

Possibility and predictors of surgical salvage of infected mature arteriovenous fistula for hemodialysis

Ahmed A. Elnaggar^a, Khaled Diab^a, Amr A. Rahim^b, Ahmed M.A. Elsayed^c, Mahmoud I. Aboelnor^d

^aDepartment of General Surgery, Faculty of Medicine, Fayoum University, Fayoum,

^bDepartment of Vascular Surgery, Faculty of Medicine, Kasr Al-Ainy, Cairo University,

^cDepartment of Vascular Surgery, Faculty of Medicine, Helwan University, Cairo, Egypt,

^dRadiodiagnosis Department, Faculty of Medicine, Fayoum University

Correspondence to Ahmed A. Elnaggar, MD, Department of General Surgery, Faculty of Medicine, Fayoum University, Fayoum 63514, Egypt. Tel: +20 100 954 3896; e-mail: aaa29@fayoum.edu.eg

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Background

Infection in arteriovenous fistula (AVF) is a common complication in patients with end-stage renal disease (ESRD) requiring dialysis. The standard management includes ligation of the AVF to prevent the progression of septicemia. Till now, there is limited evidence on the effectiveness and possibility of salvage of infected AVFs.

Aim

To evaluate the effectiveness and safety of salvage of infected mature autogenous AVF.

Methods

This prospective study was conducted at the Fayoum University Hospital from September 2015 to April 2023. We included patients with dysfunctional and functioning infected AVF. Patients with infected synthetic grafts and immature infected AVFs were excluded. We aimed to excise the infected part of the vein wall and surrounding tissues to restore fistula patent and functioning after direct vein repair. We followed-up with all patients for 1 year and examined the repaired AVFs for patency and the possibility of re-infection. Tissue cultures were obtained to identify the commonest responsible organism and the recommended antibiotics.

Results

A total of 46 patients with infected AVFs were included. At the end of the follow-up period, 11 patients were ligated, and 35 underwent AVF salvage procedures. 19 cases experienced some complications: 5 cases had hematoma required surgical intervention, 2 cases had hematoma managed conservatively, 2 patients had wound dehiscence, 3 patients required hybrid angioplasty for acute failed AVF, and 7 cases required angioplasty for failing AVF.

Conclusion

When performed correctly and with expert hands, salvage of infected mature AVFs seems possible with excellent efficacy and high patency for up to 1 year.

Keywords:

dialysis, infected arteriovenous fistula, salvage, surgical repair, vascular access

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Introduction

Chronic kidney diseases, especially end-stage renal disease (ESRD), requiring renal replacement therapy is a major problem worldwide with the increasing incidence of such patients [1,2]. Hemodialysis is the most common modality of renal replacement therapy that requires access to regular and durable treatment for better control of the progression of renal disease [3,4]. A native arteriovenous fistula is the best type of access for these patients with the best advantages and the few disadvantages, according to The Kidney Disease Outcomes Quality Initiative (KDOQI) [5]. However, these AVFs are susceptible to many complications, such as dysfunction, rupture, bleeding, thrombosis, and infection [6]. Up to 25% of hospital admissions among dialysis patients are due to AVF problems [7]. AVF Infection is a serious and common complication in patients with ESRD requiring dialysis. It represents a major cause of

morbidity and mortality for hemodialysis patients, as sepsis-related mortality has increased among ESRD patients [8–11].

The preservation of a functioning patent AVF is one of the challenges in the course of treatment of ESRD patients undergoing dialysis. The standard and the easier management options for infected AVF include a no-intervention conservative strategy in mild cases or the ligation of the AVF to prevent vein rupture and severe bleeding or progression of septicemia [12]. In addition, surgical repair of the infected AVF represents an alternative solution that preserves this AV access. It preserves the patency and functionality of the AV

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access. It avoids further intervention for new AVF, which causes vein exhaustion in patients with already limited options for new fistula creation [12–14].

Till now, there is limited evidence on the effectiveness and possibility of salvage of infected AVFs. But, in a study by Attia *et al.* [13], the surgical repair of AVF seemed to be an effective solution for infected AVF. Hence, due to this lack of evidence in medical literature, this prospective study was conducted to evaluate the effectiveness and safety of salvage of infected mature autogenous AVF.

Methods

Study population

This study was conducted prospectively on 46 patients with ESRD presented with infected autogenous AVFs to the General Surgery Department at Fayoum University Hospital. Written informed consent was obtained from all patients before enrollment in the study. The study has been approved by the Research Ethics Committee of the Fayoum Faculty of Medicine.

Our inclusion criteria were patients with ESRD on regular hemodialysis who had infected mature AVF with failed conservative medical treatment with progressive infection and those who presented with impending infected AVF or had already ruptured with a herald or profound bleeding. We excluded Patients with mild superficial infections such as cellulitis that responded to conservative medical treatment, traumatic rupture AVFs, infected anastomotic sites of newly constructed AVFs, and infected synthetic Synthetic Arteriovenous Grafts (AVGs).

All patients underwent detailed history taking, and data were collected on age, sex, and cardiovascular risk factors such as diabetes mellitus (DM) and hypertension. In addition, the duration of dialysis, age and type of access of concern, and any complications developed and interventions done since using that access were also included.

Diagnosis

This study included 46 patients with ESRD on hemodialysis presented with infected mature AVFs. Clinical manifestations of infected AVF include locally progressive redness, hotness, pain, and tenderness. Or acute swelling and herald bleeding. Cannulation site discharging pus, or abscess pointing along the course of the needling segment, or rupture and severe bleeding. As well as systemic manifestations of infection, such as fever, malaise, rigors, and toxemia, could also be included.

Duplex ultrasound imaging was performed in all patients using mid-range duplex ultrasound machines (Toshiba xario machine/logic s7 expert machine) using superficial linear ultrasound probes. In some patients, a convex probe was used in the status of marked arm swelling, especially in the obese patient in addition to the superficial probe.

The examination was done sitting with the affected upper limb exposed to the shoulder. The examination started with an assessment of the afferent artery (brachial or radial artery) the flow pattern was examined, and flow volume was measured proximal to the shunt, then the shunt site was examined for patency, and if there was stenosis. The draining vein of the shunt was examined along its length to its junction with the deep system, the draining vein was examined for stenosis, dilatation either focal or diffuse, and also for possible stealing tributaries. The effective flow of the shunt was measured.

The second step is an assessment of the surrounding soft tissue for edema, collections, abscess, and hematoma, and if there is a hematoma. The duplex examination confirmed the presence or absence of flow within (pseudo aneurysm formation). The underlying muscles were examined to assess for intermuscular/intramuscular extension hematomas or the collection and exclusion of compartmental syndrome formation.

Preoperative assessment

All patients with AVF infection were admitted to the hospital, and intravenous empirical antibiotics were initiated after wound cultures were routinely taken. Laboratory investigations were obtained (e.g., complete blood count (CBC), blood group, coagulation profile, renal and liver functions). Patients presented with severe bleeding were managed urgently, aiming at the stoppage of bleeding by direct compression on the bleeding site and resuscitation to stabilize the patient's condition. Broad-spectrum antibiotics are started, and their type and duration of treatment vary based on the culture results and the patient's clinical course.

Operation

The type of surgical technique used was based on the following:

- (1) Patient hemodynamics, preoperative findings such as toxemia (high white blood cell (WBC) count and elevated C-reactive protein (CRP)), the severity of infection, and duplex measurements.
- (2) Intraoperative findings as an extension of infection, quality of artery and vein, length of the vein, anastomotic condition.

Anesthesia and tourniquet application

General or regional (supraclavicular) anesthesia infiltration was administered. Then a pneumatic tourniquet was applied over the limb proximal or distal to the site of AVF infection but proximal to or on the AVF anastomosis. The inflation time of the cuff was kept to a minimum of not more than 2 h.

Surgical procedure

An adequate elliptical skin incision was done over the site of infection, longitudinal or transverse, according to the direction of vein expansion planning for comfortable skin closure at the end of the procedure, followed by sampling infected tissue for culture and sensitivity. Excision of all infected tissues of the skin, subcutaneous tissues, and infected venous wall and sharp dissection, followed by wound irrigation with a large amount of saline. Then control the vein proximal and distal to the infection, then deflate the tourniquet. Thrombectomy Fogarty catheter for removal of any thrombi proximal or distal to the site of infection in case of acute infected failed fistula, then irrigation of the vein with heparinized saline proximally and distally (Fig. 1).

Repair technique

All infected vein walls must be excised. We describe the infected wall as brownish red and friable and has weak or no tensile strength, while the healthy wall has whitish intima and strong elastic consistency that can maintain sutures of the repair in its place.

The lumen of the vein is retained and reconstructed according to the remaining healthy venous wall either by a direct edge-to-edge closure using polypropylene sutures, end-to-end anastomosis in tortuous vessels, or

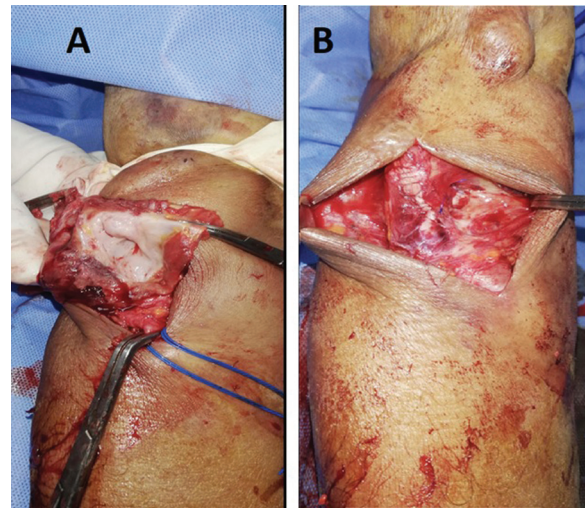
vein patch from adjacent healthy dilated part of the vein. Good liberation of wound edges by undermining and skin closure in no tension. Coverage by a local fasciocutaneous flap is needed if the primary skin closure is difficult. Fistulas with extensive infection destroying the vein, extending to the anastomotic site of AVF, no available vein wall for repair or compromise of a large part of the venous conduit is ligated (Fig. 2).

Results

Summary of included patient data

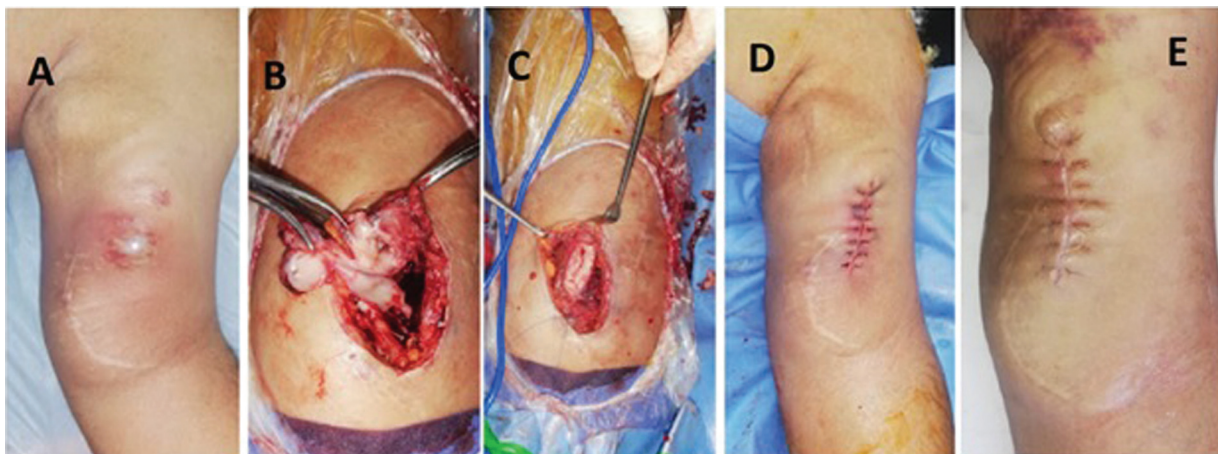
A total of 46 patients on dialysis had an infection of mature AVFs. The mean age was 47.80 years \pm 16.68, and the mean duration of dialysis was 5.58 years \pm 4.09,

Figure 1



(a) shows infected aneurysmal dilatation of right brachial cephalic AVF, with noted healthy white intima and unhealthy brownish red intima and (b) shows excised unhealthy venous wall and surrounding tissues with healthy adequate skin edges before closure of the skin.

Figure 2



Shows (a) infected left brachial basilic AVF preoperative, (b) intraoperative infected unhealthy tissues and (c) after debridement with healthy venous wall, (d) After skin closure, and (e) 10 days postoperative.

while the mean duration of AVF was 3.63 ± 3.06 years. 24 (52.2%) patients are males. In comparison, 22 (47.8%) patients are females, as presented in Tables 1 and 2. 19.6% had radio-cephalic arteriovenous fistula. In contrast, 52.2% had a brachio-cephalic arteriovenous fistula, and 28.3% had a brachio-basilic arteriovenous fistula. 69.6% of the patients had to function AVF and 10.9% of them had central venous hypertension, 10.9% suffered from failing AVF, and 8.7% had acute infected failed AVF. A high percentage of the patients (84.8%) did not have a previous intervention for their current fistula, while only 15.2% had previous interventions for fistula salvage in the form of angioplasty. 17.4% of the patients suffered from DM, 54.7% suffered from hypertension, and only 6.5% had ischemic heart disease.

Technical outcomes

Regarding the technical outcome, 35 (76.1%) were repaired, 11 (23.9%) patients were ligated, 9 had done primary ligation without repair, and 2 were ligated after 5 days of repair. Seven (15.2%) of the patients suffered from hematoma within 2 weeks of the operation, 3 (6.5%) experienced failing fistula, 2 (4.3%) cases suffered an extension of infection and bleeding ended with ligation of the infected vein, and 2 (4.3%) cases had wound dehiscence within 1 week needed re-

Table 1 Age of the patients, duration of dialysis and duration of AVF

	N	Mean	SD
Age	46	47.80	16.68
Duration of dialysis/years	44	5.58	4.09
Duration of AVF/y	46	3.63	3.06

Table 2 Characteristics of the patients and arteriovenous fistula

	N (%)
Sex	
Male	24 (52.2)
Female	22 (47.8)
Type of AVF	
Radial cephalic	9 (19.6)
Brachial cephalic	24 (52.2)
Brachial basilic	13 (28.3)
State of AVF function	
Functioning	32 (69.6)
Central venous hypertension	5 (10.9)
Failing	5 (10.9)
Failed	4 (8.7)
Previous intervention for current fistula	
No	39 (84.8)
Yes	7 (15.2)
DM	
No	38 (82.6)
Yes	8 (17.4)
HTN	
No	25 (54.3)
Yes	21 (45.7)
IHD	
No	43 (93.5)
Yes	3 (6.5)
Technical outcome	
Repaired	35 (76.1)
Ligated	11 (23.9)
1 week follow-up and complications	
None	32 (69.6)
Hematoma	7 (15.2)
Failing fistula	3 (6.5)
Extension of infection and bleeding ended by ligation	2 (4.3)
Wound dehiscence needed reintervention	2 (4.3)
Interventions done in the first 3 months	
Angioplasty for failing AVF	7 (15.2)
Hybrid angioplasty for acute failed AVF	3 (6.5)

intervention in the form of good debridement of the infected perivascular tissue and making a healthy pocket for the vein then closure of the debrided edges of the skin. Seven (15.2%) patients needed angioplasty for their failing AVF within the follow-up period of 1 year, only three (6.5%) patients needed hybrid angioplasty for acute failed AVF, and only one case reinfected after 3 months at the same site and managed by the same method but the vein needed coverage by a local fasciocutaneous (Keystone) flap.

Correlation between technical outcomes and the general and clinical characteristics of the included patients

Among 35 patients with successful repair, 18 were males, while 17 were females. On the other hand, 6 males and 5 females underwent ligation of AVF. There was no significant difference between males or females who underwent AVF repair and those who underwent AVF ligation; $P=0.857$; Table 3.

The brachio-cephalic was associated with the highest rate of successfully repaired AVF; 18 out of 35 (75%) patients. However, there was no significant difference between all AVF Types and the technical outcomes (either repaired or ligated); P greater than 0.999.

Table 3 Association between technical outcome and characteristics of the patients and AVF

	Technical outcome		P value
	Repaired	Ligated	
Sex			
Male N (%)	18 (75.0%)	6 (25.0%)	0.857
Female N (%)	17 (77.3%)	5 (22.7%)	
Type of AVF			
Radial cephalic N (%)	7 (77.8%)	2 (22.2%)	>0.999
Brachial cephalic N (%)	18 (75.0%)	6 (25.0%)	
Brachial basilic N (%)	10 (76.9%)	3 (23.1%)	
State of AVF function			
Functioning N (%)	29 (90.6%)	3 (9.4%)	0.006
CVH N (%)	2 (40.0%)	3 (60.0%)	
Failing N (%)	2 (40.0%)	3 (60.0%)	
Failed N (%)	2 (50.0%)	2 (50.0%)	
Previous intervention for current fistula			
No N (%)	29 (74.4%)	10 (25.6%)	>0.999
Yes N (%)	6 (85.7%)	1 (14.3%)	
DM			
No N (%)	29 (76.3%)	9 (23.7%)	>0.999
Yes N (%)	6 (75.0%)	2 (25.0%)	
HT			
No N (%)	19 (76.0%)	6 (24.0%)	>0.999
Yes N (%)	16 (76.2%)	5 (23.8%)	
IHD			
No N (%)	33 (76.7%)	10 (23.3%)	0.569
Yes N (%)	2 (66.7%)	1 (33.3%)	

Chi-square test was used to compare between technical outcome and characteristics of the patients and AVF.

The functioning AVF was associated with a statistically significant higher incidence of successful repair in 29 out of 32 compared with Central Venous Hypertension (CVH), failing, and failed AVF; $P=0.006$.

Patients with no history of previous intervention for the current AVF were associated with a higher incidence of successful repair, 29 out of 35 (74.4%). However, there was no significant difference between those with previous and without intervention; P greater than 0.999.

Regarding the role of comorbidities, patients with no history of DM, Hypertension (HTN), and Ischemic Heart Disease (IHD) were associated with a higher incidence of successful repair than those with comorbidities. However, there was no significant difference between the number of patients who underwent repair or ligation of AVF in both comorbidity groups; P greater than 0.999, 0.999, and 0.569, respectively; Table 3.

As for age, dialysis duration, and AVF duration, there was no significant relationship with the technical outcome, either repaired or ligated. The mean age of those who underwent repair and those who underwent ligation was 48.37 ± 16.01 and 46 ± 19.41 , respectively; $P=0.686$; Table 4.

Discussion

This study found that infected AVF can be salvaged rather than ligated with good patency rates up to 12 months of follow-up. Out of 46 patients, 35 (76.1%) had a successful repair compared with 11 (23.9%) patients who underwent ligation. The success of the AVF repair was not associated with any clinical variant except for the functioning condition of the AVF before the repair process. The Functioning AVF was

Table 4 Comparison between technical outcome and age of the patients, duration of dialysis and duration of AVF

	N	Mean	SD	P-value
Age				
Repaired	35	48.37	16.01	0.686
Ligated	11	46.00	19.41	
Duration of dialysis/years				
Repaired	35	5.30	3.97	0.378
Ligated	9	6.67	4.64	
Duration of AVF/ y				
Repaired	35	3.61	2.91	0.963
Ligated	11	3.66	3.66	

Independent sample t-test was done to compare between technical outcome and age of the patients, duration of dialysis and duration of AVF. It showed no statistically significant difference.

associated with a statistically significant higher incidence of successful repair in 29 out of 32 (90.6%) compared with dysfunctional AVF, 2 out of 5 cases (40%) with CVH, 2 out of 5 (40%) failing AVF, and 2 out of 4 (50%) failed AVF; $P=0.006$.

The Kidney Disease Outcomes Quality Initiative (K/DOQI) standards promote the increased use of native vascular access because of superior patency rates and lower complication rates than grafts once established [5]. Regarding the effect of age, sex, and comorbidities on the incidence of AVF site infection, in our study, there was no significant difference between males and females with AVF infection. This was different from what is reported by Attia *et al.* [13], Salahi *et al.* [15], and Rodriguez *et al.* [16]. They reported a predominance of infection in male patients. On the other hand, Taylor *et al.* [17] and Cinat *et al.* [18] reported female predominance. This can be explained by the fact that these studies included surgical site infection of newly constructed AVF. Our sample mean age was 47.80 years \pm 16.68, nearly similar to the previously mentioned study population.

The incidence of salvage failure in central venous hypertension cases was higher as CVH causes limb edema that may be severe enough to cause difficult dissection. Also, the bleeding field increases the incidence of postoperative hematoma and impairs the availability of good skin flaps for good wound closure. Blood flow acts as a barrier against infection spread in functioning AVF. While in acute failed AVF, the thrombus in the vein acts as a culture media for the spread of the infection. We did not find difficulty in skin closure after excision of the infected skin and subcutaneous tissue overlying the infected vein because we could easily dissect the skin and SC tissues over the undersized vein after repair that was acting as a tissue expander during its dilation.

The presence of polyproline sutures for repair of the debrided vein may increase the incidence of persistence of infection that will erode the venous repair with rupture of the vein. Still, fortunately, this sequel did not happen except in two cases after 5 days of repair ended by ligation of the fistula [19]. We may explain the regression of infection to good debridement and excision of all infected tissues, then irrigation of the wound with a large amount of saline before closure. High vascularity at the infected site due to vasodilatation caused by in release of inflammatory mediators at the area of infection and rapid blood flow within the vein secondary to AVF. On the other hand, the thick mature wall of the repaired

veins aided in fighting the infection [20] except in 1 of the 2 cases that had been ligated after 5 days of repair where the conduit vein was very thin, and the fistula age was 17 years, the other case that was ligated after 5 days were repaired after infected failed AVF.

Although DM is a well-known disease affecting the immune defense mechanisms against infections, our sample showed that only 8 patients (17.4%) had DM, while the majority had no DM. This was consistent with what is reported by Taylor *et al.* [17], who reported no significant difference between the infected and noninfected patients regarding the incidence of DM, with 12% and 18% for each group, respectively. On the other hand, this differed from what was reported by Attia *et al.* [13] and Katneni and Hedayati [21]. Attia *et al.* [13] reported the association between DM and vascular infection in 45.3% of their patients. The latter reported a significant increase in vascular access infections in DM and a significant relationship with the positivity of the culture swaps obtained from the infection site [21].

Regarding the technical outcomes of infected AVF, there is a lack of medical literature regarding the salvage of infected AVF. The study by Attia *et al.* [13] shares some of our objectives; they included the newly formed infected AVF in their population. However, our main difference was targeting only infected mature AVF. In our study, 35 patients out of 46 (76.1%) underwent surgical repair, while 11 (23.9%) required AVF ligation. This is similar to the results reported by Attia *et al.* [13]. Among 64 patients, 50 (78.1%) patients of them underwent surgical repair, while 14 (21.9%) of them underwent ligation of the AVF. Mature infected AVF, as evidenced by late infection (> 30 days), was only noted in 35 cases, of which 30 (85.7%) cases were repaired. Of the 50 cases that underwent repair, 45 remained patent after a 1 month follow-up. In addition, during the 6 month and 1 year follow-up period, 42 cases and 41 cases remained patent, respectively. Most of the failed AVFs after repair were due to re-infection or aneurysmorrhaphy. Taylor *et al.* [17] studied the efficacy outcomes in synthetic, bovine, and autogenous AVF. They reported that infection happened in two patients with mature infected autogenous AVF in the form of puncture site infection. One case ended with ligation, and the other was salvaged by new anastomosis between the artery and vein in a clean field. Nevertheless, they did not repair the infection site directly as we did [17].

In our results, seven cases underwent angioplasty for failing AVF in the follow-up period, while 3 cases

required hybrid angioplasty for acute failed AVF. Moreover, we reported hematoma in seven cases similar to that found by Attia and colleagues. The hematoma can be explained by the vasodilatation caused by the accumulation of inflammatory mediators, hypervascularity of the failed caused by arterialization of veins, venous hypertension, and bleeding diathesis in renal failure patients.

An important factor that should be studied in the upcoming studies is the role of the AVF site. In our study, we included patients with three types of fistula, with the majority of patients with brachial cephalic followed by brachial basilic and the least number of patients with radial cephalic. Although we did not establish a relationship between the type of fistula and the development of infection or the technical outcome, it may represent a predictor of the development of infection. In their trial, Attia *et al.* [13] reported that upper arm AVF was the most common infected fistula (84.4%), which is similar to results reported by previous studies [22,23]. This was evidenced by the higher incidence of infection in the proximal elbow region accounting for 73.4% of complications compared with the distal wrist region, with an incidence of 24.5%, as reported by Belli *et al.* [23]. This could be explained by the higher colonization of skin bacteria flora in the cubital fossa compared with other regions [24].

Limitations

The small sample size of our study is the main limitation. So, it is difficult to generalize the results of our study to different populations. Also, patients with functioning AVF before the repair were greater than those with other AVF states. So, results may be applicable only for those with functioning AVF rather than CVH, failing or failed AVF. So, we recommend conducting a multicentric trial on patients with different demographic and clinical characteristics with long-term follow-up periods to reach reliable and generalizable evidence.

Conclusion

Infected AVF could be salvaged with a trial of repair rather than ligation. It revealed excellent efficacy and high patency for up to one year. There was no significant predictor of the success of the AVF repair. However, we found that the state of the infected AVF was the only significant variable to predict the technical outcome.

Conflicts of interest

There are no conflicts of interest to disclose in relation to this research.

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