Preservation of Vascular Access

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ABSTRACT
Preservation of vascular access is critical in the long-term successful management of hemodialysis pa-
tients. Dialysis access abnormalities are the most common cause of hospitalization in this patient
group, and access problems can increase the morbidity and cost involved in the care of these patients.
Native fistulas are preferable to synthetic grafts because of longer survival and a lower complication
rate. Venous outflow stenosis is the most common site of obstruction in a failing graft. The pathophysi-
ology of access failure is poorly understood, but it seems to be related to intimal hyperplasia in the
native vessel downstream from the anastomosis. The stimulation of local growth factors by needle punc-
ture may also play a role. An assessment of access adequacy includes careful physical examination,
laboratory evaluation, and ultimately, angiography. Measurements of recirculation and venous pressure are commonly used to screen for access dysfunction, and their appropriate use will lower the incidence of graft loss in dialysis units. Treatment is usually either angioplasty or surgery, with some centers having success with thrombolytic therapy. New techniques such as atherectomy and stent placement may prove to be beneficial, but this requires further study.

Key Words: Dialysis access, access failure, ESRD, graft thrombosis

The patient is a 45-yr-old, 77-kg woman with ESRD secondary to hypertension. In March 1990, she had a right subclavian catheter and a left arteriovenous (AV) fistula placed and began hemodialysis (HD). In April 1990, the fistula failed and a left forearm synthetic graft was placed. This graft clotted in September 1990, and after unsuccessful declotting, a left subclavian catheter was inserted. A right arm angiogram in October 1990 revealed subclavian stenosis, and after successful angioplasty, a right forearm graft as well as a left internal jugular percutaneous was placed. An angiogram of the left arm venous system was not performed. The right forearm access was used in November 1990 and then clotted in August and December 1991. After the declotting in December 1991, recirculation studies were performed with a two-needle recirculation of 5.6% and a three-needle value of 15% (simultaneously) at blood flows of 450 mL/min. Dialysis time was 2.5 h. Venous pressures (VP) were 250 to 350 mm Hg and post/pre-BUN ratios were variable but ranged from 0.3 to 0.4 at blood flows of 450 mL/min. The ratio did increase to more than 0.5 before the patient's last two clotting episodes. Another right arm angiogram was performed and showed native venous occlusion just downstream to the right lower arm graft anastomosis in the basilic vein with retrograde flow down a native vein and ultimately filling of a patent subclavian vein. The lesion was not amenable to angioplasty, and the graft was ultimately revised.

BACKGROUND

Dialysis access problems are the most common cause for hospitalization in dialysis patients. Carlson et al. in 1984 reviewed the charts of 946 dialysis patients in the upper-midwestern United States to examine the frequency, duration, and cause for hospitalization (1). They found that 25% of hospitalization episodes and 21% of the days hospitalized were related to access problems. HD access malfunction accounted for 70% of the access admissions. Preservation of vascular access is clearly important in limiting the morbidity and cost involved in the care of ESRD patients. In this review, the types of permanent vascular access, their complications, the pathophysiology of access failure, an assessment of access adequacy, and the treatment of access dysfunction will be examined.

CLINICAL FEATURES

Every potential dialysis patient has a limited number of possible dialysis access sites. Given this limited number of sites, the length of survival of each access is critical. As the population beginning dialysis ages, the number of potential access sites diminishes secondary to atherosclerosis and the loss of superficial veins; therefore, it becomes more difficult to place an AV fistula. Numerous reviews have demonstrated a survival advantage of AV fistulas over synthetic polytetrafluoroethylene (PTFE) grafts (2-4). Zibari et al. found the mean patency rate to be significantly greater in native versus PTFE accesses (2.85 versus 1.75 yr) (2). They also demonstrated that the incidence of thrombosis was much lower in native versus synthetic grafts (11 versus 64%). Kherbakian et al. found a 50% synthetic graft survival at 36 months, but a 64% survival of native fistulas in a comparison of 100 native versus synthetic grafts (3). Rizutti et al. reported a 50% patency rate at 36 months in a series of 189 PTFE grafts in 131 patients over 7 yr (5). These series demonstrate that the incidence of early (<30 days) thrombosis is greater in fistulas compared with grafts because of technical failures (inadequate inflow), but beyond that point, the total number of thromboses is clearly greater in synthetic grafts (2-4). Other complications of vascular access include infection, pseudoaneurysms, and arterial steal. These are all more common in synthetic grafts and lead to decreased graft survival (Table 1) (2-4). There are a number of anatomic abnormalities that account for access failure, and the location of the abnormality greatly affects management. Obstruction to venous outflow anywhere along the venous return accounts for 85% of these abnormalities (6). The obstruction typically occurs within 5 to 6 cm of
the AV anastomosis in a fistula and within 2 to 3 cm of the venous anastomosis of a graft, but may be more proximal in 15 to 20% of the cases. Areas of anatomic narrowing that may become hemodynamically significant at high-flow rates include the axillary vein, the cephalic vein at the elbow, and the subclavian vein between the clavicle and the first rib. In addition, sites of hypertrophied venous valves may also account for proximal stenoses and are located in both the axillary and subclavian veins. Perhaps most importantly, sites of intimal trauma from old temporary catheters may lead to proximal stenoses in those central veins. This syndrome of subclavian stenosis is well documented in the literature (7). Schwab et al. performed 50 venograms in 47 dialysis patients seen for thrombosis, arm edema, poor access blood flow, or increased access venous pressures (7). They found subclavian stenosis in 12 patients. Prior ipsilateral subclavian vein cannulations, longer catheter presence, and increased number of catheters were all more common in the group with subclavian stenosis (7). Arterial stenosis is uncommon and accounts for only 5% of the documented anatomic abnormalities causing access failure, with a combination of venous and arterial stenoses present in 10% of cases (6). With aggressive efforts, most thrombotic events will be found to have an anatomic cause; occasionally, however, there is no documented abnormality found and the clotting event is attributed to hypotension (8).

PATHOPHYSIOLOGY OF ACCESS FAILURE

The central factors important in determining access survival and longevity are not well understood. Several studies have attempted to examine this issue. Zamora et al. (9) placed femoral AV PTFE grafts in 10 dogs and examined their hemodynamic and morphologic changes. Cardiac output increased, and peripheral vascular resistance decreased. Intimal hyperplasia was found most prominently in the proximal vein near the venous anastomosis. The venous pressures in the graft were close to normal, despite high flow, suggesting that it was neither venous hypertension nor transmission of arterial pulsatility that led to intimal hyperplasia. They postulated that the proximal vein’s greatly increased flow is turbulent and that this might generate shear stress on the endothelium, leading to intimal hyperplasia (9). Swedberg et al. obtained native and PTFE graft vein samples of occluded or severely narrowed segments in five patients and compared them with the normal PTFE vein anastomoses obtained from two patients for other reasons (4). Lesions were evaluated by light microscopy, electron microscopy, and immunocytochemistry. In those failed grafts, the lumen was occluded by a proliferative thickening of the intimal layer in the native vein just downstream from the venous anastomosis. The cell type was found to be smooth muscle cells. They did not find any luminal fibrin or macroscopic thrombus, nor did they note any lipid, foam cells, or macrophages. This suggested that the predominant lesion was smooth muscle cell hyperplasia. They postulated several different mechanisms, including one similar to that of Zamora et al. (turbulent flow leading to increased shear stress leading to intimal hyperplasia). Another theory suggested that puncture of the graft with a needle stimulates platelet aggregation and release of platelet-derived growth factors at the puncture site, which stimulates smooth muscle cell proliferation and leads to luminal narrowing downstream from the anastomosis. This mechanism would explain the different locations of stenosis in native versus synthetic fistulas, because the needle placement relative to the venous anastomosis is different in the two types of access (4).

ASSESSMENT OF ACCESS ADEQUACY

The nephrologist and technical staff must be ever vigilant to the clues of access dysfunction (Table 2). Venous stenosis must be considered when delayed clotting at puncture sites occurs in a patient on a stable anticoagulation regime. Other signs include pseudoaneurysm formation; excessive fluid loss on dialysis (due to obligate increased transmembrane pressure on nonvolumetric machines); swelling and venous pulsations of the distal extremity, chest, or neck; or a change in the access thrill to a pulsation. Arterial stenosis should be considered when inadequate flow rates occur, when inflow lines collapse, and when there is increased negative arterial pressure during dialysis runs. Laboratory tests suggestive of access malfunction include increased recirculation (RE), increased VP, and increases in the post-BUN to pre-BUN ratio.

Local RE occurs when dialyzed blood being returned through the distal/venous end of the access mixes with blood being drawn into the proximal/arterial end of the dialyzer circuit. It is calculated by the formula \( \frac{(P - A)}{(P - V)} \) where P is the simulta-

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<th>Sign of Access Dysfunction</th>
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<td>Prolonged Bleeding from Puncture Sites</td>
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<td>Access Extremity Edema</td>
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<td>Unexpected Excess Fluid Loss on Dialysis</td>
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<td>Change in Character of Thrill or Bruit</td>
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<td>Decreased Dialysis Efficiency</td>
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<td>Aneurysm and Pseudoaneurysm Formation</td>
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<td>Increased Venous Pressure</td>
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<td>Increased Recirculation</td>
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<td>Decreased Dialysis Efficiency (Measured Kt/V)</td>
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<td>Without Change in Prescription</td>
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TABLE 2. Signs of Access Dysfunction
neous BUN from the peripheral circulation, A is the BUN from the arterial port, and V is the BUN from the venous port. When RE is zero, the peripheral and arterial samples are identical. RE is affected by needle placement, location of access, and blood flow. As blood flow increases, RE increases. Windus et al. (10) performed standard RE studies in 103 patients over 14 months. Indications included recent access surgery, routine screening, and worsened dialysis efficiency. The patients were on high-flux HD with blood flows averaging near 400 mL/min. Samples were obtained within the first 15 min of dialysis. Ninety-six percent of patients with RE > 15% had synthetic grafts. Those patients who had two consecutive RE > 15% underwent angiography. Twenty-two of 25 patients agreed to angiography, and 18 of 22 had significant abnormalities. Seventeen of 18 patients were treated in some fashion for their stenoses, with a mean pretreatment RE of 33%, which decreased to 11% after treatment (10).

The “three-needle technique” has been the standard method by which to measure RE and is done early in the dialysis procedure in order to maximize the concentration differences between the samples. The peripheral sample is obtained by venipuncture of the opposite arm. As RE measurements have become more routine, a different technique has been developed in order to save patients a peripheral venipuncture. The “two-needle technique” has been used by some centers; in this method, the peripheral sample is obtained by turning the blood pump down to 50 mL/min or less and withdrawing blood from the arterial port, thus simulating a peripheral sample. In a variant of this method, called the stop-flow technique, the blood pump is turned off completely and the arterial line is clamped beyond the access port. The line is then flushed with saline before the “peripheral” sample is obtained. Several studies have documented that the “two-needle technique” consistently underestimates the “3-needle technique”. Sherman and Levy (11) compared both methods in 15 patients with RE > 15% by the standard method. Eight patients had native fistulas, and seven had synthetic grafts. All patients were on standard dialysis with blood flows of 300 mL/min, and samples were obtained after at least 1 h of dialysis. Five patients without RE were also studied. Although there was a good correlation between the two methods (r = 0.77), and two-needle method consistently underestimated the standard method (mean RE, 15.2 versus 27.6). Even if one decreased the normal cutoff from 15 to 7% by the two-needle method, 8 of 26 studies would have missed significant RE > 15% by the standard method. The underestimation of RE was more evident in native fistulas than in synthetic grafts. Clearly, recirculated blood is returned through the arterial needle, which affects the interpretation of the “peripheral” sample in this technique. The authors concluded that the two-needle method was an inadequate screening test (11). More recent data from Depner et al. (12) suggest, however, that the true peripheral sample may overestimate the BUN. They found that from 60 to 120 min into dialysis the peripheral BUN was statistically greater than the BUN obtained from the arterial side of the AV graft when occluded or free flowing. Their interpretation of these results was that the contralateral arm venous BUN was higher because the blood being sampled was dialyzed at an earlier time (and therefore has a higher BUN) and that slower flow through the venous system might allow for more complete equilibration of urea between compartments (12). In another study that compared RE methods, Emoven et al. (13) studied the stop-flow technique, the contralateral arm venipuncture technique, and the stop-dialysis technique. The stop-dialysis technique stops dialysate flow and transmembrane pressure but continues blood flow. They found that there was no difference in RE among the three methods when done at 30 min and that RE increased in each method by 90 min, with the greatest increment in the contralateral arm venipuncture method (13). Collins et al. not only demonstrated the previously mentioned findings of the blood flow, time, and method dependence of RE, but also showed that access location affected RE as the blood flow was increased (14). In their study, when the blood flow was increased from 300 to 400 mL/min, there was a significant increase in RE in both radial fistulas and brachial AV grafts, but not in upper arm grafts. They performed angigrams on patients with RE > 15% and found 58% true positives and 42% false positives at 20% < RE < 30%. As RE was increased, the true-positive rate increased, but at RE values of 15 to 19%, there was only a 20% true-positive rate (14). A separate confounding factor in measuring access RE has recently been noted. Cardiopulmonary RE describes a parallel blood circuit to the systemic tissue compartment consisting of the extracorporeal circuit and the peripheral access. Blood returning to the heart from this parallel circuit (dialyzed blood) mixes with blood returning from the systemic tissue compartment. This phenomenon may account for a lower BUN measured in dialyzer "arterial" blood and may as a result lead to overestimation of access RE (15). In summary: (1) RE measurements should be done within the first 30 min of dialysis; (2) when done at 30 min, the method used does not appear to matter and should be selected on the basis of the skill and comfort of the person doing the study; (3) RE > 15% for blood flows of 300 mL/min and RE > 20% for blood flows of 400 mL/min or more should prompt angiography.

Venous pressures should also be assessed in patients with suspected access dysfunction. Schwab et
al. measured VP in all of their chronic HD patients over a 2.5-yr period. VP was measured at blood flows of 200 to 225 mL/min during the first 30 min of treatment. Patients with VP > 150 mm Hg for three consecutive readings were offered fistulograms. Seventy-three patients were found to have elevated VP, and 58 agreed to further study. Fifty of 58 had stenoses on venography. Of the eight patients without stenoses, five ultimately normalized their VP. Thirteen of 15 patients who refused venography had subsequent thromboses, and 6 of these patients required a new access. One hundred forty-three patients had normal VP throughout the study, and 14 of these patients were randomly selected for angiography. One (7%) of 14 had a venous stenosis. They calculated a specificity of 93% and a sensitivity of 86% for VP > 150 mm Hg. Their access replacement per patient year decreased from 0.26 to 0.07 by this screening and interventional approach (16). Unfortunately, VP varies with the type of access, its location, and flow. At high blood flows, VP is not a useful measurement in terms of predicting access failure; Windus et al. demonstrated this in their study of VP and RE at a blood flow of 400 mL/min in which VP was not correlated with RE (10). Schwab et al., however, found VP to be more sensitive than RE > 15% for patients on conventional HD for detecting anatomic abnormalities (17).

Kinetic modeling is now commonly used to help assess dialysis efficiency. A fall in a patient’s measured Kt/V or an increase in the post/pre-BUN ratio that occurs without an obvious explanation may also be a sign of access dysfunction because dialysis efficiency will fall as RE increases.

RE studies and VP measurements provide the clinician with clues to access dysfunction; however, angiography is required for defining anatomy and planning rational therapy. In order to visualize both the arterial and venous limbs of the access, a blood pressure cuff needs to be inflated proximal to the anastomosis during the injection. Cine pictures are obtained with the hand rotated for multiple views. The anastomosis should be carefully examined at the end of an injection with the cuff deflated to evaluate the speed of fistula flow. Imaging of the high proximal veins is also necessary to rule out proximal stenoses. Pressure gradients should be measured across the anastomosis and any stenoses. A gradient greater than 20 mm Hg occurring abruptly is consistent with a significant lesion (18).

TREATMENT OF ACCESS DYSFUNCTION

The treatment of access dysfunction requires a combined medical, surgical, and radiologic approach. The primary nonsurgical therapy is angioplasty. Success is partially operator and technique dependent.

The basic approach requires the use of balloons 20 to 30% larger than the normal adjacent vein for the treatment of venous stenoses. Up to 15 atm of pressure are generated, and multiple brief inflations are performed. For arterial and anastomotic lesions, smaller balloons are used. Any dilation may be painful and requires local anesthesia. In addition, significant vasospasm may occur, which can be resistant to most therapies. Patients are typically heparinized during the procedure. Some radiologists directly enter the graft, whereas others use a femoral approach. The procedure is generally done in an outpatient setting (18). Glanz et al. (19) reported their experience with 141 percutaneous transluminal angioplasty (PTA) procedures in 95 patients over 7 yr. Indications for angiography included graft thrombosis. RE, high VP, unilateral arm edema, and aneurysms. Sixty percent of the patients who initially underwent angiography were not felt to have lesions amenable to PTA. No attempts were made to dilate intra graft stenoses. Lesions longer than 4 cm were treated surgically. One hundred twelve PTA were done in PTFE grafts, and 29 were done in native fistulas. Ninety-three of 141 stenoses were graft anastomotic venostenoses. The initial success rate for angioplastied lesions was on the order of 80% with a 1-yr patency of approximately 45 to 50%. There were nine complications (6%) including six graft thromboses within 48 hours and three venous ruptures. No patient required a transfusion or emergency surgery (19). These results are roughly comparable to those of other authors.

The mechanism of PTA as determined by an intravascular ultrasound study by Davidson et al. includes either vessel stretch or recoil (20). Stretch implies that the vessel lumen stays as open as the balloon used, and recoil means the vessel lumen collapses to significantly less than its initially dilated size. Plaque dissection can occur with either vessel stretch or recoil and occurred in 42% of the total cases. The authors studied 38 consecutive PTA in venous stenoses and used intravascular ultrasound to determine vessel diameter, cross-sectional area, plaque composition, shape, and mechanism of PTA. The vast majority of plaques were soft and eccentric. Elastic recoil occurred in 64% of central vein lesions, whereas vessel stretch occurred in 63% of brachial vein lesions, with a similar incidence of dissection in both groups. They also found residual thrombus not detected by angiography. Unfortunately, sufficient data were not provided to correlate restenosis rate or PTA failure with the mechanism of PTA. The comparison of PTA versus surgery for comparable lesions has not been addressed in any large, prospective, randomized study, although there have been several small studies with mixed results. Clearly, the advantages of PTA include its ability to prolong access life and spare alternative sites, the opportunity to
assess the vascular anatomy and treat the lesion in one sitting, the availability of the access for use immediately postprocedure, and its relative lack of morbidity.

Thrombolytic therapy was attempted in the mid-1980s as an alternative medical treatment of acute thrombosis. Initial studies reported high complication rates, with most patients developing significant postprocedure bleeding. Bookstein et al. reported successful thrombolysis and fewer complications with a modification they termed “pulsed-spray pharmacomechanical thrombolysis” (21). This technique involves the placement of two special catheters with multiple side holes into the thrombus, oriented in opposite directions. Urokinase is then injected in small pulses as the catheters are advanced and withdrawn. Patients were also systemically heparinized and received 250,000 to 500,000 U of urokinase. They used this technique in 41 patients with 47 thrombi, including 29 patients with PTFE grafts. They reported a 97.9% success rate with the mean time to total lysis of 63 min. Their complications included 3 of 47 patients with possible embolic events that resolved and three hemorrhagic complications. They concluded that it was a more effective therapy than other thrombolytic methods (21). The advantages and disadvantages of the various therapeutic approaches to access dysfunction are summarized in Table 3.

Anticoagulants and antiplatelet agents have been used in patients with recurrent graft thrombosis on the basis of a rationale similar to their use in patients with peripheral vascular and coronary grafts. Several issues should be addressed before the institution of these agents in a dialysis patient. An anatomic cause for thrombosis must always be ruled out as the explanation for repeated thrombosis before the institution of anticoagulation, because in most instances, a cause for graft thrombosis can be identified (8). In addition, a hypercoagulable state should be eliminated as a contributing factor to thrombosis in patients with systemic lupus erythematosus. There are no prospective, randomized studies to demonstrate a beneficial effect of coumadin in preventing graft thrombosis. Old studies documented a benefit of aspirin and sulfonpyrazone in preventing thrombosis in external AV shunts. There have not been any recent studies that have identified a benefit to the use of antiplatelet agents without the price of significant bleeding complications in patients with synthetic or native fistulas. Newer techniques that may be useful in the near future for better diagnosis and treatment of graft thrombosis include intravascular stents, angiography, and directional atherectomy.

CONCLUSIONS

1. Vascular access malfunction and complications are a major cause of morbidity and cost in the care of dialysis patients. (2) Native fistulas are preferable to synthetic grafts. (3) Venous outflow stenosis is the most common anatomic cause of graft dysfunction, but central venous stenosis should always be ruled out in the evaluation of a poorly functioning graft. (4) Intimal hyperplasia is the most common finding in obstructed grafts. (5) RE is affected by access location, type, needle placement, blood flow, method, and time of the study. The three-needle RE technique has been the gold standard screening method for abnormal RE, but more recent data suggest that the stop-flow or stop-dialysis technique is equivalent when done at 30 min and is more convenient. RE studies should be performed at 30 min into the dialysis. RE > 15% in patients on conventional HD (blood flow, 300 mL/min) should prompt angiography. RE > 20% warrants angiography for patients on high-flux HD (blood flow, ≥400 mL/min). However, these threshold values have not been firmly established in a prospective study with all patients undergoing angiography. (6) VP > 150 mm Hg measured at blood flows of 200 to 250 mL/min warrant angiography, but the test is not predictive at higher

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<th>TABLE 3. Therapeutic approaches to access dysfunction</th>
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<td><strong>Angioplasty</strong></td>
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<tr>
<td>Wide availability</td>
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<td>Access usable immediately</td>
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<td>Sparing of alternative sites</td>
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<td>Stenosis may recur with frequency on the basis of location</td>
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blood flows. (7) The ideal frequency of screening is not determined, but all patients with graft dysfunction should undergo angiography. Units that do have a screening program have reported a decrease in graft thrombosis. (8) Therapy for access dysfunction includes angioplasty and surgery. Routine thrombolytic therapy for acutely clotted grafts is not indicated unless done in a center with expertise in this area. Several new methods that may be useful in the management and treatment of access failure include atherectomy, angiography, intravascular stents, and intravascular ultrasound. There is no solid proof of the benefit of anticoagulants and antiplatelet agents in recurrent clotted grafts, and side effects are common.

ACKNOWLEDGMENTS

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REFERENCES