
Endovascular Arteriovenous Fistula (endoAVF) Creation: everlinQ Update

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University Health Network

Toronto General Hospital Toronto Western Hospital Princess Margaret Hospital

Disclosures

- Shareholder – TVA Medical
- Consultant
 - CR Bard
 - Gore Medical
- I'm Canadian



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Learning Objective

Upon completion of this activity, participants will be able to:

Describe AVF updates



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50+ Years of the AV Fistula

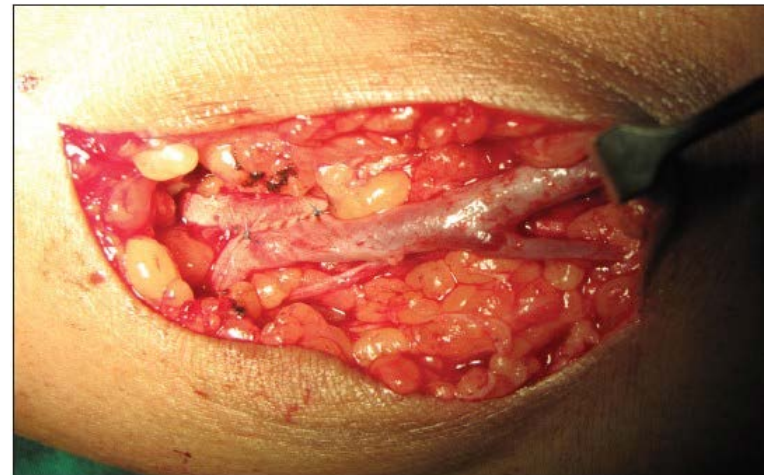
‘First’ AV Fistula, 1966

- Brescia, Cimino and Hurwich
- Side to side surgical anastomosis of cephalic vein and radial artery near the wrist



AV Fistula in 2017

- Surgical anastomosis of vein and artery
- Most commonly the cephalic vein and radial artery near the wrist or cephalic vein and brachial artery in upper arm



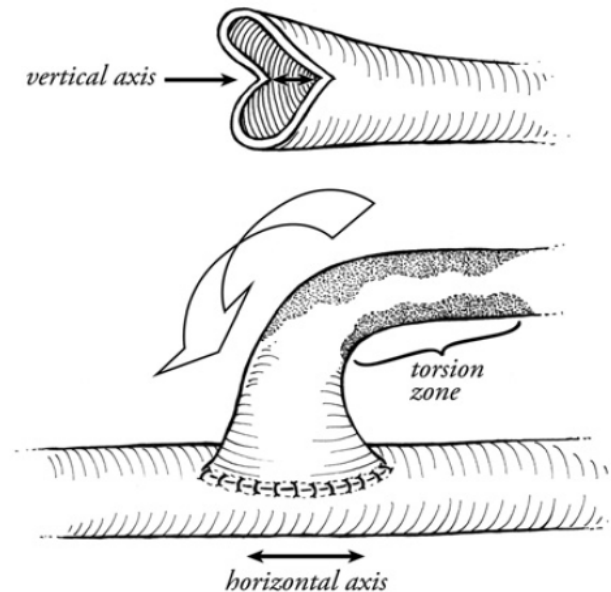
- 20-60% of AVF fail to mature
- 80% of patients start dialysis on a CVC
- 30% of patients refuse AVF surgery



Why Do Surgical AVFs Fail?

Flow limiting lesions often at the site of surgery associated with maturation failure¹

- ~30% AVFs report stenosis at 6-weeks post-op¹
- Surgical manipulation of the vein is associated with neointimal hyperplasia and primary fistula failure²



From Bharat et al. JVS 2012;55(1):274-80

1. Cheung et al. J Am Soc Nephrol. 2017 Oct;28(10):3005-3013.
2. Roy-Chaudhury et al. JASN 2006;17:1112-27



endoAVF with everlinQ

Potential endoAVF Benefits

No scar

Few interventions to maintain patency¹⁻³

Expands anatomic options for AVF creation

Preserves options for future surgical AVF

1. Rajan et al. J Vasc Interv Radiol 2015; 26:484–490.
2. Yang et al. J Vasc Access 2017;28;18 (Suppl. 2):8-14.
3. Lok et al. Am J Kidney Dis. 2017; 70(4): 486-497

endoAVF
Creation Site

Arterialized superficial
veins for cannulation



Example of an endoAVF patient at 2.5 yrs post creation

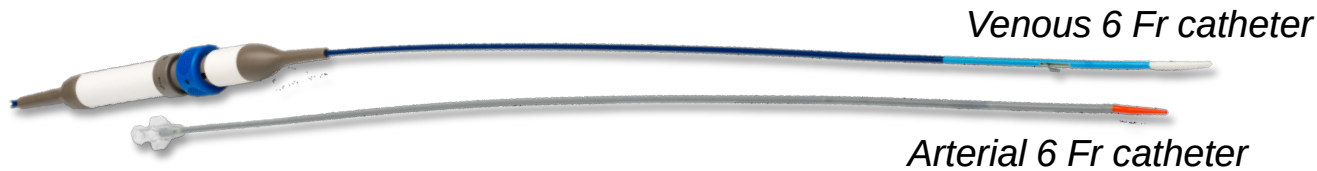
Disclaimer: This patient image is shared as an example of a potential outcomes for endoAVF patients. Individual patient outcomes can and do vary based on the condition of the patient, severity of disease, extent of surgery, and response to treatment. The everlinQ and everlinQ 4 endoAVF Systems have been issued European CE Mark for the creation of an arteriovenous fistula for hemodialysis and are not approved for sale in the United States.



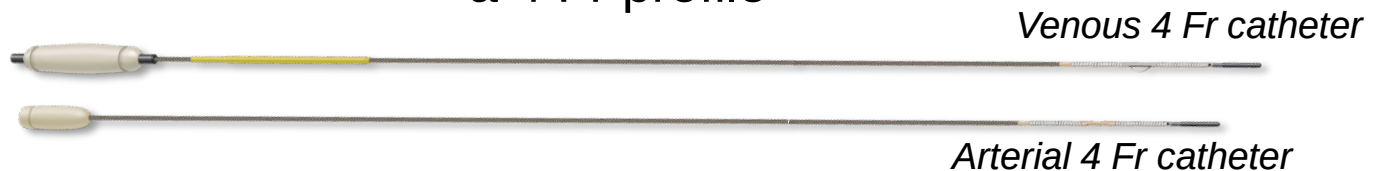
TVA everlinQ endoAVF Platform



Endovascularly creates a
functional AVF



Accesses vessels with
a 4 Fr profile



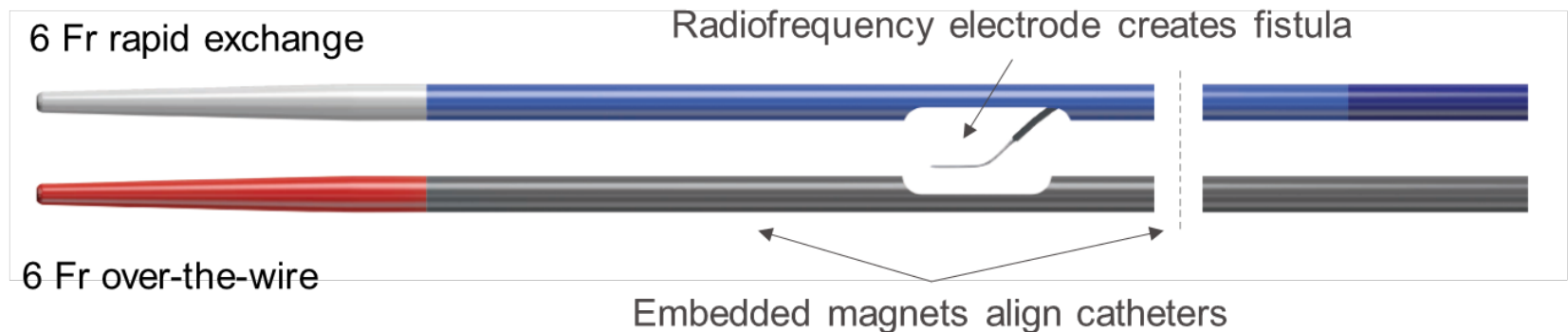
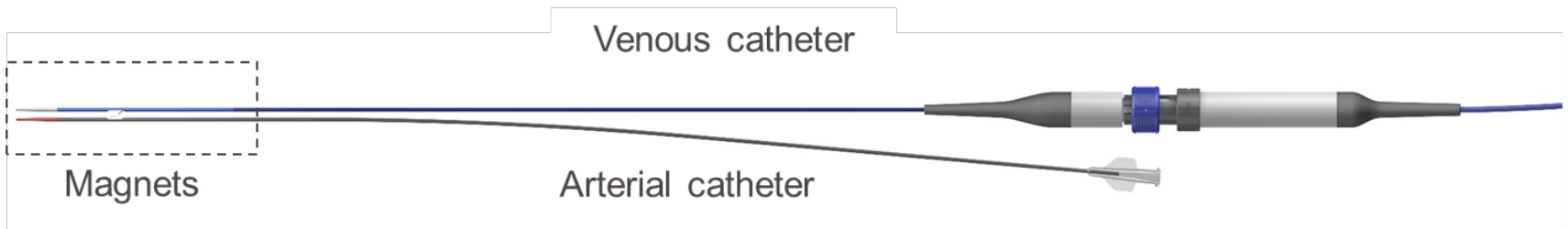
RF Generator



DISCLAIMER: The everlinQ and everlinQ 4 endoAVF Systems have been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis and are not approved for sale in the United States.

TVA everlinQ endoAVF System

Dual catheter system utilizing RF energy to create an autologous fistula



RF Generator



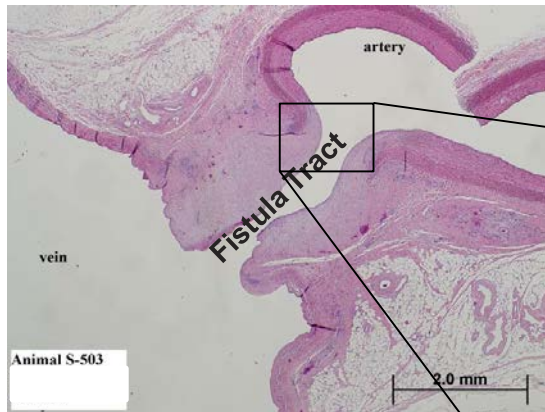
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endoAVF Histology and Gross Anatomy

Shows minimal vessel trauma of the everlinQ endoAVF

- Well-healed endoAVF tract with organized, mature fibrous remodeling
- Lining of endoAVF tract well covered in endothelial cells



30 days post-op

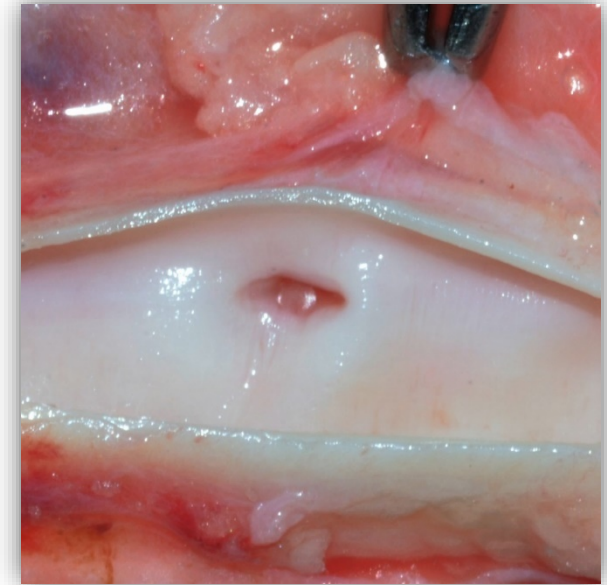
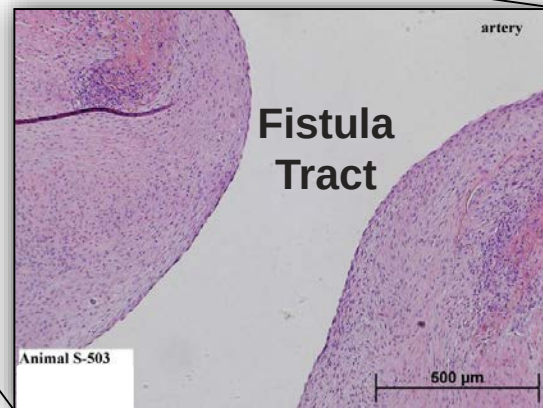


Image of an endoAVF at day 30 viewed from a dissected iliac artery of a sheep model.



Patient Eligibility

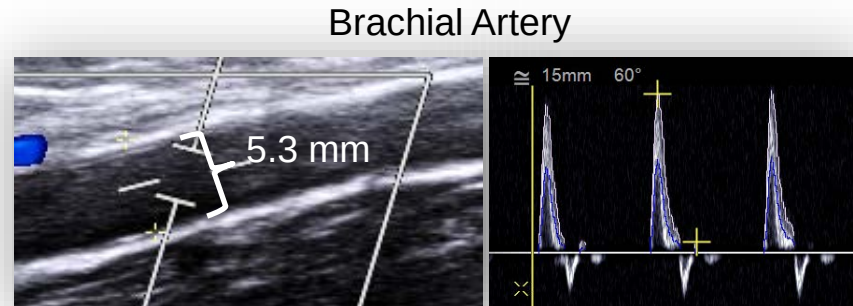
- ✓ Surgical AVF candidate
 - Adequate heart function (ie. not NYHA Class III or IV heart failure)
 - Adequate upper arm veins for dialysis
- ✓ On dialysis with CVC and/or failing AVF or AVG, or predialysis patient in need of an access
- ✓ Anatomic suitability for endovascular procedure



AVF Screening Similar to Surgical AVF

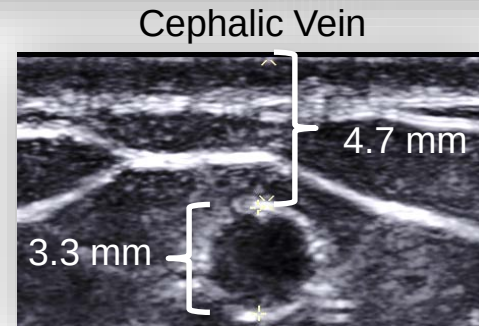
✓ **Good Inflow**

Brachial artery ≥ 2 mm
Triphasic flow



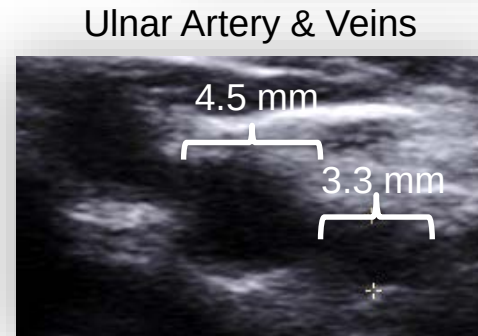
✓ **Good Outflow**

Cephalic or basilic vein ≥ 2.5 mm
Depth ≤ 6 mm (or eligible for elevation)

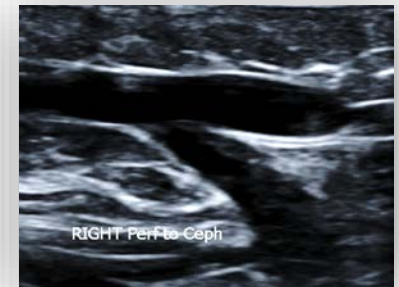


✓ **Good Creation Site**

Proximal ulnar artery and vein ≥ 2 mm
Patent perforator with communication to outflow veins



Perforator to Cephalic



everlinQ Case Example



Disclaimer: This case example is shared as an example of a potential outcomes for patients being assessed for an endoAVF. Individual patient outcomes can and do vary based on the condition of the patient, severity of disease, extent of surgery, and response to treatment. The everlinQ and everlinQ 4 endoAVF Systems have been issued European CE Mark for the creation of an arteriovenous fistula for hemodialysis and are not approved for sale in the United States.

endoAVF Building Momentum in the Peer-Reviewed Literature

Percutaneous Creation of an Arteriovenous Fistula for Hemodialysis Access

Dheeraj K. Rajan, MD, Adrian Ebn...
Jesus M. R...

ABSTRACT

Purpose: Arteriovenous fistulas (AVFs) created by conventional surgical techniques have long-term patency. This study investigated the feasibility of creating fistulas with percutaneous AVFs (pAVFs) in providing hemodialysis access.

Materials and Methods: From August 2012 to September 2013, a percutaneous pAVF was created in 33 patients. The patency of the pAVF at 6 months was recorded, as was clinical effectiveness at 6 months.

Results: A pAVF was successfully created in 32 of 33 patients (97%). Four causes unrelated to the procedure, one patient was lost to follow-up. Of the 32 patients, 28 patients had a pAVF at 6 months. Two additional patients had usable access at 6 months. The patency of the pAVF at 6 months was 96.2% (26 of 27; standard error, 3.8%). Mean time to pAVF maturation was 1.5 months (range 0.5-3.5 months). Mean time to pAVF maturation was 1.5 months (range 0.5-3.5 months). Mean time to pAVF maturation was 1.5 months (range 0.5-3.5 months).

Conclusions: Although larger studies are required to validate efficacy in a hemodialysis access successfully created with an endovascular catheter-based system, the results of this study suggest that pAVFs may be a viable alternative to surgical techniques.

ABBREVIATIONS

AVF = arteriovenous fistula; pAVF = percutaneous arteriovenous fistula; RF = radiofrequency

Two million people worldwide rely on hemodialysis to sustain life (1). Creating and maintaining a useable vascular access is essential in the care of patients undergoing hemodialysis. Traditionally, vascular access is created by one of three methods: (i) creation of an

From the Division of Vascular and Interventional Radiology (D.K.R.), Peter Munk Cardiac Center, University of Toronto, Toronto, Ontario, Canada; Cardiovascular Services (A.E.), Mount Sinai Hospital, Toronto, Ontario, Canada.

AJKD

Original Investigation

Endovascular Proximal Forearm Hemodialysis Access: Results of a Novel Endovascular Approach

Charmaine E. Lok, MD, MSc,^{1,2} Dheeraj K. Rajan, MD,³ Ravi Sidhu, MD, MEd,⁴ Christine Dipchand, MD, MSc,⁵ Louise Moist, MD, MSc,⁶ on behalf of the NEAT

Background: Hemodialysis arteriovenous fistulas (AVFs) with maturation, early thrombosis, and patient nonacceptance without open surgery offers another hemodialysis vascular access option.

Study Design: Prospective, single-arm, multicenter study.

Settings & Participants: Consecutive adult non-dialyzed patients with a proximal forearm AVF.

Intervention: Using catheter-based endovascular techniques, a proximal forearm AVF was created between target vessels, resulting in an endovascular proximal forearm AVF.

Outcomes: Safety, efficacy, functional usability, and patency.

Measurements: Safety as percentage of device-related complications; efficacy as percentage of patients with a functional AVF at 6 months; functional usability of endovascular proximal forearm AVFs to primary and cumulative endovascular proximal forearm AVF patencies per standard.

Results: 80 patients were enrolled (20 roll-in and 60 part 1). 80 patients were enrolled (20 roll-in and 60 part 1). 80 patients were enrolled (20 roll-in and 60 part 1).

Conclusions: Endovascular proximal forearm AVFs were created in 98% of participants; 8% had a related complication. 87% were physiologically suitable for dialysis (eg, dialysis flow > 600 mL/min).

Limitations: This study was a single-arm study with no control group. The results of this study suggest that endovascular proximal forearm AVFs may be a viable alternative to surgical techniques.

Conclusions: Endovascular proximal forearm AVFs were created in 98% of participants; 8% had a related complication. 87% were physiologically suitable for dialysis (eg, dialysis flow > 600 mL/min).

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JVA

ISSN 1129-7298

J Vasc Access 2017; 00 (00): 000-000
DOI: 10.5301/jva.5000723

ORIGINAL RESEARCH ARTICLE

Comparison of post-creation patency between surgical and an endovascular arteriovenous fistula creation

Shuo Yang¹, Charmaine Lok², Renee Arnold^{2,3}, Dheeraj Rajan², Marc Glickman⁴

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²University Health Network, University of Toronto, Toronto - Canada
³Icahn School of Medicine, Mt Sinai Hospital, New York, NY - USA
⁴Eastern Virginia Medical School, Norfolk, Virginia - USA

ABSTRACT

Introduction: Due to early and late failures that may occur with surgical arteriovenous fistulas (SAVFs), post-creation procedures are commonly required. This study compared SAVF post-creation procedures and their outcomes with a new endovascularly created AVF (endoAVF).

Methods: A 5% random sample from Medicare Standard 2820 creation procedures and associated costs for SAVF created the 6 months prior to and after the AVF creation was required. Physician claims were used to identify post-creation procedures. Comparative procedural information on endoAVF was obtained from the NEAT.

Results: Of 3764 Medicare SAVF patients, 60 successfully matched baseline demographic and clinical characteristics. 1 year was lower for endoAVF patients (0.59 per patient-year; p<0.05). In the endoAVF cohort, event rates of a

primary or secondary failure were 0.001 and 0.001, respectively. In the SAVF cohort, event rates of a primary or secondary failure were 0.001 and 0.001, respectively.

Conclusions: EndoAVFs were created in 98% of participants; 8% had a related complication. 87% were physiologically suitable for dialysis (eg, dialysis flow > 600 mL/min).

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Cardiovasc Intervent Radiol
DOI 10.1007/s00270-017-1750-x

CIRSE CrossMark

CLINICAL INVESTIGATION

Endovascular Creation of an Arteriovenous Fistula (endoAVF) for Hemodialysis Access: First Results

Christoph Georg Radosa¹, Julia Caroline Radosa², Norbert Weiss³, Christine Schmidt⁴, Sebastian Werth⁵, Thomas Hofmoeckel¹, Verena Plodeck¹, Christian Gatzweiler⁴, Michael Laniado¹, Ralf-Thorsten Hoffmann¹

Received: 10 April 2017 / Accepted: 14 July 2017

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Abstract

Introduction: Surgical creation of a radiocephalic fistula is the gold standard of vascular access for hemodialysis. Recently, an endovascular approach for upper arm fistula creation (endoAVF) has been developed, which may be an alternative to open surgery. We describe a case series of eight cases showing feasibility, early complications and

outcome of endoAVF.

Materials and Methods: In 2016, we created 8 endoAVFs for end-stage renal disease (ESRD) patients. Patient characteristics, technical success, total patient radiation time to maturation of endoAVF, and patency at six months were assessed.

Results: EndoAVF was successfully created in 8 patients (100%). The mean age was 68 years (range 55-78 years). The mean time to maturation of endoAVF was 1.5 months (range 0.5-3.5 months). The mean time to maturation of endoAVF was 1.5 months (range 0.5-3.5 months).

Conclusions: EndoAVFs were created in 98% of participants; 8% had a related complication. 87% were physiologically suitable for dialysis (eg, dialysis flow > 600 mL/min).

Limitations: This study was a single-arm study with no control group. The results of this study suggest that endovascular proximal forearm AVFs may be a viable alternative to surgical techniques.

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Real World Experience

Improved Outcomes and Cost Savings

Pivotal Study

Proof of concept

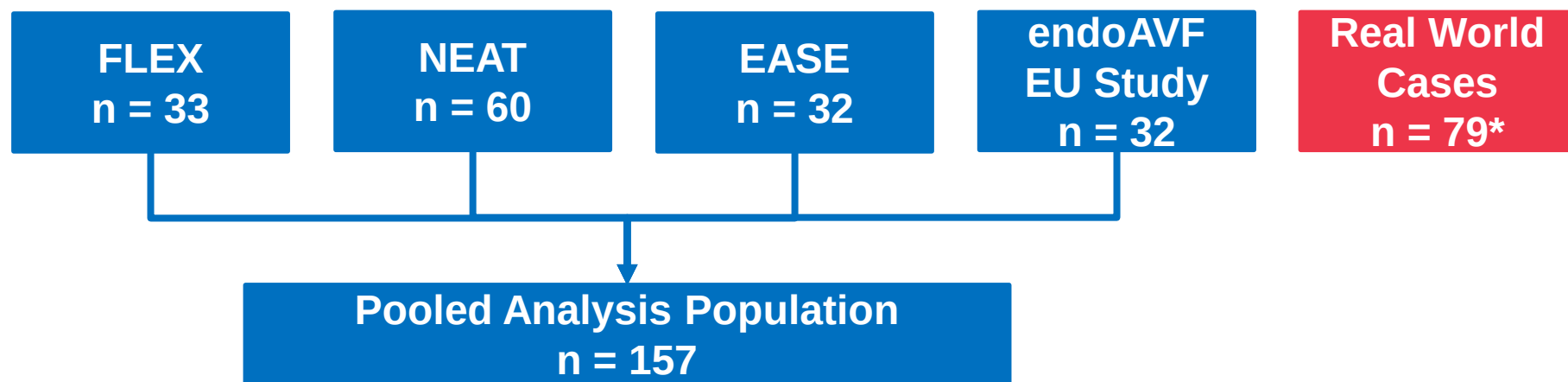


Global endoAVF Experience

- endoAVF cases have been performed with the everlinQ endoAVF system globally in Germany, UK, Greece, Switzerland, Netherlands, Paraguay, Australia and Canada
- endoAVF EU Post-Market Study
 - Multicenter, single arm, prospective study
 - Up to 120 patients 12 month follow-up
- Non-study EU cases
 - Site-reported procedure outcomes tracked
 - All events adjudicated by independent Clinical Events Committee



endoAVF Global Meta-Analysis



Data as of August 2017 from 28 sites in Canada, Australia, Germany, UK, Netherlands, Paraguay, Switzerland

*Represents the number of cases where adequate data could be collected to evaluate procedural safety and effectiveness

DISCLAIMER: The everlinQ and everlinQ 4 endoAVF Systems have been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis and are not approved for sale in the United States.



endoAVF Global Demographics

Characteristic	Pooled (N=157)
Sex: Male	70.7%
Age (years)	57.0 ± 13.8
Race/ethnicity:	
Caucasian	50.8%
Black	0%
Asian	6.5%
Other	12.9%
Hispanic	42.7%
Body Mass Index (BMI)	27.1 ± 5.7
Comorbidities	
Diabetes	58.6%
Hypertension	87.9%
Coronary artery disease	17.7%
Cerebrovascular Disease	12.9%
Peripheral arterial disease	2.4%
On hemodialysis at screening	65%

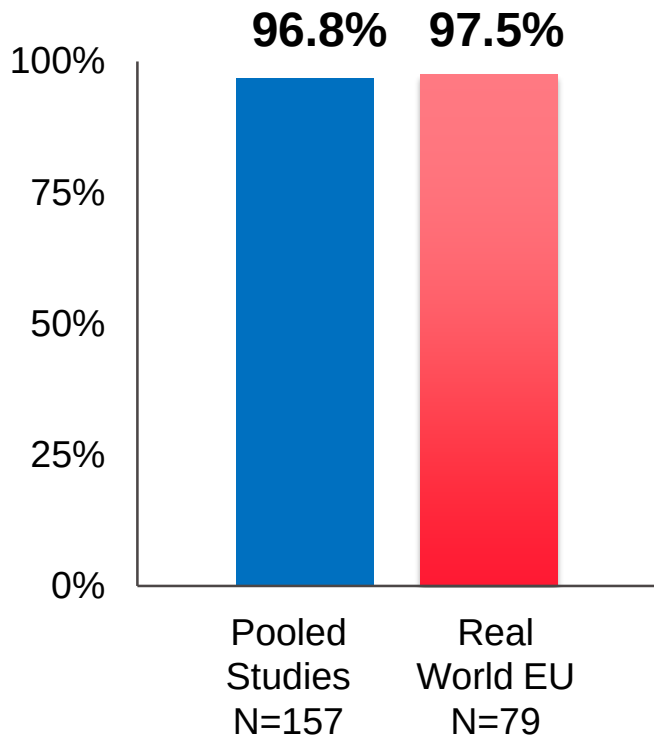
NOTE: Demographic data on “Real World” cases were not collected.

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Procedure Outcomes

Procedure Success



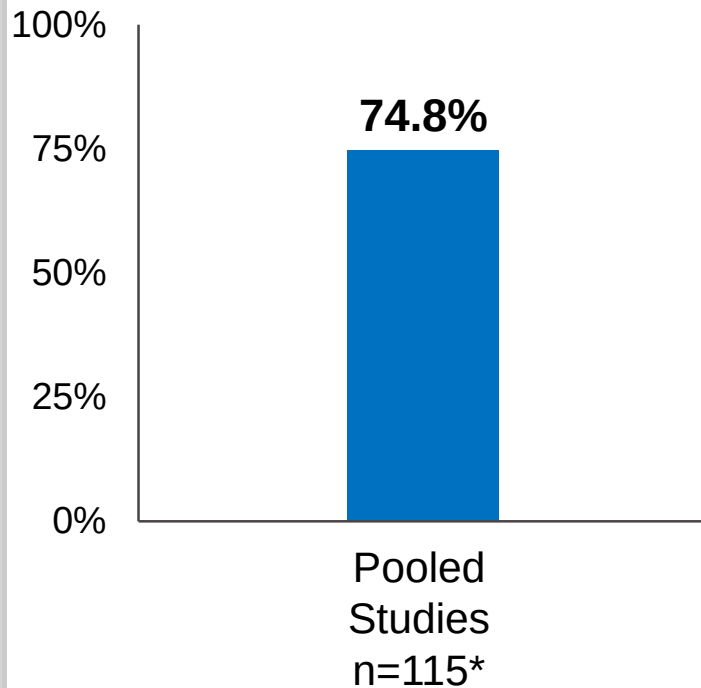
Procedure Outcomes

- Mean baseline vein diameter: $2.7 \pm 0.7\text{mm}$
- 12% of patients experienced a procedure-related serious adverse event in the pooled studies
 - Proper vessel access and closure are important
 - 6 patients experienced complications related to closure device
 - Manual compression is recommended
- 3.8% of patients experienced a procedure-related serious adverse event in “Real World” cases



Cannulation Outcomes

2-needle Cannulation at 6 months



Pooled Studies

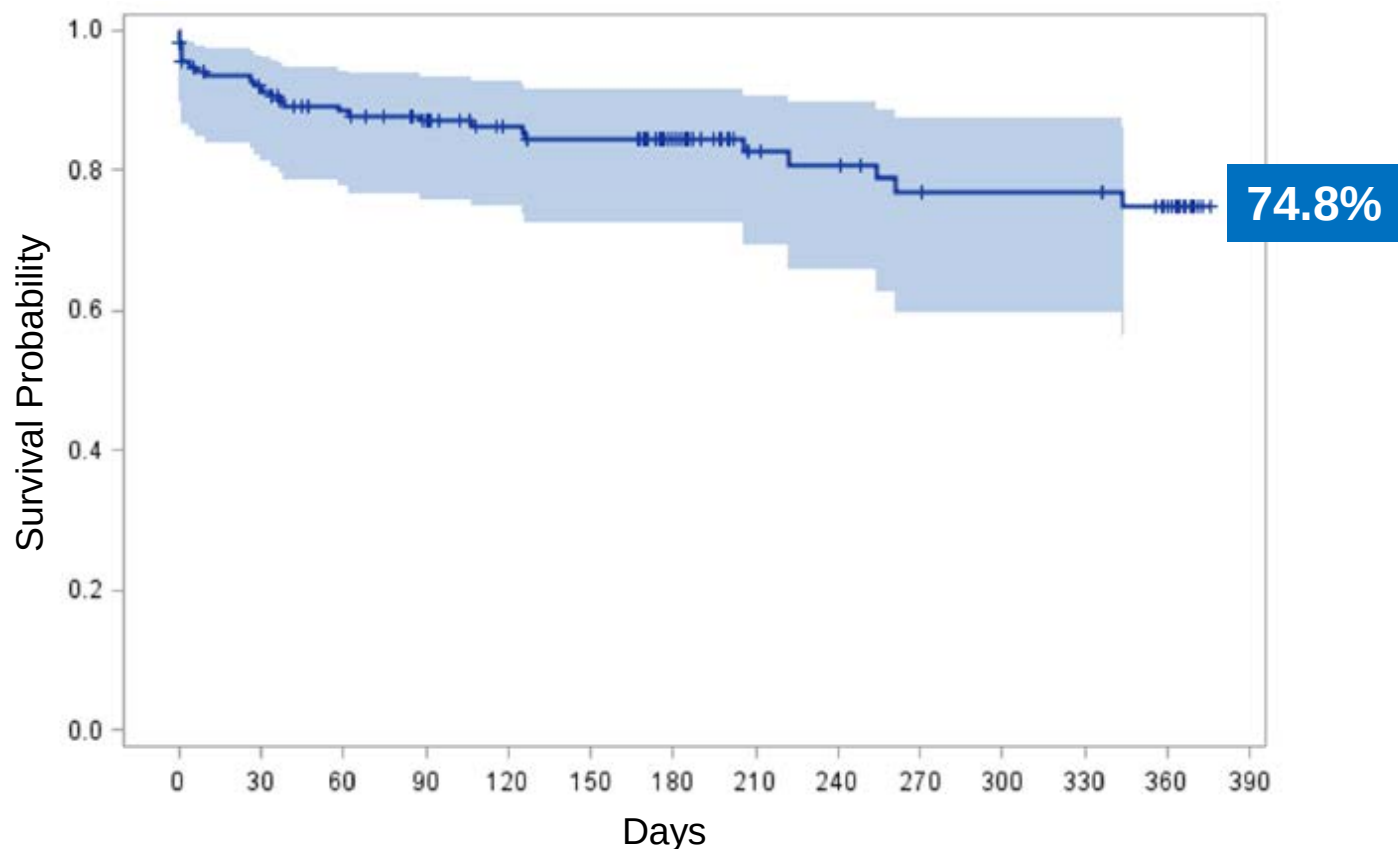
Time to cannulation, months (median, range)	2.1 [1.6,3.2]
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- Only 14.6% of predialysis patients initiated dialysis with a CVC
- Only 18.6% of patients on dialysis at enrollment were using a CVC at 12 months

*Represent evaluable patients at 6 months. Patients were excluded due to lost to follow-up, missed visits and early exits from the study.



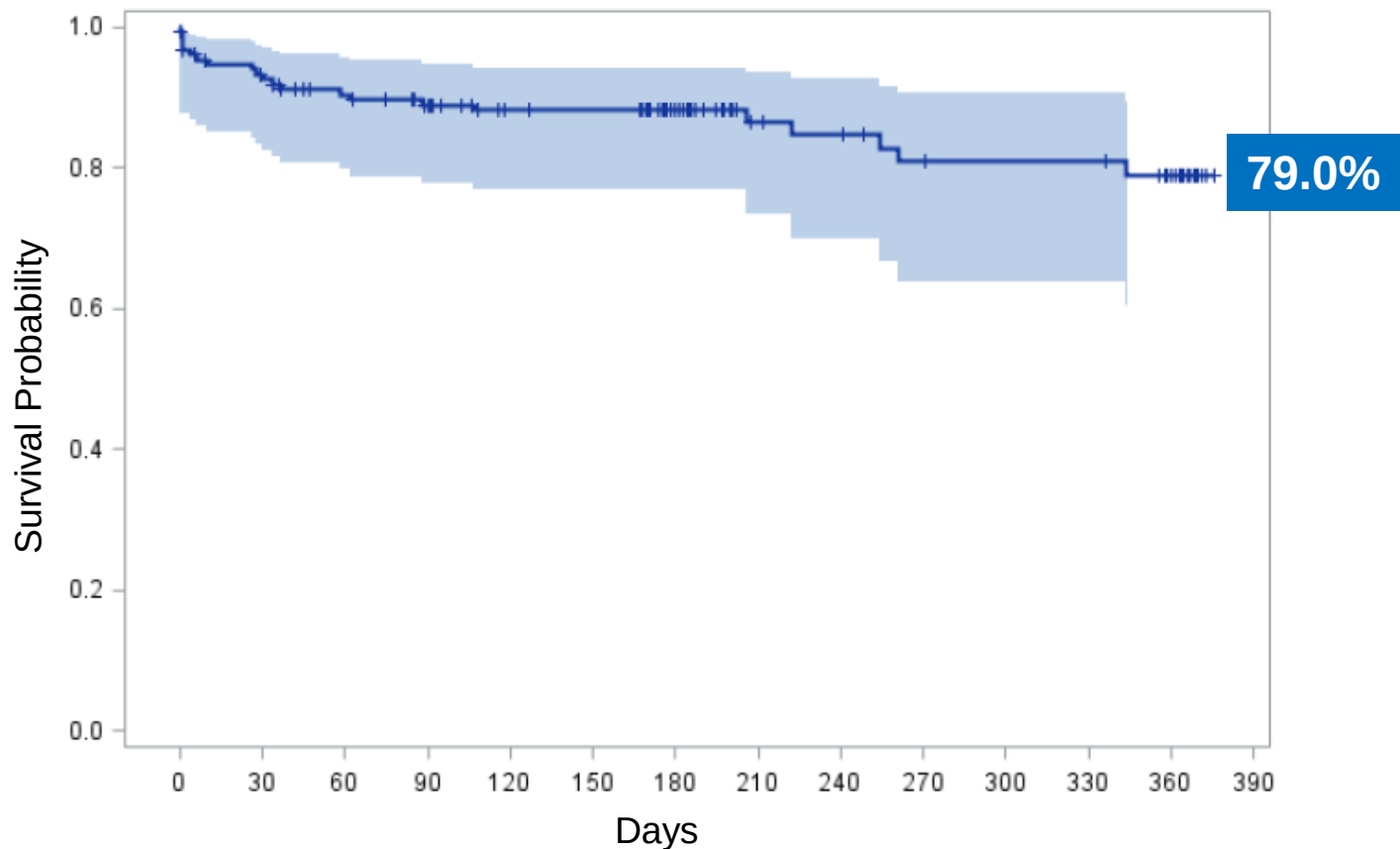
TVA everlinQ Primary Patency



		+ Censored 95% Equal Precision Band												
Interval (days)	0	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	301-330	331-360	361-390
At Risk	157	150	131	121	112	103	100	70	45	43	39	38	38	29



TVA everlinQ Secondary Patency



Interval (days)	+ Censored 95% Equal Precision Band												
	0	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	301-330	331-360
At Risk	157	152	133	124	116	107	106	76	50	48	43	42	42

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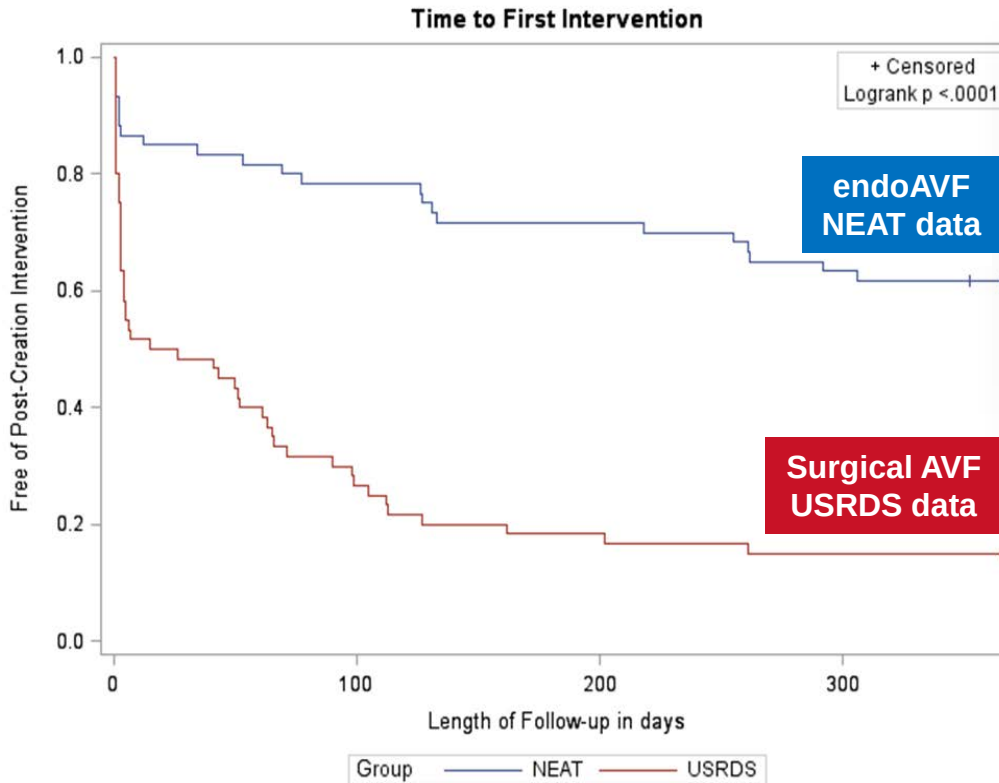
Interventions

Intervention	Pooled (N=157)
Subsequent vein embolization	19
Balloon angioplasty	7
Stent	0
Thrombectomy	1
Thrombolytic therapy	0
Transposition	6
Surgical AVF/AVG	4
Other	18
Total Interventions	55
% of patients with ≥ 1 intervention	24%

76% of patients required no interventions to mature/maintain the endoAVF



endoAVF vs. Surgical AVF: USRDS Comparison



- 1 month after fistula created, 50% of surgical AVF patients need an additional intervention compared to only 15% with endoAVF
- At 1 year, 85% of surgical AVF patients have had an additional intervention compared to only 38% of endoAVF patients

Comparison of NEAT to a propensity-score matched surgical AVF cohort from the United States Renal Database System

endoAVF patients experience fewer interventions than surgical AVF patients

Arnold, R., Rajan, D, et al. Submitted Manuscript

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Comparison of post-creation procedures and costs between surgical and an endovascular approach to arteriovenous fistula creation

Shuo Yang¹, Charmaine Lok², Renee Arnold^{1,3}, Dheeraj Rajan², Marc Glickman⁴

¹Quorum Consulting, San Francisco, California - USA

²University Health Network, University of Toronto, Toronto - Canada

³Icahn School of Medicine, Mt Sinai Hospital, New York, NY - USA

⁴Eastern Virginia Medical School, Norfolk, Virginia - USA

The average first year cost per patient was estimated at US\$11,240 USD lower for endoAVF than for SAVF.

This study compared patients with SAVF to patients with a new endovascularly created AVF (endoAVF).

Methods: A 5% random sample from Medicare Standard Analytical Files was abstracted to determine post-creation procedures and associated costs for SAVF created from 2011 to 2013. Medicare enrollment during the 6 months prior to and after the AVF creation was required. Patients' follow-up inpatient, outpatient, and physician claims were used to identify post-creation procedures and to estimate average procedure costs. Comparative procedural information on endoAVF was obtained from the Novel Endovascular Access Trial (NEAT).

Results: Of 3764 Medicare SAVF patients, 60 successfully matched to endoAVF patients using 1:1 propensity score matching of baseline demographic and clinical characteristics. The total post-creation procedural event rate within 1 year was lower for endoAVF patients (0.59 per patient-year) compared to the matched SAVF cohort (3.43 per patient-year; $p < 0.05$). In the endoAVF cohort, event rates of angioplasty, thrombectomy, revision, catheter placement, subsequent arteriovenous graft (AVG), new SAVF, and vascular access-related infection were all significantly lower than in the SAVF cohort. The average first year cost per patient-year associated with post-creation procedures was estimated at US\$11,240 USD lower for endoAVF than for SAVF.

Conclusions: Compared to patients with SAVF, patients with endoAVF required fewer post-creation procedures and had lower associated mean costs within the first year.



Conclusions

- ever**linQ** endoAVF platform adds additional fistula options for patients and physicians
- Multiple clinical studies and real-world experience have shown:
 - High technical success and acceptable complication rates
 - High cannulation success
 - High patency with low interventions

