Thermal Resistance Anastomosis Device for the Percutaneous Creation of Arteriovenous Fistulae for Hemodialysis

Jeffrey E. Hull, MD, Guillermo Elizondo-Riojas, MD, Wendy Bishop, BHSc, RVT, and Yesenia L. Voneida-Reyna, MD

ABSTRACT

Purpose: To evaluate the safety and efficacy of arteriovenous fistula (AVF) creation with a thermal resistance anastomosis device (TRAD).

Materials and Methods: From January 2014 to March 2015, 26 patients underwent ultrasound (US)-guided percutaneous creation of proximal radial artery–to–perforating vein AVFs with a TRAD that uses heat and pressure to create a fused anastomosis. Primary endpoints were fistula creation, patent fistula by Doppler US, two-needle dialysis at the prescribed rate, and device-related complications.

Results: Technical success rate of fistula creation was 88% (23 of 26). Procedure time averaged 18.4 minutes (range, 5–34 min), and 96% of anastomoses (22 of 23) were fused. At 6 weeks, 87% of AVFs (20 of 23) were patent, 61% (14 of 23) had 400-mL/min brachial artery flow, 1 patient was receiving dialysis, 2 fistulae had thrombosed, and 1 patient had died unrelated to the procedure.

Conclusions: Percutaneous AVFs created with a TRAD met the safety endpoints of this study. Midterm follow-up demonstrated intact anastomoses and fistulae suitable for dialysis.

ABBREVIATIONS

AVF = arteriovenous fistula, TRAD = thermal resistance anastomosis device

The arteriovenous fistula (AVF) is the preferred access for hemodialysis in the United States and throughout the world (1–3). The predominant method of creating an AVF with a sutured anastomosis has remained unchanged since the original description by Brescia et al in 1966 (4). Minimally invasive methods for AVF creation have recently been developed. A two-catheter electrosurgical radiofrequency anastomosis device that cuts precisely aligned linear incisions has successfully created ulnar artery–to–ulnar vein fistulae in the interventional suite with promising initial results (5). The thermal resistance anastomosis device (TRAD) was designed as a single-catheter venous access system to create percutaneous fistulae under ultrasound (US) guidance. This anastomosis device uses applied pressure and thermal resistance energy (ie, direct heat) to fuse artery and vein adventitia.
together and then cut an elliptical anastomosis between the proximal radial artery and perforating vein. The present report prospectively evaluates the initial safety of the use of a TRAD in a 6-week study with 12–24-month follow-up.

**MATERIALS AND METHODS**

The study was a single-arm prospective 6-week evaluation of the Ellipsys Vascular Access System (Avenu Medical, San Juan Capistrano, California) for the creation of AVFs for hemodialysis access (ClinicalTrials.gov: NCT02816398). The primary efficacy endpoints were (i) creation of a fistula with the TRAD device and (ii) fistula patency by Doppler US examination. The secondary endpoints were brachial artery US examination. The secondary endpoints were brachial artery flow volume > 400 mL/min and/or three sessions of two-needle dialysis at the prescribed rate. The safety endpoints were (i) less than a 50% incidence of minor complications and (ii) less than a 1% incidence of major device-related complications as defined in vascular access reporting standards (6,7). Additional complications evaluated included electrical shock causing tissue injury and significant embolization in a previously uninvolved arterial territory with associated tissue ischemia. Inclusion and exclusion criteria are listed in Table 1. Continued follow-up of the 20 patients with patent fistulae after the initial 6-week evaluation was performed by review of dialysis records, Doppler US examination results, and additional procedures for a period of 12 months or greater.

**Patient Population**

The present study complies with Declaration of Helsinki guidelines for research in human subjects. The initial 6-week protocol and the extended follow-up data collection had regulatory approval from the Federal Commission for the Protection against Health Risks and hospital investigational review board approval. Between January 2014 and March 2015, patients eligible for a surgical fistula were evaluated for the study. Screening resulted in 26 of 45 patients being enrolled as meeting inclusion criteria for the study. All patients enrolled had an assessment of medical history and a physical examination, laboratory studies, and Doppler US examination, and signed informed consent. All patients were Hispanic, 38% were male, 62% were female, and all were undergoing catheter hemodialysis. Patient demographics are summarized in Table 2. The pre- and postprocedural Doppler US vein-mapping examination was performed with a SonoSite M-Turbo linear 5–13-MHz transducer (SonoSite, Bothell, Washington) according to a modification of the Society of Vascular US guidelines as previously described (8).

The TRAD consists of three main components: an access needle, an over-the-wire tissue fusion and cutting catheter, and a power controller. The TRAD catheter has a 6-F proximal diameter with opposing active surfaces between the base and the coned 5-F distal tip (Figs 1, 2c). The power controller delivers direct current to the catheter heating element that is controlled with feedback from two temperature sensors and a gap sensor detecting the temperature and the opening distance of the catheter. A thumb tab in the handle of the device controls the catheter opening and closing and the fusion pressure. The combination of time, temperature, and pressure results in tissue fusion and cutting of an elliptical anastomosis.

**Table 1. Inclusion and Exclusion Criteria**

**Inclusion Criteria**

1. Age > 18 y and < 80 y
2. Patients diagnosed with CKD classification stage IV/V
3. Adequate quality vein based on preoperative assessment
   a. Adjacent vein diameter of > 2.0 mm at target anastomosis site
   b. Confirmed adequate outflow vein ≥ 2.0 mm
4. Adequate quality radial artery based on preoperative assessment
   a. Arterial lumen diameter of > 2.0 mm at target anastomosis site
5. Adequate collateral arterial perfusion
6. Negative Allen test results for ulnar artery insufficiency

**Exclusion Criteria**

1. Pregnancy or patients currently breast feeding
2. Diagnosed hypercoagulable state
3. Acute or active infection
4. Use of immunosuppressive medication
5. History of organ transplantation
6. Upper-extremity arterial stenosis (> 20 mm/Hg systolic BP difference between arms)
7. Radial artery–adjacent vein proximity > 1.5 mm

**Table 2. Demographic Characteristics of Study Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic race</td>
<td>26 (100)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>10/16</td>
</tr>
<tr>
<td>Age (y)</td>
<td>45.5 ± 13.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.7 ± 5.1</td>
</tr>
<tr>
<td>Obesity*</td>
<td>7 (27)</td>
</tr>
<tr>
<td>IDDM</td>
<td>11 (42)</td>
</tr>
<tr>
<td>NIDDM</td>
<td>6 (23)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>24 (92)</td>
</tr>
<tr>
<td>Left arm fistula</td>
<td>24 (93)</td>
</tr>
<tr>
<td>Previous AVF</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Previous catheter</td>
<td>26 (100)</td>
</tr>
</tbody>
</table>

Note: Values presented as mean ± standard deviation where applicable. Values in parentheses are percentages.

AVF = arteriovenous fistula; BMI = body mass index; HTN = hypertension; IDDM = insulin-dependent diabetes mellitus; NIDDM = non–insulin-dependent diabetes mellitus.

*Defined as BMI > 30 kg/m².
Procedure

Patients were pretreated with aspirin 325 mg/d for 48 hours and clopidogrel 75 mg/d for 5 days or 300 mg the day before the procedure. Local/regional anesthesia with conscious sedation was used. Initial venous access was at the cubital vein or brachial vein with US guidance and a standard micropuncture needle and wire (Cook, Bloomington, Indiana). Under continuous US guidance, the micropuncture needle was advanced over the wire to the junction of the perforating vein and radial artery (Video 1 [available online at www.jvir.org]). The micropuncture needle was advanced into the radial artery (Fig 2) and exchanged for a sheath (6-F Slender radial artery sheath; Terumo, Somerset, New Jersey). The TRAD catheter was advanced over a 0.014-inch wire (Nitrex; ev3, Plymouth, Minnesota) and positioned in the sheath with the distal tip in the artery and base in the perforating vein. The sheath was retracted, allowing capture of the artery and vein between the catheter base and tip (Fig 2c). The catheter was closed, compressing the artery and vein together. The power controller was activated, applying pressure and thermal resistance energy until complete closure of the catheter was indicated by feedback from the gap sensor signifying anastomosis completion. The catheter and sheath were removed, and hand-held pressure was applied at the access site until hemostasis was achieved. Completion Doppler US examination was performed after fistula creation.

Subsequent endovascular procedures to prepare fistulae for hemodialysis were performed in an endovascular suite with fluoroscopy (GE Medical Systems, Milwaukee,
Wisconsin) and US (SonoSite). These procedures were performed to direct flow into arm veins and achieve a palpable superficial target vein with adequate length and diameter for two-needle cannulation as described in the National Kidney Foundation’s “rule of sixes” (9). The preferred target vein was the cephalic vein, followed by retrograde flow in the median vein, and finally, the basilic vein, requiring elevation. Inadequate inflow of less than 400 mL/min was increased by balloon dilation of the juxtaanastomotic segment from fistula access or transradial artery access at the wrist (10,11). Deep flow was directed to the superficial veins by embolization of the brachial vein with coils (12), typically when the brachial vein flow volume was greater than 300 mL/min. Banding of the median basilic vein was used to direct flow from the basilic vein into the cephalic vein by using the technique described by Miller et al (13). Flow was directed into the median forearm vein by percutaneous valvulotomy by using an over-the-wire valvulotome (LeMaitre, Burlington, Massachusetts) as previously described (14). Target veins that were deep were superficialized by surgical elevation.

Patients had scheduled clinical and Doppler US examinations at 24 hours and 1, 2, and 6 weeks. Additional assessments of the patients with patent fistulae were obtained from medical records at 3, 6, 12, and as late as 24 months. Assessments included physical examination, Doppler US examinations, and dialysis records.

**Definition of Terms**
Technical success was defined as creation of a fistula demonstrating flow by Doppler US. The procedure time was the time from initial access to catheter removal. Failed access was the inability to achieve initial venous and/or arterial access. The fused anastomosis was the direct connection of artery and vein without interruption, intervening nonvascular tissue, or pseudoaneurysm. The juxtaanastomotic segment includes the anastomosis and the proximal 4 cm of the fistula. A tract fistula was a fistula tract of nonvascular tissue in which the separation of artery and vein was greater than 5 mm on US or fistulography. A functional fistula allowed two-needle dialysis for three dialysis sessions at the prescribed rate. Clinical success was fistula flow by Doppler US, flow volume in the brachial artery of 400 mL/min, or functional fistula. Functional patency was survival analysis of fistulae after the first two-needle access for dialysis (15).

**Data Analysis**
Descriptive qualitative, quantitative, and statistical analysis was performed. Quantitative assessments were performed by using Excel (Microsoft, Redmond, Washington) and included calculation of minimal, maximal, and average values, standard deviation, and paired Student t test results. Kaplan–Meier analysis of functional fistula patency from first use for dialysis to

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**Figure 3.** TRAD anastomosis in a postprocedural fistulogram: (a) proximal radial artery at the fused anastomosis (arrow), brachial artery (BR), and perforating vein (P, a and b). (b) Same image as a with the venous outflow image added shows the cephalic vein (C) and basilic vein (B). (c) Digital subtraction fistulogram at 6 weeks, immediately after dilation of juxtaanastomotic segment with a 4-mm balloon. The anastomosis is indicated by the arrow. Flow volumes were 691 mL/min in the brachial artery, 561 mL/min in the median cephalic vein (MCV), and 108 mL/min in the median basilic vein (MBV). The cephalic vein was cannulated for dialysis. (d,e) US images of the fused anastomosis (plus symbols) between the radial artery (RA) and perforating vein (PV) at 688 days in longitudinal and transverse images, respectively.
abandonment as described by Huijbregts et al (15) was performed by using MedCalc for Windows (version 12.5; MedCalc, Ostend, Belgium).

RESULTS

The technical success rate in percutaneous AVF creation was 88% (23 of 26). All three technical failures were the result of access failure: one caused by venous bleeding from the initial puncture and two as a result of vasoconstriction. Procedure times averaged 18.4 minutes ± 7.7 (range, 5–34 min). On day 1, the initial mean brachial artery flow volume increased from a preprocedural measurement of 49.8 mL/min ± 37.3 (range, 10.8–118 mL/min) to 380.5 mL/min ± 166.3 (range, 57–718 mL/min). The anastomosis length, width, and cross-sectional area were 2.12 mm ± 0.57 (range, 1.2–3.2 mm), 1.6 mm ± 0.38 (range, 1.0–2.3 mm), and 2.76 mm² ± 1.25 (range, 1.1–5.8 mm²), respectively. A fused anastomosis was achieved in 96% of patients (n = 22) and remained intact throughout the initial 6-week and subsequent follow-up study (Fig 3). A tract fistula developed and resulted in a functioning fistula in one patient.

At 6 weeks, additional procedures were performed on 48% of AVFs (n = 11). Early thrombosis developed in two fistulae, and one patient died of causes unrelated to the fistula. Balloon dilation of the juxtaanastomotic segment was the most common secondary procedure, performed in 10 patients during the first 6 weeks, and significantly increased the brachial artery flow volume from 257.8 mL/min (range, 0–806 mL/min) to 783.5 mL/min (range, 353–1,640 mL/min; P = .0002). The average balloon size for dilation of the juxtaanastomotic segment was 5.0 mm ± 0.8 (range, 4–6 mm).

At 6 weeks, 77% of patients (20 of 26) had met the primary clinical endpoint: 14 had brachial artery flow volume greater than 400 mL/min, one was receiving dialysis, and five had patent fistulae (Fig 4). The mean brachial artery flow volumes and the total venous outflow flow volumes at 6 weeks were 597.5 mL/min and 544.0 mL/min, respectively, with a nonsignificant 53.5-mL/min difference (P = .28; Table 3).

The initial 6-week Doppler US data, combined with the follow-up data, demonstrated that the anastomotic cross-sectional area, flow volumes, and vessel diameters increased through 360 days (Table 4). Beyond 360 days, these parameters appeared stable. During the last available Doppler US examination in 10 patients at a mean of 506 days ± 105 (range 397–688 d), the mean brachial artery flow volume was 1,175 mL/min ± 393.6 (range, 542–1,965 mL/min), and the target vein flow volume was 960.9 mL/min ± 234.4 (range, 599–1,305 mL/min). The data in Table 4 show a direct relationship between anastomotic cross-sectional area and brachial artery flow (Pearson $r = 0.94$). Average time to dialysis was 108 days ± 61 (range, 33–295 d). The average number of days receiving dialysis (16 patients total) was 354 days ± 177 (range, 0–617 d). The average brachial artery flow volume in dialyzed fistulae at 3 months was 841 mL/min ± 425 (range, 470–1,836 mL/min), and target vein flow volume was 540 mL/min ± 212 (range, 277–844 mL/min). The cumulative functional patency rates were 88% and 75% at 6 and 12 months, respectively (Fig 5).

Overall, in the first 12 months, 36 additional procedures were performed in 23 patients with fistulae, equating to 1.57 procedures per patient per year. The types of procedures performed were 26 endovascular and 12 surgical procedures that included balloon dilation, brachial vein embolization, basilic vein transposition, basilic vein ligation, and median vein valvulotomy (Table 5).

There were no major device-related anastomosis complications (Table 6). The patients with access failure remained suitable for surgical fistula creation.
Early fistula thrombosis occurred in three fistulae (< 6 wk), two within 24 hours and one at 13 days. All three cases of early fistula thrombosis involved the anastomosis; two had partial thrombosis of the perforating vein. There was neither arterial thrombosis nor emboli. One anastomotic occlusion that occurred at 2 hours was dilated open with a 4.5-mm balloon, and two were abandoned. Two other minor complications included a minor hematoma during the access portion of a procedure and creation of a tract fistula that went on to be employed for successful dialysis. During the follow-up period after 6 weeks, three fistulae were abandoned or thrombosed, and an additional four deaths unrelated to the device or fistula occurred.

**DISCUSSION**

In the initial 6-week evaluation in the present study, the TRAD demonstrated successful creation of percutaneous anastomoses between the proximal radial artery and perforating vein with low complication rates. The initial and follow-up evaluation demonstrated that the anastomoses and fistulae were safely created, underwent maturation procedures without complications, and were durable. The percutaneous fistulae created with the TRAD were comparable to surgical and percutaneous fistula results reported in the literature in terms of early thrombosis (16), 6-month fistula failure rate (15–17), and functional patency (5,18). The percutaneous approach to fistula creation has the potential advantage of being minimally invasive and creating anastomoses between in situ vessels without dissection, twisting, or dislocation of vessels thought to cause intimal hyperplasia (5,19). However, percutaneous AVFs are currently limited by anastomosis type and location (5). Percutaneous AVFs have multiple outflow veins, which potentially pose challenges in the development of hemodialysis cannulation sites. In the present study, anastomosis creation was followed by a tailored approach for each fistula to achieve adequate flow for dialysis and to direct flow into a target vein suitable for two-needle cannulation for hemodialysis.

<table>
<thead>
<tr>
<th>Table 3. Flow Distribution at 6 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Distribution</strong></td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Artery</td>
</tr>
<tr>
<td>CV</td>
</tr>
<tr>
<td>BV</td>
</tr>
<tr>
<td>BrV1</td>
</tr>
<tr>
<td>BrV2</td>
</tr>
<tr>
<td>Median vein</td>
</tr>
<tr>
<td>Total vein</td>
</tr>
</tbody>
</table>

Values are presented as mean ± standard deviation

*Artery = brachial artery flow, BV = basilic vein at mid-upper arm, BrV1 and BrV2 = brachial vein in distal upper arm (which are usually paired), CV = cephalic vein at mid-upper arm, median vein = median vein in the proximal forearm, total vein = sum of venous outflow (CV + BV + BrV1 + BrV2 + median V).

†Difference in flow volume in artery and total vein was 53.5 mL/min (nonsignificant difference, P = .28, Student t test).

![Figure 5. Kaplan–Meier curve of functional patency of fistulae from the first two-needle cannulation to abandonment.](image)

**Table 4. Vessel Diameter and Flow**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Preprocedure</th>
<th>1 d</th>
<th>7 d</th>
<th>14 d</th>
<th>42 d</th>
<th>90 d</th>
<th>180 d</th>
<th>360 d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 26)</td>
<td>(n = 23)</td>
<td>(n = 23)</td>
<td>(n = 23)</td>
<td>(n = 20)</td>
<td>(n = 16)</td>
<td>(n = 14)</td>
<td>(n = 12)</td>
</tr>
<tr>
<td>BA diameter (mm)</td>
<td>2.9</td>
<td>3.3</td>
<td>3.4</td>
<td>3.4</td>
<td>3.7</td>
<td>4.5</td>
<td>3.8</td>
<td>5.3</td>
</tr>
<tr>
<td>Cephalic diameter (mm)</td>
<td>2.7</td>
<td>3.4</td>
<td>3.7</td>
<td>3.4</td>
<td>4.0</td>
<td>4.4</td>
<td>4.5</td>
<td>10.8</td>
</tr>
<tr>
<td>Basilic diameter (mm)</td>
<td>3.6</td>
<td>4.9</td>
<td>4.8</td>
<td>5.0</td>
<td>5.6</td>
<td>5.0</td>
<td>6.1</td>
<td>10.5</td>
</tr>
<tr>
<td>Length (mm)*</td>
<td>–</td>
<td>2.2</td>
<td>2.1</td>
<td>2.0</td>
<td>2.6</td>
<td>2.7</td>
<td>3.2</td>
<td>3.4</td>
</tr>
<tr>
<td>Width (mm)*</td>
<td>–</td>
<td>1.6</td>
<td>1.6</td>
<td>1.7</td>
<td>1.9</td>
<td>2.1</td>
<td>2.8</td>
<td>3.0</td>
</tr>
<tr>
<td>CSA (mm²)†</td>
<td>–</td>
<td>2.9</td>
<td>2.6</td>
<td>2.8</td>
<td>4.1</td>
<td>4.9</td>
<td>6.4</td>
<td>8.1</td>
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<tr>
<td>BA flow (mL/min)†</td>
<td>49.8</td>
<td>379.7</td>
<td>347.3</td>
<td>327.0</td>
<td>597.5</td>
<td>597</td>
<td>605</td>
<td>1284.2</td>
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<tr>
<td>Target vein flow (mL/min)†</td>
<td>–</td>
<td>271.4</td>
<td>228.3</td>
<td>201.0</td>
<td>380.1*</td>
<td>483</td>
<td>568.4</td>
<td>1023.7</td>
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*US measurements of anastomosis.
†US measurements of anastomosis.
*CSA and BA flow measured by Doppler US show significant positive correlation (Pearson r = 0.94).
The TRAD fuses and cuts an elliptical connection between the deep and superficial arm veins. Adequate dilation of the perforating vein was an important element of increasing flow to the superficial system.

Directing flow toward a target vein for hemodialysis required a variety of procedures, including brachial vein embolization, basilic vein ligation, valvulotomy, and basilic vein transposition. Reduction of deep flow by brachial vein embolization was required in 26% of patients (n = 6). This was less than the 100% brachial vein embolization rate reported by Rajan et al (5) in percutaneous AVFs created between the ulnar artery and vein. In that series (5), brachial vein embolization was performed at the time of anastomosis creation, so it is unclear whether this procedure would be needed in all patients.

The overall additional procedure rate was 1.56 per patient per year in the present study (36 in 23 patients). Rajan et al (5) reported a lower secondary procedure rate of 0.6 per patient at 6 months by not directing flow into a single target vessel and by incorporating embolization of the brachial vein into the initial procedure. The best strategy for preserving vein,
achieving ideal flow rates, and providing adequate cannulation sites should be examined in future studies. Limitations of the present study include its design as a single-site, single-arm, prospective 6-week feasibility study. Primary fistula patency was not an intended outcome for this study, and it therefore deviates from the typical surgical series (18). Fistulae were not in common use at the treatment center before the outcome for this study, and it therefore deviates from study. Primary single-site, single-arm, prospective 6-week feasibility cannulation sites should be examined in future studies.

4. Brescia MJ, Cimino JE, Appel K, Hurwich BJ. Chronic hemodialysis procedures to adjust the current paradigm, all percutaneous and acceptable maturation and dialysis rates. In the current paradigm, all percutaneous fistulae require procedures to adjust flow, prevent unwanted deep flow, or direct flow into the target vein for cannulation. Additional investigation is warranted and under way.

REFERENCES