



NON-MATURED ARTERIOVENOUS FISTULAE FOR HAEMODIALYSIS: DIAGNOSIS, ENDOVASCULAR AND SURGICAL TREATMENT

MARKO MALOVRH*

Department of Nephrology, University Medical Centre Ljubljana,
Zaloška 7, 1525 Ljubljana, Slovenia

* Corresponding author

ABSTRACT

Non-maturation is a feature of autologous vascular access. The autologous arteriovenous fistula needs time to mature and for the vein to enlarge to a size where it can be needled for dialysis. A fistula that fails early is one that either never develops adequately to support dialysis or fails within the first three months of its use. Two variables are required for fistula maturation. Firstly, the fistula should have adequate blood flow to support dialysis and secondly, it should have enough size to allow for successful repetitive cannulation. Three main reasons for maturation failure are: arterial and venous problems and the presence of accessory veins. Early diagnostics and intervention for fistula maturation minimizes catheter use and its associated complications. The identification of immature fistulae is relatively simple. Physical examination has been highlighted to be a valuable tool in assessing fistula. Any fistula that fails to mature adequately and demonstrates abnormal physical findings should be studied aggressively. Ultrasonography can successfully identify candidates who fail to meet the recently developed criteria for immature fistulae. In recent years, digital subtraction angiography and contrast-enhanced magnetic resonance angiography has been introduced for assessment of dysfunctional haemodialysis conduits, including immature fistulae. A great majority of non-matured fistulae can be successfully salvaged using percutaneous techniques. In addition to endovascular techniques, surgical intervention can also be an option. This paper reviews the process of fistula maturation and presents information regarding how to obtain a mature fistula.

KEY WORDS: haemodialysis, arteriovenous fistula, vascular mapping, non-maturation, endovascular treatment, surgical treatment

INTRODUCTION

When the time arrives for creation of an arteriovenous access for long-term dialysis, current recommendations indicate that native veins should be preferred over prosthetic material and that the arteriovenous communication should be performed as distally as possible (1,2). The construction of a functional radial-cephalic fistula can be challenging, and high initial failure rates have been reported in many publications. Estimates of non-maturation rates vary from just under 10% in brachiocephalic fistulae to between 25% and 33% in radiocephalic fistula (3-5). Currently, there are no well established criteria that define fistula maturation. Non-maturation may be defined clinically on the basis of insufficient vessel development one month after creation, difficulties in cannulation, or impossibility to achieve more than 300 mL/min, needed for successful dialysis treatment or defined as an fistula that had been created for at least eight weeks but had not matured enough to allow successful cannulation or use during haemodialysis (6,7). Frequently, these patients are consigned to a dialysis catheter for dialysis therapy. Non-maturation is also an issue for tertiary procedures like brachiocephalic or brachio basilic fistulae where fistula is formed between larger veins and arteries (8).

Non-maturation

The most important determinant of fistula maturation is likely to be the response of both the feeding artery and the drainage vein to the increase in shear stress that occurs following the creation of an arteriovenous anastomosis. An increase in shear stress invariably results in vascular dilatation in an attempt to return shear stress levels back to normal. If arteriovenous fistula is created in patients with severe vascular disease and diabetes, it is possible that the conventional wisdom about the linkage between higher shear stress rates and vascular dilatation may not always hold true. Similar reasons may result in a failure of venous dilatation. Aggressive push towards trying to create a native arteriovenous fistula whenever possible could result in the use of a poor venous segment that has lost the ability to vasodilate because of prior vein puncture. Predictive models for fistula stress the importance of age or cardiovascular disease as well as diabetes. In addition, other factors are associated with fistula non-maturation. There are identifiable venous stenosis and accessory branch veins (9). Accelerated venous intimal hyperplasia is the reason for venous stenosis. There are two factors responsible for intimal hyperplasia: first, fistula configuration and

consequently low shear stress what could result in focal areas of neointimal hyperplasia and vasoconstriction and second, vascular injury associated with mobilization and manipulation by the surgeon during the procedure. Normally, increments in blood flow begin to occur soon after the construction of arteriovenous fistula. Won et al. found significant increase in blood flow from average 20,9 mL/min in the radial artery average 174 mL/min in the fistula only ten minutes after creation of anastomosis (12). Major changes in the fistula blood flow and size occurred within four weeks after fistula construction (13). No significant changes in these two parameters were noted in the second, third or fourth month after fistula creation. Good medical practice would suggest that a fistula should be evaluated for adequacy of development within 4-6 weeks. Two important issues highlight why early identification and intervention approach is critical. Firstly, a majority of fistulae with early failure demonstrate stenotic lesions within the access circuit. In addition, vascular stenosis is a progressive process. This is an important consideration as the stenosis will eventually culminate in complete occlusion leading to access thrombosis. In this context, the opportunity to salvage an immature fistula may be lost. Secondly, and perhaps more importantly, if a patient has an immature fistula and has initiated dialysis therapy using dialysis catheter is now exposed to all of complications related to catheter use. Hence, early intervention to identify and salvage immature fistula becomes an important part of preventing fistula loss and minimizing complications related to dialysis catheters (3).

Pre-operative vascular mapping

Vascular mapping before arteriovenous fistula construction has been shown to result in decrease of non-matured arteriovenous fistulae. For optimal results, both arterial and venous evaluation is required for fistula creation. Physical examination is a simple tool that can be employed to conduct vascular mapping. Venous evaluation is performed to assess the diameter, cannulation segment length and approximate distance of the vein from the surface. A tourniquet is placed around the upper arm and veins of the extremity are inspected. Pulse examination and differential blood pressure measurement can be easily performed using physical evaluation. Utility of physical evaluation is less than optimal. If the veins are not seen easily with the naked eye after application of the tourniquet, the patient is considered to not have good veins for arteriovenous fistula creation. A recent study documented that visibility of veins by clinical inspection was present in only 54

of 116 consecutive patients (46.5%) whereas poor clinically visible or clinically absent veins were found in 62 (53.5%). A majority (77%) of these 62 patients showed adequate veins in duplex ultrasonography (10). Beside physical examination, ultrasound is the method of choice. Because of its non-invasive nature, ease of performance, safety and success, ultrasonography has emerged as a critically important tool for vascular mapping. Duplex sonography helps identify the optimal location for successful creation of vascular access and the time necessary for its development. The criteria used to determine suitability of arteries are internal diameter, thickness and morphology of the artery wall, resistance index and blood flow before and after reactive hyperaemia, and for suitability of veins internal diameter, and distensibility of the vein (10,11). Malovrh concluded that duplex ultrasonography helps identify the optimal location for successful fistula creation and the time necessary for its development (10). Arterial narrowing and calcification are relatively common in patients with chronic kidney disease. While ultrasound examination provides an accurate assessment of peripheral vasculature, it does not provide direct visualization of the central veins, a weakness which could potentially result in development of swelling associated with central stenosis after arteriovenous fistula placement. Vascular mapping can also be conducted using radiocontrast administration. This technique allows for direct visualization of the peripheral as well as the central veins.

Diagnosis of an immature fistula

The identification of candidates with immature arteriovenous fistula is relatively simple. Physical examination is a valuable tool. The mature arteriovenous fistula has a soft pulse and it is easily compressible. There is a prominent thrill at the anastomosis which is present throughout entire structure during systole and diastole. When the extremity is elevated the fistula will generally collapse, at least partially. With juxta-anastomotic stenosis, a bounding pulse is felt at the anastomosis. The thrill is present only in the systole. After completely occluding the access several centimetres downstream from the arterial anastomosis it may be found a weak pulse as a result of a poor arterial inflow. Accessory vein can be diagnosed by inspection only. Examination by palpation can detect accessory vein by the presence of thrill over its trunk. Finally, with downstream stenosis, arteriovenous fistula becomes more forcefully pulsatile with predominantly systolic thrill. When extremity is elevated, the portion of fistula distal to stenosis remains distended with proximal portion col-

lapse in the normal fashion (14). Based on the above on the above information, physical examination may be the most practical approach to the evaluation of fistula maturation. This evaluation should be undertaken between 4-6 weeks by a skill examiner. Any fistula that fails to mature adequately and demonstrates abnormal physical findings should be studied aggressively and abnormalities that are detected should be corrected before a plan to create a new access is made. Beside clinical examination, non-invasive investigation using colour-Doppler ultrasonography (CDUS) has been shown to be a valuable diagnostic modality in the prevention and management of complications of haemodialysis access. Grogan et al. claim the routine CDUS surveillance of newly created arteriovenous fistulae 4-6 weeks post-operatively will lead to increased early intervention and an increased functional utilization rate of arteriovenous fistula (15). Clinically immature fistulae frequently showed one or more potentially remediable problems seen at postoperative CDUS, which may be useful in triaging the subsequent treatment of immature fistulae to the appropriate surgical or endovascular service (16). Digital subtraction angiography (DSA) is invasive, but a major advantage over the other imaging modalities is the possibility of performing the endovascular intervention immediately, in case a hemodynamically significant stenosis has been detected. Depiction of the access tree and endovascular treatment may be performed after femoral artery puncture, followed by selective catheterisation of upper limb bearing the vascular access, or through brachial artery catheterisation (17, 18). Contrast-enhanced magnetic resonance angiography (CE-MRA) has been introduced for non-invasive assessment of dysfunctional haemodialysis conduits, including immature fistulae. CE-MRA is minimally invasive, lacks ionizing radiation, provides angiographic map of the complete vascular access tree and has a high accuracy for stenosis detection (19). CE-MRA, as CDUS, facilitates the interventionalist to perform a DSA and angioplasty through providing appropriate puncture location. Drawbacks of CE-MRA are high imaging costs, limited availability of MR scan time and the absence of MR-guided access intervention. Planken et al. found that CE-MRA enables detection of upper arm extremity arterial and venous stenosis and occlusions, related with vascular access failure and non-maturation, with substantial to almost perfect inter-observer agreement and that this is a valuable tool for prediction of vascular access early failure and non-maturation with a better positive predictive value (77%) than CDUS (20).

Treatment of non-matured fistulae

Recent studies have demonstrated that the two most common problems observed in early fistula failure are the presence of stenosis and accessory veins (6,21). However, more and more incident patients may present with poor quality arteries as the consequence of diabetes, smoking, hypertension, dyslipemia or increasing age. Nowadays, there are two methods of treatment of non-matured fistulae: endovascular and surgical treatment.

By use of an aggressive approach and employment of two basic techniques, balloon angioplasty and vein obliteration, nephrologists can successfully salvage and subsequently utilize an otherwise failed fistula. In a prospective observational study, 100 patients with early failure underwent evaluation and treatment. Vascular stenosis and the presence of a significant accessory vein alone or in combination are found to be the culprits in most instances. Venous stenosis was present in 78% of the cases. A majority of these lesions (48%) were found to be close to the anastomosis. A significant accessory was present in 46% of the cases. Percutaneous balloon angioplasty was performed with a 98% and vein obliteration with a 100% success rate. After intervention, it was possible to initiate dialysis using the fistula in 92%. Actuarial life table analysis showed that 68% were functional at 12 months. The overall complication rate in this series was 4% (6). Delayed maturation of radial-cephalic fistulas can be due to lesions of the radial artery that are amenable to percutaneous dilation. Turmel-Rodrigues et al. demonstrated the successful application of endovascular techniques to salvage fistulae that failed to mature. Seventy four patients who were included had undergone attempted percutaneous dilation of the forearm artery feeding an immature radiocephalic fistula. Technical success was achieved in 73/74 cases following angioplasty. All but two fistulas were then successfully used for dialysis. Primary patency rates at 12 and 24 months were significantly better for pure arterial lesions, with 65% and 61% compared to 42% and 35% in cases of concomitant venous stenosis ($P < 0.04$). The secondary patency rates were 96% and 94% at 1 and 2 years, respectively (18). These results indicate that forearm arteries feeding dialysis fistulae that do not dilate spontaneously because of stenosis or wall abnormalities, respond well to percutaneous balloon dilatation. Several investigators conclude that lack of maturation is caused by underlying stenosis in every patient, and they advocate angioplasty in all non-maturing fistulae (22, 23). In their opinion, the rationale for embolization of collaterals may leave stenosis untreated. On the other

hand, it can be argued that lack of maturation is commonly caused by competing veins (6, 7). Embolization or ligation of these veins will augment flow within the intended outflow vein and thereby enable maturation. Moreover, Planken et al. recently observed that ligation of accessory veins during initial fistula creation can potentially reduce non-maturation rates (24). While interventional techniques are growing, surgery still plays a strong role. Fistulae that fail immediately are the consequence of poor selection of vessels, or poor surgical technique. The non-maturing fistula is one that has worked for at least 24 hours. It is important to be able to identify non-maturing fistula in clinical practice and to have a plan to intervene in a timely manner, to avoid undue delay in correcting problems. If there is persistent low flow and no sign of vein enlargement despite an absence of other identifiable factors predisposing to fistula failure, then ligation and creation of a new fistula is advisable. Accessory veins are best ignored if small. If large and diverting significant flow, they can be ligated under local anaesthesia, through small stab incisions adjacent to the vein. Venous stenosis within the body of a fistula is best treated with balloon angioplasty. Juxta-anastomotic stenosis may be treated surgically or percutaneously. A prospective non-randomized study of 64 patients showed that outcomes were similar using angioplasty or surgery. Restenosis rates were significantly higher following angioplasty (25). The surgical approach is usually performed under local anaesthesia, the vein is mobilised proximally and reanastomosed to the proximal part radial artery. This procedure is more difficult at the elbow and it is often easier to attempt balloon angioplasty, reserving surgery for those that fail. Poor arterial inflow should be identified pre-operatively by ultrasound, but this is not always possible. Part of the assessment of the non-maturing fistula should include detailed assessment of the inflow circuit. Arterial stenosis greater than 50% coupled with poor flow should undergo angioplasty. If this fails to improve fistula flow rates, it is unlikely that surgical bypass will be of help. Deciding to revise or replace a non-maturing fistula is easy when the fistula shows no sign of maturation (i.e. persistent low flow and no enlargement). In this situation the surgeon and patient will recognize the need to move to a new site. The problem is what to do when there is some evidence of maturation and simple steps have not produced immediate or adequate results. It is recommended in this situation to begin the assessment of the patient again, starting out on the pathway from the beginning.

CONCLUSION

Non-maturing of autologous arteriovenous fistulae is a significant, even increasing problem in vascular access. To maximize the likelihood of success, it is important to plan surgery carefully, assessing both inflow artery and the venous outflow. Physical examination should be basic method and should be performed by every nephrologist. Additional examination of arteries and veins by non-invasive ultrasound is an objective assessment and provides an excellent evaluation of both arteries and veins for creation of an arteriovenous fistula. Failure to achieve maturation in 4-6 weeks should prompt for a search for reversible aetiologies. Post-operative fistula ultrasonography may be useful in triaging the subsequent treatment of the non-maturing fistula to the appropriate endovascular or surgical intervention. The use of this strategy will help to optimise the number of fistulae that mature to use for dialysis.

Conflict of interest statement. None to declare.

REFERENCES

- (1) Vascular Access Work Group. Clinical practice guidelines for vascular access. *Am. J. Kidney Dis.* 2006;48: S176-S273.
- (2) Tordoir J., Canaud B., Haage P., et al. EBPg on vascular access. *Nephrol. Dial. Transplant.* 2007; 22(Suppl 2):ii88-ii117.
- (3) Miller P., Tolwani A., Luscly C., et al. Predictors of adequacy of arteriovenous fistulas in haemodialysis patients. *Kidney Int.* 1999; 56:275-280.
- (4) Aacher E., Gade O., Hingorani A. et al. Changes in the practice of angioaccess surgery: impact of dialysis outcome and quality initiative recommendations. *J. Vasc. Surg.* 2000;31:48-92.
- (5) Tordoir J.H., Rooyens P., Dammers R., van der Sande F.M., de Haan M., Yo T.I. Prospective evaluation of failure modes in autogenous radiocephalic wrist access for haemodialysis. *Nephrol. Dial. Transplant.* 2003;18:378-383.
- (6) Beathard G.A., Arnold P., Jackson J. et al. Aggressive treatment of early fistula failure. *Kidney Int.* 2003; 64:1487-1494.
- (7) Nassar G.M., Nguyen B., Rhee E. et al. Endovascular treatment of "the failing to mature" arteriovenous fistula. *Clin. J. Am. Soc. Nephrol.* 2006;1:275-280.
- (8) Casey K., Tonnessen B.H., Mannava K. et al. Brachial versus basilic vein dialysis fistulae: a comparison of maturation and patency rates. *J. Vasc. Surg.* 2008;36:237-241.
- (9) Lok C.E., Allon M., Moist L. et al. Risk equation determining unsuccessful cannulation and failure to maturation in arteriovenous fistulas. *J. Am. Soc. Nephrol.* 2006;17: 3204-3212.
- (10) Malovrh M. Native arteriovenous fistula: preoperative evaluation. *Am. J. Kidney Dis.* 2002;39:1218-1225.
- (11) Malovrh M. Non-invasive evaluation of vessels by duplex sonography prior to construction of arteriovenous fistulas for haemodialysis. *Nephrol. Dial. Transplant.* 1998; 13:125-129.
- (12) Won T., Jang J.W., Lee S. et al. Effects of intraoperative blood flow on the early patency of radiocephalic fistulas. *Ann. Vasc. Surg.* 2000; 14: 468-472.
- (13) Robbin M.L., Chamberlain N.E., Lockhart M.E. et al. Haemodialysis arteriovenous fistula maturity: US evaluation. *Radiology* 2002; 225:59-64.
- (14) Asif A. How can we make fistulae mature? In: Tordoir J., ed. *Vascular Access*. Salezzia:Edizione Minerva Medica 2009:29-34.
- (15) Grogan J.F., Castilla M., Lozanski L. et al. Frequency of critical stenosis in primary arteriovenous fistulae before haemodialysis access: should duplex ultrasound surveillance be the standard of care? *J. Vasc. Surg.* 2005;41:1000-1006.
- (16) Singh P., Robbin M.L., Lockhart M.E. et al. Clinically immature arteriovenous haemodialysis fistulas: effect of US on salvage. *Radiology* 2008; 246:299-305.
- (17) Song H.H., Won Y.D., Kim Y.O. et al. Salvaging and maintaining non-maturing Brescia-Cimino haemodialysis fistulae by percutaneous intervention. *Clin. Radiol.* 2006; 61:404-409.
- (18) Turmel-Rodrigues L., Boutin J.M., Camiade C. et al. Percutaneous dilatation of the radial artery in nonmaturing autogenous radiocephalic fistulas for haemodialysis. *Nephrol. Dial. Transplant.* 2009; 24:3782-3788.
- (19) Doelman C., Duijm L.E.M., Liem Y.S. et al. Stenosis detection in failing haemodialysis access fistulas and grafts: comparison of color-Doppler ultrasonography, contrast-enhanced magnetic resonance angiography and digital subtraction angiography. *J. Vasc. Surg.* 2005;42:739-746.
- (20) Planken R.N., Leiner T., Nijenhuis L.E.M. et al. Contrast-enhanced magnetic resonance angiography findings prior to haemodialysis vascular access creation: a prospective analysis. *J. Vasc. Access* 2008; 9:269-277.
- (21) Natário A., Turmel-Rodrigues L., Fodil-Cherif M. et al. Endovascular treatment of immature, dysfunctional and thrombosed forearm autogenous ulnar-basilic and radial-basilic fistulas for haemodialysis. *Nephrol. Dial. Transplant.* 2010;25:532-538.
- (22) Shin S.W., Do Y.S., Choo S.W. et al. Salvage of immature arteriovenous fistulas with percutaneous transluminal angioplasty. *Cardiovasc Interv. Radiol.* 2005;28:434-438.
- (23) Manninen H.I., Kaukanen E., Maekinen K. et al. Endovascular salvage of nonmaturing autogenous haemodialysis fistulas: comparison with endovascular therapy of failing mature fistula. *J. Vasc. Interv. Radiol.* 2008;19:870-876.
- (24) Planken R.N., Duijm L.E., Kessels A.G. et al. Accessory veins and radial-cephalic arteriovenous fistula non-maturation: a prospective analysis using contrast-enhanced magnetic resonance angiography. *J. Vasc. Access* 2007;8:281-286.
- (25) Tessitore N., Mansueto G., Lipari G. et al. Endovascular versus surgical pre-emptive repair of forearm arteriovenous fistula juxta-anastomotic stenosis: analysis of data collected prospectively from 1999 to 2004. *Clin. J. Am. Soc. Nephrol.* 2006;1: 448-454.