An Implanted Blood Vessel Support Device for Arteriovenous Fistulas: A Randomized Controlled Trial

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Rationale & Objective: Reducing turbulent blood flow through dialysis arteriovenous fistulas (AVFs) and radial stretching of their venous wall may attenuate hyperplasia and stenosis and improve AVF outcomes in hemodialysis patients. The goal of this study was to evaluate the safety and efficacy of the VasQ implant, which intervenes on these mechanisms by physically supporting the surgical arteriovenous anastomosis.

Study Design: Prospective, randomized, controlled, multicenter study.

Settings & Participants: 40 consecutive patients with kidney failure referred for creation of a brachiocephalic fistula in 4 vascular access centers in the United Kingdom and Israel.

Interventions: AVF surgical creation with placement of the VasQ implant (treatment) versus AVF placement without the implant (control).

Outcomes: Safety assessed as percentage of severe device-related adverse events was the primary outcome. Secondary outcomes were efficacy assessments including: (1) AVF maturation at 3 months, defined as cephalic vein diameter ≥ 5 mm and flow ≥ 500 mL/min; (2) functional cumulative patency, defined as successful 2-needle cannulation for two-thirds or more of all dialysis runs for 1 month in study participants receiving dialysis; (3) cephalic vein diameter and blood flow; and (4) primary and cumulative patency at 6 months.

Results: No severe device-related adverse events were observed. There was no significant difference in maturation at 3 months or primary patency at 6 months between treatment and control (85% vs 80% and 80% vs 66%). Significantly larger vein luminal diameters were observed in the treatment group versus controls at 3 and 6 months (8.27 ± 2.2 vs 6.69 ± 1.8 mm [$P = 0.03$] and 9.6 ± 2.5 vs 7.56 ± 2.7 mm [$P = 0.03$]). Functional patency at 6 months was significantly greater in the treatment group (100% vs 56% [$P = 0.01$]).

Limitations: Small sample size, limited power for secondary end points.

Conclusions: No safety signals were detected for the VasQ external support of brachiocephalic AVFs. Higher functional patency and vein luminal diameters were achieved with the device at 3 and 6 months. VasQ may safely intervene on mechanisms associated with the disturbed hemodynamic profile in the juxta-anastomotic region.

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The functional success of arteriovenous access is the backbone of hemodialysis (HD) adequacy and patient survival.[1,2] Although autogenous arteriovenous fistulas (AVFs) remain, for most patients, the preferred primary vascular access due to improved patency, reduced complications, and overall cost,[3] they have high rates of maturation failure, stenosis, and occlusions requiring continuous surgical and endovascular maintenance to assist maturation and maintain patency.

Although the mechanism of AVF dysfunction remains largely unclear, observational studies of "failing-to-mature" fistulas have described several possible causes. Inherent and acquired factors related to vascular dysfunction, such as female sex, diabetes, age older than 65 years, history of peripheral vascular disease, and coronary artery disease, have been linked to early fistula failure.[4-6] Moreover, anatomical and surgical factors directly affect the functional outcome. Absence of suitable vascular anatomy, inadequate surgical technique during mobilization of the vein, and lack of surgical expertise have all been identified as contributing factors in AVF failures.[7,8]

Development of stenosis during the maturation period accounts for >90% of AVF dysfunction, and failure can occur anywhere along the fistula circuit[9] due to juxta-anastomotic stenosis in 40% and proximal venous stenosis in 60% of cases.[10] The complex AVF geometry in conjunction with a direct exposure of the vein to high-pressure pulsatile arterial flow triggers hemodynamic changes in the juxta-anastomotic region (JAR) characterized by multidirectional flow, oscillating wall shear stress (WSS), and a substantial increase in radial forces with cyclic stretching of the intima and media.[11] The complex hemodynamic profile is believed to stimulate remodeling and intimal hyperplasia–related failure through a pathway that involves endothelial cell (EC) activation and the secretion of prothrombotic and vasoconstrictive factors, known to promote intimal growth through proliferation and migration of vascular smooth muscle cells and extracellular matrix deposition.[12] In vitro studies have evaluated EC responses to different flow rates and related shear stress patterns,[13] linking unidirectional WSS and reduced circumferential strain with EC quiescence and outward vein remodeling.

We studied the safety and efficacy of a novel biocompatible device, VasQ (Laminate Medical Technologies Ltd), designed to reduce flow disturbances at the JAR.[5,14] The device is a blood vessel external support implant that consists of 2 nickel titanium components: (1) a laser-cut brace that wraps the artery at the JAR, regulating anastomotic angulation at 40° to 50°, and creating a 1-mm radius of curvature; and (2) an external mesh braid that determines vascular diameter and gradient (cone shape) in the first 25 mm of the juxta-anastomotic vein without contact with blood flow (Fig 1A). It is hypothesized that optimization of JAR geometry could improve a unidirectional flow pattern with uniform WSS that will favorably stabilize the hemodynamic conditions in the JAR and limit progressive intimal hyperplasia associated with undesirable inward vein remodeling.

In randomized preclinical testing using a sheep model of femoral artery to femoral vein AVF, VasQ has been shown to be safe and fistulas treated with the device remained patent at 3 months of follow-up, without exceptional injury or inflammation to the vessels.

In a first-in-human single-center single-arm study,[14] 20 patients had a single-size device implanted. This first study reported freedom from device-related adverse events (AEs), 79% unassisted maturation at 3 months, 79% primary patency, and 93% functional patency in patients receiving dialysis after 6 months in brachiocephalic AVFs.

Following the first-in-human phase, final geometric and structural modifications were implemented to improve device usability, and 3 sizes of the device were configured: model 5B for a vessel diameter range of 2.5 to 4.8 mm, model 6B for 4.8 to 5.5 mm, and model 7B for 5.5 to 6.0 mm, allowing a more accurate fit for a wide range of artery and vein diameters.

This prospective, multicenter, open-label, randomized, controlled trial was an extension of the first-in-human study. The aim of the current study was to validate the safety and efficacy in newly created brachiocephalic AVFs with VasQ in its final design, compared to standard surgical practice.

Methods

Study Design

In this prospective, multicenter, open-label, randomized, controlled trial, 40 patients were enrolled at 3 sites in the United Kingdom and 1 site in Israel between September 2015 and February 2017. Patients were equally randomly assigned to the treatment (VasQ) and control (standard surgical practice) arms and were followed up for 6 months post–AVF creation (Fig 2).

The study was conducted in compliance with the Declaration of Helsinki and Good Clinical Practice guidelines. All participants provided written informed consent before random allocation. The study was approved by the National Health Service Research Ethics Committee (reference number 14/EE/0062) for the UK sites and the Ethics Committee of Sheba Medical Center (reference number 2331-15-SMC) for the Israeli site.

Patient Population

Consecutive adult patients with kidney failure who were eligible for creation of a new brachiocephalic AVF based on a surgeon's clinical evaluation and vein mapping Doppler ultrasound were further evaluated according to study eligibility criteria. Patients were deemed eligible if they had a minimum brachial artery and cephalic vein diameter of 3 mm at the antecubital fossa, upper arm cephalic vein depth ≤ 8 mm, with no presence of stenosis in the veins of the upper arm defined as a peak systolic velocity ratio > 2 in the outflow vein or luminal stenosis > 50% and no ipsilateral central venous stenosis

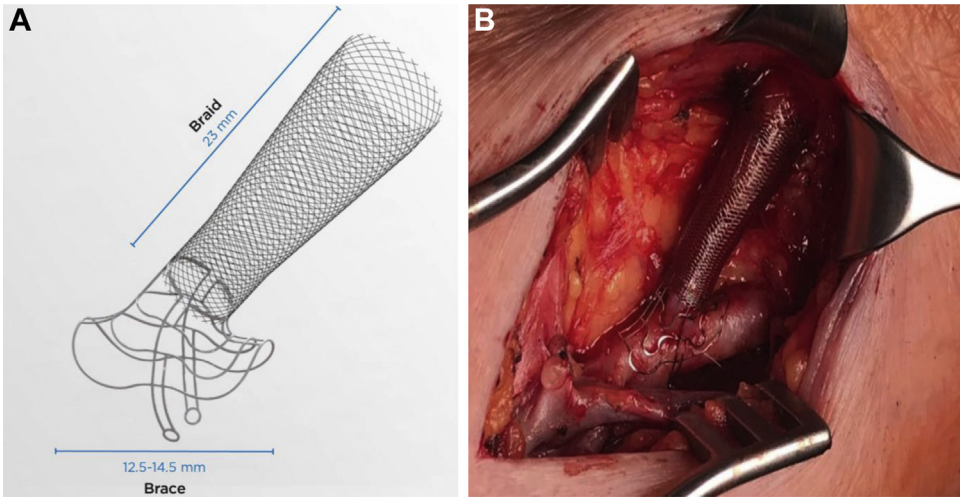

Figure 1. (A) The VasQ device, consisting of a brace and a braid. (B) VasQ implant in its final expanded state over the anastomosis and juxta-anastomotic region of a brachiocephalic arteriovenous fistula.

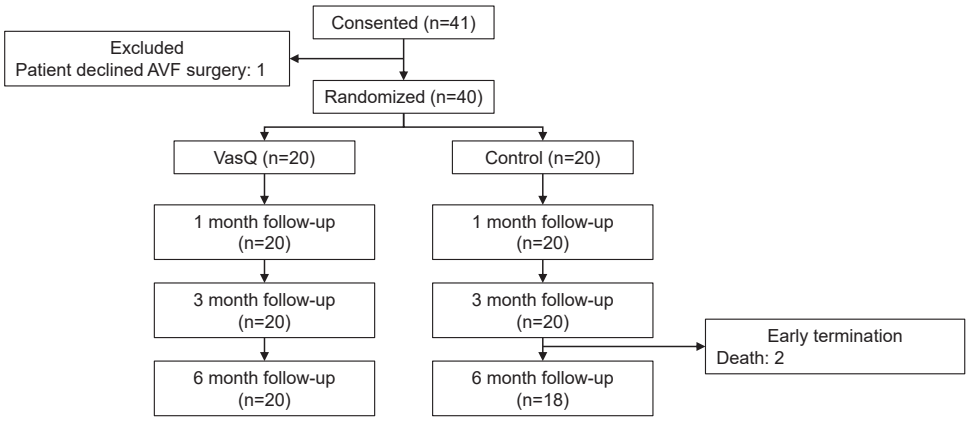

Figure 2. CONSORT (Consolidated Standards of Reporting Trials) flow chart. Abbreviation: AVF, arteriovenous fistula.

(eligibility criteria are available in Item S1). Cephalic vein and brachial artery quality were categorized as excellent (absence of scarring/calcification), fair (mild to moderate scarring/calcification), or poor (severe scarring/calcification) for vein/artery, respectively.

Randomization

Patients were randomly assigned in a 1:1 ratio to either the control or treatment arms, using sealed randomization envelopes that were provided by an independent statistician (BioStat).

Treatment

All study participants underwent end-to-side brachiocephalic AVF creation under local anesthesia. Patients in the treatment group were additionally treated with implantation of the VasQ device. The device was provided sterile along with a model selection tool. A transverse 4- to 6-cm incision was performed at the antecubital fossa, followed by dissection of the cephalic vein and brachial artery. Dissection and mobilization of the cephalic vein was identical in the intervention and control groups. Venous and/or arterial side branches were tied off with ligatures, avoiding the use of surgical clips that would interfere with deployment of the device. A dedicated model selection tool was used to gauge the external diameter of the artery to aid selection of the appropriate device size. The procedure continued with division of the vein, occlusion of arterial flow, and creation of a 5- to 7-mm arteriotomy. At this stage, the VasQ was placed around the vein and held in a nonexpanded state with an atraumatic bulldog clamp. A standard end-to-side vein-to-artery anastomosis with a nonabsorbable suture, for example, polypropylene 6/0, was fashioned. The arterial and venous clamps were subsequently released, and the patency of the anastomosis was confirmed. Any leaks were corrected as required. The surgeon then performed a quick interruption of the arterial inflow to facilitate the next step. With the vein collapsed, the VasQ was deployed to its final expanded state over the vein and around the anastomosis. The device was secured in position around the artery with a nonabsorbable suture through 2 small eyelets at each edge of the arterial end of the device (Fig 1B). The arterial inflow was then restored and the AVF was inspected and palpated to confirm patency. The surgical incision was closed in routine fashion.

Patients in the control group underwent a standard end-to-side brachiocephalic AVF procedure as described, without use of the VasQ device.

Patient Follow-up

On-site follow-up visits were conducted 1, 3, and 6 months postsurgery and included clinical assessment of patency and maturation, Doppler ultrasound, and review of patient records. Clinical examination included AVF inspection, palpation for the presence of thrill and vein size, auscultation for the presence of audible bruit, assessment of hand circulation, and detection of AVF-related complications. Doppler ultrasound included measurement of vein diameter, volume flow rate in the outflow vein, and detection of the presence and location of stenoses. AEs and serious AEs were recorded at each visit.

Outcome Measures

The primary end point of the study was freedom from severe (ie, performance of daily activities is compromised) or unanticipated device-related AEs 6 months postprocedure. Secondary efficacy outcome measures included percentage of AVFs physiologically matured at 3 months, primary and secondary patency 6 months postprocedure, and cephalic vein outflow at 1, 3, and 6 months.

Successful physiologic maturation was defined as a minimum of a 5-mm cephalic vein diameter with volume outflow > 500 mL/min confirmed using color duplex spectral analysis.

Primary patency was defined as percentage of patent AVF free from surgical or endovascular interventions. Secondary patency was defined as percentage of patent AVF

following surgical or endovascular interventions. Patency was confirmed by the presence of an audible bruit in the cephalic vein.

Additional analyses were performed following study completion, including comparative analysis of cephalic vein diameter (by Doppler ultrasound), cumulative functional patency at 3 and 6 months defined as successful 2-needle cannulation of patent fistulas for two-thirds or more of all dialysis runs for 1 month, and occurrence of stenosis > 50% or complete occlusion anywhere along the access vein.

Statistical Analysis

This was an extension phase of a first-in-human trial and so was not powered for statistical significance. Rather, the aim of the study was to provide preliminary assessment of both the safety and effectiveness of the device compared to standard surgical practice.

Baseline characteristics and outcomes were compared between the 2 study groups. Categorical and continuous variables were compared using χ^2 and 2-sided t test, respectively. Fisher exact test was used for calculating P values for binary outcomes. Continuous data were expressed as mean ± standard deviation or median and range for non-normal distributions. The level of statistical significance was set at 5%. All analyses were conducted using JMP 13.2.0 software (SAS Institute).

Results

Study Participants

Overall, 40 patients were enrolled in the study, 20 in the control and 20 in the treatment group, between September 2015 and February 2017. The last patient completed 6 months' follow-up in September 2017. Table 1 summarizes baseline characteristics by treatment group.

Mean age was significantly younger in the treatment group, although the percentage of patients 65 years or older was not. No other statistically significant differences in baseline characteristics were observed.

Surgical Procedure

VasQ was successfully implanted in 100% (20/20) of patients randomly assigned to the treatment arm with no intraoperative exclusions. Table 2 summarizes intraoperative characteristics of blood vessels and the implantation procedure.

No intraoperative device–related AEs were reported. Mean total surgical time (from incision to skin closure) was not significantly different: 58 ± 17 versus 49 ± 27 minutes for treatment versus control, respectively.

Safety

No severe device-related AEs were reported during the study. Two control patients with a background of known cardiac disease died between the 3- and 6-month follow-up due to cardiac events (cardiac arrest and asystole), both with a functioning fistula at the time of death. No deaths occurred in the treatment group. There were no statistically significant differences between the treatment group and controls in access-related AEs (Table 3).

No episodes of access-site infection occurred in either arm. Two patients in each group developed steal syndrome. Events in the treatment arm were graded as mild and moderate and did not require intervention. In the control arm, events were graded as moderate and severe, requiring surgical ligation of 1 AVF due to hand ulceration.

AVF Maturation

Proportions of patients with assisted and unassisted maturation and physiologic variables of the AVFs are reported in Table 4. There was no difference in achieving successful assisted and unassisted maturation between the treatment and control arms 1 and 3 months postsurgery.

At 3 months postsurgery, functional patency was achieved in 90% (9/10) of treated patients established on HD versus 45% (5/11) in the control group ($P = 0.06$). At the end of the study (6 months' follow-up), 100% (14/14) functional patency was achieved in the treatment group versus 56% (5/9) in the control group ($P = 0.01$).

Mean cephalic vein lumen diameters, measured using duplex ultrasound ~8 cm proximal to the anastomosis (a common cannulation site for HD), 3 and 6 months post–AVF creation were 8.27 ± 2.2 versus 6.69 ± 1.8 mm ($P = 0.03$) and 9.6 ± 2.5 versus 7.56 ± 2.7 mm ($P = 0.03$), for device versus control, respectively.

Mean AVF volume flow rates measured at the above point at 1, 3, and 6 months in the treatment and control groups were 1,259.06 ± 398.6 versus 1,208.35 ± 543.2 mL/min ($P = 0.8$), 1,500.71 ± 518.9 versus 1113.5 ± 661.6 mL/min ($P = 0.06$), and 1,393.7 ± 673.6 versus 1046.88 ± 625.5 mL/min ($P = 0.1$), respectively.

AVF Patency

There was no statistically significant difference in primary and cumulative patency between the treatment and control arms 6 months postsurgery. Primary patency was achieved in 80% (16/20) versus 66% (12/18) in treatment and control, respectively ($P = 0.5$). Cumulative patency was 85% (17/20) in the treatment group versus 72% (13/18) in the control group ($P = 0.6$).

Stenosis, defined as >50% reduction in luminal diameter anywhere between the anastomosis and the cephalic arch (inclusive), measured using Doppler, was detected in 15% (3/20) of patients in the treatment arm versus 50% (10/20) in the control group ($P = 0.04$) during the follow-up period. Although the incidence of stenosis was not associated with a significant decrease in primary and cumulative patency, mean AVF volume flow rate and vein diameter at 6 months were significantly lower in AVFs with stenosis versus AVFs free from stenosis

Table 1. Patient Demographic and Clinical Characteristics by Treatment Group

Characteristic	Treatment (n = 20)	Control (n = 20)	*P*
Age, y	60.7 ± 12.7	68.9 ± 11.6	0.04
Age ≥ 65 y	40% (8)	70% (14)	0.1
Male sex	14 (70%)	13 (65%)	0.9
Race			0.7
White	9 (45%)	10 (50%)	
Asian	6 (30%)	3 (15%)	
African	3 (15%)	5 (25%)	
Caribbean	2 (10%)	2 (10%)	
BMI, kg/m^2	31.3 ± 7.2	29.4 ± 7.4	0.4
Mean arterial blood pressure, mm Hg			
Systolic	138 ± 19.5	140 ± 13	0.7
Diastolic	71 ± 14.7	76 ± 12.2	0.2
Cause of kidney disease			0.2
Diabetes mellitus	12 (60%)	9 (45%)	
Hypertensive nephrosclerosis	2 (10%)	1 (5%)	
Polycystic disease	2 (10%)	3 (15%)	
Interstitial nephritis	1 (5%)	0 (0%)	
Chronic pyelonephritis	1 (5%)	0 (0%)	
Other	2 (10%)	7 (35%)	
Smoking status			0.3
Never smoked	9 (45%)	7 (35%)	
Ex-smoker	5 (25%)	4 (20%)	
Current	4 (20%)	2 (10%)	
Unknown	2 (10%)	7 (35%)	
Significant comorbid conditions			
Diabetes	13 (65%)	12 (60%)	0.7
Hypertension	19 (95%)	18 (90%)	0.5
Coronary/cardiac disease	5 (25%)	4 (20%)	0.7
Cerebrovascular disease	1 (5%)	0 (0%)	0.2
Previous access in the same limb	5 (25%)	3 (15%)	0.4
Dialysis status			
Active dialysis at screening	9 (55%)	9 (55%)	0.9
CVC use at screening	6 (67%)	8 (89%)	0.3
Total prior access procedures (all limbs and types)			0.9
0	6 (30%)	8 (40%)	
1	9 (45%)	8 (40%)	
≥2	5 (25%)	4 (20%)	
Prior access procedures in study limb			0.4
0	15 (75%)	17 (85%)	
≥1	5 (25%)	3 (15%)	
Indication for index access procedure			0.7
First time access	13 (65%)	14 (70%)	
Failed autogenous access	7 (35%)	6 (30%)	
Cephalic vein external diameter, mm	4.0 ± 1.24	4.0 ± 1.0	0.7
Brachial artery external diameter, mm	4.1 ± 0.77	4.5 ± 1.1	0.2
Cephalic vein quality			0.7
Excellent	12 (60%)	13 (65%)	
Fair	8 (40%)	7 (35%)	
Poor	0 (0%)	0 (0%)	
Brachial artery quality			0.5
Excellent	16 (80%)	16 (80%)	
Fair	4 (20%)	3 (15%)	
Poor	0 (0%)	1 (5%)	

Abbreviations: BMI, body mass index; CVC, central venous catheter.

(698.8 ± 560.2 vs 1,488.9 ± 552.3 mL/min [P = 0.001] and 6.07 ± 3.7 vs 8.92 ± 3.1 mm [P = 0.03]).

Discussion

We report on an initial assessment of the safety and potential of VasQ, an external support device, to improve maturation and patency outcomes by optimizing the geometrical configuration of the JAR with the aim of reducing flow disturbance. Disturbed flow patterns in the JAR are characterized by increased turbulence, oscillating WSS, and increased wall tension in the JAR of the outflow vein. Suboptimal hemodynamic patterns that develop in response to the abnormal artery-vein connection have been described as key factors associated with undesirable inward vein remodeling[15] through the development of neointimal hyperplasia resulting in stenosis and eventually occlusion of the AVF. This rapid formation of a neointimal layer occurs in response to the hemodynamic changes that promote EC activation, increased expression of growth factors, and secretion of prothrombotic and vasoconstrictive substances.[11,16]

The association between geometrical characteristics of the arteriovenous anastomosis and AVF outcomes has been investigated in several retrospective clinical studies and computational fluid dynamics models. However, to date, these have not been translated to a technology that improves clinical outcomes. Sadaghianloo et al[17] associated anastomotic angles <30° with decreased patency and higher reintervention rate in radial-cephalic AVFs. Anastomotic angle had no effect on outcomes of brachiocephalic fistulas; however, the median angle reported for brachiocephalic fistulas was 90° (range, 10°-170°), suggesting a practical limitation in controlling the anastomotic angle. Analysis of WSS profiles in side-to-side versus end-to-side anastomosis by Hull et al[18] concluded that the most uniform WSS profile occurs in side-to-side anastomoses, followed by 45° end-to-side and then 90° end-to-side configuration.

Similarly, an implantable anastomotic connector made of siliconized polyurethane (OptiFlow, Bioconnect

Table 2. Intraoperative Characteristics of Brachiocephalic AVF Procedure

Characteristic	Treatment (n = 20)	Control (n = 20)	*P*
Skin incision to skin closure time, min	58 ± 0.17	49 ± 0.27	0.2
Cephalic vein diameter, mm	4.0 ± 1.24	4.0 ± 1.0	0.7
Brachial artery diameter, mm	4.1 ± 0.77	4.5 ± 1.1	0.2
Cephalic vein quality			0.7
Excellent	12 (60%)	13 (65%)	
Fair	8 (40%)	7 (35%)	
Poor	0 (0%)	0 (0%)	
Brachial artery quality			0.5
Excellent	16 (80%)	16 (80%)	
Fair	4 (20%)	3 (15%)	
Poor	0 (0%)	1 (5%)	
Access limb			
Right	8 (40%)	6 (30%)	0.5
Dominant	7 (35%)	5 (25%)	0.5
VasQ device model[a]			
5B	13 (65%)	NA	
6B	5 (25%)	NA	
7B	2 (10%)	NA	

Abbreviations: AVF, arteriovenous fistula; NA, not applicable.
[a]Model 5B is for a vessel diameter range of 2.5 to 4.8 mm; model 6B, for 4.8 to 5.5 mm; and model 7B, for 5.5 to 6.0 mm.

Table 3. Access-Related Adverse Events

Event	Treatment (n = 20)	Control (n = 20)	*P*
All-cause mortality	0 (0%)	2 (10%)	0.5
AVF-related mortality	0 (0%)	0 (0%)	0.9
AVF revascularization	2 (10%)	2 (10%)	0.9
Thrombectomy	1 (5%)	0 (0%)	
Fistuloplasty	1 (5%)	2 (10%)	
Access site complications			0.7
Loss of AVF patency	3 (15%)	4 (20%)	
Thrombosis	3 (15%)	2 (10%)	
Surgical ligation	0 (0%)	2 (10%)	
Steal syndrome	2 (10%)	2 (10%)	0.9
Postoperative wound infection	0 (0%)	0 (0%)	0.9
Postoperative bleeding	0 (0%)	0 (0%)	0.9
Neuropathy	5% (1)	0 (0%)	0.3
Hypoesthesia	1 (5%)	2 (10%)	0.5
Arm swelling	0 (0%)	1 (5%)	0.3

Abbreviation: AVF, arteriovenous fistula.

Systems Inc) with a predefined angle and cross-sectional area has been tested.[19,20] Although there are some conceptual similarities between the Optiflow and the VasQ, there are several fundamental and possibly crucial differences between the 2. Use of OptiFlow dictated a change in surgical technique with the use of special instruments and intravascular placement of synthetic material; VasQ does not require the introduction of prosthetic material to the bloodstream and deployment of the device over the arteriovenous anastomosis is performed using standard surgical equipment. In terms of efficacy, OptiFlow failed to demonstrate a clinical benefit in functional patency rates with an associated high rate of outflow vein thrombosis.

In this first randomized post–CE (Conformité Européenne) mark study, no severe or serious device-related AEs were reported. No differences were observed between treatment and control with regard to the type, severity, and rate of complications. Complete loss of patency at the end of the 6-month follow-up period was reported in 15% of treated patients and 25% of controls, with no postoperative wound infection or bleeding in any of the study groups. The safety profile reported here is consistent with reports from first-in-human, single-arm, pre–CE mark studies in which no device-related AEs or serious AEs were reported. With a small sample size, our study was not powered to identify differences in AEs. However, because the device is completely external to the blood vessels, covers a limited segment of the JAR without extending into the cannulation segment, and is made of nickel titanium, a compound with well-established biocompatibility, it is not expected to increase the rate of known complications or introduce new risks.

Patient demographics and baseline medical background were well-balanced between the control and treatment groups for most variables. However, mean patient age was younger in the treatment (60.7 ± 12.7 years) compared to the control (68.9 ± 11.6 years) group ($P = 0.04$). Although age has been reported as an independent risk factor for AVF failure,[21] several studies have failed to confirm a negative correlation between age and AVF outcome.[22-24] In our study, age had no effect over any measured outcome, including primary patency (odds ratio [OR], 1.03; 95% CI, 0.97-1.09; $P = 0.4$), secondary patency (OR, 1.05; 95% CI, 0.98-1.12; $P = 0.1$), functional patency (OR, 0.97; 95% CI, 0.91-1.02; $P = 0.3$), vein diameter ($\beta = -0.002$; 95% CI, −0.09 to 0.08; $P = 0.9$; $R^2 = 0.0001$), or volume flow rate ($\beta = -6.5$; 95% CI, −21.5 to 8.37; $P = 0.4$; $R^2 = 0.02$).

There was no difference between study arms in achieving successful assisted and unassisted physiologic maturation 1 and 3 months postsurgery. At 3 months postsurgery, functional patency was achieved in 90% (9/10) of patients established on HD in the treatment group versus 45% (5/11) in the control group ($P = 0.06$). At 6 months, functional patency was achieved in all patients established on HD in the treatment group (100% [14/14]) versus 56% (5/9) in the control group ($P = 0.01$).

AVFs have been proven to be superior to prosthetic grafts and tunneled lines in maintenance HD patients. Current guidelines dictate that the majority of incident patients should commence dialysis through a functioning AVF.[25,26] A functional AVF is an access circuit able to deliver adequate flow, usually between 350 and 400 mL/min, without recirculation for the total duration of dialysis. Several factors have been described as possible predictors of functional patency. Demographic and comorbid

Table 4. AVF Outcomes and Physiologic Characteristics

Outcome/Characteristic	Treatment	Control	*P*
Assisted maturation[a]			
1 mo	85% (17/20)	85% (17/20)	0.9
3 mo	85% (17/20)	80% (16/20)	0.9
Unassisted maturation[a]			
1 mo	80% (16/20)	80% (16/20)	0.9
3 mo	80% (16/20)	80% (16/20)	0.9
Functional patency[b]			
3 mo	90% (9/10)	45% (5/11)	0.06
6 mo	100% (14/14)	56% (5/9)	0.01
Cephalic vein volume flow, mL/min			
1 mo	1,259.06 ± 398.6	1,208.35 ± 543.2	0.8
3 mo	1,500.71 ± 518.9	1,113.5 ± 661.6	0.06
6 mo	1,393.7 ± 673.6	1,046.88 ± 625.5	0.1
Cephalic vein diameter, mm			
1 mo	6.94 ± 1.4	6.65 ± 1.3	0.5
3 mo	8.27 ± 1.3	6.69 ± 1.8	0.03
6 mo	9.6 ± 2.5	7.56 ± 2.7	0.03
AVF patency			
Primary patency at 6 mo	80% (16/20)	66% (12/18)	0.5
Secondary patency at 6 mo	85% (17/20)	77% (14/18)	0.6

Note: Values given as percentage (number affected/number at risk) or mean ± standard deviation.
Abbreviation: AVF, arteriovenous fistula.
[a]Physiologic maturation defined as patent fistula with cephalic vein diameter ≥ 5 mm and AVF volume flow rate > 500 mL/min.
[b]Successful establishment on hemodialysis through study AVF using 2-needle cannulation in patients actively dialyzed with a patent fistula for two-thirds or more of all dialysis runs for 1 month.

condition factors such as age 65 years or older, diabetes, and body mass index ≥ 27 kg/m^2 were described as negative predictors,[27] as were clinical care processes such as timing of the first postoperative follow-up visit more than 2 weeks and longer from surgery to initial cannulation (OR for each additional month, 0.81; 95% CI, 0.76-0.88).[28] Higher blood flow and larger vein diameter measured using ultrasound 6 weeks postsurgery were reported to be associated with successful unassisted and overall clinical maturation by Robbin et al.[29]

Our results show no difference in outflow volume treatment and control 1, 3, and 6 months postsurgery. Mean vein lumen diameter measured at the cannulation area (8 cm proximal to the arteriovenous anastomosis) was larger in treatment vs control 3 and 6 months postsurgery. It could be postulated that the physical dimensions of the target vein are directly related to the success of cannulation; that is, larger veins are more accessible and easier to cannulate by vascular access nurses. Functional patency could also be influenced by additional factors such as cannulation skills, patient factors (eg, preference for using a central venous catheter), or study effect because this was not a blinded study. We did not detect a center effect when assessing functional patency. Of note, 3 of 4 participating centers were in the United Kingdom and contributed the vast majority of study participants (38/40). Moreover, fistula cannulation in UK dialysis centers is performed according to the clinical practice guidelines published by the British Renal Society Vascular Access Special Interest Group and Vascular Access Society of Britain & Ireland, which provide a detailed framework encouraging adherence to nursing training and sign-off, thus reducing variation among centers and limiting potential bias.

Stenosis (>50% reduction in lumen diameter) was detected in fewer patients in the treatment arm versus control. Although this did not translate to a 50% reduction in maturation or patency, in our study, AVFs with stenosis had significantly lower flow and vein diameter compared with AVFs with no evidence of stenosis. Progression of stenotic lesions over a longer period could result in further decline in outflow volume, requiring endovascular/surgical interventions to salvage the access, causing further deterioration of the AVF. Because the device targets the JAR, where the development of stenosis is frequent, it could be postulated that reducing flow disturbances in this area could prevent the occurrence of stenosis in this area. This could assist in maintaining a more constant outflow over time and potentially reduce proximal stenosis formation as well. Confirming this hypothesis requires larger studies with longer follow-up time.

In conclusion, in this randomized controlled study, no safety concerns were detected using VasQ external support in brachiocephalic fistulas. There was no difference between treatment and control in unassisted maturation at 3 months and primary patency at 6 months postsurgery. At 3 and 6 months, we observed improved functional patency and larger vein luminal diameter in the treatment group versus control. VasQ may prevent some of the complications associated with the disturbed hemodynamic profile

in the JAR. Larger longer-term prospective studies are required to confirm the clinical benefit of the device.

Supplementary Material

Supplementary File (PDF)

Item S1: Eligibility criteria.

Article Information

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