Chapter 39
In Patients with New Arteriovenous Fistulas, Are There Effective Strategies to Enhance AVF Maturation and Durability Beyond Waiting?

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Abstract Autogenous arteriovenous fistulas are optimal conduits for hemodialysis due to their excellent long-term patency, low rates of infections and lower mortality rates. Yet, they are associated with a higher rate of failure to mature. As such, patient factors should be identified and modified, if possible, along with patient-centered surgical planning that includes the choice of vessels and techniques to yield the best possible outcomes for maturation. Furthermore, the postoperative period often requires a multidisciplinary team approach as arteriovenous fistula durability and maturation can be improved with appropriately timed endovascular or surgical interventions.

Keywords Arteriovenous fistula maturation • Creation • Durability • BAM • Neointimal hyperplasia • Anastomosis

Introduction

Autogenous arteriovenous fistulas (AVFs) are optimal conduits for hemodialysis. They have excellent long-term patency, low infection rates, less incidence of steal syndrome, stenosis, and lower mortality. Therefore, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI), Society for Vascular Surgery (SVS), and Fistula First Breakthrough Initiative (FFBI) recommend an AVF should be placed at least six months prior to the anticipated need for hemodialysis (HD) [1–5]. Clear documentation exists discussing the deleterious effects of tunneled dialysis catheters (TDC) and recommending early placement of AVF [1–4]. The 2003 guidelines of FFBI had set a prevalence goal of 66% AVF, to be met by

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2009, for those undergoing dialysis [5]. However, despite our increased prevalence of AVF creation, we have not met the goal. The U.S. Renal Data System Annual Data Report for 2013 (USRDS) reports an 81 % prevalence of TDC at initiation of therapy and 58.9 % AVF creation at initiation of hemodialysis [4]. The incidence of functional AVF at the first outpatient dialysis treatment is only slightly improved from 35.5 % in 2007 to 37 % in 2011 [4].

Subsequently, once a new autogenous AVF is created, the time to maturation can be lengthy and as many as 20–60 % fail to mature [3, 4, 6–23]. This adds the need for more procedures and a tunneled dialysis access catheter. Thus, vascular access dysfunction has now become a major contributor to cost, hospitalization and the overall morbidity and mortality [4, 24]. Many studies have attempted to elucidate the cause of access dysfunction by examining preoperative, intraoperative, or postoperative issues along with some adjuvant therapies that attempt to improve maturation and durability of these fistulae.

Search Strategy

A literature search of English language publications from January 2000 to October 2014 was used to identify published data on effective strategies to enhance maturation and durability of new AVF using the PICO outline (Table 39.1). The PubMed database was utilized and the search terms included "creation of arteriovenous fistulas", "maturation of arteriovenous fistulas", "patency of arteriovenous fistulas", "durability of arteriovenous fistulas", and "end stage renal disease AND fistulas." Articles were excluded if they specifically addressed grafts, only addressed specific complications such as steal phenomena, pediatric population, lower extremity fistulas, or involved discussion of fistulas in non-human models. Abstracts of the relevant titles were subsequently obtained and evaluated for eligibility. Further, review of the full article was then completed to include or exclude each article as appropriate. We then adopted the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scheme to classify the data. We also utilized the guidelines, opinions and data discussed in FFBI, NKF-KDOQI, SVS as well as the Annual Report of the USRDS to complete this chapter.

Table 39.1 PICO table for effective strategies to enhance AVF maturation and durability beyond waiting in patients with new arteriovenous fistulas

P (Patients)	I (Intervention)	C (Comparator group)	O (Outcomes measured)
Patients with ESRD requiring arteriovenous fistulae	Preoperative, intraoperative, and postoperative measures	Waiting for maturation or failure	Enhance maturation and durability of new arteriovenous fistulas

Results

Definition of AVF Maturation

The definition of AVF maturation is as defined by KDOQI. It is the "rule of 6's." This entails that a fistula must be 6 mm in diameter with a tourniquet, less than 6 mm deep, have blood flow >600 ml/min, and should be evaluated for non-maturation within 6 weeks after creation [1, 2].

Preoperative Factors for AVF Failure (Table 39.2)

The USRDS states that of the patients who received greater than or equal to 1 year pre-ESRD nephrology care, 30 % had a maturing a fistula and 50 % had a functional fistula at initiation of dialysis. This is approximately five times greater as compared to patients who were not referred to a nephrologist [4, 27, 38]. Thus, suggesting that earlier referral to a nephrologist may be of significant benefit [29].

Selecting appropriate access sites is critical for AVF maturation and preoperative duplex ultrasound may play an important role. One randomized trial, by Nursal et al. compared physical exam findings to duplex ultrasound preoperatively for site selection and showed no difference in AVF maturation or function [39]. Two other randomized trials supported the use of preoperative duplex ultrasound over physical examination for AVF maturation rate, but these studies had significant shortcomings in follow-up and the reported definition of patency [32, 38]. A similar topic was also discussed by Patel et al. They found an increase in creation of AVF due to duplex use but possibly worse rates of AVF maturation [31]. Indeed, a prospective trial with significant power to measure differences in maturation rates between ultrasound and physical exam findings is required to investigate the true role of preoperative duplex.

Vessel diameters have also been addressed to document their effect on AVF maturation. Wong et al. reported a higher rate of fistula failure with smaller arteries, <1.6 mm in diameter [15]. A literature review by Glass et al. showed that radial artery diameter (RAD) determined patency as RAD < 2 mm vs. RAD >2 mm yielded 40 % vs. 59 % AVF maturation, respectively [35]. Kheda et al. showed that small artery elasticity (2.25 ml/mmHg vs 3.71 ml/mmHg × 100 p = 0.02) was more predictive for AVF maturation than arterial diameters [20]. Shinstock et al. further demonstrated that a one mm increase in arterial diameter was associated with 30 % decrease of AVF abandonment with a median follow-up of 379 days [24]. Current guidelines suggest a minimum arterial diameter of 2 mm for successful AVF creation at the wrist, but guidelines for other locations is lacking [3, 24, 30, 38, 40].

Similarly, studies have also addressed vein diameters. A meta-analysis by Glass et al. revealed that duplex derived cephalic vein diameters <2 mm and >2 mm resulted in 29 % vs 71 % of AVF maturation, respectively [35]. Application of tourniquets during use of duplex to assess vein diameters was addressed in studies by Lockhart et al.

Table 39.2 Studies discussing preoperative reasons for failure and ways to improve maturation and durability

Author	Discussion	Study type (quality of evidence)
Dageforde et al. [26]	N = 158 Outcome: Greater than 2/3 of AVF with < 2.7 mm minimum vein diameter (MVD) on preop duplex failed to mature in 6 months Increased MVD on preoperative duplex mapping is associated with decreased risk of failure of maturation and improved long-term patency (P = 0.005 and P = 0.001, respectively)	Retrospective (low quality)
Allon et al. [25]	N = 145 Outcome: Postoperative AVF stenosis equal in those with preexisting venous intimal hyperplasia and does that do not (46 % vs 53 % P = 0.49) Postop non-maturation 30 % of those with postop stenosis vs 7 % in those without postop stenosis (P = 0.001) More interventions needed to maintain patency in those with postoperative stenosis than those without stenosis (P = 0.008)	Prospective (low quality)
Mortaz et al. [26]	N = 130 Outcome: Diabetes does not have a negative impact on the AVF rate of patency and its duration to maturation	Retrospective (low quality)
Hanko et al. [27]	N = 508 Outcome: Pre-dialysis AVF creation rates were 79 % of those who chose and started hemodialysis (HD), 39 % of those who chose peritoneal dialysis but started HD and 50 % of those in the undecided group who commenced HD	Retrospective (low quality)
Renaud et al. [28]	N = 280 Outcome: One and 2 year primary (P = 0.547) and secondary (P = 0.990) patency rates comparable for those age <65 years vs. age ≥ 65 years	Retrospective (low quality)
Ishaque et al. [8]	N = 249 Outcome: African American (AA) males may have smaller median basilic and cephalic vein diameters. AA males more likely to have AV graft vs. non AA males (17.9 % vs. 7.1 % P = 0.009)	Retrospective (low quality)
Oliver et al. [29]	N = 1929 Outcome: 40 % had their first fistula creation 3–12 months prior to starting dialysis, 30 % AVF created > 1 year prior to dialysis, 30 % within 90 days of starting dialysis	Retrospective (low quality)

Table 39.2 (continued)

Author	Discussion	Study type (quality of evidence)
Schinstock et al. [24]	N = 293 Outcome: Risk of reduced primary patency increased with diabetes (HR = 1.54) Risk of reduced PP and SP was decreased with larger arteries (HR = 0.83, HR = 0.69) One mm increase in arterial diameter was associated with 30 % decrease of AVF abandonment with a median follow-up of 379 days	Retrospective (low quality)
Allon et al. [9]	N = 50 Outcome: Preop arterial diameter was associated with upper arm AVF maturation (p = 0.007) Medial fibrosis was similar in nonmaturing and mature AVF (60 % vs 66 % P = 0.2)	Prospective (low quality)
Lockhart et al. [30]	N = 73 Outcome: Sonography used for Radiocephalic arteriovenous fistula (RCAVF) to separate patients into group 1 (pre-tourniquet vein diameter ≥ 2.5 cm) and group 2 (pre-tournique < 2.5 cm and after application of tourniquet increased to ≥ 2.5 cm) Fistula success rate similar in both groups (39 % vs. 33 % P = 0.624) Tourniquet application increased the total number of usable forearm fistula	Retrospective (low quality)
Patel et al. [31]	N = 202 Outcome: AVF creation rate increased from 61 % to 73 %, but functional maturation rates decreased from 73 % to 57 % (P < 0.05) after implementation of preoperative imaging and aggressive vein use	Retrospective (low quality)
Wong et al. [32]	N = 402 Outcome: Improved trend of patients who underwent ultrasound preoperatively vs. clinical exam alone, started using their AVF (81 % vs. 69 % P = 0.11)	Literature review (low quality)
Kheda et al. [20]	N = 32 Outcome: Average small artery elasticity index was lower in failed than in matured fistulas (P = 0.02)	Prospective (Low Quality)

(continued)

Table 39.2 (continued)

Author	Discussion	Study type (quality of evidence)
Lauvao et al. [33]	N = 298 Outcome: AVF location (P = 0.032) and vein size (P = 0.002) significantly affected maturation in univariate analysis Only vein diameter was independent predictor of AVF functional maturation (P = 0.002)	Retrospective (low quality)
Kosoy et al. (2009)	N = 100 Outcome: Mean duration of operation was shorter in Brachiocephalic arteriovenous fistula (BCAVF) vs. Brachiobasilic arteriovenous fistula (BBAVF) (P < 0.001), but no significant differences in postop complications or morbidity or mortality. Primary patency was similar at one and 3 year follow-up (P = 0.8)	Prospective (low quality)
Lok et al. [21]	N = 422 Outcome: Internally validated risk equation found age ≥ 65 years, peripheral vascular disease (PVD), coronary artery disease, non-white rate to be predictive of failure to mature	Retrospective (low quality)
Lazarides et al. [34]	N = 1841 (13 studies) Outcome: Higher rates of RCAVF failure in elderly at 12 months and 24 months (OR = 1.525, P = 0.001 and OR 1.357, P = 0.019 Secondary analysis showed effect in favor or elbow BCAVF vs. RCAVF in elderly (P = 0.004)	Literature review (moderate quality)
Glass et al. [35]	N = 433 for RAD and 386 for CVD, 20 studies Outcome: Mean radial artery diameter (RAD) yielding fistula success for (RAD) > 2.0 mm and RAD < 2.0 mm, 59 % vs. 40 %, respectively Fistula success rate between cephalic vein diameter (CVD) > 2.0 mm and CVD < 2.0 mm was 71 % vs 29 %, respectively	Literature review (low quality)
Monroy-Cuadros et al. [36]	N = 831 Outcome: Incidence of primary failure = 10 % Age > 65 years (P = 0.001), history of diabetes (P = 0.007), history of smoking (P < 0.001), presence of forearm fistula (P < 0.001), and low initial intra-access blood flow < 500 ml/min (P < 0.001) were independently associated with loss of primary patency	Retrospective review (low quality)

Author	Discussion	Study type (quality of evidence)
Hingorani et al. [37]	N = 41 Outcome: Venodilatation as a percentage increase after application of tourniquet compared with native state was 37 % for distal cephalic vein, 31 % for midcephalic vein, and 32 % for midbasilic vein Venodilatation as a percentage increase after placement of regional anesthesia nerve block compared with after tourniquet application was 42 % for distal cephalic, 19 % for midcephalic, 26 % for midbasilic veins Venodilatation is augmented with regional anesthesia and tourniquet compared with using a tourniquet alone and may allow more options for access creation	Retrospective (low quality)
Wayne et al. [23]	N = 73 Outcome: Absence of PVD, aspirin use, and absence of previous permanent dialysis access were associated with higher primary patency rates Higher mean arterial pressure (MAP) during maturation relative to preoperative MAP associated with lower patency Maturation period hemodynamics pay play important role in dialysis access patency	Retrospective (low quality)

and Hingorani et al. These studies suggested a role for the use of tourniquets during the duplex exam before the placement of AVF [30, 37]. Thus, NKF-DOQI recommends a minimum vein diameter of 2.5 mm for creation of AVF [1, 2, 33].

Specific Populations

In 1966, Cimino and Brescia described their novel technique for fistula creation with an 11 % failure to maturation rate. The patients' median age was 43 years with almost all having glomerulonephritis as the cause of their end stage renal disease. Today, the failure rate is fivefold as high and the age group requiring dialysis with the fastest growth is >85 years old [4, 21]. The meta-analysis by Lazarides et al. showed that in the elderly (range varying among studies from >50 to >70 years), radio-cephalic AVF (RCAVF) was significantly more likely to fail than in the non-elderly at 12 months (OR = 1.525, p = 0.001) and 24 months (OR = 1.357, p = 0.012) [34]. However, many other studies have shown conflicting data [8, 21, 23, 26, 28].

Other factors and their effects on AVF maturation have also been examined. Although the major cause of AVF failure to maturation is venous intimal hyperplasia (VIH) [41], studies have shown that AVF in those with preexisting VIH, calcifications, or stenosis were equally likely to mature than in those without these lesions [21, 25]. Studies documenting the effects of BMI have been largely inconclusive [20, 38] and studies on the effects of gender have not shown significant differences in maturation [38]. Finally, diabetes has been associated with worse primary patency [38, 42].

Intraoperative Factors Affecting AVF Failure, Maturation and Durability (Table 39.3)

Studies addressing intraoperative measures to assess maturation of AVF have largely focused on intraoperative volume flow, blood pressure (BP), tissue handling, vessel distension, and anastomosis techniques. Saucy et al. discussed intraoperative blood flow in RCAVF after completion of anastomosis using a transit time ultrasonic flowmeter as well as follow-up post op using color flow ultrasound to estimate blood flow. They found that intraoperative blood flow volume with a cutoff of 120 ml/min had 67 % sensitivity, 75 % specificity, and 91 % positive predictive value to predict early failure [12]. Others have demonstrated an association between low mean arterial pressure (MAP) on the day of fistula placement and lower maturation rate. Higher diastolic BP during maturation relative to preoperative diastolic BP has also been associated with lower maturation rate. These studies demonstrate the significance of hemodynamics in fistula maturation [23, 38].

Tissue handling has been a possible implication in "swing point" or juxta-anastomosis stenosis, thus, minimal tissue handling is advocated [18, 22, 43–45]. In a prospective randomized trial, Lin et al. discussed interrupted technique using nitinol clips to create anastomosis versus sutures. They demonstrated promising AVF

Table 39.3 Studies discussing intraoperative reasons for failure and ways to improve maturation and durability

Author	Discussion	Study type (quality of evidence)
Kotoda et al. [40]	N = 1 Outcome: Case-report of balloon-assisted creation and maturation of small caliber cephalic vein and small caliber radial artery for AVF creation	Case report (low quality)
Kanko et al. [43]	N = 67 Outcome: 89 % patency rate in 6 months using the "diamond-shape anastomosis" technique	Retrospective (low quality)
Manson et al. [44]	N = 10 Outcome: Technical feasibility (n = 10/10, 100 %), safety and clinical success of the Optiflow implant for AVF creation was addressed. One hundred percent patients had diameters > 6 mm at Day 42, but more studies needed	Retrospective (low quality)
Bharat et al. [45]	N = 125 Outcome: Decreased juxta-anastomotic stenosis in piggyback Straight Line Onlay Technique (pSLOT) patients (P = 0.04) pSLOT revealed decreased overall AVF failure rate of 16.7 %, compared with side to side technique rate of 33.3 %, and end to side rate if 40.3 %, (P = 0.01)	Retrospective (low quality)
Dukkipati et al. [46]	N = 6 studies evaluating patency rates for BBAVF N = 10 studies comparing BBAVF vs. BCAVF vs. AVGraft N = 2 studies comparing BBAVF vs. BBrAVF vs. AVG N = 3 studies comparing One-stage vs. Two-stage BBAVF Outcome: Rate of BBAVF primary failure is approx. 15–20 % (range = 0–40 %) Mean 1-year patency rate is approx. 72 % (range = 23–90 %) Mean 2-year patency rate is approx. 62 % (range = 11 –86 %) Limited evidence supports Two-stage BBAVF with increased primary patency at 15 months compared to One-stage	Literature review (low quality)
Robertson et al. [47]	N = 73 Outcome: No significant difference in functional patency rates at 6 weeks between one stage vs. two stage brachiobasilic fistula creation (76 % vs. 84 % P = 0.545). No difference observed in long-term patency (P = 0.431)	Retrospective (low quality)
Bonforte et al. [11]	N = 459 Outcome: Middle arm fistula (MAF) primary patency at 4 years from creation was 79 % Higher risk of MAF failure was found in women (P = 0.19), underweight patients (P = 0.010), and MAF implantation after starting hemodialysis (P < 0.001)	Retrospective (low quality)
Bhalodia et al. [19]	N = 58 Outcome: Primary failure was lower for proximal Radiocephalic AVF (pRCF) than distal RCF (dRCF) (32 % vs. 59 % P = 0.05) Cumulative survival similar between pRCF and dRCF (92 % vs. 86 % at 1-year and 74 % vs 76 % at 2 years P = 0.56)	Retrospective (low quality)

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Table 39.3 (continued)

Author	Discussion	Study type (quality of evidence)
Saucy et al. [12]	N = 58 Outcome: Intra-operative blood flow in functioning radiocephalic AVF was significantly higher compared to non-functioning radiocephalic AVF (230 ml/min vs 98 ml/min P = 0.007) 1-week and 4-week blood flow measurements were also higher in functioning AVF vs. non functioning (753 ml/min vs. 228 ml/min P = 0.0008 and 915 ml/min vs. 245 ml/min P < 0.0001) Intra-op blood flow of 120 ml/min revealed a sensitivity of 67 %, specificity of 75 % and positive predictive value of 91 % for functioning RCAVF	Retrospective (low quality)
Lin et al. [48]	N = 132 Outcome: Nitinol surgical clips used to compare outcomes against sutured anastomosis in forearm and upper arm fistulae Clipped forearm AVF (FAVF) had improved maturation at 6-weeks vs. sutured anastomosis (86 % vs. 69 %, P < 0.05) Clipped forearm AVF also had improved patency at 12, 24, and 36 months (P < 0.05) No difference was measured in clipped vs. sutured upper arm AVF maturation or patency	Prospective (low quality)
Fila et al. [68]	N = 93 Outcome: Significant impact and failure to mature was due to increased body-mass index (P = 0.041), artery diameter (P < 0.001), vein diameter (P = 0.004), and vein diameter after dilation using serially increasing diameter dilators (P = 0.002) Those patients with vein diameters < 2 mm, only vein diameter after dilatation significantly affected function (P = 0.004)	Retrospective (low quality)

maturation rates, 86 % at 6 weeks using clips versus 69 % with sutures (p < 0.05). However, no difference in patency was noted [48]. These data have not been replicated and the significant cost of these devices has limited their use.

Suture techniques have also been examined. There are devices that allow for sutureless anastomosis. However, minimal success was exhibited in one pilot study in humans [44]. Inconclusive reports are present on four quadrant sutures vs. continuous vs. interrupted techniques [38, 43]. Anastomosis creation in an end (vein) to side (artery) manner has become widely accepted since the report by Wedgwood et al. demonstrated a decrease in incidence of VIH [38] compared to end to end or side to side manner. Still, there are other techniques such as on-lay and posterior straight on-lay that offer similar patency; however, these were in small case series [45].

Studies discussing location of new arteriovenous fistulae are abundant. Some have discussed that distal RCAVF carry less potential for maturation compared with proximal RCAVF. Two retrospective analyses have shown equal if not better patency with proximal or middle arm RCAVF [11, 19]. However, in reality, physical limita-

tions including quality and caliber of the available artery and vein are more likely to determine the site of AVF placement.

Retrospective analyses of single-stage versus two-stage brachio-basilic AVF (BBAVF) have documented improved patency at 1-year and 2-year with two-stage procedures [46, 47]. Koksoy et al. [67] reported from a randomized prospective study the patency of single-stage BBAVF vs brachio-cephalic AVF (BCAVF). These data only included patients with prior failed RCAVF with patent upper arm veins. Their study showed that, although BCAVF creation required shorter duration of procedures, primary patency remained the same [49]. Furthermore, Ascher et al. reported similar AVF maturation rates of 91 % vs. 87 % ($p = 0.3$) for BCAVF vs. BBAVF, respectively [50].

Postoperative Factors Affecting AVF Failure, Maturation and Durability (Table 39.4)

As recommended by FFBI, every new AVF should be evaluated for maturation at 4 weeks [5]. If the access is not maturing at 4 weeks, or flow remains low (<500 ml/min), or cannulation of the AVF is not feasible, a fistulogram is recommended for evaluation [3, 54].

The four most useful surveillance methods for dysfunction, as described by NKF-DOQI, are serial access flow measurements, measurement of static venous pressure, pre-pump arterial pressure, and duplex ultrasound scanning [38]. If access surveillance is abnormal, a fistulogram can be performed [1, 2, 38]. A meta-analysis completed by Casey et al. found 12 studies addressing surveillance versus clinical monitoring [59]. Only three of these studies showed that vascular intervention after abnormal surveillance led to a significant reduction in risk of access thrombosis (RR 0.53 95 % CI 0.36–0.76) and a non-significant risk of AVF access abandonment [3]. Other studies have documented that clinical monitoring of AVF has 96 % sensitivity and 93 % negative predictive value [63]. Thus, clinical monitoring may be equal to surveillance. This, however, is not very likely to be applicable in our communities where thorough physical exams are resource intensive and rare, and surveillance may be advocated [3, 10, 59]. Indeed, if clinical exam is equivocal, duplex ultrasound can be beneficial.

Specific treatment options for non-maturing AVF rest with the physician. Ascher et al. noted that simple and extended salvage procedures may extend the lifespan of the AVF [58]. Certainly, debate exists between open surgical techniques and endovascular PTA techniques. In a retrospective analysis by Tindi and Roy-Chaudhry, it was shown that open surgical treatment may be superior to endovascular treatment. In a nonrandomized study of male Veterans' Affairs hospital patients, AVF maturation rates between endovascular or open surgical techniques were compared to the controls that did not undergo either procedure. The open surgical arm and no treatment requirement arm had similar maturation rates of 83 % vs 86 %, while only 40 % of the PTA arm AVF matured [53]. Other studies have cited secondary patency

Table 39.4 Studies discussing postoperative reasons for failure and ways to improve maturation and durability

Author	Discussion	Study type (quality of evidence)
Lynch et al. [6]	Keywords: QI Coordination Teams Increased Follow-Up But Not Maturation N = 198 Outcome: Institutional quality-improvement (QI) program developed well-defined office follow-up schedule after AVF creation Compliance within first-30 days post AVF creation increased from Pre-QI to QI group (48 % vs. 65 % P = 0.015) No difference in failure to mature rate for the pre-QI and QI group (22 % vs 21 % P = 0.816)	Retrospective (low quality)
Gorin et al. [7]	N = 30 patients, 31 AVF created Outcome: Office-based ultrasound guided angioplasty of AVF performed n = 48 for failing to mature and remaining 7 interventions performed for stenosis 90-day patency = 93 % 85 % AVF treated for FTM achieved functional status Four perifistular hematomas; three resulted in AVF thrombosis. No patients required hospitalization. Office setting valuable tool in management of dialysis access	Retrospective (low quality)
Usta et al. [69]	N = 80 Outcome: Factors influencing AVF function were radial artery diameter (P = 0.02), intraoperative flow (P = 0.01), intraoperative pulsatility index (P = 0.01), and postoperative flow (P = 0.01) Intraoperative ultrasound and postop DUS can help identify AVFs that are unlikely to function and may need early intervention	Retrospective (low quality)
Lee et al. [41]	N = 12 Outcome: Vein samples obtained from AV anastomosis at time of AVF creation showed neointimal hyperplasia in 10 of 12 specimens	Retrospective (low quality)
Tan et al. [10]	N = 44 Outcome: Patients on HD who received endovascular interventions for access problems were analyzed. No periop complications 100 % technical success rate Median time for first endovascular intervention was 13 months for AVF and 8 months for AVG Median time for restenosis or failure was 11 months for AVF and 5 months for AVG	Retrospective (low quality)
De Marco Garcia et al. [51]	N = 62 Outcome: Intraoperative balloon angioplasty utilized to upgrade small caliber veins during AVF creation 85 % remained patent and subsequently underwent Balloon assisted maturation (BAM) with a resulting functional AVF	Retrospective (low quality)

Table 39.4 (continued)

Author	Discussion	Study type (quality of evidence)
Raynaud et al. [13]	N = 25 Outcome: Percutaneous transluminal angioplasty (PTA) performed at forearm artery lesions for failing distal access maturation In 91 % of patients after PTA, accessed used for hemodialysis without difficulty Primary patency rates were 83 % (range = 60–93 %) at 1-year and 74 % (range = 47–89 %) at 2-years	Retrospective (low quality)
Rayner et al. [52]	N = 3674 Outcome: Observational data at hemodialysis, hemofiltration, or hemodiafiltration facilities in Europe and U.S. Significant differences in clinical practice currently exist between countries regarding AVF creation and timing of first cannulation Cannulation ≤ 14 days after creation was associated with 2.1 fold higher likelihood of subsequent AVF failure compared to AVF cannulated > 14 days (P = 0.006)	Prospective (high quality)
DerDerian et al. [17]	N = 30 patients, 143 Balloon-assisted maturation Outcome: Balloon-assisted maturation is a controversial method for developing AVF Average BAM per patient was 4.8 (range = 1–7 procedures) 74 developed post procedural hematoma, 76 showed increase in volume flow measurement, but no correlation (P = 0.87) Hematomas most frequently during 2nd BAM procedure (24.3 % of all hematomas) 8 mm balloon group, statistical difference was noted in percent increase in volume flow measurement (VFM) with presence of a hematoma and percent increase in VFM without presence of a hematoma (P = 0.027) Suggest a more aggressive approach to BAM with use of larger balloons to create hematoma formation and minimizing excessive dilation procedures, may have a significant effect in maturation based on VFM	Retrospective (low quality)
Lee et al. [53]	N = 89 Outcome: 46 of 89 (52 %) patients required intervention to achieve maturation. Thirty-one patients had surgical revision, 15 patients had endovascular interventions Cumulative survival longer in AVF receiving surgical interventions compared with angioplasty to promote AVF maturation (P = 0.05) One-year cumulative survival was 86 % vs. 83 % vs. 40 % for no intervention vs. surgery vs. angioplasty, respectively	Retrospective (low quality)

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Table 39.4 (continued)

Author	Discussion	Study type (quality of evidence)
Robin et al. [54]	N = 69 Outcome: Ultrasound measurements at 2–4 months post AVF creation are highly predictive of fistula maturation and adequacy for dialysis	Retrospective (low quality)
Swinnen et al. [22]	N = 68 Outcome: 33 AVF received Juxta-anastomosis Stenting (JXAS) for failure to mature, 35 received JXAS for inadequate dialysis Technical success in placement of nitinol stent was 97 %. 75 % of those that were failing to mature were brought to maturity after JXAS	Retrospective (low quality)
Geogiadis et al. [42]	N = 72 Outcome: ESRD diabetics with radial artery Monckeberg calcifications receiving Radiocephalic arteriovenous fistula (RCAVF) had worse late clinical outcomes compared with ESRD diabetics with healthy arm vessels. Long-term benefits may be lost in diabetics with extensively calcified vessels for distal RCAVF fistulae	Prospective (low quality)
Bountouris et al. [55]	N = 159 Outcome: 50 % of primary percutaneous transluminal angioplasty (PTA) required no further intervention. Fifty percent required at least one reintervention Primary assisted patency was 89 % at 6 months and 85 % at 12 months	Literature review (low quality)
Miller et al. [56]	N = 122 Outcome: Successful AVF maturation in 118/122 patients Follow-up of 109 of 118 patients was achieved (mean = 24 months, range = 0.25–60 months)	Retrospective (low quality)
Miller et al. [57]	N = 140 Outcome: Thrombosed fistulae that were never used for hemodialysis underwent endovascular salvage procedures, such as thrombectomy, BAM, elimination of competing branching veins, etc. Cost analysis revealed percutaneous procedures costs $4,881 to $14,998 less than access abandonment and new access creation	Retrospective (low quality)
Hingorani et al. [58]	N = 46 patients, 75 revisions Outcome: Simple and extended salvage procedures may allow maturation and add to the life span of AVFs for hemodialysis Suggest an advantage to open techniques as compared with percutaneous techniques but only in terms of requiring fewer subsequent procedures	Retrospective (low quality)

Table 39.4 (continued)

Author	Discussion	Study type (quality of evidence)
Casey et al. [59]	N = 1363 patients Outcome: Surveillance followed by intervention led to a non-significant reduction of risk of access thrombosis (RR, 0.82; 95 % CI, 0.58–1.16), and access abandonment (RR, 0.80; 95 % CI, 0.51–1.25) Vascular intervention after abnormal access surveillance led to significant risk reduction of access thrombosis (RR, 0.53; 95 % CI, 0.36–0.76) Potential benefit of AV access surveillance followed by interventions to restore patency is based on low quality evidence	Literature review (moderate quality)
Marks et al. [60]	N = 20 Outcome: 20 AVF underwent office guided duplex balloon angioplasties 18 of 20 were for failing AVF Excellent duplex imaging quality and technical advances in endovascular tools allowed performance of AVF balloon angioplasties in office with technical success	Retrospective (low quality)
Ascher et al. [61]	N = 25 patients, 32 angioplasties Outcome: No systemic complications. One patient developed arm hematoma One patient had focal intraluminal dissection not obstructing the flow Increase from mean volume flow from preoperative to postoperative (350 ± 180 lm/min to 933 ± 332 ml/min, P < 0.001)	Retrospective (low quality)
Gallagher et al. [62]	N = 45 patients, 185 duplex guided BAM Outcome: 99.5 % successfully dilated-one required surgical exploration due to large AVF rupture AVF failed to mature in 7 of remaining 44 patients (16 %) because of proximal vein stenosis All of the 7 subsequently matured after successful balloon angioplasty of the venous outflow	Retrospective (low quality)
Dember et al. [14]	N = 877 Outcome: Enrollment stopped after 877 participants, based on intervention efficacy. Fistula thrombosis occurred in 12.2 % assigned to Clopidogrel vs 19.5 % assigned to placebo (P = 0.018) Failure to attain suitability for dialysis did not differ between placebo and Clopidogrel.	Multicenter, prospective RCT (high quality)

with endovascular salvaging techniques to be up to 77 %, 61 % and 32 % at 12 months, 24 months, and 36 months, respectively [56]. Literature review by Bountouris et al. showed that results of PTA vs. open surgery are similar for salvaging failing fistulas and mirror the SVS guidelines that local expertise should guide therapy [3, 55]. Very limited quality of data exists due to mostly retrospective analysis to recommend firm guidelines.

Studies documenting endovascular interventions to enhance AVF maturation remain controversial [13]. Some studies describe balloon assisted maturation (BAM) as a technique that can promote VIH and cellular proliferation, leading to stenosis due to increase in luminal pressure, medial hypertrophy, or abnormal wall shear [16, 17, 64]. Other authors speculate that BAM heals into a large fibrous conduit as seen on fistulograms post BAM and contributes to increased AVF patency [17, 51]. These studies have suggested using a combination of limited interventions with large caliber balloons to achieve maturation [17, 57]. De Marco Garcia et al. achieved 85 % maturation of new AVFs after performing primary balloon angioplasty during the index procedure for creation in small caliber (<3 mm) veins and subsequent BAM within 2 months of creation [51]. Indeed, many studies have documented the safety of performing these procedures at outpatient centers [7, 56, 57, 60–62].

Other techniques of endovascular AVF maturation or salvage have shown varying results using a combination of cutting or non-cutting balloons [18, 56]. Juxta-anastomotic stenting using non-covered nitinol stents to treat VIH [22], angioplasty to treat stenosis, thrombectomy or thrombolysis as appropriate to treat access thrombosis, and embolization of collateral side branches as needed to ensure adequate fistula flow have all shown promising results [18, 56].

Furthermore, open AVF management strategies are based on treating the underlying cause of nonfunctioning of AVF. In an access that is too deep causing an AVF to become nonfunctional, but free of significant stenosis, transposition and re-tunneling with or without moving the site of anastomosis can improve functionality. Open ligation of patent side branches may be attempted if large patent branches, usually greater than 2 mm, are found to be shunting blood away from AVF and preventing adequate maturation [3].

Arterial inflow problems represent about 3–5 % of all stenoses in HD access. The site of stenosis may be anywhere in the inflow arteries. PTA with or without stenting is the preferred option for stenosis involving >50 % of arterial diameter causing insufficient inflow [3].

Poor venous outflow is another major problem for AVF maturation. After access creation, aggressive surveillance may be undertaken. Diagnosis of early venous stenosis (<7 days after creation) is usually a technical error and should be revised with open technique. Late diagnosis of these stenoses can be treated using balloon angioplasty.

Thrombosis of fistula can be divided as early or late. Early thrombosis (<30 days from creation) is usually due to technical error and a thorough evaluation of the fistula should be performed to assess the worth of re-exploration versus assessment of a new site. Management of thrombosed access begins with thrombectomy, then identifying, and treating the stenotic lesion. Shorter lesions respond well to patch angioplasty of lesions with either venous or prosthetic materials. Longer lesions require bypass of the diseased segment [3]. Endovascular options with thrombectomy and treating underlying lesions can be performed as a standard technique.

Finally, timing of first AVF cannulation may also correlate with the likelihood of failure. Rayner et al. have described time of cannulation with <14 days after creation resulting in 2.1 fold likelihood of AVF failure ($p = 0.006$) compared to AVF cannulation >14 days post creation [52].

Adjuvant Therapies

Smoking has long been recognized as a factor for vascular disease. Studies have shown early and late AVF failure among cigarette smokers [3, 36]. Osborn et al. conducted a Cochrane review of medical treatment as adjuvant therapy for improving AVF maturation. Their analysis of trials starting from 1970s to the present, including antiplatelet agents such as aspirin, clopidogrel, ticlodipine, dipyridimole, documented marginal success of these therapies. One trial comparing low dose of warfarin with placebo was stopped early due to increased bleeding in the treatment group. A trial using clopidogrel was also stopped early due to significantly decreased risk of early AVF thrombosis compared to placebo, but no difference was found in maturation [14]. A single trial of fish oil, 4 g daily, showed favorable outcomes. Yet, the quality of data from these single studies has remained insufficient to recommend use [65].

Recommendations

The systematic review of literature demonstrates the scarcity of evidence-based data available, lack of randomized controlled trials, with recommendations mostly based on retrospective analysis or observational studies in this field. Indeed, based on the data analyzed, the new autogenous AVF is prone to multitude of problems, yet remains as the best option we have for hemodialysis. Strategies to enhance AVF patency and durability extend to time well before and after the placement of a fistula.

Preoperatively, the following are recommended:

1. Smoking cessation
2. Timely referral for nephrology care and vascular access placement
3. Ultrasound imaging to ensure adequate arterial diameters of at least 2.0 mm radial artery and 2.5 mm cephalic vein at the wrist (preferably performed by the surgeon himself or herself) .

Intraoperatively, the following are recommended

1. Non-dominant, upper extremity distal fistulas recommended to preserve other sites for future access
2. End to side anastomosis is preferred
3. Intraoperative blood flow measurement, if available, of at least 120 ml/min after creation and search for cause of poor volume flow if present

Postoperatively, the following are recommended

1. Follow-up with access surgeon at 4 weeks to examine the fistula
2. No cannulation prior to 14 days
3. "Rule of 6's" to evaluate for maturation
4. If AVF does not meet the criteria for maturation, or displays signs of early failure, referral for duplex ultrasound and/or fistulogram is needed
5. BAM may have a role to improve maturation
6. Endovascular approach, including angioplasty, stenting, thrombectomy, thrombolysis, venous branch ligation may be utilized as appropriate
7. Open techniques such as fistula superficialization, interposition vein grafts, transposition or even ligation of branches may be needed for specific problems

A Personal View of the Data

AVF dysfunction is a major burden to our patients and society. Identifying patients that may require closer surveillance postoperatively is critical. Taking care of these patients requires aggressive preoperative, intraoperative and postoperative assessment to understand features that may help us improve maturation rates and durability. While there is ample data from retrospective studies, case reports, and observational prospective cohorts, there is limited to no data assessing results in randomized clinical trials to truly achieve the best outcomes. Hence, our knowledge is limited to the current published research, presentations at major meetings, as well as peer-reviewed guidelines. Nevertheless, understanding the pathophysiology of failure to mature AVFs and utilizing appropriate strategies that propose timely referral, selection of vessels for creation of AVF, followed by aggressive monitoring utilizing endovascular options first, may improve our patients' outcomes.

Recommendations

- Smoking cessation (**strong recommendation, low quality evidence**)
- Timely referral for care and access (**strong recommendation, very low quality evidence**)
- Preoperative ultrasound imaging (**strong recommendation, very low quality evidence**)
- Use arteries with diameter >2 mm (**strong recommendation, very low quality evidence**)
- Use veins with diameter >2.5 mm (**strong recommendation, very low quality evidence**)
- Distal site of non-dominant upper extremity as first access choice (**strong recommendation, very low quality evidence**)

- Surgeon follow-up within 4 weeks (**strong recommendation, very low quality evidence**)
- End to side anastomosis (moderate recommendation, very low quality data)
- Reassess AVF if intraoperative blood flow <120 ml/min (**moderate recommendation, very low quality data**)
- AVF surveillance (**moderate recommendation, very low quality evidence**)
- Endovascular or open treatment (**moderate recommendation, very low quality evidence**)
- BAM to enhance maturation (**moderate recommendation, very low quality evidence**)

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