CLINICAL STUDY

Maturation for Hemodialysis in the Ellipsys Post-Market Registry

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ABSTRACT

Purpose: To prospectively evaluate the maturation of the endovascular arteriovenous fistula system (EndoAVF) for 2-needle cannulation (2NC).

Materials and Methods: From October 2018 to June 2019, evaluation of 123 patients resulted in 95 arteriovenous fistulae, a rate of 63% (60 of 95) EndoAVF, and 37% (35 of 60) fistulae treated surgically. At 4 weeks, EndoAVF was not suitable for 2NC (defined as a palpable target vein [TV], 500 mL/min flow volume, and 5-mm diameter) underwent maturation procedures.

Results: Technical success of EndoAVF creation was 96.7% (60 of 62). At 4 weeks, 67% (40 of 60) fistulae underwent maturation procedures: 62% (37 of 60) had balloon dilation, 32% (19 of 60) had brachial vein embolization, and 30% (18 of 60) had cubital vein banding, increasing TV flow volume from 182 ± 123 mL/min to 572 ± 225 mL/min ($P < 0.0005$). Transposition was required in 33% of patients (20 of 60), reducing the mean TV depth from 10.9 to 3.7 mm ($P < .0001$). 2NC and fistula success (2NC × 3) was achieved in 87% (47 of 54); 10% of patients (6 of 60) were not on dialysis; 6.8% of patients (4 of 60) died; 5% of fistulas (3 of 60) were abandoned for arm swelling, steal syndrome, and thrombosis. Time to 2NC, fistula success, and tunneled catheter removal were 65.6 ± 45.7 days, 79.1 ± 50.9 days, and 113.4 ± 62 days, respectively. Patients achieving 2NC had brachial artery flow of 944 ± 284 mL/min; and TV flow, diameter, and depth of 674 ± 292 mL/min, 6.1 ± 0.8 mm, and 3.6 ± 1.3 mm, respectively. Major complications were arm swelling, steal syndrome, and thrombosis.

Conclusions: Most patients had EndoAVF with maturation procedures at 4 weeks that achieved rapid maturation (Ellipsys Fistula for Hemodialysis Access; NCT03828253)

ABBREVIATIONS

EndoAVF = endovascular arteriovenous fistula, 2NC = 2-needle cannulation

Creation of a percutaneous fistula for hemodialysis access has been introduced in the United States and Europe with clinical trials showing safety and efficacy and promising results over 2 years (1,2). Percutaneous fistulae were created in situ with flow into the superficial system through the perforating vein using multiple venous outflow into the brachial, basilic and cephalic veins (2,3). Data from outside the United States support advantages of the percutaneous fistula that include improved cumulative and functional patency, reduced secondary procedures, and cost savings (2,4–6). Many of these improvements rely on the ability of dialysis centers to take advantage of cannulating fistulae at nonconventional sites around the antecubital fossa (2,3,7).

Concerns about the use and adoption of the percutaneous fistula in the United States have been raised in the medical literature with attempts to understand patient selection, maturation, and cannulation (7,8). The current study evaluated these issues from a prospective registry at a single center in the United States.

MATERIALS AND METHODS

Study Design

The Ellipsys post-market registry (Ellipsys Fistula for Hemodialysis Access; NCT03828253) was a prospective evaluation of the use of the endovascular arteriovenous fistula (EndoAVF) (Ellipsys EndoAVF; Avenu Medical, San Juan Capistrano, California) at a single site within the United States, at a multidisciplinary clinic including a single interventional radiologist with 30 years' experience and 5

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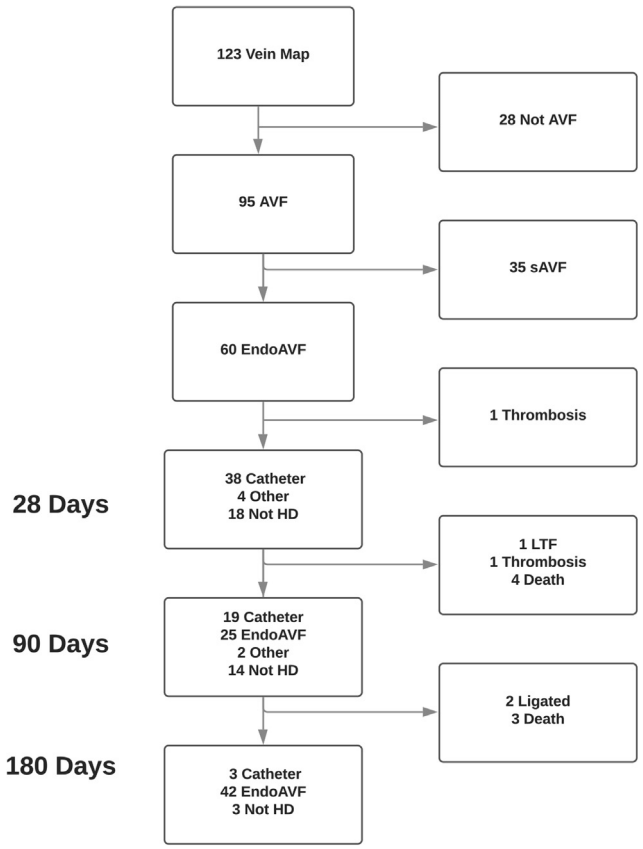

Figure 1. The flow chart shows the outcome of patients evaluated during the study. Initial evaluation included history, physical, and vein mapping evaluations. Catheter = catheter dialysis; LTF = lost to follow-up; Not AVF = fistula not created; Not HD = not on hemodialysis; Other = peritoneal dialysis, existing graft, or fistula; sAVF = surgical arteriovenous fistula.

vascular surgeons. The goals of the registry were to evaluate patient selection and fistula maturation using the best practices for early maturation identified during the US Pivotal Trial. Follow-up through 6 months was planned.

Between September 2018 and June 2019, 60 consecutive patients eligible for EndoAVF signed informed consent and were enrolled in the post-market registry. The study was performed with approval by an independent Investigational Review Board. The registry collected data for vein mapping, procedure performance, and follow-up at visits at 7, 28, 90, and 180 days. Event time-based data included all interventions, and dates of physiological maturation, referred for dialysis, 2-needle cannulation (2NC), functional fistula (fistula used in 3 of 4 sessions), catheter removal, cannulation injury, fistula thrombosis, fistula abandonment, and death. Patients were followed for a mean 282 ± 109 days (range, 103–385 days).

Patient Population

Patients with end-stage renal disease stages IV and V requiring immediate or near-term hemodialysis access underwent history, physical examination, and doppler ultrasonography examination to determine suitability for arteriovenous fistula. Evaluation of 123 patients resulted in 95 arteriovenous fistulae, 63% (60 of 95) EndoAVF and 37% (35 of 60) surgical fistulae (Fig 1). The demographics of the EndoAVF patients are summarized in Table 1.

Procedure

All procedures were performed using ultrasonography guidance with the patient under local or regional anesthesia. The antecubital fossa was prepped and draped. The vascular anatomy was confirmed by ultrasonography. Venous access with a micro-puncture needle (Cook Medical, Bloomington, Indiana) was obtained at the cubital vein in 82% (49 of 60) and the brachial vein in 18% (11 of 60). Fistula creation was performed as previously described (1). Briefly, the access needle was advanced transvenously and then into the proximal radial artery under ultrasonography guidance. A sheath (Glidesheath Slender 6; Terumo Medical, Somerset, New Jersey) was placed, and heparin (3,000 units) was injected into the proximal radial artery. The Ellipsys catheter was advanced through the sheath to the anastomosis site and activated. Balloon dilation after fistula creation was performed in all patients. The anastomosis and the outflow vein were balloon dilated with a 5- × 20-mm balloon (Sterling 4-Fr Monorail, Boston Scientific, Marlborough, Massachusetts) to 12 atmospheres until spasm resolved as previously described (1,5). In most cases the proximal radial artery was smaller than 5 mm diameter, such that the balloon was oversized. In some cases of severe mismatch between the artery and balloon diameter, the semicompliant balloon would migrate out of the artery into the perforating vein and avoid damaging the proximal radial artery. In 2 such cases, repeated balloon dilation with a 4-mm balloon was

Table 1. Demographics

Demographic	Value
Mean ± SD age, y (range)	64 ± 14 (24–90)
Males/Females	34/26
Ethnicity W/B/H/A	29/28/1/2
Mean ± SD BMI, kg/m^2 (range)	30.7 ± 9.0 (11.4–70.1)
HTN, %	57 (95)
NIDDM, %	37 (62)
IDDM, %	18 (31)
Smoker, %	12 (40)
Hemodialysis, %	44 (73)
Not on dialysis, %	16 (27)
Catheter, %	39 (65)
PD, %	3 (5)
Prior fistula or graft, %*	12 (20)

BMI = body mass index; HTN = hypertension; IDDM = insulin insulin-dependent diabetes; NIDDM = non-insulin-dependent diabetes; PD = peritoneal dialysis; W/B/H/A = White/Black/Hispanic/Asian.
*Prior fistula or graft included 2 patients who were currently using a failing graft or fistula.

performed to adequately dilate the anastomosis. Brachial artery flow volumes were obtained before and after balloon dilation. A brachial artery flow volume of >500 mL/min with a fistula wave form and visible resolution of spasm defined the ideal endpoint. The sheath was removed, and hemostasis was achieved at the venous access site by using handheld pressure. Completion of the Doppler ultrasonography evaluation was performed to ensure patency and assess for complications.

Maturation

At the 4 week visit, maturation and suitability for dialysis were assessed by physical examination; Doppler ultrasonography; flow volumes in the brachial artery; and the 3 main outflow veins: cephalic, basilic, and brachial were assessed. A fistula was considered suitable for dialysis when the fistula was palpable on physical examination and the target vein had 500 mL/min flow volume, 5-mm diameter based on the authors' experience and expert opinion (8,9). Fistulae not meeting the target endpoints underwent maturation procedures in a stepwise progression of balloon dilation of the proximal fistula (anastomosis through 4 cm of venous outflow), deep brachial vein embolization, and banding of the median basilic vein as needed. All endovascular procedures were performed in an outpatient-based laboratory. The first step was to achieve adequate inflow by a balloon that dilated the proximal fistula from anastomosis to target vein with 4-cm long balloon. A brachial artery flow volume of 800 mL/min has been recommended as a useful benchmark flow to support sustained dialysis with EndoAVF (8). The second step was to embolize the brachial vein when flow volume in this vessel was greater than 250 mL/min (according to Ellipsys instructions for use) and limited flow into the perforating vein. The third step was to band the median basilic vein to direct flow into the cephalic vein when needed to increase the flow volume or increase the palpability of the cephalic vein, or both. Banding of the median basilic vein was performed using an 0.035-inch wire in the interventional radiology suite by cut-down or Miller technique, using 4-0 proline suture (10). Surgical transposition was scheduled after adequate flow in the target vein was established, and the fistula was judged too deep for cannulation, when it was not palpable and was greater than 6 mm deep. The target vein was transposed by superficialization without tunneling, transection, or reanastomosis as previously described (11,12). Liposuction and lipectomy were also used for superficialization of the cephalic vein (13,14).

Follow-up Protocol

All patients underwent follow-up physical examinations and Doppler ultrasonography examinations at 1 and 4 weeks, 3 months, and then at 3-month intervals. All patients released for dialysis had a palpable fistula in the upper arm and a Doppler ultrasonography examination for documentation of vessel flow and diameter and to mark with indelible marker the cannulation sites for access. No ultrasonography assistance was provided at the dialysis centers during this study.

Definitions

Technical success was defined as successful deployment of the device and creation of a fistula by the Ellipsys device. In each patient, a single vein was identified as the target vein for dialysis access. Maturation procedures were secondary procedures performed prior to achieving physiological maturation of the target vein, defined as a flow volume ≥500 mL/min and diameter ≥5 mm or being used for hemodialysis as recommended by American Society of Nephrology Kidney Health Initiative (9). This definition of physiological maturation replaces the prior definition of brachial artery flow volume ≥500 mL/min and target vein diameter ≥4 mm used in prior EndoAVF trials (1,2,15). The proximal fistula was the inflow artery at the anastomosis through the first 4 cm of venous outflow. Clinical success was 2NC. Maintenance procedures were secondary procedures performed after the maturation endpoint or the patient undergoing successful 2-needle dialysis. A secondary procedure often included several interventions in a single session, although each type of procedure (ie, balloon dilation, embolization, and banding) was counted separately. Failure of the primary fistula was the inability to use a fistula for dialysis despite interventions and was classified as immediate (<72 hours), early (72 hour–90 days), or late (90–180 days) (16,17). Functional patency started at the first successful 2NC (18). Fistula success was defined as 2NC with dialysis at the prescribed rate as determined by the dialysis center during 2 of 3 of dialysis sessions (17). A thrombosed fistula had thrombosis of the anastomosis. Thrombus associated with stenosis or occlusion in the mid-fistula or central outflow were considered stenosed or occluded, respectively. Results were recorded according to reporting standards for the North American Vascular Access Consortium, Society for Vascular Surgery, and SIR (17,19,20).

Data Analysis

Clinical data were recorded on source documents and keyed into spread sheets. Descriptive qualitative, quantitative, and statistical analyses were performed. Quantitative assessments were performed using Excel for MacIntosh 2011 version 14.5.7 (Microsoft, Redmond, Washington) and were reported as mean ± SD and ranges. Kaplan-Meier survival analysis and inverse Kaplan-Meier cumulative probability analyses were performed using MedCalc version 14.12.0 software (MedCalc Software bvba, Ostend, Belgium) and reported as percentages of survival, mean ± SE, and medians (20). Patients were censored at date of death or last visit when they were lost to follow-up.

RESULTS

Doppler ultrasonography vein mapping found 92% (113 of 123) were candidates for surgical fistula and 61% (75 of 123) were EndoAVF candidates (**Fig 1**). Eighteen patients did not have arteriovenous fistulas created: 6 patients went on peritoneal dialysis, 3 patients had a surgical graft, 4 patients had not had surgery, and 5 were lost to follow-up.

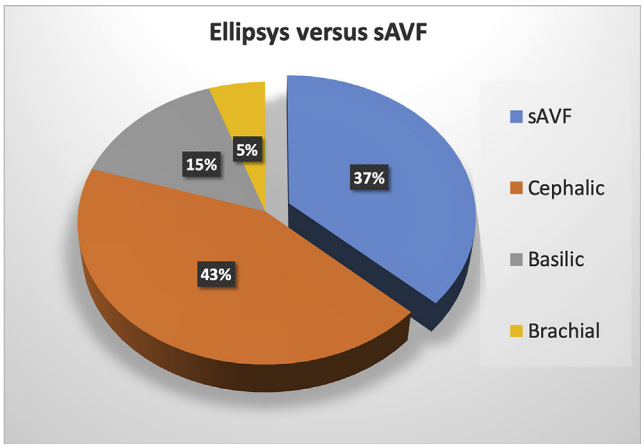

Figure 2. Distribution of fistula types for the 95 fistulas created during the study. The percutaneous fistula are represented by the target vein used for dialysis and included the cephalic, basilic, and brachial veins. The basilic and brachial vein fistulas were created in 2 stages with percutaneous fistula creation followed by surgical transposition. sAVF = surgical arteriovenous fistula.

Arteriovenous fistulae were created in 95 patients, with EndoAVF created in 63% (60 of 95) and surgical fistulae created in 37% (35 of 95) of patients. The EndoAVF procedure was contraindicated in 29 patients; 9 patients had absent perforating veins; 10 patients had perforating veins less than 2 mm in diameter; 4 patients had cubital veins <2 mm in diameter; 2 patients had incomplete palmer arch (Barbeau IV); 2 patients had radial artery <2mm; 1 patient had a thrombosed perforating vein; and 1 patient had high brachial artery bifurcation and an excessive distance between the radial artery and the perforating vein. There were 6 patients who were candidates for the EndoAVF procedure who underwent surgical AVF: 4 were candidates for wrist fistulas, and 2 chose surgery because they required transposition after EndoAVF.

Technical success with EndoAVF creation was achieved in 96.8% (60 of 62). Two patients in whom the initial creation failed due to inability to access the proximal radial artery underwent repeated procedures successfully, for a rate of 100% (60 of 60) fistula creation. Preoperative vein mapping demonstrated the mean proximal radial artery, perforating vein, and target vein diameters were 3.4 ± 1.2 mm (range, 2–9 mm), 3.0 ± 0.9 mm (range, 2–5.6 mm), and 4.0 ± 1.3 mm (range, 1.7–8.5 mm), respectively. The mean procedure time was 19.5 ± 11.3 min (range, 7–70 min). Initial brachial artery flow volume immediately after fistula creation was 323 ± 168.5 mL/min (range, 53–834 mL/min). All patients had 5-mm balloon dilation of anastomosis and perforating vein immediately after the creation which increased brachial artery blood flow volume to 649 ± 246.3 mL/min (range, 235–1277 mL/min). The ultimate target vein for dialysis was the cephalic vein in 70% (42 of 60), the basilic vein in 22% (13 of 60), and the brachial vein in 8% (5 of 60) as shown in Figure 2.

Table 2. Physical Examination

Days	Pulse			Thrill	Augment	Edema
	Doppler	1+	2+			
7	53%	44%	3%	36%	24%	2%
28	49%	39%	12%	36%	28%	4%
90	15%	52%	33%	54%	56%	8%
180	6%	63%	31%	71%	79%	4%
2NC	0%	66%	34%	80%	70%	0%

Note–Pulse was measured on the mid-distal upper arm and was Doppler only, 1+, or 2+ with a tourniquet. Thrill, augmentation, and edema were present or absent. Two-needle cannulation (2NC) was at a mean of 79.9 ± 47.3 (1–237) days.

EndoAVF Maturation

Endovascular maturation procedures were performed in 67% (40 of 60) at a mean 32.1 ± 14.6 days (range, 5–67 days) after creation, whereas 33% (20 of 60) had no maturation procedures. A total 52 endovascular procedures were required in 60 patients to achieve adequate flow and diameter in the target vein for hemodialysis, with 12 patients requiring 2 procedures. Multiple interventions were performed in individual patients during a single procedure as needed and included balloon dilation in 62% (37 of 60), brachial vein embolization in 32% (19 of 60), banding of median cubital vein in 30% (18 of 60), branch embolization in 8.3% (5 of 60), and valvulotomy in 3.3% (2 of 60), and 1 uncovered stent placement in diseased proximal radial artery. The maturation procedures increased the mean brachial artery flow volume from 602.7 ± 305 mL/min to 857.8 ± 371.4 mL/min ($P < .012$) and the target vein flow volume increased from a mean 188.9 ± 146.4 mL/min to 630.2 ± 437 mL/min ($P < .0001$). The physical examination and Doppler ultrasonography characteristics of the fistula at standard follow-up visits and key milestones are reported in Tables 2 and 3.

Transposition was performed in 30% (18 of 60) of 8 basilic vein fistulas, 5 brachial vein fistulas, and 5 cephalic vein fistulas at a mean 61.9 ± 20.8 days (range, 31–97 days). Three cephalic vein fistulas were treated with liposuction or lipectomy, or both. The pre-transposition mean target vein flow, diameter and depth was 831 ± 296 mL/min (range, 516–1,602 mL/min), 5.9 ± 1.0 mm (range, 4.0–8.4 mm), and 10.9 ± 4.5 mm (range, 6.0–23 mm), respectively. The post-target vein flow and diameter were not significantly changed at 751 ± 458.1 mL/min (range, 312–1,638 mL/min) and 6.0 ± 1.0 mm (range, 4.5–8.2 mm), respectively. The mean fistula depth was significantly diminished after transposition at 3.5 ± 1.5 mm (range, 1.6–5.4 mm) ($P < .0001$). Two basilic vein fistulas were used for dialysis without transposition. One patient not on dialysis did not undergo transposition of the basilic vein.

Kaplan-Meier Analysis

The Kaplan-Meier-derived event-time endpoints included cumulative probability of physiologic maturation, 2NC, and tunneled catheter removal and are shown in Table 4.

Table 3. Fistula Doppler Ultrasound Characteristics

Endpoint	BA Flow	TV Flow	TV Diameter	TV Depth	Palpable
1 week	716.2 ± 315.1	336.9 ± 338.7	5.1 ± 1.1	5.6 ± 0.60	47%
4 week	730.2 ± 303.2	358.6 ± 322.8	5.2 ± 1.4	4.6 ± 2.8	51%
90 days	1,024.0 ±417.5	607.1 ± 453.8	6.2 ± 1.5	4.5 ± 4.0	85%
2NC	982.6 ± 351.9	704.1 ± 323.8	6.2 ± 1.3	3.6 ± 1.3	98%
Fistula success	1,066.7 ± 381.1	721.3 ± 400.0	6.9 ± 1.7	3.3 ± 1.2	100%
TCR	1,061.0 ± 394.4	750.9 ± 349.5	7.1 ± 1.8	3.8 ± 2.0	100%

Note–The table gives fistula characteristics in terms of Doppler ultrasonography and whether a fistula was palpable in the upper arm above the elbow with a tourniquet on. The 4-week results took place before maturation procedures.
BA = brachial artery; fistula success = successful use of the fistula within 2 of 3 dialysis sessions; TV = target vein; 2NC = first two-needle cannulation.

Physiological fistula maturation was achieved in 93% (56 of 60) patients. Three patients died prior to maturation, and 1 was thrombosed. The mean time to the physiologic maturation endpoint for this trial (target vein flow ≥500 mL/min and diameter ≥5 mm) was 40.4 ± 4.3 days. In the 54 patients requiring dialysis, 87% (47 of 54) of fistulas had 2NC and achieved fistula success at a mean 65.6 ± 45.7 days (Fig 3), and 87.7 ± 8.8 days, respectively (Table 4). Tunneled catheter removal was achieved at a mean 113.4 ± 9.3 days. The 6-month cumulative and functional patency were both 94% as shown in Figures 4 and 5.

Physical and Doppler Ultrasonography Examination

The percutaneous fistula at 7 days had a doppler pulse in the mid-fistula, a weak thrill, weak augmentation, and no edema. Over the first 3 months, the pulse pressure, thrill, and augmentation improved. A summary of the physical examination findings are listed in Table 2. The ultrasonography characteristics of fistulas achieving 2NC (clinical maturation) were brachial artery flow of 943.7 ± 283.7 mL/min (range, 457–1,733 mL/min), target vein flow, diameter, and depth of 674.1 mL/min ± 291.9 mL/min (range, 305–1,638 mL/min), 6.1 ± 0.8 mm (range, 4.5–8.2 mm), and 3.6 ± 1.3 mm (range, 1.6–6.4 mm), respectively. The anastomosis cross- sectional area was 7.9 ± 3.5 mm^2 (range, 3.3–18.5 mm^2). Doppler ultrasonography findings at the time of fistula success and at catheter removal were similar and are shown in Table 3.

Catheter Use

Hemodialysis catheters were required in 47 patients. A total of 39 patients had catheters at the time of fistula creation, and 8 patients had catheters placed after fistula creation. Catheters were removed from 80% of patients (31 of 39), with a catheter in place at the time of fistula creation and 100% (8 of 8) of catheters placed after fistula placement. The mean time to catheter removal was 106 ± 54.9 days (range, 37–267 days). Three catheters are still in use, 3 patients died with their catheter in place, and 2 were lost to follow-up. Patients with catheter in use included those with fistula thromboses, massive arm swelling, and 1 patient who refused to remove the catheter despite having a functioning fistula.

EndoAVF Maintenance

Maintenance procedures were performed in 63% (38 of 60) patients and included 70 procedures at a mean 130 ± 75.6 days (range, 27–333 days). Indications included 11 with low inflow, 35 with low flow in cannulation segment (mid and central fistula), 11 with low outflow, 8 with collateral flow, 3 with thrombosis, and 2 with arm swelling. Procedures included 63 balloon dilations: 3 artery, 4 anastomosis, 39 proximal fistulae, 20 mid-fistula, 7 distal fistula, 10 central circulation; 2 stenting; deep embolization in 14; branch embolization in 5; percutaneous banding in 6; thrombectomy in 5; and valvulotomy in 1. Procedural success was divided into anatomic success of 99% (69 of 70), clinical success of 96% (67 of 70), and hemodynamic success of 99% (69 of 70) according to SIR guidelines (19). Patients requiring maintenance procedures had a mean target vein blood flow volume of 238 ± 509 mL/min (range, 0–1,561 mL/min), which increased to a mean 798 ± 356 mL/min (range, 305–2,166 mL/min; $P < .0001$). Only 2 patients achieved 2NC without an endovascular procedure or transposition.

Adverse Events

There were 2 early fistula thromboses (<30 days), one was abandoned, and the other was percutaneously declotted. There was 1 thrombosed anastomosis with all other vessels intact at 58 days, a new EndoAVF was created at the original location. Primary fistula failure occurred in 3% (2 of 60) with 1 early failure due to thrombosis of anastomosis, and 1 late failure due to intractable arm swelling (17). Two fistulae were ligated, 1 for arm swelling and 1 for steal syndrome. Seven patient deaths occurred unrelated to fistula. Two patients were lost to follow-up. A complete list of adverse events is presented in Table 5.

DISCUSSION

The post-market registry of the Ellipsys EndoAVF demonstrates real-world outpatient use of the percutaneous fistula

Table 4. Kaplan-Meier–Derived Time-Event Endpoints

Event	Number	Events	Mean Days	Median Days	Kaplan-Meier Survival (%) at 180 Days
Primary patency	60	50	52.9 ± 8.4	34.0	7%
Primary assisted	60	4	374.7 ± 9.9	NA	97%
Cumulative patency	60	4	375.2 ± 9.7	NA	96%
Functional patency	47	2	321.4 ± 7.3	NA	94%
					Cumulative probability of success (%)
BA 500 and TV 4 mm	60	58	11.4 ± 1.3	7	97%
TV 500 and 5 mm	60	54	40.4 ± 4.3	33	90%
Released for dialysis	54	47	59.6 ± 6.5	48	87%
2NC (all)	54	47	65.6 ± 45.7	61	87%
2NC (HDT0)	44	37	76.8 ± 43.1	68	84%
2NC (HDT0 No Trans)	31	25	56.8 ± 30	50	81%
2NC (HDT0 w/ Trans)	13	12	118.6 ± 35.6	114	92%
2NC (not HDTO)	10	10	23.9 ± 27.6	12.5	100%
Fistula Success	54	47	79.1 ± 50.9	71	87%
TCR (all)	47	39	113.4 ± 62	105	83%

Note–Table shows Kaplan-Meier analysis of primary patency, primary assisted patency, cumulative patency, and functional patency. The lower part of the table demonstrates cumulative probability of success (100 = survival probability in percentages) with Kaplan-Meier analysis. Endpoints include Original 90-day EndoAVF maturation endpoint of brachial artery flow volume of 500 mL/min and a target vein of 4 mm (BA 500 and TV 4) and the definition of physiologic maturation target vein flow volume of 500 mL/min and diameter of 5 mm (TV 500 and 5mm). Two-Needle cannulation (2NC) was analyzed for all patients, for patients on hemodialysis at time zero (HDT0), in patients with and without transposition (Trans), and patient not on hemodialysis at time zero (not HDT0). Time to fistula success and tunneled catheter removal (TCR) are also shown.
BA = brachial artery; TV = target vein.

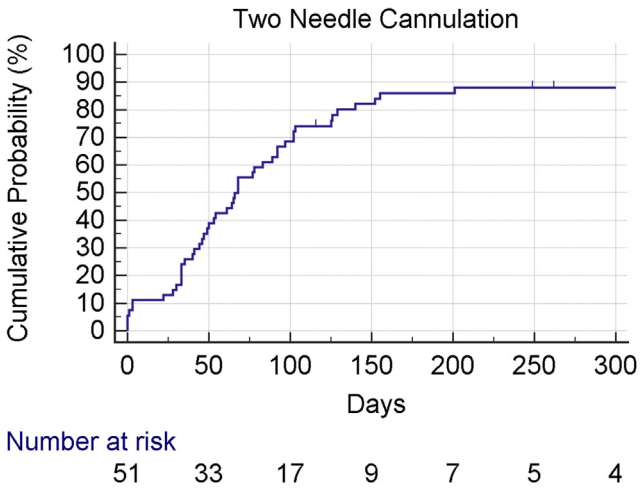

Figure 3. Kaplan-Meier curve of cumulative probability (100 = percentage of survival probability) of achieving 2-needle cannulation for all patients with percutaneous fistula. Mean time to 2-needle cannulation was 65.6 days with 87% of patients reaching this milestone.

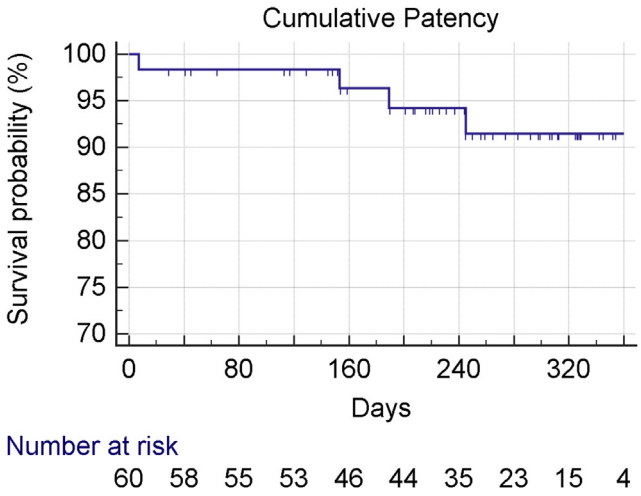

Figure 4. Kaplan-Meier survival curve of cumulative patency of fistula.

in the United States. Following standard guidelines for determining patient suitability for dialysis access creation, the Ellipsys system was used to create 63% of fistulas in the authors' practice (21). The percutaneous fistula fits between surgical fistula created at the wrist and the upper arm fistulae using the brachial artery in a logical progression from distal to central vein use. It has been recently noted that creation of percutaneous fistulae does not jeopardize future wrist fistula, allowing patients greater choice of fistula location (8). The Patients' willingness to undergo a percutaneous procedure can help to overcome reluctance to have surgery and thus increase the number of patients starting dialysis with a fistula (22). An additional 6% (6 of 95) of patients could have had EndoAVF in this series. How patient and provider preferences in choosing EndoAVF change over time will depend on long-term results and patient satisfaction (23). The 2NC milestone was achieved at a mean 76.8 days in 87% of patients compared with the reported 135 days in 64% of surgical patients (24). The ability to provide fistulae

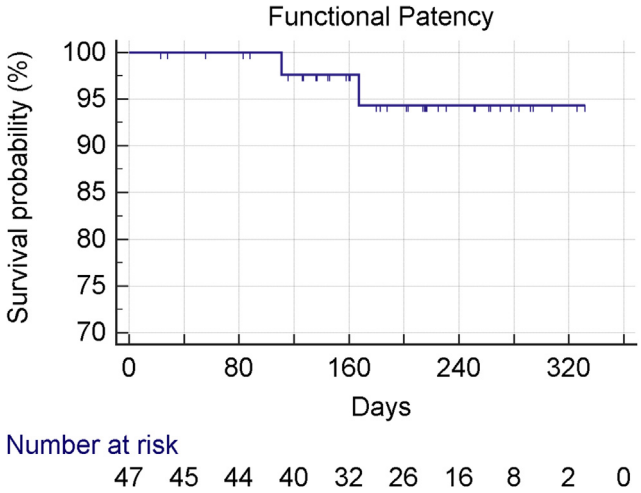

Figure 5. Kaplan-Meier survival curve of functional patency of fistula

to more incident patients while increasing fistula success to more than 85% with early 2NC should provide additional benefits in terms of reduced morbidity and mortality and reduced cost (1,3,25–27).

Standardization of EndoAVF procedures, including use of 5-mm balloon dilation of the proximal fistula at the time of fistula creation and preparation for dialysis using maturation procedures at 4 weeks to achieve a palpable pulse in the target vein demonstrated 3 important improvements compared with the US Pivotal Trial approach (1). The first improvement was resolving spasm at the anastomosis and increasing the brachial artery flow volume above 500 mL/min during the initial procedure by using 5-mm balloon dilation. The resolution of spasm and increased flow decreased the early thrombosis rate from 11% in the Pivotal Trial to 2% in the current trial and was consistent with prior reports of the flow volume needed to mature a surgical

Table 5. Adverse Events

Event		Description	Severity	Treatment	Outcome
Bleeding					
Early	None				
Puncture site					
Infection	None				
Noninfectious fluid collection		Hematoma related to cannulation injury	1	Rest fistula (2) pAVF/TCI (3)	Resolved
Hematoma	5				
Seroma	0				
Lymphocele	0				
Hematoma/post-AVF creation	1	Small hematoma at puncture site	1	Held pressure	Resolved
Anastomosis complications					
Hemorrhage	None				
Pseudo	None				
Stenosis with intimal hyperplasia	4	Stenosis	2	PTA	
Mid AV access/run-off vein complications					
Dilatation/ Aneurysm	None				
Pseudo	None				
Mid AV access stenosis	3	Stenosis	2	PTA	Resolved
Mid-AV access (cann injury)	4	Cannulation injury	2	PTA/TCI	Resolved
Mid-AV access w/ thrombus	1	Thrombosis	2	PTA	Resolved
Mid AV access w/thrombosis (cann injury)	4	Cannulation injury	2	PTA/TCI	Resolved
Stenosis post elevation	1	Post-surgical elevation	0	None	Ongoing
Access thrombosis		Description	Severity	Treatment	Outcome
Early (<30 days)	2	Thrombosis per DUS	2,3	Declotted	1 Re-do, 1 lost
Late	1	Thrombosis per DUS	2	Declotted	Re-do
AV access malfunction inability to puncture	5	CV too deep for access	2	Elevation	Resolved
Remote complications					
Steal syndrome abnormal vasculature	1	Distal arterial disease	3	Finger amputation	Ligated fistula
Venous hypertension central line thrombosis	1	Central stenosis	3		Ligated fistula
Neuropathy	None				
Total	33				

cann = cannulation injury; CV = cephalic vein; DUS = Doppler ultrasound exam; pAVF/TCI = percutaneous arteriovenous fistula and tunneled catheter insertion; pseudo = pseudoaneurysm; PTA/TCI = balloon dilation and tunneled catheter insertion.

fistulae (28,29). The second improvement was a decrease in maturation procedures required from 2.0 (205 of 103) procedures per patient to 0.87 (52 of 60) procedures per patient. Note that this reduction in procedures was achieved by increasing balloon dilation during the index procedure from 19% to 100% (1). The third improvement was decreasing the time to 2NC from 100 days to 70 days. There was no increase in complications related to the use of a 5-mm balloon dilation after EndoAVF creation.

The maturation and cannulation strategies for EndoAVF are inter-related. In the current study, secondary procedures directed flow into a single upper arm vein that produced fistulae, meeting established guidelines for fistula flow diameter depth and length (9,27). Outside the United States, percutaneous fistulas created using both the Ellipsys device and the WalvelinQ device (BD Medical, Tempe, Arizona) have used multiple outflow veins around the cubital fossa for cannulation, eliminating the need for many of the maturation procedures used in the US studies (1,2,5,8,30). The use of these multiple outflow vein EndoAVFs has required advanced cannulation techniques, including accessing cubital veins, ultrasonography guidance, and plastic access cannulas that are not currently available in the United States (5,8,31). The multiple outflow EndoAVF had obvious benefits for patients and, in terms of cost and reducing secondary procedures (2,4,5), although the primary goal remains to provide functional access usable where the patient receives dialysis. Equipoise between maturation procedures and cannulation can be reached with the EndoAVF based on patient needs and provider abilities.

Limitations of this study are that the data are derived from a modest sample size from a single site with surgeons and interventionalists experienced in the creation and management of percutaneous fistulas, allowing possible center effect bias. Patient selection, maturation, and cannulation were not compared relative to surgery or other methods or devices to create fistulas. There was no evaluation of the cannulation methods and protocols used at the dialysis centers. The study's focus on maturation does not demonstrate long-term effects of fistula creation and use.

CONCLUSIONS

Percutaneous fistulae were created in most patients at a multidisciplinary office-based laboratory. The fistulae were created with a high level of technical and clinical success, rapidly achieving the critical milestones of fistula placement, 2-needle cannulation, functional fistula, and catheter removal. The clinical characteristics of the maturing and functional single-vessel outflow percutaneous fistula were defined for the US population.

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