

Access Flow Measurements in Hemodialysis Patients: *In Vivo* Validation of an Ultrasound Dilution Technique^{1,2}

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(J. Am. Soc. Nephrol. 1996; 7:966-969)

ABSTRACT

In this study, access flow in hemodialysis patients with bridge grafts was measured by a newly developed device. The technique is based on the measurement of changes in the ultrasound characteristics of blood. These changes were initiated by an injection of isotonic saline and measured in the tubes of the extracorporeal circuit. The access flow rate (mean \pm standard variation) was 880 ± 440 mL/min (range, 166 to 1740) ($N = 46$). The mean coefficient of variation was $13.4 \pm 6.8\%$ (median, 13.0%; range 3.5 to 29.4%). Measurements correlated well ($r = 0.91$, $N = 22$, $P < 0.001$) with flow rates determined by magnetic resonance angiography and by a technique based on intra-access flow-pressure curves ($r = 0.84$, $N = 14$, $P < 0.001$). In conclusion, access flow can be measured easily, noninvasively, and reliably by the ultrasound dilution device.

Key Words: Hemodialysis, access flow, access surveillance

Access thrombosis is an important problem in the management of hemodialysis patients. It requires invasive, time-consuming, and expensive procedures, which are not without morbidity and mortality. A simple test that would identify patients at risk for thrombosis would have great clinical value. Thrombosis is often associated with access stenosis, which elevates resistance and impairs access flow. Therefore, access flow measurements are probably

useful in access surveillance. Indeed, a number of studies over the past 20 years have indicated that access flow below a certain level predicts thrombosis in the near future (1-6). The techniques proposed to measure access flow rates include constant infusion of technetium-99m (7), dye-dilution (8), electromagnetic flow meters (1,9), Doppler imaging (2-6) and magnetic resonance angiography (MRA) (10). However, each method has one or more drawbacks, such as invasiveness, low reliability, intrinsic difficulty, operator dependence, and costs. As a result, none gained widespread acceptance and most clinicians depend on dialyzer venous pressure measurements for access surveillance (11,12).

Recently a newly developed device for access flow rate measurement was introduced (13). This technique is based on the Fick principle: dilution of blood in the extracorporeal circuit by isotonic saline is measured by ultrasound. A comparison with Doppler ultrasound measurements in seven patients has been published (14). In this study, we report our experience in a large group of hemodialysis patients. There is no reference standard for this purpose. Therefore, we compared measurements with the new device with measurements by MRA, which in our hands has been proven to produce correct and reproducible results in phantom studies and patients (15,16), and with a technique based on intra-access flow-pressure curves (17). Both methods measure access flow rates in entirely different ways than the new ultrasound dilution method does.

PATIENTS AND METHODS

Studies were done in chronic hemodialysis patients. All patients had a bridge graft (either polytetrafluoroethylene [PTFE] or homologous vein) in an arm. Three (all loops) were upper-arm grafts, and 43 were forearm (40 loop and three straight) grafts. We deliberately limited the flow-rate measurements to patients with grafts, because with these patients (in contrast to patients with Brescia-Cimino fistulae), it is possible to measure flow in a single vessel, *i.e.*, the graft.

Access Flow Measurements

Measurements of access flow were obtained in 46 patients. These measurements were always done in the first 30 min of a hemodialysis session. In 22 patients, MRA was performed immediately before that hemodialysis. In 30 of the patients, coupled measurements of access flow rates with the ultrasound dilution method and the intra-access flow-pressure curve technique were obtained. Both measurements were made in random order within the first 30 min of the hemodialysis session.

Ultrasound Dilution Method. We used the Transonic Hemodialysis Monitor (Transonic Systems Inc, Ithaca, NY). The

¹ Received December 5, 1995. Accepted February 9, 1996.

² These studies were presented at the 28th Annual Meeting of the American Society of Nephrology, November 5-8, 1995, and published in abstract form (J Am Soc Nephrol 1995;6:484).

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1046-6673/0706-0966\$03.00/0

Journal of the American Society of Nephrology

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theoretical background and bench validation of this method is described in detail in a previous article (13). With this method, patients need to have two needles in the access, one facing the arterial anastomosis in countercurrent orientation (dialyzer blood inlet) and the other facing the venous anastomosis. To measure the access flow rate, the dialyzer lines are reversed from normal: the arterial inlet is downstream to the venous outlet, and the outlet then faces the access stream (Figure 1). A flow sensor is clipped on the arterial line to measure the dialyzer flow rate and for recording ultrasound dilution caused by saline injections. An additional identical flow sensor is clipped on the venous line downstream from the place of the saline injection. The indicator injected into the venous line can serve both to calibrate the sensor and to measure access flow (Figure 1). To measure access flow, 5 mL of isotonic saline is injected into the venous line. The indicator is mixed with the blood flowing in the access. The fraction of the indicator detected by the sensor on the arterial line is determined by the ratio between flows in the extracorporeal circuit and the access. Knowing the blood flow rate in the extracorporeal circuit, the access flow rate can be calculated from this ratio (13). Flow determinations consisted of five single measurements, which were averaged. All measurements were done during a fixed dialyzer pump speed, usually 250 mL/min. The ultrafiltration rate was turned off 3 min before the start of measurements. After flow-rate measurements were done, the dialyzer lines were reversed back to normal.

Magnetic Resonance Angiography (MRA). Patients were studied with nontriggered two-dimensional phase-contrast MRA using a 1.5-tesla whole-body magnetic resonance system with shielded gradients (Gyrosan ACS/NT15, Philips Medical Systems, Best, the Netherlands). Reproducibility within a single session was tested in 11 patients, and the coefficient of variation was $4.8 \pm 2.8\%$. Measurements were done as described in other studies (15,16).

Flow-Rate Estimation from Intra-Access Flow-Pressure Curves. For this purpose, an additional needle was placed into the venous part of the graft downstream of the venous needle of the extracorporeal circuit. A pressure module was connected (Hewlett Packard, King of Prussia, PA). At a dialyzer blood flow rate of 0 mL/min, the pressure recorded by the pressure module is caused by the spontaneous access blood flow. When the spontaneous blood flow is stopped by digital compression between the arterial and venous needle, the intra-access pressure measured through the additional needle is exclusively determined by the dialyzer blood flow.

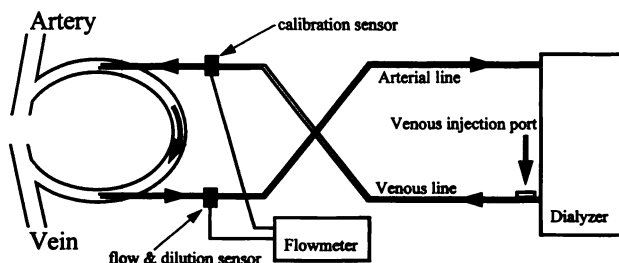


Figure 1. Access-flow rate measurement in a hemodialysis patient. The arterial and venous lines of the extracorporeal circuit are reversed from normal. The sensor for calibration is clipped on the venous line downstream of the place of saline injection, and the sensor for flow and dilution measurement is placed on the arterial line.

By increasing the dialyzer blood flow rate in 50-mL/min steps from 0 to 500 mL/min, a dialyzer blood flow-pressure curve can be constructed. The pressure taken at each step of the dialyzer blood-flow pressure curve represented the mean of at least 10 pressure recordings. The dialyzer blood flow causing an intra-access pressure identical to the spontaneous intra-access pressure will represent the spontaneous access blood flow rate. In patients who have access blood flow rates greater than 500 mL/min (equaling the maximum dialyzer blood flow rate), the access blood flow rate can be estimated by extrapolation (Figure 2). Because this will be hazardous with flow rates far beyond 500 mL/min, we only evaluated recordings indicating access flow rates below 1000 mL/min.

Statistical Analysis

Means \pm SD and range where indicated are given. Coefficient of variation was calculated by dividing the SD by the mean. Univariate regression analysis was done on the means. A *P* value of less than 0.05 was considered to indicate statistical significance.

RESULTS

The average values of graft flow measured by the ultrasound dilution method were 880 ± 440 mL/min (median, 880 mL/min, and range, 166 to 1740 mL/min; *N* = 46). The mean coefficient of variation of the five consecutive measurements was $13.4 \pm 6.8\%$ (median, 13.0%; range, 3.5 to 29.4%). The mean coefficient of variation in the lowest, middle, and highest third of flows was, respectively, $16.1 \pm 5.9\%$, $12.2 \pm 6.0\%$, and $12.1 \pm 8.1\%$ (not significant).

In 22 patients, MRA was also performed. The MRA flow rate was 1084 ± 413 mL/min (range, 482 to 1831 mL/min) and the flow rate measured by the ultra-

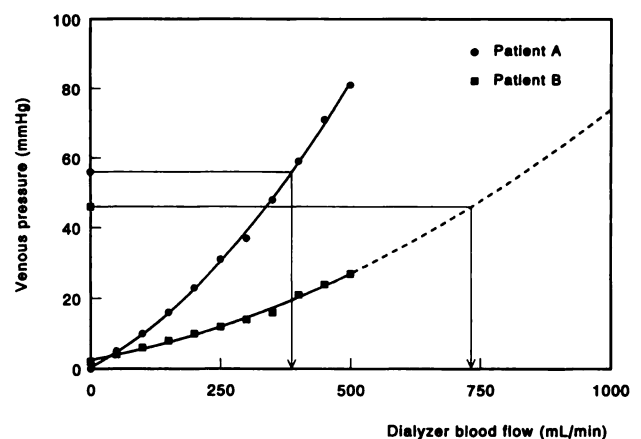


Figure 2. Flow measurement based on intra-access flow-pressure curve. In Patient A, venous pressure at dialyzer blood flow rate 0 mL/min is 57 mm Hg. The relation between dialyzer blood flow and venous pressure during compression of the graft between the two needles indicates that the access blood flow rate is 390 mL/min. In Patient B, the flow-pressure relation is extrapolated above 500 mL/min. In this patient, the pressure at a dialyzer flow rate of 0 mL/min is 47 mm Hg and the flow rate is estimated to be 740 mL/min.

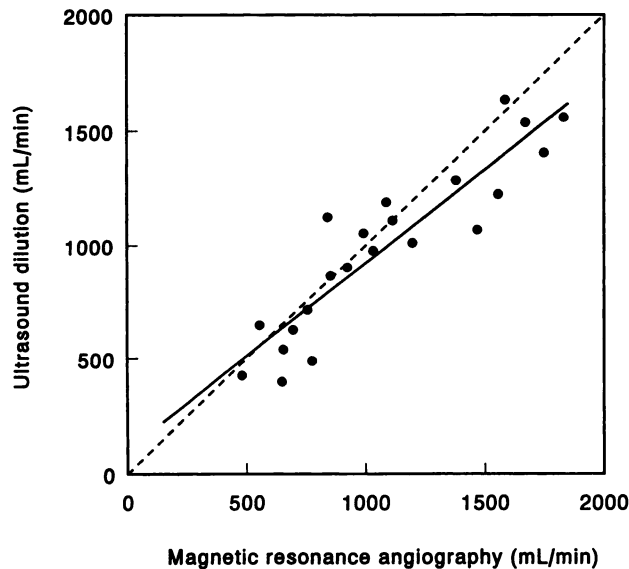


Figure 3. Relation between access flows measured by the ultrasound dilution method and MRA ($N = 22$). The dotted line represents the line of identity, and the solid line the regression line. Correlation was 0.91 ($P < 0.001$; ultrasound dilution = $0.82 \times \text{MRA plus } 100$).

sound dilution technique was 990 ± 372 mL/min (range, 399 to 1635 mL/min). The correlation between the MRA and the ultrasound dilution flow-rate measurements was $r = 0.91$ ($P < 0.001$; ultrasound dilution = $0.82 \times \text{MRA plus } 100$) (Figure 3).

In 30 patients, the flow rate was determined on the basis of the intra-access flow-pressure curves and using the ultrasound dilution technique. In 16 of the 30 paired measurements, access flow rates were estimated to be more than 1000 mL/min by both methods. In this range, an exact estimation of the access flow rate from the dialyzer blood flow-pressure curves is hazardous. The flow rate measured on the basis of the flow-pressure curves in the remaining 14 patients was 533 ± 219 mL/min (range, 181 to 901 mL/min) and the flow rate measured by the ultrasound dilution technique was 486 ± 249 mL/min (range, 166 to 903 mL/min). The correlation was $r = 0.84$ ($P < 0.001$; ultrasound dilution = $0.95 \times \text{flow based on flow-pressure curve} - 20$) (Figure 4).

DISCUSSION

The flow measurements by the ultrasound dilution method are based on the indicator dilution principle. Techniques based on this principle have been used for more than a century for blood-flow measurements and are considered to be reliable. Our results on access flow measured by the ultrasound dilution method are in the range reported in the literature for volume flow in hemodialysis grafts. The measurements show good correlation with the MRA over a wide range of flow rates. Within the flow rate range of 0 to 1000 mL/min, the results show good correlation with

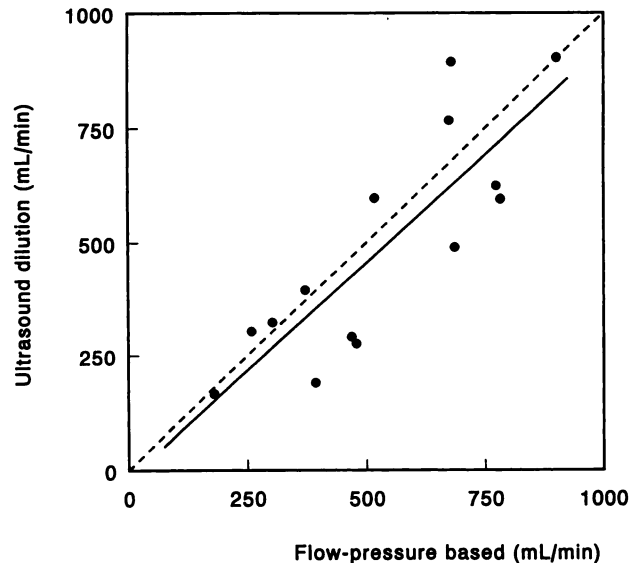


Figure 4. Relation between access flow rates measured by the ultrasound dilution method and based on intra-access flow-pressure curves. Only the results of patients with flow rates below 1000 mL/min are shown ($N = 14$). The dotted line represents the line of identity, and the solid line the regression line. Correlation was $r = 0.84$, ($P < 0.001$; ultrasound dilution = $0.95 \times \text{flow based on intra-access flow-pressure curve} - 20$).

the assessments based on intra-access flow-pressure curves. The mean coefficient of variation is 13.4%. *In vitro* reproducibility is reported to be 2.8% (13). However, *in vivo*, the variability of the results is not only determined by the technique but also by blood pressure, which may show sudden changes during dialysis. A change in blood pressure will affect flow in the nonautoregulating graft. Complete mixing of the indicator in the graft flow is essential for proper measurement of flow rate with the technique presented here. It is conceivable that the mixing may be less complete during low access flows, resulting in a higher variability of the results. However, the mean coefficient of variation of the lowest third of flow rates was not different from that of the other two thirds. Theoretically, the access flow rate is not influenced by the flow through the dialyzer. Indeed, it was shown that the flow rate did not change when the dialyzer flow rate was reduced from 334 to 177 mL/min (14). A shortcoming of this new technique is the need for two needles in the graft. Therefore, it is impossible to use the technique during single-needle dialysis. In addition, we think that the technique is less suitable for use in native fistulae because one cannot be certain that the access between the two needles is a single vessel.

It is of obvious clinical relevance that the ultrasound dilution method is able to discriminate low flow rates. Low access blood flow rates are associated with an increased risk of thrombosis. Although Alfrey *et al.* (1)

already noted that low flow rates in external shunts predicted imminent thrombosis, it was not until Doppler ultrasonography became available that more data were published. To date, several studies, all using Doppler ultrasonography, have indicated that access flow rates below 300 to 500 mL/min predict thrombosis in the near future (2–4,6). Whether measurement of a low access flow rate by the ultrasound dilution method has a similar predictive value remains to be established. A theoretical advantage of the ultrasound dilution method is that it measures actual volume flow. Conventional Doppler ultrasound, by contrast, primarily measures flow velocity, and volume flow has to be calculated from flow velocity and graft diameter. This means that a laminar flow is assumed, which probably does not exist in any graft. Another problem with conventional Doppler ultrasound is that it depends highly on the skills of the operator. Perhaps these difficulties explain why in one study using Doppler ultrasound access, thrombosis was predicted with flow rates under the rather high level of 1300 mL/min (5). Finally, Doppler ultrasound is time-consuming, and, in contrast to the method presented here, is often not available as a bedside technique.

In previous phantom studies in our hospital, MRA has been proven to produce reliable and reproducible results in volume flow measurements (15). Also, in hemodialysis patients, this method is reported to be adequate. In one study, a good correlation was found between access-flow measurements with MRA and a dye dilution technique (10). The correlation with the ultrasound dilution technique applied in the study presented here is good, and close to the line of identity. On average, however, MRA measurements tended to give somewhat higher flow rates. Perhaps this is related to the fact that measurements by MRA were done before the dialysis session, and measurements by the ultrasound dilution device were done only after the patient has been connected to the extracorporeal circuit. In the latter condition, blood pressure may be somewhat lower, thus blood flow in the graft will be lower as well. It appears from our results that the ultrasound dilution method not only can reliably distinguish low access flow rates, but also high blood flows, which may be relevant in the management of patients with cardiac failure.

The access-flow measurement based on the construction of intra-access flow-pressure curves is very simple and seems quite sound on theoretical grounds. This principle was already proposed almost two decades ago (17), although the actual implementation in the study presented here was slightly different from that described in the original study. Despite the simplicity of the principle, the method has not gained widespread recognition, perhaps because it is invasive and labor-intensive.

In conclusion, the newly developed ultrasound dilution method offers the opportunity to measure flow in the vascular access of hemodialysis patients. The

method provides reproducible results, is noninvasive, easy to perform as bedside measurement, and needs little investment in time, making it superior to the other methods. The technique does not require physical manipulation of the shunt, which means an obvious advantage in terms of risk for the patient. The clinical usefulness to distinguish patients at risk for access thrombosis remains to be established.

ACKNOWLEDGMENT

Dr. Bosman is supported by a grant from the Dutch Kidney Foundation.

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