Validation in the sheep of an ultrasound velocity dilution technique for haemodialysis graft flow

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Abstract

Background. A simple, rapid, inexpensive method for measuring the flow in a patient’s vascular access would permit routine monitoring during haemodialysis, and hence provide information of access graft deterioration sufficiently early to increase the success of minimally invasive remedial procedures. This paper reports the validation of such a method in animals.

Methods. A PTFE graft was implanted in sheep between the carotid artery and the jugular vein. While the sheep was under general anaesthesia and on a haemodialysis circuit, ultrasound velocity in its blood was perturbed by the injection of a 5–10 ml bolus of isotonic NaCl. The pump tubing flow was measured by a transit-time blood flow meter. This flow was combined with the areas of perturbation generated by the injection before and after mixing in the access flow to estimate graft flow. The calculated graft flow was compared to flow measured directly by a transit-time probe on the same carotid artery.

Results. Over a 10-fold range, 120–1260 ml/min, graft flow measured by ultrasound velocity dilution agreed well with graft flow measured directly with a scatter of 76 ml/min about the regression line.

Conclusion. Ultrasound velocity dilution provides a method for measuring flow in the graft accurate enough for clinical evaluation of patients on dialysis.

Key words: graft flow validation; haemodialysis; transit-time; ultrasound velocity; vascular access flow

Introduction

Changes in vascular access graft blood flow may portend graft failure and are therefore of considerable importance to patients on dialysis. Vascular access flow in patient grafts has been measured by dilution techniques, often whilst assessing other methods e.g. [1–4]. A flow-meter based on the dilution principle capable of easily measuring vascular access flow during routine haemodialysis has recently become available [5]. This reversed line method is minimally invasive and depends on perturbations of the velocity of sound in the blood passing through the dialysis circuit [6]. This velocity is determined mainly by the total concentration of protein in the blood [7]. The injection of a small bolus of isotonic NaCl (Figure 1) dilutes the haemoglobin and plasma proteins and thereby transiently perturbs the ultrasound velocity. A transducer of a transit-time blood flow meter applied to the dialysis tubing provides two signals, one differential, from which the blood flow in the tubing is derived, and a second that is a function of the time of passage of the sound between the crystals of the probe. Perturbation of sound velocity within the window of the probe changes this second signal. The bolus is injected into the dialysis tubing, and the area generated by the velocity change plotted against time is measured simultaneously with the blood flow at the same site, probe transducer T × 1 (Figure 1). With the lines reversed from their normal configuration during haemodialysis, the same bolus is then further diluted by mixing with the access flow and the corresponding area, now reduced, is sampled by T × 2. Since an area so generated is inversely proportional to the dialyser flow, the access flow can then be derived from the ratio of the two areas and the known dialyser tubing flow. Because both probes experience the same bolus, the volume injected need not be known. Note that in the arrangement shown in Figure 1 the needles have been reversed from their normal configuration. With the needles in the normal configuration, the same apparatus permits any access flow recirculation that is present to be quantified [8].

In order to validate this technique it is desirable to compare it to the graft flow measured by an independent, reliable method. In the dialysis patient the colour Doppler technique has been used. Although agreement with this method has been reported [9,10], the Doppler method has the disadvantage of high variability, and of the estimate of graft flow being somewhat dependent on the operator. The standard for flow measurement, the transit-time flow meter requires surgical implantation, and hence cannot be employed in a patient for ethical reasons. It can, however, be used in a suitable...
Fig. 1. Experimental arrangement of the sheep with arteriovenous graft and dialysis circuit for measurement of access flow directly by a perivascular flow probe and indirectly by an ultrasound dilution method. Note that the needles are inserted in the graft reversed to the normal configuration during patient dialysis.

Methods

Animal protocols were approved by the Institutional Animal Care and Use Committee of Cornell University. For instrumentation anaesthesia was induced with ketamine, and maintained with isoflurane in oxygen in a circle rebreathing system. Two adult ewes were equipped with a perivascular flow probe (6R Transonic Systems Inc., Ithaca, NY) on the right carotid artery. A 4–7 mm PTFE graft (S#47048, W. L. Gore and Associates Inc., Flagstaff, AZ) was introduced between the same carotid artery and the jugular vein. The graft was sutured end to end to the proximal carotid artery, and end to side of the ipsilateral jugular vein. The loop of the graft was tunnelled beneath the skin of the neck, up towards the midline. The lead to the perivascular probe was exteriorized at the back of the neck where it could be tucked beneath a bandage.

Observations were made after the graft incision had healed and the signal received from the perivascular flow probe had stabilized. In order to minimize changes in graft flow caused by excitement, observations were made on each sheep anaesthetized under the same protocol used for surgery. Dialysis needles (15-gauge, Terumo Medical Corp., Elkton, MD) were inserted into the graft with the points directed away from each other in the configuration shown in Figure 1, and separated by ~18cm. The dialyser pump circuit (National Medical Care, Rockleigh NJ) was connected but without a dialyser filter (Figure 1). Flow through the dialyser tubing, 170–370 ml/min, was controlled by a roller pump (Drake Willock Model 7401, Portland OR). Dialyser flows were not varied systematically over the range of access flows; the smaller dialyser flows were mainly grouped in the first sheep that had the smaller access flows. Access graft flow was measured as in a patient by the ultrasound velocity dilution method [6] using an HD01 Hemodialysis Monitor (Transonic Systems Inc., Ithaca NY). The carotid arterial perivascular probe was connected to a T106 flow meter.

The flow meters were calibrated for each series of observations in three stages, but with the needles connected to the dialysis circle in the normal position, i.e. reversed from Figure 1. In this state, compression of the graft between the needles with the dialysis pump switched off completely occluded the graft, giving a zero flow reading for both the probe measuring tubing flow and the perivascular probe reading carotid flow. In the second stage the dialyser pump was started while the graft was still occluded. In this state, the same flow passed through both probes, allowing their sensitivities to be compared directly. Finally, after disconnecting the dialysis tubing, the carotid probe was calibrated using a syringe to withdraw and reinject measured volumes of blood through the proximal needle with the graft compressed and occluded distally. For each withdrawal and reinjection, the area generated by the flow signal against time divided by the volume of blood gave an absolute calibration of the meter sensitivity [12]. Correction for calibration becomes important if flow through the carotid probe is not axial to the probe. In our situation the release of tension on the carotid artery caused by insertion of the graft resulted in minor kinking of the vessel within the window of the probe and a consequent reduction in probe flow sensitivity. The correction for zero was always small.

Dialyser flow and sound velocity transients were collected at 16 Hz and graft flow was calculated from ultrasound dilution with standard software (Transonic Systems Inc.,
Ithaca NY) provided with an additional channel for monitoring the carotid arterial flow. Flow through the graft was decreased by light compression between the needles. Flow was stimulated by an intravenous drip of 0.3 mg/min dobutamine. Relationships between variables were examined by standard regression analysis.

**Results**

When the two sheep were standing quietly, flow in their grafts was \( \sim 0.6 \) and \( \sim 1.0 \) l/min. During collection of data the sheep was anaesthetized and graft flow measured concurrently by ultrasound dilution and by the perivascular probe. In three sessions, 54 comparisons of flow were made on the first sheep and 36 during two sessions on the second. Graft flows measured by the perivascular probe, \( 450 \pm 170 \) (SD) ml/min, were lower in sheep 1, than the corresponding flows, \( 940 \pm 270 \) (SD) ml/min, in sheep 2. Regression lines were fitted of \( Q_D \), the graft flow by ultrasound dilution, against \( Q_P \), flow by perivascular probe. The standard deviations of the points about the two regression lines were \( \pm 72 \) and \( \pm 84 \) ml/min, the slopes, 0.995 and 1.022, and the intercepts, 56 and 10 ml/min respectively. Because these parameters of each regression line did not differ significantly, data from the two sheep were combined to give 90 comparisons of flow measured directly by perivascular probe and indirectly by ultrasound dilution over a range of access graft flow from 120 to 1260 ml/min (Figure 2).

The slope of the regression line of the combined data, \( Q_D = Q_P \times (0.993 \pm 0.025) + 39 \pm 18 \), did not differ significantly from that of the line of identity. The scatter of the individual data about the regression line was \( \pm 76 \) ml/min. The intercept of the regression line reached statistical significance (\( P = 0.033 \)).

To investigate the influence of dialyser flow, \( Q_b \), on the accuracy of access flow measurement, the data were divided in two groups with low \( Q_b \), 170–230 ml/min (access flow \( 479 \pm 276 \) ml/min (mean \( \pm \) SD)), and high \( Q_b = 231–370 \) ml/min (access flow \( 761 \pm 308 \) ml/min(mean \( \pm \) SD)). The difference, dilution flow-perivascular sensor flow was \( 6 \pm 76 \) for low \( Q_b \) and \( 55 \pm 68 \) ml/min for high \( Q_b \) (mean \( \pm \) SD, \( n = 37 \) and 53 respectively).

**Discussion**

Usually the introduction of new medical technology requires a theory, bench validation, animal validation, clinical study on patients, and comparison with existing technologies. Theory and bench validation, mostly related to mixing conditions and sound velocity dilution technology, were analysed by Krivitski [5,6]. Where ultrasound dilution has been compared with colour Doppler [9,10] or magnetic resonance [13] methods, encouraging agreement has been shown. Nevertheless these Doppler and magnetic resonance methods cannot be considered definitive validation because of their variability. The most accurate, but of necessity, invasive, measurement of access flow is to use a calibrated perivascular probe directly on the arterial supply of the access flow. In this study the ultrasound dilution method is compared with concurrent measurement with a perivascular probe.

Graft flow measured by ultrasound velocity dilution closely followed the flow measured by a probe on the artery supplying the graft over a 10-fold range. The scatter of points about the regression line (Figure 2) appeared to be distributed uniformly across the flow range, suggesting it was not a function of the flow. Moreover, this scatter was small enough to ensure that the dilution method is sufficiently accurate for clinical application.

Even with \( Q_b \) in the low range of 170–240 ml/min with the access flow below 700 ml/min, good accuracy was achieved. This does not contradict a previous recommendation [5] that \( Q_b \) should be 250–300 ml/min that was designed to cover access flows up to 3 l/min. In this study with relatively low range of access flows but with sufficient distance between the needles (\( \sim 18 \) cm) and the outflow needle facing the access flow, mixing appeared to be adequate.

Fortunately the systematic error detected by observing the positive intercept, 39 ml/min, in the regression of Figure 2 is small enough to be disregarded in a clinical access flow measurement. Although \( Q_D - Q_P \) is significantly \((0.005 > P > 0.001)\) less for low \( Q_b \) than high \( Q_b \), we cannot conclude that the \( Q_b \) is the source of the systematic error because there was a tendency for the low \( Q_b \) to be associated with lower access flows.

Access flow is an important criterion for assessing graft condition [14]. When account is taken of the short time it takes for a nurse to make a measurement of access flow, and the negligible cost of the saline injection, ultrasound dilution supplies a feasible method for routine monitoring during haemodialysis of changes in access flow over the life of a graft. This would encourage detection of graft deterioration early
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enough to permit the use of minimally invasive salvage procedures, thereby improving patient care by prolonging the usefulness of a working vascular access [15].

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References

8. Depner TA, Krivitski NM, MacGibbon D. Hemodialysis access recirculation measured by ultrasound dilution. ASAIO J 1995; 41: M749–M753
9. Depner TA, Krivitski NM. Clinical measurement of blood flow in hemodialysis access fistulae and grafts by ultrasound dilution. ASAIO J 1996; 41: M746–M749
10. Sands JJ, Glidden D, Miranda C. Hemodialysis access flow measurement—comparison of ultrasound dilution and duplex ultrasonography. ASAIO J 1996; 42: M899–M901

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