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Reprinted Article "Factors Associated with Early Failure of Arteriovenous Fistulae for Haemodialysis Access"[☆]

V. Wong [b], R. Ward [a], J. Taylor [a], S. Selvakumar [a], T.V. How [b], A. Bakran [a,*]

[a] *Renal Transplant Unit, Royal Liverpool Hospital, Prescott Street, Liverpool L7 8XP, UK*
[b] *Department of Clinical Engineering, University of Liverpool, PO Box 147, Liverpool L69 3BX, UK*

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Abstract The radiocephalic arteriovenous fistula remains the method of choice for haemodialysis access. In order to assess their suitability for fistula formation, the radial arteries and cephalic veins were examined preoperatively by ultrasound colour flow scanner in conjunction with a pulse-generated run-off system. Intraoperative blood flow was measured after construction of the fistulae. Post-operative follow-up was performed at various intervals to monitor the development of the fistulae. Radial artery and cephalic vein diameter less than 1.6 mm was associated with early fistula failure. The intraoperative fistula blood flow did not correlate with the outcome of the operation probably due to vessel spasm from manipulation. However, blood flow velocities measured non-invasively 1 day after the operation were significantly lower in fistulae that failed early compared with those that were adequate for haemodialysis. Most of the increase in fistula diameter and blood flow occur within the first 2 weeks of surgery.

Introduction

The Cimino-Brescia radio-cephalic arteriovenous fistula is the method of choice for the establishment of haemodialysis vascular access in patients with end- stage renal failure. The fistula is relatively simple to perform under local anaesthesia and, when successfully established, is easy to needle and relatively free from complications. However, a significant proportion (up to 30%) of fistulae fail early, within 3 months of surgery.[1] Some thrombose in the first 24 h of the operation, usually as a result of technical errors, others fail to mature or the blood flow through them is not sufficiently high for haemodialysis. The cause of most early failures is often unclear although the quality of the vessels is thought to play an important role. Small sized or stenosed or partially thrombosed cephalic veins and atherosclerotic or small sized radial arteries have been

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* Corresponding author. Mr A. Bakran, Consultant Transplant and Vascular Surgeon, Renal Transplant Unit, Royal Liverpool University Hospital, Prescott Street, Liverpool L7 8XP, UK.

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suggested as possible causes.[2] This study was designed to address some of these issues.

Initially, an objective and non-invasive method of assessing the quality of the patient's cephalic vein and radial artery preoperatively was developed in order to define those factors which correlate with successful arteriovenous fistula formation. Also, intraoperative blood flow was measured in the exposed cephalic vein immediately after construction of the fistula to try and correlate this parameter with the outcome of operation. The fistulae were then followed-up by means of non-invasive measurement of diameter and blood flow using an ultrasonic colour flow scanner. The objectives of this part of the study were to determine the patency of the fistulae, to provide data which may help in the understanding of the development of fistulae and to investigate factors which relate to fistulae maturation.

Method

All patients with end-stage renal failure requiring a vascular access were invited to take part in this study. Prior to the operation, the patient's cephalic vein and radial artery were assessed clinically by the surgeon and the quality of each vessel was classified into one of the following categories: good, poor or absent. An attempt at fistula construction was made in all cases where the cephalic vein was present, even when the vein was classified as poor by the surgeon. The fistulae were created at the wrist with the anastomosis constructed in end vein-to-side artery fashion since this is considered to be haemodynamically efficient and the risk of venous hypertension in the hand is minimised.[2]

Non-invasive ultrasound assessment was carried out preoperatively by means of a colour flow scanner (Acuson 128XP Computed Sonography System, Acuson Corp.) provided with a 7.0 MHz linear array probe (Type L7384) which operates at 5 MHz in Doppler mode. In order to improve visualisation of the cephalic vein, a pulse generated run-off (PGR) system (Oak Medical Ltd.) was used in conjunction with the ultrasound scanner. The PGR has been used for determining the patency of runoff vessels in the calf prior to femorodistal bypass.[3] It consists of a pressure cuff driven by compressed air producing controlled inflation and deflation of the cuff. Best results were obtained when the pulsatile pressure within the cuff was set to fluctuate between 0 and 100 mmHg at a rate of 100 pulsations per minute. This pulsatile pressure cuff, measuring 3 cm wide, was placed around the patient's hand. A second cuff was applied to the upper arm and was inflated to a constant pressure of 40 mmHg. The resulting pressure difference between the wrist and the upper arm generated a pulsatile flow in the veins of the forearm. This pulsatile venous flow could then be detected by the colour flow scanner. The vein was imaged longitudinally, without compression, and its diameter measured at 5 cm intervals from the wrist to the antecubital fossa. Stenoses were identified by changes in the luminal diameter and the presence of flow disturbances. Occlusion due to thrombosis was easily recognised by the sudden loss of flow information. Major branches along the vein could also be observed and when present, their location and diameter were recorded.

Intraoperative measurement of blood flow through the fistulae was made using an ultrasonic transit-time flowmeter (Model HT107, Transonic Systems Inc.). Immediately after the fistula was constructed, an ultrasonic perivascular probe (Model H4S, Transonic Systems Inc.) designed for vessels of diameter 2.5–4 mm was placed over the vein at least 1 cm downstream of the anastomosis. Sterile ultrasound gel was used between the vessel and the probe. The blood flow signal was recorded over a period of 40 s and was stored in a microcomputer for subsequent analysis.

Postoperative follow-up was carried out at the following times after the operation: 1 day and 2, 4, 6, and 12 weeks. This consisted of non-invasive Doppler flow measurement and B-mode and colour flow imaging of the cephalic vein, radial artery and the anastomotic region. The diameters of the proximal and distal artery and the cephalic vein and the blood flow through them were determined. In the case of the cephalic vein the flow measurements were made between 5 and 10 cm downstream of the anastomosis where the flow was less disturbed. When stenotic lesions were detected in the cephalic vein or at the anastomosis, their location and degree of narrowing expressed as percentage cross-sectional area reduction were recorded.

Statistics

The data are presented in terms of mean $\pm$ S.D. Comparison of mean values between different groups are made using Student's two-tailed test for unpaired samples with separate variance. When comparing groups, a p-value of less than 0.05 was considered significant.

Results

Patients

Sixty patients with arteriovenous fistulae have been followed-up for at least 12 weeks. There were 37 men (age range: 17–77 years, mean: 59 years) and 23 women (age range: 20–77 years, mean: 57.5 years). One patient had received a renal transplant which subsequently failed and seven had diabetes. Of the sixty patients, three subsequently died and three were lost to follow-up.

Preoperative

The mean diameter of the cephalic vein measured preoperatively was 2.6 mm at the wrist, 3.0 mm in mid-forearm and 3.2 mm at the elbow. The radial artery was generally smaller, with mean diameter of 2.2 mm (Table 1). Localised venous stenoses were found in 11 patients. Most stenoses were mild (<50% area reduction) and only one, with cross-sectional area reduction of >75%, was haemodynamically significant. In five patients, particularly those with a small cephalic vein, the stenosis progressed after creation of the fistula and became haemodynamically significant (>75%).

A major side branch with diameter similar to that of the main cephalic vein was found in 20 patients. Multiple branches were rarer, with two patients having two and a further two having three branches within 5 cm of the

Table 1 Preoperative mean diameter of the radial artery at the wrist and the cephalic vein at the level of the wrist, mid-forearm and antecubital fossa measured by ultrasound colour flow scanner.

Vessel	Mean diameter (mm)	S.D. (mm)	n
Vein (wrist)	2.6	0.7	53
Vein (mid-forearm)	3.0	0.9	49
Vein (antecubital fossa)	3.2	0.7	49
Artery (wrist)	2.2	0.5	53

wrist. It was necessary to ligate the side branches in two patients with multiple branches in order to improve fistula maturation. Both fistulae subsequently matured and were used satisfactorily for haemodialysis.

Intraoperative

Intraoperative fistula blood flow measured in 26 patients ranged from 10 to 360 ml/min, (125 ± 102 ml/min). There was no correlation between intraoperative blood flow and the size of the cephalic vein measured preoperatively. Moreover, the intraoperative flow did not relate with the outcome of the operation.

Postoperative

The outcome of the operations is summarised in Fig. 1 and the cumulative patency rates determined by life table analysis are shown in Fig. 2. Four fistulae thrombosed early, two within 24 h and the other two within 1 week of the operation. In another four cases, the fistula was patent but haemodynamically failed (flow too low to be measured reliably). Six of these eight patients whose fistulae thrombosed or had poor blood flow were referred for secondary access procedures all of which were successful.

Of the 46 patients who have been followed-up for at least 12 weeks, 38 had a patent fistula that was suitable for dialysis. The diameter and flow through the proximal and distal segments of the radial artery and cephalic vein measured in the 46 patent fistulae are given in Table 2. All the patent fistulae are being used for routine dialysis. The remaining eight fistulae were judged clinically to be inadequate for dialysis because of poor flow (<150 ml/min) or failure to dilate (cephalic vein diameter < 3 mm) or both. The underlying causes were the presence of a significant stenosis (>75% cross-sectional area reduction), small vessel size and major branches which diverted a large proportion of the flow from the cephalic vein. Significant stenoses were found in four inadequate fistulae, two at the anastomosis, and two in the mid forearm. One of the midforearm stenoses was present preoperatively and the other was detected during the first routine postoperative examination. In two cases, the cephalic vein had major divisions within 5 cm of the anastomosis and both were demonstrated by preoperative examination.

Fig. 3 shows the relationship between the 1-day postoperative blood flow velocity and the outcome of the fistulae at 12 weeks. The patients were divided into two groups. The failed group ($n = 14$) includes the fistulae that failed early (6, excluding 2 which thrombosed within 24 h) and those that were inadequate for dialysis (8). The successful group ($n = 38$) comprises patients with fistulae that were on satisfactory dialysis. In general, the higher the velocity of flow, the more likely was a fistula to be patent and adequate for dialysis. The blood flow velocity for these two groups were as follows: Failed: 0.18 ± 0.09 m/s, and Successful: 0.53 ± 0.15 m/s. The difference between these two groups is statistically significant ($p < 0.01$).

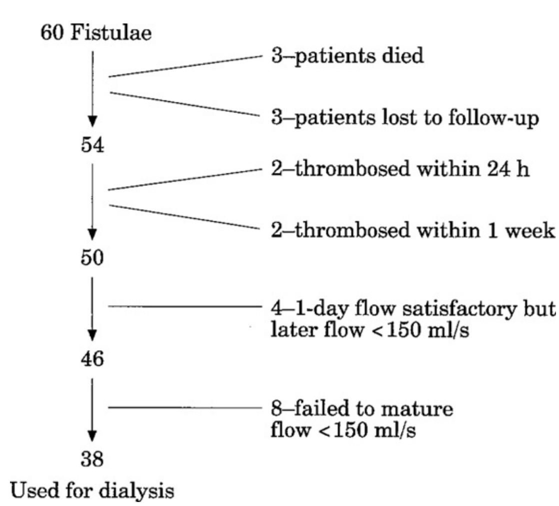

Figure 1 Summary of the results of arteriovenous fistulae surgery.

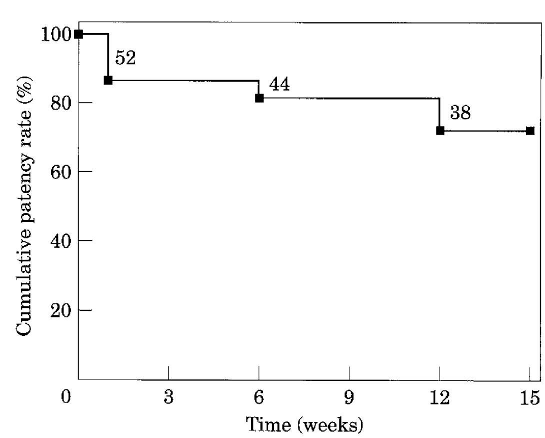

Figure 2 Patency results, calculated from life table analysis, for the radiocephalic arteriovenous fistulae performed in the group of 60 patients.

Table 2 Postoperative diameter and flow in the cephalic vein, the proximal and distal segments of the radial artery. Measurements were made at 12 weeks by means of the colour flow scanner in patients with fistulae which were adequate for haemodialysis. Note that the distal radial artery flow was generally retrograde. Only in one case was the flow antegrade. In two further cases no flow was detected in the distal artery.

Vessel	Diameter (mean $\pm$ S.D) (mm)	Flow (mean $\pm$ S.D) ml/min
Cephalic vein	5.8 $\pm$ 1.2	710 $\pm$ 318
Proximal radial artery	4.2 $\pm$ 0.8	550 $\pm$ 210
Distal radial artery	3.2 $\pm$ 0.6	137 $\pm$ 170

In order for a fistula to mature properly, the inflow and outflow vessels should be unrestricted and free from disease. The diameter of these vessels is important since the resistance to flow through a cylindrical vessel is inversely proportional to the fourth power of the radius.[4] Fig. 4 shows the relationships between the cephalic vein and radial artery diameters measured preoperatively by ultrasound and the outcome of the performance of the fistula. There appeared to be a lower limit for the vessel diameter below which the fistula invariably failed. Of the six fistulae involving a radial artery of diameter $\leq$ 1.6 mm, two thrombosed and four failed to mature satisfactorily. In two other cases where the fistula failed to develop and the radial artery was greater than 1.6 mm diameter the cause of failure was due to the presence of a significant stenosis in the vein. There were also three cephalic veins of diameter $\leq$ l.6 mm which failed to mature satisfactorily. However, in the other cases of early thrombosis and haemodynamic failure, the vessel diameters varied widely, indicating that vessel calibre is only one of several factors affecting the outcome of the operation.

Fig. 5 shows the change in the vein diameter with time after the construction of the fistulae. In all patent fistulae, both those which were adequate and inadequate for dialysis there was a marked increase in diameter in the first 2 weeks after the operation. Whilst those in the successful group the vein diameter continued to increase after 2 weeks, albeit at a reduced rate, those in the failed group (inadequate for dialysis) the vein diameter decreased gradually with time up to the maximum follow-up time of 12 weeks. A similar pattern was found in the case of blood flow (Fig. 6).

Preoperative clinical assessment and ultrasound measurement compared with clinical outcome

The results of the preoperative clinical assessment of the cephalic vein are summarised in Table 3. In the failed group ($n = 16$), six cephalic veins were considered to be of poor quality while nine were moderate or good. The remaining vein was difficult to palpate because of the overlying adiposity. Of the 38 fistulae with successful outcome, 25 were associated with moderate to good veins, six with poor veins and the remaining seven were not assessable.

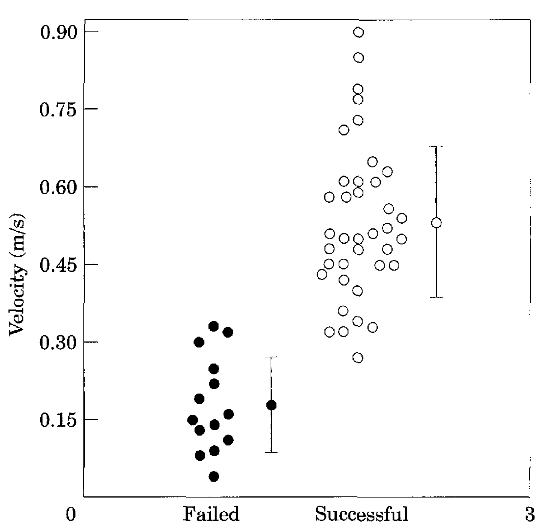

Figure 3 Blood flow velocity measured at 5—10 cm from the anastomosis one day after surgery. The velocity in the failed group ($n = 14$) was 0.18 $\pm$ 0.09 m/s and in the successful group ($n = 38$) 0.53 $\pm$ 0.15 m/s. The difference between the two groups is significant ($p < 0.01$).

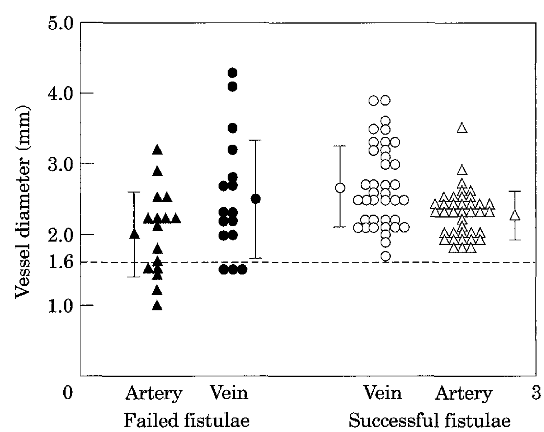

Figure 4 Relationship between radial artery and cephalic vein diameters measured preoperatively by ultrasound and the outcome of the operation. The diameter of the cephalic vein in the failed group was 2.6 $\pm$ 0.8 mm compared with 2.7 $\pm$ 0.6 mm in the successful group. The radial artery diameter in the failed group was 2.0 $\pm$ 0.6 mm and in the successful group it was 2.3 $\pm$ 0.3 mm. Although the diameters were slightly larger in the successful than in the failed group, the differences were not significant. However, radial artery and vein diameter equal to or less than 1.6 mm were associated with failed fistulae.

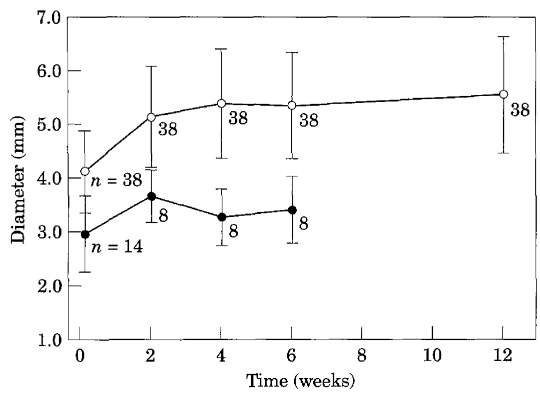

Figure 5 Plot of the mean diameter of fistulae as a function of time. The measurements were made at 5–10 cm downstream of the anastomosis. (o) successful fistulae ($n = 38$), (●) fistulae that failed within 12 weeks.

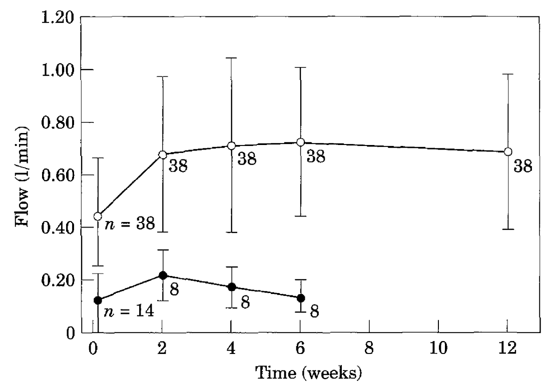

Figure 6 Plot of the mean blood flow through the fistulae as a function of time. The measurements were made at 5–10 cm downstream of the anastomosis. (o) successful fistulae ($n = 38$), (●) fistulae that failed within 12 weeks.

The relation between the preoperative ultrasound results and the outcome of surgery are summarised in Table 4. For the purposes of this study, the criteria used for an abnormal ultrasound scan are: (a) a vessel with diameter less than 1.6 mm or (b) the presence of a stenosis in the cephalic vein. Of the 16 failed fistulae, seven had abnormal scans while nine were classified as normal. In the successful group, none had an abnormal scan according to the above criteria.

To compare the preoperative ultrasound findings with clinical assessment, the sensitivity, specificity, positive and negative predictive values, as defined by Altman,[5] were calculated and the results are presented in Table 5. Neither test was particularly sensitive since less than half of the failed fistulae were correctly predicted. However, ultrasound assessment was better in two respects. All fistulae that were classified as normal from the ultrasound scans had a successful outcome (sensitivity of 1.0) and all fistulae that met the criteria for abnormal scan subsequently failed (positive predictive value of 1.0). The total correct predictions for ultrasound assessment was 0.83 (7 + 38/54) compared with 0.67 (6 + 25/46) for clinical assessment.

Discussion

Long-term haemodialysis of patients with chronic renal failure is dependent on maintaining a patent and functioning vascular access. An established CiminoBrescia arteriovenous fistula is widely accepted as the best form of access in these patients. This and other studies[6] indicate that these fistulae are associated with a relatively high early (<3 months) failure rate. It should be pointed out that in this study, all patients, even those with poor cephalic veins, on clinical evaluation, had an arteriovenous fistula created. Also the mean age of the patients was high (58 years) reflecting the increasing availability of dialysis to the elderly. These older patients often have diseased vessels. There have been very few studies to identify the factors, such as the size and quality of the cephalic vein and radial artery and the blood flow through them, that may have an influence on these early failures. This is important since it may enable the surgeon to select the best type of vascular access for a particular patient and ensure that operations on vessels associated with a poor outcome are avoided. Increasingly, clinical experience shows that in many patients, the cephalic veins are being cannulated for infusion of fluids or drugs making successful outcome for fistula surgery less likely. This study has shown that such sites of stenosis following cannulation can be detected prior to surgery.

Assessment of patients' vessels prior to access surgery usually consists of confirmation of the presence of a radial pulse and the degree to which the cephalic vein dilates after application of a proximal tourniquet. Whilst in most cases it is possible qualitatively to assess the vessel size and to recognise the presence of thrombosis, in patients who are obese or have deep lying veins, this is difficult to accomplish since the veins are not readily visible or palpable. Even so, clinical

Table 3 Relation between the outcome of surgery and clinical assessment of cephalic veins. Veins that were not readily visible or palpable and were not assessed are excluded.

Clinical assessment	Outcome		
	Failed	Successful	Total
Poor	6	6	12
Good	9	25	34
Total	15	31	46

Table 4 Relation between the outcome of surgery and preoperative ultrasound assessment. The ultrasound scan is defined as abnormal if the vessel is of diameter less than 1.6 mm and/or a stenosis is detected in the cephalic vein.

Ultrasound assessment	Outcome		
	Failed	Successful	Total
Abnormal	7	0	7
Normal	9	38	47
Total	16	38	54

assessment only appeared to predict probable successful outcome of fistula surgery in 25 out of 38 patients and failure in six out of 16 patients. With the advent of high resolution ultrasound colour flow scanners it is now possible to obtain non-invasive and quantitative data on the vessel size and blood flow velocity prior to and following the operation. These scanners have also been found to be useful for early diagnosis and treatment of fistula complications.[7–9] The accuracy of blood flow velocity measurements using Duplex scanning depends on the vessel being uniformly insonated and the flow laminar and axisymmetric.[10] Since flow rate is determined by the product of mean velocity and vessel cross-sectional area, the accuracy in measuring the vessel diameter is important. The best resolution that can be achieved with the scanner used in this study is of the order 0.2 mm (i.e. the wavelength at 7 MHz). Since the smallest fistula at 2 weeks was about 4 mm in the successful group, the theoretical error associated in flow determination is about 11%. In the case of the inadequate fistulae, the maximum error increases to about 25%. Note that the values of velocities shown in Fig. 3 are not affected by these errors since the measurement of diameter is not required. The cephalic vein lies very superficially in many patients and are susceptible to compression during the measurement unless care is taken to avoid any pressure being exerted on the skin surface by the probe. All the ultrasonic imaging was performed by one of the authors to ensure consistency of the measurement procedure and liberal quantities of ultrasonic coupling gel was used to avoid direct contact between the probe and the skin surface. Moreover, when fistula flow was determined, measurements were also made in the proximal and distal radial arteries to verify the inflow was similar to the outflow. In all cases, good agreement was obtained and the maximum discrepancy between the inflow and outflow was less than $\pm$20%.

Noting the poorer results obtained with female patients, Kinnaert et al.[11] indicated that the small arteries often encountered in these patients may be responsible for some of the early failures. The present study shows that vessel diameter was not a sensitive predictor of outcome and it is only one of several factors that determine the success or failure the fistula. When the diameter was 1.6 mm or less or a stenosis was found, the fistula invariably failed. A small radial artery could limit the flow through the fistula because of the strong influence of radius ($1/r^4$) on pressure drop. Since it is generally more difficult to anastomose small vessels it is likely that when their diameters are less than about 1.6 mm, there may be a greater risk of technical errors leading to poor blood flow.

The majority of fistulae (65%) had at least one branch along the efferent vessel and 80% of these branches were detected in the preoperative examination. In cases where there was more than one branch division within 5 cm of the anastomosis, a significant proportion of the flow was diverted from the mainstream and the fistulae consequently failed to mature. Since most branch divisions could be detected preoperatively, ligation of these should be considered at the time of fistula construction or soon thereafter.

In a study comparing end-to-side to side-to-side fistulae, Wedgewood et al.[12] found that successful fistulae have a significantly higher intraoperative blood flow than those which subsequently failed. The present study did not show any correlation between intraoperative flow and the outcome of the fistula operation. Reliable flow measurements on small diameter vessels in such a confined space was technically demanding even with the miniature transit-time ultrasound probes used in this study. Because of the unavoidable handling of the vessels during the operation, several cases of vessel spasms were observed resulting in poor fistula flow. This was also observed by Anderson et al.[13] in almost half of the patients in whom flow measurements were made. However, most of these vessels recovered fully by the following day and in the majority of the cases the flow greatly increased compared with intra-operative values. Consequently, the blood flow velocity measured the day after the operation correlated better with early failure of the fistula than intraoperative volume blood flow. If an early prediction of the fistula unsuitability for dialysis can be made with accuracy, patients can be selected for secondary vascular access sooner rather than waiting 4–6 weeks for fistula maturation. Our results suggest that measuring the flow velocity at day 1 post-operatively would be beneficial in this regard. In those with

Table 5 Analysis of data obtained from clinical assessment and ultrasound assessment.

	Clinical assessment	Ultrasound assessment
Sensitivity	0.4	0.44
Specificity	0.81	1.0
Positive predictive value	0.5	1.0
Negative predictive value	0.74	0.81
Total correct predictions	0.67	0.83

satisfactory initial flow velocity, vein size at weeks would confirm whether the fistula would mature adequately to enable successful haemodialysis.

In conclusion, the sizes of the radial artery and cephalic vein, determined by either ultrasound or clinical assessment, do not correlate with the outcome of fistula constructions. However, a primary access should not be performed if the diameter of either vessel $\leq$ 1.6 mm. Non-invasive blood flow velocity measured at 24 h is predictive of fistula success or failure. Branch divisions can be detected preoperatively by ultrasound and may therefore be ligated at the time of fistula creation.

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