Surgical treatment for primary infected aneurysm of the descending thoracic aorta, abdominal aorta, and iliac arteries. *J Vasc Surg* 2002;36:746–750.
- Silverberg D, Halak M, Yakubovitch D, et al. Endovascular management of mycotic aortic aneurysms. *Vasc Endovascular Surg* 2010;44:693–696.
- Lee WK, Mossop PJ, Little AF, et al. Infected (mycotic) aneurysms: Spectrum of imaging appearances and management. *Radiographics* 2008;28:1853–1868.
- Ting AC, Cheng SW, Ho P, Poon JT. Endovascular stent graft repair for infected thoracic aortic pseudoaneurysms—A durable option? *J Vasc Surg* 2006;44:701–705.
- Bisdas T, Teebken OE. Mycotic or infected aneurysm? Time to change the term. *Eur J Vasc Endovasc Surg* 2011;41:570.
- Leo PJ, Pearl J, Tsang W. Mycotic aneurysm: A diagnostic challenge. *Am J Emerg Med* 1996; 14:70–73.
- Hsu RB, Lin FY, Chen RJ, et al. Antimicrobial drug resistance in *Salmonella*-infected aortic aneurysms. *Ann Thorac Surg* 2005;80:530–536.
- Macedo TA, Stanson AW, Oderich GS, et al. Infected aortic aneurysms: Imaging findings. *Radiology* 2004;231:250–257.
- Gomes MN, Choyke PL, Wallace RB. Infected aortic aneurysms. A changing entity. *Ann Surg* 1992; 215:435–442.
- Hsu RB, Tsay YG, Wang SS, Chu SS. Surgical treatment for primary infected aneurysm of the descending thoracic aorta, abdominal aorta, and iliac arteries. *J Vasc Surg* 2002;36:746–750.
- Dubois M, Daenens K, Houthoofd S, et al. Treatment of mycotic aneurysms with involvement of the abdominal aorta: Single-centre experience in 44 consecutive cases. *Eur J Vasc Endovasc Surg* 2010;40:450–456.
- Kyriakides C, Kan Y, Kerle M, et al. 11-year experience with anatomical and extra-anatomical repair of mycotic aortic aneurysms. *Eur J Vasc Endovasc Surg* 2004;27:585–589.
- Weis-Müller BT, Rascanu C, Sagban A, et al. Single-center experience with open surgical treatment of 36 infected aneurysms of the thoracic, thoracoabdominal, and abdominal aorta. *Ann Vasc Surg* 2011;25:1020–1025.
- Kan CD, Lee HL, Yang YJ. Outcome after endovascular stent graft treatment for mycotic aortic aneurysm: A systematic review. *J Vasc Surg* 2007;46:906–912.
- Clough RE, Black SA, Lyons OT, et al. Is endovascular repair of mycotic aortic aneurysms a durable treatment option? *Eur J Vasc Endovasc Surg* 2009;37:407–412.
- Sörelus K, Mani K, Björck M, et al. Endovascular repair of mycotic aortic aneurysms. *J Vasc Surg* 2009;50:267–274.
- Svensson LG, Kouchoukos NT, Miller DC, et al. Expert consensus document on the treatment of descending thoracic aortic disease using endovascular stent-grafts. *Ann Thorac Surg* 2008; 85(1 Suppl):S1–41.
- Bitseff EL, Edwards WH, Mulherin JL, Jr., Kaiser AB. Infected abdominal aortic aneurysms. *South Med J* 1987;80:309–312.
- Zhou T, Guo D, Chen B, et al. Endovascular stent-graft repair of mycotic aneurysms of the aorta: a case series with a 22-month follow-up. *World J Surg* 2009; 33:1772–1778.
- Chiu CH, Ou JT. Risk factors for endovascular infection due to nontyphoid *Salmonellae*. *Clin Infect Dis* 2003;36:835–836.
- Chiu CH, Lin TY, Ou JT. Predictors for extraintestinal infection of non-typhoidal *Salmonella* in patients without AIDS. *Int J Clin Pract* 1999;53:161–164.
- Chiu CH, Su LH, Chu C. *Salmonella enterica* serotype Choleraesuis: Epidemiology, pathogenesis, clinical disease, and treatment. *Clin Microbiol Rev* 2004;17:311–322.
- Guiney DG. The role of host cell death in *Salmonella* infections. *Curr Top Microbiol Immunol* 2005;289:131–150.
- Luo CY, Yang YJ. Surgical experience with *Salmonella*-infected aneurysms of the abdominal aorta. *J Formos Med Assoc* 1997;96:346–352.
- Chan P, Tsai CW, Huang JJ, et al. Salmonellosis and mycotic aneurysm of the aorta. A report of 10 cases. *J Infect* 1995;30:129–133.
- Chiu CH, Wu TL, Su LH, et al. The emergence in Taiwan of fluoroquinolone resistance in *Salmonella enterica* serotype Choleraesuis. *N Engl J Med* 2002;346:413–419.

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