Percutaneous Angioplasty of Juxta-Anastomotic Stenosis of Failing Distal Radio-Cephalic Hemodialytic Arteriovenous Fistulas: Our Techniques in Comparison, an Attempt to Standardize the “Optimal Technique”

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Abstract

Purpose: Juxta-anastomotic area is the critical zone of the distal radio-cephalic fistula for higher frequency of presentation of lesion and lower patency rates versus non-juxta-anastomotic stenosis. Our purpose was to describe our techniques for the treatment of juxta-anastomotic stenosis of failing distal radio-cephalic shunt and evaluate the effectiveness of venous and anastomotic Percutaneous Transluminal Angioplasty (PTA) compared to venous PTA alone of this region.

Materials and methods: We retrospectively reviewed 175 patients with distal radio-cephalic arteriovenous fistulas (AVFs) with Echo-Color-Doppler (ECD) evidence of venous stenosis of the juxta-anastomotic region without any dynamically significant anastomosis stenosis, treated between 2008 and 2011, having at least 1-year follow-up.

Two groups were recognized: 1) 103 patients treated with venous juxta-anastomotic and anastomosis PTA (“V configuration PTA”); 2) 72 patients treated only with venous PTA (“Z or V2 configuration PTA”). Surviving Times and Primary patency at 6 and 12 months were evaluated for both groups.

Results: The immediate post-procedural technical and clinical success was 100% for all the patients. Patients treated with “V configuration PTA” – group 1 showed higher survival rate free of target lesion reintervention compared to patients who underwent “Z or V2 configuration PTA” - group 2, with a statistically significant difference (P-value=0.0001) in Surviving Time. PP at 6 and 12 months were respectively 97% and 79.6% in the group 1 and 79.8% and 54.1% in the group 2.

Conclusions: We always treat venous juxta-anastomotic stenosis of distal radio-cephalic hemodialytic AVFs with PTA of the whole juxta-anastomotic region in presence or not of dynamically significant stenosis at anastomosis.

ABBREVIATIONS

PTA: Percutaneous Transluminal Angioplasty; AVF: Arterio-Venous Fistula; ECD: Echo-Color-Doppler; PP: Primary Patency; SP: Secondary Patency

INTRODUCTION

The number of patients who undergo hemodialysis will increase in the future for the progressively ageing population and the high incidence of diabetes. End stage renal disease...
(ESRD) is a very common condition: 65,000 new patients undergo hemodialysis in Europe and more than 350,000 in United States with an estimated growth of up to 500,000 in 2020 [1].

The rate of failure of native, arteriovenous fistula (AVF) is still very high; most dysfunctions of the shunt are caused by stenosis of the dialytic circuit that can lead to thrombosis and loss of vascular access [2]. As it is well known, stenotic lesions of distal radio-cephalic arteriovenous shunts occur mainly in the anastomotic site in up to 64% of cases [2-6].

The juxta-anastomotic area is the region within 3 cm of the arteriovenous anastomosis [7] and it is the critical zone of the distal radio-cephalic fistula for higher frequency of presentation of lesions and lower patency rates after percutaneous transluminal angioplasty (PTA) in comparison with PTA of non juxta-anastomotic stenosis.

Reviewing the literature, we noticed that there are no authors describing in detail the exact technique to perform an effective angioplasty. Therefore, we decided to review angioplasties of distal radio-cephalic AVFs performed at our hospital, in order to understand in which way the different techniques we have used can affect the effectiveness of the treatment and to try to standardize "the optimal PTA technique". To be effective a balloon catheter has to tear the intimal layer as well as the internal elastic lamina and at least parts of the tunica media in order to prevent elastic recoil of a stenotic vasal segment. As a response of this vascular trauma a cascade of biological reactions is initiated to repair the injured wall structures with possible, consecutive formation of neo-intimal hyperplasia [8]. We evaluated if the treatment of a non stenotic, "well-functioning" anastomosis, in association with venous PTA, in case of hemodynamically significant venous, juxta-anastomatic stenosis, is recommendable in improve primary and secondary patency.

We think that the juxta-anastomotic area has to be considered a single compartment to be treated in its entirety with angioplasty to be always performed crossing the anastomosis with the guidewire and inflation of balloon in "V shape configuration", as it will be described below. We believe in fact that anastomosis is always involved in the dysfunctional dialytic access due to juxta-anastomotic stenosis also without or not so obvious ECD appearance.

Therefore, the purpose of our study was to describe our different PTA techniques for the treatment of distal radio-cephalic hemodialytic arterio-venous shunt and evaluate the effectiveness of venous and anastomotic PTA compared with venous PTA alone.

MATERIALS AND METHODS

The IRB of the participating institution does not require approval for the type of research we performed: observational, retrospective, historical cohorts study.

All the principles of the Declaration of Helsinki were followed.

We retrospectively reviewed 298 patients with AVF, treated at our hospital between 2008 and 2011: 175 patients were assessed for eligibility and 123 patients, not meeting inclusion criteria, were excluded.

The eligibility criteria were the presence of a native, distal radio-cephalic hemodialytic fistula with clinical signs of failing dialysis access, Echo-Color-Doppler (ECD) evidence of venous juxta-anastomotic stenosis without any dynamically significant anastomotic stenosis and any other stenotic lesion of inflow or outflow, confirmed with phlebography of the upper arm, completed with cavography, having, at least, one year follow up.

After the evaluation of the eligible 175 patients, we recognized two groups in this sample: 1) 103 patients with venous juxta-anastomotic stenosis treated with venous and anastomosis’s PTA ("V configuration PTA"); 2) 72 patients with venous juxta-anastomotic stenosis treated with simple venous site PTA ("Z configuration or V2-configuration PTA"); all cases in absence of hemodynamically significant anastomosis, inflow and outflow stenosis at ECD, as required in the eligibility criteria.

When clinical and physiological indicators demonstrated that the fistula was going to fail we always performed and ECD and the treatment was always performed as soon as we found hemodynamically significant venous juxta-anastomotic stenoses.

All AVFs were always minutely studied in advance with ECD, in order to show the localization and cause of the dysfunction (stenosis, thrombotic occlusion), to evaluate the degree of stenosis, the venous outflow and the conditions of all arteries of the upper arm, to map the AVF, to measure vessel diameters, to plan the treatment and to choose the best site to perform the ultrasound-guided percutaneous access.

Treatment was most of times performed with retrograde access in venous outflow, always under ultrasound guidance, placement of 5 to 6 introducer sheaths (Radiofocus® Introducer II, Terumo, Tokyo, Japan; Prelude PRO™ Merit Medical), intravenous administration of 2500 units of heparin, to avoid thrombotic events, and selective digital subtraction angiography to outline the anatomy of AVF and evaluate the lesions already studied with ultrasound. Every preliminary study was completed with phlebography of the upper arm and cavography, which always confirmed the results of ECD about the absence of other outflow stenosis.

In the group 1 (175 patients, 59% of the whole sample) balloon was delivered and inflated according to the "V shape" configuration (Figure 1a). This means that juxta-anastomotic stenosis and anastomosis were crossed with coaxial technique with 4 F, angled catheter and thin guidewire (0.014"), which was retrogradely advanced into the proximal radial artery. The balloon catheter was then passed over the guidewire and inflated in the entire juxta-anastomotic region for at least 2 minutes.

When the guidewire did not advance in the artery from the venous retrograde approach, we performed an arterial antegrade access with micro-puncture system (Micropuncture® Access Set, Cook Medical), and we crossed anastomosis and venous stenosis with a guidewire antegradely advanced in the venous outflow, this guide was pulled back and snared inside the introducer sheat previously placed in the venous retrograde access, recovered from this site and the treatment was performed from the venous approach. Even when the arterial access is required we always prefer to recover the guide from the artery to the vein and carry out the angioplasty from the venous access where usually a bigger introducer sheat is placed.
In the group 2 (72 patients, 41% of the whole sample) we crossed anastomosis with 0.014” guidewire that was retrogradely advanced in the proximal radial artery, in “V shape” configuration (Figure 1b), exactly as described before, in this case called as “V2 configuration”, or antekradely advanced in the distal radial artery, in “Z shape” configuration (Figure 1c). In any case, in the group 2 the balloon was delivered and inflated only on the venous part of juxta-anastomotic region without any dilation of the anastomosis.

Venous juxta-anastomotic stenosis’s PTA was always performed, in both groups, with balloons of suitable diameter, never undersized. We usually used 3-3.5-4 mm, low profile, and compliant PTA dilatation catheters for the whole juxta-anastomotic region in the group 1 and only for the venous juxta-anastomotic region for the group 2. Multiple inflations were used for resistant lesions, using growing PTA balloons, inflated for 2 minutes at least to avoid elastic recoil.

The two groups of patients did not show any other arterial or venous stenosis except the juxta-anastomotic lesion, but in our daily practice, in presence of simultaneous non juxta-anastomotic outflow lesions we usually use suitable size standard balloons or, when this is not enough to achieve optimal results, high-pressure balloons, cutting balloons or scoring balloons.

All AVFs of the two groups were matured; matured fistulas were defined, with the “Rule of six”, as AVF with venous diameter ≥ 6 mm, blood flow rate ≥ 600 ml/min and skin depth < 6 mm, evaluated with ultrasound 6 weeks after the creation of the dialytic circuit. All AVFs were correctly used for dialysis at least two months. Both of these groups were homogeneous samples, with similar patient’s characteristics: mean age 71 years in the group 1 and 69 in the group 2; male gender 80% in the group 1 and 83.7% in the group 2; hypertension 50% in the group 1 and 59.3% in the group 2; hyperlipidemia 42% in the group 1 and 26.7% in the group 2; diabetes mellitus 57% in the group 1 and 69.8% in the group 2; AVF mean age 25 months in the group 1 and 22 months in the group 2; all patients of both groups had matured, distal, radio-cephalic fistulas, with “de novo” venous, juxta-anastomotic stenosis (Table 1). Main objective of our study was to evaluate the Surviving Time in the two groups to estimate the effectiveness of PTA of the whole juxta-anastomotic region compared to PTA of the venous side of juxta-anastomotic region.

Surviving Time was defined in accord with the Kidney Disease Outcomes Quality Initiative recommendations as absence of dysfunction of the vascular access, patent lesion or residual stenosis <30% and no need for further intervention of the target lesion (TLR). Primary patency (PP) after PTA was evaluated with ECD at 6 and 12 months for both groups. Data were statistically analysed: the Survival Curves was estimated using Kaplan-Meyer analysis and compared with Logrank test.

RESULTS

First treatment technical and clinical successes were 100% for all the patients in both groups.

Technical success after PTA was defined as the reactivation of “thrill” and residual stenosis <30%; clinical success after PTA was defined as the ability to perform a regular dialysis immediately after the treatment. The ECD controls at 6 and 12 months showed respectively 100 and 82 patent AVFs in the group 1 and 57 and 39 patent AVFs in the group 2; so the 6 and 12 months Primary Patency rates were respectively 97% (100/103) and 79.6% (82/103) in the group 1 and 79.8% (57/72) and 54.1% (39/72) in the group 2 (Table 2). Surviving Times were evaluated in the two groups.
PTA showed higher mean survival rate and longer free period from reintervention of the target lesion in comparison with patients who underwent only venous PTA with a statistically significant difference (P-value=0.001) in Surviving Time evaluating the survival curves with the Logrank Test (Table 4). In fact the mean survival is 359 (SE: 3.141; 95% CI for the mean: 353.455 to 365.768) in the group 1 and 326 (SE: 8.992; 95% CI for the mean: 308.835 to 344.082) in the group 2. The Kaplan-Meyer analysis (Figure 2) showed a wide gap between the two survival curves highlighting the group 1’s statistically significant higher Survival likelihood.

**DISCUSSION**

Balloon angioplasty continues to be the most accepted and cost-sensitive method of treating failing hemodialytic access [10]. Since the early reports of success, angioplasty has become the standard treatment for stenosis in both fistula and grafts. The technique has been shown to be safe, easily performed and effective[11] and it is the first treatment option in the international guidelines [12]. Numerous studies describe the technique used, but the PTA's outcomes were never evaluated in relation with the site of the balloon's inflation. DK Rajan reviewed the use and outcome of PTA technologies, past, present and future as well as some of the questions that remain unanswered with PTA [10]; he analyzed the outcomes of many studies that evaluated factors that can affect the patency: the location of stenosis, the use of different devices as standard PTA balloons, cutting balloons, cryoplasty, paclitaxel-coated balloons (PCB) and stent graft placement. He evaluated also the choice of the balloon and the relationship between patency and inflation time concluding that the different inflation times (range: 1-5 min) did not affect access patency. Some authors evaluated the use of PCB in patients undergoing transluminal angioplasty for recurrent juxta-anastomotic stenosis of radio-cephalic AVF [13]. Their sample was similar to ours concerning site of AVF and stenosis and like us they used preferably transvenous approach and, only in patients who required, the transradial access, but the exact inflation site has not been reported and their PP rates were lower than ours. Others evaluated the efficacy and outcomes of 3 different percutaneous transluminal angioplasty approaches (transarterial, transvenous and combination) [14] but the site of inflation is not clear. In some studies evaluating predictors of technical success and patency after PTA of de novo dysfunctional hemodialysis AVF [15], they obtained the access to fistula through a brachial artery puncture. Some authors reported the technical success and long term clinical outcomes of matured AVF after PTA [16], for obliterated lesions: after initial constant failure of transvenous approach in their early patients, they routinely changed to transradial artery approach for later cases; occasionally they combined transfemoral and transradial artery approach were necessary to successfully recanalize a tightly obliterated or ruptured venous segment of the venous outflow. We believe the venous retrograde approach is safer and allows the use of larger introducer sheaths with less risk than arterial antegrade access. Only when we are not able to cross the lesion or the anastomosis from the venous access we perform the transarterial antegrade approach but, in most of cases, just to cross the lesions and anastomosis, the guidewire is in fact antegradealy advanced in the venous outflow, pulled back inside.

### Table 1: Baseline and procedures.

<table>
<thead>
<tr>
<th>Baseline and procedures</th>
<th>VEN+ANAST PTA</th>
<th>VENOUS PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nr of Patients</td>
<td>103</td>
<td>72</td>
</tr>
<tr>
<td>Mean age</td>
<td>71 ± 13 years</td>
<td>69 ± 12 years</td>
</tr>
<tr>
<td>Male Gender</td>
<td>80.0% (82/103)</td>
<td>83.7% (60/72)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>50.0% (51/103)</td>
<td>59.3% (42/72)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>42.0% (43/103)</td>
<td>26.7% (19/72)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>57.0% (58/103)</td>
<td>69.8% (50/72)</td>
</tr>
<tr>
<td>AV Fistulas mean age</td>
<td>25 months</td>
<td>22 months</td>
</tr>
<tr>
<td>Stenosis type:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>de-novo</td>
<td>100% (103/103)</td>
<td>100% (72/72)</td>
</tr>
<tr>
<td>outflow lesions</td>
<td>100.0% (103/103)</td>
<td>100.0% (72/72)</td>
</tr>
<tr>
<td>First treatment’s Tech</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Success</td>
<td>100.0% (103/103)</td>
<td>100.0% (72/72)</td>
</tr>
<tr>
<td>First treatment’s Clinical Success</td>
<td>100.0% (103/103)</td>
<td>100.0% (72/72)</td>
</tr>
</tbody>
</table>

**Abbreviations:** VEN+ANAST: Venous+Anastomosis; PTA: Percutaneous Transluminal Angioplasty; Nr: Number

### Table 2: Results.

<table>
<thead>
<tr>
<th>Group</th>
<th>6 Months PP</th>
<th>12 Months PP</th>
</tr>
</thead>
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<tr>
<td>1</td>
<td>97% (100/103)</td>
<td>79.8% (57/72)</td>
</tr>
<tr>
<td>2</td>
<td>79.6% (82/103)</td>
<td>54.1% (39/72)</td>
</tr>
</tbody>
</table>

Group 1 shows higher Primary Patencies at 6 and 12 months.

**Abbreviations:** PP: Primary Patency

### Table 3: Results.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Mean Survival</th>
<th>SE</th>
<th>95% CI for the mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>359,612</td>
<td>3,141</td>
<td>353,455 to 365,768</td>
</tr>
<tr>
<td>1</td>
<td>326,458</td>
<td>8,992</td>
<td>308,835 to 344,082</td>
</tr>
<tr>
<td>Overall</td>
<td>345,971</td>
<td>4,288</td>
<td>337,567 to 354,376</td>
</tr>
</tbody>
</table>

Patients treated with venous and anastomosis’s PTA show higher mean survival rate and longer free period from TLR (Target Lesion Reintervention) compared to patients underwent only venous PTA.

**Abbreviations:** SE: Standard Error; CI: Confidence Interval

### Table 4: Results.

**Comparison of survival curves (Logrank test)**

<table>
<thead>
<tr>
<th>Chi-squared</th>
<th>15,0968</th>
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</thead>
<tbody>
<tr>
<td>DF</td>
<td>1</td>
</tr>
<tr>
<td>Significance</td>
<td>$P=0.0001$</td>
</tr>
</tbody>
</table>

Logrank test shows a statistically significant difference between the Survival Time of the two groups ($P=0.0001$), higher in the group 1.

**Abbreviations:** DF: Degrees of Freedom
the introducer sheath previously placed in the venous retrograde access, snared and recovered from this site and the treatment is performed from the venous approach.

Our results show a higher survival rate and longer free period from reintervention of target lesion in patients of the group 1, treated with PTA of the whole juxta-anastomotic region, in “V configuration”, in comparison with patients of the group 2, who underwent PTA of the simple venous side of the juxta-anastomotic region, in “V2 or Z configuration” with a statistically significant difference (P-value=0.0001) in Surviving Time. As we wrote before, there was not any dynamically significant anastomotic stenosis, as requested in the eligibility criteria. Some authors divide juxta-anastomotic region into three compartments, venous, arterial and anastomosis [9,17] and they perform PTA with the guidewire placed into the distal radial artery for dilation of purely venous stenosis and guidewire advanced into the proximal radial artery for dilation of stenosis located at the anastomosis itself or on the proximal artery [7]. We think that the juxta-anastomotic area, the region within 3 cm of the arteriovenous anastomosis [7], has to be considered a single compartment to be treated in its entirety, with angioplasty to be always performed crossing the anastomosis with the guidewire and inflation of balloon in “V shape configuration”. We believe in fact that anastomosis is always involved in the dysfunctional dialytic access due to juxta-anastomotic stenosis also without or not so obvious ECD appearance. Sometimes, for example, too angled anastomosis can create turbulence leading to stenosis, PTA in this site can help improve the anatomy of arteriovenous anastomosis, also when a hemodynamically significant stenosis is not clearly evident at ECD. Furthermore, an angioplasty performed just in the venous juxta-anastomotic site cannot ensure the treatment of the entire stenotic lesion. For these reasons, supported by our results, in our standard practice, we always use thin materials, we perform as first choice the transvenous retrograde us-guided access and we always use “V shape” inflation to treat the stenosis of the juxta-anastomotic region either in presence or not of hemodynamically significant stenosis in every compartment of the region. Although drug eluting balloons (DEB) were never used in any patients of this study, in the last years we always used them, so once a good morphological result is achieved with standard balloons we always complete the treatment with the inflation of a DEB 0.5 mm bigger than the last standard balloon used. Indeed, as shown in literature, patients treated with standard PTA and DEB have higher primary and secondary patency rates compared to patients treated just with standard PTA [18,19].

Some authors consider the surgical creation of a new and slightly more proximal anastomosis as the preferred option in the management of juxta-anastomotic stenosis in forearm [18] and proposed surgery as the preferred treatment over the percutaneous approach for its better primary patency compared to PTA [7,17,21-26]. We believe the multiple confounders in these reports do not allow a good evaluation of patency rates: most of these works have not studied a homogeneous sample for type of AVF and site of stenosis and a small number of patients with juxta-anastomotic lesions were evaluated. In addition, most of the times they did not use thin material (0.014”, 0.018”) and PTA was performed without cross of anastomosis and the use of “V shape configuration”, as we described. In this work, we think our homogeneous sample, only consisting of patients with venous juxta-anastomotic stenosis and distal radio-cephalic AVFs, gave us an objective evaluation of primary patency and survival rates.

We believe the technical tips we described in this study can really affect PTA outcomes of the juxta-anastomotic stenosis of distal radio-cephalic fistulas, in fact our primary patency rates are higher than the results showed from other authors, with promising higher 6 and 12 months PP than the literature [2,6,7,20-28]. So we think that PTA performed in this way has to be considered the golden standard and first choice treatment in malfunctioning arteriovenous access, especially to preserve all the way distal radio-cephalic AVF and that the surgical proximalization has to be reserved only to patients who cannot be treated with endovascular approach.

The use of this technique seems to be effective and to improve primary and secondary patency and decrease reinterventions of target lesion in juxta-anastomotic stenoses of failing distal radio-cephalic arteriovenous shunts with a statistically significant difference between the two groups examined and could make present and future technologies and devices more effective.

REFERENCES

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Cite this article