

# Color doppler ultrasound assessment of juxta-anastomotic stenosis in radiocephalic arteriovenous fistulas: endovascular or surgical approach

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Received for publication: 13 Jan 2018

Accepted in revised form: 1 Mar, 2018

## ABSTRACT

**Background:** Juxta-anastomotic stenosis (JAS) is a common complication of radiocephalic arteriovenous fistulas. There is diverging data as to the best therapeutic approach being angioplasty or surgery. Pre-operative color Doppler ultrasound (CDU) is accurately used for initial assessment of the vascular access and follow-up monitoring. The aim of this study was to evaluate immediate and long-term results of endovascular versus open surgical intervention of juxta-anastomotic venous stenosis of forearm radiocephalic fistulas and to test if CDU assessment can be used to ameliorate preoperative strategy and long-term outcomes.

**Methods:** This retrospective cohort study included 63 patients with JAS radiocephalic fistulas referred to vascular access consultation. CDU was used to assess preoperative morphological, functional and hemodynamic stenosis characteristics and according to specific criteria, allocate patients to endovascular or surgical treatment.

**Results:** Surgical revision was proposed in 68.2% of patients (N=43), namely the creation of a new proximal fistula (N=41), while angiographic evaluation was proposed in 31.7% of the cases (N=20). Mean follow-up time was 720±524 days with a maximum follow-up of 4.6 years. In the surgical group, primary patency was 92% and 84% at 6 and 12 months respectively, while in the endovascular group, it was 76% and 47% (p=0.013). There was no significant difference in the assisted primary patency between the interventional groups at 12 months: 94% in the endovascular vs. 93% in the surgical group (p=0.542).

**Conclusion:** Pre-operative CDU assessment of JAS and specific allocation criteria with an access-centered approach choosing the best option in each fistula allowed the correct diagnosis of the lesion, improved the global results of the treatment and optimized the financial resources by reserving PTA for selected cases where surgery could be more difficult with higher risk of access loss.

**Keywords:** Assisted primary patency, color doppler ultrasound, juxta-anastomotic stenosis, neo-anastomosis, percutaneous transluminal angioplasty, primary patency.

## ■ INTRODUCTION

Arteriovenous fistulas (AVF) commonly complicate with flow-limiting stenosis, an independent risk factor for AVF failure. Usually stenosis develops significantly earlier in radiocephalic AVF compared to other type of upper limb fistula<sup>1</sup>. The best approach to juxta-anastomotic stenosis (JAS) in radiocephalic AVF is still controversial. Significant stenosis can be treated either with surgery or percutaneous transluminal angioplasty (PTA)<sup>2</sup>, the latter allowing better native venous preservation and being less invasive<sup>3</sup>.

Most importantly, early pre-emptive intervention, either PTA or surgical correction, results in lower incidence of AVF thrombosis<sup>4</sup>. The two procedures are considered equally valid, complementary for pre-emptive treatment of stenosis in radiocephalic AVF<sup>5</sup>. The choice depends on technical availability, local expertise or patient's choice.

Color Doppler ultrasound (CDU) has been proven to be a reliable AVF screening tool<sup>6</sup>, giving insight into preoperative morphological and functional characteristics of the vessels used for AVF construction<sup>7</sup> but also having high sensitivity and specificity for diagnosing and characterizing JAS<sup>8-10</sup>.

Our approach was based on the fact that pre-operative CDU assessment of JAS allows an access centered approach by choosing the best therapeutic option in each fistula based on specific CDU criteria. The aim of this study was to evaluate immediate and long-term results of endovascular versus open surgical intervention of juxta-anastomotic venous stenosis of forearm radiocephalic fistulas using CDU based criteria for allocation to surgical or endovascular procedure.

## ■ METHODS

### ■ Study design, setting and patient population

A total of 1300 vascular access (VA) consultations belonging to 6 hemodialysis (HD) centers performed between 1 March 2011 and 31 October 2015 were retrospectively reviewed. Sixty-three patients with radiocephalic fistulas with hemodynamic significant JAS were identified. Patients were referred to VA consultations whenever impaired VA was suspected, including changes on physical examination, decreasing flow (Qa) measured by BTM® (Fresenius Medical Care),

low Kt/v or cannulation difficulty. Following the routine procedure of our center, JAS from radiocephalic AVF that required intervention were selected and PTA or surgical procedures were performed in the interventional radiology unit as an outpatient procedure, after written informed consent. Follow-up examinations were performed systematically every month with clinical examination and Qa measurements.

### ■ Preoperative vascular evaluation

The diagnosis of JAS was made combining clinical data and CDU examination using a 7-15 MHz linear 38 mm transducer (Ultrasound System; General Electric Pro scanner) carried out by the same experienced nephrologist. VA assessment included combined physical examination and repeated CDU calculation of fistula flow rates while in the VA consultation. All dysfunctional AVF were evaluated with CDU allowing localization and characterization of the stenosis before allocating patients to surgical or PTA treatment.

Stenoses were considered hemodynamically significant in the presence of clinical signs associated with decreased dialysis dose, cannulation difficulties and low blood flow (<500 ml/min) or a blood flow reduction of more than 25% if Qa < 1000 ml/m. Otherwise Stenoses were considered hemodynamically significant only if there was at least one of the following additional ultrasound criteria:<sup>1</sup> resistance index in the radial artery >0.7,<sup>2</sup> residual stenosis diameter <2.0 mm.

### ■ Outcomes and study definitions

JAS was defined as the stenosis affecting the anastomosis site, including the radial artery and cephalic vein usually within 3 cm of the anastomosis, or a combination of both, sparing the puncture areas<sup>11</sup>.

The primary outcomes were post intervention primary patency (PP) and post intervention assisted primary patency (APP).

Post intervention primary patency (PP). PP is the interval from the time of any surgical or endovascular intervention until thrombosis or the time of measurement of patency<sup>12</sup>.

Post intervention assisted primary patency (APP). APP is the interval from the time of intervention until first access thrombosis or the time of patency

measurement, including all intervening similar manipulations (surgical or endovascular interventions) designed to maintain the functionality of the access<sup>12</sup>.

Patients who were transferred to different angiographic centers, who received kidney allograft or died, were included until last known follow-up consultation with patent AVF.

### Statistical Analysis

Continuous variables are presented as mean  $\pm$  standard deviation or median and interquartile range (IQR), and categorical variables as a percentage of the number of studied cases. Chi-square test was used to assess differences between proportions of categorical variables. Patency was analyzed using Life Tables and Kaplan-Meier statistics and the difference between surgical or endovascular interventions were compared using the log-rank test. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) 23.0 for windows (SPSS Inc. Chicago, IL, USA). P-values less than 0.05 were considered statistically significant.

## RESULTS

This study included 63 patients with a mean age of 72  $\pm$  11 years, all undergoing hemodialysis for a mean of 6.6  $\pm$  5.1 years. The majority of patients were male (63.5%; N=40) with 49.2% being diabetic (N=31) and 68% (N=43) hypertensive. Most patients had previous cardiovascular disease with 17.5% (N=11) having peripheral arterial disease and 25.4% (N=16) coronary heart disease. The most frequent etiology of patient's chronic kidney disease was diabetic nephropathy, followed by the undetermined one (Table 1). The majority of patient referral was due to clinical diagnosis of JAS (N=24), followed by thrombosis (N=17), decreased Qa (N=10), decreased Qb (n=5), decreased Kt/v (N=3), outflow stenosis (N=2), cannulation difficulties (N=1) and one patient simply needed vascular access monitoring. After clinical and echo-Doppler assessment, A presumed diagnosis of JAS at the following sites was made: anastomosis site (n=3), radial artery (n=9) and radiocephalic vein (n=51). Four patients had simultaneous outflow stenosis.

Depending on CDU assessment of the AVF, patients were allocated into the two different treatment groups: Endovascular procedure was conducted when: 1) radial

**Table 1**

Patient baseline characteristic

Patient demographic and baseline characteristics	Value
No. of radiocephalic AVF	63
Age (year; mean $\pm$ SD)	72 $\pm$ 11
Male gender (%)	63.5
Time on hemodialysis (years; mean $\pm$ SD)	6.6 $\pm$ 5.1
Mean follow up time (days; mean $\pm$ SD)	720 $\pm$ 524
CARDIOVASCULAR DISEASE	%
Coronary artery disease	25.4
Peripheral vascular disease	17.5
Hypertension	68
Other comorbidities	%
Diabetes	49.2
Neoplasia	12.7
CHRONIC KIDNEY DISEASE ETIOLOGY	N (%)
Undetermined	21 (33.3)
Diabetic nephropathy	28 (44.4)
Chronic glomerulonephritis	6 (9.5)
Autosomal polycystic kidney disease	4 (6.3)
Others	4(6.3)

artery diameter was <2.5 mm; 2) significant calcified radial artery walls that could turn a proximal neo-anastomosis technically difficult; 3) new anastomosis with humeral artery, carrying out a higher risk of inducing AVF related ischemia like small caliber and significant calcified or stenotic radial or ulnar artery; 4) surgery would be required or there was a prediction of significant loss of vein length; 5) there was a damaged outflow vein wall with fibrosis proximal to the stenosis that preclude surgical revision; 6) multiple stenosis; 7) whenever the use of a central venous catheter would be necessary if the surgical revision was performed.

The surgical approach with the creation of a proximal neo-anastomosis was preferentially conducted whenever: 1) the diameter of radial artery was >3mm; 2) there was an intact cephalic vein wall with a diameter >3mm without any nearby stenosis allowing wider preservation of the vein length and easier cannulation the day after the procedure; 3) when there were more than 2 PTA in less than 3 months.

After applying CDU criteria, surgical revision was proposed and performed in 43 cases, with creation of a new proximal fistula the most common procedure (N=41), and 2 patients having surgical angioplasty performed. Of the 41 patients submitted to a new anastomosis, 2 patients had immediate thrombosis after procedure, needing construction of a new

humeral-cephalic AVF and at the same time a HD central venous catheter. In 17 patients JAS was diagnosed after thrombosis had already occurred. In all cases, the outflow vein was patent, allowing its characterization. In these patients, 16 were successfully treated surgically with CDU guiding the best location for the new proximal anastomosis. Only one patient needed a central venous catheter. One patient had multiple stenoses that were solved with a hybrid approach. Patients with occlusion of the outflow vein, needing thrombectomy, were excluded from the study. The angiographic procedure was performed in 20 patients; all patients had functioning AVF after the procedure. There was no misdiagnosed stenosis with CDU compared with angiography in the endovascular group and surgical patients had no significant outflow stenosis after JAS correction.

Mean follow-up time was  $720 \pm 524$  days (median: 706, IQR: 214-1204) with a maximum follow-up of 4.6 years. During the follow-up, 10 patients died, 3 were transplanted and 2 were transferred to another angiographic center.

Thrombosis was observed in 3 AVF, 2 from the endovascular group and 1 from the surgical group. Thirty-five per cent of patients (7/20) submitted to a first

**Table 2**

Primary patency and assisted primary patency comparisons between the two intervention groups (endovascular or surgery) by Kaplan-Meier; cumulative proportion surviving at the end of 6 months, 1 and 2-years estimated by life tables

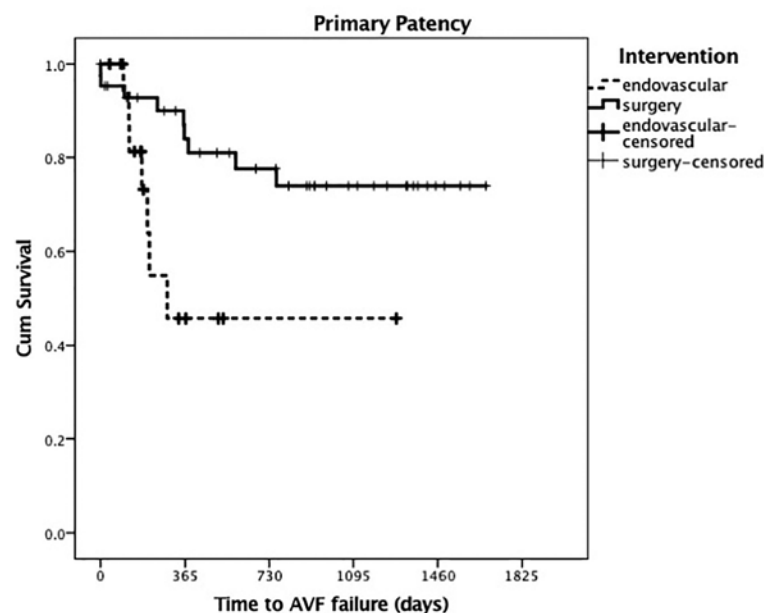
	PTA (%)	Surgery (%)	p value
<b>Primary Patency</b>			
6 months	76	92	0.013
1-year	47	84	
2-years	47	77	
<b>Assisted Primary Patency</b>			
6 months	94	93	0.542
One-year	94	93	
2-years	79	93	

angiographic proceeding relapsed, not statistically different from the 18.6% (8/43) who relapsed when submitted to initial surgical approach ( $p=0.155$ ).

In the surgical group, primary patency was 92% and 84% at 6 and 12 months respectively, significantly better than the endovascular group (76% and 47%:  $p=0.013$ ). There was no significant difference in the assisted primary patency between the interventional groups at 12 months: 94 % in the endovascular vs. 93% in the surgical group ( $p= 0.542$ ). (Figure 1; Table 2).

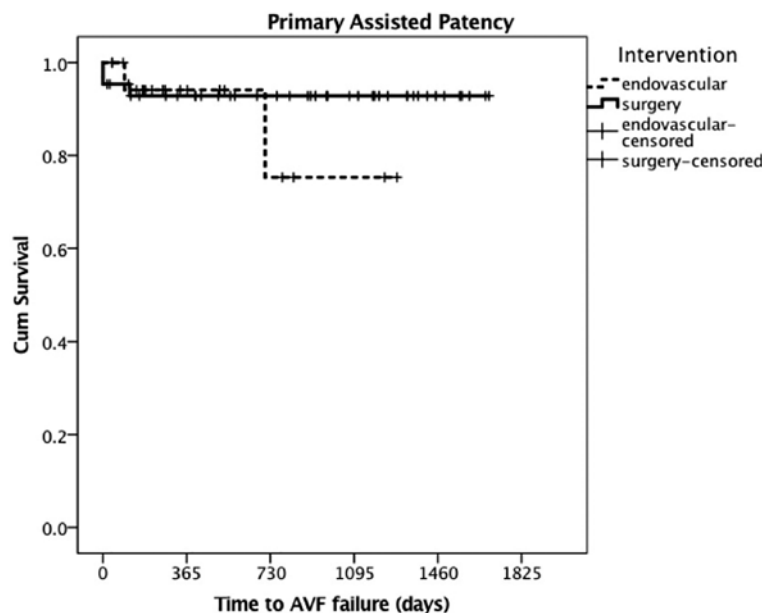
**Figure 1**

Kaplan-Meier analysis of primary patency (endovascular and surgical intervention)



**Figure 2**

Kaplan-Meier analysis of assisted primary patency (endovascular and surgical intervention)



## DISCUSSION

The cornerstone of AVF salvaging is the accurate identification of stenotic lesions. In radiocephalic AVF, JAS is the most common finding, even more common after CDU assessment, as previously reported in other studies<sup>13,14</sup>. There is still controversy about which method is the best approach to manage JAS, surgery or endovascular proceeding. Recent reports suggest that stenosis can be safe and successfully managed using either endovascular procedure or surgery<sup>13,15</sup>. Previous studies show that surgical and endovascular interventions do not differ significantly when it comes to primary patency although re-intervention rates may differ<sup>8,16,17</sup>. Although PTA is less invasive, there is a higher restenosis rate<sup>5,16,18</sup> probably due to balloon-induced vascular wall injury which accelerated the neointimal hyperplasia promoting more neo-intimal hyperplasia and stimulating smooth muscle cell proliferation<sup>19</sup>. Restenosis develops faster than a virgin stenosis. The key is in appropriate timing of PTA procedures<sup>20</sup>. In our study, there were no significant differences between primary assisted patency but primary patency was significantly better in surgical patients even when we included patients whose first presentation of JAS was thrombosis, a sign of worse prognosis in access survival. Similar to our study, PP at

18 months was higher in the surgically repaired group as demonstrated in the meta-analysis of four non-randomized cohort studies<sup>15</sup>. This was noteworthy with post-treatment primary and APP rates after proximal neo-anastomosis<sup>21</sup>. A small study that included only endovascular treatment of JAS demonstrated that long-term good results are possible, except when the residual stenosis after the first procedure is 50% or more<sup>22</sup>. Patients should know that when submitted to endovascular proceedings, multiple maintenance interventions might be needed<sup>5,23</sup>.

Independently of the procedure, either surgical or endovascular, the final decision usually depends on individual preference, technique availability, surgeon, interventional radiologist and nephrologist experience, as well as economic and material resources. Our perspective is that the two methods are complementary and not competitive and in JAS treatment CDU could be the answer to which is the best treatment for each access. CDU is a non-invasive method that requires no radiation or contrast. It allows stenosis characterization and hemodynamic evaluation, establishing any need for intervention in the AVF stenosis. The CDU criterion to allocate patients into 2 groups of intervention proposed in this study allowed an individualized vascular-access-centered approach. A better patient allocation significantly decreases the number of re-interventions,



having a positive impact on PP, patient morbidity and costs by also decreasing major complications and inconvenience associated with the intervention.

Our therapeutic option took into consideration the immediate risk of vascular access loss when a more complex surgery is performed, such as in AVF with a <2.5 mm diameter, significant calcified radial artery walls or damaged outflow vein wall with fibrosis or whenever there is an extensive loss of venous capital, especially when needing a central venous catheter to undergo hemodialysis. Even with this caution, 2 patients had immediate thrombosis after surgical procedure. PTA is not free of complications such as thrombosis and vein wall rupture with severe and uncontrolled hemorrhage needing immediate access ligation after balloon dilation. However, there is no proven risk factor associated with worse outcome regarding PTA stenosis treatment and the risk of immediate access loss seems to be lower compared to surgery. PTA's main benefit is still preservation of proximal vein length and higher immediate success after procedure. The surgical approach can be associated with higher primary failure and complications as insufficient vein length for cannulation after the procedure. In these cases, we propose an initial PTA assuming that several other endovascular proceedings may be needed. Depending on the time of the recurrence, if inferior to 3 months, we propose the construction of a new proximal AVF, even though a temporary central venous catheter may be needed. PTA is preferred if there is a high ischemic risk related to a new AVF construction using the humeral artery.

Study limitations include its retrospective design, a single vascular access center and the lack of ability to detect significant predictors of access failure as a result of the small number of patients. Using the pre-operative CDU assessment, our team chose the salvage technique without randomization, which can be also a study limitation.

To the best of our knowledge, this is the first study that allocates JAS to endovascular or surgical therapeutic intervention based on CDU assessment. This approach with specific allocation criteria choosing the best option in each fistula allowed the correct diagnosis of the lesion, improved the global results of the treatment and optimized the financial resources by reserving PTA for selected cases where surgery could be more difficult with higher risk of access loss.

**Disclosure of potential conflicts of interest:** none declared

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