Access flow reduction and recurrent symptomatic cephalic arch stenosis in brachiocephalic hemodialysis arteriovenous fistulas

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ABSTRACT
Background: Recurrent cephalic arch stenosis (CAS) has been linked to high flow and has a high rate of recurrence following angioplasty. This study investigates the effectiveness of access flow reduction in decreasing rapidly recurrent symptomatic CAS.

Methods: A retrospective study of patient records from February 2005 to April 2009 was conducted. Patients with brachiocephalic fistulas who had undergone two or more instances of cephalic arch angioplasty within 3 months, and thereafter underwent flow reduction via banding of the access inflow (n=33) were included. A before-and-after analysis was conducted: the rates of cephalic arch angioplasty were calculated for each patient before and after the banding procedure, and compared via a paired t-test.

Results: At 3, 6, and 12 months, the cephalic arch primary lesion patency was 91%, 76%, and 57%. The cephalic arch intervention rate was reduced from 3.34 to 0.9 per access-year (t=7.74, p<.001). The average follow-up time was 14.5 months (range, 4.8-32).

Conclusion: Flow reduction of a brachiocephalic arteriovenous hemodialysis fistula may effectively diminish the incidence of symptomatic CAS.

Key words: Cephalic arch stenosis, Cephalic arch, Brachiocephalic fistula, Flow reduction, MILLER banding, Hemodialysis

INTRODUCTION

The Fistula First Initiative has increased the number and proportion of arteriovenous fistulas (AVFs) placed for hemodialysis (HD) use in the USA. Although AVFs generally require fewer interventions than arteriovenous grafts (AVGs) to maintain patency, a few sites of venous stenoses account for a large portion of repeat interventions (1). A particularly troublesome site within brachiocephalic AVFs is the cephalic arch (2, 3).

Cephalic arch stenosis (CAS) has been implicated in 19.5-77% of brachiocephalic fistula failures (4-6). Angioplasty of stenotic lesions involving the cephalic arch has limited efficacy as immediate elastic recoil, venous perforation, and rapid re-growth of venous intimal hyperplasia results in a 42% primary patency at 6 months (5, 7, 8). Placement of bare nitinol stents improves immediate patency, but does not significantly improve 6-month primary lesion patency compared to angioplasty alone (5, 9). In many patients, rapid re-stenosis occurs and repeat interventions become necessary to maintain access patency and HD adequacy.

High flow within the venous outflow of an AV access is correlated with intimal hyperplasia. Various reasons for venous intimal hyperplasia have been proposed; however, the most likely cause of intimal hyperplasia is intimal injury due to turbulence (10), and has a direct correlation with hypervolemic flow (11, 12). Therefore, such a trigger for intimal hyperplasia should be mitigated by reducing flow within the AVF (13). This study examines the effect of fistula flow reduction via banding of the juxta-anastomotic segment on the recurrence of CAS.

MATERIALS AND METHODS

Patient population and study design

Patients were referred to our vascular access outpatient clinic by 18 surrounding dialysis centers with an estimated 4,000 HD patients. A retrospective analysis of the medical records of 183 patients who were treated with Minimally Invasive Limited Ligation Endoluminal-assisted Revision (MILLER) banding for steal syndrome (n=114) or hypervolemia (n=69) from February 2005 to April 2009 was conducted. Patients’ medical records were assessed for demographic information,
Access flow in CAS

Prior to each intervention, a complete fistulagram was performed (GE OEC 9800 C-arm). Oxilan (Guerbet, Bloomington, IN) intravenous contrast was used for imaging. All instances of CAS (Figs. 1, 2) were treated with angioplasty (Ultra-thin Diamond Balloon, Boston Scientific/Meditech, Watertown, MA; Conquest, Bard, Covington, GA), or angioplasty followed immediately by bare nitinol stent placement (Protégé EverFlex, ev3, Minnesota, USA) if lesions exhibited elastic recoil or recurred within 3 months. Banding of HD accesses was performed in accordance with the MILLER procedure (15, 16) (Figs. 3, 4).

Flow reduction was assessed through palpation (17, 18). Additionally, for six patients, pre- and post-banding procedure flow measurements were obtained upon the acquisition of a Flow Transonic machine (Transonic Systems Inc, Ithaca, NY).

Study endpoints and definitions

All patients with an access dysfunction related to CAS were treated with angioplasty and/or stent placement at including co-morbidities, gender, and age.

Inclusion and exclusion criteria. The inclusion criteria were: a brachiocephalic AVF as the only HD access, angioplasty of the cephalic arch at a rate of ≥2 times per 3 months prior to the banding procedure, lead-in period ≥120 days, and follow-up period ≥120 days. Patients with anatomically variant cephalic veins (ie supraclavicular cephalic arches) were excluded.

Determination of steal and hypervolemia was based on clinical symptoms. The symptoms of steal included numbness and coldness of the hand which were exacerbated at dialysis and alleviated by temporary shunt occlusion (Tab. I). Accesses were considered hypervolemic if they were found to have congestive heart failure directly attributable to AV access placement, visibly notable aneurysm growth, or problematic elevation of venous pressures at dialysis. (High flow has previously been defined as exceeding 1500 mL/min) (14). Angiography was performed to confirm these findings.

Angiography criteria. Following angioplasty of the cephalic arch, patients were scheduled for a follow-up evaluation after 3 months. Patients returning prior to 3 months were referred from their HD unit due to clinical findings such as prolonged post-dialysis bleeding; high arterial, intra-access or venous pressure; and thrombosis. Patients who returned at 3 months and did not have any of these symptoms were not studied angiographically and were rescheduled for an evaluation after an additional 3 months.

Intervention criteria. A hemodynamically significant venous stenosis was defined as a stenosis of at least 50%, with clinical signs such as elevated venous pressure and prolonged post-dialysis access bleeding. All significant lesions were treated at each visit.

**TABLE I - CLASSIFICATION OF STEAL SYNDROME BY SEVERITY**
[from (39)]

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Retrograde diastolic flow without complaints; steal phenomenon</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Pain on exertion and/or during hemodialysis</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Rest pain</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Ulceration/necrosis/gangrene</td>
</tr>
</tbody>
</table>
the lesion site. A before-and-after analysis was conducted. Time zero was defined as the time of banding, and the rates of cephalic arch interventions (ie symptomatic CAS) prior to the banding procedure were compared to the rates following the banding.

Patients were evaluated for primary cephalic arch lesion patency, cephalic arch interventions per access-year, thrombotic events per access-year, and secondary access patency. Follow-up information was obtained from patient charts and phone calls.

In accordance with the Society of Interventional Radiology guidelines, primary lesion patency was defined as the interval between the banding procedure and any subsequent intervention across the cephalic arch. Secondary access patency was defined as the time of patency from the banding procedure until the access was surgically revised. Follow-up ended with death, kidney transplantation, or most recent records of dialysis use (19).

Statistical analysis

A Kaplan-Meier analysis was performed to construct a life-table estimate of the patencies. The pre- and post-banding cephalic arch angioplasty rates were calculated and compared using a paired t-test.

RESULTS

Outcomes

Within the 33 (18% of the original 183-patient cohort) patients who fitted the study criteria, the average cephalic arch intervention rate prior to the banding procedure was 3.34 per access-year. Following the banding procedure, this was reduced to 0.9 interventions per access-year. Comparison of these rates via a paired t-test revealed a significant difference between the pre- and post-banding rates of interventions at the cephalic arch (t=7.74, p<.001).

At 3, 6, and 12 months following the banding procedure, the primary lesion patency at the cephalic arch was determined to be 91%, 76%, and 57%, respectively (Fig. 5). At 12 months, the secondary access patency was 97% (Tab. II). The thrombotic event rate was 0.18 per access-year. In order to treat thrombosis or inadequate access flow, two patients had their bands stretched.

The indications for banding were symptomatic steal syndrome (n=18) or hypervolemia (n=15). The average patient age was 61 (range, 33-87) and 16 (48%) patients were female (Tab. III).
brachiocephalic AVFs being 37 times more likely to contain CAS than radiocephalic AVFs (5). This disparity in the prevalence of CAS between brachio- and radiocephalic fistulas is likely accounted for by differing hemodynamics at the cephalic arch (12).

The cephalic arch has a unique architecture. In addition to containing a high concentration of valves and having a steep angulation, it crosses multiple tissue planes, bridging the superficial and deep venous systems while being tethered to rigid extravascular structures (20). In the context of a brachiocephalic fistula, these factors combine to make the cephalic arch particularly vulnerable to the development of stenotic lesions, as changes in vessel compliance produce turbulent flow (5,7).

When an anastomosis is created between the brachial artery and cephalic vein, the flow within the cephalic vein is increased and the vessel begins to dilate. However, the tissues surrounding the cephalic arch preclude its expansion, so that the cephalic vein narrows as it approaches its junction with the central veins. This sudden reduction in the circumference of a high-flow pathway results in an inflow-outflow mismatch, potentiating turbulence and the increased shear stress associated with it.

Although various reasons for venous intimal hyperplasia have been proposed (21-23), turbulence is likely the primary etiologic factor in contributing to injury-induced hyperplasia (11, 13, 20, 24-31). The Reynolds number, which is a measure of fluid turbulence (13, 24), is most closely correlated with development of CAS (12):

$$Re = \frac{Q \times L}{\eta \times A}$$  [Reynolds equation]

where $Q$ is the flow rate, $L$ is the tube length, $\eta$ is the viscosity, and $A$ is tube’s cross-sectional area (13). Hence, changes in flow direction and vein lumen, along with valves which increase flow velocities and create local eddies, further amplify turbulence (20, 32). The amount of flow necessary to induce turbulence depends on the extravascular architecture, angle of vein curvature and pre-arteriovenostomy cephalic arch diameter, and will therefore vary among individuals (20).

Given the aforementioned reports concerning the role

### TABLE II - PATENCIES OF 33 BRACHIOCEPHALIC FISTULAS

<table>
<thead>
<tr>
<th>Time (Months)</th>
<th>Cephalic Arch Lesion Patency (%)</th>
<th>Secondary Access Patency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>91</td>
<td>100</td>
</tr>
<tr>
<td>6</td>
<td>76</td>
<td>100</td>
</tr>
<tr>
<td>12</td>
<td>57</td>
<td>97</td>
</tr>
</tbody>
</table>

### TABLE III - PATIENT DEMOGRAPHICS (n=33)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>26 (79%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12 (36%)</td>
</tr>
<tr>
<td>Mean age (range)</td>
<td>61 (33, 87) years</td>
</tr>
<tr>
<td>Female sex</td>
<td>16 (48%)</td>
</tr>
<tr>
<td>Left arm</td>
<td></td>
</tr>
<tr>
<td>brachiocephalic fistula</td>
<td>22 (67%)</td>
</tr>
<tr>
<td>Right arm</td>
<td></td>
</tr>
<tr>
<td>brachiocephalic fistula</td>
<td>11 (33%)</td>
</tr>
<tr>
<td>Mean banding diameter (range)</td>
<td>4 (3, 5) mm</td>
</tr>
</tbody>
</table>

### Flow measurements

In order to analyze better the relationship between flow and banding, a flow measurement device was obtained, and utilized in six consecutive patients. The mean pre-banding flow was 2226 mL/min and the mean post-banding flow was 1225 mL/min. The banding procedure resulted in a mean flow reduction of 42% (range, 24-55%) (Tab. IV).

### Follow-up

The average follow-up time was 14.5 months (range, 4.8-32). Two patients expired during follow-up.

### DISCUSSION

In a cohort of radiocephalic and brachiocephalic AVFs, the incidence of CAS was observed to be 15%, with

### TABLE IV - ACCESS FLOW REDUCTIONS IN SIX PATIENTS

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Initial Flow (mL/min)</th>
<th>Final Flow (mL/min)</th>
<th>Net Decrease (mL/min)</th>
<th>Net Decrease (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3800</td>
<td>1700</td>
<td>2100</td>
<td>55.3%</td>
</tr>
<tr>
<td>2</td>
<td>2500</td>
<td>1400</td>
<td>1100</td>
<td>44.0%</td>
</tr>
<tr>
<td>3</td>
<td>1625</td>
<td>770</td>
<td>855</td>
<td>52.6%</td>
</tr>
<tr>
<td>4</td>
<td>1700</td>
<td>1300</td>
<td>400</td>
<td>23.5%</td>
</tr>
<tr>
<td>5</td>
<td>1130</td>
<td>780</td>
<td>350</td>
<td>31.0%</td>
</tr>
<tr>
<td>6</td>
<td>2600</td>
<td>1400</td>
<td>1200</td>
<td>46.2%</td>
</tr>
<tr>
<td>Average</td>
<td>2226</td>
<td>1225</td>
<td>1001</td>
<td>42.1%</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>952</td>
<td>374</td>
<td>642</td>
<td>12.4%</td>
</tr>
</tbody>
</table>
of turbulence in the genesis of CAS, we surmise that the creation of a strictured band in the juxta-anastomotic segment will effectively diminish the tendency toward turbulence. We recognize that shifting a focal resistance from the cephalic arch to the juxta-anastomotic segment appears simply to change the location of a recurrent stenosis. However, we believe that the creation of a strictured band at this site will not result in frequent stenosis formation because of its straight-line, avalvular physiology. This assumption was supported by the fact that only 1.1% of patients from the original 183-patient cohort required angioplasty at the banding site.

Access flow reduction via banding of the juxta-anastomotic segment has previously been used to treat venous intimal hyperplasia in AVGs. In a study of loop AVGs placed in canine subjects, Fillinger et al demonstrated that banded grafts have lower rates of venous intimal hyperplasia than non-banded grafts (13). While extensive intimal hyperplasia was observed in the venous limb of non-banded grafts, only negligible amounts were found in banded grafts. The average flow reduction in banded grafts was 55% (from 1017-462 mL/min), suggesting that a significant reduction in flow results in a corresponding decrease in venous intimal hyperplasia.

Previous studies of CAS treatment have obtained 6-month primary patencies of 42-47% with angioplasty and/or bare metal stent placement (4, 5), 82% with covered nitinol stent placement (9), and 69-70% with surgical approaches (33-35). The 6-month primary cephalic arch patency of 76% achieved with our banding technique is comparable to those attained with covered stents (9) or surgical revision (33, 34) (Tab. V). Furthermore, a marked difference exists between the cephalic arch patency of our banding cohort and that of the most comparable control group: the bare metal cohort of Shemesh et al achieved a 6-month patency of 39%, with no access having a patent cephalic arch at 12 months (9). As well, our before-and-after study yielded a significant reduction in the rates of symptomatic CAS, with a decline from 3.34 to 0.9 interventions per access-year (t=7.74, p<.001).

Our secondary access patency was 97% at 12 months, suggesting that this banding procedure does not compromise access durability in fistulas with recurrent CAS. Previous endovascular treatment studies have obtained thrombosis rates of 0.13-0.57 per access-year in fistulas (36-38). Given these results, our thrombosis rate of 0.18 per access-year is comparable to those studies, suggesting that banding improves the access suitability of hypervolemic brachiocephalic fistulas without an increased number of repeat thrombotic events.

We consider our relatively high cephalic arch primary lesion patencies to provide evidence in support of the use of flow reduction in the treatment of this type of lesion, which is a less expensive and invasive treatment than covered stent placement or surgical revision. Prior to our observation that banded brachiocephalic fistulas required fewer cephalic arch re-interventions, our treatment was limited to frequent angioplasty and stent placement. We now perform banding as an adjunct procedure for the treatment of rapid symptomatic cephalic arch re-stenosis and believe that the MILLER procedure is an appropriate alternative treatment for CAS. However, large-scale, randomized studies are necessary to provide definitive evidence of this treatment’s utility.

The limitations of this study include its retrospective nature, lack of a control group, and the absence of flow measurements for the initial 27 patients. Because patients were selected based on clinical findings, rather than precise flow measurements, there may be a bias toward undertreating low-pressure AV accesses following banding and subclinical stenoses would not have been detected. However, nearly all of the patients had follow-up angiography at the time of publication, confirming patency of the arch. Randomized, controlled studies would greatly improve our understanding of the treatment of CAS.

ACKNOWLEDGEMENTS

Michael Alesi, RT, and James Smith, RT, provided expert technical advice in order to make these procedures possible and successful.

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment / Group</th>
<th>n</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shemesh et al (9)</td>
<td>Bare stent</td>
<td>12</td>
<td>39%</td>
<td>39%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Covered stent</td>
<td>13</td>
<td>82%</td>
<td>82%</td>
<td>32%</td>
</tr>
<tr>
<td>Kian et al (33)</td>
<td>Vein bypass</td>
<td>13</td>
<td>92%</td>
<td>69%</td>
<td>39%</td>
</tr>
<tr>
<td>Chen et al (34)</td>
<td>Venovenostomy</td>
<td>10</td>
<td>80%</td>
<td>70%</td>
<td>60%</td>
</tr>
<tr>
<td>Presented data</td>
<td>Flow reduction</td>
<td>33</td>
<td>91%</td>
<td>76%</td>
<td>57%</td>
</tr>
</tbody>
</table>
Conflict of Interest: We have had no involvements that might raise the question of bias in the work reported or in the conclusions, implications, or opinions stated.

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