Original Article

Arterio-Venous Fistula Flow Dynamics and Results of Surgical Revision using Distal Inflow in Patients with Massive Limb Edema from Central Venous Occlusion

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Objective: To investigate the flow dynamics and outcomes of AVF flow reduction surgery using distal inflow in such patients.

Materials and Methods: A prospectively collected data on AVF flow dynamics of 19 hemodialysis patients with neck or arm edema from central venous occlusion and the outcomes of eight flow reduction procedures between February 2011 and December 2014 were retrospectively reviewed. AVF flow rate was measured by duplex Doppler ultrasound. Flow reduction surgery was performed in patients with high flow AVF by switching the inflow to radial or ulnar artery. Outcomes of surgery were assessed in terms of AVF flow rate reduction and relief of edema.

Results: Of the 19 patients included, the mean age of AVFs was 5.3±3.6 years. Fifteen patients (79%) had brachial artery inflow AVF and the remaining four patients (21%) had radial artery inflow fistula. The mean flow rates of brachial and radial artery based AVFs were 2,191±1,367 ml/min and 1,455±560 ml/min, respectively. Eight AVF surgical revisions using distal inflow were performed in seven patients, which resulted in a significant reduction of mean flow rate from 2,900±1,256 ml/min to 860±480 ml/min ($p<0.001$). Relief of edema was achieved in 7 out of 8 instances.

Conclusion: AVF flow rate tended to be high in most of the circumstances. The surgical revision using distal inflow significantly reduced AVF flow rate and improved limb edema. This procedure could be a viable option in high flow AVF patients.

Keywords: Arterio-venous fistula, Central venous occlusion, Edema, Limb swelling

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Upper limb edema from central venous occlusion is a major complication facing chronic renal disease patients who have hemodialysis treatment via their arteriovenous fistula (AVF)[1]. Although not common, a presentation can significantly incapacitate the patient's well-being with disfigurement, heaviness, pain and movement limitation[1]. In addition, it can cause needling difficulty leading to inadequate dialysis and subsequent loss of AVF patency[2]. This unfavorable event also precludes the possibility of creating a new AVF on the affected limb, resulting in an increase risk of morbidity and mortality in a patient.

In contrast to the usual low flow rate associated with occlusive lesions of the efferent venous limbs, we observed a paradoxically high AVF flow in many swollen limb or neck patients associated with central venous occlusion. Several authors have proposed risk factors for central venous stenosis among hemodialysis patients[3,4]. Nevertheless, little is known about the natural history of central venous occlusion, especially the flow dynamics of affected AVFs. From a surgical viewpoint, knowing the course of disease would guide vascular surgeons in providing proper investigations and suitable management to affected patients. In addition, those patients who experience this adverse event would be thoroughly counseled regarding the natural history of disease, plan of treatment, and AVF prognosis.

The objective of the present study was to determine the AVF flow dynamics of patients who had arm or neck edema due to central venous occlusion. A further aim was to investigate outcomes of AVF flow reduction surgery by using distal inflow in patients with high in flow AVF.

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Materials and Methods

Study population

The prospectively collected data of successive patients who had hemodialysis treatment via AVF and presented with ipsilateral limbs or neck edema from central venous occlusion to our hospital between February 2011 and December 2014 were retrospectively reviewed. The authors included patients with edema that persisted for at least three weeks. The circumference of symptomatic limb must be at least 20% higher than the contralateral side, which corresponded to a 44% increase in the cross-sectional area. An imaging confirmation (e.g. AVF venography, CT

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venography or ultrasonography) of central venous occlusion must be obtained. The degree of venous stenosis was considered significant if it was 90% or greater. The exclusion criteria were patients with post-AVF creation edema. The study received approval from the Vajira Institutional Review Board (approval number 30/2557) and was performed in accordance with the Declaration of Helsinki.

Data collection

The data were collected following the standard protocol which included: patients' demographics; age and type of AVF; type of AVF conduit (autogenous vein or prosthetic graft); edema duration; related symptoms and physical findings; and magnitude of edema measured by mid upper-arm and upper third of forearm circumferences, or neck circumferences, as relevant to particular patients. In the cases with arm edema, the contralateral upper arm and forearm circumferences were also recorded.

All patients underwent ultrasonographic examination (model LOGIQ 9, GE Healthcare, Milwaukee, WI) by experienced vascular surgeons. The collected data included: AVF diameter, AVF flow rate, brachial artery diameter, brachial artery flow rate and radial artery flow rate. The flow rates were computed using scanner program assuming vessel circularity. The efferent venous segments, continuing from the anastomosis without prior branching, with homogeneous unidirectional flow as viewed in the color Doppler mode, were used for AVF flow rate measurement. The locations were recorded for further re-measurement to assess the results of flow reducing surgery among patients who underwent surgical revision of high flow AVF. The brachial artery diameter and flow rate were measured at the proximal one-third of the upper-arm. The upper arm and forearm cross-sectional areas were calculated from the measured circumferences assuming limb circularity and used for surgical outcome assessment.

Surgical revision of high flow AVF and outcome assessment

Flow reduction surgery was offered to patients with AVF flow rate of more than 1,500 ml/min that coexisted with occlusive lesions of the central vein at a site, which were unapproachable without thoracotomy, extra-anatomical bypass surgery or using endovascular technique. Each individual patient was informed of the innovative nature of the utilization of surgical methods and consent was obtained before the operation. Only patients who did not have pre-existing cause of arm edema would be included. Operations were performed following the strategy of: 1) Conversion of AVF arterial inflow distally to radial or ulnar artery, which was not previously subjected to flow increasing adaptation; and 2) Autogenous vein or standard wall 5 mm polytetrafluoroethylene prosthetic graft interpositioning between the new distal inflow and the AVF limb (Figure 1). Based on this strategy, the anastomosis of patients with brachial artery based AVF would be switched to the radial or ulnar artery, whereas the anastomosis of the radial artery based AVF would be switched to the ulnar artery. Prophylactic intravenous cefazolin was routinely given.

Outcomes of surgery were assessed in terms of AVF flow rate reduction and relief of edema, which were monitored on day x after surgery. The location of AVF flow rate measurement, the ultrasound machine used, and the upper arm and forearm measurement were done using similar techniques to those performed before the operation.

Statistical analysis

All statistical analyses were performed using SPSS software version 22.0 for Windows (IBM corporation, Armonk, NY, USA). Continuous variables are presented as median with range. Categorized variables are displayed as number (percentage). The Mann Whitney U test was used to compare continuous parameters. A value of $p<0.05$ was considered statistically significant.

Results

Nineteen successive patients at our vascular clinic from February 2011 to December 2014 met the inclusion criteria. Seventeen patients presented with arm and forearm edema and two patients presented with neck and face edema. Most of AVFs (n = 16, 84.2%) were autogenous type. The mean fistula age was 5.3±3.6 years (range 1 to 13 years). The mean duration of swollen symptoms was 18±26 weeks (range 3 to 104 weeks). Among patients with limb edema, the mean circumferences of the upper arm and forearm were 32.7±4.1 cm (range 26 to 40 cm) and 30.5±3.6 cm (range 25 to 37 cm), respectively. The calculated cross-sectional areas of the upper arm or forearm in the swollen side were larger than the normal contralateral size by the mean value of 93±71 percent (range 31 to 422 percent). The dermal hyperpigmentation and liposclerosis, which are typical characteristics of chronic

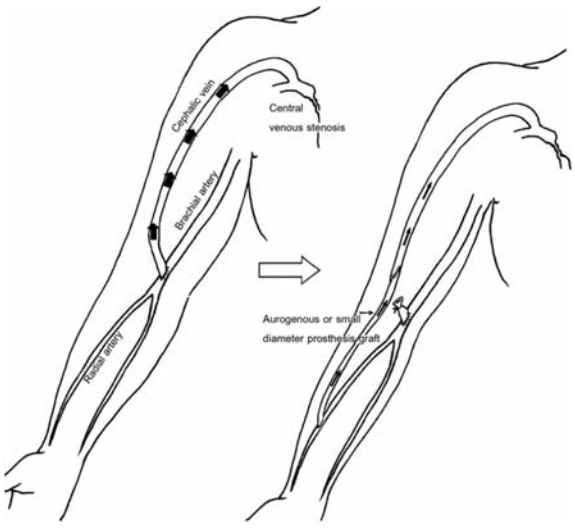


Figure 1. Flow reduction surgery.

venous insufficiency were noted in three patients. The clinical characteristics of these patients are presented in detail in Table 1.

For the brachial artery based fistula (n = 15) and radial artery based AVF (n = 4), the mean AVF flow rates were 2,191±1,367 ml/min (range 463 to 4,695 ml/min) and 1,455±560 ml/min (range 621 to 1,791 ml/min), respectively. The mean diameter of brachial artery of the limb with more than 1,200 ml/min AVF flow rate was significantly larger than that of the limb with the AVF flow rate less than 1,200 ml/min (6.7±1.7 mm, range 4.8 to 11.3 mm vs. 4.7±0.5 mm, range 4.2 to 5.3 mm, $p = 0.009$).

Seven patients had eight AVF surgical revisions using distal inflow. The patients' details and the surgical results are summarized in the Figure 2. The locations of central venous occlusion in these patients were: superior vena cava (n = 1), brachiocephalic vein (n = 1), and subclavian vein (n = 3). Five (71.4%) were complete obstructive lesions while the other two lesions (28.6%) were stenosis. Seven of eight operations were performed under local anesthesia. The pre-operative mean AVF flow rate was 2, 900±1,256 ml/min (range 1,642 to 4,695 ml/min), which was significantly reduced to 860±480 ml/min (range 260 to 1,612 ml/min, $p<0.001$) post operatively. There were no operative complications.

Table 1. Clinical characteristics of 19 chronic renal disease patients with upper limb swelling from central venous obstruction

Characteristic	Total (n = 19)
Age (years)	
Mean (SD)	55 (15)
Range	28 to 78
Sex, n (%)	
Male	7 (36.8)
Female	12 (63.2)
Side of fistula, n (%)	
Left	11
Right	8
Fistula age (years)	
Mean (SD)	5.3 (3.6)
Range	1 to 13
Type of AVF, n (%)	
Autogenous brachiocephalic type	10 (52.6)
Autogenous brachiobasilic with venous transposition	2 (10.5)
Autogenous radiocephalic type	4 (21.1)
Forearm loop prosthesis brachiobasilic type	2 (10.5)
Upper-arm loop prosthesis brachiobasilic fistula	1 (5.3)
Duration of swelling symptoms (weeks), median (IR)	
Mean (SD)	18 (26)
Range	3 to 104
Central venous occlusion site, n (%)	
Brachiocephalic trunk	8 (42.1)
Subclavian vein	6 (31.6)
Brachio-cephalic subclavian junction	2 (10.5)
Cephalo-subclavian junction	2 (10.5)
Superior vena cava	1 (5.3)

AVF = arterio-venous fistula; IR = interquartile range; n = number; SD = standard deviation

Alleviation of edema was achieved in seven circumstances including two operations for a patient who presented twice with face and neck edema. The initial operation in this patient was a conversion of brachiocephalic to radiocephalic AVF using the available forearm cephalic vein, which completely resolved her swelling symptoms. Three and a half years later, her symptoms recurred, presumably from adaptive flow increase of the AVF (2,062 ml/min). The re-distalization with 5 mm interposition graft between the distal end of radial artery and upper arm cephalic vein resulted in complete resolution of her edema. In five patients whose arm edema was relieved, the percent excess cross-sectional area of the swollen arms over the contralateral arms was significantly reduced compared with the pre-operative value (upper arm, pre-operative mean 97±27 percent [range 59 to 134 percent) vs. postoperative mean 58±47 percent [range 0 to 111 percent), $p = 0.016$; and forearm, pre-operative 91±6 percent [range 82 to 96 percent) vs. postoperative mean 25±26 percent [range 0 to 56 percent), $p<0.01$). One limb failed to improve despite significant reduction of the AVF flow rate (4,496 ml/min to 1,612 ml/min).

Discussion

Evidence suggests that limb edema from central venous obstruction in hemodialysis patients is caused by outflow restriction. In this regard, the reduction of AVF flow rate is expected. For venous obstructive lesions in arms, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) guidelines advocate the association of AVF flow below 600 ml/min with the presence of efferent venous limb stenosis or obstruction[5]. In contrast to the KDOQI guidelines, the present study found that only a small proportion of swollen limbs associated with central venous occlusion had low flow AVF regardless of the lesion being completely obstructed in the majority of circumstances. The mean flow rates of brachial artery based AVF and radial artery based AVF and proportion of the high flow AVF observed in this study surpassed the documented flow characteristics of normal AVF reported by several authors[6-8]: 2,191 ml/min vs. 1,247 to 1,290 ml/min[6-8], 1,455 ml/min vs. 647 to 1,063 ml/min[7,8] and 40% vs. 15%[8], respectively (Figure 3). The authors hypothesize that the edema develops as a result of the flow increasing adaptation that exceeds the capacity of the venous collateral drainage around the pre-existing flow of occlusive lesions. This is supported by our findings that: 1) The brachial arteries of higher flow AVF were significantly larger than the lower flow AVF; 2) the majority (81%) of the patients had the brachial based autogenous AVF which inherently delivers a higher flow compared to the radial artery based[9] or the prosthetic

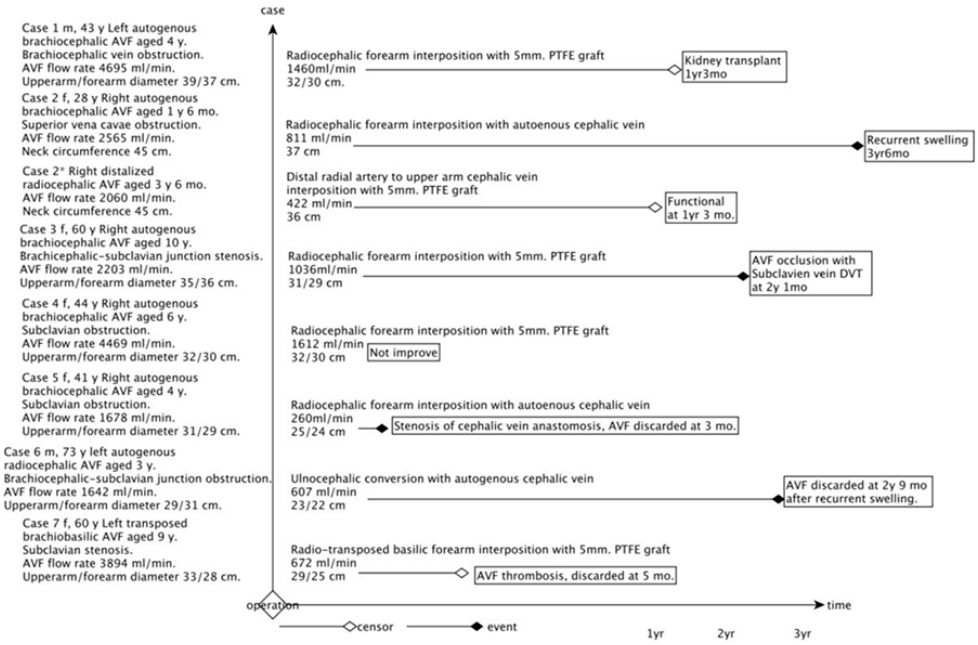


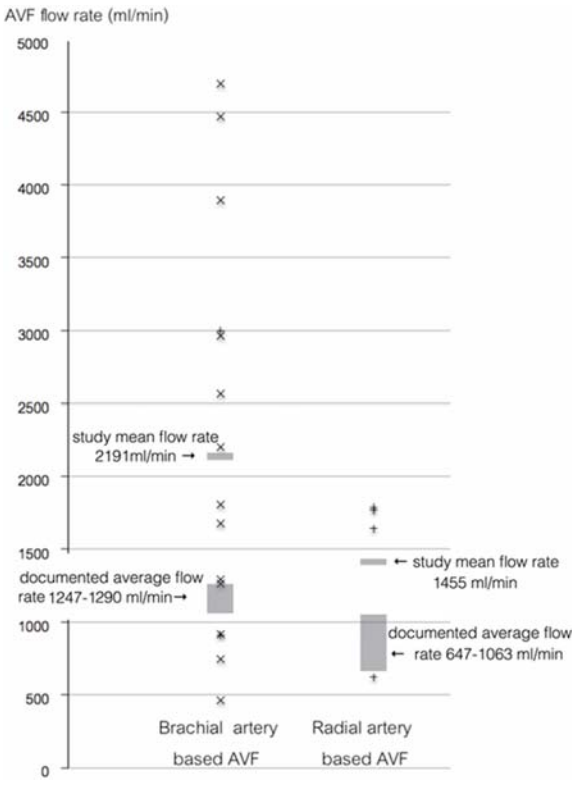
Figure 2. Patients' details and results of 7 patients who underwent surgical revision (case 2 underwent surgical revision for 2 times).

graft AVF; 3) the swelling symptoms developed long after the AVF creation, allowing time for the vessels' adaptive dilatation; and 4) flow reduction surgery resulted in edema alleviation despite the residual occlusive lesions. The paradoxical high flow coexisted with occlusive lesions[10,11], the predominant type of autogenous AVF with brachial artery inflow[11-14] and the symptoms that manifested long after AVF creation[11,12] have previously been observed in AVF complicated by steal syndrome, heart failure or swollen limbs.

Surgical revision using distal inflow has been described for the treatment of high flow AVF complicated by steal syndrome or congestive heart failure[15-17]. The present study reported the innovative utilization of this technique for the edematous complication of the central venous occlusion. By distalization of the AVF, arterial inflow to the wrist connects back to the fistula with a small diameter conduit, preferably to the in situ autogenous vein, and the AVF flow rate could be effectively reduced. This resulted in resolutions of arms or neck edema of the participants in this preliminary study. With this technique, the augmentation of a fistula's resistance was achieved by incorporating the small diameter system of the whole forearm, back (conduit) and forth (radial or ulnar arteries). In the majority of patients with brachial artery based AVF, inflow distalization could be performed by switching the anastomosis to radial or ulnar artery. For the radial artery based AVF, the anastomosis could be switched to the ulnar artery. This is a low risk surgery and no major complications materializing in the present study. However, the resolution of swelling symptoms is not prompt, usually takes 1 to 2 weeks and the placing of a prosthetic graft on the massively swollen limb could potentially predisposes to wound complication.

Although the configuration of the distalized AVF is similar to normal autogenous or straight prosthesis forearm AVF and reasonable patency was achieved in the majority of the patients in the present study, the small size of the prosthetic grafts, the suboptimal quality of the available autogenous veins and the size discrepancy between the interposition grafts and the gigantic AVF may account for the early failure in some patients.

Several techniques have been proposed as therapeutic options for central venous occlusion among hemodialysis patients. The bypass surgery to the right atrium has been reported for the symptomatic central venous obstructive cases. This technique is invasive, so it is considered high risk and regarded as a last resort option[18-20]. Aside from this, extra-anatomical bypass, such as axillary to internal jugular vein, axillary to femoral vein or direct repair of subclavian vein have been reported in a small number of patients[21-24]. Another save and less invasive technique is the endovascular stenting of the central venous obstruction site. However, this method usually requires re-intervention to maintain optimal AVF patency rate[11,25,26]. To be noted, correction of central venous occlusive lesion of the high flow AVF could lead to even higher AVF flow. Cardiac complications as a consequence of high AVF flow rate, although not common, have been reported in several studies[5,7,16,27,28]. In this regard, based on our findings, in approaching the swollen limb patients with central venous



AVF = arterio-venous fistula

Figure 3. The mean flow rates of brachial artery based AVF and radial artery based AVF among patients with high flow AVF compared to flow characteristics of normal AVF.

occlusion, the AVF flow status should be investigated. In patients with high flow AVF, the fistula revision using distal inflow is a viable option.

The limitation of the present study is the small number of enrolled patients caused by the sporadic nature of the condition. Hence, our results needed to be confirmed in other settings with different population backgrounds. Furthermore, the present study focused only on short-term outcomes after surgery, including AVF flow rate reduction and relief of edema, and the duration of postoperative follow-up in each patient was less than four year. So, further research with larger sample size and longer follow-up period is required to determine the patency of AVF after this surgical procedure as well as quality of life among patients with high inflow of AVF.

Conclusion

AVF flow rate tended to be high in most of the circumstances. The surgical revision using distal inflow significantly reduced AVF flow rate and improved limb edema. This procedure could be a viable option in high flow AVF patients.

What is already known on this topic?

Upper limb edema from central venous occlusion among chronic renal disease patients who have hemodialysis via their AVF can significantly incapacitate patient's well-being with disfigurement, heaviness, pain, movement limitation and needling difficulty leading to inadequate dialysis. It is known that occlusive lesions of the efferent venous limbs are associated with low flow rate. However, we observed a paradoxically high AVF flow in many swollen limb or neck patients associated with central venous occlusion.

What this study adds?

Only a minority of swollen limbs associated with central venous occlusion had low AVF flow regardless of the lesion being completely obstructed in the majority of circumstances. In contrast, the mean flow rate and proportion of high flow AVF surpassed the documented characteristics of normal AVF. Hence, in approaching the swollen limbs of patients with central venous occlusion, AVF flow status should be investigated. In high flow AVF, surgical revision using distal inflow was effective for the treatment of arm or neck edema.

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Potential conflicts of interest

The authors declare no conflict of interest.

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