The Arteriovenous Fistula

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The ground-breaking article by Brescia and Cimino in 1966 (1) revolutionized the creation of the vascular access, and the Cimino fistula was soon used in almost all dialysis patients. Unfortunately, subsequent wide-spread use of PTFE grafts instead of AV fistulae occurred because of the ease of the surgical technique, the immediate availability of the graft for puncture, the need of high blood flow for high-efficiency, short-duration hemodialysis sessions, and because of financial disincentives against the AV fistula. PTFE grafts currently account for 80% of primary vascular accesses created in the United States (2,3), but they are less frequently used in other countries. It has been increasingly recognized that outcomes of PTFE grafts are poorer. In the DOQI guidelines (4), this has led to the recommendation that AV fistulae should be the first option; however, this advice has not been followed uniformly. One impediment may be the astonishingly high rate of primary failures of AV fistulae, up to 50% in some centers (4). The DOPPS study (Figure 1) documented substantial differences between survival of PTFE grafts and AV fistulae and differences of survival of AV fistulae between the United States and other countries (3). On the basis of our experience, we are of the opinion that primary failure rates can be substantially improved by attention to small but important details of surgical technique. The DOQI guidelines state that AV fistulae are feasible only in 50% of the patients, but we (5) and others (6) found that construction of native AV fistulae is feasible in up to 90%.

It is the purpose of this article (a) to provide some insights into the fascinating cellular biology and pathophysiology underlying the vascular adaptation to the creation of an AV fistula and (b) to describe some small, often neglected, but important technical details that determine the success of the procedure. It is the intention to improve results and to influence patterns of practice.

Vascular Remodeling and Adaptation to High Flow

Wedge and Cimino (7) measured flow rates in the radial artery before and immediately subsequent to the creation of an end-to-side fistula. Flow increased from 21.6 ± 20.8 ml/min to 208 ± 175 ml/min immediately after operation. In well-developed fistulae, flow rates may ultimately reach values of 600 to 1200 ml/min.

Flow increases as a result of both vasodilation and vascular remodeling. The latter has been studied using echo-tracking techniques (8). It was found that the diameter of the proximal antecubital vein increased progressively while the intima media thickness remained unchanged. Venous dilation caused reduction of mean shear stress, which had returned to normal values by 3 mo. The venous limb of the AV fistula underwent eccentric hypertrophy as documented by increased wall cross-sectional area. In parallel, remodeling of the radial artery was seen without arterial hypertrophy, despite a marked increase in diameter and blood flow (9).

The changes in blood flow after creation of an AV fistula initiate compensatory responses that have been elegantly elucidated in experimental models (10). Apart from primarily NO-mediated vasodilation, adaptive remodeling of the vessel wall is induced by reorganization of cellular and extracellular components, ultimately altering wall geometry. Elevated flow after creation of an AV fistula enlarges the arterial diameter (10). Kamiya and Togawa (11) documented that after creation of a carotid to jugular anastomosis the flow-loaded artery enlarged until wall shear stress had returned to baseline values. This response usually occurred rapidly, but when extremely high shear stress was induced, it required up to 6 mo (12), for example in the monkey iliac artery subjected to a 10-fold increase of flow.

Endothelial cells play a central role in adaptive remodeling (13). Shear stress, i.e., the frictional force generated by blood flow, acts on the apical cell surface to deform the cell in the direction of blood flow, thus eliciting rapid cytoskeletal remodeling and activating signaling cascades with the consequent acute release of nitric oxide (NO) and prostacyclin followed by activation of transcription factors, including NF-κB, c-fos, c-jun, and SP-1. The mediators of the adaptive response include integrins, focal adhesion–associated proteins, and stretch-sensitive calcium channels. The crucial importance of endothelial cells is illustrated by the observation (14) that de-endothelialization eliminates the dilation resulting from an increase of flow. Acute flow-induced endothelial release of nitric oxide (NO) (15) as well as increased vessel wall cGMP content (16) have been documented in high flow models. Inhibition of NO by L-NAME interfered with flow-induced vascular enlargement (17).
The first step of remodeling involves controlled removal of preexistent vessel wall constituents. The arterial wall of an AV fistula exhibits early tears and fragmentation of the internal elastic lamina (18) and enlarged fenestrae (19), increasing arterial distensibility. The loss of the internal elastic lamina results from degradation by metalloproteinases, which are released from endothelial cells (20). A role for oxidative stress is suggested by the observation that endothelial cells of flow-loaded carotid arteries stain positive for nitrotyrosine, which is indicative of the presence of peroxynitrite (21), and this is abrogated by administration of L-NAME. The urokinase type of plasmin activator is also upregulated. This observation is important, because the plasminogen-plasmin system activates pro-metalloproteinases. It is therefore not surprising that non-selective inhibitors of metalloproteinases diminish flow-mediated arterial enlargement in a rat AV fistula model (22).

The involvement of the above systems raises the issue whether remodeling is normal or not in uremia. It is well known that generation of NO is reduced in uremia (22), and numerous specific abnormalities have been described in endothelial cell monolayer cultures (HUVEC) exposed to uremic serum: increased ELAM-1 and VCAM expression, increased presence of von Willebrand factor on the extracellular matrix (23), abnormal cell morphology, accelerated growth, and increased expression of tissue factor mRNA (24). Platelet deposition on extracellular matrix, which had been synthesized in the presence of uremic serum, is also increased. Interestingly an antibody to human tissue factor prevented the increase in platelet deposition observed on “uremic” extracellular matrix, a finding potentially relevant for the genesis of fistula stenoses. There are few formal analyses of vascular remodeling in uremia. Amann et al. (25) investigated remodeling in first-order branches of the mesenteric arteries exposed to high-flow or low-flow conditions. A highly significant increase in intimal thickness and intimal cell proliferation was noted in arteries of uremic compared with sham-operated animals when exposed to low-flow conditions, and this was abrogated by endothelin receptor antagonists. Under high-flow conditions, there was an increased number of PCNA-positive cells in the media, which again was abrogated by endothelin receptor antagonists. Obviously the responses of the intima to low flow and of the media to high flow are exaggerated. Against this background, it is remarkable that remodeling is largely appropriate in uremic patients (8,9).

Although not directly related to uremia, the processes underlying the development of stenoses in coronary saphenous vein grafts are of interest for understanding the development of fistula stenoses. It is thought that the changes provoking delayed stenoses are initiated during surgery and consist of denudation of the surface endothelial cells and insudation of granulocytes and monocytes with deposition of fibrin and thrombocyte-containing thrombi (26). CRP induces a pro-inflammatory phenotype of saphenous vein endothelial cells, which is reversible with the administration of endothelin receptor antagonists (27); of interest in view of the microinflammatory state of uremia and the role of endothelin receptor antagonists in experimental models of uremia (25). Interventions interfering with smooth muscle cell accumulation in the neointima further suggest a role of PDGF (28), angiotensin subtype AT-1 receptors (29), VEGF (30), and leptin (31), among others.

One important aspect in the evolution of the AV fistula of uremic patients is iatrogenic remodeling resulting from puncture of the AV fistula (32). Puncture displaces tissue, and the defect caused by the cannulation is replaced by a thrombus causing a slight increase in tissue mass. Even after healing, the edges of the puncture hole stay apart as shown by applying tattoo marks. This causes cumulative and progressive enlargement of the fistula depending on the number of punctures per unit area. This holds true if the cannula does not punch out tissue, but rather displaces tissue as seen with anti-coring cannulas, in which only the anterior half of such cannulas makes sharp cuts.
There are three options for cannulation (Figure 2); (a) the rope ladder pattern, (b) the area puncture pattern, and (c) the buttonhole pattern. In the rope ladder pattern, the punctures are regularly distributed along the entire length of the arterialized vein. In contrast, with the area puncture technique they are restricted to a small area. With the buttonhole technique, punctures are always performed through the exactly identical spot. This procedure displaces the thrombus undergoing organization; with time, a cylindrical scar wall is formed by the subcutaneous tissue and the venous wall.

With the rope ladder technique, the technique most frequently used, progressive dilation is induced along the entire length of the fistula. The worst scenario, i.e., circumscribed dilation, disruption of wall texture, and aneurysm formation, is usually a result of the area puncture technique. Such aneurysms are a composite of true and false aneurysms, intact parts of the wall alternating with scar tissue. Thinning of the wall of the vein causes progressive enlargement of the aneurysm, because wall stress increases progressively with increasing lumen diameter according to the Laplace law.

Evaluation of the Patient Before Surgery

It is important to instruct the patient in time and to motivate him that forearm veins are preserved. Puncture of a vein will leave a scar. When a fistula is created, such scars interfere with harmonious dilation and remodeling, cause turbulent flow, and predispose to stenosis. The veins of both arms, not only of the dominant arm, should remain untouched. For venipuncture, the veins of the dorsum of the hand should be used as an alternative. If difficulties arise, the hand should be warmed by a hot bath.

There is no consensus on the optimal timing of fistula surgery. The DOQUI guidelines recommend to establish vascular access when the serum creatinine concentration exceeds 4 mg/dl and the estimated GFR is ≤ 25 ml/min (4); at any rate, at least 3 to 4 mo before the scheduled beginning of dialysis. One serious impediment to timely creation of an AV fistula is the high rate of late referrals. Astor et al. (33) reported an impressive relation between timing of referral and the frequency of the initiation of dialysis treatment with central catheters for vascular access.

There has been much disagreement concerning the time when a fistula is ready for puncture. The DOQI (4) guidelines recommend puncture after 3 to 4 mo. This may be too restrictive. We measured fistula flow and found that there is an immediate tenfold and more increase of blood flow rate in the radial artery, which progressively increases during the first 10 d (7) and tapers off later on. This pattern is in line with the time course established in experimental studies (10). It is therefore the practice of the authors to puncture the fistula no sooner than 10 d after operation. We do not feel, however, that there is a rationale to consistently wait any longer unless there are specific circumstances such as skin lesions, infection, etc.

One decade ago (34), we and others started to use ultrasonography and Duplex sonography as valuable tools for assessing an established fistula. It has recently been recognized, however, that this technique is also valuable for preoperative assessment (Figure 3) that will provide useful information to the surgeon. The primary aim is the indication to the surgeon whether an anastomosis at the usual site above the wrist will be successful and whether a steal phenomenon is a likely outcome.

The lumen of the radial artery and the vein should be measured (Table 1). It is well known (35) that a large proportion of the blood flow in the fistula is provided by the ulnar artery via the palmar arch in up to one third of patients. The vasodilatory capacity of the palmar arch should therefore be assessed by calculating the resistance index from post-ischemic diastolic blood flow after fist clenching (Figure 3). This is an index of vascular reactivity to shear stress and of vascular reserve (36). Improvement of fistula outcome by preoperative assessment has been documented by Silva (37).

Creation of an AV fistula is an interdisciplinary task. In several countries, the task of coordination is delegated to a “fistula manager” who integrates the activities of the nephrologist, the ultrasonographer, the surgeon, or the interventional radiologist (38). The creation of fistulae should be delegated to a restricted number of dedicated surgeons, because good results are only achieved by surgeons with considerable expertise.

Surgical Technique

Today, the most frequently used technique of anastomosis is the (artery) side to (vein) end technique (in the following, the sequence is always artery to vein). Historically, the first anastomoses used (1) were side-to-side; later on, the end-to-end
technique was introduced, but today the side-to-end technique is the most commonly used approach. All three techniques have advantages and disadvantages.

**Side-to-Side Anastomosis.** The advantage of side-to-side anastomosis is its technical simplicity. It is also easy to test the distensibility of the proximal vein from the distal venous limb, particularly before it is ligated after creation of the anastomosis.

The disadvantage is a definite risk of venous hypertension with swelling of the hand. This can be avoided by ligation of the distal run-off vein, thus achieving a functional side-to-end anastomosis. The risk of venous hypertension in the distal venous limb is a particular problem of anastomoses in the elbow area.

**End-to-End Anastomosis.** The advantage of end-to-end anastomosis is that the fistula flow is limited, thus avoiding a hypercirculatory state. The disadvantage is that the anastomosis is technically more demanding. Problems particularly arise when there are large discrepancies of the luminal diameters between artery and vein. The most serious problem is, however, that ligation of the distal limb of the radial artery may predispose to ischemia of the hand. The risk is particularly high in elderly and diabetic patients. One of the maneuvers to optimize flow in a fistula is to avoid acute angles when the vessels are anastomosed, but when the radial artery is sclerosed acute angles cannot be consistently avoided with the end-to-end technique. A final disadvantage is that if venous thrombosis supervenes it will automatically extend into the arterial limb of the fistula.

**Side-to-End Anastomosis (Figure 4).** Although several techniques for anastomosis are available, the side-to-end anastomosis has deservedly become the most commonly used technique. It is absolutely indicated when artery and vein are far apart and must be brought closely together to create an anastomosis. The side-to-end technique will then allow anastomosis of the vessels without creating an acute angle. As a further advantage, a venous thrombosis will affect only the venous limb if it supervenes. If the fistula has to be revised, it is easy to create an anastomosis at a more proximal site.

This type of anastomosis poses a number of technical problems, detailed below, which probably explain the high primary malfunction rates reported in some series (39,40,41).

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**Figure 3.** Preoperative imaging of the radial artery by color flow duplex sonography. Doppler frequency spectrum shows a high-resistance flow with a clenched fist (typical tricyclic flow; left) and a low-resistance flow after release (right; typical low resistance with a RI 0.67 causing high diastolic flow).

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RI = \frac{\text{Maximal systolic flow velocity} - \text{Diastolic flow velocity}}{\text{Maximal systolic flow velocity}}
\]

**Figure 4.** (Panel A) B-mode sonogram showing a longitudinal section of an arteriovenous fistula created by anastomosing the cephalic vein (V) to the radial artery (A) at the wrist in a side-to-end fashion. (Panel B) With the same sectional view, Color Doppler sonography shows turbulent flow at the av anastomosis. The radial artery (A) is feeding the shunt vein (V).

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**Table 1.** Prediction of poor av-fistule outcome

- Arterial diameter < 1.5 mm (internal diameter)
- Venous diameter < 2.5 mm (using a tourniquet)
- Resistance index > 0.8 (after fist clenching)

*Preoperative imaging by Color Doppler sonography.*
Technical Points Determining Success

An AV fistula transforms a vein into a high-flow vessel. It is obvious that obstacles to flow must be avoided, e.g., kinking, acute angles, torque etc. They create turbulence, damage endothelial cells, and increase the risk of stenosis formation.

Transverse cutaneous incisions should be avoided, and we recommend longitudinal incisions if possible.

It has been recommended that veins should be mobilized so that they can be more easily adapted to the artery. This maneuver removes adventitial layer and vasa vasorum, thus predisposing to sclerosis and stenosis. There is no doubt that veins occasionally have to be used for transposition or superficialization, but this should not be done at the time of the first surgical intervention, when veins are still thin-walled. During a second procedure, when veins have matured and remodeled, they can be used. For this purpose, one can even create a temporary AV anastomosis; not to obtain a fistula for puncturing, but to create a vein suitable for later transposition or superficialization.

Endothelial cell damage from clamping thin-walled veins should be avoided to prevent late stenoses. Digital compression is safe for interruption of blood flow. Instead of forcefully dilating a spastic venous segment, e.g., with a Fogarty catheter, we enter a venous catheter from the distal limb of the veins and gently dilate the vein by injecting warm saline. If this is not sufficient, papavarin and nitroglycerin are administered locally.

The length of the arteriotomy must be guided by the angle that will be achieved when adapting the vein to the artery, as illustrated in Figure 5.

When mobilizing the vein, one should avoid torque, causing luminal narrowing, turbulence, and stenosis. Torque can be relieved if the vein is rotated in an antegrade direction as illustrated in Figure 6.

It is not advisable to ligate run-off veins at the time of first fistula surgery, because it is impossible to predict the future function of the fistula. Venous tissue may be extremely useful later on, e.g., for patches, grafts etc. If venous hypertension develops, veins can then be ligated in a targeted fashion.

An anastomosis at the level of the wrist is only sensible if both artery and vein are able to dilate (7) so as to accommodate an increase in blood flow by a factor of 20 to 100. Therefore the ultrasonographer and later the surgeon must evaluate the quality of the vessels, particularly of the artery. This is increasingly important because of the rising proportion of elderly and

Figure 5. (Panel A) The venous stump is cut in a direction parallel to the artery. If an acute angle is created between the artery and the vein, the result will be a long arteriotomy, exceeding by far the diameter of both artery and vein. (Panel B) If the vein approaches the artery at an angle of 90 degrees, the length of the anastomosis will equal the diameter of the vein.

Figure 6. (Panel A) If a distant vein is mobilized and the venous stump is made to meet the artery without any adaptation, there is a high risk that the vein undergoes torsion, which is often responsible for early failure and thrombosis. (Panel B) An outward directed rotation of the vein avoids this risk of torsion. Variable rotation between 60 and 120 degrees has to be imposed. The necessary degree of rotation can be estimated before starting to suture the anastomosis by injecting heparinized saline into the proximal stump of the vein after it has been compressed with the finger.
diabetic patients with sclerosed or calcified radial arteries. It is of interest that, in contrast to the carotid and coronary arteries, the radial artery rarely develops atherosclerotic plaques. When evaluating the arteries and veins during surgery, it is useful to do this with the aid of magnification glasses or even a microscope.

At the level of the wrist, the cephalic vein divides into a smaller branch that lies closer to the radial artery and a larger branch running across the dorsum of the hand. The smaller branch usually has a valve impeding venous run-off, and the lumen of the vessel is often unable to accommodate high flow rates. In view of such anatomy, it is often wise to select a more proximal site for anastomosis.

Selection of the vessels and the site for the anastomosis in some ways resembles chess; one must always anticipate the next two or three moves and must consider what possibilities remain after the fistula has potentially failed. Ideally, creation of the fistula should not preclude future corrective surgery.

In selecting the length of the anastomosis, one must consider the anticipated blood flow. The higher the site of anastomosis, the higher the future blood flow for any given area of the anastomosis, and the smaller should the anastomosis consequently be. We do not recommend anastomoses exceeding 6 mm in length at the level of the brachial artery.

The suture technique proposed by Tellis (42) is extremely useful and is suitable even for the very small vessels of children. The suture starts in the center of the back wall of the arteriotomy and venotomy. Suturing is continued passing the corners with excellent visualization throughout the procedure as shown in Figure 7.

When closing the skin, it is important to consider that the uremic patient, particularly the diabetic uremic patient, is at high risk of infection. We avoid sutures that act as a wick, use only subcutaneous sutures, and close the skin incision by adapting the edges with tapes.

By using the above strategies, we have managed to achieve a thrombosis rate of eight episodes per 100 patient-years (43), substantially below the DOQI target of 25 episodes per 100 patient-years for AV fistulae.

**Perioperative Management**

One has three anesthesia options: local anesthesia (infiltration), regional anesthesia (brachial plexus block), or general anesthesia.

Local anesthesia is simple and commonly well tolerated, but it has the disadvantage of causing local edema thus, increasing the risk of infection. Furthermore, arterial and venous spasms are more common and more severe than with regional or general anesthesia.

Regional anesthesia by infiltration of the brachial or axillary plexus has the advantage of significantly reducing the frequency of vascular spasms. It also allows easy surgery-site change, e.g. from wrist to elbow. The disadvantage is that an experienced anesthesiologist is required.

General anesthesia is required when time-consuming operations in more proximal parts of the arm are anticipated or when patients have severe comorbid conditions (44).

We advise against routine perioperative use of antibiotics. In diabetic patients and other patients at high risk of bacterial infection, however, a single dose of an antibiotic, preferably an aminoglycoside with dose adjustment for renal failure, is advisable. Perioperative administration of antibiotics is obviously necessary if an infected fistula or graft is operated upon.

There is also no need for routine use of platelet inhibitors (45,46). Adequate surgical techniques are more important than pharmacologic intervention. When surgical problems cannot be corrected, however, it may be advisable to administer aspirin (47) or, in complex cases, even a combination of aspirin and clopidogrel (48). There is little evidence that routine screening of hemostasiologic parameters is of any use before the primary surgical intervention. If recurrent thrombosis has occurred, however, a careful screen for items such as antiphospholipid antibodies, genetic abnormalities (prothrombin polymorphism, factor V Leiden mutation, protein C, and protein S deficiency), hyperhomocysteinemia, and antithrombin VIII is indicated.

The DOPPS data show that malfunction of the primary fistula is less when calcium channel blockers are used (49). This finding is not unexpected in view of the vasodilatory properties of calcium channel blockers. With respect to long-term fistula function, it is of interest that patients on ACE inhibitors have less delayed fistula closure, at least when PTFE grafts are used (50,51). This observation presumably illustrates that vascular remodeling depends on endothelin and angiotensin II, respectively (25).

It remains controversial whether use of intermittent venous congestion through cuff inflation in the postoperative period yields any benefit for long-term fistula function. A priori, it seems unlikely that an intermittent increase in intravascular pressure (and by implication of wall stress) will affect remodeling of the vein which is primarily the result of increased shear stress. There is no clear evidence of a beneficial effect on late outcomes.

Similarly, the widely recommended practice of hand exercises, such as squeezing a rubber ball at frequent intervals,
confers no documented benefit. It will increase venous blood flow, however, and thus appears to be at least sound on physiologic grounds.

**Monitoring of the Fistula**

Nurses should be trained to recognize fistula problems and to pay attention to a progressive increase of venous inflow pressure and post-puncture bleeding time. Regular “fistula visits” are advisable, i.e., inspection and physical examination of the fistula every 6 or 8 wk. The main purpose is to detect development and progression of stenoses in time to prevent eventual thrombosis, so that one is not forced to surgically correct an established thrombosis.

The pathophysiology underlying stenosis formation is turbulence of blood flow (Figure 8), which activates platelets and endothelial cells. In this context, a particular role has been postulated for platelet-derived growth factor (PDGF) (52).

The final trigger causing thrombosis is a critical reduction of fistula blood flow. Many studies document that low fistula flow is the best predictor of thrombosis. The critical flow rate is different in PTFE grafts and in AV fistulae (Table 2). For the latter, we found that all fistulae thrombosed in which the flow rate was $< 200 \text{ ml/min}$. This is of course far less than what is required for optimal blood flow during dialysis. As a result of low blood flow, dialysis will become ineffective and recirculation will occur, but measurements of recirculation are considerably less sensitive to predict fistula malfunction and thromboses than direct measurements of fistula flow rates (53). The time course is more important than the absolute values. Figure 8 shows the typical findings when a stenosis develops.

A number of indicators and predictors of fistula thrombosis have been discussed in the literature, such as MCP-1, lipid abnormalities, homocysteine, etc., but nothing has emerged which would be helpful for routine monitoring.

Several procedures help recognition of critically low blood flow rates and impending stenoses at the bedside:

- Auscultation (high frequency bruits at the site of stenosis)
- Hand elevation test (collapse of the post-stenotic venous segment and persisting congestion of the pre-stenotic segment)
- Prolonged bleeding after removal of the needle from the puncture site
- Elevated venous inflow pressure during hemodialysis sessions, particularly progressively increasing venous inflow pressures during consecutive dialysis sessions

Once a critically low fistula flow and stenosis have been documented, one has two alternatives: interventional radiology or corrective surgery.

Although this is still controversial, we believe as a rule of thumb that interventional radiology using intraluminal dilation with high pressure exceeding 20 atm ($\approx 2026 \text{ kpa}$) and stenting is sensible in the majority of cases for central stenoses at the level of the axillary vein and above, while most of peripheral stenoses should primarily be addressed by surgical correction. The reason for this recommendation is that the acute post-interventional blood flow rates after dilation are admittedly substantial, but the 1-yr and 2-yr unassisted or assisted patency rates are not impressive, presumably because damage to endothelial cells predisposes to recurrence of stenosis and thrombosis. After this maneuver, primary patency rates of 49% for

![Figure 8](image-url)

**Figure 8.** (Panel A) B mode sonogram showing a longitudinal section of an AV fistula created by connecting a PTFE graft (PTFE) to a native vein (V). At the site of anastomosis, incipient shunt stenosis with myointimal proliferation (arrows) is seen. (Panel B) Turbulent Color Doppler flow signals in the region of an anastomotic stenosis (arrows) are seen resulting from endothelial and fibromuscular hyperplasia at the graft (PTFE)/vein (V) anastomosis 18 mo after surgery.

**Table 2. Critical shunt flow volume in dialysis access**

<table>
<thead>
<tr>
<th>Access Type</th>
<th>Minimum Flow Rate</th>
<th>Recirculation Problems</th>
<th>Clotting Problems</th>
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</thead>
<tbody>
<tr>
<td>AV Fistula</td>
<td>350 to 400 ml/min</td>
<td>&lt;300 ml/min</td>
<td>&lt;200 ml/min</td>
</tr>
<tr>
<td>PTFE Graft</td>
<td>800 to 1000 ml/min</td>
<td>&lt;600 ml/min</td>
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*Estimation of shunt blood flow rate: $Q_b = TAV \times A \times 60$. Blood flow ($Q_b$; flow volume in ml/min) is the product of cross-sectional area of the vessel ($A; \text{cm}^2$) and the time averaged velocity ($TAV; \text{cm} \times \text{sec}^{-1}$).
salvaged forearm and 9% for salvaged upper arm AV fistulae have been reported (54). The reported 12-mo primary patency rate was only 27%, and the overall patency rate of 51% (55). Our results after surgical intervention are more favorable, and reconstruction of the lumen is usually also curative (56).

Alternative Surgical Approaches

An increasingly higher proportion of patients requires approaches other than the classical Cimino fistula at the level of the wrist (1), because an increasing proportion of diabetic and elderly patients are unable to achieve high flow rates for optimal fistula function when the radial artery is used for anastomosis. The solution may be anastomosis at a more proximal level.

We compared the primary actuarial fistula patency rate in diabetic and nondiabetic patients (57). In contrast to many reports, we found no difference between diabetic and nondiabetic patients. The explanation is that we had created a primary anastomosis at the level of the elbow in 74% of the diabetic patients compared with 32% in nondiabetic patients. While the high fistula undoubtedly has potential disadvantages and risks, this strategy seems justified, because the life expectancy of the elderly type 2 diabetic patients on dialysis is relatively low (58). A more frequent use of anastomoses at the elbow level with or without transposition of basilic veins has also been recommended by others (59).

Many nephrologists are hesitant to use the brachial artery for primary anastomosis out of fear of provoking hypercirculation and cardiac decompensation. This risk can be minimized if one adopts the procedure of Gracz (60,61). The principle of this procedure is to use the perforating vein for anastomosis. It connects the superficial and deep veins in the anticubital region. The perforating vein can dilate and remodel only to a limited extent, thus interposing a natural throttle between the artery and the run-off vein. This limits the maximal blood flow. Using this approach, we have not seen a single case of cardiac decompensation from high cardiac output in a series of more than 600 patients. Because of flow limitation, the risk of a steal phenomenon and peripheral ischemia is reduced as well. In obese patients, the cephalic vein (or even a mobilized basilic vein) has to be brought up often in a second step into a subcutaneous position. The first superficial segment of the basilic vein in the region of the elbow is too short in many patients, providing only a short stretch of the vessel for cannulation. Here again the subcutaneous superficialisation of the basilic vein along the medial aspect of the upper arm can yield satisfactory longerterm results. It is important to leave the proximal third of the basilic vein untouched to allow venous drainage during later surgical corrections, e.g., PTFE bridge grafts, etc.

Today numerous rescue operations are available for stenoses, fistula thrombosis, aneurysms, etc. The type of intervention should be based on pathophysiologic considerations. We present two examples that illustrate that limited reconstruction, if necessary with the use of a short PTFE interposition graft, allows preservation of a fistula and avoids fistula abandonment and a PTFE loop graft installation instead (Figures 9 and 11).

Complications of the AV Fistula

Steal Phenomenon. In recent years, ischemic lesions resulting from an arterial steal phenomenon have become more frequent in the population of highly comorbid elderly patients with vascular disease and diabetes mellitus. Concerning the interventional strategies, it is important to distinguish two varieties. First, high-flow steal, i.e., when fistulae with very low resistance “suck-off” blood flow from the palmar arc and the opposite ulnar artery, thus creating critical ischemia of the fingers. In theory, this type of lesion should be relatively easy to correct by limiting the size of the anastomosis and reducing fistula flow (63,64). Because the resistance goes with the $4^{th}$ power of the radius according to Poiseuille’s law, only drastic reduction of the fistula’s lumen will be effective. To create an effective yet safe lumen is tricky, however, and poses the risk of low flow and thrombosis.

More difficult, but unfortunately increasing in frequency, is the steal phenomenon in patients with low fistula flow. It is primarily the result of stenosed peripheral arteries so that even normal blood flow in the fistula will create critical ischemia in distal vascular beds. Preoperative monitoring helps to predict the risk of low-flow steal from the limited vasodilation of the
palmar arc arteries as indicated by abnormally low post-ischemic diastolic flow after fist clenching (Table 1, Figure 3). There are only a few therapeutic options. One is to close the fistula and use a central catheter. An alternative procedure has originally been proposed by Schanzer (65) and recently renamed DRIL (distal revascularization–interval ligation) (66). The principle is illustrated in Figure 10. The artery distal to the anastomosis is ligated so that the fistula no longer sucks blood off from peripheral vessels. In a second step, the peripheral artery is fed via an interposed segment of saphenous vein or PTFE graft to raise the perfusion pressure. An unresolved issue is whether for such patients, in analogy to hemodilution in patients with peripheral arterial disease, moderately low hematocrit values should be aimed at to avoid rouleaux formation and microcirculatory stasis or, conversely, whether high hematocrit values are beneficial by raising pO2 and tissue oxygenation. Calcium channel blockers may be contra-productive by increasing the run-off from ischemic tissue into adequately vasodilating parts of the circulation.

Congestive Heart Failure. One advantage of the native AV fistula is that hypercirculation and congestive heart failure from high fistula flow are very rare indeed, in contrast with what is seen with PTFE grafts (67,68). Hypercirculation ensues if outflow resistance is too low; in other words, when the anastomosis is too wide. This problem is more common with PTFE grafts and brachial artery fistulae. The only reliable diagnostic measure is to quantitate fistula flow. Banding procedures, i.e., artificial narrowing of the anastomosis have been recommended, but the result is very unpredictable. Apart from the desperate act of ligating the fistula, the best intervention is to recreate a narrower anastomosis. The results of narrowing are often unsatisfactory for reasons explained above (Poisson’s law).

Stenosis of Central Veins (Paget Schroetter Syndrome). A central venous stenosis may unfortunately be clinically asymptomatic before creating the vascular access and become
symptomatic only when flow is increased. If a critical stenosis is unable to accommodate increased flow rates, the result will be swelling of the arm and cyanosis as well as formation of collaterals on the chest wall. Central stenoses are usually the result of past subclavian catheters (69,70), but alternative causes have to be considered, e.g., pacemaker cables (71), primary thrombosis in patients with antiphospholipid antibodies or coagulation disorders, compression by tumors, etc. One therapeutic option is to ligate the anastomosis and use the other arm after appropriate imaging to exclude bilateral stenosis. A preferable intervention is to correct the stenosis, either by dilation with stenting (72,73) or by surgical correction (74). The latter intervention involves major surgery, however, and carries a considerable surgical risk. It is therefore the less desirable option.

Aneurysm. Aneurysms of the AV fistula are usually the result of destruction of the vessel wall and replacement by biophysically inferior collagenous tissue. Once aneurysms have formed, the law of Laplace predicts that there is a tendency to progress spontaneously, because wall stress becomes greater with increasing diameter of the aneurysm. Aneurysm formation is favored by replacement of the vessel wall by scar tissue after repetitive puncture of the same vessel segment. A pre-stenotic rise of outflow pressure. Major complications are rupture, infection (which is favored by intra-aneurysmatic thrombi), and in rare cases orthograde or retrograde embolism. Before intervention, adequate imaging using ultrasonography is absolutely indispensable for identification of thrombi, assessment of the degree of outflow stenosis, and evaluation of the surrounding tissue. The surgical correction includes partial or complete resection of the aneurysmatic sac, correction of accompanying stenoses, and reconstruction of an adequate lumen as illustrated in Figure 11.

Conclusion

It is the intention of this brief review to point out that the biology of the AV fistula is fascinating and that adequate management of the fistula and its complications should be based on pathophysiologic reasoning. There is no single standard approach, and surgical management must be individualized. One key to success is early referral and early establishment of a vascular access after preoperative assessment using ultrasonography. Regular monitoring of the fistula is indicated, and fistula flow should be assessed in critical cases as the single most important predictor of fistula thrombosis. It must be the aim to prevent thrombosis rather than to intervene on established thrombosis.

Our personal experience as well as several registry reports document that native AV fistulae can be established in more than 80% of the patients. The results are superior to those of PTFE grafts. We are aware that there are powerful disincentives against the AV fistulae, but we hope that nephrologists can be motivated to try a native AV fistula in all dialysis patients.

References


