The role of angioplasty in haemodialysis patients with symptomatic venous hypertension owing to central venous stenosis

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Background
Central venous stenosis (CVS) is a serious problem in hemodialysis (HD) patients, often presenting with symptoms of venous hypertension. Endovascular treatment is aimed to provide symptomatic relief and to maintain HD access patency.
Aim
To evaluate our experience in the endovascular treatment of CVS in HD patients and to determine the relationship between the temporary catheter insertion, the type of arteriovenous fistula, and development of CVS.
Patients and methods
A prospective study was carried out on 30 patients with End Stage Renal Disease (ESRD) undergoing HD presented with symptomatic venous hypertension in the same side of vascular access, between October 2015 and October 2017. All the patients underwent endovascular treatment and were analyzed.
Results
A total of 30 (20 male and 10 female) patients underwent endovascular interventions for CVS during a time period of 2 years, where 20 stenotic segments were in subclavian vein, six in innominate vein, and four in iliac veins. The technical success rate for endovascular treatment was 80%. Eighteen (75%) patients were treated by ballooning of the stenosed segment alone, whereas six (25%) patients needed primary stenting owing to tight recoiling of the stenotic lesion. Four patients needed reintervention during follow-up (three cases managed by balloon dilatation alone and one needed venous stent after dilatation).
Conclusion
Endovascular treatment is safe and effective in managing CVS. The incidence of CVS is higher with central venous catheter insertion and proximal arteriovenous fistula.

Keywords:
angioplasty, central venous stenosis, endovascular, hemodialysis, stent

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Introduction

During the recent decades, there have been significant advances in quality of care and life span of hemodialysis (HD) patients. Consequently, it is very common for HD patients to have exhausted their arteriovenous access options in both upper and lower limbs and develop many complications [1].

Arteriovenous fistulas have many complications either systemic or local. Systemic complications include high cardiac output and heart failure, especially with proximal fistulas, and local complications include venous hypertension, steal syndrome, and aneurysmal dilatation of the outflow vein of the anastomosis [2].

Central venous occlusive disease (CVOD) is defined as the occlusion or stenosis of 50% or greater involving the lumen of the internal jugular, subclavian, axillary, innominate or superior cava veins. It is a major problem in patients on HD causing significant morbidity (venous hypertension) and may lead to access dysfunction [3].

The causes of central venous stenosis (CVS) in such patients are venous trauma caused by the repeated punctures and cannulations, hypercirculation accompanied by turbulences especially with proximal arteriovenous fistula (AVF), aggregation of thrombocytes and occurrence of thrombi leading to intimal hyperplasia and fibrosis at the site of the original stenosis [4].

The site of insertion of the central venous catheter is considered an important risk factor for development of CVS. The catheters placed in subclavian veins carry the

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highest risk, with a 42% incidence of CVS compared with 0–10% incidence in cases of internal jugular vein access [5].

Therefore, in patients with renal impairment, central and peripheral venous access placement should be avoided as much as possible. The insertion of peripheral venous lines should be reduced to preserve future peripheral potential access sites [6].

Symptomatic CVS typically present with arm edema, dilated collateral neck and chest wall veins, and prolonged bleeding from puncture site after HD, whereas asymptomatic CVS can be detected by elevated static venous pressures or elevated pump pressures during dialysis sessions that may need ligation of the fistula to relieve symptoms if severe [7].

Surgical and endovascular treatments are available for treatment of central venous stenosis (CVS). Although high primary patency rates (80–90% at 1 year) have been reported with open surgical repair of the central veins, it carries a high rate of postoperative morbidity and mortality. Endovascular management has been widely accepted as the treatment of choice for CVS [8].

The endovascular options include percutaneous transluminal angioplasty with or without stent deployment. The Kidney Disease Outcomes Quality Initiative guidelines recommend endovascular treatment with percutaneous transluminal angioplasty first, with second-line stent deployment as the preferred treatment line to CVS [9].

Objectives

The aim of this study was to evaluate our experience with endovascular treatment of COVD in HD patients (indications, success rate and complications). Moreover, we aimed in this study to determine the effect of temporary central venous dialysis catheters and the type of the AVF on the development of CVS.

Patients and methods

Patients

This is a prospective study carried out at Menoufia University Hospitals on 30 patients with End Stage Renal Disease (ESRD) on HD complaining of symptomatic venous hypertension in the form of ipsilateral arm, chest, or facial edema; ipsilateral arm pain; color changes; cyanosis; ulceration; distended collateral veins over the access limb or chest wall; or prolonged bleeding from access puncture site at the end of dialysis sessions owing to CVS with functioning AVF or AVG during the period from October 2015 to October 2017. The study was granted an ethical approval from the Institutional Review Board at Faculty of Medicine, Menoufia University, Egypt.

All patients were subjected to endovascular options (balloon angioplasty with or without stenting) after failure of conservative measures in form of limb elevation and elastic compression to relieve their symptoms.

All patients were subjected to following:

(1) Medical history.
(2) Clinical examination including vascular examination focusing on rest pain or during dialysis, edema of the limb with AVF, skin changes like change in color, cyanosis, and ulceration.
(3) Investigations either laboratory such as coagulation profile or radiological such as duplex ultrasonography to assess the preoperative and postoperative blood flow in the fistula and computed tomography venography to detect the site and length of lesion.

Methods

All cases were operated in an angioplasty operating room with peripheral vascular capabilities under complete aseptic conditions using nonionic contrast medium (Ultravist, Bayer company, Germany), using balloons and stents of different sizes (from 7 to 18 mm). A balloon size 10% larger than the nonstenotic vein of interest was typically selected. The procedure was done under either local, regional, or general anesthesia using balloon angioplasty alone or combined with venous stent according to each case.

Each case was documented individually according to anesthesia (local, regional, or general), site of puncture, duration of the procedure, equipment used (sheath French size; guide wire, balloon, or stent type; or guiding catheter if used) and pressure used.

All patients received a loading dose of 300 mg of clopidogrel 12 h before the procedure and intraprocedurally, and then received a bolus of 5000 IU of heparin (70 : 100 U/kg) after insertion of the sheath. In cases in which the wire succeeded to cross the lesion, a high-pressure balloon was positioned and expanded, and if there was greater than 30% residual stenosis, a second angioplasty was performed, using a cutting balloon and/or self-expanding stent Fig. 1.

Technique

Venous access was obtained through AVF in all cases of CVS, and we trialed to traverse the stenotic site using a 0.035-inch hydrophilic guide wire (Terumo, India). In difficult cases where the guide wire failed to cross the stenotic lesion, the stiff end of the guide wire was also used, which succeeded in two cases. Moreover, microcatheters and micro-guide wires (coronary wires) were used and succeeded in only one case. Combined approach using both AVF and femoral vein was used in five cases and succeeded in only one case.

All patients were evaluated immediately postoperative and then followed up in the outpatient clinic after 3, 6 and 12 months for feasibility of the fistula for dialysis, duplex to detect the improvement of blood flow through the fistula, and postoperative complications Fig. 2.

Outcomes

The primary outcome was to evaluate the improvement of blood flow rate through the fistula after balloon angioplasty with or without stenting for treating the CVS. Secondary outcome was to determine the relationship between the central venous temporary dialysis catheters, the site of the AVF, and development of CVS.

Failure of the guide wire to cross the stenotic or occluded segment of the vein was considered as primary failure of the procedure.

Statistical analysis

Results were statistically analyzed by SPSS, version 22 (SPSS Inc., Chicago, Illinois, USA) and the following was performed: (a) descriptive analysis for the quantitative data, for example, percentage, mean, and SD, and (b) paired *t*-test for parametric data. *P* value was considered significant if up to 0.05.

Results

Our study included 30 patients with ESRD on regular HD who presented with symptomatic venous hypertension owing to CVS. The male to female ratio was 2 : 1. The mean age of the patients was 52.5 years. A total of 14 (46.7%) patients had diabetes mellitus, nine (30%) patients had hypertension and five (16.7%) patients had heart diseases as shown in Table 1.

In our study, it is apparent that venous hypertension is not linked to particular sex or age group. The endovascular management interventions were used as primary line of treatment after failure of conservative measures to relieve symptoms of venous hypertension. In our study, 20 (66.7%) patients were operated under local anesthesia, six (20%) patients received general anesthesia, and the remaining four (13.3%) patients received regional (spinal anesthesia).

Computed tomography venography in the studied patients demonstrated stenosis of subclavian vein in 20 (66.7%) patients, six (20%) patients had stenosis in innominate vein, four (13.3%) patients had iliac vein stenosis, and no patient had stenosis or occlusion of internal jugular vein or superior vena cava.

Regarding primary outcome in this study, the blood flow rate through the fistula improved significantly after the endovascular interventions (balloon angioplasty with or without stenting) with mean fistula flow rate of 593 ml/min preoperatively and 1964 ml/min postoperatively (P=0.001), as shown in Table 2.

Table 1 General characteristics and associated comorbidities of patients

General characteristics	Study group (n=30) [n (%)]
Age (years)	
Mean±SD	52.53±6.60
Range	35–65
Sex [n (%)]	
Male	20 (66.7)
Female	10 (33.3)
Comorbidities [n (%)]	
Hypertension	9 (30)
DM	14 (46.7)
Hypertension and DM	23 (76.7)
Heart diseases	5 (16.7)

DM, diabetes mellitus.

Table 2 Distribution of the studied group regarding the flow rate (ml/min) before and after intervention

	Total flow (ml/min)			Paired *t*-test	*P* value
	Before (mean±SD)	After (mean±SD)	Relative change		
In all patients (n=22)	593.18±134.63	1964.54±598.28	1371.36±552.86	11.63	<0.001*
Increased flow (n=21)	601.90±131.43	2047.61±465.21	1445.71±439.59	15.07	<0.001*
In patients with access (n=20)	586.0±138.95	1956.0±628.10	1370.0±581.19	10.54	<0.001*
Initial flow ≤580 ml/min (n=11)	477.27±55.33	1801.81±679.15	1324.54±659.45	6.66	<0.001*
Initial flow >580 ml/min (n=11)	709.09±73.81	2127.27±481.85	1418.18±449.64	10.46	<0.001*

*Statistically significant value.

In our study, 15 (50%) patients had brachiocephalic fistula, 10 (33.3%) patients had brachiobasilic fistula, four (13.3%) patients had femoral arteriovenous synthetic grafts, and one (3.3%) patient had radiocephalic fistula as documented in Table 3. This indicated that the incidence of CVS was higher in the patients with proximal AVF than those with distal ones, and this was considered one of the secondary outcomes in this study (the relationship between type of fistula and development of CVS).

Moreover, all patients (100%) had history of temporary central venous catheter insertion at the ipsilateral limb complicated with venous hypertension. Twenty-one (70%) patients had previous subclavian vein catheters, five (16.7%) patients had internal jugular vein catheters, and four (13.3%) patients had femoral vein dialysis catheters, as shown in Table 3. This indicated that the insertion of temporary dialysis catheters for HD is a very potent precipitating factor for development of CVS, especially with subclavian vein catheter insertion.

Table 3 Medical characteristics of the studied groups

Medical characteristics	Study group (*n*=30)
Duration of chronic renal failure (years)	
Mean±SD	9.62±7.17
Range	1–24
Duration of fistula (m)	
Mean±SD	3.63±2.74
Range	1–12
Limb	
Upper	26 (86.7)
Lower	4 (13.3)
Site of previous catheter insertion	
Subclavian vein	21 (70)
Femoral vein	4 (13.3)
Internal jugular vein	5 (16.7)
Stenosed central vein	
Subclavian	20 (66.7)
Iliac	4 (13.3)
Innominate	6 (20.0)
Site of fistula	
Right upper	10 (33.3)
Right lower	1 (3.3)
Left upper	16 (53.3)
Left lower	3 (10.0)
Type of fistula	
BCF	15 (50)
BBF	10 (33.3)
RCF	1 (3.3)
Femoral	4 (13.3)
Sheath introduction	
Fistula access	25 (83.3)
Fistula access+femoral vein	5 (16.7)

BBF, brachio basilic fistula; BCF, brachio cephalic fistula; RCF, radio cephalic fistula.

In six (20%) patients, the guide wire failed to completely cross the stenotic or the occluded lesion, which was considered as primary failure, whereas in 24 (80%) patients, endovascular interventions were successful, and results were satisfactory [18 (75%) patients were treated by ballooning of the stenosed segment alone whereas six (25%) patients needed primary stenting owing to tight recoiling of the stenotic lesion].

Four (13.3%) patients needed reintervention during the first 6 months from the first angioplasty: three cases were managed successfully by balloon dilatation only, whereas the forth one needed balloon dilatation and venous stent deployment. Only one (4.2%) patient was complicated by subclavian stent fracture and one (4.2%) patient died after 1 year from nonvascular cause. Immediate technical success was achieved in 24 (80%) cases. The primary patency rate at 3, 6, and 12 months was 80, 63, and 63%, respectively (Table 4).

Discussion

Venous hypertension is a significant problem for HD patients that may result in severe limb edema, arteriovenous access dysfunction, and ligation of the fistula in severe cases [10].

The incidence of CVS is increasing because of its association with the use of central venous catheters, especially subclavian vein, as evaluated by many authors. Kundu [11] has reported that the incidence of CVS in patients with ESRD on HD in the USA has decreased significantly after the widespread transition from subclavian to jugular access for HD catheters.

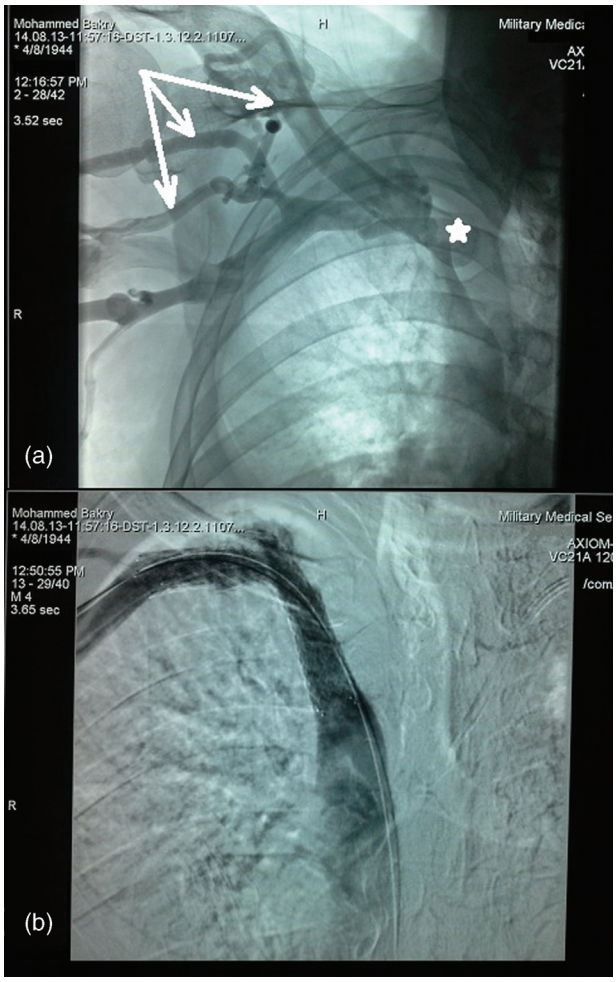
Hossny [12] has reported in his study that venous hypertension was mostly owing to a preoperative undiagnosed subclavian vein outflow problem caused by an ipsilateral subclavian catheter.

All these mentioned studies are in agreement with the results in our study, in which 70% of our patients with

Table 4 Follow-up of the studied group

Outcome	Follow-up [*n* (%)]		
	After 3 months (*N*=30)	After 6 months (*N*=24)	After 12 months (*N*=24)
Improved	24 (80)	19 (79.2)	23 (95.8)
Primary failure	6 (20)	–	–
Stent or balloon	–	4 (16.7)	–
Stent fractures	–	1 (4.2)	–
Died	–	–	1 (4.2)

Figure 1



Example of endovascular management of CVS (a), showing right subclavian vein stenosis at the site of star, and arrows indicating collateral veins as a result of subclavian stenosis (b), showing subclavian stent deployed, improvement of flow and disappearance of collateral veins.

CVS had history of subclavian vein catheter insertion in the ipsilateral side of venous hypertension.

The recent study by Trerotola *et al.* [13] revealed higher incidence of symptomatic CVS in patients with arteriovenous grafts (52%) compared with 29% in AVFs. This may be owing to greater capacitance of AVF than grafts, but these results did not match with our results and may be owing to the higher incidence of usage of synthetic graft outsides compared with autogenous fistula. They also revealed that the incidence of symptomatic CVS is higher in patients with upper arm access than those with forearm access regardless of the access type, and these results match with the results in our study.

COVD can be symptomatic or asymptomatic. Symptoms vary depending on progression and the anatomic position of the disease. Stenosis and occlusions in subclavian veins can cause venous hypertension in upper limbs, characterized by edema, cyanosis, varicose veins, hyperpigmentation and even ulcers. Stenosis in the innominate vein can cause facial and chest edema and collateral veins over the chest wall. In patients on HD, output may be reduced and venous pressure increased, leading to inefficient dialysis [14].

At present, endovascular treatment is the treatment of choice for Central Venous Disease (CVD), which can be done by balloon angioplasty with or without stenting, and more recently, cutting balloon and stent graft have been used. Rates of immediate technical success of balloon angioplasties alone can vary from 70 to 90% as shown in the study done by Bakken *et al.* [15] on 47 patients with ESRD presented with symptomatic CVS who underwent balloon angioplasty, where the primary patency rates at 3, 6, and 12 months were 58, 45, and 29%, respectively, compared with 80, 63, and 63%, respectively, in our study.

Moreover, a recent study by Yadav *et al.* [16] reported a technical success rate of 81.8%, which is nearly similar to our result (80%).

The optimal management strategy is still not clear. Primary stenting has been advocated by some for the treatment of CVD, whereas others have advocated balloon angioplasty as the primary treatment, reserving stenting for treatment failure or restenosis, and we applied the last strategy in our study [17].

Jones *et al.* [18] reported 70–90% immediate technical success rate of angioplasty for CVS in their study, which is significantly similar to the success rate in our study (80%). The 6-month primary patency rates ranged from 23 to 63% compared with 63% in our study. Bare metal stent provided higher patency rates (55–100%) in 6 months. Stent grafts prevent in-stent stenosis from intimal hyperplasia and provide an 81% primary patency at 6 months after placement.

The advantages of these covered stents is that they provide a relatively inert and stable intravascular matrix for endothelization that could reduce the intimal hyperplasia response, reducing restenosis rates after angioplasty. Kundu *et al.* [19] published a study in which they employed eight covered stents for treatment of CVS, reporting primary patency at 3, 6 and 9 months of 100%.

In our study, seven venous stents were used, where six were used primarily at the first intervention owing to

Figure 2

Example of clinical improvement of upper limb swelling (a), preoperative right upper limb edema (b), 1-year postoperative indicating relieving of edema, which was following subclavian stent deployment indicated in Fig. 1.

recoiling tight stenotic lesion, whereas the seventh one was used in the secondary reintervention owing to restenosis, and no stent grafts were used.

Conclusion

Placement of central venous catheters or venous interventions are the most important risk factors for COVD. So, prevention is necessary, including rational use of central venous access and appropriate planning of creation of AVFs in predialytic patients.

COVD is also more common in HD patients with proximal fistulas than distal ones.

The endovascular treatment is an effective and safe method for treatment of CVD in patients undergoing HD. It has a high technical success rate without significant morbidity or mortality. In spite of that, the patients may develop restenosis or occlusion later on that may require multiple interventions to maintain patency. The use of stent graft decreases the incidence of in-stent intimal hyperplasia and stenosis and improves patency.

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Conflicts of interest

There are no conflicts of interest.

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