Endovascular Treatment of the “Failing to Mature” Arteriovenous Fistula

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In recent literature, surgically created hemodialysis (HD) arteriovenous fistulas (AVF) have high rates of primary failure. Endovascular treatment holds promise to salvage these fistulae. The outcomes of 119 patients who had a “failing to mature” AVF and presented for endovascular management were evaluated prospectively. All patients underwent a fistulogram. Stenotic lesions underwent balloon angioplasty, and accessory veins underwent obliteration. Technical success was determined immediately after the procedure. AVF salvage was determined by successful use during HD. Patients were followed up for 1 yr, during which primary and secondary AVF patency rates were measured. The distribution of stenoses was as follows: Artery, 6 (5.1%); arterial anastomosis, 56 (47.1%); juxta-arterial anastomosis, 76 (63.9%); peripheral vein, 70 (58.8%); and central vein, 10 (8.4%). Significant accessory veins were present in 35 (29.4%). Mixed lesions were found in 85 (71.4%). The technique was successful in 107 (89.9%), and the AVF was salvaged in 99 (83.2%). Follow-up of salvaged fistulae showed a total event rate of 0.38/access-year, thrombosis rate of 0.12/access-year, and loss rate of 0.04/access-year. Endovascular treatment of “failing to mature AVF” is safe and effective when performed in a dedicated center.


The low prevalence of the arteriovenous fistula (AVF) among US hemodialysis (HD) patients (1,2) has initiated nationwide measures to increase AVF creation and prevalence (3–20). Among these are providing educational programs, setting forth guidelines and goals (3,4), implementing multidisciplinary approaches (4–9), encouraging preoperative venous mapping (14–19), and asking surgeons to create AVF instead of arteriovenous grafts (AVG) (10–21).

Overall, an increase in AVF prevalence is occurring in the United States, albeit at a slow rate (14–20). One impediment has been high primary failure rates, which in recent series ranged between 23 and 46% (9,12–14). The use of ultrasound or other means of preoperative venous mapping is likely to decrease the incidence of primary AVF failures (14–19). However, the increasing demand to create more fistulae may lead to their creation in borderline vessels, thereby increasing primary failure rates (21–23). Thus, salvage of these primary failures will be essential for increasing AVF prevalence in the United States.

In our dedicated endovascular suite, we used percutaneous angioplasty and accessory vein obliteration in attempts to salvage fistulae with primary failure. Because most did not present with thrombosis, we elected to refer to their fistulae as “failing to mature.” In this article, we report our initial success rates as well as follow-up on a series of 119 consecutive patients who were referred for salvage of their “failing to mature” AVF.

Materials and Methods

Definitions

The “failing to mature” AVF in our series was defined as an AVF that had been created for at least 8 wk but had not matured enough to allow successful cannulation or use during HD. This includes (1) fistulas that were never cannulated for HD be cause of obvious lack of maturity; (2) fistulas that failed first cannulation attempts and were abandoned; (3) fistulas that were cannulated successfully but could not be used because the blood flow was insufficient to sustain HD; this may have been because of high venous pressure or poor arterial inflow; and (4) fistulas that thrombosed before any attempts at HD. Juxta-arterial anastomosis segment refers to the initial 5 cm of the AVF starting at the arterial anastomosis. Peripheral vein refers to the venous outflow tract of the AVF that starts proximal to the juxta-arterial segment and ends at the distal edge of the subclavian vein. Central vein refers to subclavian vein, innominate vein, or superior vena cava. The interventionalist is the physician performing the procedure. Technique success was determined by the interventionalist on the basis of initial and final angiogram results. Successful angioplasty was defined by a <30% residual narrowing on final angiogram. Successful accessory vein obliteration was defined as complete cessation of flow in the accessory vein. Successful AVF salvage was defined as the ability to begin using the AVF for HD within 4 wk after the last elective endovascular intervention. A minimum of six consecutive successful uses were required to label the AVF as salvaged successfully. Primary and secondary patency rates were determined only in salvaged fistulae. Primary unassisted patency refers to AVF patency without the need for additional intervention. Secondary patency refers to AVF patency with the use of interventional procedures such as angioplasty or thrombectomy to maintain patency.
Patient Referral and Selection Criteria

Patients with AVF dysfunction were referred to our center by many community and university nephrologists. Referrals were initiated either by the nephrologists or by the HD unit nurses. In one case, the patient was referred by a vascular surgeon. Referred patients came to us from 27 separate HD units largely but not exclusively from the Houston area. Every patient who was referred for endovascular treatment of dysfunctional AVF was screened for the presence of “failing to mature” AVF. When the AVF was thrombosed on presentation, it was excluded only when the thrombosed AVF was not palpable by physical examination. Other exclusions were physical evidence of AVF-related infection, patients with history of major allergic reaction to intravenous radiocontrast agents, and patients who were unwilling to undergo the procedure. No exclusions were based on the duration of time interval from creation of the AVF to referral.

Diagnostic Procedures

Every patient underwent a physical examination that included palpation and auscultation of the AVF. Cannulation was done using a 21-G needle that allowed introduction of a 0.018-in guide wire over which a 5F sheath was inserted and exchanged for a wider sheath if necessary. Physical examination helped to direct initial cannulation. Thus, when the AVF was easily collapsible, it was suspected of having an inflow problem, and initial cannulation was attempted away from the arterial anastomosis with the needle pointing upstream. When the AVF had a strong pulse in its initial course, a downstream venous stenosis was suspected, and cannulation was done close to the arterial anastomosis with the needle pointing downstream. A fistulogram then was performed, and radiocontrast was traced to the central veins. This allowed identification of all vascular lesions that were contributing to failure of the AVF to mature. A second cannulation of the AVF was done in the opposite orientation to the first cannulation, when necessary, for diagnostic or treatment purposes.

Interventional Procedures

Intervention included balloon angioplasty of vascular stenoses and obliteration of accessory veins. A necessary requirement for balloon angioplasty was successful passage of a guide wire through the vessel that required dilation. Balloon angioplasty was attempted initially by inflating a Workhorse balloon (Angiodynamics, Queensbury, NY) up to a maximum of 20 atmospheres (atm). For resistant lesions, a Conquest balloon (Bard, AZ) was used instead and was inflated up to 35 atm. Accessory veins were obliterated by selective cannulation of the vessel by a 5F infusion catheter and the subsequent deployment of an intraluminal thrombogenic stainless steel coil (Cook, Bloomington, IN). In all cases, a final fistulogram was obtained to determine technical success.

Data Collection

Demographic, clinical, and radiographic data were recorded for all patients, including the results of initial fistulogram as well as any subsequent interventions. Specifically, data on the location of the AVF and sites and severity of lesions were recorded in the chart.

Follow-Up

All patients were required to have follow-up visits during which the AVF was evaluated by physical examination. A decision then was made either to begin using the AVF for HD or to perform additional endovascular intervention. A follow-up visit, with similar decision-making, was required after every intervention. Thirty-five (29.4%) patients required more than one session of intervention. When an AVF failed intervention or failed to be used successfully for HD despite a series of interventions carried out in a 2-mo period, the AVF was abandoned and considered a treatment failure. When the AVF was used successfully during HD, follow-up was initiated at 3-mo intervals through a telephone communication with either the patient or the HD unit. Any AVF derangements, loss, or subsequent intervention with angioplasty or thrombectomy were recorded.

Statistical Analyses

Technical success and AVF salvage rates were presented as simple percentages. To test for an association between AVF salvage and age, we used the t test. To test for an association between AVF salvage and other demographic data, we used the $\chi^2$ test. $P < 0.05$ was considered significant. AVF event rates were presented as events per access-year. Long-term patency rates were presented using death- and kidney transplantation–censored Kaplan-Meier survival curves.

Results

Patient Population

A total of 123 patients fulfilled the definition of “failing to mature” AVF. Of these, two were excluded because their AVF was thrombosed and the interventionist could not feel the venous outflow tract of the AVF on physical examination. One was excluded because of local infection and one because of unwillingness to undergo the procedure. Thus, a total of 119 patients were included in the study. The mean age was 57 ± 14 yr. There were 77 (64.7%) men and 42 (35.3%) women. Black and white patients were equally represented (36.1% each), Hispanic patients composed 17.7%. Diabetes was present in 69 (58%; Table 1). The median and mean of the duration of time from AVF creation to first intervention was 4 and 4.6 ± 4.2 mo, respectively (range 2 to 24 mo). The types of AVF are presented in Table 2.

Sites of Lesions

Multiple derangements were present in 85 (71.4%) individuals. A single derangement was present in 34 (28.6%). Of these, six (5.0%) were due to the presence of a deep AVF with varying degree of tortuosity. Significant accessory veins were present in 35 (29.4%) but as the only cause of AVF dysfunction in four (3.4%; Table 3). The frequency and the distribution of vascular stenoses were as follows (Table 4): Artery, six (5.1%); arterial stenoses, 12 (9.8%); venous stenoses, 32 (26.3%); venous stenoses, 14 (11.4%); venous stenoses, 21 (17.7%); venous stenoses, 10 (8.4%); venous stenoses, 2 (1.7%); venous stenoses, 69 (58%).

Table 1. Patient demographics

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<table>
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<tbody>
<tr>
<td>$N$</td>
<td>119</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>57±14</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>77 (64.7%)</td>
</tr>
<tr>
<td>female</td>
<td>42 (35.3%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>white</td>
<td>43 (36.1%)</td>
</tr>
<tr>
<td>black</td>
<td>43 (36.1%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>21 (17.7%)</td>
</tr>
<tr>
<td>Asian</td>
<td>10 (8.4%)</td>
</tr>
<tr>
<td>Native American</td>
<td>2 (1.7%)</td>
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<tr>
<td>Diabetes</td>
<td>69 (58%)</td>
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peripheral vein, 70 (58.8%); and central vein, 10 (8.4%). Complete peripheral vein occlusion was present in 25 (21%).

Technique Outcomes
In 107 (89.9%) patients, the angiographic procedure succeeded in increasing the AVF blood flow. In Figure 1, we show a sample of two successful interventions. In three patients, the angiographic procedure was a contributor to successful AVF use. Of these, one was a deep brachial-cephalic AVF, and outlining the location and the depth of the AVF helped successful cannulation. In the other two cases, a brachial-cephalic AVF was actually done by connecting the brachial artery to the median antecubital vein, which diverted the blood to the deeper basilic vein. On the basis of the angiographic data, the vascular surgeon was instructed to ligate the connection between the median antecubital vein and basilic vein, thereby assisting these two AVF to become usable subsequently. These three cases were included among the successfully salvaged fistulas because we believed that the angiographic procedure provided valuable information that was instrumental in AVF salvage. In nine (7.6%) patients, the technique failed for the following reasons: Complete occlusion of venous outflow tract (n = 4), venous outflow tract was deep and tortuous (n = 3), venous outflow tract was severely strictured (n = 1), and juxta-arterial segment was strictured (n = 1).

AVF Salvage Rates
Ninety-nine (83.2%) fistulas became usable during HD. Twenty (16.8%) fistulas failed to become usable during HD. Of these, nine were due to technique failure as described above and 11 were due to persistence of AVF “immature” state despite apparently successful endovascular treatment. A summary of the reasons for failure of AVF salvage is listed in Table 5. Successful AVF salvage was not associated with age (P = 0.875), gender (P = 0.215), race (P = 0.514), the presence of diabetes (P = 0.630), or the location of the AVF (P = 0.395).

Follow-Up
All 99 patients whose fistulas were salvaged successfully were followed up for a minimum of 3 mo with a mean duration of follow-up of 8.9 ± 5.9 mo. This amounted to a total of 882 patient-months of follow-up. During this period, there were a total of 11 deaths and three kidney transplants in patients with a functioning AVF. Three patients lost their AVF as a result of thrombosis, and 17 required a total of 25 repeat endovascular treatments. The latter involved 19 angioplasty procedures and six successful thrombectomies. The total AVF event rate was 28 events per 882 patient-months (3.18 per 100 patient-months) or

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Table 2. Types of AVF

<table>
<thead>
<tr>
<th>Type</th>
<th>N</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Radiocephalic</td>
<td>75</td>
<td>(63%)</td>
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<tr>
<td>Brachial-cephalic</td>
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<td></td>
</tr>
<tr>
<td>nontransposed vein</td>
<td>28</td>
<td>(23.5%)</td>
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<tr>
<td>transposed vein</td>
<td>1</td>
<td>(0.8%)</td>
</tr>
<tr>
<td>Brachial-basilic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>nontransposed vein</td>
<td>6</td>
<td>(5.1%)</td>
</tr>
<tr>
<td>transposed basilic vein</td>
<td>9</td>
<td>(7.6%)</td>
</tr>
</tbody>
</table>

*AVF, arteriovenous fistula.

Table 3. General overview of AVF derangements

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<tr>
<th>Derangement</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two or more derangements</td>
<td>85</td>
<td>(71.4%)</td>
</tr>
<tr>
<td>stenosis (≥1) and significant accessory vein</td>
<td>35</td>
<td>(29.4%)</td>
</tr>
<tr>
<td>stenosis (≥2) without significant accessory vein</td>
<td>50</td>
<td>(42%)</td>
</tr>
<tr>
<td>Single derangement only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>significant accessory vein</td>
<td>4</td>
<td>(3.4%)</td>
</tr>
<tr>
<td>deep AVF</td>
<td>6</td>
<td>(5%)</td>
</tr>
<tr>
<td>stenosis</td>
<td>24</td>
<td>(20.2%)</td>
</tr>
</tbody>
</table>

Table 4. Frequency and distribution of vascular stenoses

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral artery stenosis</td>
<td>6</td>
<td>(5.1%)</td>
</tr>
<tr>
<td>Arterial anastomosis stenosis</td>
<td>56</td>
<td>(47.1%)</td>
</tr>
<tr>
<td>Juxta-arterial anastomosis stenosis</td>
<td>76</td>
<td>(63.9%)</td>
</tr>
<tr>
<td>Peripheral vein stenosis</td>
<td>70</td>
<td>(58.8%)</td>
</tr>
<tr>
<td>Peripheral vein occlusion</td>
<td>25</td>
<td>(21%)</td>
</tr>
<tr>
<td>Central vein stenosis</td>
<td>10</td>
<td>(8.4%)</td>
</tr>
<tr>
<td>Arterial with juxta-arterial stenosis</td>
<td>45</td>
<td>(37.8%)</td>
</tr>
<tr>
<td>Juxta-arterial with peripheral vein stenosis</td>
<td>46</td>
<td>(38.7%)</td>
</tr>
</tbody>
</table>

Figure 1. A sample of two vascular lesions that were encountered during salvage procedures on “failing to mature” arteriovenous fistulas (AVF). (A) A tight juxta-arterial anastomosis stenosis (arrow) is preventing the maturation of an upper arm brachial-cephalic AVF. (B) Successful angioplasty led to resolution of the stenosis. (C) An extremely tight venous outflow tract stricture (short black arrows) has prevented successful maturation of a radiocephalic AVF. A collateral vein has developed (white arrow). (D) Successful angioplasty led to resolution of the stricture, and the collateral vein is now undetectable by angiography.
0.38/access-year. The AVF thrombosis rate was 0.12/access-year, and AVF loss rate was 0.04/access-year. Longitudinal follow-up of AVF patency rates is presented in Figure 2.

Complications

Complications included local hematoma formation in approximately 15% of patients. These occurred either at the site of vessel cannulation or angioplasty. In most cases, the hematoma was self-limiting and was contained simply with application of local pressure. In three patients, however, the blood from the hematoma dissected into the surrounding tissues, causing pain and a large area of ecchymosis. Conservative measures successfully treated all of these patients. Three patients had local pain and erythema around the site of coil insertion, which subsided with conservative measures. In one patient, steal phenomenon developed and the AVF required elective ligation. It is interesting that this was a brachial-basilic AVF that had been declared unsuccessful because of its depth. None of our patients lost an AVF as a result of the procedure.

Discussion

The AVF that composed this series never matured to sustain HD. Our evaluation of these fistulas uncovered significant underlying pathology, exemplified by the severity and the multiplicity of lesions. Thus, 75% of cases required intervention at more than one anatomic location. Such underlying pathology clearly explains why these fistulas never matured enough to be used during HD. It also suggests that these fistulas are unlikely to mature with additional time or with physical exercise of the ipsilateral arm, as is commonly advised. Thus, waiting on these “failing to mature” fistulas in the hope of spontaneous improvement is unrewarding and may result in AVF thrombosis and irrecoverable loss.

Our results demonstrate that endovascular evaluation coupled with angioplasty of vascular stenosis and accessory vein obliteration results in high salvage rates of these “failing to mature” fistulas. Our success rates are comparable but modestly lower than those reported by Beathard et al. (24) in their series on early AVF failure. However, this difference may relate to disease severity. In their series, early AVF failure was defined as a fistula that never matured or that failed within the first 3 mo of use. Our series of 119 cases strictly comprises fistulas that could never be used successfully for HD. Hence, we suspect that the extent and the severity of lesions in our series are likely to be worse. In both series, however, AVF salvage rates with endovascular treatment was very encouraging. Thus, the commonly practiced approach of abandoning the “failing to mature” AVF should be discouraged and considered obsolete.

The locations of the vascular lesions, judged to prevent the maturation of the AVF, are largely in agreement with previous reports by Beathard et al. (24–26). The most common lesion in our series is stenosis of the juxta-arterial anastomosis segment. Very frequently, this lesion is associated with narrowing of the arterial anastomosis or with downstream venous stenosis (Tables 3 and 4) (24). The juxta-arterial anastomosis lesion significantly restricts the flow to the AVF, prevents the maturation process, and may progress to complete occlusion if untreated.

Table 5. Reasons for unsuccessful AVF salvagea

<table>
<thead>
<tr>
<th>Causes</th>
<th>n</th>
<th>AVF Type</th>
</tr>
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<tbody>
<tr>
<td>Occlusion of venous outflow tract</td>
<td>4</td>
<td>All cases R-cephalic</td>
</tr>
<tr>
<td>Stricture of venous outflow tract</td>
<td>7</td>
<td>All cases R-cephalic</td>
</tr>
<tr>
<td>Deep venous outflow tract</td>
<td>5</td>
<td>B-cephalic (2); B-basilic (3)</td>
</tr>
<tr>
<td>Arterial and JXTA anastomotic stenosis</td>
<td>4</td>
<td>B-cephalic (2); B-basilic (2)</td>
</tr>
</tbody>
</table>

*aFailure rate from all causes is 16.8%. R, radial; B, brachial; JXTA, juxta-arterial.

Figure 2. Survival curves of salvaged AVF. These curves are generated by using death- and kidney transplantation–censored Kaplan-Meier analysis. (A) Primary unassisted patency refers to AVF patency without the need for additional interventional procedures. (B) Secondary patency refers to AVF patency with the use of interventional procedures to either maintain or restore patency.
Often, it leads to the presence of “hammer pulse” close to the arterial anastomosis, which can be detected by physical examination (27,28). Accessory veins as the sole cause of AVF dysfunction were responsible for a minority of the primary AVF failures in our series. More often than not, they are found in association with other stenotic lesions, which may have assisted in their growth.

Once the “failing to mature” AVF is salvaged, the focus becomes on its long-term patency. In this series with a total of 882 patient-months of follow-up, we show that the majority of salvaged AVF maintain good patency rates. Recurrence of vascular stenosis or thrombosis with a total event rate of 0.38 per access-year is not surprising given the proliferative nature of the vascular lesion as well as induction of scar formation by vessel wall injury from balloon angioplasty (29). Fortunately, recurrent stenoses respond very well to repeat angioplasty, which frequently provides an opportunity to perform the necessary dilation with a larger size angioplasty balloon because the AVF then is generally more developed. It is interesting that our data as well as those of Beathard et al. (24) show that once these ‘failing to mature’ fistulas undergo salvage treatment and become usable during HD, they demonstrate comparable patency to other studies that have followed fistulas that did not require intervention for initial use (12,13,22,30–32).

Endovascular treatment of the “failing to mature AVF” does not eliminate the need for additional vascular surgery in some patients. However, we strongly believe that endovascular treatment should be attempted before surgery is considered for the following reasons: (1) We and others (22–24,33) have demonstrated that endovascular treatment is associated with excellent success rates, low complication rates, and promising long-term patency rates (24). Most important, this is done without the introduction and assistance of synthetic polytetrafluoroethylene grafts. (2) Because vein manipulation is incriminated in juxta-arterial anastomosis stenosis, avoidance of surgery, if possible, eliminates the risk for recurrent stenosis at sites of new arterial and juxta-arterial anastomosis. (3) During endovascular treatment, AVF mapping is an inherent part of the procedure. This uncovers all of the contributing lesions to AVF dysfunction. Such information is valuable and is the basis for any successful treatment approach. This increases the chances of successful surgical revision. In other instances, it may mean totally abandoning the existing AVF and saving the patient from unnecessary surgical revision.

Limitations of this article lie inherently in the design of the study, which is a case series study. Thus, our results are subject to criticism because of lack of a randomized design in which an alternative approach is implemented. Obviously, alternative approaches include surgical revision of the AVF, creation of a new AVF at a new site, insertion of short segments of polytetrafluoroethylene to bypass stenosed segments, and creation of an AVG. These alternative approaches continue to be viable options, and despite the promising success of our approach with endovascular treatment of failing to mature AVF, we do not provide proof that endovascular treatment is superior to these alternatives. In addition, this article does not provide data on the cost of these procedures, which is beyond the scope of this article.

Conclusion
Endovascular treatment of “failing to mature AVF” is both safe and effective. When it is performed in a dedicated access center, it is associated with high success rates, low complication rates, and promising AVF primary and secondary patency rates.

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References
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Functioning vascular access is the lifeline of the hemodialysis patient. Please refer to the Disease of the Month article in the April issue of JASN (available online at www.jasn.org) on vascular access to complement the papers by Nassar et al., Asif et al., and the access data from DOPPS in this issue of CJASN.