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Vascular Access as a Determinant of Adequacy of Dialysis

Andrew J. Cortez, William D. Paulson, and Steve J. Schwab

Vascular accesses consist of permanent arteriovenous (AV) accesses (autogenous fistulas and synthetic grafts) and venous accesses (central venous catheters [CVCs]). AV accesses have fewer complications than venous accesses, and are therefore the preferred hemodialysis access. An important additional issue is whether the type of access influences adequacy of dialysis (i.e. Kt/V). Key limiting factors in delivering adequate Kt/V are blood pump speed (Q_B), access recirculation, and treatment time. In general, AV accesses support higher Q_Bs with less negative inflow arterial pressures than CVCs. Well-functioning AV accesses are also less likely to exhibit recirculation. Nevertheless, recirculation commonly develops when AV accesses (usually grafts) develop stenosis with decreased access blood flow. Although extension of treatment time can offset the effects of reduced Q_B and recirculation, this is often impractical and poorly accepted by patients. In conclusion, AV accesses are superior to venous accesses because they are less prone to complications and are more likely to deliver prescribed Kt/V within prescribed treatment time.
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Hemodialysis was first introduced by Kolff as a therapy for renal failure in Nazi-occupied Holland during World War II.[1] By the end of the 1950s, the technique had proven its effectiveness as a life-sustaining procedure for acute renal failure. The concept of repetitive hemodialysis treatments for patients with chronic renal failure was tested in the 1960s and emerged as a viable therapy by 1970.[1] This development was followed by efforts to establish a quantitative dosing standard for renal replacement therapy as opposed to relying on subjective measures of therapy.

The National Cooperative Dialysis Study (NCDS) was commissioned by the National Institutes of Health in 1974 to address the issue of adequate hemodialysis dose.[2] In this multicenter clinical trial, a 2 × 2 design was used to determine the relative benefits of 2 levels of time-averaged urea concentration and 2 levels of dialysis treatment time (duration was used as a surrogate for middle molecule clearance). Gotch and Sargeant then retrospectively developed a mathematical model of urea clearance to interpret the results of the NCDS.[3] They represented the dose of dialysis during a treatment as the unitless quantity Kt/V, where K is urea clearance (mL/min), t is treatment time (min), and V is urea distribution volume (mL). Kt/V represents the total volume of urea cleared by the dialyzer normalized for the urea distribution volume (ie, body size). It subsequently was shown that Kt/V correlated with patient morbidity and mortality in the NCDS and other datasets.[4] Despite some debate, Kt/V subsequently became accepted as a measure of dialysis dose adequacy in the individual patient. A consensus gradually emerged that a Kt/V of 1.0 was a minimum threshold for adequate dialysis.

Subsequent to the NCDS, another National Institutes of Health–sponsored multicenter clinical trial (the 5-year Hemodialysis (HEMO) study) was undertaken to determine the optimum dose of hemodialysis.[5] This study indicated that the then current National Kidney Foundation Dialysis Outcome Quality Initiative (NKF-K/DOQI) hemodialysis goal of single-pool Kt/V of 1.3 appeared to be as beneficial as a higher value of 1.7. Thus, a single-pool Kt/V target of 1.3 currently is taken to indicate adequate hemodialysis when delivered 3 times per week. However, the use of Kt/V involves a number of assumptions. The least reliable is that the prescribed dialyzer blood flow (Q_B, which is driven by the dialysis machine blood pump) is reached and sustained throughout each session. The vascular access is a principal determinant of Q_B and therefore has a strong influence on the adequacy of dialysis.

Section of Nephrology, Hypertension, and Renal Transplantation, Department of Medicine, Medical College of Georgia, Augusta, GA.
Address reprint requests to Steve J. Schwab, MD, Chairperson, Department of Medicine, Medical College of Georgia, 1120 15th St, BIW 546, Augusta, GA 30912-2941. E-mail: sschwab@mcg.edu

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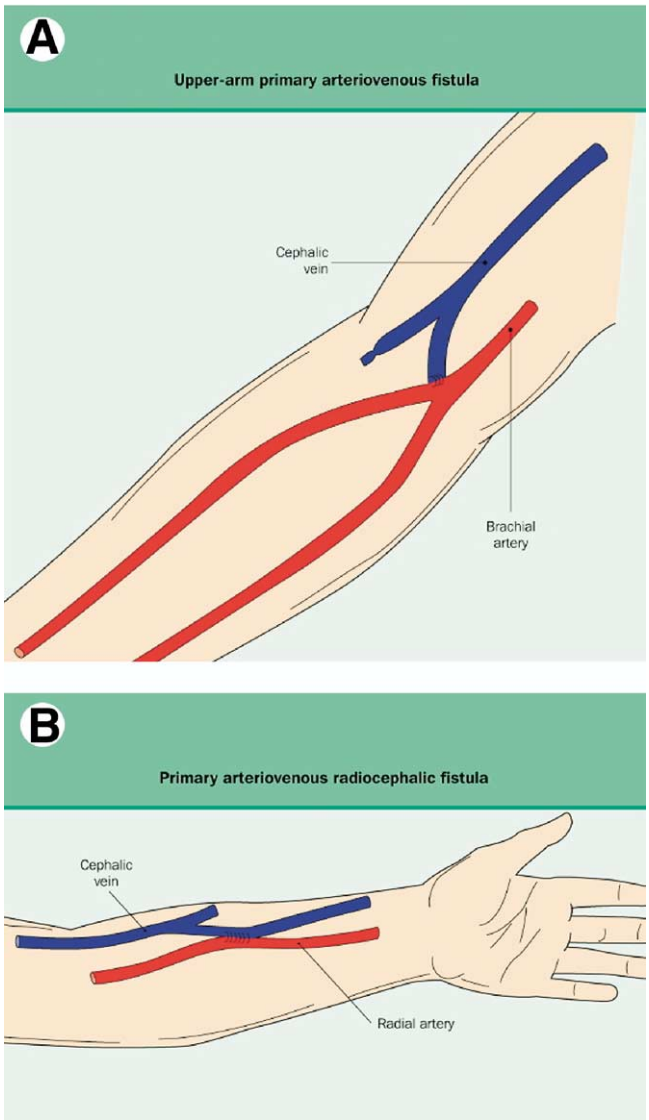

Figure 1 Examples of (A) brachiocephalic and (B) radiocephalic autogenous AV fistulas. (Color version of figure is available online.)

Hemodialysis Vascular Access

Vascular accesses may be divided into 2 categories: permanent arteriovenous (AV) accesses (autogenous fistulas [Fig 1] and synthetic grafts), and venous accesses (cuffed tunneled chronic central venous catheters [CVCs] [Fig 2] and uncuffed acute CVCs). In addition, CVCs with subcutaneous hemodialysis ports are now approved for use in the United States. Figure 3 shows sites and configurations of both common and rare AV accesses. Current NKF-K/DOQI Clinical Practice Guidelines recognize AV fistulas as the optimal vascular access.[6] Once established, fistulas have lower rates of thrombosis, infection, and abandonment than grafts, and are associated with lower mortality.[7,8,9,10] Young fistulas usually have lower blood flows than grafts, but this difference generally resolves as the luminal diameter gradually increases with time. Unfortunately, inadequate vasculature may force a patient to rely on a graft rather than a fistula.[11] Venous accesses have higher morbidities and mortalities than AV accesses. Consequently, the NKF-K/DOQI Guidelines discourage their use as a chronic access.[12]

Does the Type of Access Matter?

The urea clearance (K) and the urea distribution volume (V) theoretically are independent of vascular access type. Patients usually are provided large surface area dialyzers and high dialysate flow rates (eg, 800 mL/min), so that the limiting factors in achieving dialysis adequacy are treatment time and Q_B. This brings us to the central issue in this article: when considering adequacy of dialysis, does the type of vascular access matter? Is there a relation between vascular access and delivered Kt/V?

In considering this question, we should keep in mind that K depends on a number of variables, including the clearance capacity of the dialyzer (determined by surface area and permeability), Q_B, and dialysate flow. The surface area and permeability of current dialyzers are manufactured with good quality control. Also, most modern dialysis machines deliver accurate dialysate flows, and flow distribution abnormalities along dialyzer membranes have been largely corrected.

In contrast, inability to reach and sustain the prescribed Q_B from treatment to treatment is a common cause of low Kt/V. Another common cause is access recirculation. When access blood flow is less than Q_B, the inflow artery cannot supply enough blood to match the rate of blood uptake by the arterial needle of the dialysis circuit.[13] Consequently, dialyzed blood returning to the access through the venous needle recirculates back to the arterial needle. Low Q_B and recirculation both lower the delivered K.

The Q_B indicated on the dialysis machine usually overestimates the actual Q_B.[14,15,16] This overestimate is influenced strongly by the type and performance of vascular access. Q_B is varied by adjusting the dialysis machine roller pump speed. Increasing Q_B results in a more negative pressure in the arterial portion of the dialysis circuit (Fig 4). Depner et al[14] have shown that the discrepancy between the displayed Q_B and the ultrasonically measured value correlates with the subat-

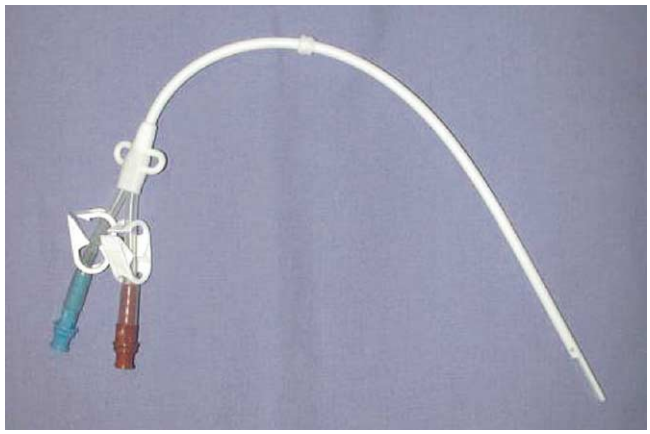

Figure 2 Example of cuffed CVC commonly used in chronic hemodialysis. (Color version of figure is available online.)

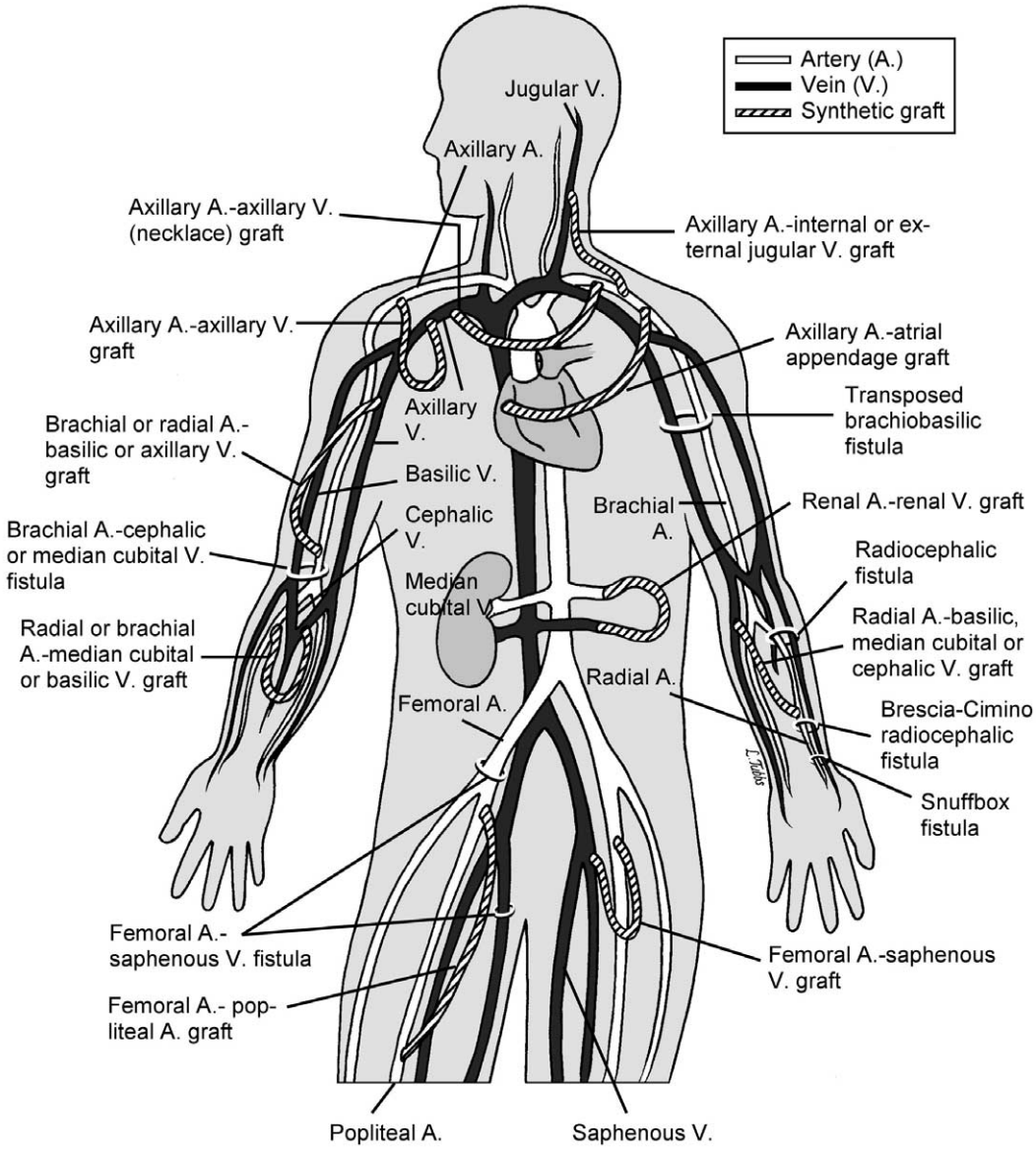

Figure 3 Sites and configurations of AV fistulas and synthetic grafts.[18]

mospheric pressure in the inflow blood tubing. At -200 mm Hg, the true Q_B averaged 8.5% less than the indicated flow, whereas at -400 mm Hg, the true Q_B was 33% less. The proposed mechanism for this discrepancy is negative pressure, which causes a decrease in the luminal cross-sectional area of the prepump roller segment of the inflow tubing (Fig 4).[17] Q_B and this inflow pressure are coupled variables. Thus, as inflow tubing pressure decreases to less than (becomes more negative than) -200 mm Hg, the Q_B indicated by the dialysis machine progressively overestimates delivered Q_B. This fundamental observation is true regardless of the type of vascular access.

CVCs

When using CVCs, the prepump inflow pressure is influenced by catheter length and luminal diameter as well as by the location of the catheter insertion. NKF-K/DOQI Guidelines recommend a CVC blood flow of at least 300 mL/min.[6,12] Poiseuille's Law for fully developed laminar flow in a rigid straight tube indicates that flow (Q) is determined by the following equation:

$$Q = \pi \Delta P D^4 / 128\ \mu L,$$

in which ΔP is the pressure drop along the length L of the tube, D is the luminal diameter, and μ is dynamic viscosity. Poiseuille's Law indicates that Q increases very rapidly as D increases.[19,20] Thus, it might seem logical to use large luminal diameters to ensure maximal Q_B. However, this approach is limited by the consideration that as the CVC luminal diameter becomes larger, the difficulty and risks associated with CVC insertion increases, and the likelihood of vein thrombosis increases because the CVC fills the vein lumen to a greater extent.[19,20]

It is important to appreciate that Poiseuille's Law assumes

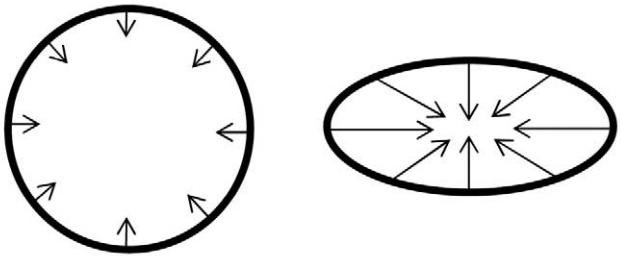

Figure 4 Distortion of lumen of prepump segment of dialysis tubing as pressure becomes increasingly negative (indicated by length of arrows). This distortion decreases the cross-sectional area of the lumen, resulting in higher flow resistance and decreased delivered blood pump speed (Q_B). Adapted from Depner et al.[14]

the tube is straight. CVCs, however, may bend into one or more curves depending on their insertion location, and these curves increase resistance to flow. For example, Oliver et al[21] have shown that flows in right internal jugular catheters are approximately 40% higher than in left internal jugular catheters. This may be owing to the less tortuous course of the right internal jugular vein. Moreover, when tunneling a cuffed CVC, it is important to ensure that the catheter makes a gentle curve without kinks as it travels from the exit site in the skin to the entrance to the central vein. In general, the fewer curves a CVC makes, the fewer the complications and the better the blood flow.

The location of the CVC tip influences catheter blood flow. The larger the blood vessel, the less likely the inflow to the CVC (ie, Q_B) will exceed the vessel's flow capacity. When this capacity is exceeded, dialyzed blood from the outflow lumen recirculates back to the inflow lumen of the catheter. Because all of cardiac output flows through the right atrium, right atrial CVCs are far less likely to exhibit recirculation than femoral CVCs.[21] In comparing recirculation in CVCs versus AV accesses, it is conceptually useful to consider the catheter lumens equivalent to the arterial and venous needles in the AV access, and the right atrium or central vein equivalent to the AV access.

In general, acute temporary CVCs do not perform as well as chronic tunneled cuffed CVCs because acute CVCs are optimized for rapid and easy bedside insertion.[19] Acute CVCs usually have smaller luminal diameters (allowing easy bedside guidewire insertion) with CVC tips in central (eg, iliac) veins rather than in the right atrium (negating the need for fluoroscopy during insertion). In contrast, cuffed tunneled CVCs have larger luminal diameters (requiring a peel-away sheath) and require fluoroscopy during right atrial placement.[19] Thus, dialysis efficiency is optimized by inserting the largest possible CVC via a straight route into the right atrium.

AV Access (Grafts and Fistulas)

In general, AV accesses support higher Q_Bs with less negative inflow arterial pressures than CVCs.[15] This is possible because AV access blood flows are generally 800 to 1,800 mL/min. Thus, a well-functioning AV access can supply flow far in excess of demands by dialysis machines. However, blood is pumped to and from the AV access through dialysis needles, and the needles have small luminal diameters with large flow resistances that decrease delivered Q_B. Sands et al[15] showed that 15-gauge needles provide an 8.4% lower Q_B than 14-gauge needles when the machine Q_B is set at 400 mL/min. With a 15-gauge needle, AV accesses often can yield inflow arterial pressures smaller (less negative) than -200 mm Hg at Q_Bs of 400 mL/min. Nevertheless, Q_Bs greater than 400 mL/min may require 14-gauge needles to avoid negative arterial pressures of greater than -200 to -250 mm Hg. Increasing the Q_B when arterial pressure already exceeds -200 mm Hg yields a further but limited increase in delivered Q_B.[17,19,21-23]

Machine limits on negative arterial pressure limit the maximal possible delivered Q_B.[17,23,24] When attempting to reach the prescribed Q_B, it is common practice to increase the machine-indicated Q_B gradually until arterial pressures approach -250 to -300 mm Hg. This is considerably less than the negative pressures (approximately -400 mm Hg) at which the prepump blood tubing may collapse (thereby possibly causing hemolysis).[14,25,26]

Clinical Practice

CVCs are the access of choice in acute settings, but also are used widely in chronic hemodialysis. Tunneled cuffed CVCs placed in the right atrium appear to have negligible recirculation and many are capable of sustaining Q_Bs of 350 mL/min or more.[27,28] There are multiple CVC types and configurations and each has advantages and disadvantages. In general, the larger the luminal diameter of the CVC the greater the dialysis efficiency, but also the greater the complications associated with insertion and use. Properly placed acute uncuffed CVCs often have recirculations of approximately 5% at their maximal blood flow (Q_B), and reach sustainable Q_Bs of 250 to 300 mL/min.[21] The insertion location and catheter characteristics influence performance. Short, 15-cm, acute femoral CVCs may reach recirculations of 30%.[23] Reversal of inflow and outflow lines is an all too common practice that is used to increase flow through a malfunctioning CVC.[21] Such reversal may increase recirculation to as high as 35%.[21,23,27]

AV accesses also can yield high levels of recirculation. For example, access stenosis may decrease access blood flow, so that Q_B exceeds access flow. As another example, if access anatomy is identified incorrectly, the arterial needle may be placed in the venous segment of the access, and the venous needle may be placed in the arterial segment.[29] The penalty for significant recirculation is commonly a decrease in Kt/V.[16,30]

Current NKF-K/DOQI Guidelines recommend monthly estimation of dialysis adequacy.[31] This approach is based on the assumption that monthly measurements provide a representative Kt/V. In reality, however, such measurements are snapshots in time that often are based on optimal treatment conditions.[32] These snapshots use optimal patient and staff adherence to the dialysis prescription with optimal Q_Bs and limited interruptions.[29,33] Thus, these snapshots are not representative of the usual delivered Kt/V. In our experience, treatment time is not increased routinely when frequent dialysis machine alarms

(with associated stopping or slowing of blood pump) cause a decrease in the average Q_B. A decreased Q_B and a decreased treatment time are the most important causes of under-dialysis.[29,33]

Patient adherence to prescribed treatment time is an important factor in attaining adequate dialysis. Arriving late or signing-off early are all too common occurrences in daily practice.[24,29,33] Time constraints of patients and dialysis centers permit little margin for error in the treatment schedule, and this is exacerbated by low dialyzer Q_B.[16] Patients often are unwilling to extend their treatments during inefficient sessions, and dialysis units may limit treatment times (eg, a maximum of 5 h).[4,24,34,35] Large patients may not be able to achieve treatment goals within practical time limits unless they have reliably high Q_Bs (which CVCs may not be able to provide). In our experience, recurring decreases in Q_B may decrease the dialysis dose up to 30% on less-optimal nonmodeling days. Also, a pilot study from our institution indicated that use of CVCs yielded 20% to 30% decreases in desired liters of blood processed per month.

Online Kt/V monitoring during each dialysis treatment provides a more representative measure of dialysis adequacy than the monthly determination.[36,37] In addition, it allows for immediate adjustment in the dialysis prescription so that the target Kt/V can be reached, and it provides a valuable teaching tool for patients.

Despite the various access-related factors that can decrease the Kt/V, adequacy goals, in principle, can be met by extending treatment time. In clinical practice, however, this is not generally practical in the United States. Patients (especially larger patients) may not reach their goal because they (and, to a lesser extent, the dialysis facility) may be unwilling to tolerate longer treatment times (4-6 h). In such situations, AV accesses are more likely to provide adequate dialysis within the practical time frame. We also must recognize that our patients' time is important to them and their families. Until studies show that slow-flow long-duration dialysis decreases morbidity and mortality, it seems our patients' wishes should be paramount. We should try to deliver an adequate dialysis treatment within a reasonable time frame.

Conclusion

In order, to reach goals of dialysis adequacy, we must provide a sufficient Q_B within the available treatment time. To answer our earlier question as to whether the type of access matters when attempting to deliver adequate dialysis, the answer is that it does matter. Nevertheless, despite the many advantages provided by AV accesses over CVCs, the majority of patients do achieve adequate Kt/V with both types of vascular access.[38,39] Results of the HEMO Study do not support exceeding the currently recommended Kt/V.[5] It must be cautioned, however, that patients in the HEMO Study reliably achieved their dialysis prescription at each session. Larger patients may require higher Q_Bs (which are less reliably delivered by CVCs) or may require treatments of 5 hours or more.

The purpose of a higher Q_B is to provide an adequate Kt/V within a tolerable treatment time, thereby increasing patient adherence with the dialysis prescription. Moreover, higher Q_Bs may allow shorter treatments, thereby decreasing the cost/treatment by increasing the number of shifts per day. Just as we maximize other aspects of dialysis, we must strive to optimize Q_B, especially in larger patients who achieve a marginal Kt/V. AV accesses are most likely to allow us to reach these goals. Patients who move from AV to venous access may require increased treatment times. Online Kt/V monitoring allows us to measure adequacy during every treatment so that we can make real-time, not retrospective, changes in prescription. This is especially useful in patients with unreliable accesses. Finally, we should recognize that increased treatment time is the only variable that will nearly always allow us to attain an adequate Kt/V.

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