Graft infection after endovascular abdominal aortic aneurysm repair

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Introduction: **Although the natural history and management of infected open abdominal aortic aneurysm (AAA) repair is well described, only sporadic case reports have described the fate of patients with infected endografts placed in the abdominal aorta. The present study describes a tertiary referral center's experience with infected endovascular aneurysm repairs (EVARs).**

Methods: **The medical records of 1302 open and endovascular aortic procedures were queried from January 2000 to January 2010. The cases were reviewed for prior aortic procedures, prosthetic implants, and etiology of current open procedure. Demographics, operative details, and perioperative courses were documented.**

Results: **Nine patients (1 woman) with a mean age of 71 years had an EVAR that later required an open procedure for explantation and surgical revision for suspected infection. All grafts were explanted through a midline transperitoneal approach, with a mean time to explant of 33 months. The explanted endografts included 4 Zenith (Cook, Bloomington, Ind), 2 Ancure (Endovascular Technologies, Menlo Park, Calif), 2 Excluders (Gore, Flagstaff, Ariz), and 1 AneuRx (Medtronic, Minneapolis, Minn). Eight of the nine original EVARs were performed at other hospitals; 1 patient had EVAR and open explant at the University of Michigan. All patients had preoperative computed tomography scans, except one who was transferred in extremis with a gastrointestinal hemorrhage. Three patients also had a tagged leukocyte scan, and two had magnetic resonance imaging to further reinforce the suspicion of infection before explantation and bypass planning. Rifampin-soaked Hemashield (Boston Scientific) in situ grafts were used in four patients, with extra-anatomic (axillary-bifemoral) bypass used in the other five. The in situ group had no positive preoperative or postoperative cultures, with the exception of the unstable patient who died the day of surgery. For the other five patients, positive tissue cultures were found for *Bacteroides, Escherichia coli*, coagulase-negative *Staphylococcus*, *Streptococcus*, and *Candida*. Three patients were found to have aortic-enteric fistula, two of whom died before discharge from the hospital. The remaining seven survived to discharge. Average length of stay was 22 days, with a median follow-up of 11 months.**

Conclusion: **This series of infected EVARs is the largest group of infected AAA endografts reported to date. Because EVAR of AAAs is presently the most common method of repair, development of endograft infection, while rare, can be managed with acceptable mortality rates. Patients presenting with aortic-enteric fistula after EVAR appear to have a more virulent course. (J Vasc Surg 2011;54:58-63.)**

The incidence of aortic endograft infection is low, 0.2% to 0.7%,[1] but represents a challenging management problem in aortic surgery. The incidence seems to be similar to aortic graft infection after open abdominal aortic aneurysm (AAA) repair, with a predictable high risk of death. Although much attention has been given to the more common problem of endoleak management, there is still much to learn about the late complication of endograft infection. This study evaluated the experience at a tertiary referral center in managing endograft infections after AAA repair.

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METHODS

This was a retrospective, single-institution review. Medical records of the 1302 open and endovascular aortic procedures performed at University of Michigan were queried from January 2000 to January 2010. The cases were identified using Current Procedural Terminology code 35907 and for prior aortic procedures, prosthetic implants, and etiology of current open procedure. We identified nine patients who underwent open aortic endograft explantation for a suspected infection. Demographics, operative details, culture results, and perioperative courses were documented. Any patients with identified aortic endograft infection managed medically were not included in this study design. The Institutional Review Board at University of Michigan reviewed and approved this study (#HUM00035996).

RESULTS

Eight of the nine identified patients were men with a mean age of 71 years (range, 54-84 years). Eight of nine initial endovascular aneurysm repairs (EVARs) were performed at outside institutions (patient 5 had both procedures at University of Michigan). The endografts placed included 4 Zenith (Cook, Bloomington, Ind), 2 Ancure

Table. Nine patients managed operatively for aortic endograft infection after endovascular aneurysm repair

Patient	*Age, years*	*Sex*	*Initial endograft*	*Intervening procedures*	*Interval, months*
1	77	M	Zenith	Endoleak	37
2	67	M	Zenith		28
3	73	M	Zenith		20
4	68	M	AneuRx	Endoleak; abscess drained	41
5	75	M	Excluder		15
6	73	M	Ancure	Groin, I & D, fem-pop	6
7	84	M	Ancure		24
8	54	M	Excluder	Abscess drained	45
9	66	F	Zenith	Endoleak	80

ABFB, Axillary bifemoral bypass; *CT,* computed tomography; *Dapto,* daptomycin; *GI,* gastrointestinal; *I & D,* incision and drainage; *Meropen,* meropenem; *RSHG,* rifampin-soaked Hemashield graft; *Staph, Staphylococcus*; *Strep, Streptococcus*; *UTI,* urinary tract infection; *Vanc,* vancomycin.

(Endovascular Technologies, Menlo Park, Calif), 2 Excluders (Gore, Flagstaff, Ariz), and 1 AneuRx (Medtronic, Minneapolis, Minn; Table). Mean time to endograft explant was 33 months (range, 6-80 months).

Presentation of aortic graft infection is described in the literature in one of three typical ways: gastrointestinal (GI) hemorrhage, chronic low-grade sepsis, or severe sepsis. All of the patients in this study had one or more of these except patient 2, who was diagnosed at a follow-up computed tomography (CT) scan only. Seven patients presented with clinical manifestations of sepsis, one of which was severe.

Patient 11 had nagging back and pelvic pain with associated abdominal fullness (in the setting of an enlarging AAA with no evidence of endoleak). Patient 3 had fever, chills, and night sweats for approximately 1 month. This patient presented with fever of 102.4°F, but no other signs of severe sepsis.

Patient 4 presented with fevers and was found to have a psoas abscess on CT scan. This was illuminated as a frank abscess in the terminal aorta during explant. A sigmoid mass was discovered as well, and perforated diverticulitis diagnosed. Patient 5 had severe sepsis and presented to the emergency department with mental status changes, hypotension, leukocytosis, anemia, and complaints of abdominal pain.

Patient 6 presented with multiple infections, including a groin infection leading to bacteremia, a septic ankle, and osteomyelitis of the lumbar and sacral spine. He had been on chronic antibiotics for the 6 months between implant and explant. Signs of chronic sepsis were also present in the last two patients. Patient 8 presented with 1.5 years of back pain, 6 months of abdominal pain, weight loss, and fevers up to 101°F. A new heterogenous fluid collection was found adjacent to the juxtarenal aorta seen on CT. Patient 9 presented with severe back pain radiating down her leg and fever of 103°F, her third episode of bacteremia in the prior year.

Other global risk factors such as comorbidities and smoking status were also evaluated. Patients 8 and 9 were current smokers and patients 2, 3, 4, and 5 were former smokers all with >40 pack-years each. Patients 1 and 4 were obese, and the rest were at or below the normal weight range. Only patient 5 had documented diabetes. No other immunosuppressive factors were identified in any of the other patients, such as steroid use or chemotherapy.

Endoleaks with subsequent endovascular procedures were present in two patients. Patient 1 had a type III leak due to poor apposition of the left iliac limb. He underwent embolization of the main left hypogastric artery on two occasions (coils, and then pushable cores) before explant later the same year. No antibiotics were given during this procedure. Patient 4 had a type II leak, with six attempts at embolization of various arteries, including the right iliolumbar and branches of the right hypogastric. Intravenous antibiotics were initiated only after the last revision when a psoas abscess was discovered. In patient 2, a type III endoleak was identified at the time of infection diagnosis.

Patient 7 presented with a GI hemorrhage and was later discovered to have an aortic-enteric fistula (AEF). This patient had presented to another emergency department with GI bleeding two weeks before arrival at our facility. Endoscopy was done at that time, with biopsy of the duodenum. The cause of bleeding was not identified, and the patient was discharged. He then presented to our institution in extremis, having been intubated and received seven units of packed red blood cells in route. In addition to this patient, AEFs were also discovered in patients 3 and 9. They did not present with GI bleeding. The AEFs were discovered at explantation only after axillary-bifemoral bypass was completed. Patients 3 and 7 experienced excessive operative bleeding and were not expected to survive. They were packed, closed, and transported to the intensive care unit, where they died within hours. Patient 3 was in hemorrhagic shock due to an unidentified source of bleeding and cardiac arrested several times intraoperatively. Patient 7 became extremely coagulopathic despite resuscitation, and the family agreed to withdraw care.

In general, workup for diagnosis of graft infection varied slightly by patient. CT was common to all patients except patient 7 due to his emergent status (Fig 1). Radiographic interpretations such as "multiple foci of gas" and "adjacent fluid collection" were suggestive of aortic endograft infection. Patients 1, 4, and 9 underwent tagged leukocyte scans to confirm suspicion of infection noted on CT; uptake was visualized in the aortic lumen, "aneurysm sac adjacent to endograft," and fluid collection anterior to

Table. Continued.

Clinical symptoms	*Antibiotics before resection*	*Diagnostic tests*	*OR cultures*	*Treatments*	*Follow-up*
Back pain	None	CT; WBC scan	Negative	RSHG	Alive; 8 months
None	None	CT	Negative	RSHG	Alive; 6 months
Fever, chills	IV Zosyn, Vanc ×6 weeks	CT	*Bacteroides, Candida*	ABFB	Dead
Fever, abscess	Ceftriaxone ×4 weeks	CT; WBC scan	Negative	ABFB	Alive; 21 months
Back pain, UTI	Zosyn ×1 weeks	CT	*E. coli*	ABFB	Alive; 21 months
Multiple infections	Unknown ×6 months	CT; MRA	*Staph*	ABFB	Alive; 3 months
Acute GI bleed	None	Endoscopy	*Bacteroides, E. coli, Strep*	In situ graft	Dead
Back pain fever, chills	Meropen, Dapto ×1 week	CT; MRI	Negative	RSHG	Alive; 7 months
Back, leg pain	Nafcillin ×2 weeks	CT; WBC scan	*Staph, E. coli*	ABFB	Alive; 2 months

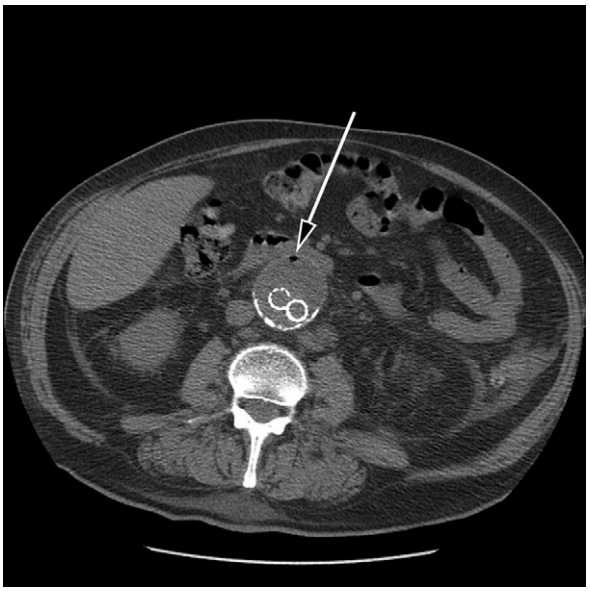

Fig 1. Computed tomography without contrast of patient 5 shows air in the abdominal aortic aneurysm sac (*arrow*).

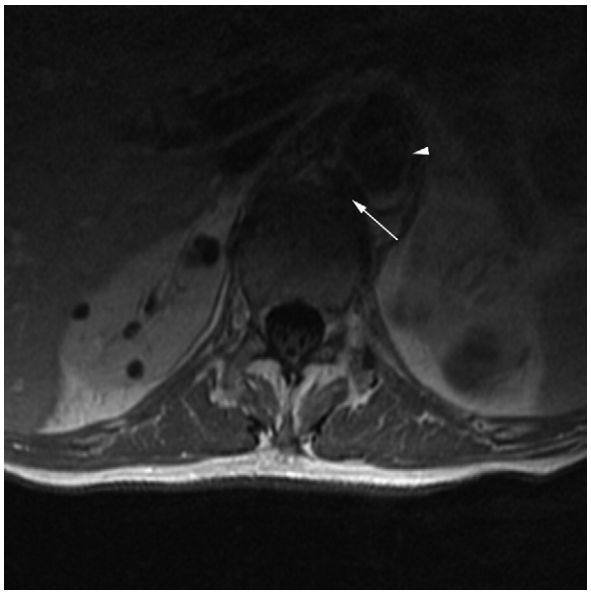

Fig 2. T1-weighted axial magnetic resonance imaging from patient 8 demonstrates a focal defect in the anterior vertebral body (*arrow*) indicating contiguous spread from aortic graft infection (*arrowhead*).

the iliac bifurcation, respectively. MRI was the confirmatory test for patients 6 and 8, elucidating lytic changes of adjacent vertebral bodies (Fig 2). Operative findings described as "frank purulence" or "infected-appearing thrombus" were visual confirmation of an infectious nature in six patients. The remaining two had "inflammatory reactions" seen in the AEF cases.

All grafts were explanted through a midline transperitoneal approach because this is the preferred approach of the senior author. Total excision of the endograft was performed in all cases, often using a suprarenal or supraceliac clamp, except in patient 2 secondary to overall poor medical condition and wanting to avoid a suprarenal aortic cross clamp. An axillary-to-bifemoral bypass was done before explantation in patients 3, 4, 5, 6, and 9, whereas the other four underwent simultaneous in situ graft placement. The axillary-to-bifemoral bypasses were performed with polytetrafluoroethylene the day before explants, except on the same day in patient 6. In situ grafts were rifampin-soaked Hemashield (Boston Scientific Corp) in three of the patients; the last was patient 7 who exsanguinated due to disseminated intravascular coagulation immediately after placement of a graft.

Complications during the operative procedure included significant hypotension requiring cardiopulmonary resuscitation in patient 3 after finding an AEF during explantation of the endograft. A sigmoid mass was found in patient 4, and a colostomy was performed for diverticulitis. Patient 5 was taken back to the operating room later in the day for explantation for hypotension and bleeding from an internal iliac artery as a result of a calcium plaque going through the front wall.

Antibiotics were given to many of the patients before resection of the endograft (Table). Patient 3 had been on

intravenous and then oral antibiotics for 3 months before graft explantation. Patients 4 and 8 had been on intravenous antibiotics for 1 to 4 weeks due to local abscesses and patients 5 and 9 for treating suspected remote infections. Patient 6 also underwent treatment for remote infections for the entire 6 months between EVAR and graft explantation. Although preoperative antibiotics can influence intraoperative culture results, our series did not demonstrate a clear pattern between presence or length of preoperative antibiosis and intraoperative culture results.

Results of graft or perigraft fluid cultures at the explant operation are reported in the Table. Four patients had negative cultures from graft and aortic material, all of whom had "frank pus" described at explantation. An in situ graft had already been decided and started for three of these patients; patient 4 was given an axillary-to-bifemoral bypass. Of the patients with positive cultures, two had purulence or infected-appearing thrombus; the other two were described as having inflammatory reaction only. Four of five of this group of patients underwent axillary bifemoral bypasses. From the thrombus and endograft, gram-positive coagulase-negative *Staphylococcus* or *Streptococcus* spp were cultured in three patients. Gram-negative bacteria (*Bacteroides* and *Escherichia coli*) were grown in four patients. One patient also had a positive fungal culture (*Candida glabrata*). Both patients who died had positive cultures for gram-negative bacteria.

All surviving patients received broad-spectrum antibiotics until bacterial culture identification allowed for replacement by selective antibiotic regimen for 4 to 6 weeks after discharge. Patients were monitored by the Infectious Disease Service, and of the surviving patients, five have records that indicate they are being maintained on lifelong oral antibiotics. Interestingly, patient 4 required replacement for a septic knee approximately 20 months after explantation.

AEFs are rare and difficult to manage. Patient 3 had a large 4-cm defect found in the aortic wall and fourth part of the duodenum. The aneurysm of patient 7 appeared to have mucosa directly eroded into it. The duodenum of patient 9 was found densely adherent to the aneurysm sac by the retroperitoneal abscess. The exact cause of fistula formation is not known, but is hypothesized to be due to erosion of the graft fabric into the duodenum. What role stents or hooks have on this process (ie, namely with aortic pseudoaneurysm formation) would be purely speculative.

Two of the patients found to have AEFs died before discharge from the hospital. The remaining seven patients survived to discharge with an average length of stay of 22 days (range, 9-55 days). Mean follow-up of the surviving patients was 11 months (range, 3-21 months).

DISCUSSION

Several studies have suggested a similar incidence of aortic graft infections in open and endovascular cases.[1-3] Open aortic graft infections have been well documented in the literature; however, endovascular graft infections have been reported only in case reports and small series totaling 110 patients.[1,4,5] This therefore is the largest single-institution case series known to date of graft infections after EVARs.

The largest studies of open AAA graft infections show aortic graft infections presenting close to 2 to 5 years after implantation.[6,7] More recent data showed that aortic graft infections (open and endovascular) occurred most commonly in the first year after surgery. This is possibly due to improved imaging reducing the time to diagnosis.[1,2] We found that the average time to explants for this series of endografts was substantially longer, at 33 months. One possible explanation is patients being lost to follow-up or transferring care from the institution that performed the original procedure.

Endovascular aortic stent graft infections have been shown to present roughly one-third as chronic sepsis, one-third as severe acute sepsis, and one-third as AEFs.[1,4,8] Symptoms are important, and were present in eight of nine patients in this study. Many patient complaints and symptoms were vague and relatively nonspecific, as has been described previously,[9] leading to a delay in the correct diagnosis. Current follow-up guidelines for EVAR recommend periodic CT scans (yearly) and therefore may enable more rapid identification of gas or fluid that can spur investigation of suspicions for infection. Nonoperative treatment exists as an option for selected patients presenting with infected endograft after EVAR. This is primarily reserved for patients who cannot tolerate an open surgical procedure, because mortality rates of 36% have been reported.[4] These patients are usually managed with percutaneous drainage, instillation of antibiotics through drains, and intravenous antibiotics for at least 6 weeks.

The cause of aortic graft infections in general, and specifically endograft infections, has been hypothesized. Vogel et al[2] concluded in 2008 in a population level analysis that aortic graft infections were associated with periprocedural infections for both endovascular and open AAA repairs.[2] Unfortunately, due to the retrospective nature of our study and the fact that most initial procedures were at outside hospitals, complete periprocedural data for the original EVARs are not available for this study.

Although experimental data have shown that endovascular devices offer less bacterial resistance and increased adherence[8,10] than grafts placed during open surgery, some studies have shown similar rates of aortic graft infections between open and endovascular approaches to AAA repair.[2,3] EVAR largely eliminates the contamination associated with placement due to sterile sheaths and delivery systems. Contrary to this, however, are studies that show decreased sterility in endografts placed in interventional suites compared with traditional operating theaters.[4,11] These effects may balance out and produce equal rates of aortic graft infections in open and endovascular cases. If endografts are placed in operating room or sterile endovascular suites, then the sources of infection must arise from elsewhere. Data appear to point to a hematogenous source of secondary bacterial seeding of endografts causing aortic graft infections. In six of nine patients in this study, there

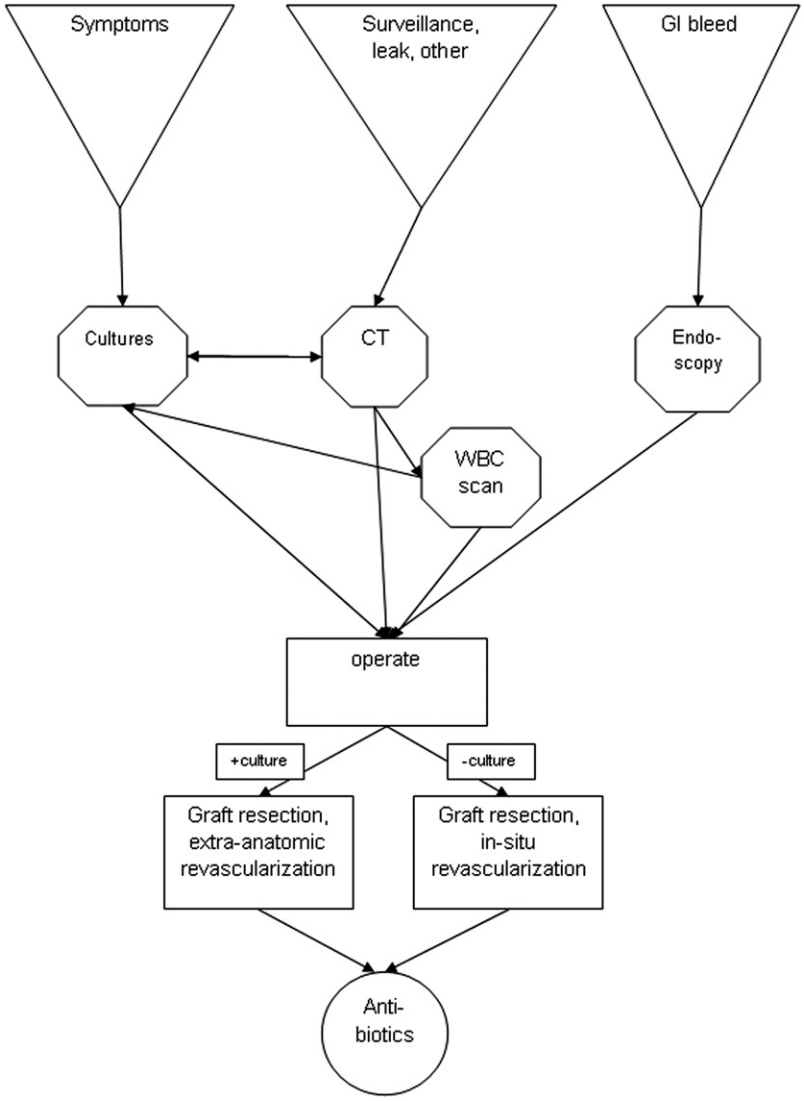

Fig 3. Proposed algorithm for workup and management of patients with infected endograft after endovascular aneurysm repair. *CT,* Computed tomography; *GI,* gastrointestinal.

were certainly remote sources of infection retrospectively identified to support this hypothesis. However, it is difficult to determine causality because the time course is unclear. Other sources of infection include perioperative contamination, mechanical erosion (stent migration, excessive angulation) leading to AEF, aortic thrombus as a nidus, or contamination from additional procedures (for endoleaks).

Identified sources in this group include multiple intervening endovascular procedures in two patients (patients 1 and 4) and immediate preceding or concurrent presentation of remote infections in four patients. Patient 5 had pneumonia 2 months prior and a urinary tract infection at admission, patient 6 had groin infection, spinal osteomyelitis, and a septic ankle diagnosed before explantation, patient 8 had a retroperitoneal perispinal abscess drained 2 months before presentation, and patient 9 had a urinary tract infection, with the first of three episodes of bacteremia starting 1 year before presenting. Possible sources for infection of the aortic endograft may be that the original AAA in patient 2 was ruptured and an increased bacterial load could have been introduced during the emergent procedure (operative records unavailable). In addition, the AAAs done emergently could have been mycotic in nature. Patient 3 had an open repair for aortic occlusive disease 11 years before an endovascular repair for a proximal anastomotic pseudoaneurysm, which was 12.5 years before the endograft explantation. The pseudoaneurysm was suspicious for the presence of an infection at that time.

The literature has shown that positive cultures are not always found in cases of suspected endograft infection. The Gilling-Smith group[1] reported only 68% of cases demonstrated a positive culture. Three of four patients in our in

situ group had no postoperative positive blood or tissue cultures, despite the appearance of frank purulence. The exception is patient 7, who was too unstable to consider alternative surgical management and died the day of surgery. Correspondingly, four of five patients managed with an axillary-to-bifemoral bypass had positive intraoperative graft or tissue cultures. Patient 4 did not, but had a positive culture for *Streptococcus* from his psoas abscess earlier in the hospital course. This is a small sample size, but begs inquiry and investigation into decision making for management of infected aortic endografts. The presence of frank purulence did not necessarily correspond with positive OR cultures. It would be helpful to have a way of knowing preoperatively which cases would have positive cultures and decide for an extra-anatomic bypass to decrease bacterial spread.

The few surgeons who performed these endograft resections and revascularizations were not following a preset guideline, but made independent decisions on a patient-by-patient basis. Looking retrospectively at this series of patients, and understanding that culture data are not always available before operative decisions are made, a proposed algorithm to manage patients presenting with a suspected infected endograft after EVAR is found in Fig 3. It suggests that when blood or abscess cultures are positive, an extra-anatomic reconstruction and graft resection is preferable. In contrast, when all obtainable preoperative cultures are negative, an in situ graft placement after resection is suggested.

The most common culture reported in the literature has been gram-positive bacteria, with the specific bacterial organism *Staphylococcus* spp representing 23% to 88% of all positive cultures.[1,3,5,12] Our study did not support this and unexpectedly had more gram-negative bacterial cultures than positive. Also in opposition to previously reported literature, *Candida glabrata* was present in one of four patients with positive cultures. These could reflect local bacterial patterns and virulences, or simply a small study size.

Limitations of this study include a possible exclusion bias as a result of a limited coding scheme. Short follow-up time is noted, due to most of the procedures being within the last 2 years of included time period. Bias may also be present due to the single-institution, referral nature of this study.

Further studies are needed to identify patients at greatest risk for infection, which would necessitate enhanced surveillance, longer treatment of intervening infections, or prophylactic antibiotic treatment before any invasive procedures attempting to preserve the original endograft. This will be difficult to accomplish due to the low incidence of infected EVARs.

CONCLUSIONS

This experience with infected EVARs contributes to the body of literature currently available largely in the form of case reports. Infection of an endograft after EVAR, like that after open AAA repair, is rare, difficult to manage, and potentially lethal. There are multiple presenting symptoms associated with endograft infection, but the presence of an AEF increases the virulence of a patient's course. Further investigation into the role of culture positivity in management decisions is required.

AUTHOR CONTRIBUTIONS

Conception and design: AL, GU
Analysis and interpretation: AL, GU
Data collection: AL, NB
Writing the article: AL, JR, JE, EC, GU
Critical revision of the article: AL, NB, JR, JE, EC, GU
Final approval of the article: AL, NB, JR, JE, EC, GU
Statistical analysis: AL
Obtained funding: GU
Overall responsibility: GU

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