Effect of regional versus local anaesthesia on outcome after arteriovenous fistula creation: a randomised controlled trial

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Summary

Background Arteriovenous fistulae are the optimum form of vascular access in end-stage renal failure. However, they have a high early failure rate. Regional compared with local anaesthesia results in greater vasodilatation and increases short-term blood flow. This study investigated whether regional compared with local anaesthesia improved medium-term arteriovenous fistula patency.

Methods This observer-blinded, randomised controlled trial was done at three university hospitals in Glasgow, UK. Adults undergoing primary radiocephalic or brachiocephalic arteriovenous fistula creation were randomly assigned (1:1; in blocks of eight) using a computer-generated allocation system to receive either local anaesthesia (0·5% L-bupivacaine and 1% lidocaine injected subcutaneously) or regional (brachial plexus block [BPB]) anaesthesia (0·5% L-bupivacaine and 1·5% lidocaine with epinephrine). Patients were excluded if they were coagulopathic, had no suitable vessels, or had a previous failed ipsilateral fistula. The primary endpoint was arteriovenous fistula patency at 3 months. We analysed the data on an intention-to-treat basis. This study was registered with ClinicalTrials.gov (NCT01706354) and is complete.

Findings Between Feb 6, 2013, and Dec 4, 2015, 163 patients were assessed for eligibility and 126 patients were randomly assigned to local anaesthesia (n=63) or BPB (n=63). All patients completed follow-up on an intention-to-treat basis. Primary patency at 3 months was higher in the BPB group than the local anaesthesia group (53 [84%] of 63 patients *vs* 39 [62%] of 63; odds ratio [OR] 3·3 [95% CI 1·4–7·6], p=0·005) and was greater in radiocephalic fistulae (20 [77%] of 26 patients *vs* 12 [48%] of 25; OR 3·6 [1·4–3·6], p=0·03). There were no significant adverse events related to the procedure.

Interpretation Compared with local anaesthesia, BPB significantly improved 3 month primary patency rates for arteriovenous fistulae.

Funding Regional Anaesthesia UK, Darlinda's Charity for Renal Research.

Lancet 2016; 388: 1067–74

Published Online August 1, 2016 http://dx.doi.org/10.1016/S0140-6736(16)30948-5

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Introduction

Arteriovenous fistulae are the haemodialysis access modality of choice for patients with end-stage renal disease.[1,2] They are associated with a six-times reduction in the risk of systemic sepsis[3] and have lower all-cause and cardiovascular mortality than tunnelled central venous catheters.[4]

However, about a third of arteriovenous fistulae fail at an early stage.[5–10] Early failure of radiocephalic fistulae made from the small, distal vessels at the wrist is particularly common.[7,8] The likelihood of failure is affected by the preoperative arterial and venous diameters, arterial inflow, and early postoperative blood flow through the arteriovenous fistulae.[11,12] Although some anaesthetic techniques can directly affect venous diameter and intraoperative and postoperative blood flow,[13] no conclusive evidence exists that any particular anaesthetic technique can significantly affect either early patency or long-term arteriovenous fistula outcome.

General anaesthesia, regional anaesthesia, and local anaesthetic infiltration are all acceptable anaesthetic techniques for arteriovenous fistula creation. Although general anaesthesia increases intraoperative vasodilatation, it is associated with increased cardiorespiratory complications in patients with end-stage renal disease.[14,15] Regional anaesthesia, such as a brachial plexus block (BPB), involves targeted injection of a local anaesthetic to specifically block the motor and sensory nerves that supply the operative site, avoiding the need for general anaesthesia. Both local anaesthetic infiltration and regional anaesthesia avoid the risks associated with general anaesthesia, but only regional anaesthesia produces an associated sympathetic nerve block. This sympathetic blockade increases venous diameter and arterial flow both intraoperatively and in the early post-operative period.[16,17] Maintenance of adequate blood flow through the fistula in the perioperative period can prevent thrombosis and early fistula failure, and can assist in maturation.[17] Additionally, arterial and venous spasm has been shown to be more common with local anaesthetic infiltration than with regional (or general) anaesthesia.[18]

Several observational cohort studies have previously shown that, compared with local anaesthetic infiltration, a BPB results in better immediate arteriovenous fistulae patency rates[19–21] and an improved surgical ability to identify the optimum site for intervention.[22] However, so far, no evidence suggests that any short-term benefits of regional anaesthesia can affect long-term

Research in context

Evidence before this study

Arteriovenous fistulae are the vascular access modality of choice for patients with end-stage renal disease requiring haemodialysis. Unfortunately, however, their universal use is limited by high early failure rates. Different anaesthetic techniques can affect both preoperative arterial and venous diameters and early blood flow within the fistula, factors which in turn are known to affect arteriovenous fistula maturation. Although a regional anaesthetic brachial plexus block (BPB) results in sympathetic blockade, which increases both peri-operative blood vessel diameters and brachial artery blood flow, this has not yet been shown to improve medium-term or long-term arteriovenous fistula patency.

We searched PubMed, Embase, and MEDLINE for manuscripts published in English between database inception and April 30, 2016, using the search terms "arteriovenous fistula" AND "anaesthesia" OR "regional anaesthesia" OR "brachial plexus block" OR "local anaesthesia". Several small, single-centre, observational, cohort studies have previously shown that, compared with local anaesthetic infiltration, a BPB results in better immediate arteriovenous fistula patency rates and improved surgical ability to identify the optimum site for intervention. So far, to our knowledge, no evidence has been published that any short-term benefits of regional anaesthesia (ie, immediate patency) can affect medium-term (3 months) or long-term (>12 months) arteriovenous fistula patency. Only two small randomised trials have been published comparing BPB and local anaesthesia. One detected increased arteriovenous fistula flow rates for up to 8 weeks in patients who received a BPB compared with local anaesthesia, but did not find a difference in primary patency. The other trial reported increased vessel diameters in the BPB group.

Added value of this study

This is the first randomised controlled trial comparing arteriovenous fistula patency in patients having creation under either local anaesthesia or BPB. We have shown that primary patency at 3 months is higher in arteriovenous fistulae created using BPB than with local anaesthesia (84·1% *vs* 61·9%; OR 3·3; p=0·005). This difference was more marked for radiocephalic fistulae (76·9% *vs* 48·0%; OR 3·6; p=0·03). BPB, but not local anaesthesia, resulted in perioperative vascular dilatation and increased brachial artery blood flow.

Implications of all the available evidence

Our findings support previously published data that BPB increases venous diameter and arterial blood flow both intra-operatively and postoperatively. Several previous observational studies have suggested that these changes in blood flow translate into improved early arteriovenous fistula patency with BPB. For the first time, our findings not only confirm these observations in a randomised controlled trial, but also show that the more relevant clinical outcome of primary patency is increased medium term after a BPB. We would advocate that BPB be used as the anaesthetic technique of choice for uncomplicated arteriovenous fistulae.

arteriovenous fistula patency. In a small, randomised trial,[23] a single-shot BPB significantly increased fistula blood flow for up to 8 weeks after surgery, but this effect did not translate into any difference in fistula patency, the ultimate determinant of arteriovenous fistula success.

We hypothesised that immediate and medium-term arteriovenous fistula patency could be improved by use of regional anaesthesia (BPB) rather than local anaesthesia. We aimed to conduct a randomised controlled trial to answer the question: does regional anaesthesia, compared with local anaesthetic infiltration, improve medium-term (ie, 3 months after surgery) arteriovenous fistula patency?

Methods

Study design and participants

This observer-blinded, randomised controlled trial recruited patients from three university teaching hospitals in Glasgow, UK (Stobhill Ambulatory Care Hospital, Western Infirmary, and Queen Elizabeth University Hospital). All adult patients (aged 18 years or older) who were having primary radiocephalic or brachiocephalic fistulae created were eligible to participate. A member of the research team approached patients preoperatively and assessed suitability for inclusion in the trial. We excluded patients who were unable or unwilling to provide informed, written consent, who had undergone previous ipsilateral attempts at arteriovenous fistula creation, and whose radial or brachial artery was less than 1·8 mm or whose cephalic vein was less than 2 mm at the wrist or less than 3 mm at the elbow on preoperative ultrasound (without tourniquet). We used preoperative ultrasound to ensure suitable vessels for arteriovenous fistulae creation. We also excluded patients with allergy to local anaesthesia, coagulopathy, infection at the anaesthetic or surgical site, significant peripheral neuropathy or a neurological disorder affecting the upper limb, or known ipsilateral central vein stenosis (even if treated).

Ethical approval for this trial was granted by the West of Scotland Research Ethics Committee 5 (12/WS/0199). The research was undertaken in accordance with the Declaration of Helsinki and adhered to the standards of International Conference on Harmonisation Good Clinical Practice. All participants provided written, informed consent. The protocol has previously been published.[24]

Randomisation and masking

We randomly assigned patients 1:1 to either BPB or local anaesthetic technique. We generated the randomisation sequence (in blocks of eight) using a web-based computer random-sequence generator. A colleague, independent of the research team, produced sequentially numbered, opaque, sealed envelopes allocating patients to trial groups. Patients who were suitable and willing to participate were assigned a study number and sealed envelope. The sealed envelope was opened by the anaesthetist immediately before the operation. Due to the nature of the intervention, it was not possible to blind the patient, surgeon, anaesthetist, or study team involved at the time of surgery. However, the vascular access nurse specialist who assessed the primary endpoint was independent and blinded to the randomisation.

Procedures

The surgical procedures were done by a total of nine experienced consultant vascular access surgeons (or senior trainees under consultant supervision). No formal operative technique was stipulated within the study protocol to permit individual surgeons to react to variations in anatomy that might be encountered intraoperatively. Nevertheless, surgeons largely followed a standard operating technique. All surgeons used operating loupes with ×8 magnification and microinstruments. A standard approach to access the vessels was used, with transverse skin incision at, or just below, the elbow crease for brachiocephalic fistulae, and with longitudinal skin incision at the wrist for radiocephalic fistulae. Surgeons dissected and skeletalised the cephalic vein (or the median cubital vein if suitable at the elbow) for a short length proximally. Visible branches were ligated and divided. The vein was then divided and spatulated, and flushed with heparinised saline. The surgeon then dissected the artery and controlled it with bulldog clamps. At the elbow, surgeons created a true brachiocephalic fistulae in every case rather than proximal radiocephalic fistulae. The decision of whether to use the median cubital, perforating branch, or the true outflow cephalic vein to make the fistula was left to the surgeon's discretion. Similarly the size of the arteriotomy was at the surgeon's discretion, based on risks and benefits for the individual patient (eg, vessel quality, risk of steal, etc). Generally, arteriotomies on the brachial artery were between 3 mm and 5 mm in length, whereas radial artery arteriotomies were slightly larger (7–10 mm). An end-to-side anastamosis of the vein to the artery was then performed using continuous 6·0 (elbow) or 7·0 (wrist) prolene. Most procedures were done as day-case surgery.

Two consultant anaesthetists skilled in BPB (or senior trainees under consultant supervision) did all of the BPBs in this study. All patients in the BPB group received an ultrasound guided BPB. Anaesthetists chose the supraclavicular approach, unless there was a contraindication, in which case they did an axillary block. A 1:1 mixture of 0·5% L-bupivacaine and 1·5% lidocaine with epinephrine (1 in 200 000) was injected up to a maximum volume of 40 mL.[25] The maximum dose limits were set at 2 mg/kg for bupivacaine and 7 mg/kg for lidocaine with epinephrine, recognising that these drug doses are additive. The time taken to do the block and any technical problems during block insertion (intravascular puncture, paraesthesia) were recorded. The anaesthetic team measured the sensory block of the musculocutaneous, median, radial, and ulnar nerves every 5 min by using a previously validated 3-point scale using a cold test: 0 is no block, 1 is analgesia (can feel touch but not cold), and 2 is anaesthesia (patient cannot feel touch). Motor block of musculocutaneous, median, radial, and ulnar nerves was graded as either 0 (no block), 1 (paresis), and 2 (paralysis).[26] The anaesthetic team continued making measurements until either the sensory block was adequate in the operative area distribution or a maximum of 20 min had elapsed, at which point the anaesthetist supplemented the block with targeted axillary or midhumeral supplementation, as appropriate, by use of ultrasound. If a BPB block failed despite supplementation, the anaesthetist used local anaesthetic infiltration. This was recorded as a failed block. If additional analgesia or conversion to general anaesthesia was needed, this was regarded as a failed block.

The operating surgeon gave patients in the local anaesthetic infiltration group infiltration of local anaesthetic into the surgical site under sterile conditions, using a combination of 0·5% L-bupivacaine and 1% lidocaine injected subcutaneously immediately before the commencement of surgery. The maximum dose limits were set at 2 mg/kg for bupivacaine and 3 mg/kg for lignocaine, again recognising that these drug doses are additive.

A member of the study team, experienced in ultrasound assessment of peripheral vessels, performed preoperative vein mapping and Doppler ultrasound assessment of the upper limb arterial tree on all patients before the administration of anaesthesia. The investigator recorded, in triplicate, measurements of the cephalic vein diameter 2 cm above the wrist and at the elbow, and of the basilic vein at the elbow. They also recorded in triplicate, radial and brachial artery diameters, and brachial artery blood flow. The investigator made similar assessment of the vasculature after administration of anaesthesia, immediately preoperatively, and at 3 month follow-up. At the 3 month follow-up visit, the investigator measured the diameter of the outflow cephalic vein at 5 cm, 10 cm, and 15 cm intervals above the anastomosis.

Outcomes

The primary endpoint was primary patency at 3 months. Secondary endpoints were immediate patency (at time of discharge from hospital), functional patency (assessed clinically and by ultrasound) at 3 months, and the change in brachial artery blood flow and diameter and cephalic vein diameter immediately after administration of anaesthesia and after 3 months. Additionally, we also assessed the need for additional administration of local anaesthesia, pain scores, and patient satisfaction scores. We recorded operative and anaesthetic complications.

A vascular access nurse specialist, blinded to the mode of anaesthesia, assessed primary patency at 3 months. Primary patency was defined clinically as the presence of a thrill or bruit in the absence of any additional intervention to re-establish function. The research team also assessed clinically the immediate postoperative patency (patency at time of discharge from hospital—ie, presence of thrill or bruit, or both). The research team assessed functional patency at 3 months, both clinically (used for dialysis or in predialysis patients deemed suitable for cannulation by the vascular access nurse specialist) and by ultrasound (>6 mm diameter, <6 mm from skin surface, flow rate >600 mL/min).[25,26] A member of the research team obtained all ultrasound measurements in triplicate before anaesthesia, immediately after anaesthesia, and at 3 months' follow-up, as described previously. The investigator recorded pain scores with a verbal numerical rating scale (0 [no pain] to 10 [worst pain ever]) immediately after and 1 h after the procedure. The investigator recorded patient satisfaction scores before discharge with a verbal numerical rating scale (0 [very dissatisfied] to 10 [highly satisfied]).

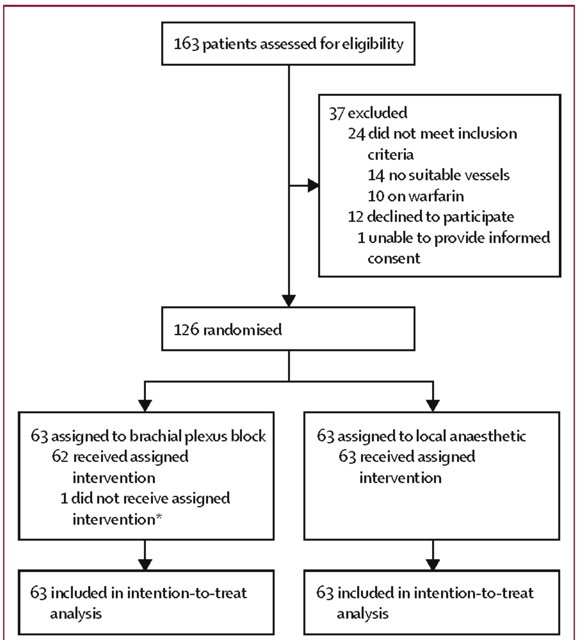

Figure: **Trial profile**
*Protocol breach: patient was randomly assigned to brachial plexus block before vessel assessment and was then found to have no suitable vessels.

Statistical analysis

We calculated a priori that a total of 126 patients (63 in each group) would be needed to detect an improvement in primary patency at 3 months from 65% to 85% in patients having arteriovenous fistulae creation under BPB with 80% power and significance ($p<0·05$), allowing for 10% loss to follow-up or mortality. The 65% primary patency rate at 3 months is representative of maturation rates for arteriovenous fistulae described elsewhere in the scientific literature.[6,10] We anticipated that an increase in primary patency at 3 months from 65% to 85% was a conservative estimate in view of that local observational data had previously shown arteriovenous fistula patency of 93% in patients having BPB compared with 52% in patients having arteriovenous fistula creation under local anaesthesia.[20]

We analysed results using SPSS Statistics v.22 (IBM Analytics, Armonk, NY, USA). We tested data for normality. Assuming normal distribution, we used a student's t test (2-tailed) to compare continuous data and a χ^2 or Fischer's exact test to compare categorical data. We used Mann-Whitney U tests for non-normally distributed data. We considered $p<0·05$ significant. Missing data were limited and assumed to be missing at random. If a data point was missing, this case was removed from analysis of the specific variable of interest. We analysed the data on an intention-to-treat basis.

This study was registered with ClinicalTrials.gov, number NCT01706354.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data validation, data interpretation, or writing of the report. All authors had full access to all the data in the study and the corresponding author had final responsibility for the decision to submit for publication.

Results

Between Feb 6, 2013, and Dec 4, 2015, 163 patients were considered for participation (figure).[27] 37 were excluded and 126 patients were randomly assigned to a group. 125 patients completed the study protocol (63 local anaesthesia *vs* 62 BPB). One patient had a protocol breach having been randomly assigned before vein mapping ultrasound, at which point no suitable vessel was found for radiocephalic or brachiocephalic fistula creation. This patient was followed up on an intention-to-treat basis. All 126 patients completed the study and follow-up period.

The groups were similar in terms of age, sex, comorbidities, medications, and renal replacement modality (table 1). We found no significant difference between the groups with regard to operating surgeon or site of arteriovenous fistulae. We found no significant differences in any of these baseline variables between BPB and local anaesthesia groups.

51 (40%) of 126 patients randomly assigned had radiocephalic fistula creation, with the remainder having brachiocephalic fistula creation (n=75 [60%]). Mean brachial artery blood flow was 30·7 mL/min (SD 13·1; table 2). Preoperative brachial artery blood flow in patients who had arteriovenous fistula creation under BPB was similar to that in the local anaesthesia group (table 2). In patients undergoing radiocephalic fistula creation, mean preoperative radial artery diameter was 2·10 mm (SD 0·29) and cephalic vein diameter (wrist) was 2·28 mm (0·49). In brachiocephalic fistulae, mean brachial artery diameter was 3·05 mm (0·57) and cephalic vein diameter (elbow) was 3·23 mm (0·75; table 2). There was no significant intraobserver variability (appendix).

Primary patency at 3 months was higher in patients having their arteriovenous fistulae created under BPB than under local anaesthesia (53 [84%] of 63 patients *vs* 39 [62%] of 63 patients; odds ratio [OR] 3·3 [95% CI 1·4–7·6], p=0·005; table 3). This difference was seen for both radiocephalic and brachiocephalic fistulae, but the effect size seemed to be greater in radiocephalic fistulae (table 3). Immediate patency was also better in patients having BPB than it was in patients given local anaesthetic (table 3). We found no significant difference in functional patency between groups at 3 months overall; however, a difference in favour of BPB was seen in radiocephalic fistulae (table 3) We found 100% concordance for functional patency at 3 months when assessed clinically and by ultrasound.

Patients in the BPB group had a significant increase in the diameters of the cephalic vein at elbow, basilic vein at elbow, and both radial and brachial arteries after administration of anaesthesia (table 4). A similar change was not seen in the local anaesthesia patient group (table 4). An increase in brachial artery blood flow was also seen in the BPB group that was not seen in the local anaesthesia group when comparing immediately before and immediately after administration of anaesthesia (table 4). At 3 months' follow-up, we found no significant difference between the groups in the diameter of the outflow vein at 5 cm, 10 cm, or 15 cm above the anastomosis in mature fistulae. There were more patients in the BPB group with brachial artery flows higher than 250 mL/min at 3 months' follow-up than in the local anaesthetic group (43 [68%] of 63 patients *vs* 27 [43%] of 63 patients; OR 2·9 [95% CI 1·5–5·9], p=0·01).

Patients in the BPB group had a mean volume of 23·7 mL (SD 4·0) of 0·5% L-bupivacaine plus 1·5% lidocaine with adrenaline (1 in 200 000), whereas a mean volume of 14·7 mL (5·0) of 0·5% L-bupivacaine plus 1% lignocaine was infiltrated in the local anaesthesia group. Mean time taken to administer anaesthesia was significantly longer in the BPB group (17·0 min [SD 5·7] *vs* 3·4 min [2·5]; p<0·0001). No patient developed any anaesthetic complications. Both groups of patients achieved excellent anaesthesia, with all patients reporting pain scores of 0, both during and 1 h after completion of surgery. Significantly fewer patients in the BPB group needed additional local anaesthetic supplementation than in the local anaesthesia group (two [3%] of 63 patients *vs* nine [14%] of 63 patients; p<0·001). For the two patients in the BPB who required additional anaesthesia, one responded to targeted supplementation with an axillary block and one had a failed block necessitating local anaesthetic field infiltration. No patient required conversion to general anaesthesia.

	Overall patient population (n=126)	Brachial plexus block (n=63)	Local anaesthetic (n=63)
Age (years)	60·8 (14·8)	59·5 (15·3)	62·1 (14·3)
Sex			
Male	79 (63%)	40 (63%)	39 (62%)
Female	47 (37%)	23 (37%)	24 (38%)
Primary renal disease			
Diabetes	21 (17%)	10 (16%)	11 (17%)
Multisystem	16 (13%)	9 (14%)	7 (11%)
Interstitial	41 (33%)	16 (25%)	25 (40%)
Glomerulonephritis	24 (19%)	15 (24%)	9 (14%)
Unknown	24 (19%)	13 (21%)	11 (17%)
Comorbidities			
Diabetes	34 (27%)	17 (27%)	17 (27%)
Ischaemic heart disease	48 (38%)	22 (35%)	26 (41%)
Cerebrovascular accident	9 (7%)	3 (5%)	6 (10%)
Hypertension	93 (74%)	40 (63%)	53 (84%)
Obesity (BMI >30 kg/m^2)	41 (33%)	22 (35%)	19 (30%)
Drugs			
Antihypertensives*	2 (1–4)	2 (1–4)	2 (1–4)
Aspirin	85 (67%)	42 (67%)	43 (68%)
Clopidogrel	29 (23%)	13 (21%)	16 (25%)
Statin	73 (58%)	38 (60%)	35 (56%)
RRT modality at time of randomisation			
Haemodialysis	63 (50%)	30 (48%)	33 (52%)
Pre-dialysis	63 (50%)	33 (52%)	30 (48%)
Site of arteriovenous fistulae			
Radiocephalic	51 (40%)	26 (41%)	25 (40%)
Brachiocephalic	75 (60%)	37 (59%)	38 (60%)
Surgeon†			
1	35 (28%)	16 (25%)	19 (30%)
2	23 (18%)	13 (21%)	10 (16%)
3	16 (13%)	8 (13%)	8 (13%)
4	16 (13%)	8 (13%)	8 (13%)
5	14 (11%)	8 (13%)	6 (10%)
Others	22 (17%)	10 (16%)	12 (19%)
Anaesthetist‡			
1	NA	36 (57%)	NA
2	NA	27 (43%)	NA

Data are n (%), mean (SD), or median (IQR), unless stated otherwise. BMI=body-mass index. RRT=renal replacement therapy. NA=not applicable. *Mean number of antihypertensive drugs per patient (range). †Each number represents an individual surgeon. ‡Local anaesthetic was administered by the surgeon.

Table 1: **Baseline characteristics**

See Online for appendix

	Overall patient population	Brachial plexus block	Local anaesthetic
Brachial artery blood flow (mL/min; n=124)	30·7 (13·1)	31·3 (14·2)	30·1 (15·1)
Radiocephalic fistulae (n=51)			
Radial artery diameter (mm)	2·10 (0·29)	2·11 (0·31)	2·08 (0·36)
Cephalic vein (wrist) diameter (mm)	2·28 (0·49)	2·21 (0·20)	2·32 (0·55)
Brachiocephalic fistulae (n=75)			
Brachial artery diameter (mm)	3·05 (0·57)	3·09 (0·52)	3·02 (0·61)
Cephalic vein (elbow) diameter (mm)	3·23 (0·75)	3·30 (0·89)	3·16 (0·76)

Data are mean (SD). All measurements have been obtained in triplicate.

Table 2: **Preoperative baseline vessel diameters and brachial artery blood flow**

	Brachial plexus block (n=63)	Local anaesthetic (n=63)	Odds ratio (95% CI)	p value
All arteriovenous fistulae				
Primary patency at 3 months	53 (84%)	39 (62%)	3·3 (1·4–7·6)	0·005
Immediate patency*	58 (92%)	46 (73%)	4·3 (1·5–12·5)	0·005
Functional patency at 3 months	26 (41%)	18 (29%)	1·8 (0·8–3·7)	0·15
Radiocephalic fistulae				
Primary patency at 3 months	20/26 (77%)	12/25 (48%)	3·6 (1·1–12·0)	0·03
Immediate patency*	23/26 (88%)	15/25 (60%)	5·1 (1·2–21·7)	0·02
Functional patency at 3 months	19/26 (73%)	10/25 (40%)	4·1 (1·2–13·2)	0·02
Brachiocephalic fistulae				
Primary patency at 3 months	33/37 (89%)	27/38 (71%)	3·4 (1·0–11·8)	0·05
Immediate patency*	35/37(95%)	31/38 (82%)	3·9 (0·8–20·5)	0·08
Functional patency at 3 months	7/37 (19%)	8/38 (21%)	0·9 (0·3–2·7)	0·95

Data are n (%) or n/N (%). *Immediate patency is patency at time of discharge from hospital.

Table 3: **Patency rates of arteriovenous fistulae**

Four patients had a change in operative plan after administration of BPB. Initial decision to create a brachiocephalic fistula was modified to radiocephalic fistula as the diameter of the cephalic vein at the wrist increased after BPB. We found no difference in the duration of surgery between BPB and local anaesthesia groups (62·1 min [SD 11·8] *vs* 62·8 min [12·2]; p=0·77). One patient in the BPB group developed a superficial wound infection and three patients in the local anaesthesia group developed clinically significant steal necessitating operative intervention. No patient in the BPB group developed steal. Patient satisfaction scores were higher in the BPB group than the local anaesthesia group (9·8 [SD 0·6] *vs* 9·4 [1·0]; p=0·02).

Discussion

Our results show superiority of BPB for the creation of arteriovenous fistulae, with improved medium-term (3 month) primary patency rates compared with local anaesthesia. The effect size of this difference seemed to be more marked in radiocephalic fistulae and was associated with immediate and significant increases in both vessel diameter and brachial artery blood flow after administration of BPB. Patient satisfaction was high in both groups, but superior in the BPB group. To our knowledge, this is the first randomised controlled trial to show benefit of a BPB on medium-term arteriovenous fistula patency and one of the few studies in which anaesthetic technique affects surgical outcome.

Our findings are consistent with other recent studies, which show an improvement in arterial blood flow and vasodilatation with regional anaesthesia.[23,28–30] The effect size of this difference seemed to be greater in distal radiocephalic fistulae with small vessels. The biological plausibility of these observations is supported by the observed changes in the haemodynamics of the vascular tree. Dilatation of both artery and vein makes the anastomosis technically less challenging (particularly in very small vessels), whereas improved arterial inflow,[16,23] increased venous compliance,[28] and reduced pulsatility index[31] promote blood flow through the arteriovenous fistulae immediately after creation and reduce early thrombosis within the first hours to days. Once laminar, so-called fistula-type blood flow has been established, the rate of thrombosis seems similar between the two groups. Like other authors who found improved blood flow at 8 weeks with BPB compared with local anaesthesia,[23] we observed that more patients in our BPB cohort had good blood flow via the arteriovenous fistulae at 3 months (brachial artery blood flow >250 mL/min). This finding could merely be because there were more patent arteriovenous fistulae in the BPB group, rather than because of any lasting effect of the BPB itself.

The benefits of BPB compared with local anaesthesia in the promotion arteriovenous fistula maturation seemed to occur early, with the difference in patency between the two groups manifesting immediately (at time of hospital discharge) but persisting until at least 3 months. Similarly the benefits were more marked in achieving a patent fistula rather than in obtaining functional patency with a fistula capable of sustaining dialysis. This discrepancy was most marked in the brachiocephalic fistulae, which achieved 80% primary patency at 3 months but only 20% functional patency. These functional patency rates fall below those seen in other retrospective series.[32] The explanation for this is likely to be multifactorial. We do not perform assisted-maturation at our institution, and none of the arteriovenous fistulae in this study had received any procedure to promote functional maturation by 3 months' follow-up. We anticipate that with future interventions, subsequent functional patency rates will improve. Secondly, it is well recognised that advancing age, coronary artery disease, and peripheral vascular disease are associated with inadequate maturation.[33,34] The patients in this study had significant comorbidities. Finally more than a third of patients had a body-mass index higher than 30 kg/m², for whom superficialisation is likely to be needed to achieve functional patency.

Unlike other studies that have used vessel diameter and arterial blood flow as a surrogate for the success of regional anaesthesia and arteriovenous fistulae, our study assessed primary patency at 3 months. We believe that the choice of a clinically relevant endpoint is one of the major strengths of our study. The endpoint was assessed both clinically and (in the case of functional patency) by ultrasound with 100% concordance, adding validity to the results. An early endpoint was chosen to minimise the multiple confounding factors (eg, cannulation technique, outflow stenosis, etc) that are inherent to the assessment of vascular access. Primary functional patency assessed by ability to sustain dialysis would arguably have been a superior endpoint. However, because of the large number of patients who were predialysis at the time of arteriovenous fistula creation, this was not feasible.

A further benefit of regional anaesthesia is that, as shown elsewhere,[29] the operative plan in our study was modified in several cases due to the vasodilatation from BPB, and more distal arteriovenous fistulae were created. In one study[31] of patients deemed not to have any suitable vessels for autologous access, a third of patients listed for arteriovenous graft insertion successfully underwent arteriovenous fistula creation after BPB.

The administration of the BPB is operator-dependent and it is well recognised that the failure rate of BPB is higher if the operator is inexperienced.[35] In this study only two consultant anaesthetists, both experienced in ultrasound guided BPB, did the procedure to minimise inter-operator variability. No complications and only one block failure occurred, which was a combination of poor ultrasound views and patient discomfort during the nerve block leading to a decision to change to a local anaesthetic, which would be quicker for the patient. Complications of supraclavicular blocks such as pneumothorax can occur, and adequate training is necessary to do these blocks.[36] Nevertheless with the advent of ultrasound guidance this block is now commonly used for upper limb surgery.[37] It is possible that other approaches to the BPB confer the same benefit because all approaches result in sympathetic blockade, but this theory cannot be inferred with certainty from our data.

BPB took significantly longer than local anaesthesia to do (17·0 min *vs* 3·4 min; $p<0·0001$) and necessitated the presence of a skilled anaesthetist, which is not the case for local anaesthesia. Performing regional anaesthesia and surgery in parallel rather than sequentially can help improve efficiency and minimise operative delays between patients.[38] Although an analysis of cost was outside of the scope of this study, any additional costs associated with employing an anaesthetist to do the BPB could potentially be offset against the cost savings of improved arteriovenous fistula maturation, reduction in the need for second and subsequent surgeries, and the complications of tunnelled central venous catheter use.

	Brachial plexus block	Local anaesthetic	p value
Change in cephalic vein (wrist) diameter (mm; n=87)	0·1 (–0·03 to 0·5)	–0·5 (–1·7 to 3·2)	0·37
Change in cephalic vein (elbow) diameter (mm; n=124)	0·5 (0·2 to 1·2)	0·1 (–0·1 to 0·2)	0·006
Change in basilic vein (elbow) diameter (mm; n=121)	0·5 (0·2 to 1·4)	0·1 (–0·4 to 1·3)	0·09
Change in radial artery diameter (mm; n=124)	0·1 (0 to 0·4)	0 (–2·4 to 4·7)	0·01
Change in brachial artery diameter (mm; n=124)	1·6 (0·5 to 2·6)	0·2 (–0·4 to 0·3)	<0·0001
Change in brachial artery blood flow (mL/min; n=120)	45 (13 to 75)	1 (–10 to 9)	0·0006

Data are median (IQR), with change reflecting post-anaesthetic minus pre-anaesthetic.

Table 4: **Change in vessel diameters before and immediately after administration of anaesthesia**

The high early thrombosis rate of arteriovenous fistulae reported in the Dialysis Access Consortium randomised controlled trial[10] published in 2008, coupled with an increasingly elderly, co-morbid population, have resulted in a growing body of opinion advocating alternatives to autologous vascular access in the past 10 years.[39,40] Furthermore, political pressure (such as the tariff for dialysis depending on which access modality the patient used imposed by the Government in England and Wales) focuses on optimising prevalent, rather than incident, vascular access.[41] Many of these prevalent patients have complex vascular access needs such as multiple failed arteriovenous fistulae, prolonged tunnelled central venous catheter use, and central venous stenosis.[42] To obtain vascular access in such patients is time consuming, costly, associated with significant morbidity, and generally has poor outcomes.[43] Conversely, this study has focused on simple radiocephalic and brachiocephalic fistula creation, mainly in incident patients with no previous vascular access. We have shown that good outcomes from autologous vascular access can be achieved in this patient group and that a simple modification to the anaesthetic technique (BPB) can improve immediate and long-term patency.

This randomised controlled trial compared BPB with local anaesthesia for arteriovenous fistula creation and showed superiority of BPB, with significant improvement in the primary outcome of patency at 3 months. On the basis of these findings, consideration should be given to using BPB for all arteriovenous fistula creation.

Contributors

EA was principally responsible for recruitment. EA collated and analysed the data and wrote the final manuscript. AJ assisted with recruitment and data collection. RK and AM designed the study and wrote the protocol. JK was involvied in reviewing the design of the study and revision of the final manuscript. MC conceived the study and was the principal surgeon. AM and MS were anaesthetists for the trial. AM had principal responsibility for the study.

Declaration of interests

We declare no competing interests.

Acknowledgments
We thank the patients, surgeons, and nursing staff at the Western Infirmary, Stobhill Hospital Glasgow and Queen Elizabeth University Hospital, Glasgow. We are also grateful to the Trial Steering Committee and statistician. EA's salary was funded by Darlinda's Charity for Renal Research. AM received funding from Regional Anaesthesia UK.

References

1 Vascular Access Working Group. Clinical practice guidelines for vascular access. *Am J Kidney Dis* 2006; **48** (suppl 1)**:** S248–73.
2 National Kidney Care Audit. National kidney care audit vascular access report. Leeds: NHS Information Centre, 2011.
3 Thomson PC, Stirling CM, Geddes CC, Morris ST, Mactier RA. Vascular access in haemodialysis patients: a modifiable risk factor for bacteraemia and death. *QJM* 2007; **100:** 415–22.
4 Bray BD, Boyd J, Daly C, et al. Vascular access type and risk of mortality in a national prospective cohort of haemodialysis patients. *QJM* 2012; **105:** 1097–103.
5 Riella MC, Roy-Chaudhury P. Vascular access in haemodialysis: strengthening the Achilles' heel. *Nat Rev Nephrol* 2013; **9:** 348–57.
6 Rodriguez JA, Armadans L, Ferrer E, et al. The function of permanent vascular access. *Nephrol Dial Transplant* 2000; **15:** 402–08.
7 Golledge J, Smith CJ, Emery J, Farrington K, Thompson HH. Outcome of primary radiocephalic fistula for haemodialysis. *Br J Surg* 1999; **86:** 211–16.
8 Fernstrom A, Hylander B, Olofsson P, Swedenborg J. Long and short term patency of radiocephalic arteriovenous fistulas. *Acta Chir Scand* 1988; **154:** 257–59.
9 Nguyen TH, Bui TD, Gordon IL, Wilson SE. Functional patency of autogenous AV fistulas for hemodialysis. *J Vasc Access* 2007; **8:** 275–80.
10 Dember LM, Beck GJ, Allon M, et al. Effect of clopidogrel on early failure of arteriovenous fistulas for haemodialysis: a randomised controlled trial. *JAMA* 2008; **299:** 2164–71.
11 Lin PH, Bush RL, Nguyen L, Guerrero MA, Chen C, Lumsden AB. Anastomotic strategies to improve hemodialysis access patency—a review. *Vasc Endovasc Surg* 2005; **39:** 135–42.
12 Hofstra L, Bergmans DC, Leunissen KM, et al. Anastomotic intimal hyperplasia in prosthetic arteriovenous fistulas for hemodialysis is associated with initial high flow velocity and not with mismatch in elastic properties. *J Am Soc Nephrol* 1995; **6:** 1625–33.
13 Wong V, Ward R, Taylor J, Selvakumar S, How TV, Bakran A. Factors associated with early failure of arteriovenous fistulae for haemodialysis access. *Eur J Vasc Endovasc Surg* 1996; **12:** 207–13.
14 Howell SJ, Sear YM, Yeates D, Goldacre M, Sear JW, Foëx P. Risk factors for cardiovascular death after elective surgery under general anaesthesia. *Br J Anaesth* 1998; **80:** 14–19.
15 Lee TH, Marcantonio ER, Mangione CM, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999; **100:** 1043–49.
16 Shemesh D, Olsha O, Orkin D, et al. Sympathectomy-like effects of brachial plexus block in arteriovenous access surgery. *Ultrasound Med Biol* 2006; **32:** 817–22.
17 Mouquet C, Bitker MO, Bailliart O, et al. Anesthesia for creation of a forearm fistula in patients with endstage renal failure. *Anesthesiology* 1989; **70:** 909–14.
18 Konner K, Nonnast-Daniel B, Ritz E. The arteriovenous fistula. *J Am Soc Nephrol* 2003; **14:** 1669–80.
19 Shemesh D, Zigelman C, Olsha O, Alberton J, Shapira J, Abramowitz H. Primary forearm arteriovenous fistula for hemodialysis access–an integrated approach to improve outcomes. *Cardiovasc Surg* 2003; **11:** 35–41.
20 Zaliunate R, Kearns R, Clancy M, Macfarlane AJ. Does regional compared to local anaesthesia influence outcome after arteriovenous fistula creation? European Society of Regional Anaesthesia; Dresden, Germany; Sept 7–10, 2011. 584.
21 Glover G, Bowie R, Stoves J, Wilkinson D, Mercer K. Brachial plexus block for formation of arteriovenous fistula is associated with improved patency. *Anaesthesia* 2007; **62:** 424–27.
22 Laskowski IA, Muhs B, Rockman CR, et al. Regional nerve block allows for optimization of planning in the creation of arteriovenous access for hemodialysis by improving superficial venous dilatation. *Ann Vasc Surg* 2007; **21:** 730–33.
23 Sahin L, Gul R, Mizrak A, et al. Ultrasound-guided infraclavicular brachial plexus block enhances postoperative blood flow in arteriovenous fistulas. *J Vasc Surg* 2011; **54:** 749–53.
24 Macfarlane AJR, Kearns RJ, Aitken EL, Kinsella J, Clancy MJ. Does regional compared to local anaesthesia influence outcome after arteriovenous fistula creation? *Trials* 2013; **14:** 263.
25 Soares LG, Brull R, Lai J, Chan VW. Eight ball, corner pocket: the optimal needle position for ultrasound-guided supraclavicular block. *Reg Anesth Pain Med* 2007; **32:** 94–95.
26 Rodriguez J, Taboada-Muniz M, Barcena M, Alvarez J. Median versus musculocutaneous nerve response with single-injection infraclavicular coracoid block. *Reg Anesth Pain Med* 2004, **29:** 534–38.
27 Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *Trials* 2010; **11:** 32.
28 Meena S, Arya V, Sen I, Minz M, Prakash M. Ultrasound-guided supraclavicular brachial plexus anaesthesia improves arteriovenous fistula flow characteristics in end-stage renal disease patients. *South Afr J Anaesth Analg* 2015; **21:** 131–34.
29 Reynolds T, Kim K, Dukkipati R, et al. Pre-operative regional block anaesthesia enhances operative strategy for arteriovenous fistula creation. *J Vasc Access* 2011; **12:** 336–40.
30 Lo Monte AI, Damiano G, Mularo A, et al. Comparison between local and regional anaesthesia in arteriovenous fistula creation. *J Vasc Access* 2011; **12:** 331–35.
31 Schenk W. Improving arteriovenous access: regional anaesthesia improves arteriovenous fistula prevalence. *Am Surg* 2010; **76:** 938–42.
32 Wilmink T, Hollingworth L, Powers S, Allen C, Dasgupta I. Natural history of common autologous arteriovenous fistulae: consequences for planning of dialysis access. *Eur J Vasc Endovasc Surg* 2016; **51:** 134–40.
33 Lok C, Allon M, Moist L, Oliver MJ, Shah H, Zimmerman D. Risk equation determining unsuccessful cannulation events and failure to maturation in arteriovenous fistulas (REDUCE FTM I). *J Am Soc Nephrol* 2006; **17:** 3204–12.
34 Masengu A, Maxwell A, Hanko J. Investigating clinical predictors of arteriovenous fistula functional patency in Europe. *Clin Kidney J* 2016; **9:** 142–47.
35 Sandu N, Manne J, Medabalmi P, Capan, L. Sonographically guided infraclavicular brachial plexus block in adults: a retrospective analysis of 1146 cases. *J Ultrasound Med* 2006; **25:** 1555–61
36 Sites BD, Chan VW, Neal JM, et al. The American Society of Anesthesia and Pain Medicine and the European Society of Regional Anaesthesia and Pain Therapy joint committee recommendations for education and training in ultrasound guided regional anaesthesia. *Reg Anaesth Pain Med* 2010; **35:** S74–80.
37 Perlas A, Lobo G, Lo N, Brull R, Chan V, Karkhanis R. Ultrasound-guided supraclavicular block: outcome of 510 consecutive cases. *Reg Anesth Pain Med* 2009; **34:** 171–76.
38 Chazapis M, Kaur N, Kamming D. Improving the peri-operative care of patients by instituting a "block room" for regional anaesthesia. *BMJ Qual Improv Report* 2014; **3:** u204061.w1769-u204061.w1769.
39 Tozzi M, Franchin M, Ietto G, et al. Initial experience with the Gore Acuseal graft for prosthetic vascular access. *J Vasc Access* 2014; **15:** 385–92.
40 Aitken EL, Jackson AJ, Kingsmore DB. Early cannulation prosthetic graft (Acuseal) for arteriovenous access: a useful option to provide a personal vascular access solution. *J Vasc Access* 2014; **15:** 481–85.
41 Lok CE. Fistula first initiative: advantages and pitfalls. *Clin J Am Soc Nephrol* 2007; **2:** 1043–53.
42 Agarwal AK, Patel BM, Haddad NJ. Central vein stenosis: a nephrologist's perspective. *Semin Dial* 2007; **20:** 53–62.
43 Bakken AM, Protack CD, Saad WE, Lee DE, Waldman DL, Davies MG. Long-term outcomes of primary angioplasty and primary stenting of central venous stenosis in hemodialysis patients. *J Vasc Surg* 2007; **45:** 776–83.