

 **Original Article** 

Outcomes of Central Venoplasty in Haemodialysis Patients

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Objective: To review the outcomes of central venoplasty in the treatment of symptomatic central vein stenosis in patients undergoing haemodialysis via an ipsilateral arteriovenous fistula (AVF).

Methods: Data were collected retrospectively, and included all the consecutive cases of central venoplasty between January 2008 and December 2015.

Results: A total of 132 central venoplasties in 76 patients were performed, with incidence of symptomatic central vein stenosis at 7.4%. Of the patients, 66% were male and the mean age was 61 years. The most frequent indication was decreased dialysis access flow rates (58%) and 52% of all the patients had symptoms of upper limb swelling. The patients who had previous ipsilateral tunneled internal jugular vein dialysis catheters made up 58% of the patients. The mean time from AVF creation to first central venoplasty was 24 months, and 74% of the cases required a second central venoplasty and the mean time to second venoplasty was 7 months. The overall post intervention assisted primary patency rate was 87%, 74%, 63%, and 42% at 6, 12, 18, and 24 months respectively. Statistically significant differences were found in primary assisted patency ($p=0.025$) and time to second procedure ($p=0.039$) comparing those with and without a history of ipsilateral tunneled dialysis catheter.

Conclusion: Central venoplasty is technically feasible with low procedural risk. The maintenance of the AVF patency

usually requires multiple procedures at average interval of 7 months. Patients with a history of upper limb tunneled dialysis catheter ipsilateral to the side of central vein stenosis or AVF have a less favorable outcome compared to those without.

Keywords: central venoplasty, percutaneous angioplasty, haemodialysis, renal access, arteriovenous fistula

Introduction

A well-established outflow tract clear of any obstruction is essential for an arteriovenous fistula (AVF) to mature and to function efficiently. Central vein stenosis (CVS) leads to AVF outflow obstruction and venous hypertension in the effected limb which compromises the AVF patency and can result in an incapacitating upper limb edema.¹ It is defined as a narrowing of 50% or more in the superior vena cava, brachiocephalic, or subclavian veins.

Owing to the high frequency of prior placement of an ipsilateral upper limb central venous dialysis catheter resulting in central vein injury and subsequent restorative process and stenosis, patients with end-stage renal failure (ESRF) are particularly at risk.² The incidence of CVS in symptomatic ESRF patients is 16%–19% overall and 27% in those with a history of ipsilateral central venous catheter placement.^{3,4}

The treatment of CVS is evolving and optimal management remains unknown. The results of studies evaluating the safety and efficacy of endovascular techniques such as balloon angioplasty and venous stenting in CVS are encouraging; however, assisted primary patency rates tend to decrease within the first 12 months and the need for secondary procedures to maintain the AVF patency is common.⁵

We aim to review the outcomes of central venoplasty in the treatment of symptomatic CVS in patients who undergo haemodialysis (HD) via an ipsilateral AVF.

Methodology

We conducted a single-center retrospective review of central venoplasties performed in a 1300-bed university-

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affiliated tertiary hospital between January 2008 and December 2015. Excluded from the data collection were patients without an AVF or who were undergoing central venoplasty during dialysis catheter exchange. Demographic, procedural and follow-up data were obtained from our institution's electronic patient records system.

Patients presenting with clinical or radiological evidence of venous outflow obstruction were evaluated for CVS by central venography. Central venoplasty was carried out at the discretion of the attending interventional radiologist.

Central venoplasties are performed at the intervention radiology suite by Vascular Intervention Radiologists. Procedures are performed under local anesthesia with sedation. Access is usually obtained via the venous limb of AVF or the femoral vein. After an ultrasound-guided puncture and 7Fr sheath insertion, an 0.035" Glidewire (Terumo, Tokyo, Japan) with 4Fr Berenstein 2 support catheter (Cordis, Milpitas, CA, USA) is used to cross the stenosis. On crossing the lesion, wire is exchanged to Amplatz Super Stiff (Boston Scientific, Marlborough, MA, USA) and central venoplasty is performed with either 10mm/12mm Mustang (Boston Scientific, Marlborough, MA, USA), 10mm Conquest (Bard, Covington, GA, USA) or 12mm Atlas (Bard, Covington, GA, USA) balloons. Central vein stenting is reserved for cases of vein rupture and occasionally for recalcitrant lesions. Commonly used stents include Atrium Advanta V12 (10 to 16mm), Bard Fluency Plus (10 to 13.5mm) sizes, Gore Viabahn (10 to 13mm) and Bentley BeGraft 10mm. For recalcitrant lesions, we use a bare-metal nitinol self-expanding stent, most commonly Optimed Sinus-XL (16 to 36mm). The patient is subsequently discharged home if well and may resume HD via the AVF at his/her next dialysis session. The dialysis flow rates are reviewed at vascular outpatient clinics at 6 weeks.

Definitions

Central venoplasty is defined as balloon angioplasty of the brachiocephalic vein, subclavian vein, or superior vena cava. First and second central venoplasty is defined as the first and second central venoplasty performed since the creation of the AVF affected by CVS. Technical success is defined as the successful inflation of the angioplasty balloon within a central vein without radiological evidence of residual stenosis or significant recoil and technical failure as the failure of the angioplasty balloon inflation or radiological evidence of residual stenosis or significant recoil.

Residual stenosis and significant recoil are defined as >30% stenosis post venoplasty at the time of the procedure or at repeat venogram respectively, as per the National Kidney Foundation Kidney Disease Outcomes Quality Initiative 2006 Guidelines.

Post intervention primary assisted patency is as described by the Journal of Vascular Surgery (JVS) recommended standards for reports dealing with arteriovenous HD accesses.⁶⁾

Statistical analysis

The GraphPad Prism 7.0b software (GraphPad Software, La Jolla, CA, USA) was used to perform all the statistical analysis. The Gehan–Breslow–Wilcoxon test was used to calculate the survival curve comparison. The measured values are given as means or percentages. Patency rates are reported according to the JVS recommended reporting standards criteria⁶⁾ and the Kaplan–Meier survival analysis was used to calculate the patency rates.

Results

Within the study period, 1030 AVFs were created and the incidence of symptomatic CVS was 7.4%. A total of 132 central venoplasty procedures were performed in 76 patients, and 66% of the patients were male. The mean age was 61 years. The co-morbidities included hypertension (97%), diabetes mellitus (70%), ischemic heart disease (55%), peripheral arterial disease (26%), stroke (20%), and cardiac failure (20%) (Table 1). On review of the medication history, the patients were receiving single and dual antiplatelet therapy in 64% and 8% respectively and 28% were receiving none. Of the patients, 3% only were receiving anticoagulation. 53% of vascular access grafts were brachiocephalic AVF, 24% were brachiobasilic transposition AVF, 18% radiocephalic AVF and 5% were synthetic arteriovenous grafts.

The right/left innominate vein were the most common central veins to be angioplastied in both first and second central venoplasty (R/L = 33%/42% and 41%/32% respectively).

The most common indication for first and second central venoplasty was upper limb swelling (51% and 50% respectively). Complete central venous occlusion was

Table 1 Population characteristics

Study population	76
Incidence of central vein stenosis (%)	76/1030 (7.4%)
Total central venoplasties performed	132
Male:female (%)	50:26 (66:34)
Mean age (range)	61 (35–84)
Smokers (%)	21 (28%)
Hypertension (%)	74 (97%)
Diabetes mellitus (%)	53 (70%)
Ischemic heart disease (%)	42 (55%)
Cardiac failure (%)	15 (20%)
Stroke (%)	15 (20%)
Peripheral arterial disease (%)	20 (26%)

Table 2 Outcome data

Complications	n (132) (%)
Puncture site haematoma	3 (2%)
Puncture site infection	1 (1%)
Cardiac arrhythmia	0 (0%)
Central vein rupture	6 (5%)
30 day related readmission	6 (5%)
30 day mortality	0 (0%)

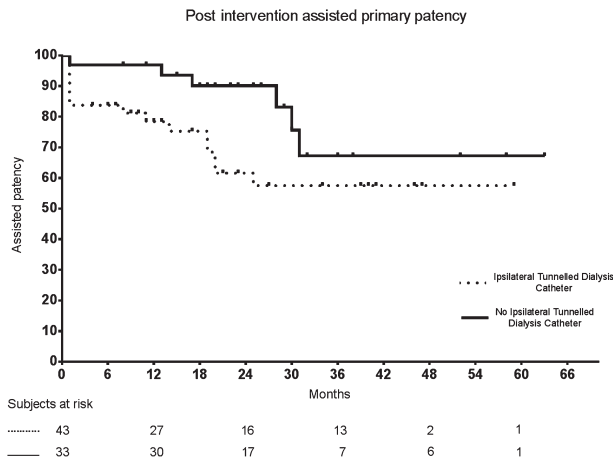


Fig. 1 Post intervention primary assisted patency in patients with vs. without ipsilateral tunneled dialysis catheter. Kaplan–Meier survival curve comparing post intervention primary assisted patency rates in patients with vs. without a history of ipsilateral tunneled dialysis catheter.

reported in 59 of 132 intra-procedure central venograms (45%); however, all were crossed by the angioplasty wire. Overall technical failure rate was 11% (15 of 132 procedures). Residual stenosis was observed in 32 of 132 procedures (24%). A total of 3 central venous covered stents were placed; 1 at primary central venoplasty and 2 at the second procedure. All the 3 stents were placed to treat central vein rupture resulting from central venoplasty.

There was no 30-day mortality rate and 30-day readmission rate was 5%. The reasons for readmission were fistula thrombosis (n=3), worsening upper limb swelling (n=1), hyperkalemia (n=1) and upper limb cellulitis (n=1). The overall complication rate was 8% (10 of 132 procedures) (Table 2). There were 3 puncture site haematomas (2%), 1 puncture site infection (1%) and no patients had a cardiac arrhythmia. The incidence of central vein rupture was 5% (6 of 132 procedures), 3 of which were treated by stent insertion and the other 3 treated by balloon tamponade.

The mean time from AVF creation to first central venoplasty was 24 months. Of the 76 patients who underwent an initial central venoplasty, 56 (74%) required a second central venoplasty within the study period. The mean time between the first and the second venoplasty was 7 months.

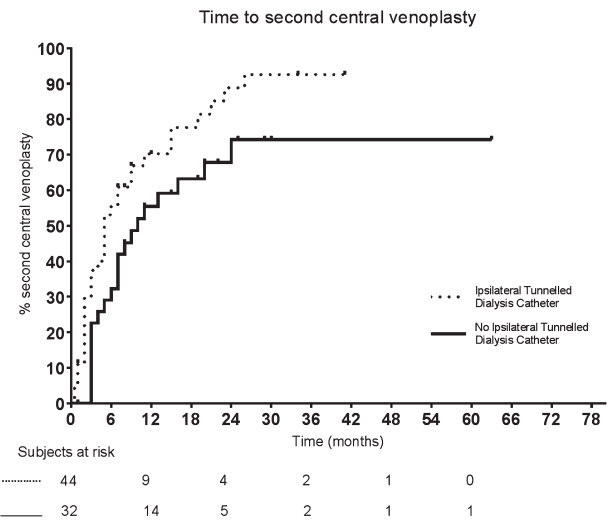


Fig. 2 Time to second central venoplasty in patients with vs. without ipsilateral tunneled dialysis catheter. Kaplan–Meier survival curve comparing the time between first and second central venoplasty in patients with vs. without a history of ipsilateral tunneled dialysis catheter.

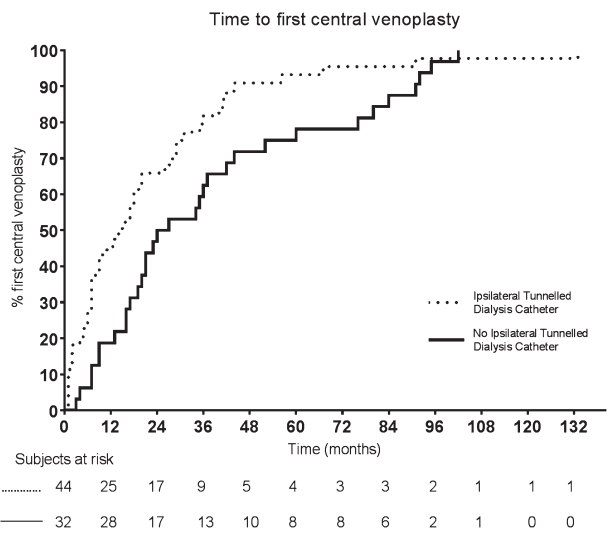


Fig. 3 Time to first central venoplasty in patients with vs. without ipsilateral tunneled dialysis catheter. Kaplan–Meier survival curve comparing the time between haemodialysis access creation and the first central venoplasty in patients with vs. without a history of ipsilateral tunneled dialysis catheter.

Post intervention primary assisted patency rates were 87%, 74%, 63%, and 42% at 6, 12, 18, and 24 months respectively.

The patients who had a history of tunneled upper limb dialysis catheter ipsilateral to the side of the AVF and CVS were 58%. All the tunneled dialysis catheters were internal jugular vein catheters. Comparing the survival curves between the patients with against the patients without prior ipsilateral tunneled dialysis catheter showed statisti-

cally significant differences in post intervention assisted primary patency ($p=0.025$) (Fig. 1).

A comparison of the same groups also revealed a shorter time to second central venoplasty in patients with an ipsilateral tunneled dialysis catheter which reached statistical significance ($p=0.039$) (Fig. 2); however, no statistically significant difference in time to first central venoplasty was found between the two groups ($p=0.11$) (Fig. 3).

The findings that are unique to our study are found in the comparisons between patients with and without a history of tunneled dialysis catheter ipsilateral to the CVS undergoing treatment as this comparison is not found in the current literature. In a comparison of these groups, we found patients with a history of ipsilateral tunneled dialysis catheter ($n=44$) had a significantly reduced primary assisted patency ($p=0.025$). In the same group the time until a second central venoplasty was required was significantly reduced ($p=0.039$).

Discussion

For clinicians involved in the maintenance of vascular access, CVS remains a challenge. Its prevalence is high among HD patients and it poses a significant threat to AVF maturation and patency. The etiology of CVS in the HD population has been largely attributed to the combination of vein trauma resulting from central venous catheterization for temporary access and increased flow and turbulence from AVF creation.⁷ The pathophysiology is not understood fully. Animal models of vein injury have demonstrated the need for “critical area” of injury leading to the development of platelet microthrombi within 24h of injury, followed by smooth muscle proliferation over 7–8 days.⁸ The analysis of subclavian vein arthrectomy specimens from patients with symptomatic stenosis or occlusion have shown intimal hyperplasia and fibrous tissue changes.⁹

Largely due to a variation in study design, the data describing the epidemiology of CVS is inconsistent. Studies tend to focus on either symptomatic or asymptomatic/unsuspected CVS; however, the definition of symptomatic CVS between reports varies a great deal. In our study, we have collected data on all patients undergoing a central venoplasty within a particular timeframe and, therefore, our quoted incidence value of 7.4% in our HD population is an estimate only. The prevalence of CVS is likely being greatly underestimated as the majority of studies follow a similar methodology and study only those patients presenting with either access complications or upper limb swelling necessitating a diagnostic venogram. Such studies have reported an incidence of 19%–41% on central venography.^{3,4,10} These studies were performed in

the current era of preferential internal jugular vein use for tunneled dialysis catheter placement.

The association between upper limb tunneled dialysis catheter placement and the development of CVS is well established. For those with a history of subclavian vein catheters, the risk of CVS is elevated further and guidance advocating the preferential use of internal jugular vein for tunneled dialysis catheter placement have been introduced.^{10–14} Our study population included no patients with a known history of subclavian vein cannulation. The earliest report linking central venous catheter (CVC) placement and the development of CVS is from Fourestie et al.¹⁵ More recent studies have shown a significantly higher risk of developing CVS with longer indwelling duration of central catheters.¹⁶ In a study of 154 follow up venograms post upper limb CVC placement, a longer duration of CVC placement was associated with a significantly increased risk of the development of CVS.¹⁷

The literature is consistent in the description of the pattern presentation of symptomatic CVS. If 40%–50% present with upper limb swelling, 30% will present with high venous pressures complicating dialysis.^{5,18} Our findings are in keeping with the literature. Indications for central venoplasty in our cohort were upper limb swelling in 51% and high venous pressures in 37%.

Advances in endovascular technology have provided clinicians safe and feasible first line therapies in the treatment of CVS. Before the widespread acceptance of percutaneous angioplasty (PTA) and endovascular stenting, the mainstay of treatment was open surgery in the form of extra-anatomical bypass using either endogenous vein or polytetrafluoroethylene graft.^{19,20} The evidence in support of open surgery in CVS is limited to several small case series of patients who either re-occlude post endovascular management or are deemed unsuitable for endovascular options. Chandler and colleagues describe a series of 12 patients who failed conservative management and PTA without stenting. Post-operative primary patency was reported as 80%, 60%, and 25% at 1, 2, and 3 years respectively. No patients died as a result of the procedure; however, post-operative complications and morbidity are not commented on.¹⁹

The earliest report of PTA for CVS is from Glanz et al. in 1988, who reported post interventional primary patency rates of 35% and 6% at 1 and 2 years respectively.²¹ Advancement in endovascular technology has since allowed for improvements in technical success and patency rates. A 2007 study from Bakken et al. of primary central venoplasty vs. primary venous stenting in CVS reported post interventional primary patency rates of 45%, 29%, and 7% at 6, 12, and 24 months respectively, with no statistical difference in patency between primary angioplasty and primary stenting there being significantly less residual

stenoses in the stenting group.⁵⁾ The frequent need for repeat or “maintenance” procedures using this approach is well recognized and in the same study post interventional primary assisted patency rates are more encouraging at 77%, 73%, and 57% at 6, 12, and 24 months. Our post interventional primary assisted patency rates were similar to current literature at 87%, 74%, and 42% at 6, 12, and 24 months respectively. The proportion of central venograms reported as showing residual stenosis post angioplasty in our population is half of that reported by Bakken et al.; however the term residual stenosis does invite a degree of interpretation bias.

The indications for stent placement in CVS vary between institutions. In our local setting stenting is reserved for cases of intra-procedure central vein rupture and occasionally for resistant lesions. Primary stenting for central venous lesions is controversial. Improved primary patency rates and less frequent need for secondary procedures compared with venoplasty alone have been reported²²⁾; however, there are conflicting studies reporting no significant difference in primary patency.^{5,23)} There are observational studies in the literature describing the use of stenting in lesions which are resistant to central venoplasty which report encouraging patency rates; however these do not include any comparative data.²⁴⁻²⁶⁾

Conclusion

Within our study population, the incidence of symptomatic CVS is 7.4% and central venoplasty is technically feasible with low procedural risk. However, patients are likely to require multiple procedures at average interval of 7 months, to maintain the AVF patency. Patients with a history of upper limb tunneled dialysis catheter ipsilateral to the side of central vein stenosis/AVF have significantly lower AVF patency rates post central venoplasty and require maintenance procedures sooner compared to those without. The authors recommend that in patients likely to require permanent renal access in the form of an upper limb AVF, to avoid reduced AVF patency, the site of any temporary tunneled dialysis catheter should be carefully considered.

Additional Remarks

This article is the largest series of central venoplasty to date and the findings were presented as an oral presentation at the Charing Cross Symposium in April 2017.

Disclosure Statement

None conflicts of interest to declare.

Author Contributions

Study conception: ZJL, SC, JK

Data collection: GAC, JK

Analysis: GAC

Investigation: GAC, ZJL

Writing: GAC, ZJL

Funding acquisition: not applicable

Critical review and revision: all authors

Final approval of the article: all authors

Accountability for all aspects of the work: all authors

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