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4

Vascular Access for Hemodialysis

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1. Introduction

A progressive rise in the number of patients accepted for renal replacement therapy has been reported world wide [1]. Permanent vascular access (VA) is the life-line for the majority of these patients, when hemodialysis is the treatment of choice. Thus, the successful creation of permanent vascular access and the appropriate management to decrease the complications is mandatory. A well functional access is also vital in order to deliver adequate hemodialysis therapy in end-stage renal disease (ESRD) patients. Unfortunately, despite the advances in hemodialysis technology, the introduction of the polytetrafluoroethylene (PTFE) graft and the cuffed double lumen silicone catheter were the only changes in the field of vascular access in the last years. However the cost of vascular access related care was found to be more than fivefold higher for patients with arteriovenous graft (AVG) compared with patients with a functional arteriovenous fistula (AVF) [2]. It seems that the native arteriovenous fistula that Brescia and Cimino described in 1966, still remains the first choice VA [3]. Thereafter, vascular access still remains the "Achilles' heel" of the procedure [4] and hemodialysis vascular access dysfunction is one of the most important causes of morbidity in this population [5]. It has been estimated that vascular access dysfunction is responsible for 20% of all hospitalizations; the annual cost of placing and looking after dialysis vascular access in the United States exceeds 1 billion dollars per year [6, 7]. Nowadays, three types of permanent vascular access are used: arteriovenous fistula (AVF), arteriovenous grafts (AVG) and cuffed central venous catheters. They all have to be able to provide enough blood flow in order to deliver adequate hemodialysis, have a long use-life and low rate of complications. The native forearm arteriovenous fistulas (AVF) have the longest survival and require the fewest interventions. For this reason the forearm AV is the first choice, followed by the upper-arm AVF, the arteriovenous graft (AVG) and the cuffed central venous catheter as a final step [8-10].

2. History of vascular access

Vascular access for hemodialysis is closely associated with the history of dialysis. Glass needles were employed as vascular access when hemodialysis came into view in 1924. The first haemodialysis treatment in humans was carried out by Haas G. who used glass cannulae to acquire blood from the radial artery and reverting it to the cubital vein [11]. Venipuncture needles were used as means for blood acquisition from the femoral artery and its reinfusion to the patient by vein puncture, in 1943 by Kolff W. [12, 13]. Regular hemodialysis treatments were possible in 1950s through the use of a medical apparatus (Kolff 's twin-coil kidney [14]), thus projecting the problem of a reliable, capable of repeated

use vascular access. Nowadays, the artery-side-to-vein-end-anastomosis has become a standard procedure [15]. In 1952, Aubaniac had described the puncture of the subclavian vein [16].

In the 60s, by using Alwall's experience, Quinton, Dillard and Scribner developed arteriovenous Teflon shunt [17]. This procedure involved two thin-walled Teflon cannulas with tapered ends inserted one into the radial artery and the other into the adjacent cephalic vein. The external ends were connected by a curved Teflon bypass tube. Later, the Teflon tube was replaced by flexible silicon rubber tubing. After the advancement of permanent vascular access, the possibility of maintenance hemodialysis was a fact and therefore a groundbreaking procedure.

In the subsequent years, many variants of the AV shunt were used, with the majority of them concerning temporary vascular access from the onset of chronic dialysis treatment, compensating for the time of AV fistula's absence or maturity. In 1961, Shaldon performed hemodialysis procedures by inserting catheters into femoral artery and vein, using the Seldinger-technique [18, 19]. Over time, vessels in different sites were used, including the subclavian, jugular and femoral vein.

In 1962 Brescia MJ described a 'simple venipuncture for hemodialysis' [20]. In 1963 Fogarty TJ et al invented an intravascular catheter with an inflatable balloon at its distal tip, designed for embolectomy and thrombectomy [21]. The first surgically created fistula was placed in 1965, followed by further 14 operations in 1966 [22]. In 1966 Brescia, Cimino, Appel and Hurwich published their paper about arteriovenous fistula. Appell had performed a side-to-side-anastomosis between the radial artery and the cephalic antebrachial vein. One year later, in 1967, Sperling M. et al reported the successful creation of an end-to-end-anastomosis between the radial artery and the cephalic antebrachial vein in the forearm of 15 patients using a stapler [23]. In the next few years this type of AV anastomosis received widespread acceptance. However this procedure was cast aside as first choice AV, due to the increasing numbers of elderly, hypertensive and diabetic patients with demanding vessels and high risk of steal syndrome. End-to-end-anastomoses are still a common place technique in revision procedures but it seems that they correlate with higher mortality risk due to infection [24].

In 1968 Röhl L. et al published thirty radial-artery-side-to-vein-end anastomoses [25]. After anastomosis was performed, the radial artery was ligated distal to the anastomosis, thus resulting in a functional end-to end-anastomosis. Today, the artery-side-to-vein-end-anastomosis has become a standard procedure [15]. In 1970, Girardet R. [26] and Brittinger W.D. [27] described their experience with the femoral vein and artery for chronic hemodialysis. Experimental trials have been done by several authors in order to establish a permanent vascular access using subcutaneous tunnel. Brittinger W. was the first to implant a plastic valve as a vascular access in an animal model but unfortunately his efforts did not proceed to a human one [28]. Moreover, during the early 70s, Buselmeier T.J. developed a U-shaped silastic prosthetic AV shunt with either one or two Teflon plugged outlets which communicated to the outside of the body. The U-shaped portion could be totally or partially implanted subcutaneously [29]. Subsequently pediatric hemodialysis patients were extremely favored by this procedure. New materials for AV grafts were presented in 1972, one biologic and two synthetic. In 1976, Baker L.D. Jr. presented the first results with expanded PTFE grafts in 72 haemodialysis patients [30]. In the years to come, several publications indicated the benefits and the shortcomings of the prosthetic material in question, remaining the primary choice of graft for hemodialysis VA to date. The same year, two authors, Mindich B. and

Dardik H., had worked with a new graft material: the human umbilical cord vein [31, 32]. Regrettably so, this material did not succeed in becoming a revolutionary graft material, due to its inadequate resistance against the trauma of repeated cannulation and its complications (aneurysm and infection). After the subclavian route for haemodialysis access was firstly introduced by Shaldon S et al in 1961, it was further processed in 1969 by Erben J et al, using the intraclavicular route [33]. In the next 20 years or so, the subclavian vein was the preferred access for temporary vascular access by central venous catheterization. Today, due to phlebographic studies revealing a 50% stenosis or occlusion rate at the cannulation site, subclavian route has been discarded. Subclavian stenosis and occlusion predispose to oedema of the arm, especially after creation of an AV fistula [34].
The first angioplasty described by Dotter CT et al who introduced a type of balloon, was immensely conducive to the resolution of one of the most significant predicaments in vascular surgery and vascular access surgery [35].
In 1977, Gracz KC et al created the "proximal forearm fistula for maintenance hemodialysis", a variant of an AV anastomosis [36]. An adjustment of this AVF became quite significant in the old, hypertensive and diabetic patients on the grounds that it allows a proximal anastomosis with a low risk of hypercirculation [37]. In 1979 Golding A.L. et al developed a "carbon transcutaneous hemodialysis access device" (CATD), commonly known as "button", by which, blood access does not require needle puncture [38]. As a procedure of third choice, these devices were expensive and never gained widespread acceptance. Shapiro F.L. described another type of "button", a device similar to that developed by Golding [39].

3. Angioaccess classification

Years after the initial efforts to create the appropriate vascular access in order to perform a safe hemodialysis, modern Nephrologists have now the possibility to select the appropriate access for their patients. Thus, the first distinction is made between temporary and permanent VA [40]. Temporary VA with expected half-life less than 90 days, peripheral arteriovenous shunts and non cuffed double lumen catheters are included. Mid-term VA with expected half-life from 3 months to 3 years include veno-venous accesses (tunneled cuffed catheters and port catheter devices) and arteriovenous internal shunts, requiring vascular graft synthetic (PTFE) or biologic (saphenous vein, Procol, etc.) material ,or external shunt. Long-term VA with an expected half-life more than 3 years includes virtually the native arteriovenous fistulas [4] and the new generation of PTFE grafts .

3.1 Acute hemodialysis vascular access

When an urgent hemodialysis has to be performed, the need for an appropriate vascular access becomes immediate. This type of access must have some specific features such as ease of insertion and availability for immediate use. Two types of such accesses are currently available: non-tunnelled dialysis catheters and cuffed, tunnelled dialysis catheters (Figure 1-5).
Double-lumen, non-cuffed, non-tunnelled hemodialysis catheters are the preferred method for immediate hemodialysis when a long-term access is not available. They are made of polymers which are rigid at room temperature to facilitate insertion but soften at body temperature to minimize vessel injury and blood vessel laceration. In order to minimize recirculation, the distance between the proximal and distal lumens should be at least 2cm [41].

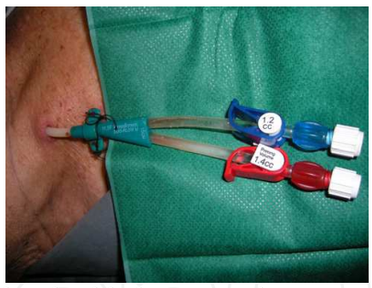


Fig. 1. Non cuffed internal jugular double lumen catheter

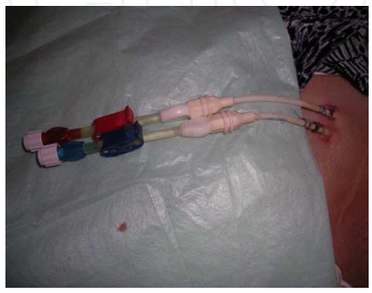


Fig. 2. Cuffed tunnelled internal jugular double lumen catheter

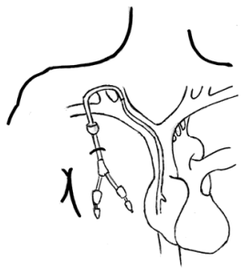


Fig. 3. Permanent cuffed jugular catheter

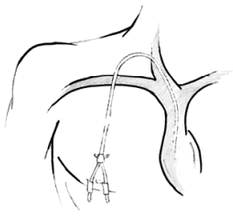


Fig. 4. Acute non-cuffed jugular catheter

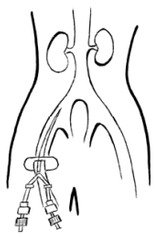


Fig. 5. Femoral non-cuffed catheter

Central veins such as jugular, subclavian or femoral, can be used as insertion routes of these catheters [42]. The femoral artery can be used as an access central vein when all other central veins have been excluded. For their insertion a modified Seldinger guide wire technique is used. In order to minimize immediate insertion complications, image guided assistance is recommended. Non-cuffed catheters are also suitable for use at the bedside of the patient [43, 44].
The 2006 National Kidney Foundation Dialysis Outcomes Quality Initiative (K/DOQI) guidelines recommend, after internal jugular or subclavian vein insertion, identifying radiographically any potential complications and confirming tip placement prior to either anticoagulation or catheter use [45]. Nowadays, the subclavian catheters should be generally avoided because of the high incidence of vein stenosis and thrombosis.
The maximum blood flow with this class of catheters is usually blood pump speeds of 300 mL/min, with an actual blood flow of 250 mL/min or less [46, 47]. Femoral catheters have to be at least 18 to 25 cm in length in order to have lower recirculation. The routine use-life of these catheters varies depending on the site of insertion. Generally speaking, internal jugular catheters are suitable for two to three weeks of use, while femoral catheters are usually used for a single treatment (ambulatory patients) or for three to seven days in bed bound patients [48]. However, the KDOQI guidelines suggest that non-cuffed, non tunnelled catheters should be used for less than one week. Tunnelled catheters should be placed for those who require dialysis for longer than one week [45]. More recently, a non-cuffed, non-tunnelled triple-lumen dialysis catheter has been developed. The purpose for third lumen is blood drawing and intravenous administration of drugs and fluid. In a multicenter, prospective study, blood flow rates and infectious complications were similar with double lumen catheter [49].
Infectious complications are the principal reason for catheter removal.

3.2 Permanent vascular access

Taking patient factors into consideration, such as life expectancy, comorbidities, the status of the venous and arterial vascular system, is very important in order to prescribe the appropriate access. Other factors are determined by the type of access itself, such as arteriovenous fistula (AVF), arteriovenous graft (AVG), or TC which have a different effect on circulatory system. Also, the duration of their functionality and the risk for infection and thrombosis are important factors to consider. Each type of surgical anastomosis has advantages and disadvantages [50]. In 2002 the American Association for Vascular Surgery and the Society for Vascular Surgery published reporting standards according to which three essential components of VA should be mentioned: conduit (autogenous, prosthetic), location and configuration (strait, looped, direct, etc.) [51].

3.2.1 Arteriovenous fistula

An AVF is the preferred type of vascular access; it has the lowest complication rates for thrombosis (one-sixth of AVGs) and infection (one-tenth of AVGs) [52, 53].
There are 3 types of AVFs:

- First type when artery and vein are connected in their natural position, either with a side-to-side or a side-artery-to-vein-end anastomosis.
- Second type, where a vein is moved to connect to an artery in end-to-side fashion to either bridge a larger anatomical distance, or to bring the vein to the surface where it is accessible for cannulation and requires a tunnel to position the vein in its new location.

- Third type where a vein is removed from its anatomical location and is connected to an artery and vein in end-to-end fashion.

Both second and third types require the formation of a tunnel [54] (Figure 6-9). End-to-end anastomoses are now rarely performed, since the complete disruption of the artery imposes a risk for peripheral ischemia and thrombosis. The most common surgical technique today is the side-to-end anastomosis. However, technical problems such as cutting the end of the vein in an oblique angle may create functional problems due to stenosis. An anastomosis more proximal in the arterial system should be smaller to prevent steal symptoms and limit maximal fistula flow, with the inherent complication of ischemic steal or heart failure [54]. Arteriovenous fistula creation is often performed under local anaesthesia, with low morbidity and requires time for maturation. Data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) indicate that AVFs should mature at least 14 days before use [55]. Fistula size and flow increase over time of 8–12 weeks and the initial blood flow rates has a range of 200–300 mL/min.



Fig. 6. Forearm AVF



Fig. 7. Side to side forearm AVF



Fig. 8. End to end forearm AVF



Fig. 9. Side to end forearm AVF

Placement of AVFs should be initiated when the patient reaches CKD stage 4, or within 1 year of the anticipated start of dialysis. A physical examination should document blood pressure differences between the upper extremities[56] and an Allen test should be performed as the lack of a well-developed palmar arch predispose for vascular steal symptoms in case the dominant artery is used for the VA creation [57].

Ultrasound must be done before surgical implantation because it can provide information for maximal surgical success by mapping arteries and veins; e.g. a preoperative arterial lumen diameter >2 mm is associated with successful fistula maturation [56], while a diameter of <1.6 mm predicts failure of the procedure [58]. Kidney Disease Outcomes Quality Initiative (KDOQI) Vascular Access guidelines, suggest that a working AVF should have a blood flow >600 mL/min, a diameter >0.6 cm, and be at a depth of 0.6 cm (between 0.5 and 1.0 cm) from the surface, 6 weeks after its creation. In fistulas that are successfully maturing, flow increases rapidly post-surgery, from baseline values of 30–50 mL/min to 200–800 mL/min within 1 week, generally reaching flows >480 mL/min at 8 weeks [59, 60]. The AVFs must be evaluated 4–6 weeks after placement, and experienced examiners (e.g., dialysis nurses) can identify non-maturing fistulas with 80% accuracy [61].

3.2.2 Arteriovenous graft

AVGs (Figure 10-12) were the most commonly used type of dialysis access in the U.S. [62]. However, they do not last as long as AVFs and they have higher rates of infection and thrombosis [52]. Grafts present a second choice of VA when AVF is not able to be performed because of vascular problems. They can be placed in the forearm, the upper arm, and the thigh, and can have a straight, curved or loop configuration. They may offer a large surface area for cannulation. AVGs can be cannulated about 2-3 weeks after placement, although there are studies suggesting that immediate assessment after placement for PTFE AVGs is possible [63, 64]. This interval is needed in order to allow the surrounding tissue to adhere to the PTFE conduit, to reduce the postsurgical oedema and the risk for local complications such as perigraft hematoma and seroma [65].



Fig. 10. Upper arm AVG

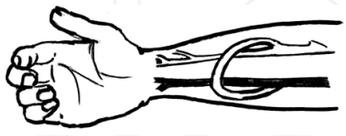


Fig. 11. Looped Forearm AVG



Fig. 12. Straight femoral AVG

3.2.3 Tunnelled hemodialysis catheter

TCs (Figure 2,3) are used when AVFs or AVGs are not possible to be created for several reasons such as multiple vascular surgeries, which lead to vascular thrombosis, or when patients have severe peripheral vascular disease or very low cardiac output. This is more frequently encountered in paediatric and very old patients.

Unfortunately, these are associated with the highest infection rate and they are not a very long-term access option. Studies have revealed that central venous catheters are colonized within 10 days of placement; however, colonization of the catheter biofilm does not correspond to positive blood cultures or clinical signs of bacteremia [66]. It seems that outcome of the infection treatment does not differ if, in addition to antibiotic therapy, the catheter will be guidewire changed or completely removed [67]. Recently Power A. et al published their experience with 759 TCs. The survival rate at 1, 2 and 5 years was 85%, 72% and 48% respectively. The infection rate was 0.34 per 1000 catheter days showing that with careful and appropriate use of TCs, they can provide effective and adequate long-term hemodialysis and rates of access related infection almost similar to AVGs' [68].

When conventional venous accesses have been exhausted and peritoneal dialysis is impossible, it is mandatory to use alternative procedures for VA in order to continue HD. Translumbar inferior vena caval CVCs belong to this category and it seems that they can offer relatively safe and effective long-term HD access [69]. Another alternative is the transhepatic hemodialysis catheters; they seem to be a potentially viable option with low rates of morbidity due to placement, high rates catheter-related maintenance and possibility of long-term functionality [70].

4. Hemodialysis vascular access in children

The choice of replacement therapy in children is variable. The registry of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) reports that of patients initiating renal replacement therapy in paediatric centres [71, 72]: one quarter of children underwent preemptive renal transplantation, one half were started on peritoneal dialysis and one quarter were started on hemodialysis. Kidney transplantation remains the preferred therapy for paediatric patients. Therefore, many of them receive maintenance HD through an indwelling catheter in perspective of short HD period [73]. In the United States, less than 800 paediatric patients receive maintenance HD therapy. The majority of smaller patients especially those less than 10kg or less than 2 years old, receive PD [74-76].

However, hemodialysis can be performed successfully in infants and very young children, as well [77]. Children who will undergo hemodialysis will need evaluation of their vasculature for placement of an arteriovenous (AV) fistula, arteriovenous graft, or cuffed double lumen catheter. The use of an AV fistula, which is the recommended type of vascular access in adults, is limited in children due to the size of their vessels. In the 2008 NAPRTCS annual report, vascular access for hemodialysis included external percutaneous catheter in 78% of patients, internal AV fistula in 12%, and internal and external AV shunt in 7.3 and 0.7 %, respectively [72]. K/DOQI has encouraged greater use of AV fistulas in larger children receiving hemodialysis who are not likely to receive a transplant within 12 months, with a goal of achieving more effective dialysis with fewer complications than the ones occuring with catheters. The choice of catheter size and configuration depends on the size of the patient. It is suggested that in children as small as 4 to 5 kg, a dual-lumen 8 Fr catheter can

be well tolerated, and as the child becomes larger in size, a larger volume access can be placed [78]. Vascular access should be able to provide sufficient blood flow and adequate dialysis with a Kt/V greater than 1.2. A recommended flow rate of 3 to 5 mL/kg/min is acceptable in most patients due to the fact that flow rates in paediatrics vary by the size of catheter depending on the size of the patient, [79].

5. Vascular access complications and survival

Studies have shown a mortality risk dependent on access type, with the highest risk associated with central venous dialysis catheters, followed by AVGs and then AVFs [80, 81]. Additionally, patients who had a catheter as first VA, had more complications and higher mortality [82]. Same results have been presented by Ng LJ et al who examined hospitalization burden related to VA type among 2635 incident patients [83]. The CHOICE study examined mortality based on access type in 616 hemodialysis patients for up to 3 years of follow-up. Central venous catheters and AVGs were associated with approximately 50% and 26% increased mortality respectively, compared with AVFs with prevalence in men and elderly patients [84, 85]. Despite these findings and the KDOQI recommendations, dialysis access data from 2002–2003 showed that only 33% of prevalent hemodialysis patients in the US were being dialyzed via AVFs. On the contrary in Europe and Canada, the majority of the patients (74% and 53% respectively) were being dialyzed via AVFs [86].

Vascular access admissions continue to fall, with more procedures now performed in an outpatient setting, and are 45% below than in 1993. Among African American patients, the relative risk of an all-cause hospitalization or one related to infection is almost equal to that of Caucasians; the risk of a vascular access hospitalization, however, is 24 percent higher [87]. Thrombotic occlusion remains a major event, leading to permanent failure in 10% of AVFs and 20% of grafts each year. Interventional (percutaneous transluminal angioplasty and/or stent implantation) or surgical revision of thrombosed accesses has similar outcomes with a high rate of reinterventions. The elderly diabetic population with peripheral arteriosclerotic obstructive disease is in particularly prone to angio-access induced hand ischemia. [88]. It has been shown that patients with AVGs and TCs have higher levels of chronic inflammation than those with AVFs, and increased requirements in epoetin [89]. In our previous work with 149 hemodialysis patients who had undergone 202 vascular access procedures (177 Cimino-Brescia fistulae and 25 PTFE grafts) we found that the Cimino-Brescia fistula was used as the first choice of vascular access in all patients, except one in the elderly group. PTFE grafts were the second or third choice in 7 patients younger than 65 and 15 in the elderly group (p: NS). The only reason for technique failure was vascular thrombosis in both groups (p: NS). Other complications were: aneurysms (10/48 and 14/101, p: NS), infections (0/48 and 2/101 p: NS) and oedema (0/48 and 6/101, p: NS). (Table 1) Five-year technique survival of the first AV fistula in the two groups was 35% and 45% respectively (log-rank test, p: NS). (Figure 13) Our findings suggested that there was no difference in vascular access complications across age groups and the survival of the first AV fistula was independent of age [8]. Similar reports have been published by Swindlehurst N et all according to which the creation of permanent hemodialysis access in the elderly with AVF is not only possible but also proved to have a short hospital stay, high patency rates, and an acceptable rate of further intervention [90].

	Group A (age>60)	Group B(age<60)	P
Thrombosis	14/48	39/101	N.S.
Aneurysm	10/48	14/101	N.S.
Oedema	0/48	6/101	N.S.
Infection	0/48	2/101	N.S.

Table 1. Complications of vascular acces (Reference 8)

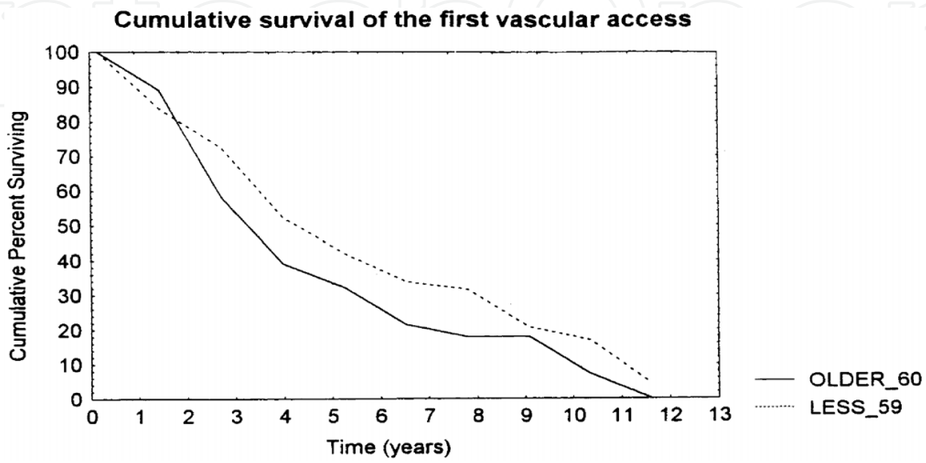


Fig. 13. Cumulative survival of first VA accord1ing to the patients' age(Reference 8)

In 2010 USRDS Annual Data Report, hospitalization in 2008 increased again, to a point 46% above their 1993 level. In 2007–2008, women treated with hemodialysis were 16 % more likely to be hospitalized, overall, than men. They also had a greater risk than men of cardiovascular, infectious and vascular access hospitalizations 11%, 14%, and 29% greater, respectively. Recently unpublished, our data are different than those we published in 1998. Our findings showed that among 189 patients, the female ones had had more possibility to start HD with double lumen catheter than the male ones, and also patients with heart failure independent of gender. Female patients had PTFE grafts as first vascular access (p=0,023) and the elderly patients had more complications and more vascular access procedures (p=0.026).

5.1 Non-tunnelled double lumen catheters complications

The non-tunnelled double lumen catheters' complications concern the early ones during the insertion and the late ones such as infection and thrombosis of the vessels.

The severity of acute complications varies with the site of insertion. The lowest rate is in the femoral position. A significant complication is perforation of the femoral artery. Bleeding usually resolves within minutes of direct compression and large femoral or retroperitoneal hematomas occur occasionally [91]. Subclavian insertion complications are more serious. Over-insertion of guide-wire can occasionally lead to atrial or ventricular arrhythmias but they are frequently transient [92]. Penetration or cannulation of the subclavian artery can lead to hemothorax, which may require a thoracotomy tube. The incidence of pneumothorax varies from less than 1 percent to more than 10 percent of insertions, depending on the skill and experience of the physician. Pericardial rupture and tamponade also have been described [93, 94]. There is less likelihood of arterial puncture or pneumothorax in ultrasound-guided catheter insertion [95]. Subclavian insertion from the left has an

increased risk of pneumothorax and atrial perforation which can be presented with acute hemopericardium upon initiation of dialysis. Internal jugular vein is the preferred site of insertion because of subclavian stenosis and loss of the ipsilateral arm for future hemodialysis access. This complication appears to occur more often with subclavian (40 to 50 %) than with internal jugular insertions (up to 10 %) [96, 97]. At internal jugular insertions a carotid artery penetration may occur, but there is also a lower risk of pneumothorax (0.1 percent).

Prevention and treatment of catheter thrombosis are important clinical issues. To prevent formation of thrombus, both lumens of the double lumen catheter are instilled with heparin following hemodialysis [41]. Lytic agents such as urokinase and alteplase are effective in treatment of catheter thrombosis. Alteplase has effectiveness rates in thrombosis treatment comparable to the ones observed with urokinase [98]. Central vein catheters are associated with the development of central vein stenosis [99]. The K/DOQI guidelines therefore recommend avoiding placement in the subclavian vein, unless no other options are available. If central venous thrombosis is detected early, it responds well to directly applied thrombolytic therapy [99] or to percutaneous transluminal angioplasty when the fibrotic stenosis can be crossed with a guidewire [100]. The infection risks associated with temporary double lumen catheters include local exit site infection and systemic bacteremia, both of which require prompt removal of the catheter and appropriate intravenous antibiotic therapy [45, 101, 102]. Bacteremia generally results from either contamination of the catheter lumen or migration of bacteria from the skin through the entry site, down the hemodialysis catheter into the blood stream [103-105]. Skin flora, Staphylococcus and Streptococcus species, are responsible for the majority of infections.

There is conflicting evidence concerning the risk of infection based upon the site of insertion. In a large prospective randomized study (750 patients), the risk of infection was not reduced with jugular versus femoral venous catheterization [106]. But other prospective nonrandomized studies suggest, that the infection risk appears to sequentially increase for hemodialysis catheters inserted into the subclavian, internal jugular, and femoral veins, respectively [101, 107]. Coagulase-negative staphylococci, Staphylococcus aureus, aerobic gram-negative bacilli, and Candida albicans most commonly cause catheter-related bloodstream infection. In most cases of non-tunneled CVC-related bacteremia and fungemia, the CVC should be removed. The decision should be based on the severity of the patient's illness, documentation that the vascular-access device is infected, assessment of the specific pathogen involved, and presence of complications, such as endocarditis, septic thrombosis, tunnel infection, or metastatic seeding [108].

Overall, compared with the subclavian vein, the internal jugular vein remains the preferred access site in ambulatory patients. In the Intensive Care Unit, either femoral or internal jugular vein placement is satisfactory, with the use of ultrasound making internal jugular vein placement safer.

The best solution is to prevent the infection by proper placement technique, optimal exit site care and management of the catheter within the HD facility [41, 109].

5.2 Arteriovenous fistulas complications

Complications of AVFs can be divided into early and late causes.

Early causes include inflow problems due to small or atherosclerotic arteries, or juxta-anastomotic stenosis, so a pre-operative evaluation for suitable access sites has to been performed [110].

The aetiology of this acquired lesion is not entirely clear, but may be related to manipulating the free end of the vein, torsion, poor angulation, or loss of the vasa vasorum during anatomic dissection. More often than not, this lesion can be adequately treated with angioplasty [111, 112] or by surgical revision [113]. Outflow problems may include accessory veins that divert blood flow from the intended superficial vessel to deeper conduits, or central venous stenosis in patients with prior central venous catheters. Vessels, smaller than one-fourth of the fistula diameter, are usually not hemodynamically relevant. Juxta-anastomotic stenosis and accessory veins are the most common causes for early failure AVFs when pre-operative evaluations for suitable access sites have been performed [110].
Late causes for failure of AVFs include venous stenosis, thrombosis, and acquired arterial lesions such as aneurysms or stenoses. Venous stenosis may become apparent as flow decreases over time, worsening weekly Kt/V ([dialyzer clearance
_ time]/body volume) or increasing recirculation. Native fistulas will not typically thrombose until flow is severely diminished. Thrombectomy of fistulas, although technically more challenging than in AVGs, is often successful and if flow is re-established, primary patency is longer than in grafts [114]. Aneurysms may form over the course of years as the fistula increases with increased flow and, unless associated with stenotic lesions, are more a cosmetic than functional concern. If the skin overlying the aneurysm is blanching or atrophic, or if there are signs of ulceration or bleeding, surgical evaluation should be obtained urgently [115]. Rupture of such aneurysms in high-flow fistulas can lead to exsanguination and death. (Figure 14)



Fig. 14. Aneurysm in forearm AVF

5.3 Arteriovenous graft complications

Functional survival of AVGs is much sorter than AVFs. The natural course of AVGs is thrombosis due to venous stenosis caused by neointimal hyperplasia. The increased production of smooth muscle cells, myofibroblasts, and vascularisation within the neointima is the main cause of thrombosis. There is also angiogenesis and numerous macrophages in the tissue around the graft.[116, 117] Within the neointimal lesion, growth factors (GF) such as PDGF (platelet derived), VEGF (vascular endothelial), and basic FGF (fibroblast) are present.[117] Vascular endothelium is regulated by the presence of shear stress, [118, 119] and that flow within AVGs is likely to be different from native veins. Understanding the pathophysiology of neointimal hyperplasia would allow targeted therapy. Current studies are evaluating the role of radiation,[120] decoy peptides against transcription factors [121, 122] and local delivery of drugs with cell-cycle inhibitory effects (e.g., paclitaxel [123] and sirolimus). Cell-based strategies seek to take advantage of endothelial progenitor cells that release endogenous inhibitors of proliferation and thrombosis, such as nitric oxide (NO) and prostacyclin.[124] Venous stenosis in AVGs

leads to decreased blood flow and thrombosis, at a rate of 1–1.5 times/patient/ year [52]. In most cases, thrombosis is associated with anatomical stenosis, which is mostly located in the venous anastomosis (60%), followed by the peripheral vein (37%), and within the graft (38%) [125]. Percutaneous angioplasty is safe and effective in treating venous stenosis [126] with a success rate from 80%–94%, and primary patency around 60% at 6 months and 40% at 1 year. Placement of self-expanding nitinol endovascular stents, appears to prolong patency in cases where focal lesions are resistant to repeated angioplasty [127]. Central stenosis is technically more difficult to treat, and stenotic lesions often recur within 6 months [54].

Thrombosis of an AVG is usually the result of multiple factors; such as the stenosis, hypotension, and the excessive compression for haemostasis. Haemodialysis' nurses have to be careful in order to avoid these factors. The risk for thrombosis increases with decreasing blood flow (BF). May RE et al found a 19% risk of thrombosis in 3-month period for an AVG with BF between 1010 and 1395 mL/min. This risk increased continuously with decreased BF; 1.67-fold at a BF of 650 mL/min, and 2.39-fold at a BF of 300 mL/min [128]. Graft thrombosis can be treated in outpatients by endovascular therapy. Angiographic search for a venous stenosis is always appropriate, and angioplasty is often indicated. Timely pharmacological thrombolysis or mechanical removal of the thrombus with a Fogarty catheter, and thrombo -aspiration or thrombectomy with a mechanical device [129] can prevent placement of a dialysis catheter.

AVG infections are serious complications and are the second leading cause of dialysis access loss. The incidence of hemodialysis-related bacteremia is more than 10-fold higher in AVGs than AVFs: 2.5 episodes per 1000 dialysis procedures versus 0.2 [130]. Patient have to be more careful for their hygiene because it seems to be the most important modifiable risk factor [131].

Pseudoaneurysms should be referred to a surgeon for resection when they are >2 times wider than the graft, rapidly increasing in size, or the overlying skin appears under duress (thin, bleeding, blanching) [132].

Ischemia, as a result of access placement is more common for AVGs than AVFs: vascular steal syndrome and ischemic monomelic neuropathy are two important clinical entities to distinguish.

Physiologic steal occurs in 73% of AVFs and 90% of AVGs, .Thus, in a radiocephalic fistula, arterial blood from the palmar arch may also deliver blood into the fistula. Unless there is the capacity for collateralization, this can lead to ischemia in the hand, ranging from complaints about cold hands to necrotic fingertips. Most of these complaints improve over time, but 1% of AVFs and up to 4% of AVGs require surgical revision [133]. Ischemic monomelic neuropathy is characterized by warm hands with a good pulse, but the hands are tender and swollen, usually immediately after surgery, and there is muscle weakness [134]. The cause is likely ischemia of the nerves and rapid surgical re-evaluation is needed. Nevertheless, there is evidence that the only differences between patients with PTFE older than 65 years old and younger ones are minor. Wound and skin complications and greater incidence of thromposis of VA associated with recombinant human erythropoietin have been reported (rHuEPO) [135].

5.4 Tunneled catheter complications

Early or late catheter dysfunctions are the functional complications of TCs. Kinking and unsuitable positioning of the catheter tip may be the cause of early dysfunction and can be

addressed under fluoroscopic guidance. Among late causes of failure, are fibrin sheaths and thrombi around or at the catheter tip. Fibrinous sheaths can be disrupted by balloon angioplasty with improved flow through a new catheter in the same location. Symptomatic occlusions of the central veins usually require the removal of the catheter and system anticoagulation and must be weighed in the context of a continued need for dialysis and other available access options. Catheter use is linked to higher rates of infection and could compromise dialysis adequacy [136, 137]. Catheter related infections (CRI) are associated with increased all cause mortality and morbidity. 8-10% of MRSA bacteraemia in the UK occurs in patients receiving long term haemodialysis. It recently seems that the appropriately chosen antimicrobial lock solutions (ALS) reduce frequency of infections in HD patients [138]. Prophylaxis with gentamicin of the catheter lumens reduces bacterial infection morbidity and mortality related bacteremia of catheter without obvious bacterial resistance, making such use advisable [139]. Del Pozo et al in their prospective study showed that evaluation of tunnelled catheters with intra-catheter leukocyte culture helps in early HD catheters colonization, giving the possibility to eradicate biofilm without the removal of catheter [140].

6. Final remarks and conclusions

The radiocephalic and the humerobasilic AVF are the two types of VA with the longest duration of function, although a high rate of initial failure is seen with the radiocephalic AV fistula[141]. It is the preferred VA on account of the longest duration, its low complications rates and its ease of puncture [142-144].

Age, female gender, presence of diabetic nephropathy, start of dialysis with a catheter and failure to wait for initial maturation of the VA are risk factors and account for the majority of VA failures during RRT. Repeated VA failure has been identified as a risk factor for mortality [145].

The brachiocephalic AV fistula is the preferred type of VA, if the radiocephalic approach fails. In case of diabetic patients this seems to be the primary fistula if adequate vessels are not available, this is a frequent finding. Four year permeability rates of 80% have been reported [146]. In Rodriguez et al study, survival of brachiocephalic AV fistula was lower than radiocephalic; slightly more than one-half of patients have patent fistulae after 4 years and one –third after more than 8 years. It also shoed that more than two-thirds of patients in whom the first VA developed successfully did not have any subsequent VA failure, whereas initial failure increased the risk of subsequent failure. Female gender and presence of diabetes were risk factors related to VA failure [141].

The effort to create fistula first, has successfully increased the prevalence of AVFs [147]. However, the number of TCs has also increased, and those placed for bridging a patient to a functional AVF may stay in place longer [62]. Studies about fistula placement success from the US and European countries differ, significantly in the primary patency rate of AVFs at one year. US studies that include diabetic patients, report patency rates as low as 40%–43% [148, 149].

Konner et al reports a primary patency rate in diabetic patients of 69%–81%, depending on gender and age (results reported from 748 AVFs over 5 years) [150].

Chemla et al performed 552 AVFs in 4 years, achieving a primary patency rate at 22 months of 80% in 153 patients with radiocephalic fistulas [151].

Korsheed et al report that AVF formation resulted in a sustained reduction in arterial stiffness and BP as well as an increase in LVEF. These data state that the lower mortality of these patients with AVF, may be due to factors beyond VA associated infections and dysfunctions [152].

However, data from 1996 to 2006 collected from DOPPS indicate a growing use of catheters in many countries [153]. Also, our data in 2011 shows increased patency for TCs in female gender patients. Rayener et al report growing use of catheter according to DOPPS data. They also indicate that in facilities with the practice of early cannulation of AVF (within 4 weeks from their creation) and promptly performed VA surgeries with success in creating VA in older, diabetic women greatly enhance the odds of their patients for using a permanent access rather than TC [153]. In new dialysis patients, early referral to a nephrologist and early patient education strongly predict a successful functioning permanent VA at dialysis initiation and it also seems that the patients have better metabolic and clinical situation at the beginning of HD, lower long-term morbidity and higher survival for the first two years [154-158]. AV fistula is better when used for the first haemodialysis treatment compared to starting haemodialysis with a catheter [55, 159, 160]. Graft is, however, a better alternative than catheter for patients, where the creation of an attempted AVF failed or could not be created for different reasons [161].

In conclusion, as far as literature and our experience are concerned, arteriovenous fistula has to be the first choice in vascular access when suitable vessels are available. Arteriovenous grafts and Central Venous Catheters may be also a good alternative as fist choice when suitable vessels are not available or as a second choice when there is AVF failure. Female gender and old patients are more likely to start hemodialysis with a TC. Finally, a well matured vascular access is important for long access survival and early referral to nephrologists is mandatory.

7. Acknowledgements

Acknowledgements to Ioannis T. Papadakis Director of Nephrology Department Hippokration General Hospital and to the patients of Renal Unit who gave us the permission to add their pictures in our chapter. Also acknowledgements must be given to Mrs Sofia Andrikou for her designs of VA.

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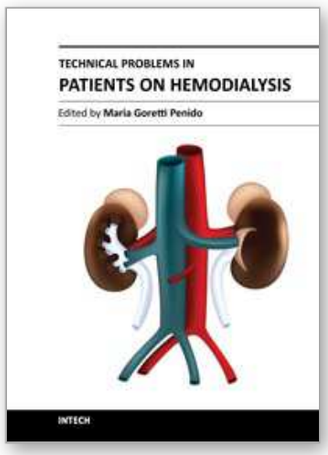
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Technical Problems in Patients on Hemodialysis

Edited by Prof. Maria Goretti Penido

ISBN 978-953-307-403-0
Hard cover, 312 pages
Publisher InTech
Published online 07, December, 2011
Published in print edition December, 2011

This book provides an overview of technical aspects in treatment of hemodialysis patients. Authors have contributed their most interesting findings in dealing with hemodialysis from the aspect of the tools and techniques used.Each chapter has been thoroughly revised and updated so the readers are acquainted with the latest data and observations in the area, where several aspects are to be considered. The book is comprehensive and not limited to a partial discussion of hemodialysis. To accomplish this we are pleased to have been able to summarize state of the art knowledge in each chapter of the book.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Konstantinos Pantelias and Eirini Grapsa (2011). Vascular Access for Hemodialysis, Technical Problems in Patients on Hemodialysis, Prof. Maria Goretti Penido (Ed.), ISBN: 978-953-307-403-0, InTech, Available from: http://www.intechopen.com/books/technical-problems-in-patients-on-hemodialysis/vascular-access-for-hemodialysis

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