



Review Article

Haemodialysis and Vascular Access in the End Stage Kidney Disease

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Abstract: The efficiency of haemodialysis treatment relies on a functional status of vascular access. A vascular access makes life-saving haemodialysis treatments possible. The efficiency of haemodialysis treatment relies on a functional status of vascular access. The purpose of this review was to discuss the role of haemodialysis and vascular access in end stage kidney disease. Vascular access and its related problems represent the main factors that determine a rise in the rate of incidence of the disease among haemodialysis patients and, consequently, a rise in the healthcare expenses. Vascular access can be divided into three categories: arteriovenous fistula, central venous catheter and arteriovenous graft. Central venous catheter has a number of disadvantages, including a considerable risk of infection and mortality. It also has negative implications for the use of a fistula for dialysis. In contrast, arteriovenous fistula is the most beneficial method, as it has a low risk of infection and mortality, and can ensure long-term functional access. Furthermore, there are three configurations of native arteriovenous fistula that can be used for haemodialysis providing flexibility of approach depending on risk factors of the individual patient.

Keywords: Haemodialysis, Vascular Access, End Stage Kidney Disease

1. Introduction

Chronic Kidney Disease (CKD) is a critical condition with considerable public health implications describes as abnormal kidney function and/or structure [1]. Progressive and permanent renal failure is most frequently treated with haemodialysis. Since 2009, the number of patients receiving home haemodialysis has increased by 23%, from 636 to 780 patients with median age of 66 years [2]. Haemodialysis has been used to treat renal failure since the 1960s [3]. Renal Replacement Therapy (RRT) with haemodialysis does not provide true replacement of renal function. However, by removing waste solutes, excess body water and restoring biochemical and acid-base balance, haemodialysis has considerably improved the morbidity and mortality of ESRD patients.

The first haemodialysis performed in a human was by Haas in 1924 [4]. Twenty years later Willem Kolff provide a primitive form of vascular access, establishing effective

anticoagulation and producing reliable equipment for widespread use when he created the rotating drum kidney in 1943 [5, 6].

A suitable type of vascular access has to be created to establish a connection between the circulation system of the patient and the haemodialysis cycle, in order to provide haemodialysis in ESRD patients. There are generally three types of vascular access that can be used for haemodialysis. Of these, the AVF is considered to provide the best long-term functional vascular access, with a reduced risk of thrombosis or infection and is most cost-effective [7]. In addition, AVF does not necessitate multiple interventions and has a lower mortality and morbidity rate among different types of vascular access [8]. The purpose of this review was to discuss the role of haemodialysis and vascular access in end stage kidney disease.

2. Mechanism of Haemodialysis

The current haemodialysis machine bears little resemblance to that devised by Kolff in 1943 although the design adheres to similar principles [5, 6]. This centres on removing blood from the intravascular compartment, passing it through an extracorporeal circuit into a dialyser and removing waste solutes and excess water by exposure to conditions that promote diffusion, convection, and movement in response to hydrostatic pressure gradients. Dialysed blood is then returned to the patient through the venous system. The volume of plasma cleared of solute per unit time by dialysis is expressed as the solute clearance. Diffusion is the predominant method by which solute clearance from plasma is achieved by haemodialysis. The process of diffusion is dependent upon blood from the extracorporeal circuit flowing through the dialyser, a collection of microfilament fibres bathed in dialysate fluid, which circulates in the opposing direction to blood flow. Blood is withdrawn from the fistula via the needle by a peristaltic pump, circulated through the dialyser, and returned to the fistula downstream through the needle. Heparin is infused downstream from the blood pump.

These conditions are favourable to the rapid diffusion of solutes through pores within the microfilament fibres, down a concentration gradient from blood to dialysate or vice-versa. The rate of diffusion varies with the degree of concentration gradient between compartments, the surface area of the microfilament membrane, the number and size of pores within the membrane, the molecular size of the solute and the relative flow rates of both extracorporeal blood and dialysate [9].

It can be seen that key determinants in the success of haemodialysis are the characteristics of the selectively permeable membranes used to form the microfilament tubes within dialyser units. Membranes may now be classified by the type of material used in their manufacture (synthetic, cellulose and substituted cellulose), their capacity, surface area, ultrafiltration coefficient, flux and in some cases, their ability to be reused [10].

3. Functional Outcomes of Haemodialysis

A high level of serum albumin has been considered as a positive measure of survival prediction in patients receiving dialysis due to the fact that it is an indicator of improved nutrition and reduced inflammatory burden [11]. Block *et al.* [12] have demonstrated that a reduced concentration of calcium phosphate is also a measure of increased survival rate as it is an indicator of efficient treatment of bone disease. Renal anaemia, reflected by low haemoglobin levels [13], and low dialysis doses [14] is associated with unsatisfactory and poor outcomes of haemodialysis [15].

Arteriovenous fistula is the first option considered for the construction of vascular access for dialysis. The construction of the fistula should be undertaken at least a month prior to the beginning of the dialysis treatment, as specified in the NKF-KDOQIa guidelines [16]. By doing this, a number of potential problems can be prevented, including the urgent

need for a catheter and its associated complications, such as infection, bleeding, thrombosis and vessel damage; additionally, the period spent in hospital also is reduced. According to Rayner *et al.*, a fistula needs two to six weeks to fully mature [17]. The main objective of health care is to create an AVF for the majority of patients prior to formal haemodialysis for the first time. Among the advantages of native AVFs are increased blood flow, reduced risk of sepsis, and durability.

4. Vascular Access

Vascular access problems represent the main determinant of morbidity among haemodialysis patients and put a considerable degree of financial pressure on the healthcare sector [2, 18]. The three types of constructions of AVFs, which are usually employed, are radiocephalic, brachiocephalic and brachiobasilic. The pre-surgery non-invasive scan imaging help clinicians in the decision making process as to which of these three types would be more suitable for the patient. Often, more than one type could be suitable and the one that is believed to have a higher success rate is chosen. However, when all three options are on the same level of success, a number of other aspects are included in the decision making, such as using the non-dominant arm or a more distally placed fistula (radiocephalic) to allow in future an easier formation of proximal fistula (brachiocephalic or brachiobasilic) and forming a brachiocephalic fistula over a brachiobasilic fistula due to its ease of formation and less surgical stress.

4.1. Type of Vascular Access

Successful haemodialysis depends on the provision of safe, efficient, and durable vascular access. Establishing and maintaining effective vascular access is a demanding process for both patients and renal services. These demands are set to increase in response to an RRT population that is becoming increasingly dependent on haemodialysis, whilst also increasing in population size, age, and co-morbidity.

Initially, vascular access methods relied on repeated peripheral cannulation to deliver arterial blood to the dialysis machine and return it to an accompanying vein. In 1949, Alwall, made the first attempt to connect an artery and a vein, using glass cannula and rubber tubing [6, 19]. This device would allow blood to be diverted onto an extracorporeal circuit for dialysis when required. His attempt was unsuccessful although it provided the template for the arteriovenous Teflon Shunt developed by Quinton *et al.* [20]. Their device consisted of two Teflon cannula inserted into the wrist, one in the branch of the brachial artery in the forearm and one in the accompanying antecubital vein. The cannula had its external ends connected by flexible tubing from which connection to an extracorporeal circuit could be made. This provided nephrologists with the first permanent vascular access device and was a decisive breakthrough in the provision of haemodialysis to the ERF population. The 'Scribner' shunt, as it came to be known, underwent many refinements before being ultimately superseded by the

successful development of arteriovenous fistulae, arteriovenous grafts, and central venous catheters. Nonetheless, the Scribner shunt played a key role in the development of permanent vascular access devices.

4.1.1. The Arteriovenous Fistula

Cimino and Brescia described a technique where haemodialysis was conducted through a simple puncture of the most accessible forearm vein. Patency of the vein was assured by the use of an inflatable tourniquet. This allowed needles of varying sizes to be used with resultant haemodialysis flows of 150-400 ml/min. Whilst successful, this technique was limited by the poor longevity of peripheral veins in comparison with that of Scribner's external arteriovenous shunt. Logical development of this technique, however, led to the creation of the first internal arteriovenous fistula. The successful use of the new technique was reported in a landmark paper [21]. The thought process of AVF was based on Cimino treating veterans of the Korean war; some of whom had traumatic AVF due to gunshot wounds and Cimino noted that venesection in these patients was very easy. They reported 12 cases in which successful primary function of an AVF had been achieved by creating a side-to-side connection at the wrist between the cephalic vein and radial artery. Exposure to high-pressure arterial flow was found to promote enlargement and thickening of the venous wall. After approximately six weeks maturation, a robust vessel wall had developed that could sustain repeated cannulation and allow regular haemodialysis to take place.

Arteriovenous fistula created by connecting an artery directly to a vein, frequently in the forearm. This artificial connection allows the vein to become larger and for the walls of the vein to thicken, a process termed maturation. A year later the technique had been amended to allow the construction of an end-to-end anastomosis in the lower arm between the cephalic vein and the radial artery [22]. This technique restricted arterial inflow into the AVF to that blood delivered by the feeding radial artery led to a high risk of developing steal syndrome.

This is a clinical condition caused by arterial insufficiency distal to haemodialysis AVF due to diversion of blood into AVF. Consequently, the technique latterly became regarded as a secondary option available to surgeons when considering surgical revision of a failed AVF. It is the technique that has become the standard AVF creation procedure of choice and has allowed AVF creation surgery to evolve and successfully provide a range of potential sites for AVF creation, predominately within the upper limbs [6].

Upper arm fistulae are more likely to cause ischemic symptoms compared to forearm fistulae. The presence of poor peripheral vasculature secondary to diabetes, calcification and peripheral arterial disease is the primary etiological factor. For practical purposes AVF creation is best conducted on the non-dominant arm with use of distal sites where possible; preserving the proximal vascular tree should vascular access surgery be required in the future. The longevity, durability, and favourable complication rate of the AVF have established

it as the leading method of establishing permanent haemodialysis vascular access. Around two thirds of haemodialysis patients in the UK dialyse using an AVF [23].

4.1.2. Arteriovenous Grafts

An alternative to the AVF is the synthetic arteriovenous graft (AVG). This was devised following the introduction of the Scribner shunt, which was noted to employ a length of flexible tubing to connect the arterial and venous blood flow. Thomas [24] developed this principle by replacing the cannula with Dacron patches sutured into the vessel wall and bringing out a loop of connecting silastic material to the skin surface. By avoiding the use of intraluminal cannula, this device was less prone to thrombosis. Meanwhile, the first vein graft had been performed using a length of excised saphenous vein, to connect the brachial artery to its accompanying vein. By combining each of these three principles direct anastomosis of vessels to tubing, looping a section of tubing to connect artery to vein and subcutaneous tunnelling of the connecting loop, the modern AVG was created [6]. Whilst initially Dacron was the most commonly used graft material, the emergence of the synthetic material polytetrafluoroethylene (PTFE) as a pliable, biocompatible material that may be repeatedly cannulated yet maintain its structural integrity, led to significant improvement in the durability of the AVG.

The brachial artery and the basilic vein are usually connected by way of an AVG. However, it is also common to connect the radial artery and the basilic vein or the brachial artery and the axillary vein with the use of grafts. When vascular access in the upper limbs is exhausted, synthetic grafts can be used to establish vascular access using the subclavian or axillary vessels, femoral vessels, or may even be anastomosed between the arterial system and the right atrium. Approximately 3% of haemodialysis patients in the UK dialyse via an AVG at present [23].

4.1.3. Central Venous Catheters

In the early years of haemodialysis, the demand for experienced surgeons to create arteriovenous shunts, fistula and grafts outstripped supply. The paucity of vascular and transplant surgeons prepared to perform these procedures provoked one UK nephrologist, Stanley Shaldon, to develop hand-made cannulae that could undergo insertion into the femoral artery and accompanying vein to permit immediate haemodialysis access. He made use of the Seldinger insertion technique - a method that enables safe catheter placement into the vascular tree introduced [24].

It was noted that arterial cannulation, in contrast to venous cannulation, is accompanied by an abnormally high risk of bleeding and was soon abandoned. Gradually different insertion sites were used including the jugular and subclavian veins. These had the advantage of allowing central venous pressures to be estimated in patients with extracellular fluid depletion [26], a common occurrence in many individuals suffering from acute kidney failure requiring dialysis. The insertion of a cannula into the subclavian vein became the favoured approach for CVC insertion until the early 1990s when angiographic data demonstrated a significantly

increased risk of central venous stenosis at the site of cannulation. This predisposed patient to a high risk of limb oedema, which could impair the ability to create and maintain a functioning AVF [27].

Insertion into the internal jugular veins is now regarded as standard practice although femoral venous cannulation is also performed. CVCs are frequently used temporarily to provide vascular access for haemodialysis whilst the patient awaits creation or maturation of an AVF or AVG or because they have run out of suitable options for permanent vascular access [28]. Some CVCs may be tunnelled subcutaneously en-route to entering the vein with a securing cuff to stabilise the position of the catheter and reduce potential for periluminal infection. Direct transcutaneous cannulation of the vein is often performed acutely and tends not to involve subcutaneous tunnelling or use of a securing cuff. Polyurethane and silicone are the two materials most commonly used in the manufacture of haemodialysis catheters although polymers such as carbothane are increasingly common [29]. These materials provide sufficient flexibility, durability, and biocompatibility for intravascular use.

The catheters are the least preferred modality and, in an ideal setting, no patient should have a catheter as access. Despite the risks associated with dialysis catheters, their use has increased to almost 70% of incident dialysis initiation with catheters [30]. The different methods of obtaining vascular access allow haemodialysis to be a viable treatment for most of ESRD patients. The diversity of vascular access options available can help nephrologists address a range of clinical scenarios more effectively. Late presentation of ESRD is one frequently experienced scenario that may have a significant impact on vascular access provision. In this setting, the time in which RRT is required to start may arrive before the patient can undergo vascular assessment, surgery, and successful maturation of their fistula. This phenomenon is often used to explain the relatively high prevalence of ESRD patients using CVCs as their first haemodialysis access modality. In the UK renal registry vascular access survey of 2006, 66% of patients started haemodialysis on a CVC compared with 34% using an arteriovenous fistula or an arteriovenous graft. After one year, the percentage of individuals treated with a CVC reached 28% compared with 71% using an AVF or AVG [23]. UK Renal Association [2] suggested that 2/3 of all patients requiring dialysis should start with an autologous fistula and the remaining 1/3 with CVC as these are described as the “Crash Landers” who have acute or undiagnosed renal failure and do not have time for AVF creation and maturation. Similarly, when an AVF or AVG fails, CVCs are a rapid means of establishing vascular access and thus play a significant part in providing urgent vascular access.

4.2. Functional Outcomes of Vascular Access

As noted by several researchers [31, 32], surgical interventions of vascular access and their associated problems are important causes of morbidity, hospitalisation, and financial pressure. In the US, more than 20% of the total number of haemodialysis patients were admitted to hospital as a result of vascular access and its

complications. The costs generated annually amounts to almost \$1 billion [31]. Studies have shown that dialysis grafts made of PTFE are not as long lasting as autologous fistulae [33, 34]; furthermore, they are more likely to develop repeated thrombosis, stenosis, and infection. The NKF-KDOQIa guidelines [16] recommend the use of AVFs over AVGs due to the advantages of the fistula; the AVGs should only be employed when the creation of natural AVFs is due to the exhaustion in the use of the patient's veins.

Clearly, there are logistical hurdles to this late presentation to renal services, fitness for surgery, suitable peripheral vascular anatomy, delays due to primary or secondary access failure and slow rates of AVF maturation. Consequently, there remain situations, especially when starting RRT, where use of an AVG or CVC may be required. This is demonstrated by the relative prevalence of CVC use in patients starting RRT around the world. Similarly, CVC insertion is the mainstay of vascular access provision to the acute renal failure population who require haemodialysis. There is a strong association between catheter use, comorbidity, and in-patient care. The question of whether the adverse features related to catheter use, such as catheter thrombosis and bacteraemia, are specifically related to use of a catheter or are simply related to the greater level of comorbidity expressed by the population who require catheter insertion has been subject to controversy [35].

Catheters are prone to develop infection from 3.8 to 5.5 episodes per 1000 days [36]. Infection can be localized or spread systematically leading to bacteraemia or sepsis [37]. In AV graft or within its outflow vein where the graft stitched to the vein, stenotic lesions are found time and again [38]. The underlying mechanism is the marked increase in shear stress in the thin-walled outflow vein, which activates focal fibromuscular hyperplasia and initiates a fibrotic venous lesion to develop [39].

5. Conclusion

A vascular access makes life-saving haemodialysis treatments possible. The efficiency of haemodialysis treatment relies on a functional status of vascular access. Each access type (CVC/AVG/AVF) has its relative attributes, it is important to consider the differing degrees of reliability, durability, and complications associated with each approach. Whether considering an individual patient's circumstances or planning vascular access provision at a population level, understanding the range of complications expressed by each access type and which factors predispose to these complications is of fundamental importance in deriving maximum benefit with minimal risk.

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