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Nonmaturing Fistulae: Epidemiology, Possible Interventions, and Outcomes

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Autogenous arteriovenous fistulae are the best method for prolonged, successful dialysis access. However, a substantial limitation of dialysis fistulae is their high primary failure rate, estimated to be as high as 70% for radiocephalic fistulae. Fistula maturation is influenced by demographic risk factors as well as anatomical barriers, the latter of which can be readily identified by noninvasive ultrasound imaging and physical examination. These barriers can be categorized as inflow problems (native arterial disease, arteriovenous anastomotic stenosis, and juxta-anastomotic stenosis) or outflow problems (proximal venous stenosis or collateral veins). Venous stenoses represent the most commonly observed barrier to fistula maturation. By treating these barriers with a systematic approach, interventionalists can significantly improve the likelihood of a fistula's usability for dialysis.

KEYWORDS dialysis, dialysis interventions, arteriovenous fistula

Introduction

The autogenous arteriovenous fistula is the preferred method of vascular access for dialysis.[1] Relative to grafts, fistulae require fewer interventions to maintain patency, have a lower rate of thrombosis, and have longer access lifespans.[2] Moreover, the rates of infection and steal syndrome are lower for fistulae than for grafts.[3] These benefits translate into a mortality benefit for patients undergoing dialysis via fistulae.[4]

However, a substantial limitation of dialysis fistulae is their high primary failure rate. Various studies have shown that between 30% and 70% of fistulae are never able to be used for a single successful session of dialysis.[5] Ironically, following the Fistula First Initiative (FFI) in 2003, an increase in the use of central venous catheters was seen, at least in part owing to the increased attempts to place fistulae, and the resultant increase in primary failure.[6] Indeed, there were a higher percentage of patients initiating dialysis on catheters in the late 2000s following FFI than in the late 1990s before FFI, likely because of the use of catheters until fistula maturation.[5] "Fistula First" has thus given way to "Fistula First and Lines Last," with grafts considered acceptable when necessary.

A functioning fistula remains the best form of dialysis access. In this article, we will discuss reasons why fistulae fail to mature, and the diagnostic tools that are available to identify the most common causes. We will also describe several interventional techniques that can be employed to promote fistula maturation.

What Defines a "Nonmaturing" Fistula?

Nonmaturing fistulae, or fistulae that exhibit early suitability failure, are defined as accesses that, despite appropriate interventions, are unable to be used for dialysis within 3 months of formation.[7] Depending on practice patterns, the readiness of a fistula for cannulation may be determined by the creating vascular surgeon or the dialysis nurse. However, even experienced nurses are able to

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determine access maturity with an accuracy of only approximately 80%.[8] Moreover, in the United States, it is common practice not to attempt cannulation for 3 months after fistula formation, though in Europe cannulation at 4 weeks is standard. Thus, given the subjectivity of evaluating a fistula's readiness for cannulation, the above definition of a mature fistula is not only problematic but also somewhat of a tautology.

A practical definition for a mature fistula is one that allows repeated successful cannulation and one that sustains enough blood flow to provide adequate clearance. K-DOQI offers a slightly more objective rubric to evaluate fistula maturity in the form of the simple "rules of 6": (1) able to support blood flow of 600 mL/min, (2) located less than 6 mm from the skin surface, and (3) measure greater than 6 mm in diameter. A corollary to these rules is that the fistula should have a relatively straight segment at least 6 cm in length (though ideally longer) for cannulation. Ultrasound imaging can also offer quantitative assessments of fistula flow, diameter, and access depth; this modality's utility in evaluating fistula maturity and identifying causes of failure are discussed subsequently. Additionally, while it is not common practice, an interventional radiologist could improve a dialysis center's primary patency rate by training and supervising the use of ultrasound guidance for cannulation. Image-guided access may allow a fistula to be used earlier and possibly spare the patient a visit to the procedure suite for a central venous catheter placement.

Causes and Epidemiology of Nonmaturing Fistulae

Following fistula formation, the anastomosed vein experiences a sudden increase in shear stress and blood pressure. These factors, through a pathway that involves nitric oxide release, result in dilatation of the vein and remodeling of the vessel wall. In the setting of poor vessel elasticity, flow-limiting stenoses, or dissipation of flow by accessory or collateral veins, this maturation process does not occur.

Demographic Risk Factors for Nonmaturation

Although interventionalists have understandably paid more attention to anatomical hurdles, it is important to appreciate the multiple demographic risk factors that have been associated with fistula nonmaturation. Female sex and diabetes have been linked with early fistula failure,[9] though a recent study casts doubt on diabetes as a risk factor.[10] In the largest published series, a predictive model identified age greater than 65 years, history of peripheral vascular disease or coronary artery disease, and white race as clinical predictors for fistula nonmaturation.[11]

Anatomical Causes of Nonmaturation

Anatomical causes for fistula nonmaturation can occur anywhere along the fistula circuit and are typically multifactorial. They can be generally classified as inflow problems (native arterial disease, arteriovenous anastomotic stenosis, and juxta-anastomotic stenosis) or outflow problems (proximal venous stenosis or collateral veins). Inadequate arterial inflow due to peripheral arterial disease accounts for a small proportion (~5%) of nonmaturing fistulae, though anastomotic stenoses are seen more frequently (~40%).[12,13] The most commonly identified lesion in a nonmaturing fistula is a venous stenosis (~60%). Accessory or collateral veins (~20%) are also considered as important findings in nonmaturing fistulae.[14,15] Veins that are too deep to allow for palpation-guided cannulation account for 5% of nonmaturing fistulae.[15]

The prevalence of these risk factors for nonmaturation varies with anatomy: not all fistulae are created equal. Radiocephalic fistulae are the K-DOQI-preferred first choice for dialysis access owing to the lower rates of steal syndrome and the fact that a more proximal fistula can still be created should the radiocephalic fistula fail. However, radiocephalic fistulae have the highest rates of primary failure; up to two-thirds will never be suitable for dialysis.[16] The most common cause of failure is venous stenosis, and the most common location is a juxta-anastomotic stenosis. A stenosis at this location is seen more frequently in radiocephalic fistulae than in any other fistulae. The causes of juxta-anastomotic stenoses are not completely understood, but the stenosis may be a ramification of the skeletonization and mobilization of the vein during surgical fistula creation.[17]

Brachiocephalic fistulae have higher patency and faster maturation rates than radiocephalic fistulae.[18] However, given the higher rate of steal syndrome[19] and preclusion of subsequent distal forearm fistula formation, the radiocephalic fistula is still preferred. On the contrary, brachiocephalic fistulae have higher rates of primary patency compared to radiocephalic fistula in patients with risk factors for nonmaturation, including age greater than 65 years, diabetes, and female sex and may therefore be appropriate in these high-risk patients.[16] Venous stenosis is also the principal culprit for nonmaturation of brachiocephalic fistulae.

Following venous stenosis, the next most common cause of fistula failure are accessory or collateral veins. Accessory veins are naturally present branches arising from the fistula outflow vein, whereas collateral veins are bypass channels that form in response to a downstream, flow-limiting stenosis. Accessory or collateral veins transform a serial circuit (single outflow vein) into a parallel circuit (multiple outflow veins), reducing the blood flow within each individual vein and thus impeding the maturation process.

Diagnostic Tools for Nonmaturing Fistulae

Physical Examination

A fistula's suitability for dialysis access can be determined by physical examination at 4-6 weeks after creation. If a