Management of symptomatic arterial and venous aneurysms in hemodialysis patients related to arteriovenous fistulas

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AIM: *Our aim in this study is to present the management of the symptomatic aneurysms that are related to AVF.*
MATERIAL AND METHODS: *Between January 2011 and January 2017, 50 patients who were operated due to symptomatic AVF aneurysms were evaluated. Forty-four (88%) patients' fistulas were closed for symptomatic venous aneurysm. In 6 (12%) patients true brachial artery aneurysm were present and a segmental artery resection with its repair was performed.*
RESULTS: *The most common symptomatic aneurysm was seen on the brachiocephalic fistula (n=32, 64%). The symptoms of the patients were; aneurysm thrombosis (n=15, 30%), steal syndrome (n=9, 18%), rupture/massive bleeding (n=7, 14%), infection (n=7, 14%), skin necrosis (n=5, 10%), venous hypertension (n=4, 8%) and high output cardiac failure (n=1, 2%). Nine (18%) patients had two or more symptoms. While the mean duration of dialysis of patients who underwent venous aneurysmectomy was 6.9 ± 4.2 years, patients who underwent arterial aneurysmectomy and brachial artery repair was 11.7 ± 3.6 years (p = 0.012).*
DISCUSSION: *Arterial aneurysm is a rare complication of vascular access. Although it causes serious symptoms including those of related such as thrombosis, ischemia, nerve compression, the most important complication is aneurysm rupture. Therefore, preoperative evaluation and appropriate surgical interventions will prevent morbidities that may arise.*
CONCLUSION: *The choice of a treatment modality in patients with a symptomatic arteriovenous fistula aneurysms is to maintain the continuity of the arteriovenous fistula but when acute bleeding occurs in an unstable patient, ligation of fistula should be considered.*

KEY WORDS: Aneurysm arterial, Hemodialysis, Vascular access, Venous access

Introduction

Renal transplant is the most suitable treatment for the patients with a renal failure. However, hemodialysis (HD) has become the most widely used renal replacement treatment due to scarcity of cadaver organ in our country as well as in the world [1,4]. A potent vascular access (VA) is a major prerequisite for an adequate HD. VA related problems are one of the most prominent reasons among the patients hospitalisation and morbidity who have end stage renal failure [5,6]. Autogenous arteriovenous fistulas (AVFs) are more effective and safe then the other methods owing to lower complication rates, higher patency and long-term survival ratesIt has also a lower cost in comparison to arteriovenous grafts (AVGs) or tunneled central venous catheters (CVCs) [5,6]. In the early period after AVF operations, thrombosis, hematoma, hemorrhage, infection can be seen, and in the late period, local complications such as thrombosis, extremity edema, steal syndrome, graft infection, aneurysm, pseudoaneurysm can be seen [2,3]. Furthermore, systemic complications like cardiac insufficiency may develop depending upon the

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fistulas high flow rate [7]. In the presence of aneurysm, if the patient is asymptomatic, intervention is usually not recommended [5]. AVF closure is recommended in hemodynamically unstable aneurysmal bleeding patients and for patients who have a functioning renal allograft [8].
The purpose of this study is to present our results for different treatment options in symptomatic AVF aneurysm patients at our center.

Patients and Methods

Selection of Patients and Evaluation

Between January 2011 and January 2017, 680 patients that were under hemodialysis programme were operated to create VA or to treat VA complications at our center. We evaluate 50 patients (7.35%) who operated due to symptomatic AVF aneurysms during these 6 year period. Patient data including age, sex, existence of hypertension (HT) and diabetes mellitus (DM), location of AVF, fistula type, duration of fistula and surgical indications were evaluated.

Indications for treatment of AVF aneurysm were;
a. Signs of local infection (erythematous, purulent discharge, or a draining sinus tract);
b. Pain around the regions with aneurysms;
c. Existence of successful renal transplantation;
d. Ulceration and/or bleeding on AVF aneurysm;
e. Loss of an adequate cannulation site;
f. Dialysis access induced ischemic symptoms;
g. Venous hypertension
h. Congestive cardiac insufficiency related to AVF.

Preoperation Evaluation

All patients were evaluated with Color Duplex Doppler Ultrasound (CDDUS) preoperatively except the ones admitted to the operation due to massive bleeding from the aneurysm. The purpose of CDDUS was to assess presence of thrombi, to identify stenosis, to determine the aneurysm site (arterial or venous-related), and to measure the flows. It was also used to assess availability of other access options on ipsilateral and/or contralateral limb for a potential AVF construction.

Surgery Details

All operations were performed under local anesthesia in the operating room. All patients received 1 g of prophylactic cefuroxime intravenously, and prilocaine was used for local anesthesia. First, a longitudinal or transverse incision was made over the pulsating mass in the upper extremity. The aneurysm, artery and vein was dissected. Following the administering of 1 ml heparin (5000 IU) intravenously, proximal and distal vascular structures were clamped. Forty-four (88%) patients' fistulas were ligated for symptomatic venous aneurysm with aneurysm excision. In 6 (12%) patients with brachiocephalic fistula, true brachial artery aneurysm was present and a segmental artery resection with its repair was performed due to extensive calcific deposits in the arterial segment where anastomosis was performed. Autogenous venous graft was used in 1 (16.7%) of these patients who underwent arterial repair (Fig. 5A). Prosthetic grafts were used in 3 (50%) (5 mm polytetrafluoroethylene (PTFE) in 1 and 6 mm PTFE in 2 patients) (Fig. 4) and in 2 (33.3%) patients, an end-to-end repair was performed without tension by releasing the distal and proximal parts of the brachial artery. Finally, the incision was closed after homeostasis was achieved. The defect was closed with local flap techniques when the skin tissue was lost (Fig. 5B).

Post-Operative Follow-Up

In the early period following the operation and prior to the discharge of the patients, radial and ulnar arterial pulses were evaluated with physical examination. Patients were reevaluated one week later after discharge. Subsequent follow-ups were made in the first and sixth months. CDDUS was not used for follow-up in venous aneurysm patients who did not have postoperative complaints. It was used for patients who underwent repair of the brachial artery aneurysm. All patients completed a mean 10.9-month follow up period (range, 1-28 months).

Statistical Methods

Data analysis was performed by using IBM SPSS Statistics version 17.0 software (IBM Corporation, Armonk, NY, USA). Whether the metric discrete variables were normally distributed or not was determined by Shapiro Wilk test. While, the metric discrete variables were expressed as mean ± standard deviation, otherwise, number of cases and percentages were used for categorical data. The mean differences between groups were compared by Student's t test. Categorical data were evaluated by Fisher's exact test. A p value less than 0.05 was considered as statistically significant.

Results

Fifty patients who had autogenous AVF were operated because of symptomatic venous and/or arterial aneurysm during the study period. The median age of these patients was 49.3 ± 15.6 (21-88), and the number of

Table I - *Patient characteristics.*

	n= 50
Age (Years)	49.3±15.6
Age Range (Years)	21-88
Sex	
Men	25 (50.0%)
Women	25 (50.0%)
HT	36 (72.0%)
DM	7 (14.0%)
Localisation	
Right	16 (32.0%)
Left	34 (68.0%)
Fistula Type	
Brescia	16 (32.0%)
Brachiocephalic	32 (64.0%)
Brachiobasilic	2 (4.0%)
Fistula Duration (Years)	7.5±4.4
Fistula Duration Range (Years)	0.5 - 17
Indication	
Thrombosis	15 (30.0%)
Existence Of Successful Renal Transplantation	13 (26.0%)
Steal, schemia	9 (18.0%)
Rupture	7 (14.0%)
Infection	7 (14.0%)
Skin Necrosis	5 (10.0%)
Venous Hypertension	4 (8.0%)
Heart Failure	1 (2.0%)
Trasplantation Duration (Years)	4.2±3.0
Transplantation Duration Range (Years)	0.5 - 12
Arterial Repair	6 (12.0%)

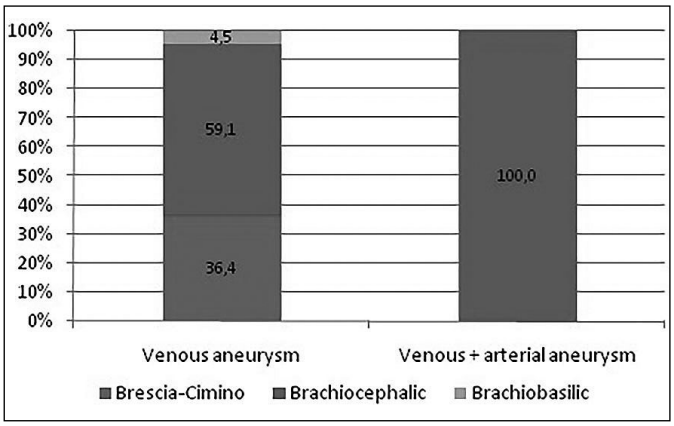

Fig. 2: Fistula type distribution of venous aneurysmectomy and venous with arterial aneurysmectomy patients.

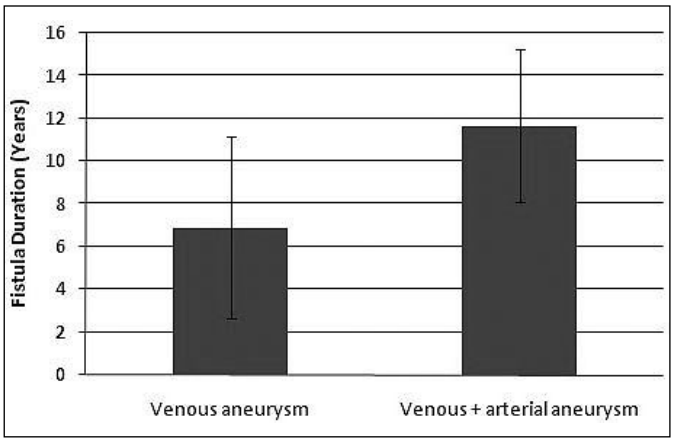

Fig. 3: Venous aneurysmectomy and venous + arterial aneurysmectomy patients' duration of fistula use

Fig. 1: Patient who had insufficient flow during dialysis determined type III thrombus and brachial artery aneurysm in doppler USG

females and males was equal. Co-morbidities, including diabetes mellitus in 7 (14%) patients and hypertension in 36 (72%) patients were present. The most common symptomatic aneurysm was seen on the brachiocephalic fistula (32 patients, 64%), and of 18 patients (36%) aneurysm was seen on radiocephalic AVF. Arteriovenous fistulas of 27 patients (54%) constructed at different centers and they were referred to our hospital due to symptomatic aneurysm. Seven patients (14%) had undergone unsuccessful radiologic interventions before surgery. The signs and symptoms of the patients were; aneurysm thromboses (n=15, 30%) (Fig. 1), steal syndrome (n=9, 18%), rupture/massive bleeding (n=7, 14%), infection (n=7, 14%), skin necrosis (n=5, 10%), venous hypertension (n=4, 8%) and high output failure (n=1, 3.2%). Nine (18%) patients had two or more symptoms. The demographic and clinical characteristics of patients are shown in Table I. AVFs were closed via ligation following a successful renal transplant was carried out on average 4.2 ± 3.0 (0.5-12) years later.

All aneurysmectomy materials that were examined by the pathology department revealed true venous aneurysm characterized by extensive calcification of all layer of the vessel wall (Fig. 6A), extensive fibrosis and calcification in the media layer of the brachial artery wall, and chronic inflammation in the adventitia layer (Fig. 6B).

Six patients with brachiocephalic fistulas (12%) had brachial artery aneurysm. One of these patients were

Table II - *Demographic and clinical features of cases of groups according to repair of brachial artery*

	Venous Aneurysmectomy (n=44)	Arterial Aneurysmectomy with Artery Repair (n=6)	p-value
Age (Years)	48.9±16.0	51.8±13.4	0.672†
SEX			0.189‡
Men	24 (54.5%)	1 (16.7%)	
Women	20 (45.5%)	5 (83.3%)	
HT	33 (75.0%)	3 (50.0%)	0.331‡
DM	7 (15.9%)	0 (0.0%)	0.576‡
LOCALISATION			>0.999‡
Right	14 (31.8%)	2 (33.3%)	
Left	30 (68.2%)	4 (66.7%)	
FISTULA TYPE			
Brescia	16 (36.4%)	0 (0.0%)	0.159‡
Brachiocephalic	26 (59.1%)	6 (100.0%)	0.075‡
Brachiobasilic	2 (4.5%)	0 (0.0%)	>0.999‡
FISTULA DURATION (YEARS)	6.9±4.2	11.7±3.6	0.012†

† Student's t test, ‡ Fisher's probability test with exact result.

Fig. 4: Patient with brachial artery repair with PTFE graft.

male (16.7%), 5 were female (83.3%). Three of these patients had hypertension. There were no patient with diabetes mellitus. Fistulas of the patients that underwent ligation with arterial aneurysm excision were all brachiocephalic fistulas located at the antecubital region (Fig. 2).

There were no statistical difference between age, sex, presence of co-morbidities (HT, DM), fistula localization and fistula type when patients underwent arterial repair after arterial aneurysmectomy and ligation of fistula with venous aneurysmectomy were performed. The mean duration of dialysis from the existing fistulas of patients who underwent venous aneurysmectomy was 6.9 ± 4.2 years, while the mean duration of dialysis from the existing fistulas of patients who underwent arterial aneurysmectomy and brachial artery repair was 11.7 ± 3.6 years, which was statistically significant (p = 0.012) (Fig. 3). The demographic and clinical characteristics of patients who underwent arterial repair after aneurysmectomy due to arterial aneurysm and underwent only venous aneurysmectomy are shown in Table II.

Median nerve damage developed in one patient (2%) who had been operated for massive hemorrhage. Among all the patients that their fistulas closed due to steal syndrome, resting pain was reduced in the early period after surgery, and findings of circulatory impairment in their hands improved. None of the patients developed arterial thrombus.

Discussion

One of the long-term AVF complications is aneurysmal degeneration. In studies frequency of aneurysm among the patients under hemodialysis changes from 6-60% [6,8,9]. However, the prevalence of aneurysmal degeneration is unclear due to the reduced life expectancy of patients with chronic renal failure.

Technical problems in anastomosis, construction of the fistula in the proximal region, using synthetic grafts, and infection may cause AVF related aneurysms. Central venous stenosis related to previously placed central venous catheter is another important factor which leads to increase venous pressure and accelerate the formation of aneurysms. Repeated cannulation on the same site during hemodialysis may result in tissue damage to the vessel wall resulting in weakening of the vessel wall and aneurysm [8]. The main indication for treatment of an AVF aneurysm is its clinical It is recommended that asymptomatic aneurysms of hemodialysis accesses do not require intervention and can be managed by abandoning cannulation of the aneurysmatic areas [4,10]. The diameter of the AVF aneurysm is not an indication for the treatment [4,10]. Pain related with the aneurysm, massive bleeding, inadequate blood flow, steal syndrome in the

Fig. 5: (A) Patient who underwent emergency surgery due to massive bleeding and extensive skin necrosis and brachial artery repair was performed with saphenous vein, (B) repair of tissue defect in the same patient with rotational skin flap

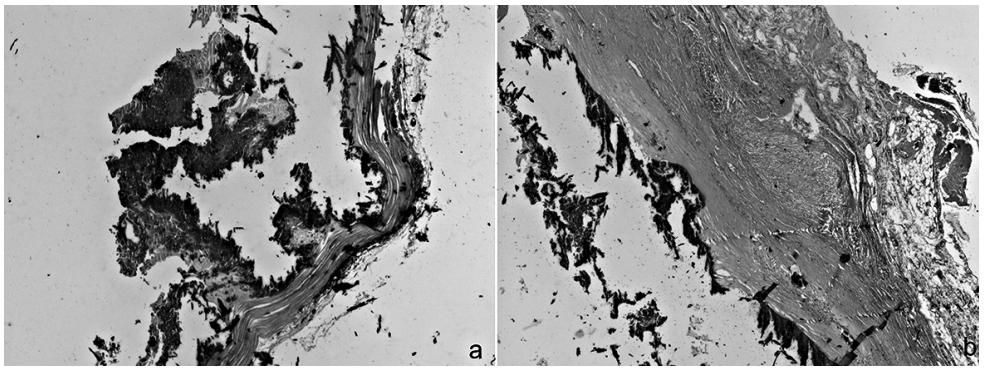

Fig. 6: (A) Venous aneurysm characterized by extensive calcification of vessel wall. (hematoxylene and eosin, x20), (B) Arterial aneurysm with medial thickening and fibrosis, extensive calcification and chronic lymphocytic adventitial inflammation (hematoxylene and eosin, x20)

ipsilateral extremity and congestive cardiac insufficiency due to high flow aneurysm are the indications for the treatment of AVF aneurysm [8]. Treatment indications related to our patients are shown in Table I.

Aneurysm-related pain is a rare symptom that can occur as a result of peripheral neural compression of the aneurysm. In differential diagnosis, uremic or diabetic polyneuropathy should be considered [8]. In our study, we did not consider pain complaints alone as an indication for surgery in our patients with aneurysms.

Aneurysmal bleeding is a serious and potentially fatal complication. It is usually seen after removal of hemodialysis needles, but may also be caused from a spontaneous or traumatic injury. The predisposing factors for aneurysm bleeding are: thinning or erosion/ulceration of the overlying skin layer, a rapidly expanding aneurysm, hypertension, high pressure of vascular access, use of anticoagulant agent, ipsilateral extremity edema and prolonged bleeding time [11]. Seven of our patients (14%) underwent aneurysmectomy due to massive bleeding. Five of them were admitted with bleeding after dialysis and 2 with spontaneous bleeding because of erosion of the overlying skin layer. Bleeding from an aneurysm can lead hemorrhagic shock. One of our patients whom was operated due to spontaneous hemorrhage had hemorrhagic shock symptoms with significant drop in blood pressure, changes in mental status occur, heart rate and respiratory rate are significantly elevated (more than 120 BPM). The ligation of the access is the first, lifesaving procedure. Ligation or the closure with aneurysm excision of the fistula was performed in all emergent bleeding patients because there were wide defects in the wall of the ruptured aneurysm and the hemodynamics of all patients were unstable.

Nearly 80% of the patients with AVF have asymptomatic or physiologic steal with a distal perfusion pressure decrease [15]. Physiological steal is generally well tolerated. Arterial collaterals and vasodilatation in the distal vascular bed usually prevents the occurrence of the symptoms. However, when these mechanisms fails due to atherosclerosis, diabetic microangiopathy and uremic calcific syndrome, an adequate distal perfusion pressure cannot be achieved, and symptomatic steal syndrome may occur. The steal syndrome occurs in 1.6% to 8% with different incidences depending on the type AVF [15]. Cold extremity, numbness, pain during dialysis, resting pain, atrophic changes in tissues, necrosis and tissue loss can occur clinically. According to the classification [15] described by Thermann et al. in order to determine the treatment options in the steal syndrome, our patients were clinically evaluated as stage 4 and ligation of fistula with aneurysm excision was performed.

Peripheral artery aneurysms are rarely seen, but brachial artery aneurysms are even less common. Brachial artery aneurysms may be associated with infection, trauma, congenital defects, or iatrogenic injuries. Aneurysms can also develop in the inflow arteries after construction of AVFs for hemodialysis [18,22]. In patients with chronic renal failure, AVF increases the production and release of nitric oxide and matrix metalloproteinases 2 and 9, and those lead to vasodilatation. Blood flow and vessel diameter increase in the anastomosed vein and artery. The anas-

tomosed vein of AVF are known to develop accelerated phlebosclerosis with aneurysm formation and lipid accumulation [6,12,13]. Elasticity loss and thickening are observed due to storage of calcium and phosphate in the media and / or intima layers of the arterial wall. While intimal calcification causes atherosclerosis, medial calcification causes increased vascular stiffness and results in a decrease in vascular compliance. High blood flow in the AVF stimulates endothelial endothelin-1 (ET-1) release. ET-1 is a mitogen for smooth muscle cells and acts as a chemotactic factor for monocytes, causing sclerotic changes, intimal thickening, lipid accumulation on both anastomosed artery and vein wall layers [14]. As a consequence of all of these, aneurysmal degeneration begins [22]. In our study, extensive calcification in the venous aneurysm wall and extensive fibrosis and calcification in the media layer of the brachial artery aneurysm wall and chronic inflammation findings in the adventitia layer were detected.

The importance of the cannulation method in the incidence of AVF aneurysm development has been emphasized in many studies. There are three options for cannulation. The most frequent method of cannulation uses change of cannulation place on every dialysis (rope-ladder technique), which is difficult to achieve in patients with short fistula. The "buttonhole technique of access cannulation has been recommended as a method which significantly reduces the existing aneurysm enlargement. With this method, cannulas are inserted at exactly the same spot at consecutive dialysis sessions, thus developing a channel in the arteriovenous fistula. This technique is probably not suitable for arteriovenous grafts, because of the fragile wall and higher pressures. In contrast aneurysm formation, is usually a result of the "area puncture technique because cannulation restricted to a small area [16,17,25]. We use the entire length of an arteriovenous fistula (rope-ladder technique), in order to prevent aneurysm formation. In our study, 32 (64%) patients underwent surgery due to brachiocephalic fistula aneurysm. Brachial artery repair was performed in six patients due to brachial artery aneurysm. This suggests that aneurysmal formation may occur due to cannulation difficulties in short fistulas.

The usage period of the same fistula is another factor that increases the incidence of aneurysm formation. Jankovic et al. [6] found that aneurysms were more likely to develop in patients entering the same fistula for longer than 5.7 years in hemodialysis. In our study, the mean duration of fistula use was 7.4 years when all patients are considered. Patients whom underwent venous aneurysmectomy red only, this time was 6.9 years. In patients who underwent arterial aneurysmectomy, the duration of fistula use was 11.7 years. The duration of HD from AVF was significantly longer in patients with arterial aneurysms ($p = 0.012$). Although 64% of all patients with arterial aneurysm had a brachiocephalic fistula, the type of vascular access was not statistically significant ($p > 0.05$).

Arterial aneurysms can develop from a few days to years after AVF creation [19]. In our series, the onset time of brachial artery aneurysms (with a mean time of 11.7 years) is similar with previous studies [6,19]. Basile et al showed that vascular access closure does not prevent the development of the arterial aneurysm [20]. Brachial artery aneurysms can appear years after AVF ligation. But no arterial aneurysm was seen after closure of AVFs in our patients' follow-up.

AVFs often remain patent after kidney transplantation. There is no consensus on fistula closure after a successful and functional renal transplantation. Indications for fistula ligation after successful transplantation include painful thrombosis, aneurysm development, venous hypertension with oedema, distal hypoperfusion, heart failure with high flow AVF, and poor cosmetic appearance [22]. Corticosteroids and immunosuppressive treatments used after transplantation are also suggested to be the cause of vasculopathies leading to aneurysmatic dilatations [21]. We performed AVF ligation with aneurysm resection following a successful renal transplant in 13 (26%) patients after a mean of 4.2 ± 3.0 (0.5-12) years. We performed surgery for one of these patients due to painful thrombosis of aneurysm and 12 for poor cosmetic appearance. No arterial aneurysm was detected in any of these patients.

In patients with symptomatic AVF aneurysms, it is important to differentiate if it is venous and/or arterial aneurysm to reduce complications. Patients who are in a risk group should be evaluated with CDDUS before surgery. It should be kept in mind that especially patients with hypertension and under long hemodialysis programme period may be at higher risk for arterial aneurysm. The parallel result between the duration of the hemodialysis programme and the risk of arterial aneurysm development demonstrated statistical significance ($p = 0.012$) in our study. While only ligation of fistula is sufficient for patients with venous aneurysm, it may be necessary to use native or prosthetic materials for arterial repair in patients underwent arterial aneurysm excision. For this reason, prosthetic conduit should be available in the operating room.

Conclusion

Aneurysms formation can be prevented by appropriate precautions such as preferring distal anastomoses, determining anastomotic diameter appropriately, identifying patients with comorbidities that may be caused by vasculopathies, avoiding central venous catheterization, early construction of the fistula (preemtive patients), avoiding cannulation in the same localization. The choice of a treatment modality that is important in symptomatic arteriovenous fistula aneurysms is to maintain the continuity of the arteriovenous fistula [23,24]. Arterial aneurysm is a rare complication of vascular access and especially

exist in brachiocephalic AVF. Although it causes serious symptoms including those of related such as thrombosis, ischemia, nerve compression, the most important complication is aneurysm rupture. Ligation of fistula should be considered when acute bleeding in an unstable patient occurs. Preservation and repair of arterial structures in patients undergoing arterial aneurysm excision and fistula ligation may prevent extremity problems due to loss of arterial circulation. Therefore, preoperative evaluation and appropriate surgical interventions will prevent morbidities that may arise.

Riassunto

Studio sul trattamento degli aneurismi sintomatici correlati con fistola artero-venosa, condotto su 50 pazienti operati tra gennaio 2011 e gennaio 2017. n 44 pazienti (88%) la fistola era chiusa per la presenza di aneurisma venoso sintomatico. n 6 pazienti (12%) si trattava di vero aneurisma arterioso dell'arteria brachiale ed un segmento dell'arteria è stato asportato con successiva riparazione.
I più comuni aneurismi sintomatici sono stati osservari a livello della fistola brachiocefalica: 32 pazienti (64%). I sintomi erano rappresentati da trombosi dell'aneurisma (15 casi = 30%), sindrome da furto (9 casi = 18%), emorragia massiva da rottura (7 casi = 14%), infezione (7 casi = 14%), necrosi cutanea (5 casi = 10%), ipetensione venosa (4 casi = 8%), insufficienza cardiaca ad alta gittata (1 caso = 2%).
Nove pazienti (18%) presentavano due o più sintomi. Mentre la durata media della dialisi dei pazienti sottoposti ad aneurismectomia venosa era di 6,9 ± 4.2 anni, nei pazienti sottoposti ad aneurismectomia arteriosa e riparazione dell'arteria brachiale la durata media era di 11.7 ± 3.6 anni (p=0.012).
L'aneurisma arterioso rappresenta una complicazione rara dell'accesso vascolare per la dialisi. Nonostante esso provochi sintomi importanti inclusi quelli correlati a trombosi, ischemia, compressione nervosa, la complicanza maggiore è la rottura dell'aneurisma. Pertanto una valutazione preoperatoria ed una procedura chirurgica adeguata può prevenire le patologie che potrebbero insorgere.
La scelta delle modalità del trattamento nei pazienti con aneurismi sintomatici di fistole arterovenose è finalizzata a mantenere la continuità della stessa fistola arterovenosa, ma nel caso di insorgenza di una emorragia acuta in paziente emodinamicamente instabili bisogna prendere in considerazione la legatura della fistola.

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