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Endovascular Repair for Aorto-enteric Fistula: A Bridge Too Far or a Bridge to Surgery?

M.I.L. Danneels,[1]* H.J.M. Verhagen,[2] J.A.W. Teijink,[3] Ph. Cuypers,[4] A. Nevelsteen[5] and F.E.G. Vermassen[1]

[1]*Ghent University Hospital, Gent, Belgium;* [2]*University Medical Center Utrecht, Utrecht,* [3]*Atrium Medical Center Heerlen, Heerlen,* [4]*Catharina Hospital Eindhoven, Eindhoven, The Netherlands; and* [5]*University Hospitals Leuven, Leuven, Belgium*

Purpose. *To review our experience of endovascular treatment of aorto-enteric fistula (AEF).*
Methods. *Between March 1999 and March 2005, 15 patients in five university and teaching hospitals in Belgium and The Netherlands were treated for AEF by endovascular repair. Twelve (80%) were male. The mean age was 67 years. Thirteen (87%) had had previous aortic or iliac surgery, 1.7–307 months before. All patients showed clinical or biochemical signs of bleeding. Eight (53%) were in shock, five (33%) had systemic signs of infection.*
Eight (53%) patients were treated in an emergency setting. Ten (67%) were treated with an aortouniiliac device, three (20%) with an aortobiiliac device, one with a tube graft and one with occluders only. All patients received antibiotics postoperatively for a prolonged period of time.
Results. *All AEF were successfully sealed, the 30-days mortality was nil. Mean hospital stay was 20 (2–81) days. One patient died 2.7 months later of postoperative complications, one died of lung cancer. Until now, there are no signs of reinfection in four (27%) patients (mean follow-up 15.7 (1–44) months). However, reinfection or recurrent AEF occurred in nine (60%) patients after 9.5 (0.61–31) months. Seven patients were reoperated successfully, two patients died after reintervention.*
Conclusion. *Endovascular sealing of AEF is a promising technique, which provides time to treat shock, local and systemic infection, and co-morbidity. This creates a better situation to perform open repair in the future with possibly better outcome. Danger of reinfection remains high. Endovascular sealing of AEF should, therefore, be seen as a bridge to open surgery when possible.*

Keywords: Aorto-enteric fistula; Endovascular treatment; Endoprosthesis.

Introduction

Aorto-enteric fistula (AEF) is a severe complication after aortic surgery and currently appears in 0.4–4%[1,2] of cases after an average interval of approximately 6 years. Untreated, AEF is almost always fatal. The widely accepted treatment is open surgery with thorough debridement followed by either in situ replacement of a graft or extra-anatomical reconstruction. Even in contemporary series the mortality rate after open surgery still approximates 33%.[3] Because of the high morbidity and mortality rate of conventional surgical treatment, the use of an aortic endoprosthesis has been described with various outcomes.[4–11] Most reports in literature, however, are anecdotal. This multicentre study aimed to evaluate retrospectively the use of an aortic endoprosthesis in patients with AEF in Belgium and The Netherlands.

Patients and Methods

Between March 1999 and March 2005, 15 patients in five university and teaching hospitals were treated endovascularly for AEF. The data for this study were collected from patient files in the cooperating centres as listed in Addendum. A structured file was completed for each patient containing the main clinical, diagnostic and surgical parameters. The outcome in terms of morbidity, mortality, reinfection or recurrence of AEF was analysed. Data analysis was performed using GraphPad Prism version 3.00 for

*Corresponding author. Dr M. Danneels, MD, Department of Thoracic and Vascular Surgery, Heilig-Hartziekenhuis Roeselare-Menen, Wilgenstraat 2, 8800 Roeselare, Belgium.
E-mail address: mdanneels@hhr.be

1078–5884/000027 + 07 $35.00/0

Table 1. Cardiovascular risk factors

	Cardiovascular risk factors
Arterial hypertension	10 patients (67%)
History of smoking	10 patients (67%)
Coronary artery disease	6 patients (40%)
Hyperlipidaemia	5 patients (33%)
Diabetes mellitus	1 patient (7%)

Windows (GraphPad Software, San Diego, CA, USA). The male:female ratio was 12:3. The mean age at the moment of diagnosis was 67 (43–82) years. The cardiovascular risk factors are summarized in Table 1.

Thirteen patients (87%) developed a secondary AEF with a mean interval of 77 (1.7–307) months after aortic or iliac surgery. The secondary AEF developed after elective primary aortic surgery in eight (53%) patients with a mean interval of 110 (42–307) months and after emergency treatment for ruptured abdominal aortic aneurysm in one patient (interval 60 months). The AEF developed after previous surgery for infected aortic grafts in four (27%) patients with a mean interval of 11 (1.7–35) months. One primary AEF was probably caused by tuberculous aortitis, for the other primary AEF no cause could be determined. Twelve patients (80%) had previous abdominal surgery for non-vascular reasons. The relevant patient history is summarized in Table 2.

At presentation, all patients showed clinical or biochemical signs of bleeding. Eight patients (53%) presented with haematemesis, eight (53%) presented with melena and seven (47%) with anal blood loss. Five patients showed two of these signs, two patients showed haematemesis, melena and anal blood loss. Eight patients (53%) were in haemodynamic shock at presentation. Eleven (73%) patients complained of abdominal pain. Five patients (33%) had systemic signs of infection, of which four also had abdominal pain.

Eleven (73%) patients were anaemic at admission (haemoglobin $\leq$11.5 g/dL). The white cell count was elevated ($\geq 10^7$/L) in eleven (73%) patients. C-reactive protein level was elevated in eight out of eleven measurements (72%). Only one patient had both a normal white cell count and a normal C-reactive protein level.

To confirm the diagnosis CT-scan was performed in thirteen patients. All CT-scans performed were suspect for AEF: there were no false-negatives. Esophagogastroduodenoscopy (EGD) was performed in 10 patients. Seven (70%) EGD procedures were positive or suspect for AEF, three (30%) were negative. One rectoscopy was performed and showed a pulsating mass. One arteriogram was performed, which showed no bleeding sites. In our study no leukocyte- or PET-scans were performed to confirm diagnosis.

All eight patients presenting with shock were treated in an emergency setting (within 6 h after admission). Because of severe haemodynamic shock with systolic pressure of 40 mmHg in the intensive care unit, one patient was stabilized using an aortic occluding balloon at the presumed level of the AEF before transport to the operating theatre.

All procedures were performed under general anaesthesia, although in one patient, the groin incision and deployment of the endoprosthesis were performed under local anaesthesia and general anaesthesia was started afterwards for placement of the femorofemoral crossover graft. Access was through standard cut down of the groins in 13 patients. One patient had a retroperitoneal approach to the iliac artery, one patient had a temporary conduit on the iliac axis for access.

Nine patients (60%) were treated with an aortoniiliac device. Seven of these patients also had an adjunctive femorofemoral crossover graft in the same procedure. The two other patients already had a femorofemoral crossover graft placed before. One of these patients also had a distal thrombectomy. Four patients (27%) were treated with an aortobiiliac device. One patient was treated with a tube graft only. Another patient was treated with two occluders and gentamycin sponges at the level of the AEF and a right axillofemoral bypass graft with distal anastomosis on a pre-existing femorofemoral crossover graft.

Two (13%) patients were treated with a staged, hybrid approach. In one patient, haemodynamic stabilization was achieved by division of the AEF and direct suture of both aorta and duodenum. Four days later, an aortic tube device was placed because the surgeon felt the direct suture of the aorta was insufficient. Another patient was treated with an aortobiiliac device for haemodynamic stabilization. Three days later, a second procedure was performed with resection of the fistula, partial resection of the jejunum and omentoplasty. The endoprosthesis was not removed.

Ten patients (66.7%) were treated with a Talent device (Medtronic Inc., Minneapolis, MN, USA), four patients (27%) were treated with a Zenith Tri-Fab device (Cook Inc., Bloomington, IN, USA), one patient was treated with a Vanguard device (Boston Scientific Co., Natick, MA, USA)

In the two hybrid procedures it was possible to obtain local microbiology cultures that revealed *Citrobacter Freundii* in one patient and both *Enterobacter* sp. and *Bacteroides* sp. in the other patient.

Table 2. Patient history, treatment and postoperative follow-up in 17 patients treated with endoprosthesis for AEF

	History	Treatment	Follow-up
Patient A, M, 49 years	Multiple aneurysms, AIG for infrarenal AAA 5 years before, arterial homograft AIG for aorto-enteric erosion 3 years before, aneurx endoprosthesis for pseudo-aneurysm on the proximal anastomosis 6.1 months before, open cholecystectomy, protein S deficiency, lumbar sympathectomy	Aortomonoiliac device+femorofemoral cross-over graft, meropenem for 3 weeks; clindamycin life long	3.2 months postoperative: septic emboli due to recurrence of AEF, treatment: right axilloiliac and hepatorenal bypass in first stage; left aortorenal and aortomesenteric bypass+resection of endoprosthesis in second stage, complications: renal insufficiency, pneumonia, pulmonary haematoma, 7.2 months postoperative: ok
Patient B, M, 71 years	AFG for Leriche's syndrome 12 years before, irresectable lung carcinoma	Aortobiiliac device, gentamycin/metronidazol/penicillin for 2 weeks	Died of lung carcinoma
Patient C, M, 76 years	AFG for Leriche's syndrome 26 years before, 1975: open cholecystectomy, 1965: gastrectomy (benign ulcer), adhesiolysis	Aortomonoiliac device+femorofemoral cross-over graft, meropenem for 3 weeks; levofloxacin/metronidazole lifelong	6.1 months postoperative: back pain and infectious blood results due to recurrence AEF at duodenum, treatment: bilateral axillofemoral graft and resection of endoprosthesis, complications: myocardial infarction, pneumonia, 21 months postoperative: ok
Patient D, M, 59 years	Thrombolysis and stenting iliac axis for aortic thrombosis, miliary tuberculosis, billroth II gastrectomy, ostial left renal artery stenosis	Aortomonoiliac device+femorofemoral cross-over graft, teicoplanin/fluconazole for 41 days; meropenem/vancomycin for 7 days	Died 81 days postoperative (multiple organ failure)
Patient E, M, 72 years	Left below knee amputation for osteomyelitis, claudication right leg, AFG 4 years before, appendectomy	Aortobiiliac device, 2 days later wedge excision of jejunal fistula+omentoplasty, amoxicillin/clavulanate/fluconazole for 4 days; co-trimoxazole lifelong	7.5 months postoperative: ok
Patient F, M, 70 years	Thrombosis of popliteal aneurysm, cystectomy and bricker derivation, low grade infection groin, adhesiolysis, AFG for rupturing AAA 5 years before	Aortomonoiliac device+femorofemoral cross-over graft, amoxicillin/clavulanate for 19 days; doxycyclin lifelong	2.8 months postoperative: abscess right groin (*E. Coli* and *S. Viridans*), treatment: surgical drainage+antibiotics, 5 months postoperative: ok
Patient G, M, 73 years	Bilateral lumbar sympathectomy, AFG for Leriche's syndrome 16 years before, AEF treated with closure of fistula and omentoplasty 1.67 months before, open cholecystectomy, ischaemic colitis	Aortobiiliac device, piperacillin/tazobactam for 8 days; co-trimoxazole life long	31 months postoperative: recurrence of AEF between jejunum and right graft limb, treatment: suture of right graft limb, closure of jejunum, omentoplasty, 10 days later: new AEF between duodenum and proximal aorta, treatment: closure of duodenum, rectus abdominis muscle flap, 1 week later excision of prosthetic graft, AFG arterial homograft, bilateral aortorenal bypass, died of sepsis and multiple organ failure 33 months postoperative
Patient H, F, 77 years	Coronary artery bypass grafts 10 days before	Aortomonoiliac device+femorofemoral cross-over graft+distal thrombectomy, gentamycin for 10 days; amoxillin/clavulanate life long	9 months postoperative abscess in left psoas muscle and recurrence of AEF with infected endoprosthesis, treatment: excision of endoprosthesis and prosthetic graft, silver impregnated right aortoiliac graft, closure of jejunum, omentoplasty, 23 months postoperative: ok
Patient I M, 47 years	Left renal artery dilation, AFG for Leriche's syndrome 10 years before, femorofemoral crossover graft right to left, left iliofemoral graft, left supragenual femoropopliteal graft, excision infected crossover graft 7 years before, left aorto-popliteal graft 1 year before, hartmann procedure after intestinal perforation during aortopopliteal grafting, excision infected iliofemoral graft+closure enterocutaneous fistula 2.23 months before	Temporary sealing of fistula with aortic balloon, proximal and distal occluders with gentamycin sponge in between, right axillofemoral bypass, antibiotic treatment: not specified, life long	10.3 months postoperative: ok

(*continued on next page*)

Table 2 Continued

	History	Treatment	Follow-up
Patient J, M, 61 years	Tube interposition from celiac trunk to aortic bifurcation for type IV thoracoabdominal aneurysm 7 years before, osteosynthesis for discitis L3–L4	Aortobiiliac device, extraction of loose pedicle screw, ciprofloxacin life long	0.6 months postoperative: acute arterial blood loss in left groin, treatment: left aortomonoiliac endoprosthesis, femorofemoral silver impregnated crossover graft, excision of migrated osteosynthesis material between inferior caval vein and prosthesis, 1.4 months postoperative: ok
Patient K, M, 78 years	AIG for AAA 4 years before	Open division of aortoenteric fistula, 4 days later sealing with endovascular tube graft device, gentamycin/cefuroxim/metronidazole for 4 weeks; amoxicillin/clavulanate for 2 weeks; co-trimoxazole for 4 months	44 months postoperative: ok
Patient L, M, 75 years	AIG for AAA 11 years before	Aortomonoiliac device+femorofemoral cross-over graft, gentamycin for 7 days; amoxicillin/clavulanate life long	12 months postoperative: recurrence of AEF (actinomyces+bacteroides), treatment: resection of all infected prosthetic grafts, left aortoiliac prosthetic graft (rifamicyn soaked), closure of two duodenal perforations, omentoplasty, 20 months postoperative: ok
Patient M, M, 81 years	Tube interposition for AAA 8 years before, barrett oesophagitis and duodenitis, Transvesical prostatectomy, diverticulosis, polycystic kidney disease, chronic obstructive lung disease, atrial fibrillation	Aortomonoiliac device+femorofemoral cross-over graft, piperacillin/tazobactam for 7 days; amoxicillin/clavulanate life long	1 month postoperative: ok
Patient N, F, 73 years	Stenting left renal artery, AFG for Leriche's syndrome 5 years before, axillobifemoral graft for occluded AFG 4 years before, appendectomy and drainage of psoas abscess	Aortomonoiliac device, amoxicillin/clavulanate life long	12 months postoperative: recurrence of AEF, treatment: excision of endoprosthesis, prosthetic patch on aorta, closure of duodenal lesion, 2 days later: haemodynamic shock, new bleeding, further treatment refused by patient, patient died 12.03 months postoperative
Patient O, F, 43 years	Extraperitoneal aortoiliac disobliteration according to LeVeen,[16] endarterectomy and patch of the infrarenal aorta, AIG for occlusion after endarterectomy, suture and femorofemoral cross-over graft for ruptured distal false aneurysm caused by appendicitis 3 years before, draining of abscesses in right groin, retroperitoneal, etc.	Aortomonoiliac device, amoxicillin/clavulanate life long	8.7 months postoperative: abscess in rectovesical excavation (Douglas' pouch), treatment: CT-guided puncture, 9.5 months postoperative: ok

AAA, abdominal aorta aneurysm; AFG, aortobifemoral bypass graft; AIG, aortobiiliac bypass graft; F, female; M, male; where time interval is mentioned, always between event and endovascular treatment of AEF.

All patients received antibiotics postoperatively for at least 14 days according to the empirical guidelines from the departments of microbiology of the various co-operating hospitals. Four patients were treated with antibiotics for a period between 6 weeks and 9 months. At discharge from the hospital, eight patients were prescribed life long antibiotic treatment.

Results

All AEF were successfully sealed. The 30-days mortality was nil. Mean intensive care stay was 6.7 (0–61) days. Mean hospital stay was 20 (2–81) days. Six patients (40%) had no postoperative complications. All postoperative complications and reinterventions in nine patients (60%) are summarized in Table 3. The in-hospital mortality was 7%: one patient with infectious, vascular, and cardiac complications died on the 81st postoperative day.

Another patient died of lung cancer within the first postoperative year. Four (50%) out of eight patients with life long antibiotics stopped the treatment: three because of serious antibiotic related gastrointestinal complaints, one patient stopped without apparent reason.

Until now, there are no signs of recurrent infection or AEF in four out of 13 (31%) patients, including the two patients who had a hybrid procedure. The mean follow-up in these four patients is 16 (1–44) months. Reinfection occurred in nine (69%) patients after a mean interval of 9.5 (0.6–31) months. Two thirds of these nine patients had a new AEF. The symptoms, treatment and outcome of these patients are summarized in Table 2.

All patients were reoperated on successfully. One patient had recurrent bleeding some days after reintervention. She refused all surgical treatment and died 2 days after diagnosis of the recurrent bleeding. One patient developed multiple organ failure and died 2 months after reoperation. Until now, the other patients have an uneventful course after reoperation with a mean follow-up of 16 (1–44) months.

During the follow-up period no dislocation or endoleak of the grafts have been observed.

Kaplan–Meier analysis showed an overall survival of 92% at 6 months, the 95% confidence interval (CI) is 78–100%. At 1 year the survival is 79% (CI 52–100%), at 2 years the survival is 66% (CI 33–98%) as shown in Fig. 1. The freedom of recurrence of AEF is 65% (CI 40–90%) at 6 months. At 1 and 2 years the freedom of recurrence is 29% (CI 3–55%) as shown in Fig. 2.

Discussion

AEF is the most serious late complication of aortic graft placement and occurs in 0.4–4%.[1,2] According to Busutill *et al*.[3] the mean interval between initial surgery and diagnosis of AEF is approximately 6 years, although it has been described as early as 2 weeks after aortic surgery. It is caused by erosion of the gastro-intestinal tract by the prosthetic graft, with or without formation of a false aneurysm. Menawat *et al*.[12] found that AEF seems more frequent after surgery for aorto-iliac occlusive disease than after aneurysmal disease. In this retrospective study, we were not able to confirm these findings, due to the small number of patients. Most patients had aortic surgery in their medical history. This is consistent with literature findings.[13] Four patients (27%) already had aortic reinterventions because of a previous AEF or infected aortic graft. One of these patients already had an endoprosthesis for a false aneurysm on an arterial homograft. The interval between previous aortic surgery and the clinical presentation of an AEF was

Table 3. Postoperative complications after endovascular treatment for AEF

	Postoperative complications
Renal (four patients)	Chronic renal insufficiency: three patients, of which one patient started haemodialysis 3 years later
	Acute renal insufficiency
Gastro-intestinal (three patients)	Duodenal necrosis and perforation, treated by surgical drainage on postoperative day 51
	Subobstruction treated conservatively
	Choledocholithiasis treated conservatively
Infectious (three patients)	Catheter sepsis with MRSE
	Postoperative bacteraemia
	Groin abscess, treated by surgical drainage on postoperative day 13
Pulmonary (two patients)	Exacerbation of chronic obstructive lung disease necessitating reintubation
	Tracheotomy for difficult postoperative weaning
Cardiac (two patients)	Pulmonary oedema
	Myocardial infarction on postoperative day 7, followed by pulmonary oedema
Vascular (one patient)	Hepatorenal shunt 26 days postoperative for right renal artery stenosis
	Puncture through femorofemoral cross over graft during drainage of an abdominal mass (same patient)

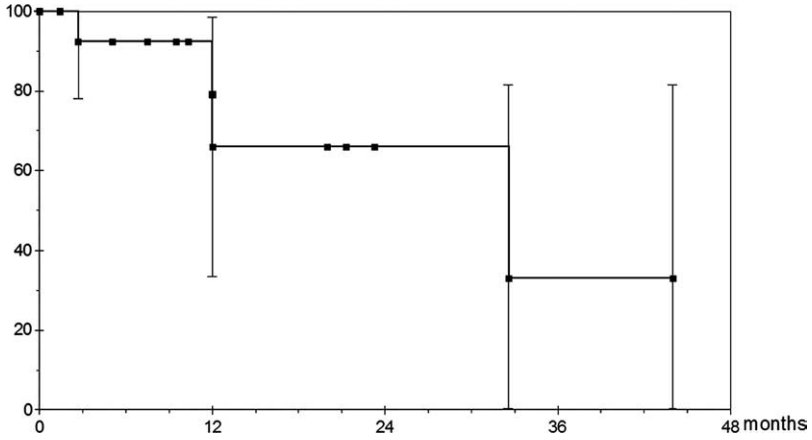

Fig. 1. Kaplan–Meier analysis including confidence interval: overall survival.

significantly shorter in this subgroup compared to patients without reinterventions on the aorta ($p=0.01$).

In every patient with clinical evidence of infection or bleeding of the gastrointestinal tract after aortic surgery, AEF should always be suspected. According to the classic triad of symptoms in AEF, all our patients had one or more signs of gastrointestinal bleeding (haematemesis, melena, haematochezia, anaemia). One in three had clinical symptoms of infection. All but one patient had biochemical signs of infection and all had various abdominal complaints. One third of the patients were in shock at presentation at the emergency ward or at transfer from another hospital.

In case of severe haemodynamic shock, prompt treatment should be undertaken. In less urgent situations, a CT-scan followed by EGD can be performed to rule out other causes of disease. However, a negative result does not exclude AEF. In our series every abdominal CT-scan performed was positive or suspect for AEF. EGD was positive or suspect in 70%. One preoperative angiography was performed and was negative.

Taking in account the high co-morbidity, previous laparotomies and/or shock at presentation, the risk of conventional repair was considered too high in this patient group. Although various mortality rates can be found in literature, mortality after conventional repair for AEF is now considered to be approximately 33% with a high co-morbidity.[3,14] In our series the total AEF-related mortality is 20%, of which two thirds occurred following reintervention at the moment of recurrent infection or new AEF.

In the postoperative care, antibiotic treatment is of the uttermost importance. In contrast to conventional repair, it is not always possible to obtain a good sample of the infectious agent. Consequently, antibiotic and/or antifungal treatment remains empirical. On the other hand, infected prosthetic material is not resected. This probably maintains a subclinical infectious process. One can expect a high rate of recurrent infection when the antibiotic spectrum is not

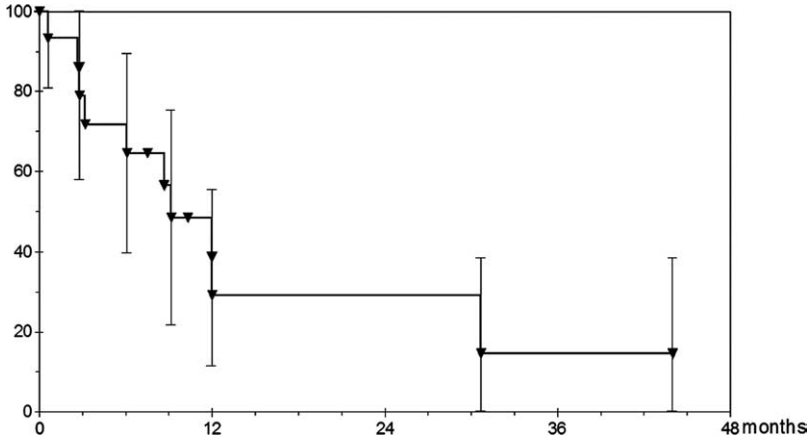

Fig. 2. Kaplan–Meier analysis including confidence interval: freedom of recurrent infection or new AEF.

adequately chosen or when the treatment is stopped early. This emphasizes the need for prolonged antibiotic treatment, preferably lifelong. Our study revealed, however, that half of the patients stopped their 'lifelong' treatment after a while, mostly because of a (presumed) gastrointestinal intolerance.

Several case reports with good long-term outcome can be found in the literature.[7,8,10] Burks *et al*.[15] reported three patients with persistent postoperative sepsis after EVAR, but no recurrence of AEF in a group of seven patients (follow-up 11–67 months). However, in our series seventy percent of all patients had a recurrent infection or new AEF within 1 year, even with adequate antibiotic treatment. Due to the high recurrence rate in our series, we feel that resection of the infected prosthesis, debridement and extra-anatomical or *in situ* revascularisation remains the treatment of choice for patients without shock and in fair general condition at the moment of presentation.

Every patient with an AEF with a high operative risk for open surgery should be considered for endovascular treatment. We think the high reinfection rate justifies open repair as soon as the patient's risk factors are reduced to a minimum. We now believe surgery should be performed before recurrent infection or new AEF has become apparent. This avoids the extra risk of an urgent or semi-urgent open procedure in an infectious and/or haemodynamically unstable patient.

Endovascular treatment of AEF should, therefore, be seen as a short bridge to surgery, except for patients remaining unfit for open surgery even after maximal supportive therapy. In those patients, long-term antibiotic treatment and lifelong surveillance are mandatory.

5. Addendum

The participating centres were:

Ghent University Hospital (four patients)
University Medical Center Utrecht (four patients)
Atrium Medical Center Heerlen (three patients)
Leuven University Hospitals (three patients)
Catharina Hospital Eindhoven (one patient).

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