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The Surgeon, Journal of the Royal Colleges of Surgeons of Edinburgh and Ireland
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Arteriovenous fistula in dialysis patients: Factors implicated in early and late AVF maturation failure

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ARTICLE INFO

Article history:
Received 17 October 2015
Received in revised form
9 February 2016
Accepted 12 February 2016
Available online 15 March 2016

Keywords:
Arteriovenous fistula
AVF
Dialysis
End stage renal disease
Dialysis access
Access survival
Primary AVF patency
Fistula maturation
AVF failure
AVF non-maturation
Brachiobasilic arteriovenous fistula
Far-Infra Red

ABSTRACT

Increasing numbers of patients are being diagnosed with end-stage renal disease (ESRD), and the demand for on haemodialysis (HD) is rising. Arteriovenous fistulae (AVFs) remain the best conduit for adequate HD, with fewer complications associated with long-term use compared to bypass grafts and central venous catheters. However, it is known that many newly formed fistulae do not mature to provide useful HD access. The paper provides a narrative overview of factors influencing the process of AVF maturation failure.

Introduction

The number of patients with end-stage renal disease (ESRD) has been growing steadily, thus increasing the demand for haemodialysis (HD).[1,2] Arteriovenous fistula (AVF) has been shown to be the best route for delivering HD.[3–5] The main disadvantage of AVF is the rate of non-maturation (failure to use the new fistula for successful haemodialysis sessions); as the newly formed conduit needs to mature into a low resistance circuit, allowing frequent cannulation with increased flow rates. There is no universal definition for a mature AVF;

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http://dx.doi.org/10.1016/j.surge.2016.02.001

the one adopted in the updated NKF-KDOQI guidelines has been widely in use. KDOQI introduced the role of 6s to define maturation (Flow of 600 ml/min, an AVF located less than 6 millimetres from the skin surface to facilitate successful repeated cannulation by HD staff and finally a minimal diameter of 6 millimetres).[6] A mature fistula should be consistently cannulatable, and should allow blood flow of at least 300–400 ml per minute. This review summarises current knowledge about why so many fistulae fail to mature.[7,8] Additionally, it provides an overview of the current practice and understanding of the complex nature of the process of AVF maturation by the authors of this review.

Methods

Pubmed and Embase were searched using a number of search terms (maturation, arteriovenous fistula, AVF, non-maturation, prediction, failure, end-stage renal disease and haemodialysis) in different combinations. Retrieved articles were included based on relevance to the subject of the narrative overview after assessing all abstracts. Although we agree that a detailed assessment of the quality of the individual studies included would increase the rigour of the review; however, we feel it can be addressed in a future systematic review, as this article is intended as a narrative review.

Patient characteristics: sex, age and diabetes mellitus

Various patient factors have been suggested to be associated with poor AVF maturation, including diabetes mellitus (DM), female sex and age. However, those factors are less important when preoperative ultrasound mappings show adequate size vessels. Preoperative US venous mapping has been proven to significantly aid the decision of placing an AVF that will have better odds of successful maturation.[9–11]

Salmela et al., found that diabetes mellitus, female sex and thrombophilia were associated with decreased primary fistula patency rates.[12] Conversely, Sedlacek et al. reported that diabetes was not an independent risk factor for AVF non-maturation, and furthermore presence of diabetes had no effect on the prevalence of AVF creation.[13] Recently, Allon et al. reported that both diabetes and age did not influence AVF maturation outcomes, although both were significantly linked to increased intimal hyperplasia.[14] Similarly, Farber et al. found that diabetes was not associated with early thrombosis.[15]

Diabetes potentially exerts its influence on AVF maturation by affecting the bioavailability of Nitric Oxide (NO) as most of the metabolic abnormalities that take place in diabetic patients can disrupt the balance between production of NO and its degradation.[16] In addition, diabetes is a known risk factor for atherosclerosis, which can also limit blood flow through a newly created AVF. Overall, the evidence that diabetes alone can predict non-maturation is controversial, as the rate of AVF maturation in diabetics is similar to non-diabetics in some published series.

Elderly patients (e.g.: above 65 years) are thought to have worse patency rates.[17,18] Lok et al. argued that age should not be a limiting factor when considering vascular access options for HD as their study showed equal survival and procedural rates in patients above or under 65 years of age.[8] This suggests that in those fistulae that mature successfully, age is less relevant in determining cumulative patency.

A study of cumulative access survival in AVF found that age, race, diabetes, gender and peripheral vascular disease did not show significant association with access survival.[19] The number of salvage procedures was the only significant factor associated with cumulative access survival in this study, as more interventions were required in elderly patients to maintain patency.[19] Tordoir et al. argued that elderly patients are more likely to have calcified arteries and small veins, therefore suggested the use of early stick catheters and central vein catheters.[20] In the very elderly with multiple comorbidities, the authors believe that consideration should be given to dialysis via central venous catheters (CVCs) as the primary access choice to reduce the surgical burden from repeated salvage procedures usually required to maintain patency.

Some studies suggested a significant negative association between female gender and fistula patency rates and prolonged maturation.[12,17,21] Also, others have suggested that elderly female patients (65+) are at higher risk of fistula non-maturation than men are of the same age group.[14,18] However, several studies disputed the association between female sex and high risk of AVF non-maturation.[14,19,22] Recently, Bashar et al. found that female gender, history of a kidney transplant and calcium channel blocker agents at the time of fistula creation all influenced AVF maturation, with non-maturation associated with a female gender in their series ($P = 0.004$).[23]

Lee et al. studied factors implicated in AVFs maturation. They found that race, diabetes, age, gender and peripheral vascular disease did not statistically influence the outcome; however, the sole predictor of access cumulative failure in their study was the number of secondary procedures required to maintain patency.[19] Feldman et al. in a series of 348 HD patients found that non-maturation was associated with a previous history of stroke, transient ischaemic attack, increasing age and dependence on dialysis when the fistula was created.[24]

In summary, there are papers suggesting that diabetes mellitus, female sex and increasing age among other factors can decrease fistula maturation and increase failure, however other papers dispute this. Certainly none of these factors should influence the decision to proceed to AVF formation in these groups.

Pathophysiology of AVF non-maturation

Maturation of AVF depends on variable biomechanical forces induced in the vascular system following AVF formation. Remodelling of the arterial limb is characterised by outward hypertrophic remodelling of the intimal layer leading to vessel dilatation; while at the venous side, the process can result in excessive intimal thickening resulting in narrowing of the venous limb.[25] The outward remodelling of the arteries assist