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ARTERIOVENOUS GRAFT INFECTION IN HAEMODIALYSIS PATIENTS: A CLINICAL AND MICROBIOLOGICAL ANALYSIS

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Keywords:

Graft infection, Staph.aureus infection, dialysis access outcome.

Abstract

Aim: The aim of this study was to analyse the clinical outcomes and describe the microbiological profiles of arteriovenous graft infections in Jordanian Royal medical services.

Methods: We performed a retrospective study of arteriovenous graft (AVG) procedures that were performed at our institution between January 2015 and December 2018. Data on the patient's demography, site of graft insertion, and date of graft-related infection were collected from our registry. Cultures and sensitivity to antibiotics were determined for all bacterial strains using VITEK2. The treatment and outcome for patients with a graft infection were analysed**.**

Result: Of the 520 AVGs inserted during the four-year study period, 86 (16.5%) AVG infections were identified in 72 patients. The mean age of the patients was 42 years (range 18-82 years) and 56 (65%) of the patients were male. An infected AVG was identified by clinical, ultrasound, and microbiological findings. Strains of Staphylococcus spp., especially S. aureus, were the most frequent cause of infected AVG, which accounted for 52 (60.5%) of the infected grafts . The second most frequent infectious species was S. epidermidis, which was detected in 15 (17.5%) cultures. The rate of AVG infection was statistically significant for patients with diabetes mellitus p=0.003), thigh grafts (p=0.04), anaemia (p=0.01), and high White blood cells on admission (p=0.01) in infected grafts group compared with patients without grafts infection as a control group. The overall patient mortality was 19 (22%) patients; the cause of death was graft-related in 4 (4.7%) patients in this series.

Conclusion

Strains of Staphylococcus, especially S. aureus, were the most frequent cause of infected AVGs. management of patients with graft infection could be individualized by total graftectomy or partial graftectomy according to patient's condition. Because haemodialysis patients are a high-risk group precaution measures should be taken to decrease the risk of infection.

Introduction

The treatment of patients with chronic renal failure (CRF) require vascular access, which is achieved by central venous cannulation or the creation of an autologous arteriovenous fistula (AVF) or fistula with an arteriovenous vascular graft (AVG). Infection is the second leading cause of access loss, after thrombosis. Infectious complications of all types are the second leading cause of death in dialysis patients, accounting for 15% to 36%.(1,2). Impaired humoral and cellular immunity, nutritional deficiencies, and type of vascular access are among the major determinants. (3)

The breakdown of the protective anatomical barriers owing to repeated intravascular intervention required for haemodialysis is the main reason for the high prevalence of graft infection in those patients (4). The average life span of a prosthetic Arteriovenous (A-V) access is 2 years, with 20% loss as a result of infection (5). Prospective

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studies have shown that the probability of an autogenous A-V access infection is 4.5% in 1 year versus 19.7% for a prosthetic A-V access (2,6). Infected vascular access for haemodialysis is usually caused by gram-positive bacteria, in particular, strains of Staphylococcus aureus, which have been documented in as many as 68% of infections [6,7,8]. Gram-negative bacteria are not a common cause of infection, with a prevalence below 28% [7,9,10].

The primary endpoint of this study was to determine the incidence of AVG infection, to show the clinical outcome, and to perform microbiological analysis. The secondary outcome was to find the risk factors of graft infections.

Patients and Methods

The medical records of 520 patients that underwent arteriovenous graft (AVG) creation/salvage procedures in our vascular centre at Jordanian Royal Medical Services, over a four-year period from January 2015 to December 2018 were retrospectively reviewed. 86 (16.5%) prostheticpoly tetra fluoro ethylene (PTFE) AVG infections were identifed in 72 patients. Patients that had less than 4 months of follow-up were excluded. Patients were regularly monitored in our dialysis unit for infection of their vascular access. Data including the patient's demography which its included in table (1), date of graft insertion, date of graft related infection,site of graft insertion, organism responsible, management of AVG infection, outcome of the graft and patient were obtained.

All prosthetic grafts were made of polytetrafluoroethylene (PTFE) material. The configuration of infected prosthetic graft was as following: loop forearm graft, 22 patients; brachioaxillary graft, 46 patients; lower limb thigh graft, 15 patients; radiobasilic graft, 3 patients.

Infected AVGs were identified by clinical, ultrasound, and microbiological findings. Clinical presentation was categorized as a draining sinus tract, exposed graft, purulent drainage, erythema, cellulitis, pain overlying the graft, or haemorrhage. management of suspected graft infection was empirical treatment with antibiotics (ABs) coverage for both gram-positive and gram-negative organisms usually for 2 weeks, usually gentamycin and second generation cephalosporin .prior antibiotics administration, swabbing of open wound or exposed graft or aspiration by needle.Gram stains and wound cultures were routinely sent for microbiology analysis.

Treatment of AVG infections may require complex and difficult clinical decisions. Despite the risk of recurrent infection, access salvage is reasonable for limited infections. Antibiotic coverage, partial graft excision and total graft removal and arterial repair were usually the main approaches to treat graft infection in our institute. Vascular surgeons assessed the individual patient risk factors and the clinical picture in the clinic on a case by case basis before starting an appropriate therapy.

Identification of bacteria and determination of sensitivity to antibiotics

The bacterial strains were isolated from clinical materials (pus, tissue biopsy, blood, part of prosthesis) and identified with a VITEK2 ID/AST Testing System (BioMerieux, UA). The majority of bacterial sensitivity testing was investigated using VITEK2 and some were modified or confirmed by manual susceptibility testing using Etest and Disc diffusion methods based on the clinical and laboratory standard institute guidelines (CLSI).

Infection was considered polymicrobial if more than one organism were isolated in the same wound culture. Regarding the outcome, patients were considered cured if resolution of the infection occurred and the patient had recovered. Relapse was defined as recurrence of the infection owing to the same organism occurring during the follow up period. The infection location was defined as occurring at a recent incision or within the body of the graft.

Statistical analysis

Patient's characteristics were summarized using descriptive statistics analysis. Results of continuous variables were given as mean and standard deviation, and count and percentage for categorical variables. Continuous variables were analysed by a Student t-test or by the Mann-Whithney U test for non-normal distributions. Qualitative variables were analysed with a Chi-Square test or Fisher test where appropriate. A p-value <0.05 was regarded as significant

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The statistical analyses of the data were performed using SPSS v.19 for Windows statistical software (Chicago, IL, USA).

Results

Infectious complications of AVGs were found in 86/520 (16.5%) patients. Prosthetic AVG infections were identified in 72(13.8%) patients. In 14 patients (16%), a prosthesis was implanted at different times and locations as redo procedure or new graft implantation. The mean age±SD of the patients was 42 ± 18.4 (range 18-82 years). The median follow-up duration was 16 months (range 7-48 months). 56 patients were male (65%). Thigh AVG was created in 15 patients (17%) owing to exhausted upper limbs, whereas upper limb AVG was inserted in 71 patients (82.6%).

Clinical findings such as warmth and redness of the skin, local pain, oedema, serous or purulent secretion from the wound usually lead to a diagnosis of infection. 73 (85%) patients with infected AVG presented with purulent secretion from the needle puncture site or from the wound. 13 (15%) patients had Cellulitis, an exposed graft, and febrile reaction on presentation. There was pain overlying the graft as a manifestation of the infection in most patients. Duplex sonography was performed on some patients to examine graft flow, perigraft fluid collection, false aneurysm , extent of infection, and to evaluate the anastomosis .

50 (58%) of graft infections occurred within one month. 4 patients with graft infection were treated conservatively by intravenous (IV) ABs, 56 patients underwent total graftectomy and venous patch repair for the artery; 3 patients of this group later presented to our emergency room with bleeding and underwent brachial artery ligation owing to friable artery after venous patch repair. 17 patients underwent partial graftectomy and a salvage procedure by vein or graft interposition through a new route with a success rate of 65%; 6 patients of this cohort had a relapse of the infection and were treated by total graftectomy. 9 patients were managed by subtotal graftectomy. A central venous catheter was inserted and used for dialysis for a median period of 4 months. All patients received treatment according to the culture and sensitivity. , 4 patients had a minimum turbid wound discharge, low grade fever, the wound culture showed the presence of staph.aureus bacteria and the Ultrasound studies revealed normal finding were treated conservatively by IV antibiotics for 2 weeks then shifted to oral antibiotic for another 2 weeks. The overall patient mortality during the study period was 19 patients. The cause of death was graft related in 4 (4.7%) patients; 3 patients died owing to septicaemia, the fourth patient developed septic ischemic brain stroke died after few days.

Of the 520 patients with AVGs that were enrolled in this study; 434 of the patients were controls and 86 patients had infected AVGs. Bivariate analysis of categorical variables identified that the presence of diabetes mellitus [124(29%) vs. 48(56%)] and thigh graft are a risk factor for AVG infection. Considering continuous variables, high WBCs and low serum haemoglobin levels, were more frequently associated with AVG infection with a statistically significant P value (Table 1).

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Table (1) Patients' demography; DM (diabetes mellitus), HTN (hypertension), COPD (chronic obstructive pulmonary disease)

Characteristic	Number of patient with AVG (434)%	Number of patients with infected AVG(86)%	P value
Male	**335(77%)**	***56(65%)***	**0.06**
Female	**99(23%)**	***30(30%)***	**0.12**
Heart Failure	**51(12%)**	***19(22%)***	**0.06**
Coronary Disease	**64(15%)**	***27(31%)***	**0.82**
Anemia	**102(24%)**	***52(60%)***	**0.01**
COPD	**34(8%)**	***8(9%)***	**0.9**
DM	**124(29%)**	***48(56%)***	**0.003**
HTN	**116(27%)**	***28(33%)***	**0.179**
Thigh graft	**21(5%)**	***15(17%)***	**0.04**
WBCs on admission	**48(11%)**	***28(33%)***	**0.001**

The most common infectious organisms in AVGs were strains of Staphylococcus, constituting 78% of all bacteria. The most frequent species was S. aureus, which accounted for 52 (60.5%) patients of the isolates of staphylococci. The second most frequent species was S. epidermidis, detected in 15 (17.5%) of the cultures. Enterococcus faecalis was present in 6 (7%) patients and gram–negative bacteria Pseudomonas aeruginosa were the cause of 4(4.7%) episodes of graft infection. Methicillin-resistance S. aureus (MRSA) bacteria were cultured from 2 patients. Mixed polybacterial growth was detected in 7 patients (including: staph.aureus, sterp. spp, Escherichia coli, Klebsiella spp. Acinetobacter spp., Enterobacterspp). After the sensitivity results, the patients were changed to the proper antibiotics. The patients infected with mixed growth bacteria were treated with broad spectrum antibiotics containing Vancomycin. the duration of treatment depends on clinical picture and subsequent wound culture result.

Discussion

Infection is an important cause of morbidity and mortality among patients with end stage renal disease (ESRD). Patients with bacteraemia or sepsis represented 45% of those hospitalized owing to infection, whereas 23% of them were considered to have access-related infection(10,11) .Data from the United States [Renal Data System (USRDS)] showed that infection is the leading cause of death among patients with ESRD.(10-13). In the present study, the mortality rate related to AVG infection was 4.7%.

Several factors can affect the infection risk for AVG. Repeated cannulation, poor personal hygiene, increased number of hospitalizations, increased duration of AVG use, increased age, diabetes mellitus (DM), hypoalbuminemia, neutrophils dysfunction and ambulatory limitations have been reported to contribute to AVG site infections. Infection is also more common in lower extremities AVG, insufficient antisepsis during surgical procedure, technique of venepuncture with risk of hematoma creation or infection contamination have been recognized as a risk for infection (2,14, 15,16). In the present study, our analysis showed a statistically significant difference in infection of AVG for patients with DM (P = 0.003), high WBCs (P= 0.001), anaemia (P=0.01), and thigh graft (P=0.04) in comparison with the control group,This distribution was similar to what has been previously reported in the literature.

Once graft-associated infection is diagnosed, treatment involves the administration of IV ABs and some form of graft excision or total graftectomy for purulent graft infection orin septic patients. Partial graftectomy could be a treatment option for AVG infection to achieve both infection eradication and vascular access preservation in selected patients (17.18). Partial graftectomy is an attractive option in patients with limited access choice, the incorporated portions of the graft is available for immediate haemodialysis and thus obviates the need for the creation of a new access. The procedure is beneficial as it reduces the risk of arterial and nerve injury and the risk of

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arterial bleeding (14). A limited portion of AVG is removed and a new graft is inserted through adjacent sterile tissue. Partial graft excision was accompanied by access salvage and wound healing in only 74% (8) of patients. We performed a partial graftectomy for 17 patients with a success rate of 65%; 6 out of the 17 patients required a total graftectomy owing to recurrent infection. It appears that surgical removal of the access site can be individualized. Patients who are less severely ill can maintain their haemodialysis access site and be treated with 2 weeks of antibiotic therapy (2, 9). In our study, 4 patients had a minimum turbid wound discharge, low grade fever, the wound culture showed the presence of staph. aureus bacteria and the Ultrasound studies revealed normal finding were "cured" by the administration of IV ABs for 14 days followed by intake of oral ABs for 2 weeks.

Graft infections can occur at any time, but the majority of them occur within 1 month after placement (8,18). As shown in our cohort, 58% AVG graft infection occurred within the first month. Bacteria adhere more strongly to the synthetic material of the AVG, leading to resistance of the host defences compared with native arteriovenous fistula (19,20). The majority of infections are attributable to routine dialysis owing to breaks in skin integrity. (21).

Methicillin-sensitive S. aureus, which account for two-thirds of S. aureus infections among dialysis patients, may cause severe morbidity, mortality, and high cost (21, 22). Complications of Staph. Aureus infection include sepsis, endocarditis, osteomyelitis, septic arthritis, and metastatic abscesses.(23,24) . In our study group, 4 (4.7%) mortalities were related to graft infection, 3 patients developed sepsis, one patient died owing to metastatic septic embolic stroke. The incidence of invasive MRSA infection among patients undergoing chronic dialysis is >100 times higher than in the general population. Although the rate of invasive MRSA infections in patients on dialysis has declined, it still continues to be a major health problem (25,26),the resistance of S. aureus has varied from 2.1 to 38.5% (21,27). In our cohort, we isolated 2 (2.3%) cases of MRSA; the AVG infection was treated successfully with Vancomycin and total graft removal.

Our study has a number of limitations. First, a small to a modest sample size and events. Second, a single-centre study retrospective in nature makes it vulnerable to collection bias and to potential inaccuracy in data collection. Third, we excluded patients with less than 4 months of follow-up (some of them lost, the other were died) which may affect the data analysis outcome. Despite these limitations, our study showed the most important clinical events, highlights the ideal management and outcome of AVG infection and confirms that the effect of S. aureus infection on patient morbidity, access loss, and mortality is significant in patients on haemodialysis.

Conclusion

Because haemodialysis patients are a high-risk group,all measures to decrease the incidence of infection like correction of anaemia, controlling of blood sugar and trying to create graft in upper limbs may decrease risk of infection. Our result showed that management of patients with graft infection could be individualized by total graftectomy or partial graftectomy according to patient's condition. Early removal of the graft in conjunction with antimicrobial therapy to prevent fatal complications is highly recommended .Our data analysis showed that strains of Staphylococcus, especially Staph. aureus, were the most frequent cause of infected AVGs.

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