

Resolved: Fistulas Are Preferred to Grafts as Initial Vascular Access for Dialysis

ABSTRACT

There is growing concern that the Fistula First Initiative, KDOQI guidelines, and subsequent pressure from the Centers for Medicare and Medicaid Services lack reasonableness regarding likely success for fistula maturation in a heterogeneous, new-onset dialysis population. Here the various positions are examined from multiple perspectives.

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Life-sustaining hemodialysis requires durable vascular access to the circulatory system.¹ The ideal permanent vascular access must provide longevity of use with minimal complication rate and supply high enough blood flow to deliver the prescribed dialysis dosage. The native arteriovenous fistula is considered the best access to initiate patients onto hemodialysis because of its longer survival and lower complication rates as compared with other forms of vascular access, such as the synthetic graft. Large studies show a graded mortality risk from both cardiovascular and infectious diseases depending on access type, with the highest risk associated with catheters, followed by grafts, and then native fistulas.² According to one analysis, the cost of vascular access care was more than five-fold lower in those who began treatment with a functioning native fistula compared with those who were treated with a graft or permanent catheter.³

The National Kidney Foundation published the Dialysis Outcome Quality Initiative (KDOQI) guidelines and opinion-based recommendations to improve vascular access outcomes.¹ This document advocates greater use of fistulas, promotes elbow-level fistulas ahead of any graft in any anatomic location, encourages preoperative venous mapping and arterial evaluations, and vigorously endorses predialysis construction of vascular access before the need for initiation of dialysis. It also identified barriers to fistula placement in the preceding decade. These include preference by surgeon,⁴ local policies, degrees of access to tertiary care, reimbursement practices, and other financial issues penalizing fistula construction. Cardiovascular diseases, late referral, and use of catheters consistently predict shorter fistula survival, even accounting for concomi-

tant comorbidities and other prognostic factors.⁵ Other factors that I believe have an impact on fistula use include older age of patients entering dialysis programs, disproportionate presence of diabetes with its vasculopathy, and presence of multiple comorbidities as a result of more “liberal” access to dialysis. Older age, diabetes, and cardiovascular diseases are associated with poor arterial and vein quality, making the construction of distal fistulas more challenging. Indeed, the choice of the fistula is strongly related to younger age, male gender, nondiabetic status, lower body mass index, no history of angina, and absence of peripheral vascular disease.^{6,7}

To modify the observed suboptimal use of fistulas among incident patients and the continued use of synthetic graft for initial vascular access, the National Vascular Access Improvement Initiative was formulated. This evolved into the “Fistula First Breakthrough Initiative,” commonly known as Fistula First. The purpose of the initiative is to increase the likelihood that every suitable patient receives the most optimal form of vascular access (fistulas if possible) for that patient. Note the initiative does not exclude grafts or catheters. The initiative proved so successful that the goal for fistula use was revised to 66% of all hemodialysis patients by the year 2009. Whether the fistula prevalence rate can reach this goal by 2009 as desired by Centers for Medicare and Medicaid Services⁸ is uncertain.

My own experience with the Fistula First initiative suggests that multidisciplinary management is essential in increasing the likelihood of success and maintaining the fistulas as the

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preferred initial access for dialysis by avoiding construction of marginal nonmaturing or poorly functioning fistulas. Indeed, a number of US^{9,10} and Canadian¹¹ programs have successfully increased the prevalence of native fistulas by implementing multiprofessional interdisciplinary programs. During a 2-yr period (2000–2001) with such a multidisciplinary team in place, vascular access tracking database, an aggressive interventional program to foster maturation, and a surveillance program to prevent access thrombosis, I was able to increase the prevalence of fistulas from 45 to 80% in our dialysis program in West Virginia (unpublished observations). By contrast, without these tools, I have struggled to keep up with the national trend for the past 6 yr.

Multiple past observations indicate the number of access procedures needed to maintain long-term patency is much lower for fistulas than for grafts, usually 2.5- to 7.0-fold lower.^{6,12} Some argue that this difference results from patient selection biases; that is, patients with best anatomy get fistula placement. Others argue the superior patency and lower intervention rate data are old^{13–15} and no longer apply to patients currently initiating hemodialysis^{16,17}; however, some recent studies continue to show overall lower procedure rates for fistulas than grafts.¹⁸

A key factor may be the initial failure rate of fistulas compared with grafts, because a higher initial failure rate with fistulas than with grafts automatically leads to prolonged catheter dependence for patients who must initiate dialysis before a permanent access is ready for use. Primary failure of fistulas (as a result of thrombosis or failure of maturation into a functional access) used to range from 10 to 20%^{6,13} but more recently is reported two to four times higher, in the 40 to 45% range.^{6,19,20} In fact, a recent prospective, 11-center European study reported an unexpectedly high primary failure rate of 40%.²¹ In this study, patency rates (access survival from creation) and potential risk factors that affect functional patency (survival from first dialysis use) were examined. Eighty-six percent of mature fistulas were still functional at 18 mo.²¹ Functional patency was adversely affected by diabetes or absence of surveillance, producing variation in secondary failure rates per hospital from 0 to 39%. Overall secondary patency was still good at 75, 70, and 67% at 6, 12, and 18 mo, respectively,²¹ and still higher than those reported for grafts.^{9,12,15,16}

Thus, primary failure has an impact on the overall survival probability of the access. Unfortunately, the latter is frequent, occurring in up to 65% of incident patients¹⁷ despite the recommendations of KDOQI for predialysis management and access planning.¹ One-year primary (intervention-free or unassisted) and secondary (assisted) survival probabilities of fistulas are greater than those of grafts after exclusion of early events but not when early events are included in the analyses.^{18,22} Avoidance of primary fistula failure, as a result of early failure or lack of maturation, is therefore the key area for vascular access outcomes. The main challenge for the nephrologist and surgeon is to minimize risk for primary failure while attempting to provide most patients with a native fistula. The

longer period of catheter dependence in patients who are already on dialysis is associated with lower delivered dosages of dialysis and with higher infection risk.¹⁰ For some, the three-fold or more increase in catheter duration with its attendant risks for underdialysis and catheter-related bacteremia might obviate the other advantages of fistulas over grafts.¹⁷ The optimal time to do so is when the patient is incident to or is in fact predialysis.

Many elements must be in place if we are to succeed in increasing fistula prevalence without seeing the increase in catheter use that has accompanied fistulas, although there is no proof that increases in fistula placement and catheter use are in any way causally related. In my opinion, it is apathy and the underestimation of the opportunities to succeed even in “difficult” patients that produces an attitude of easy surrender and is responsible for the increasing use of catheters. I do not subscribe to therapeutic nihilism by adopting the position that a fistula in many of our elderly or morbidly obese patients is not feasible because vascular anatomy is unsuitable or veins have been ruined/exhausted by previous hospitalizations.

Autologous fistulas also remain underused among such patients because of late referral to nephrologists. Other specialists often see older patients for multiple comorbid conditions, who may engender hesitation or even reluctance to consider additional care plans. Indeed, as stated previously, the choice of the fistula implies a considerable initial effort in terms of care planning and access assistance, because in the short run, early failure or lack of maturation might be problematic.¹⁴ Although it has been reported that patients referred late to the nephrologist are likely to use catheters not only at initiation of dialysis but also in the subsequent months and are less likely to receive a fistula as permanent access, there is simply no explanation for the explicit preference for grafts over fistulas by some practices.^{4,14}

Existence of multiple associations between clinical characteristics, suboptimal care before/around dialysis initiation, and type of vascular access in use raises the issue of indication bias that must be taken into account when interpreting the results of patient survival data and access type. Unmeasured or immeasurable factors (*e.g.*, disease severity; vessel availability and degree of arterial sclerosis; other, unknown factors) mask residual confounding and predispose patients to both use of suboptimal vascular access and death.

Thus, a major issue is how to predict who is at risk for early fistula access failure from early thrombosis or failure to mature, because for these patients, the probability of failure might be so high that pursuing a fistulas is not justified; a “patient first, not fistula first, but avoid a catheter if at all possible” approach might be the best. Unfortunately, no easily accessible, valid, and reliable diagnostic test is available to provide clinicians with meaningful prognostic information that identifies risk for early thrombosis or early maturation failure. Quality (calcification)/diameter of the vessels, presence of cardiovascular diseases, normal or low BP, older age, and race all predict primary failure.^{5,19,20,22} Indeed, primary failure occurs

with similar frequency in centers where preoperative vascular mapping is routinely used to guide the choice of access type and location²² as well as in programs where routine mapping is not in place.⁵

The best tool we have is a scoring system developed by Lok *et al.*²⁰ to differentiate between early surgical failure, as a result of thrombosis or technical complications, and failure to mature. Failure to mature was defined in this study as a fistula that was used for hemodialysis and was unable to provide the prescribed dialysis dosage through two-needle cannulation consistently (in effect, two-needle cannulation for two thirds or more of all dialysis runs) for 1 mo within 6 mo of its creation, despite interventions to facilitate maturation. They found four risk categories for failure to mature (low, moderate, high, and very high) and validated a simple and easily reproducible preoperative, clinical prediction rule to determine fistulas that are likely to fail maturation. These categories predicted a risk for failure to mature estimated at 24, 34, 50, and 69% on the basis of age, coronary artery disease, peripheral vascular disease, and race.²⁰

Despite such efforts, it is unclear whether the best option for the patient at high risk for primary failure is to receive an arteriovenous graft or to receive a fistula anyway once optimal strategies to treat modifiable risk factors for early thrombosis and lack of maturation (hypovolemia and cardiac diseases) have been addressed. Indeed, a substantial proportion of patients with marginal fistulas may still undergo successful salvage procedures or receive successful placement of a new fistula after a former fistula has failed.²³ Alternatively, some advocate the placement of a forearm loop graft when the artery or veins in the forearm are unsuitable for primary fistula construction to mature the vein in the upper arm followed by a strategy of conversion to an elbow-level fistula rather than attempts to salvage a graft with repeated interventions. For some patients, I have advocated the latter.

DISCLOSURES

None.

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In the perfect world, every patient with chronic kidney disease (CKD) would have nephrology follow-up and receive an arteriovenous fistula well before initiating dialysis, every fistula would mature successfully, and, thus, every new hemodialysis patient would have a mature fistula suitable for dialysis. In the real world, many patients with CKD do not have predialysis follow-up by a nephrologist, many fistulas do not mature, and, as a result, many patients start dialysis with a catheter.¹ Currently, 75% of incident US patients initiate dialysis with a catheter.²

The conclusion that fistulas are the best type of vascular access is based on the premise that fistulas last longer than grafts and require fewer interventions (angioplasty, thrombectomy, or surgical revision) to maintain their long-term patency for dialysis.³ Careful scrutiny of the studies cited as evidence reveals a strong selection bias. First, many of these studies included only fistulas and grafts that were successfully cannulated for dialysis. Patients whose vascular access failed before it could be used for dialysis (primary failure) were specifically excluded from analysis. Given that primary failures are substantially higher for fistulas (20 to 50%) than for grafts (10 to 20%), their exclusion from the outcome analysis is unfairly biased in favor of fistulas.¹ In fact, the comparative studies that included primary failures (intention-to-treat analysis) showed equivalent cumulative survival between fistulas and grafts.^{4–6}

Second, many studies underestimated the true frequency of primary fistula failure by using surrogate outcomes. The “gold standard” for a mature fistula is one that can be cannulated repeatedly with two needles and deliver a dialysis blood flow ≥ 300 ml/min for at least 1 mo.¹ Surrogate fistula outcomes, such as lack of early thrombosis, positive thrill and bruit at the postoperative surgical visit, or ability to use the fistula for just 1 wk, erroneously classify some immature fistulas as being mature, thereby underestimating the true frequency of failure to mature. Third, even fistulas that mature require substantially longer time to successful use than do grafts (approximately 8 to 12 wk for fistulas *versus* 2 to 4 wk for grafts). This period is further prolonged if the fistula requires a subsequent radiologic or surgical intervention to achieve maturity. For the subset of patients who are already on dialysis at the time of access creation, this translates to prolonged catheter dependence.

The proportion of patients dialyzing with fistulas can be (and has been) increased by concerted efforts to encourage early nephrology referral, routine preoperative vascular mapping to increase fistula creation, and efforts to salvage immature fistulas by radiologic or surgical interventions.⁷ Clinical assessment of fistula maturity should be performed by 6 to 8 wk, and appropriate radiologic or surgical intervention should follow.^{8,9} Fruitlessly waiting 6 mo before declaring a fistula failure wastes many months that could be used to establish a new, permanent access.

Notwithstanding such efforts, several multicenter studies have highlighted important disparities in fistula use among certain dialysis subpopulations. Specifically, a lower prevalence of fistulas has been associated with female gender, black race, older age, obesity, and cardiovascular disease.¹⁰ Moreover, these same clinical features have been associated with a higher likelihood of primary fistula failure¹ and with delayed transition from a catheter to a permanent access.¹¹ A recent large, multicenter, observational study validated a simple formula for estimation of the risk for primary fistula failure.¹² Using four clinical parameters (age, race, coronary artery disease, and peripheral vascular disease), it was possible to stratify the risk for failure to mature. This risk ranged from 24% in patients with scores < 2.0 to 70% in those with scores > 7.0 . Whereas a fistula may be the ideal access choice in a young white man without cardiovascular morbidity, it may be a poor choice in an older black woman with cardiovascular morbidity.

In approximately 50% of patients who have CKD and receive their first vascular access, preoperative mapping reveals no suitable vessels for creation of a forearm fistula.¹ In such patients, the current Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommend placing an upper arm fistula.³ This approach has two drawbacks. First, it sacrifices future options for an ipsilateral forearm access. Why not place a forearm graft first? Second, if the patient is already on dialysis, then it subjects him or her to prolonged catheter dependence. Creating a forearm graft first shortens the period of catheter dependence. Moreover, the forearm graft causes dilation of veins in the upper arm. Thus, when the graft fails, a new upper arm fistula can be created and used much earlier, because vein maturation has already occurred.

Certainly, a *mature* fistula is preferable to a *mature* graft; however, a mature graft is far preferable to an immature fistula with prolonged catheter dependence. A recent study provided detailed analysis of the tradeoffs between placement of a fistula or a graft.⁵ As compared with patients receiving a graft, patients receiving a fistula were more likely to have a primary access failure, required more interventions to achieve access maturation, had a substantially longer period of catheter dependence, and experienced more episodes of catheter-related bacteremia. Conversely, among the subset of patients whose access matured, fistulas had superior longevity with a three-fold lower frequency of interventions to maintain long-term patency for dialysis.

One size does not fit all. Although fistulas may be the optimal initial vascular access for some patients, grafts may be a better choice for others. One consideration is whether the patient has already initiated dialysis. The patient with CKD may have many months before a mature access becomes necessary. Thus, one has the luxury of placing the fistula and performing subsequent interventions (if needed) to promote maturity. In contrast, prolonged catheter dependence is the tradeoff incurred when fistulas are placed in patients who are already on dialysis. Moreover, the failure rate of fistulas is higher when placed in dialysis patients, as compared with predialysis patients.¹³ In the United States, the median time from fistula placement to its first cannulation is approximately 3 mo,¹³ and this is just for patients whose fistula matures. For the substan-

tial group whose fistula fails to mature, a second access must be placed, further prolonging catheter dependence.

An unfortunate byproduct of the Fistula First initiative has been the concurrent increase in patients' undergoing dialysis with catheters. During a 5-yr period in which the proportion of patients who underwent dialysis with fistulas increased by 8% (from 27 to 35%), the proportion of catheter-dependent patients increased by 9% (from 19 to 28%).² Catheter-dependent patients pay a high price in terms of infection, dialysis adequacy, and mortality. In a recent observational study, bacteremia was observed in 35% of catheter-dependent patients at 3 mo and in 48% at 6 mo.¹⁴ Catheter-dependent patients were also three times as likely to have inadequate dialysis, as compared with those who underwent dialysis with a fistula or graft. Moreover, mortality is three-fold higher in patients with catheters, as compared with patients with a permanent access (fistula or graft), and is reduced substantially in catheter-dependent patients who transition to a permanent access.¹⁵

The goal of the Fistula First guidelines was to encourage more aggressive efforts to consider fistula placement. Unfortunately, they have been transformed into rigid rules by the dialysis networks and dialysis providers. Medical directors of individual dialysis units now receive regular feedback about the proportion of their patients with fistulas. These reports frequently do not distinguish between mature and immature fistulas. Similarly, surgeons are now judged by what proportion of their vascular accesses placed are fistulas, rather than grafts, without consideration of the primary failure rates. Of even greater concern, Centers for Medicare and Medicaid Services recently proposed a differential reimbursement for outpatient dialysis units on the basis of their proportion of patients with fistulas. Units exceeding the threshold of patients with fistulas would receive higher monthly payments, and those below the threshold would be penalized financially. There is no consideration in these "report cards" of objective differences in primary fistula failure rates among patient subsets. The optimal proportion of fistulas and grafts may well vary among dialysis units, according to their case mix of patients.

In summary, the disadvantage of fistulas is their relatively high rate of failure to mature, whereas the major problem with grafts is aggressive neointimal hyperplasia leading to recurrent stenosis and thrombosis, requiring frequent interventions to maintain their patency for dialysis. Fistula placement may be the best option for patients who are not yet on dialysis, whose clinical characteristics predict a relatively low likelihood of nonmaturation, and who have a long life expectancy. Conversely, grafts may be preferred for patients who are already on dialysis, especially if they have already had primary failure of a previous fistula; for patients whose characteristics predict a high likelihood of nonmaturation; for patients with fairly limited life expectancy; and to transition to a future upper arm fistula in patients whose vascular anatomy is unsuitable for a forearm fistula or those with a failed forearm fistula. There is currently intense, ongoing research on pharmacologic interventions to improve fistula outcomes,¹⁶ which, if successful, may shift the balance in favor of fistulas. Conversely, pharma-

cologic interventions that limit neointimal hyperplasia¹⁷ may enhance the preference for grafts over fistulas. Ultimately, the decision about which type of vascular access to place in a given patient should consider all of these factors so as to minimize the proportion of catheter-dependent dialysis patients.

DISCLOSURES

None.

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