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Original Article

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Does monthly native arteriovenous fistula blood-flow surveillance detect significant stenosis—a randomized controlled trial

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Abstract

Background. Clinical practice guidelines recommend that the preferred method of surveillance for arteriovenous fistula (AVF) is the measurement of AVF blood flow (Qa). As these recommendations are based on observational studies, we conducted a randomized, prospective, double-blind, controlled trial to assess whether Qa surveillance results in an increased detection of AVF stenosis.

Methods. A total of 137 patients were randomly assigned to receive either continuing AVF surveillance using current clinical criteria (control, usual treatment) or usual treatment plus AVF blood-flow surveillance by ultrasound dilution (Qa surveillance group). The primary outcome measure was the detection of a significant (>50%) AVF stenosis.

Results. There were 67 and 68 patients assigned to the control and Qa surveillance groups, respectively. Patients in the Qa surveillance group were twice as likely to have a stenosis detected compared with the control hazard ratio (HR) confidence interval (CI) group (2.27, 95% 0.85–5.98, $P = 0.09$), with a trend for a significant stenosis to be detected earlier in the Qa surveillance group ($P = 0.09$, log rank test). However, using the Qa results alone prior to angiography, the area under the receiver operating characteristic curve demonstrated, at best, a moderate prediction of (>50%) AVF stenosis (0.78, 95% CI 0.63–0.94, $P = 0.006$).

Conclusion. This study demonstrates that the addition of AVF Qa monitoring to clinical screening for AVF stenosis resulted in a non-significant doubling in the detection of angiographically significant AVF stenosis. Further, large multi-centre randomized trials are feasible and will be necessary to confirm whether Qa surveillance and the correction of detected AVF stenosis will lead to a reduction in AVF thrombosis and increased AVF survival.

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Introduction

The native arteriovenous fistula (AVF) is the vascular access of choice for haemodialysis due to its longevity, lower complication and mortality rates compared with arteriovenous grafts (AVG) and catheters. However, the development of a significant stenosis secondary to intimal hyperplasia necessitating the revision and/or causing thrombosis remains an important clinical problem [1]. The detection and correction of an angiographically significant stenosis before thrombosis occurs is therefore an important clinical goal [2].

The measurement of vascular access blood flow (Qa) is recommended as the preferred method of surveillance for AVF [2]. These recommendations were based on the observational studies performed predominantly in patients with AVG, demonstrating that a low Qa is associated with an increased risk of thrombosis and failure, with only one study in patients with AVF [3]. Tonelli and colleagues [4] assessed the ability of Qa measurements to detect the underlying so-called subclinical AVF stenosis, a stenosis that was not detected by using clinical monitoring such as clinical examination or reduced solute clearances. However, the number of stenoses that were detected by clinical features, in addition to Qa surveillance, is not known as they were excluded from this study. Recently, Tessitore *et al.* [5] presented a 'pseudo-randomized' (randomization was by coin toss) study in which the subjects with a stenotic AVF were allocated to either blood-flow surveillance or clinical monitoring. While the patency of AVF in the blood-flow group was significantly longer, no information was given on the number of stenoses detected and treated in each group.

Therefore, to test the hypothesis that regular blood-flow monitoring, in addition to the conventional clinical monitoring, will detect any angiographically

significant stenoses earlier, we conducted a randomized, prospective, double-blind, controlled clinical trial comparing AVF Qa surveillance in addition to standard clinical AVF surveillance *vs* standard clinical AVF surveillance alone. The primary outcome of the study was the detection of an angiographically significant AVF stenosis. The aim of this study was to determine if monthly AVF Qa surveillance was associated with an increased or earlier detection rate of angiographically significant AVF stenosis. In addition, as blood-flow measurements were performed in all subjects, we also aimed to explore the relationship between access flow, conventional clinical indicators of access dysfunction and the occurrence of access stenosis.

Methods

Patients with End Stage Renal Failure (ERSD) on haemodialysis from the Department of Nephrology at Monash Medical Centre, Melbourne, Australia, were recruited into the trial. Study participants underwent thrice-weekly haemodialysis at the satellite haemodialysis units located in the south eastern metropolitan, Melbourne. Inclusion criteria were as follows: age >18 years, able to give written informed consent, stable haemodialysis for at least 4 weeks via an AVF ≥12 weeks and a baseline AVF Qa >500 ml/min. Patients were excluded if the haemodialysis was performed using either an AVG or a central venous catheter, if they were on home haemodialysis or if there was an impending live-donor renal transplant. Written informed consent was obtained from all patients. The study protocol was approved by the Southern Health (Monash Medical Centre) Human Research and Ethics Committee, and was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association. A detailed description and analysis of the determinants of the AVF Qa at the baseline in the screened subjects has been published elsewhere [6].

Study participants were randomly assigned to receive continuing AVF surveillance using current clinical criteria (control and usual treatment) or usual treatment plus AVF blood-flow surveillance (Qa surveillance group). Randomization was performed using a computer-generated random sequence (GraphPad Statmate v1.0, GraphPad Software, San Diego, CA, USA). The surveillance allocation was performed by one investigator (K.R.P), who took no part in the clinical management of the patients enrolled in the trial. Patients and treating clinicians were blinded to group assignment. AVF Qa surveillance had not been performed in our centre prior to the commencement of this trial.

All patients underwent monthly Qa measurements using ultrasound dilution (Transonic Systems Inc., Ithaca, NY, USA). This method is well described and validated [7]. Two measurements were recorded at each time point. If the second measurement varied by >10%, then a third measurement was performed and the two closest measurements were recorded. The average was then obtained and used in the analysis. All measurements were performed in the first 2 h of the haemodialysis session [8]. Assessment of recirculation was performed prior to all Qa measurements in all patients, but these results were not used in either group as a trigger for further investigation given that they do not increase the utility of Qa screening [4].

The patients in the control group were referred for digital subtraction angiography only if there was clinical suspicion of AVF stenosis. Clinical criteria included a raised dynamic venous pressure at the prescribed or actual blood pump speed that was not resolved by needle repositioning (>150 mmHg), a low arterial pressure requiring consistent reductions in the delivered dialyser blood flow (Qb), excessive bleeding from AVF venopuncture sites, an unexplained reduction in the urea reduction ratio (URR) amount determined by the treating physician or a clinical examination suspicious of stenosis. The measurement of access recirculation using the two-needle urea-based method is not routinely performed in our unit unless specifically requested by the treating clinician. Calculation of the URR was performed routinely every 3 months in all the patients. Patients in the Qa surveillance group were referred for angiography if there was clinical suspicion of stenosis using the same clinical criteria as in the control group or if AVF Qa was <500 ml/min at the baseline or if the Qa fell by >20% once the flow was <1000 ml/min [2,4]. The clinical criteria for referral for angiography was determined by the dialysis nurses and/or the treating nephrologists. Results of the Qa measurements were available to one investigator only (K.R.P.), who determined whether the referral on Qa criteria was necessary in the Qa surveillance group. Qa results in the control group were recorded (K.R.P.) but not acted upon even if the intervention thresholds were met, as in the surveillance group.

Interpretation of all angiograms and decisions regarding further intervention were performed together by a nephrologist (P.G.K.), an interventional radiologist (K.K.P.L.) and a vascular surgeon (A.S.) blinded to treatment assignment and reason for the referral. A tourniquet was used to visualize the arteriovenous (AV) anastomosis and proximal artery. An arterial approach was performed if inadequate views of the AV anastomosis were obtained. The type of intervention (angioplasty or surgery) was determined together by both the radiologist and the surgeon with the nephrologist, based on the characteristics of the stenosis identified and other clinical factors (for example, operative risk). The follow-up was continued until 31 October 2003 and was censored for the following reasons: transplantation, patient withdrawal from the study, transfer to a non-study centre, transfer to peritoneal dialysis or death.

The primary outcome measure was the time to detection of an angiographically significant AVF stenosis, defined as a ≥50% reduction of the normal vessel luminal diameter on angiography [9] accompanied by a haemodynamic (in the case of the Qa surveillance group), functional or clinical abnormality (in the case of the control group) [2]. The secondary outcome measures were AVF thrombosis, number of interventions and the performance characteristics of the AVF Qa criteria and other clinical criteria.

Ideally, AVF thrombosis and survival would have been the primary outcome measure for the trial. However, given the lower thrombosis rate of AVF, the required sample size was larger than that performed in our unit alone. We, therefore, chose the time to detection of a significant stenosis requiring revision as a surrogate end point for AVF thrombosis. Two observational studies demonstrated revision rates (we assumed this, equated to the detection of

a significant stenosis) in AVF of 0.26 per patient year [10] and 0.21 per patient-year [11], respectively. In addition, a large observational study of AVF [4], using Qa surveillance, revealed a 20% prevalence of subclinical stenosis (these were stenoses that were deemed severe enough to require revision) with a mean follow-up of 7.7 months. According to the Australian and New Zealand Dialysis and Transplantation Association (ANZDATA) registry, ~8% of the patients in Australia require a revision of their AVF over a 6-month period using clinical surveillance criteria (no units were using Qa surveillance in Australia during that time) [12]. Using these figures, we calculated that 150 patients would be required to have an 80% power to detect the increase from 8 to 25% in the subclinical stenosis rate of AVF over a 6-month period. We planned, however, to continue the follow-up for at least 12 months from the recruitment of the last patient in order to increase the detection rate in case of poor recruitment.

All the data were presented in numerals (percentage), mean ± SD or median (range) where appropriate. The primary outcome (time to positive angiogram) was assessed using the Kaplan–Meier method and compared using the log rank test. Hazard ratios (HRs) were estimated using the Cox proportional hazards model. Differences in proportions between the two groups were assessed with the χ^2 test or the Fisher's exact test where the expected frequencies were <5% in any cell. Continuous variables were compared using the Wilcoxon rank-sum test, and the paired and unpaired *t*-tests where appropriate. Receiver-operating characteristic (ROC) curves were constructed using the Qa in all the patients in whom an angiogram was performed. All analyses were performed according to the intention-to-treat principle. We declared a finding to be statistically significant if the two-sided *P*-value was <0.05. All analyses were conducted on Intercooled Stata 8.1 (Statacorp, College Station, TX, USA).

Results

Patient recruitment began in December 2001 and was completed in June 2002. Follow-up continued until 31 October 2003. The flow of participants during the trial is outlined in Figure 1. A total of 169 patients were

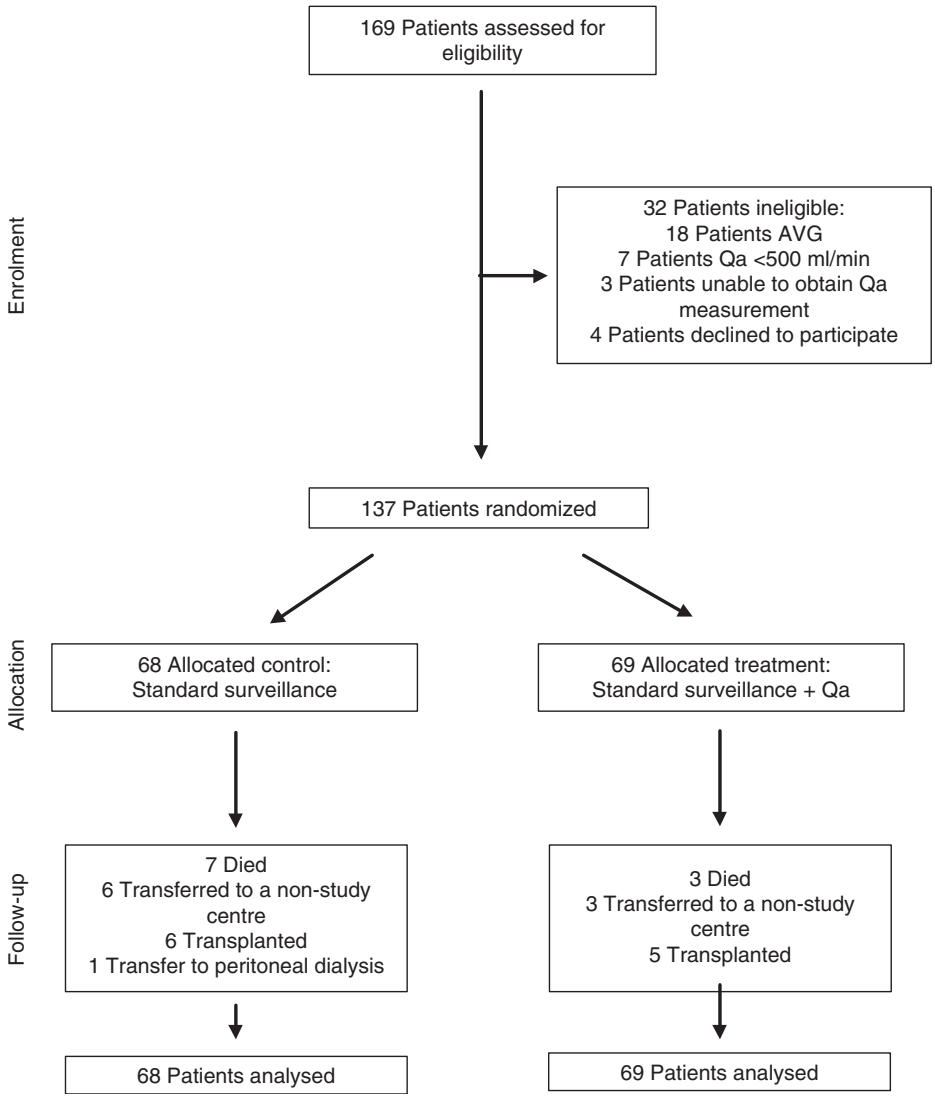

Fig. 1. Flow diagram of the randomized controlled trial of Qa surveillance in AVF.

assessed for eligibility to enter the trial. Of those, however, 30 were ineligible: 18 had an AVG, four declined to participate, three had an AVF anatomy that precluded the Qa measurement and seven had a Qa <500 ml/min at the baseline screening. Of the seven patients with a Qa <500 ml/min at the baseline screening, all had significant stenosis at angiogram. Four patients were subsequently treated (three surgically and one with angioplasty), while one received a renal transplant and the other died suddenly before surgical repair could be performed. Thus, 14 screened patients with AVF could not be recruited, and therefore only 137 patients of the intended 150 were randomized into the study. Sixty-seven patients were allocated to the control group and 68 to the Qa surveillance group. The overall median follow-up time was longer than that intended at 1.53 years (range 0.01–1.87 years). The baseline characteristics of the two treatment groups are detailed in Table 1. There were no clinically important differences between the two groups at the baseline.

Overall, 19 angiograms in 17 patients were found to have a clinically significant stenosis. There was a trend for a significant stenosis to be detected earlier in the Qa surveillance group (Figure 2, $P = 0.09$, log-rank test). Overall, the patients in the Qa surveillance group were twice as likely to have a stenosis detected compared with the control group, although this was not statistically significant (HR 2.27, 95% CI 0.85–5.98, $P = 0.09$).

Table 2 outlines the reason for the number and results of the angiograms performed in the study, divided into two groups. Thirteen angiograms were performed in the control group and 21 in the Qa surveillance group ($P = 0.12$, χ^2 test). In the control group, 6 out of the 13 (overall prevalence $6/68 = 8\%$) angiograms performed were positive for a clinically significant stenosis. Angiograms were performed in the majority (7/13) for high dynamic venous pressures, with three each for an unexplained reduction in the URR, and an abnormal clinical examination. Venous pressure was particularly poor at signifying a significant stenosis with only $1/7 = 14\%$ positive. In the Qa surveillance group, 13 of the 21 angiograms performed were positive (overall prevalence $13/69 = 19\%$). Dynamic venous pressure was also poor in this group with only two of the eight (25%) angiograms performed indicating positive. Six angiograms were

Table 1. Baseline characteristics of the trial participants

Characteristic	Control ($n = 68$)	Qa surveillance ($n = 69$)
Median follow-up (yr)	1.48 (0.08, 1.87)	1.24 (0.07, 1.87)
Gender, *n* (%) male	48 (71)	45 (65)
Race, *n* (%) white	66 (97)	61 (89)
Age (yr)	56.4 (21.4, 79.7)	60.0 (23.8, 82.8)
Primary renal disease, *n* (%)		
Glomerulonephritis	27 (40)	25 (36)
Diabetes mellitus	15 (22)	17 (25)
Hypertension/ischaemic	8 (12)	5 (7)
APCKD	10 (14)	4 (6)
Other	8 (12)	18 (26)
Comorbid conditions, *n* (%)		
Diabetes mellitus	19 (28)	24 (35)
Coronary artery disease	20 (29)	19 (28)
Peripheral vascular disaese	5 (7)	9 (13)
Cerebrovascular disease	8 (12)	8 (12)
Medications, *n* (%)		
Aspirin	22 (32)	23 (33)
Warfarin	2 (3)	6 (9)
ACE inhibitors	24 (35)	25 (36)
Epo	57 (83)	61 (88)
AVF type, *n* (%)		
Radiocephalic	42 (62)	42 (61)
Brachiocephalic	18 (27)	20 (29)
Brachiobasillic	5 (7)	5 (7)
Other	3 (4)	2 (3)
AVF age (yr)	2.39 (0.24, 8.33)	1.95 (0.15, 13.29)
Qa (ml/min)		
All AVF	1243 (515, 3950)	1145 (560, 3640)
Radiocephalic AVF	965 (515, 3630)	1040 (560, 2640)
Upper arm AVF	1530 (705, 3950)	1305 (570, 3640)
Duration on dialysis (yr)	2.09 (0.08, 8.36)	2.70 (0.05, 21.57)
Qb (ml/min)	300 (200, 350)	300 (200, 350)
Dialysis time (h)	4 (2.5, 5)	4 (3, 5)
Cardiac index (l/min/m^2)	3.15 (1.3, 6.5)	3.15 (1.7, 5.0)

Data presented as number (%) or median (range).
AVF, arteriovenous fistula; APCKD, adult polycystic kidney disaese; Epo, erythropoietin; Qb, dialyser bloof flow; Qa, AVF blood flow.

performed for a Qa <500 ml/min of which five were positive (83%). No subjects in the surveillance group had a fall of >20% in Qa with a baseline <1000 ml/min. Three out of four patients (75%) with an unexplained reduction in URR had a significant stenosis. One patient with poor clearances had a significant access recirculation using ultrasound dilution (20.1% in the month when the clearances were measured). No other episodes of true (>5%) access recirculation occurred during the study. Finally, both the clinical examination (two patients) and the excessive bleeding post-dialysis (one patient) produced positive angiograms.

Qa was significantly lower in patients with positive compared with negative angiograms [median Qa 760 (range 145–1700) *vs* 1390 (490–3820) ml/min, $P = 0.006$, rank-sum test] (Figure 3). Using the Qa results prior to the angiogram, we constructed an ROC curve for the predictive value of Qa alone for the detection of a clinically significant stenosis (Figure 4). The area under the ROC curve (AUC) demonstrated, at best, a moderate prediction (AUC 0.78, 95% CI 0.63–0.94, $P = 0.006$). With the cut-off of 500 ml/min, as used in the study, sensitivity was poor at 44% with a specificity of 93% and 67% overall correctly classified at this cut-off level. Applying a higher threshold of 800 ml/min increases the sensitivity to 62% with a corresponding reduction in specificity to 74%.

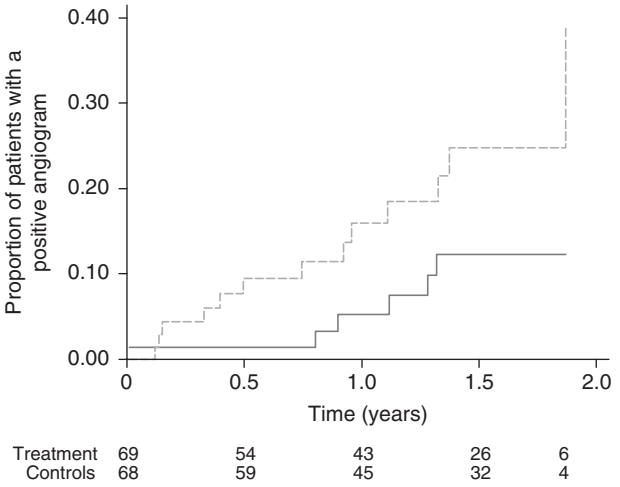

Fig. 2. Time to AVF stenosis detection comparing the control (clinical surveillance) with the Qa surveillance group ($P = 0.09$, log-rank test). Dotted line Qa surveillance group, solid line control group.

In the control group, nine patients reached the criteria for angiogram, on the flow criteria (Qa flow <500 ml/min), but did not receive an angiogram for these criteria during the trial as per protocol (cf. six performed in the treatment group). Two patients had an angiogram performed for an unexplained reduction in the URR (293 and 230 days after the first low-Qa result, respectively), both of which were positive. One subsequently had a surgical revision, whereas the other thrombosed his/her AVF while awaiting elective repair (the AVF was salvaged and repaired surgically). A further patient thrombosed his/her AVF 466 days after the low-Qa result and was salvaged surgically. Only one patient terminated the trial with a low Qa result. An angiogram requested at the termination of the trial did not demonstrate a haemodynamically significant stenosis. Of the other five positive patients, two died during the trial, at 8 and 12 weeks, following the first low-Qa result. One patient was transferred to a non-study centre, and two others were definite false-positives (one was due to hypotension during the dialysis procedure and the other as a result of needle placement with subsequent values well above the threshold. This patient subsequently had a normal angiogram, requested for raised venous pressure).

Table 3 demonstrates the indication for and type of interventions performed during the study. Of the 19 positive angiograms, 18 interventions were performed (1 patient refused surgery), 6 in the control group and 12 in the Qa surveillance group ($P = 0.20$, Fisher's exact test). In two-thirds of the patients, surgery was the preferred intervention. There were 10 thrombotic episodes during the study, producing an overall rate of 0.052 thrombosis per patient years at risk. There was no difference in the number of thrombosis between the Qa surveillance and the

Table 2. Reasons and results of AVF angiogram requests in each group

Fistulogram result	Control[a]		Qa surveillance[b]	
	Negative	Positive	Negative	Positive
Number of angiograms performed	7	6	8	13
Reason for request[c]				
Raised dynamic venous pressure	6	1	6	2
Qa <500 ml/min	–	–	1	5
Unexplained reduction in URR	1	2	1	3
Clinical examination	–	3	–	2
Excessive bleeding postdialysis	–	–	–	1

Qa, arteriovenous fistula blood flow; URR, urea reduction ratio.
[a]13 angiograms were performed in 10 patients.
[b]21 angiograms were performed in 20 patients.
[c]No angiograms were requested for a low arterial pressure.

control group (six *vs* four, respectively, $P = 0.75$, Fisher's exact test). The Qa prior to thrombosis was <500 ml/min in four patients (two each in both groups) with the overall mean Qa 619 ± 407 ml/min (in one patient a Qa result was not available). Of the patients who thrombosed their AVF, a stenosis was present in 8 out of the 10 patients. Overall, including both the patients with a positive angiogram or a thrombosed AVF, the locations of the stenoses were as follows: 11/22 (50%) had a stenosis at the anastomosis, 2/22 within 2 cm of the anastomosis, 8/22 >2 cm from the anastomosis and 1 had a subclavian stenosis. In the two patients without a stenosis at thrombectomy (both in the Qa surveillance group), one had a significant on-going AVF infection (which required surgery) while in the other patient no apparent cause for the thrombosis was found. In addition, one patient (in the Qa surveillance group) thrombosed his/her AVF within 24 h of a life-threatening contrast allergic reaction during the AVF angiography (which was positive). Three patients (two in the control group, one in the Qa surveillance group) thrombosed their AVF prior to the scheduled operative repair. In those undergoing an intervention, AVF Qa increased significantly following the intervention (mean Qa prior to intervention 719 ± 444 ml/min, Qa post-intervention 1245 ± 494 ml/min, $P < 0.001$ paired *t*-test).

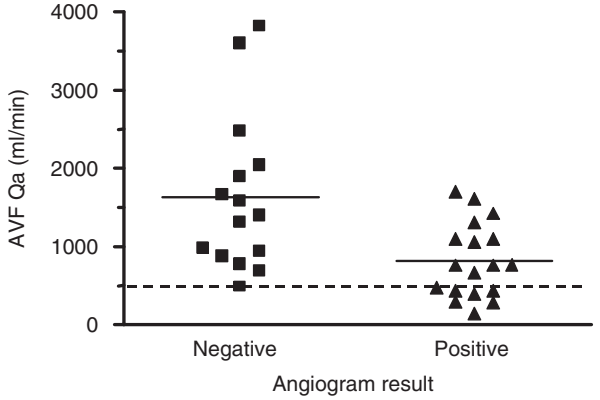

Fig. 3. AVF Qa in patients who had an angiogram performed divided into the angiogram result. The Qa value corresponds to that measured within 1 month prior to the angiogram. One subject in the positive group (treatment allocation control) did not have a Qa value recorded within 1 month of the angiogram and was not included. The solid line indicates the median Qa value and the dotted line, the Qa threshold of 500 ml/min. The Qa was significantly lower in the positive angiogram group ($P = 0.006$).

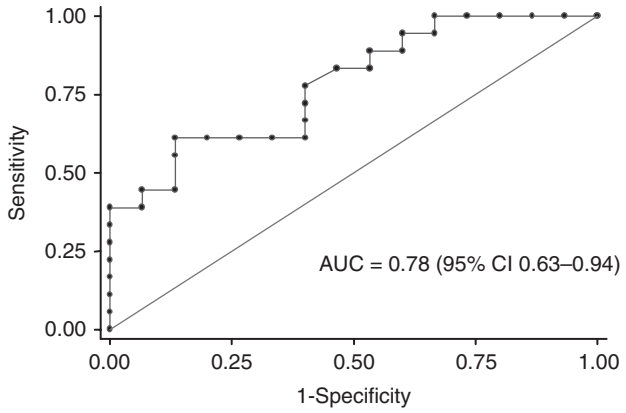

Fig. 4. ROC curve for the predictor of a significant stenosis using AVF Qa ($n = 33$).

Discussion

This study provides valuable insights into the effect of the introduction of Qa screening on a stable haemodialysis population and the interaction between the blood flow and accepted clinical indicators of AVF dysfunction. Taken overall, this study demonstrates that the addition of AVF Qa monitoring to clinical screening for AVF stenosis resulted in a non-significant doubling in the detection of angiographically significant AVF stenosis (HR 2.27) with a trend to a reduction in the time to detection of a significant stenosis in the treatment group (Figure 2). However, the data presented in Table 2 and Figure 3 illustrate that a reliance on the blood-flow threshold <500 ml/min in the treatment group would have missed an additional eight patients with a standard clinical criteria and a significant stenosis on the angiogram. This raises an important question regarding the relationship between the development of a stenosis, access blood flow, and indeed, the risk of thrombosis.

Assessing the data from Table 2 it is clear that the relationships between the access stenosis, access flow and clinical parameters of access dysfunction

Table 3. Type and reason for intervention performed during the trial

	Positive angiogram		Thrombosis	
	Control	Qa surveillance[a]	Control	Qa surveillance
Angioplasty	1	5	–	–
Surgery	5	7	4 [b,c]	6 [b,c]

[a]One patient in this group declined intervention.
[b]Includes two patients who had a positive angiogram prior to thrombosis.
[c]No subjects with a negative angiogram had a subsequent thrombosis.

are not always as we would expect. The criteria for the performance of an angiogram in the study were evidence of a functional, clinical or haemodynamic abnormality depending on the group allocation. From Figure 3 it is evident that 11 subjects with positive angiograms (i.e. a $\geq$50% reduction of the normal vessel luminal diameter on angiography [9]) did not have a 'haemodynamic abnormality' (Qa $<$500 ml/min) despite the presence of a functional or clinical abnormality. Raising the threshold for investigation would have resulted in an increased detection rate by the Qa surveillance, although likely at the expense of a higher false positive rate as suggested by the drop in sensitivity to 74% with a threshold of 800 ml/min. The resulting ROC analysis suggests that the overall performance characteristics of Qa screening alone was poor, with an AUC 0.78, below 0.8, which would be acceptable. While caution is required in the interpretation of this result as we did not perform angiography (the gold standard) on all patients and thus have not included all patients in the trial (those who were deemed negative by both the clinical and Qa criteria), this result is similar to two previous studies assessing Qa and AVF stenosis [4,13]. Tonelli *et al.* [14], in a prospective observational study, assessed 177 subjects with bi-monthly Qa measurements resulting in an ROC curve AUC for Qa to detect a stenosis in 6 months following the Qa measurement of 0.86 (95% CI not given). This study, like ours, performed angiography only in patients with either low Qa or abnormal clinical findings. However, it was assumed that those patients who did not have an angiography were negative and were included in the AUC calculation. When we applied this assumption (in the controls who reached the Qa threshold and did not have an angiogram, we have assumed that it was negative, which is the most conservative), the AUC improved a little to 0.81 (95% CI 0.71–0.92). Schwartz *et al.* [13] assessed the patients with Cimino–Brescia AVF, performing angiography on all the subjects whether the Qa result was positive or not. The AUC of the ROC curve was almost identical to ours (AUC 0.79, 95% CI 0.66–0.91). Another observational study assessed Qa measurements compared with angiography, obtaining a remarkably high AUC (0.95 $\pm$ standard error 0.02) [15]. However, it is not clear from this study as to how many of the AVF stenoses were detected as a result of the Qa screening, and at the baseline screening the stenotic AVF had a large range of flows with a large proportion exceeding the 500 ml/min threshold (similar to our results in Figure 3).

The relationship of Qa to the other clinical criteria was not always as we would expect. This is particularly apparent for an unexplained reduction in URR, where three patients were found to have a significant stenosis despite a Qa of $>$500 ml/min. For any true reduction in clearances due to a vascular access abnormality, recirculation is required for which the access flow must be less than the prescribed dialysis blood flow [16]. Thus, the reduction in URR in these patients was not due to low access flow but due to other causes such as errors in the collection of the pre- and post-urea samples, low prescribed-dialysis blood flow or the presence of a large number of collaterals in the AVF. Likewise, the three significant stenoses detected by clinical examination or excessive bleeding post-dialysis also had a Qa of $>$500 ml/min. A recent study has assessed the variability of Qa measurements between dialysis sessions [17]. Significant variability in the Qa measurements according to needle orientation was found in radiocephalic but not in brachiocephalic AVF. While this study did not show that Qa measurements were less reliable in detecting stenosis in radiocephalic AVF, it may be that this variability could be important, especially given the large number of radiocephalic AVF in this study.

Finally, dynamic venous pressure, while also easy and inexpensive to perform, was particularly poor as a surveillance method. Using the data from both groups, only 3 out of the 15 angiograms performed for high venous pressure were positive. Thus, a large number of unnecessary angiograms were performed as a result of screening on the basis of dynamic venous pressure. At present the screening using dynamic venous pressure is classed as acceptable in the current National Kidney Foundation Dialysis Outcomes Quality Initiatives (NKF-DOQI) guidelines but with the caveat that pressures will not be as accurate as direct-flow measurements [2]. To our knowledge, dynamic venous pressure has not been formally assessed in AVF. The results of this study confirm that dynamic venous pressure is poor as a screening test for AVF stenosis.

A major limitation of this study is that AVF thrombosis and/or AVF survival were not used as the primary end point for the study. The lower thrombosis and revision rate of AVF required a sample size that was beyond the size of our unit. Assuming an annual AVF thrombosis or revision rate of 12 to 15% per year, at least 300 subjects in each group would be needed to detect a reduction of 30% (relative risk (RR) 0.70, 90% power) in AVF thrombosis or revision rates as a result of blood-flow screening. Clearly, a study of this size would need to be performed in multiple centres with well-coordinated vascular access programmes. We believe that the detection of a significant stenosis is an important surrogate, and most clinicians would regard it as an important end point in its own right. In addition, the recent randomized study of Tessitore *et al.* [5] demonstrated the benefit of Qa surveillance with the patency in the blood-flow surveillance group being significantly longer compared with the clinical criteria group. This result, however, will need a confirmation in larger studies especially given that the results of two studies of Qa surveillance in AVG were negative [18,19]. Interestingly, in both these studies the Qa surveillance was effective in increasing the detection rate of significant stenosis (as in our study) in AVG but the subsequent increased intervention rate with angioplasty did not reduce the AVG thrombosis or survival. In addition, two recent randomized trials assessing the Doppler ultrasound screening

for AVG stenosis were mixed, with one demonstrating a benefit of surveillance on AVG patency [20] while the other did not [21].

A second criticism of our study is that we obtained a non-significant result due to the fact that we were not able to recruit the required 150 subjects as initially planned, and hence were under-powered. This partly relates to the exclusion of subjects with a flow of <500 ml/min at the baseline screening. In retrospect, the inclusion of those subjects would have increased the power, although it is unlikely that this would have been enough to demonstrate a significant result. In addition, we based our Qa criteria on a combination of the current NKF-DOQI guidelines and the only study performed in AVF at the time of the study, designed by Tonelli and colleagues [4]. Figure 3 demonstrates that seven of the 18 subjects with a positive angiogram had a Qa of >1000 ml/min 1 month prior to the test. Of those seven subjects, two would have met the 20% reduction in Qa regardless of the baseline flow in the months leading up to the angiogram. Both subjects were in the treatment group, and assuming that the stenosis found was responsible for the drop in Qa, it would have been detected 9 and 12 months earlier, respectively. In addition, selecting a higher threshold for angiogram would have increased the detection rate of the Qa surveillance but at the expense of a higher false-positive rate as discussed above.

Thirdly, the use of dynamic venous pressure as a clinical criteria for fistulogram could also be criticized. While it is recognized that dynamic venous pressure is not ideal as a surveillance technique in the native AVF, it is deemed acceptable by NFK-DOQI guidelines [2]. Although, our study was not designed specifically to assess dynamic venous pressures, the results here suggest that it is not an acceptable method of surveillance in AVF. In our unit, no formal surveillance programme is in place except as practiced in the control group. Thus, we felt that it was important to assess the addition of Qa measurements to our current practice, given that it is advocated as the surveillance method of choice.

In conclusion, this study demonstrates that the addition of Qa monitoring produced a modest effect on the detection of a significant AVF stenosis, although this did not reach statistical significance. The exclusion of the subjects with Qa <500 ml/min at the baseline and the limiting reductions of >20% in Qa to those AVFs with a flow below 1000 ml/min reduced the power of the study. However, this study demonstrates the feasibility of performing well-designed, randomized, controlled clinical trials in the dialysis population. Further, large, multi-centre randomized trials are feasible and will be necessary to confirm whether the increased detection and correction of AVF stenosis will lead to a reduction in AVF thrombosis and an increased AVF survival.

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Conflict of interest statement. None declared.

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