The Measurement of Hemodialysis Access Blood Flow by a Conductivity Step Method

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Background and objectives: Measurement of blood flow rate (Qa) is used to monitor dialysis access, AV fistulas, and grafts. Indicator dilution measurements of the recirculation (R) induced by reversal of hemodialysis blood lines are commonly used. This plus the dialysis circuit flow (Qb) allows calculation of Qa. R also changes the conductivity, which can be measured by a conductivity cell in the spent dialysate. The change in conductivity caused by line reversal should vary with Qa. A methodology for Qa measurement utilizing this conductivity step is proposed. This study compares conductivity step methodology against the reference method of ultrasound dilution (Qa-Trans).

Design, setting, participants, & measurements: This was an open diagnostic test study in a single academic hospital setting involving 15 hemodialysis-dependent patients. Each was studied over four hemodialysis treatments. During each treatment, two pairs of Qa measurements (conductivity step and Trans) were made. Pre- and postdialysis sodium levels were also measured.

Results: Average Qa-conductivity step was 1040 ml/min. Average Qa-Trans was 1030 ml/min. The difference was NS. The data pairs showed mean difference of 1.3 ± 17% (SD). The SD indicates a relatively large variation between data pairs. There was significant linear correlation between the Qa-conductivity step and Qa-Trans results (r = 0.91, P < 0.001). Serum sodium rose slightly but significantly over dialysis (P < 0.001).

Conclusions: Qa measurement by conductivity step may be an acceptable alternative to ultrasound dilution methodology. Care must be taken to prevent salt loading when the conductivity step is used.


The measurement of hemodialysis blood access flow rate (Qa, ml/min) in arteriovenous (AV) fistulas and grafts is common. Reduced or falling levels of Qa indicate access dysfunction and predict thrombosis (1). Most Qa measurements use indicator dilution techniques to measure the amount of recirculation induced by reversal of blood lines. This plus the dialysis circuit flow (Qb, ml/min) allows for the calculation of Qa (1). One methodology for Qa measurement involves using ultrasound velocity measurements of flowing blood and their dilution by saline using the Transonic hemodialysis monitor (Transonic, Inc., Ithaca, NY). Details of this and other technologies are given elsewhere (2). Because access recirculation is inversely related to Qa (3) and because it will lead to a decreased dialyzer urea clearance, we hypothesized that needle reversal can measure Qa by observing the effect on dialysate urea concentrations. This hypothesis was proven and the results have been published (4). Mercadal et al. (5) and Gotch et al. (6) have shown that the change in effective ionic dialysance (EID) values induced by line reversal can be used to measure Qa. As pointed out in our Discussion (4), Fresenius Medical Care (www.fmc-ag.com) had incorporated propriety software into their dialysis machine (2008K) to measure Qa utilizing EID. At that time, there was no published work regarding the accuracy and validity of this methodology beyond the original theory validation (5). Subsequently, Lacson et al. (7) of Fresenius Medical Care and Whittier et al. (8) have separately published validation data for EID incorporated into the Fresenius 2008K machine using ultrasound velocity measurements as the “gold standard” comparator. Their results showed good agreement between the methodologies. The EID-based measurements rely on two separate determinations of ionic dialysance obtained many minutes apart. Knowing the effect of line reversal on dialysate urea concentrations, we examined the possibility to directly measure Qa from the conductivity change induced by the reversal of lines (conductivity step method).

Materials and Methods

Study Design

This was a single-center open study design of 15 patients while they were undergoing hemodialyses using Integra dialysis machines fitted with Diacan (www.gambro.com). Each patient was studied during four dialyzes for a total of 60 treatments. During each treatment, two pairs of measurement for Qa were performed yielding a maximum of 120 measurement pairs. Each measurement pair consisted of one by the conductivity step method and one by ultrasound dilution. The measurement pairs were taken approximately 1 and 2 hours into each 4-hour dialysis treatment. The time between the conductivity step...
measurement and the ultrasound dilution measurement was approximately 15 minutes. Before the first pair of \( Q_a \) measurements, good access function was confirmed by the exclusion of access recirculation with lines in the normal configuration.

Patients

The study was approved by the Ethics Review Board of the University of Western Ontario and written informed consent was obtained from participating patients. The 15 patients (11 men and 4 women) had AV accesses (12 AV fistulas and 3 synthetic grafts) known to be functioning well by previous \( Q_a \) measurements \((Q_a > 100 \text{ ml/min} + \text{usual dialysis circuit blood flow rate} / [Q_b] \text{ for AV fistulae; } Q_a > 650 \text{ ml/min for grafts; no access intervention in prior month)}\).

All patients met the inclusion criteria of being over 18 years of age and receiving chronic hemodialysis for more than 3 months at London Health Sciences Centre. All patients were free from known cardiovascular instability during dialysis, active malignancy, HIV/AIDS, hepatitis B or C, pregnancy, or participation in other studies.

Hemodialysis Treatments

The dialysis prescription for each patient was followed as closely as possible. F80 polysulphone membrane dialyzers (Fresenius, Inc., United States) were used. However, the \( Q_b \) was set lower than normal (range 300 to 360 ml/min) to avoid blood pump stops during \( Q_a \) measurements. Changes in ultrafiltration (UF) rate were permissible provided that the rate was stabilized and constant during measurements; no UF profiling was used. Likewise, care was taken to ensure that \( Q_b \) was constant during measurements. Dialysate sodium concentration was 140 mmol/L and was held constant outwith EID measurements.

EID Measurement Theory

EID values accurately reflect effective urea clearances whether measured by blood or dialysate side (9). EID is derived from measurements of dialysate conductivity \((C_{d_{out}})\) at outlet \((Y_1\) and \(Y_2)\) corresponding to two different set points of dialysate conductivity at inlet \((X_1\) and \(X_2)\).

\[
EID = (Q_d + Q_{uf}) \times [1 - (Y_1 - Y_2)/(X_1 - X_2)]
\]

where \(Q_d\) and \(Q_{uf}\) are dialysate and UF flow rates, respectively. Petitclerc et al. (10) have extensively described this principle. After the measurement of \(C_{d_{out}}\) \((Y_1)\) at the prescribed value of dialysate conductivity \((X_i)\), the set point of dialysate conductivity is changed by 1 mS/cm (usually) for 2 minutes \((X_2)\). The value for \(C_{d_{out}}\) is then measured at the end of the phase \((Y_2)\). The set point of the dialysate conductivity is then moved back to the prescription value \((X_1)\) and \(C_{d_{out}}\) is measured again to confirm \((Y_1)\) and the EID is computed. To ensure an accurate reading, the Diascan requires a stable period of 7 minutes on the blood and dialysate sides because it takes 2 minutes for each of the three measurements plus 1 minute to allow for delays between inlet and outlet conductivity measurements. During this period, there should be no injections into the blood circuit or changes in \(Q_a\) or UF rates. The 7-minute period starts before the measurement of \(Y_1\) and ends after the second measurement of \(Y_2\).

**EID Measurement in These Experiments Using Diascan**

EID was measured by Diascan after both access flow measurements were done and its value was recorded.

**Conductivity Step Method for Access Flow Measurement in These Experiments Using the Integra Dialysis Machines**

This is best described by the steps required to perform the measurement and Figure 1.

1. Raise the conductivity of dialysate by 1 or 2 mS/cm, then record from the machine data screen the measured predialyzer dialysate conductivity \((C_{d_i})\) (Ci in Figure 1).
2. Wait 2 minutes, record the measured postdialyzer \(C_{d_{out}}\) \((C_n = C_{d_{out}}\) with lines in the normal configuration; Figure 1).
3. Reverse the blood lines.
4. Wait 2 minutes and then record the measured postdialyzer \(C_{d_{out}}\) \((C_r = C_{d_{out}}\) with lines in the reverse position; Figure 1).
5. Normalize dialysis fluid conductivity and blood flow direction.
6. Calculate the access blood water flow rate as:

\[
Q_{aw} = \frac{(EID - Q_{uf}) \times (C_i - C_n)}{C_i - C_n}
\]

where \(EID\) is the ionic dialysance as measured by Diascan; \(Q_{uf}\) is the UF rate in ml/min, and \(Q_{aw}\) is the access blood water flow (ml/min).

**Figure 1. Conductivity step measurement. This shows dialysate conductivity (mS/cm) plotted against time. \(C_i\) is the predialyzer dialysate conductivity after a 2-mS/cm conductivity step; \(C_n\) and \(C_r\) are the postdialyzer conductivity values with the dialysis circuit blood lines in the normal \((C_n)\) and reversed \((C_r)\) position.**
of conductivity transferred across the dialyzer membrane from dialysate to plasma water after the increment in Cl\textsubscript{aw}, and hence can be substituted for EID\textsubscript{p} in the numerator of equation 3.

To obtain whole blood access flow \((Q_a)\), \(Q\textsubscript{aw}\) needs to be corrected for the amount of nonwater substances in the blood. This is done by

\[
Q\textsubscript{aw} = Q\left[0.72 \times \text{Hct} + (1 - \text{Hct}) \left(1 - \frac{T_p}{1000}\right)\right]
\]

where \(\text{Hct}\) is hematocrit (U) and \(T_p\) is total plasma protein (g/L). This equation is a derivation of that given by Sargent and Gotch (11) but using a protein-dependent factor that is \((1 - T_p/1000)\) rather than a fixed water fraction for plasma (they give 0.94; correct for a plasma protein concentration of 60 g/L). The value of 0.72 is for the erythrocyte fraction.

### Recirculation and Access Flow Measurements by Ultrasound Dilution

The recirculation and access flow measurements were carried out using the Transonic HD01 monitor (www.transonic.com). For \(Q_a\), two measurements were taken at each time approximately 5 minutes apart. If these differed by more than 10% or 100 ml/min, a third was taken and the two measurements closest to each other were then averaged, all in accordance with the manufacturer’s instructions.

### Blood Samples

Blood was drawn from the access arterial needle before and after each dialysis was initiated to measure sodium (mmol/L). Blood samples were also taken just before the reversal of blood lines for the measurement of hematocrit (U) and \(T_p\) (g/L). The samples were sent immediately to the hospital laboratory for analysis. Sodium was analyzed by flame photometry, hematocrit by microcentrifugation, and \(T_p\) by Paramax total protein reagent (Baxter Diagnostics, Inc., Deerfield, IL).

### Reasons to Discard Data Points

Data points were discarded for the following reasons:

- Technical failure of the Integra or Transonic devices
- Ultrasound dilution measurements of \(Q\textsubscript{aw} > 4000\) ml/min
- Errors in curve fitting on the conductivity step (i.e., negative slopes on either of the two fitted lines; see Figure 1)
- Blood pump stopped during the conductivity step
- Integra machine went into bypass mode during the conductivity step
- Unintended conductivity changes during the conductivity step period
- No Diascan measurement obtained

### Statistical Analyses

Only data from complete pairs of measurements were included in the analysis. \(Q_a\) measurements by conductivity step and ultrasound dilution were compared as averages of the whole data set and as the difference in each pair. Data were given as average (minimum/maximum range) for each method and as average difference in pair \(±\) SD, respectively.

It was originally the intention to assess the repeatability of the conductivity step method for 1- and 2-mS/cm steps. However, because the measurements were made approximately 1 hour apart, any change in access flow conditions would affect the measurements obtained. Thus, the value of a comparison of between the first and second measurement was limited. Despite this, the difference between the first and second measurement was reported as average difference \(±\) SD.

The differences between groups or pairs were made by unpaired or paired \(t\) tests as appropriate assuming normal distribution of data. Correlations were made by using linear regression (Pearson coefficient) and Bland–Altman-like analysis (the differences in \(Q_a\) values between

the two methodologies were examined as a percentage of the mean \(Q_a\) value rather than the actual \(Q_a\) difference). A percentage variation was calculated for paired sequential measurements within the same method and significance tests were performed using two-tailed paired \(t\) tests.

All analyses were performed using SPSS version 15.0, released 15.0.6 (SPSS, Inc., www.spss.com)

### Results

#### Discarded Data

Twenty-eight pairs of data were discarded. Three pairs were lost because of \(Q_a\) values being too high by ultrasound dilution.

Four pairs were lost because of curve fitting difficulties and two pairs to Integra technical failure. The remainder of the discarded data was lost because manual actions had to be performed. Twelve pairs were discarded because of difficulties during blood flow reversal causing unintended blood pump stops and/or bypass. Six pairs were discarded because the Diascan measurement occurred or did not occur as it tended.

Finally, one pair was discarded because the UF rate was changed during a measurement. This left 92 measurement pairs for analysis.

#### Access Recirculation

There was 0% recirculation with lines in the normal position at the start of each patient dialysis.

#### Agreement with Ultrasound Dilution (\(Q_a\))

The average \(Q_a\) values were 1040 ml/min (421 to 4667 ml/min) as estimated by the conductivity step and 1030 ml/min (390 to 3430 ml/min) as estimated by the ultrasound dilution method. This difference was NS \((P = 0.910, \text{unpaired } t \text{ test})\).

The data were also analyzed as pairs. The difference between measurements by conductivity step and ultrasound dilution was \(-1.3\% ± 17.0\%\) (1- and 2-mS/cm steps included). Any difference was insignificant \((P = 0.469, \text{paired } t \text{ test})\).

There was a highly significant linear correlation between the conductivity step and the ultrasound dilution \(Q_a\) values \((r = 0.91, P < 0.0001)\) (Figure 2). Bland–Altman-like analysis of the same data indicated that this correlation held true over the range of access flows studied (Figure 3).

Analysis was also carried out using the respective subgroups of 1- and 2-mS/cm steps. For the 1-mS/cm step, the paired difference was \(-0.1\% ± 17.4\%\) \((n = 47)\) whereas for the 2-mS/cm steps, the paired difference was \(-2.7\% ± 16.6\%\) \((n = 45)\). Neither was significantly different from ultrasound dilution \((P = 0.098 \text{ and } 0.283, \text{respectively})\).

### Repeatability (Test/Retest) of Access Flow Measurements

The change in \(Q_a\) value between the two measurement occasions, with the conductivity step method when 1- and 2-mS/cm steps were used, was \(5.9\% ± 17.4\%\) \((n = 39)\). The corresponding changes for the 1- and 2-mS/cm subgroups were \(8.1\% ± 19.5\%\) \((n = 21)\) and \(3.3\% ± 14.7\%\) \((n = 18)\), respectively. Neither of the subgroup changes were significantly different from the changes with 1- and 2-mS/cm steps \((P = 0.668 \text{ for } 1 \text{ mS/cm}; P = 0.567 \text{ for } 2 \text{ mS/cm})\). The difference in changes between 1- and 2-mS/cm steps was also NS \((P = 0.391)\).
The corresponding change between the two ultrasound dilution measurements was 1.8% ± 15.2% (n = 51), which was not significantly different from the conductivity step method (P = 0.242).

Sodium Balance
The mean plasma sodium levels were 137.2 mmol/L before dialysis (SD 3.3 mmol/L; range 130 to 145 mmol/L, n = 57) and 139.0 mmol/L postdialysis (SD 1.6 mmol/L; range 136 to 143 mmol/L, n = 56). The mean sodium levels pre- and postdialysis treatment were significantly different (P < 0.001).

In 13 of the 15 patients’ pre- and postdialysis treatments, sodium levels were obtained for each of the four dialysis treatments. For each patient, the average plasma sodium levels were calculated for pre- and postdialysis, and these are depicted in Figure 4, which also gives the average values for the 13 patients. Paired t test analysis of these data did show a small but statistically significant (P < 0.01) increment in plasma sodium over the course of dialysis.

Discussion
The objective of this study was to test the theory that Qa can be measured by the conductivity step method.

Our results show that there were no significant differences between the results of the conductivity step method and the ultrasound dilution method. There was a close linear relationship between the respective values (r = 0.91, P < 0.001). On the other hand, the variation between the paired conductivity step and the ultrasound dilution measurements was relatively large (−1.3% ± 17%). This is also demonstrated in Figure 3. It must be noted that these paired measurements were in fact taken 15 minutes apart. It is plausible that some of this variation was due to true variations in access flow.

Variations in Qa were also recorded between the first and second measurements using the conductivity step (5.9% ± 17.4%) and the ultrasound dilution method (1.8% ± 15.2%), but the between-measurement changes were not different by method, although the study is likely underpowered to evaluate this. Again, this variation between the first and second measurements might be due to true variations in Qa; the measurements were taken approximately 1 hour apart.

The short-term variation (duplicate readings 5 minutes apart) of Qa measurement by the ultrasound method was 0.3% ± 9.2%. This SD is much smaller than that for the ultrasound dilution pairs taken 1 hour apart at 15.2%. This supports the concept that there was variability in access flow conditions over the 1-hour time between the measurements. Accepting this, the result would indicate that access flow measurements by the conductivity step were very similar to those given by the gold standard ultrasound dilution method.

The studies did show that conductivity step measurements in the setting of a dialysate sodium of 140 mmol/L can cause a significant rise in plasma sodium levels over dialysis (P < 0.001) (Figure 4). It is not possible to define the roles of the
conductivity step or the dialysate composition in this increment. This may be undesirable and contribute to extracellular fluid volume expansion and hypertension. A recent study by Manlucu et al. (12) had demonstrated the desirability of having a postdialysis sodium level less than the initial to increase salt removal and to reduce extracellular fluid volume. More work is necessary to determine the ideal dialysate sodium concentration and what conductivity step should be used.

Limitations to the studies relate mainly to the number of observations made. Although the measured results justify the conclusion that $Q_a$ measurement by conductivity step may be an acceptable alternative to ultrasound dilution methodology, one would have to accept that the study is likely underpowered to detect whether there are differences in test/retest results between the two methods. Furthermore, the study is underpowered to detect whether a 1- or 2-mS/cm step in conductivity would influence the difference between methods for $Q_a$ measurement. A further limitation is that pre- and postdialysis plasma sodium were not made at times when no conductivity steps were taken to see if we could separate the effect of the dialysate composition from the conductivity step methodology in causing the postdialysis plasma sodium rise.

Fresenius (www.fmg-ag.com) has incorporated conductivity cells and software into their 2008K machine that will measure $Q_a$ using EID. Lacson et al. (7) had reported on a clinical study involving 50 patients who had sequential $Q_a$ measurements by the Fresenius methodology using the Transonic ultrasound dilution as the reference measurement. Their results showed a significant linear correlation between the two test methods. A coefficient of variation for sequential measurements using the ultrasound dilution was 6.4% and for the EID method was 11.5%. These are probably similar to the 9.2% short-term variation of our ultrasound dilution method results. Thus, our results obtained under study rather than clinical conditions did resemble the Fresenius data. There are two major differences between the studies. The conductivity step method uses the immediate change in conductivity at the time of line reversal, whereas the EID-based measurements rely on two separate determinations of ionic dialysance obtained many minutes apart. Second, the EID-based and the conductivity step measurements correlate with blood water clearances, which have to be corrected to give $Q_a$. We measured hematocrit and total protein concentration for each subject and made the appropriate correction. Lacson et al. (7) applied a generic correction factor of 0.85 to represent the blood water fraction. The conciseness of the Fresenius results suggests that a standard correction factor may be all that is required. This possibility is worthy of further study.

Whittier and colleagues (8) prospectively evaluated hemodialysis access flow using Transonic ultrasound dilution and conductivity dialysance measurements in 48 patients. They also used the Fresenius software incorporated into the Fresenius 2008K machine. Their results were virtually identical to those of Lacson, which showed that access flow rates for ultrasound dilution and conductivity methods were comparable at access flow rates of 2000 ml/min or less, and that no single method tended to over- or underestimate flow compared with each other. Incidentally, the Whittier paper (8) made no mention of any whole blood correction factors. Furthermore, neither the Lacson nor the Whittier papers made any comment about sodium balance.

All three studies support the initial work by Mercadal (5) and Gotch (6) and indicate that $Q_a$ measurement can be done on the dialysate side using conductivity measurements. Because most dialysis machines now contain conductivity cells, the $Q_a$ measurement capability can be easily available and does not require the use of standalone expensive equipment. Further work regarding sodium balance is needed to ensure long-term safety with such technology and the ideal way to do blood water corrections should be considered.

**Disclosures**

None.

**References**