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Management of mycotic aorto-iliac aneurysms: a 30-year monocentric experience

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Abstract. – OBJECTIVE: This study aims to analyze the early and late outcomes of our 30-year experience with mycotic aneurysms of the abdominal aorta and iliac arteries.

PATIENTS AND METHODS: This retrospective cohort study compared the outcomes of all the patients with mycotic aneurysm, by analyzing prospectively collected data between September 1989 and October 2019 from the Unit of Vascular Surgery of Fondazione Policlinico Universitario Gemelli – IRCCS in Rome, Italy.

RESULTS: Twenty-three patients with mycotic aneurysm were included. Twenty-two patients underwent surgery; one patient arrived at the emergency room with unstable clinical conditions and died before being treated. Fourteen cases (60.9%) were located at the infrarenal aorta, while three cases (13.0%) were pararenal aortic aneurysms. Six cases (26.1%) had an iliac arteries localization. Seventeen patients (77.3%) underwent open surgical repair aneurysmectomy with *in situ* reconstruction, while three cases (13.6%) underwent extra-anatomic revascularization. Three patients (13.6%) underwent the placement of an endoprosthesis, of whom two underwent hybrid procedures, and one EVAR. The latter underwent an early conversion to open repair due to a type I endoleak. The mean length of hospital stay was 35 ± 18.7 days. Five patients (22.7%) died in the immediate postoperative period. In the follow-up of 45.5 ± 41.3 months (range 2-156), we documented six deaths (35.3%), of whom two (11.8%) were aortic-related for a 34.8% overall aortic-related mortality. Eleven patients were alive, with an overall survival of 47.8%.

CONCLUSIONS: Mycotic aneurysm is an extremely rare and varied pathology. Open surgical repair showed to be a safe approach because of a complete and aggressive debridement of local infected tissues, with an acceptable long-term mortality rate.

Key Words:
Mycotic aortic aneurysm, Infected aneurysm, Open surgical repair, Endovascular repair, Personalized medicine.

Introduction

The term mycotic aneurysm (MA) is commonly used to describe all infected aneurysms. Although MAs are believed to occur uncommonly, the true incidence is difficult to determine and is probably underestimated since MAs can be asymptomatic and are diagnosed only at autopsy[1]. In an autoptic study, mycotic aortic aneurysms (MAAs) were reported in 3.3% of all detected aneurysms[2]. The incidence of infected aneurysms of the aorta and iliac arteries ranges from 0.6% to 1.3%[3,4].

A recent literature review of the management of MAAs showed that therapeutic strategies are multiple, including open surgical repair (OSR) in the majority of cases, endovascular aortic repair (EVAR), which increased over the last decade, and medical treatment alone for patients unfit for any aortic repair in a very limited part[5].

We analyzed the early and late outcomes of our a single centre 30-year experience with mycotic aneurysms of the abdominal aorta and iliac arteries (MAAIA).

Patients and Methods

Study Population

This retrospective cohort study compared the outcomes of all the patients with mycotic aneurysm by analyzing prospectively collected data between September 1989 and October 2019 from the Unit of Vascular Surgery of Fondazione Policlinico Universitario A. Gemelli–IRCCS (FPUAG; Rome, Italy).

The retrospective study was performed in accordance with the Institutional Ethics Committee rules, and individual consent for this retrospective analysis was waived. All patients provided consent for intervention.

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Diagnosis of mycotic aneurysm was based on clinical presentation (pain, fever, concomitant infection, elderly patient with cardiovascular disease, and/or immunosuppressive state); laboratory findings (elevated inflammatory parameters including C-reactive protein, procalcitonin, sedimentation rate, leukocytosis, and positive blood culture); radiological findings on computed tomography angiography (CTA) or magnetic resonance imaging (saccular, eccentric, or multilobular aneurysm, periaortic mass, periaortic gas, and rapid aortic expansion) (Figure 1); and intraoperative findings[6,7]. In the case of patients without clear infectious signs and uncertain diagnosis, Indium 111 (^{111}In)-labeled white blood cell (WBC) scintigraphy or fluorine-18-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG-PET/CT) examination were used. These characteristics may not all be present in the same patient. Patients were observed with regular postoperative follow-up.

Endpoints

Primary endpoints of this study were 30-day outcomes, including early reintervention and in-hospital mortality, mean length of stay and incidence of complications, including aortic stump blow, graft occlusion, and anastomotic dehiscence and bleeding.

Secondary endpoints were late outcomes, including late reintervention, graft occlusion, graft infection, and aortic related death.

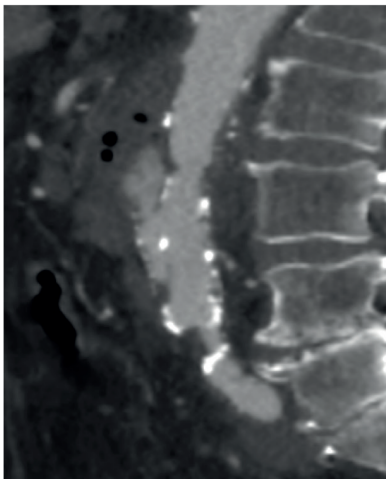

Figure 1. Computed tomography (CT) of a contained ruptured mycotic aneurysm with a polilobulated morphology and periaortic gas.

Medical Treatment

If the hemodynamic conditions allowed it, either intravenous (IV) pathogen directed antibiotic treatment after positive blood culture results or empirical broad-spectrum antibiotic treatment, for at least 3 weeks before surgery, was carried out.

Initial empirical antibiotic therapy of suspected mycotic aneurysms in people with negative blood should include an anti-Gram-negative agent (ceftriaxone, fluoroquinolones or beta-lactams) and an anti-Staphylococcus agent such as vancomycin.

After surgery, the IV therapy was confirmed or modified according to the isolated microorganism of intraoperative wall samples and the sensitivity tests, if present. The post-operative IV antibiotic therapy was continued for at least 3 more weeks after the disappearance of septic symptoms and the normalization of laboratory tests. The patient was discharged with oral antibiotic therapy for at least 6 weeks.

Operative Techniques

Open surgical repair (OSR)

The mycotic aneurysm open surgical repair consisted of two different strategies: aneurysmectomy with *in situ* reconstruction or extra-anatomic revascularization.

In the first case, the aortic access was performed through a midline transperitoneal approach. The parietal peritoneum was divided up to the ligament of Treitz and the duodenum mobilized and retracted laterally. In the case of a pararenal lesion with supravisceral aortic clamping, the proximal aorta exposure was assured through a retroperitoneal approach. After aortic neck and iliac arteries clamping, the mycotic aneurysm resection was performed with a complete and aggressive debridement of local infected tissues and lymph nodes. Abundant washes with the physiological solution were carried out.

The *in situ* aortic reconstruction was carried out with gelatin-sealed Dacron graft (Gelsoft Plus; Vascutek Terumo, Renfrewshire, Scotland, UK) with rifampin soaking, Silver impregnated polyester graft (Silver Graft; B. Braun Melsungen AG, Melsungen, Hessen, Germany), or homograft aortic tissue (Figure 2). The proximal and distal anastomoses were conducted with standard aortic anastomoses. The general rule was to fashion the anastomosis at a non-infected segment of the aortic wall, with Teflon felt reinforcement. In all the cases, the prosthesis was covered with the greater omentum.

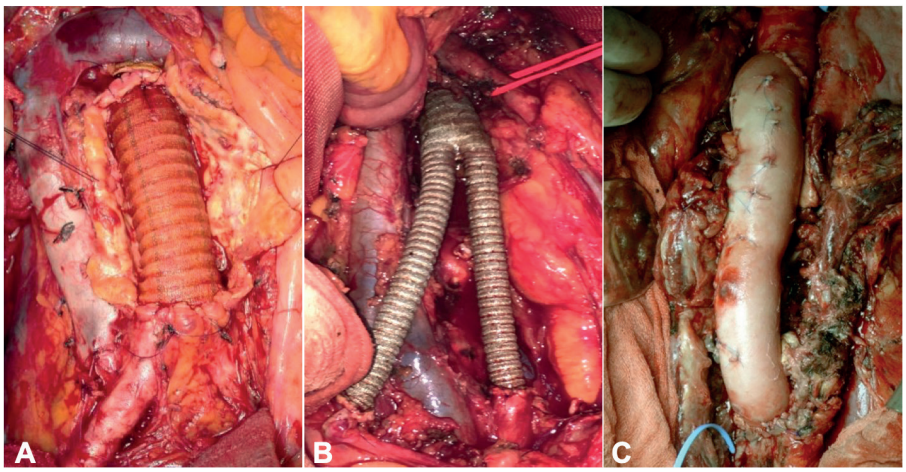

Figure 2. Intraoperative in situ final reconstruction with a gelatin-sealed Dacron graft (**A**), bifurcated Silver graft (**B**) and homograft aortic tissue (**C**).

The extra-anatomic reconstruction (EAR) was done through an axillo-bifemoral bypass or femoral-femoral bypass, in case of abdominal aorta or iliac artery localization, respectively. The indication for EAR was an important presence of contaminated regions, with pus or infected tissue.

Endovascular repair (EVAR)

In the case of patients in shock or unfit for surgery, endovascular treatment was used. General anesthesia was used in all patients with an open arterial exposure or a percutaneous approach when feasible.

Statistical Analysis

Continuous data were reported as the mean ± standard deviation or, in the case of Gaussian distribution, as the median (range). Categorical data were reported as the number and its accompanying percentage of the whole. Data analysis was performed using STATA, version 15.1 (StataCorp, College Station, TX, USA).

Results

Between September 1989 and October 2019, we treated a total of 1951 patients with abdominal aorto-iliac aneurysm at our institution. This 30-year retrospective study identified 23 patients with infected aneurysms of the aorta and/or iliac arteries, for an overall incidence of 1.17%. All the demographics, comorbidities, and anatomical features of the study population are summarized in Table I. The average age of the patients was 69 years (standard deviation, ± 12.3 years), and 20 patients (86.9%) were male. These are the comorbidities: eight patients (34.8%) had type II diabetes mellitus, six patients (26.1%) had chronic kidney disease (CKD), of whom two were undergoing hemodialysis. One patient (4.3%) had received oral corticosteroid therapy, while one patient (4.3%) had a primary immunodeficiency syndrome. Most patients presented with fever, abdominal and back pain; only five patients (21.7%) had gastrointestinal symptoms, including include vomiting, diarrhea, hematemesis, melaena, and weight loss. Fourteen patients (60.9%) presented with a systemic inflammatory response syndrome (SIRS), manifested by two or more of the following: temperature >38°C or <36°C, heart rate (HR) >90 bpm, respiratory rate (RR) >20 bpm or $PaCO_2$ <32 mmHg, white blood cells (WBC) count >12.0×10^9/L or <4.0×10^9/L[8].

Before the treatment, all the patients underwent a CTA scan; in seven patients the uncertain diagnosis was confirmed by ^{111}In-WBC scintigraphy or 18F-FDG-PET/CT examination. All aneurysm characteristics are listed in Table II. The majority of cases, fourteen (60.9%), were located at the infrarenal aorta, while three cases (13.0%) were pararenal aortic aneurysm. The median diameter of the aneurysm was 54 mm (standard deviation, ± 22.5 mm; range 24-100). Eighteen patients (78.3%) showed contained rupture of the aneurysm at the CTA with stable hemodynamic conditions, while one patient (4.3%) was free-ruptured in hemodynamic shock. Procedural details are reported in Table III. In our series, twenty-two patients out of twenty-three underwent surgery; one patient pre-

Table I. Baseline characteristics of 23 patients with mycotic aneurysm treated at Fondazione Policlinico Universitario A. Gemelli–IRCCS during a 30-year period.

Baseline characteristics	No.=23	%
Male gender	20	86.9
Mean age ± SD	69 ± 12.3	range 45-86
Smoking	9	39.1
Hypertension	13	56.5
Dyslipidemia	10	43.5
Diabetes mellitus	8	34.8
History of cardiovascular disease	7	30.4
Chronic kidney disease	6	26.1
Corticosteroid therapy	4	17.4
Primary immunodeficiency syndrome	1	4.3
Symptoms		
Fever	12	52.2
Abdominal pain	12	52.2
Back pain	10	43.5
Chest pain	2	8.7
Gastro-intestinal symptoms	5	21.7

SD, standard deviation; Gastro-intestinal symptoms, include vomiting, diarrhea, hematemesis, melena and weight loss.

sented at the emergency room in hemodynamic shock died before the treatment. Seventeen patients (77.3%) underwent open surgical repair aneurysmectomy with *in situ* reconstruction, while three cases (13.6%) underwent extra-anatomic revascularization. For the *in situ* reconstruction, we used a Dacron graft soaked in Rifampin in eleven cases (50%) and a silver impregnated polyester graft in five patients (22.7%). A cryopreserve homograft was used only in one case (4.5%) for a pararenal mycotic lesion. Three patients (13.6%) underwent an extra-anatomic reconstruction: femoral-femoral crossover and axillo-bifemoral bypass in two (9.1%) and one patient (4.5%), respectively. Three (13.6%) endovascular procedures were performed: one EVAR for a patient in hemodynamic shock and two hybrid procedures, with visceral debranching and endovascular exclusion of a pararenal aortic lesion for patients unfit for surgery. The EVAR procedure (Endurant II Stent Graft; Medtronic Inc, Santa Rosa, CA, USA) was a life-saving bridge treatment for a definitive OSR conversion, due to the presence of a type I endoleak. The two hybrid procedures consisted in: one patient who underwent debranching of the visceral vessels (right iliac-renal bypass and left iliac-mesenteric-renal bypass), coil embolization of the celiac trunk and positioning of the endograft Conformable GORE TAG (CTAG; W.L. Gore & Associates, Flagstaff, AR, USA); one patient undergoing bilateral iliac-renal bypass with a 14x7-mm grafts (Gelsoft Plus; Vascutek Terumo, Renfrewshire, Scotland, UK) and positioning of a bifurcated endograft (Endurant II Stent Graft; Medtronic Inc., Santa Rosa, CA, USA). Blood cultures and micro-organisms

Table II. Aneurysm characteristics.

Aneurysm characteristics	No.=23	%
Status of rupture		
Contained rupture	18	78.3
Free rupture	1	4.3
Intact	4	17.4
Anatomic location		
Pararenal aorta	3	13.0
Infrarenal aorta	14	60.9
Iliac arteries	3	13.0
Infrarenal aorta + iliac artery	3	13.0

Table III. Procedural details.

Procedural details	No.=22	%
In situ reconstruction	17	77.3
Dacron + Rifampicin	11	50
Silver graft	5	22.7
Homograft	1	4.5
Extra-anatomic reconstruction	3	13.6
Femoral-femoral	2	9.1
Axillo-bifemoral	1	4.5
Hybrid repair	2	9.1

Table IV. Micro-organisms cultured from specimens of the aneurysmal content and arterial wall of the mycotic aortic aneurysm and blood cultures.

Micro-organism	Gram stain	Wall cultures (no.=10)	Blood cultures (no.=10)
Staphylococcus aureus	+	4	5
Clostridium septicum	+	2	1
Escherichia coli	-	2	1
Salmonella species	-	2	2
Campylobacter fetus	-	1	0
Enterococcus faecalis	+	1	0
Enterobacter species	-	1	0
Proteus mirabilis	-	1	0
Pseudomonas aeruginosa	-	1	0
Coxiella burnetii	-	0	1

cultured from specimens of the aneurysmal content and arterial wall of the MAAIAs are listed in Table IV. Cultures from the aneurysmal content and the arterial wall were not obtained in two of the twenty-two operated patients. Fifteen patients (68.2%) had a blood and/or wall cultures positive. Gram-negative organisms predominated, even if *Staphylococcus aureus*, which is a Gram-positive, was the most common (40%). The mean length of hospital stay was 35 ± 18.7 days. Five patients (22.7%) died in the immediate postoperative period, of whom three had a contained ruptured aneurysm and two with intact one. Causes of death include cardiac arrest in two patients, gastric ischemia in one patient, internal iliac artery rupture in one case and septic shock in another one. In ten patients (45.4%) the postoperative course was complicated by fever (13.6%), hemorrhage (9.1%), abdominal lymphorrhea (9.1%), transient ischemic attack (4.5%), hepatic failure (4.5%) and acute renal failure (4.5%). In the follow-up of 45.5 ± 41.3 months (range 2-156), we documented six deaths (35.3%), of whom four were due to medical problems not related to the surgical intervention. We reported two (11.8%) aortic-related deaths for an overall aortic related mortality of 34.8%. One patient, following graft infection for *Enterobacter cloacae* and *Candida albicans*, was readmitted to the hospital for acute limb ischemia after three months from the femoral-femoral reconstruction. The patient underwent leg amputation and died due to respiratory complications. One patient died eighteen months from the OSR, due to the homograft rupture. In the follow-up we documented only one (5.9%) aortic-related complication: one patient, due to a left branch occlusion after seven years from *in situ* reconstruction, underwent percutaneous transluminal angioplasty (PTA) and stent placement.

Discussion

There are several theories to describe the pathogenesis of infected aneurysms. In the majority of the cases, the cause is attributable to septic emboli in patients with endocarditis; this group has been termed *secondary* or *embolomycotic* aneurysm[9]. The remaining parts are defined *primary* when derived from a localized periarterial suppurative process, and *cryptogenic* when the source is not proven[10].

Other etiologic factors of historical and clinical importance are syphilis, congenital defects of vessels, trauma, vascular tumors, chemical erosion, and arteriosclerosis[11]. The MAA is a rare and life-threatening disease. Infected aneurysms tend to present in immunocompromised patients, which may in part explain the increased perioperative morbidity and mortality[12]. The classic presentation is with painful, pulsatile mass with systemic features of infection, such as fever and malaise, and characteristic imaging. In the case of suspected MA, 18F-FDG-PET/CT examination is useful in diagnosis[13]. In this case series, the latter led to a final diagnosis in about one-third of patients with dubious diagnosis, in which blood and/or wall cultures were negative.

However, the real challenge is the correct management of the patient with a mycotic aneurysm. Certainly, solely medical therapy has to be excluded, as associated with an in-hospital mortality rate of 75-100% due to aneurysm rupture[14,15]. The management of this complex pathology requires a multidisciplinary team approach. A fundamental role is played by the infectiologist and both pre- and post-operative antibiotic therapy, in order to initially reclaim the infected site and to contain the bacteremia when present. The optimal

duration of antibiotic therapy is still controversial, with various recommendations ranging from 6 weeks to lifelong use. Anyway, antibiotic therapy should at least last until there is no clinical and hematological evidence of infection[4,16].

Various surgical techniques have been described for MAAIA repair. In the last decade, EVAR has been widely accepted as a valid treatment option for abdominal aorto-iliac aneurysms, with similar outcomes to OSR also in complex cases, as pararenal abdominal aortic aneurysms[17,18]. EVAR has been advocated as a less invasive technique than OSR. Semba et al[19] were the first to report the use of endovascular stent-grafts in three patients with mycotic thoracic aneurysms. Kan et al[20] suggest considering EVAR as a temporary measure to achieve hemodynamic stability in patients with aneurysm rupture or fever. In these patients, EVAR was mainly a life-saving bridge treatment. Its use occurred in a subgroup of patients who were identified based on comorbidities, anatomical features and, most of all, clinical presentations. We performed EVAR in three patients who presented in severe clinical conditions and were unfit for surgery. However, two of the three died in the immediate postoperative period. A nationwide Swedish study of 132 patients with MAA, demonstrated that EVAR was associated with improved short-term survival in comparison with OSR, without higher associated incidence of serious infection-related complications or reoperations[21]. However, despite the promising results of the latter described technique, the recently published European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms defined the open surgical repair as the gold standard for definitive treatment of MAAIA, with EVAR being an acceptable alternative to OSR (Class IIa, Level of Evidence C)[22].

Various open surgical techniques have been described for MAA repair, including *in situ* and extra-anatomic bypass prosthetic graft revascularization. Although providing similar long-term survival, Lee et al[23] described a higher complication rate for extra-anatomic bypass and suggested to consider it for patients who are unsuitable for *in situ* revascularization. In our series, the majority of the patients (77.3%) underwent open surgical repair aneurysmectomy with *in situ* reconstruction. Extra-anatomic reconstruction was performed only in three patients with an important purulent collection.

In situ reconstruction consisted mostly of synthetic conduits. Corvera et al[7] described the use of cryopreserved allograft (CPA) as a reasonable option in the setting of MAAs or infection of a prosthetic aortic graft with 64% 5-year survival. In our series, only one patient, with *Clostridium septicum bacteremia*, was treated with a cryopreserved homograft with reimplantation of the celiac trunk, superior mesenteric artery, and right renal artery. Afterward, the homograft showed an ectasia at the site of reimplantation of the right renal artery with mural thrombosis associated with incomplete infarction of the right kidney, complicated by the need for hemodialysis. Eighteen months later, the homograft rupture caused the patient's death. However, the choice of the theoretically ideal prosthesis is controversial. The majority of the prostheses that we used were rifampin-soaked, due to the risk reduction of prosthetic graft infections[24]. In 2019, Hennessey et al[25] proposed a standardized rapid real-time perioperative protocol for endovascular stent grafts. However, there are no studies that demonstrate the superiority of one material over another.

The applied surgical technique varied according to the anatomic location of MA and the severity of the infection. The extra-anatomical approach was preferred in the case of a severe purulent collection of the vessels, thus reducing the risk of graft infection, and where *in situ* replacement was not suitable. The risks of EAR include aortic stump rupture and lower rates of patency due to graft thrombosis[4,26]. One of our three EARs was complicated by a late graft infection.

Concerning this case load, preoperative antibiotic therapy, eradication of the infection, surgical aggressive debridement of local infected tissues and lymph nodes, artery reconstruction, omental coverage, and postoperative antibiotic therapy showed to be a safe MAAIAs approach (Figure 3). Indeed, the patient's condition and immunological status, as well as cardiovascular conditions, will all influence the results of any treatment. Moreover, germ types are often manifold, determining MA by either hematogenous embolism or contiguity; thus, it is necessary to understand how the infection of the aorta occurred.

The limitations of this study include retrospective data collection and a limited number of patients. Further multi-institutional and registry data are required to clarify the long-term outcomes in mycotic aneurysms surgery according to the different operative approaches and to determine whether EVAR is effective as or better than standard surgical care.

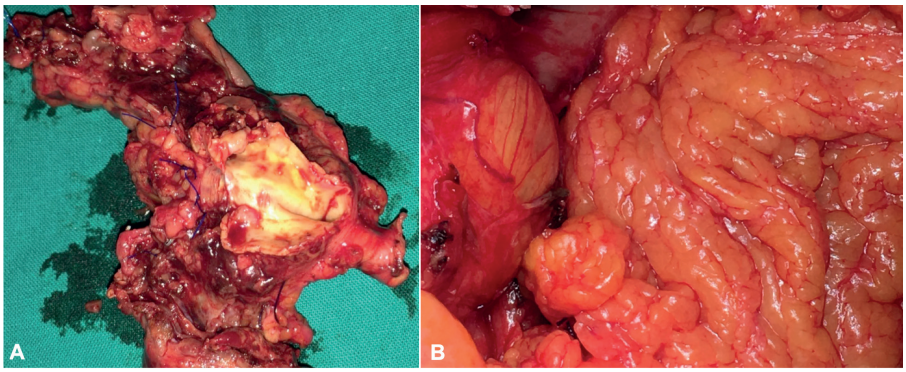

Figure 3. Intraoperative images showing the aggressive debridement of infected tissues (**A**) and final omental coverage of the artery reconstruction (**B**).

Conclusions

MAAIA is an extremely rare and varied pathology, containing so many subgroups that it is difficult to find standardized management and unique conclusions for everyone.

The management of this complex pathology requires a multidisciplinary team approach with a fundamental role of antibiotic therapy and treatment choice. Open surgical repair, associated with prolonged antibiotic therapy, proved to be a safe approach, assuring the revascularization with a complete debridement of the infected field. Nonetheless, there are still many unresolved issues precluding us from reaching a final standardized conclusion on the best management approach to MA.

Conflict of Interests

The authors declare that they have no conflict of interests.

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