Endovascular Intervention for Central Venous Stenosis in Hemodialysis Patients: A Single-center Experience

Abstract
Central venous stenosis (CVS) refers to a significant stenosis of a large intrathoracic vein, such as the subclavian, brachiocephalic, or the superior vena cava (hemodialysis, HD). Percutaneous transluminal angioplasty (PTA) with or without stent placement has been the recommended approach for CVS. A total of 10 consecutive HD patients with documented CVS over a 2-year time period from April 2017-April 2019 underwent percutaneous angioplasty and stent insertions under sedation. The procedure was performed by the interventional cardiologist in the institute. One patient underwent only PTA, whereas nine (90%) had PTA with primary stent insertion. Primary patency was 90% at 3 months, 80% at 6 months while at 12 months, it was 70% and remained at 70% at 24 months. We did not find any association between age, gender, diabetic status, dialysis vintage, or previous catheter infection with procedural patency. Central venous stenosis can be treated successfully with percutaneous angioplasty and primary stenting. Despite advances, prevention of CVS should be the primary approach.

Keywords: Central venous stenosis, hemodialysis, percutaneous transluminal angioplasty, stenting

Introduction
The term “central venous stenosis” (CVS) usually refers to a significant stenosis of a big intrathoracic vein such as the subclavian, brachiocephalic, or the superior vena cava. Stenosis is considered significant if it causes disturbance or obstruction to forward flow and usually occurs if the diameter of the stenotic portion is <50% of the unaffected portion. Central veins are commonly injured as a result of placement of intravascular devices or avascular access in hemodialysis (HD). Nearly, 80% of patients with end-stage renal disease (ESRD) in the United States initiate dialysis using a catheter and consequently central vein injury and subsequent restorative response leading to CVS are common. The effect of the stenosis depends on the flow rate and CVS may be clinically silent until an ipsilateral arteriovenous fistula (AVF) or graft is created for HD purpose. Subsequently, it often becomes a major issue because these patient present with poor fistula flow rates, sometimes making HD difficult, increased venous pressure during HD, and bleeding episodes and in more severe cases swelling of the arm bearing the AVF and AVF/graft thrombosis. The incidence of unsuspected CVS in patients with functioning grafts was reported to be 29%.\(^1\)

Percutaneous transluminal angioplasty (PTA) with or without stent placement has been the recommended preferred approach to CVS. Guideline of the Kidney Disease Outcomes Quality Initiative (K/DOQI) suggests that the percutaneous intervention with transluminal angioplasty is the preferred treatment for CVS.\(^2\) We aimed to look at the outcomes of endovascular intervention for HD patients with diagnosed CVS and poor AV fistula flow rates in our institute over a two year period from April 2017-April 2019.

Materials and Methods
A total of 10 consecutive HD patients with documented CVS with AV fistula malfunction and poor blood flow on HD over the 2-year time period from April 2017-April 2019 underwent venous angiography and percutaneous angioplasty and self-expanding metallic stent insertions under sedation. The procedure was performed by the interventional cardiologist in the institute.
All patients received antiplatelet therapy with aspirin 150 mg and clopidogrel 75 mg for thrombosis prophylaxis and this was continued post procedure for at least 4 weeks.

Results

Out of the 10 patients with CVS who underwent PTA or PTA with stenting, 7 were males with 3 females with mean age of 58.4 years ± 10.35 yrs. A total of 50% of patients had diabetes and the average time on dialysis was 15.87 ± 7.1 months [Table 1]. All patients had previous HD catheter insertions, while two (20%) of patients had documented history of catheter related infection. One patient underwent only PTA, whereas nine (90%) had OTA with primary stent insertion. Primary patency was 90% at 3 months, 80% at 6 months, whereas at 12 months, it was 70% and remained at 70% at 24 months. Figure 1 depicts the results in a patient who was intervened successfully. In one patient, though there was good postprocedural flow, the ipsilateral AVF could not be used due to distal vessel narrowing. We did not find any association between age, gender, diabetic status, dialysis vintage, or previous catheter infection with procedural patency. Two patients had a restenosis, one after 15 months and underwent repeat dilatation with adequate flow rates on dialysis, whereas the other could not be salvaged and a tunneled catheter had to be inserted on the opposite side for continuation of dialysis.

Central venous stenosis leading to ipsilateral AV fistula dysfunction and HD inefficiency can be treated successfully with percutaneous angioplasty and stenting. It is, however, important to consider the limitations of our understanding of endovascular intervention and the modulation of the endovascular response. Despite advances, prevention of CVS should be the primary approach.

Discussion

Central venous stenosis is a major and not so infrequently encountered problem in the dialysis population. It was more frequent when subclavian vein catheter were inserted for HD procedures in the 1980s.[3] In a study, out of 69 consecutive patients subjected to percutaneous placement of a tunneled right internal jugular vein (IJV) catheter who underwent prior venography, 29 (42%) were found to have unexpected stenosis or angulation.[4] In a more recent study[5] comprising 2811 HD patients in a single center from January 2000 to December 2013, CVS was diagnosed in 120 (4.3%) at a median dialysis vintage of 2.9 years (interquartile range 1.8–4.6 years).

Early attention focused on HD catheters as etiologic agents responsible for this problem. However, insertion of a variety of indwelling devices including central venous lines, pacemaker wires also leads to the development of central venous stenosis.[6,7] Central venous stenosis has also been reported in patients, however, without any previous central vein catheter placement or procedures causing thrombosis.[8] It was recognized early that dialysis catheters are associated with late vascular complications that may adversely affect the outcome of permanent vascular accesses. In a prospective study of 50 patients with subclavian catheters and 50 patients with IJV catheters, venography revealed CVS in 42% of patients in the subclavian group compared to 10% in the internal jugular group.[9] Other studies have also shown that rates of CVS at around 40%.[10] Longer time on HD and a history of previous HD catheter insertion were factors associated with stenosis. A tendency toward an increased incidence of stenosis was also observed following cannulation of the left compared to the right IJV.[11] This is thought that angulations between the left IJV, brachiocephalic vein, and superior vena cava as well as the greater length that the catheter must traverse are responsible for this increased occurrence.[12]

A majority of the affected patients remain asymptomatic. In a study of 202 patients who underwent permanent pacemaker implantation with indwelling cardiac wires inserted transvenously, 129 (64%) developed varying degrees of central venous stenosis. However, only 12 (9.3%) patients were symptomatic.[6] CVS, however, becomes clinically significant in the presence of an ipsilateral arteriovenous dialysis access that drains into the affected central veins. High venous pressure and blood flow due to the fistula overwhelms the collateral venous and lymphatic drainage, resulting in the development of tortuous collateral veins over the ipsilateral arm, neck, and upper chest. Venous hypertension may lead to severe and disabling arm edema and discomfort. Reduced access blood flow and compromised dialysis delivery occur due to access recirculation.

Endovascular intervention for CVS

The two most important endovascular means for the treatment of CVS are balloon angioplasty and endovascular stenting. Balloon angioplasty should always be the first treatment of choice. PTA has a very high initial technical success rates ranging from 70-90%.[13,14] The unassisted
| Age (years) | Sex | Comorbidities | Vintage on dialysis (months) | H/O previous catheter insertion and site | H/O catheter-related infection | Vascular access | Lesion on venogram | Type of intervention | Immediate outcome | Longer (>6-12 months) outcomes | Drug protocol |
|------------|-----|---------------|-----------------------------|-----------------------------------------|-------------------------------|----------------|------------------|---------------------|-----------------|------------------------|-------------|
| 39         | Female | HTN           |                             |                                         |                               | Left BC AV fistula | 90% stenosis at junction of right brachiocephalic and SVC | Left subclavian vein POBA S/P POBA on 11/7/2016 PTA with stenting to SVC | Adequate flow rate | Adequate flow rate | Aspirin  |
| 64         | Male   | HTN           | 19                          | NO                                      | NO                           | Right BC AV fistula | 80% distal lesion of left subclavian vein, 100% proximal obstruction of left brachiocephalic vein and SVC | PTA stenting to SVC to left brachiocephalic vein and left subclavian stenting | Adequate flow rate | Recurrent stenosis | Aspirin  |
| 59         | Male   | HTN           | 24                          | left IJV                                | NO                           | Left RC AV fistula | 90% stenosis at left brachiocephalic trunk and SVC | PTA stenting to left brachiocephalic vein and right subclavian vein | Adequate flow rate | Adequate flow rate | Aspirin  |
| 43         | Male   | HTN, DM       | 8                           | left IJV                                | YES                          | Left RC AV fistula | 90% stenosis at left brachiocephalic trunk | PTA stenting to right subclavian vein and right brachiocephalic vein | Adequate flow rate | Adequate flow rate | Aspirin  |
| 56         | Male   | HTN, DM, CVD  | 8                           | left IJV                                | NO                           | Left BC AV fistula | 70% lesion at right basilic vein, 95% lesion at right brachiocephalic vein | PTA stenting to right subclavian and brachiocephalic vein | Low flow rate | Neck edema had significantly regressed | Aspirin  |
| 67         | Female | HTN, DM, CAD, | 18                          | right IJV                               | YES                          | Right RC AV fistula | 90% stenosis at right brachiocephalic vein and SVC junction | PTA stenting to right brachiocephalic vein | Adequate flow rate | Adequate flow rate | Aspirin  |
| 63         | Male   | HTN           | 11                          | right IJV                               | NO                           | Left BC AV fistula | 90% stenosis in left subclavian vein | PTA stenting to left subclavian vein | Adequate flow rate | Limb edema had significantly regressed | Aspirin  |
| 60         | Male   | HTN           | 29                          | left IJV                                | NO                           | Left BC AV fistula | 100% occlusion of left brachiocephalic vein | PTA stenting to left brachiocephalic vein | Adequate flow rate | Adequate flow rate | Aspirin  |
| 73         | Male   | HTN, DM       | 18                          | Left BC AV fistula                      | 100% occlusion of left subclavian vein | PTA stenting to left subclavian vein | Adequate flow rate | Low flow rate | Adequate flow rate | Aspirin  |

HTN - Hypertension, DM - Diabetes mellitus, CAD - Coronary artery disease, CVA - Cerebrovascular disease, IJV - Internal jugular vein, RC - Radiocephalic, BC - Brachiocephalic, SVC - Superior vena cava, PTA - Percutaneous angioplasty, HD - Hemodialysis
patency rates reported after PTA have varied from 23 to 63% at 6 months and cumulative patency rates from 29% to 100%. At 12 months, cumulative patency rate ranged from 13 to 100%. It is to be noted that most published studies in CVS are heterogeneous with respect to severity of lesion, variable technique, and equipment. Secondary patency can be significantly better with repeated angiography. The central veins are much more likely to recoil than the peripheral veins and the success of PTA depends on the elastic or nonelastic nature of the lesion. Stents for CVS were used because of poor long lasting results of PTA alone. Guidelines for CVS recommend placement of a stent for elastic recoil of the vein that leads to significant residual stenosis after PTA or for lesions recurring within 3 months after angioplasty. The use of self-expanding metallic stents for elastic lesions has been associated with better outcomes than angioplasty alone. Stents can be used as 1) primary stent placement (PTS) after PTA without waiting for recurrence and 2) stent placement after PTA after failure or recurrence of CVS.

PTA with PTS which is what we performed in our patient group has been used to improve short- and long-term results. In a prospective study comparing angioplasty vs. stent placement in the treatment of CVS, the primary and secondary patency rates of angioplasty at 360 days were 12% and 100%, whereas the patency rates for stenting were 11% and 78%. There was no difference in patency rates (P = 0.540). Restenosis after angiography or stenting is due to intimal hyperplasia. This may be accelerated due to high flow and turbulence. After angioplasty or stenting, the stenosis usually recurs at the same site. After stent placement, however, restenosis may reoccur inside the stent or at the venous segment adjacent to the stent.

We could achieve a primary patency rate of 90% at 3 months and a 1 year and 2-year patency rate of 70%. Recurrence of stenosis occurred in two patients, one of whom underwent repeat ballooning of the stenotic area with good restoration of flow. In more recent literature, use of covered stents (also known as stent grafts or endografts) has shown promise. The technical success is high and primary and assisted patency rates are significantly better than the bare metal stents. The graft material provides a relatively inert and stable matrix for endothelialization, thereby reducing stenosis. Other potential endovascular treatments for CVS include the use of drug eluting stents and cutting balloons.

Vascular access stenosis is a harbinger of thrombosis, recurrent infections, and reduced blood flow compromising dialysis delivery. K/DOQI guidelines recommend that fistula placement should be considered first followed by prosthetic grafts if fistula placement is not possible. However more than 80% of patients with ESRD in the Indian scenario present with emergency and this mandates temporary HD catheter insertions. It is in this context that CVS continues to be a major long-term consequence of HD.

**Conclusion**

Central venous stenosis leading to ipsilateral AV fistula dysfunction and HD inefficiency can be treated successfully with percutaneous angioplasty and stenting. It is, however, important to consider the limitations of our understanding of endovascular intervention and the modulation of the endovascular response. Despite advances, prevention of CVS should be the primary approach.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Lumsden AB, MacDonald MJ, Isiklar H, Martin LG, Kilkeri D, Harker LA, et al. Central venous stenosis in the hemodialysis patient: Incidence and efficacy of endovascular treatment. Cardiovasc Surg 1997;5:504-9.
2. National Kidney Foundation: Guideline 20, K/DOQI clinical practice guidelines for vascular access. Am J Kidney Dis 2000;37(Suppl 1):S137-81.
3. Davis D, Petersen J, Felman R, Cho C, Stevick CA. Subclavian venous stenosis; a complication of subclavian dialysis. JAMA 1984;252:3404-6.
4. Taal MW, Chesterton LJ, McIntyre CW. Venography at insertion of tunneled internal jugular vein dialysis catheter reveals significant occult stenosis. Nephrol Dial Transplant 2004;19:1542-5.
5. Adwaney A, Lim C, Blokey S, Duncan N, Ashby DR. Central venous stenosis, access outcome and survival in patients undergoing maintenance hemodialysis. Clin J Am Soc Nephrol 2019;14:378-84.
6. Da Costa SS, Scalabrini Neto A, Costa R, Caldas JG, Martinelli Filho M. Incidence and risk factors of upper extremity deep vein lesions after permanent transvenous pacemaker implant: A 6 month follow-up prospective study. Pacing Clin Electrophysiol 2002;25:1301-6.
7. Teruya TH, Abou-Zamzam AM Jr, Lumin W, Wong L, Wong L. Symptomatic subclavian vein stenosis and occlusion in hemodialysis patients with transvenous pacemakers. Ann Vasc Surg 2003;17:526-9.
8. Morosetti M, Meloni C, Gandini R, Galderisi C, Pampana E, Nicoletti M, et al. Late symptomatic venous stenosis in three hemodialysis patients without previous central venous catheters. Artif Organs 2000;24:929-31.
9. Schillinger F, Schillinger D, Montagna C, Milcent T. Postcatheterisation vein stenosis in hemodialysis: Comparative angiographic study of 50 subclavian and 50 internal jugular accesses. Nephrol Dial Transplant 1991;6:722-4.
10. Macrae JM, Ahmed A, Johnson N, Levin A, Kiazii M. Central vein stenosis: A common problem in patients on hemodialysis. ASAIO J 2005;51:77-81.
11. Salgado OJ, Urdanete B, Colmenares B, Garcia R, Flores C. Right versus left internal jugular vein catheterization for hemodialysis: Complications and impact on ipsilateral access.
creation. Artif Organs 2004;28:728-33.
12. Salik E, Daffary A, Tal MG. Three-dimensional anatomy of the left central vein: Implications for dialysis catheter placement. J Vasc Intern Radiol 2007;18:361-4.
13. Beathard GA. Percutaneous transvenous angioplasty in the treatment of vascular access stenosis. Kidney Int 1992;42:1390-7.
14. Dammers R, de Haan MW, Pranken WR, Vander Sande FM, Tordoir JH. Central vein obstruction in hemodialysis patients: Results of radiological and surgical intervention. Eur J Vasc Endovasc Surg 2003;26:317-21.
15. Aruny JE, Lewis CA, Cardella JF, Cole PE, Davis A, Drooz AT, et al. Quality improvement guidelines for percutaneous management of the thrombosed or dysfunctional dialysis access. Standards of Practice Committee of the Society of Cardiovascular and Interventional Radiology. J Vasc Intern Radiol 2003; 14:S247-53.
16. Quinn SF, Schuman ES, Demlow TA, Standage BA, Ragsdale JW, Green GS, et al. Percutaneous transluminal angioplasty versus endovascular stent placement in the treatment of venous stenosis in patients undergoing hemodialysis: Intermediate results. J Vasc Interv Radiol 1995;6:851-5.
17. Farber A, Barbey MM, Grunert JH, Gmelim E. Access-related venous stenosis and occlusion: Treatment with percutaneous transluminal angioplasty and Dacron-covered stents. Cardiovasc Intervent Radiol 1999;22:214-8.
18. Duda SH, Pusich B, Richter G, Landwehr P, Oliva VL, Tielbeck A, et al. Sirolimus-eluting stents for the treatment of obstructive superficial femoral artery disease: Six month results. Circulation 2002;106:1505-9.