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Dialysis catheter malfunction

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ABSTRACT

Vascular access is a crucial factor in the treatment of hemodialysis patients. Dialysis catheters are associated with higher mortality than fistulas, meaning they should be the last choice for most patients. Although they have many drawbacks, catheters play an important role in providing a reliable vascular access in some patients.

Dialysis catheter dysfunction is a major cause of morbidity. Early dysfunction usually occurs as a result of mechanical issues while late dysfunction is most commonly due to thrombosis. The causes of dysfunction and their management are distinct, and understanding of them is essential to preserve catheter patency and improve dialysis patient outcomes.

Keywords: Dialysis catheters, fibrin sheath, thrombosis, vascular access.

INTRODUCTION

Vascular access (VA) dysfunction is a major cause of morbidity in patients undergoing hemodialysis (HD), and the need to provide a suitable VA is an ongoing challenge.

Despite recommendations by various national guidelines advocating arteriovenous fistula as the HD access of choice, the use of central venous catheters (CVCs) remains widespread among both incident and prevalent HD patients[1]. Catheters have been associated with as much as a threefold increase in mortality rate compared to fistulas[2]. Although they have many drawbacks, CVCs have some relative advantages for professionals (such as easy application, prompt use without need for maturation), patients (no skin punctures) and administrators (they can be associated with lower costs in some units[3]). Moreover, they can be a reasonable choice in two main groups; some elderly patients with multiple comorbidities, who may not live long enough to benefit from the survival advantage afforded by a fistula or graft over a catheter; and patients with thrombosis of several fistulas and grafts, with no more suitable vessels for the creation of an access[4].

Proper catheter management to preserve patency and to minimize the risk of infection is vital in improving patient outcomes. In this review we will focus on non-infectious catheter dysfunction.

DEFINITION

Central venous catheter dysfunction has a variety of definitions reported in the literature[5]. These heterogeneous designations hinder the quality assessment of renal replacement therapy, and the interpretation of studies due to different outcomes can, in the long-term, affect patient quality of life and survival. The NKF/DOQI guidelines define dysfunction as the failure to attain a sufficient extracorporeal blood flow of ≥300 mL/ minute with a pre-pump arterial pressure lower than -250 mmHg[5].

The recommendation to define catheter dysfunction as BFR <300 mL/min was opinion-based and some have advocated that this definition is excessively simplistic, because the required blood flow for adequate dialysis could be higher (up to 400 mL/min) or lower than 300 mL/min, depending on the length of each dialysis session, and catheter lumen, among other factors[6]. The definition of catheter dysfunction should not be based only on blood flow but should include more meaningful parameters for assessing the ability to provide adequate dialysis[6].

CLASSIFICATION

Based on the time of occurrence, CVC dysfunction may be classified into early or late dysfunction[7].

a) **Early** – in the early course of HD, usually as a result of mechanical issues:
   a. Malposition:
      i. Wrong vessel;
      ii. Incorrect tip location;
   b. Kinking;
   c. Catheter issues:
      i. Tip design;
      ii. Coatings;
   d. “First use” syndrome;
   e. Drug precipitation.

b) **Late** – if a catheter has been used successfully and later becomes dysfunctional, most commonly due to thrombosis:
   a. Intrinsic (intraluminal);
   b. Extrinsic:
      i. Fibrin sheath;
      ii. Thrombus;
   c. Central vein stenosis.
   d. Catheter issues:
      i. Integrity.

a) Early catheter dysfunction

a. Malposition

The optimal site for placement of tunneled venous catheters (TVCs) is the right internal jugular vein (IJV)[5]. Not only is the anatomy favorable, with a relatively straight route from the internal jugular to the right brachiocephalic vein, and thence to the superior vena cava, but also the length, typically 15 or 16 cm (as opposed to 20–23 cm for the left internal jugular) is shorter[8]. Right internal jugular catheters survive significantly longer than left internal jugular catheters, which survive longer than femoral catheters[8].

Insertion procedure should be ultrasound-guided because it improves procedure success rate and reduces complications such as arterial puncture[8]. Additionally, fluoroscopy should be used to visualize all endovascular manipulations during the catheter insertion procedure and to confirm tip position. According to published data, 29% of catheters placed without imaging guidance have a malpositioned catheter tip[7]. Blind procedure, which relies on the use of external anatomical landmarks, should not be performed[5].

Wrong vein – Final position of the catheter tip depends on the course that the guidewire takes. Even after an ultrasound-guided correct vein puncture, if the guidewire is inserted without imaging control, it can go through an erroneous vein due to tip wire angle and anatomical variations or pathology (central stenosis, for example). Malposition in a small-caliber vessel can result in low blood flow and high recirculation rate. Reinsertion of a misplaced catheter is not without potential complications and there is also the possibility of repeating the malposition if imaging is not used.

Tip position – Determining the best position for a catheter tip requires an understanding of numerous clinical variables, including catheter type, insertion site, and the patient’s body habitus, among others. Ideal position is yet to be determined. Clinical studies have demonstrated that there is significant movement of the catheter tip when the patient changes position. For example, when the patient changes from a supine to an upright or sitting position, the abdominal contents descend, the central veins lengthen, the right atrium expands, the anterior chest wall shifts downward because of gravity, and the catheter tip moves upward on average 2–3 cm[10,11]. A tunneled catheter tip that is initially positioned in the right atrium will often retract upward into the lower superior vena cava (SVC).

Several researchers have also reported that larger--diameter catheters move more than smaller ones and catheters inserted into the subclavian vein will retract more than those in the internal jugular vein[11,12].

Regarding jugular catheters, positioning the tip into the SVC can limit its ability to achieve this high level of performance because the tip may “suck” against the adjacent vascular wall when aspiration is applied. On the other hand, positioning the tip too deeply into the upper right atrium can cause arrhythmias and may also “suck” against the atria wall, which could compromise blood flow. A catheter tip that has been positioned at the SVC/right atrial junction will rarely evoke a clinically significant arrhythmia[7].

The assessment of tip location should be ideally made by fluoroscopy. However, due to resource limitations, several centers still perform standard chest X-rays to confirm location. Several radiographic landmarks have been used to help identify the position of the atrial atrium, though they are often imprecise[13-15]. Many authors have stated that the most reliable radiographic landmark to define the borders of the SVC is the right tracheobronchial angle, which is located at a median distance of 5 cm to the SVC/atrial junction[13,16]. This means that a catheter tip positioned 3 cm below the right tracheobronchial angle would always be within the SVC[7].

b. Kinking

Kinking is a possible complication of CVC tunneling, when the vein insertion site is too high and an acute angle develops during tunneling. To avoid this complication, the venotomy site in the IJV should be as close as possible to the clavicle in order to avoid a long, tortuous course in the neck, but keeping in mind that the risk of pneumothorax will increase[5]. Retrograde tunneling can also facilitate a smoother tunnel, as well as an easier and more precise tip location[6]. Also, a variety of pre-curved catheters of different lengths have been developed to avoid kinking. After insertion procedure, the top of the catheter should be evaluated to ensure a smooth curve and rapid blood flow should be easily obtained with a 10 or 20 mL syringe from both the ports of the catheter[1,6].

c. Catheter issues

Tip design – Catheter design has evolved over the last two decades to improve blood flow adequacy, reduce recirculation and prolong patency. There may be catheter design advantages, although currently, few data comparing the safety and efficacy of one type of catheter over another exist[18]. Tunneled catheters may have dual lumens, split tips, or stepped tips; cylindrical shafts, ovoid shafts, or D-shaped shafts; machine-cut side holes, laser--cut side holes, or no side holes at all[18,19].

Although a split-asymmetrical tip reduces recirculation, a correct evaluation of the tip position is more difficult. Furthermore, the split-tip design promotes vessel wall irritation and thrombosis due to rubbing of the catheter tips. The self-centering, split-tip catheter might avoid this issue because the tips remain in the center of the vessel and are not occluded through contact with the vein wall[20].

Although added holes in catheters can increase flow and diminish tip obstruction, there is increased concern about thrombosis because they allow for stagnation of blood flow at the tip and for the anticoagulant lock solution to leave the catheter tip more easily, especially if they are located very far from the distal tip[20,21]. Also, they can potentially increase the risk of infection by harboring clots, which can act as a nidus for circulating bacteria.

Nonbiased randomized controlled trials are needed to compare different types of catheters regarding their longevity and complications.

Coatings – The polymer material catheters and the surface irregularities of catheters are enough to activate an inflammatory cascade and the intrinsic pathway of coagulation[22,23]. Coatings have been developed to help improve catheter biocompatibility. Antithrombotic coatings reduce platelet adhesion, inhibit inflammatory response, and reduce thrombus formation. Nevertheless, Leblanc and colleagues suggest that the stiffness of the catheter may be more important than the surface composition in terms of chronic endothelial injury and vessel wall abrasion and irritation[22]. One study demonstrated that soft pliable silicone catheters have less thrombogenic potential than regular stiff polyethylene catheters[24].

d. First use syndrome

Gallieni and colleagues recently described this issue which occurs as a result of a "first use effect" and the contact between blood and the plastic material of the catheter, particularly inside the CVC lumen[5]. In these circumstances, blood flow is excellent after the insertion procedure, as well as at the very beginning of treatment, but it shows progressive impairment during the session. The authors recommend a 24-hour delay before using a new tunneled CVC, to ensure full anticoagulation and avoid this effect[6].

e. Drug precipitation

Nonthrombotic occlusion may also be caused by drug precipitation, which can form as a result of drug crystallization, drug-drug incompatibility, or drug-solution incompatibility[25].

■ b) Late catheter dysfunction

Catheter failure resulting from thrombosis is a common problem in hemodialysis patients. Several factors make these patients more susceptible to thrombosis formation. Hemodialysis patients have unique blood physiology. The most important features include endothelial injury during vascular access creation and during shear stress produced by turbulent blood flow; intraluminal stasis of blood in the interdialytic period; platelet activation upon attachment to the dialyzer membrane and the catheter surface; reduced levels of antithrombin III and protein C anticoagulant activity; increased levels of homocysteine and fibrinogen[27].

The location and type of thrombus can be suspected according to symptoms and signs.

a. Intrinsic

An intrinsic thrombus forms within the catheter lumen (intraluminal), on the catheter tip, or on the fibrin sheath surrounding the external surface of the catheter[28]. When a fibrin tail forms in the catheter tip, it acts as a one-way valve and there will be an ability to infuse but not withdraw blood[29].

ii. Thrombus: Insufficient anticoagulant locking solution within the catheter or leaking into the bloodstream through the side holes can promote intraluminal thrombus. The portion of the catheter distal to the side holes and toward the tip does not retain the locking solution, thus being predisposed to thrombus formation[27].

iii. Fibrin sheath: Responsible for 38–50% of dialysis catheter malfunctions[29,30]. Formation of a fibrin sheath begins at the venous insertion site and then propagates distally along the catheter. Formation often begins within 24 hours of catheter insertion and total encasement of the catheter may occur within 1 week[31]. The sheaths are composed of a combination of fibrin, collagen, endothelial cells, and thrombus (in various stages of organization). Although a clear link with biofilm has not been established, it has been shown that infectious complications increase the risk of catheter-related thrombosis[31].

b. Extrinsic:

An extrinsic thrombus may form around the catheter in the vein leading to catheter attachment to the vessel wall, or it may form in the atria. Although mural thrombi are found in at least one-third of patients with an indwelling central venous catheter of more than 1-month duration[32], only 5% develop clinical symptoms or signs of thrombosis[33]. The main cause of mural thrombus formation is vascular injury at the vascular entry site or at the catheter tip, where the cardiac cycle-associated motion causes repetitive friction[34,35]. Symptoms vary from local tenderness or pain at the site of entry to obstructive symptoms with swelling of the ipsilateral extremity, neck, or face[28,36]. Atrial thrombi may become symptomatic, with pulmonary or systemic (paradoxical) embolism or catheter dysfunction, or may be incidentally found as an atrial mass[36]. In our experience, many patients who undergo an echocardiogram bring equivocal reports describing valve vegetations versus tip catheters thrombi.

c. Central vein stenosis

According to the 1996–1998 Dialysis Outcomes and Practice Patterns Study (DOPPS), central venous stenosis occurs in up to 38% of patients with temporary central venous catheters and in 27% of patients with permanent catheters[36]. Subclavian venous catheters have the highest rate of stenosis (40–50%) compared with internal jugular venous catheters (0–10%)[37,38].

Percutaneous transluminal angioplasty (PTA) for central venous stenoses is safe and effective, but restenosis is common with primary patency rates lower than 50% at 1 year[39,40]. Stents are also used for highly rigid, tortuous, or collapsing stenosis with elastic recoil, for sealing dissections or circumscribed perforations, and for recanalization of chronic occlusions[41,42]. Surgical techniques such as jugular vein transposition and axillary-internal jugular vein or right atrial bypass grafting can be performed, but have greater morbidity[43,44].

d. Catheter issues

Integrity – Chawla and colleagues found that tunneled dialysis catheter fracture is not so uncommon[17]. In our experience, we reported two cases in which the catheter detached itself from the cuff and migrated along the tunnel.

TREATMENT

The goal in treatment is to provide safe, efficient, cost-effective and sustained catheter function while preserving future central access for AVF or graft creation. Endovascular and pharmacologic therapies are available with different success rates.

I. Endovascular:
   a. Exchange;
   b. Revision;
   c. Reposition.
II. Pharmacological:
   a. Systemic anticoagulation/antiaggregation;
   b. Lock solutions:
      i. Timing;
      ii. Type: heparin, citrate, lytic agents, others;
      iii. Dose;
      iv. Instillation method.

■ Endovascular

Effective procedures to prolong tunneled catheter patency barely exist and there is little reliable evidence on which method is best.

The method of choice advocated by the KDOQI is disruption of the fibrin sheath with a balloon and/or catheter exchange[5]. According to Valliant and colleagues, exchange procedure does not cause an increase in infectious complications and provides patency rates similar to those of *de novo* catheter placements[41].

A recent paper compared the standard "exchange" of a catheter to a "revision" procedure[42]. An exchange involves a well-described procedure where the catheter is really exchanged over a wire, the venotomy site is not entered and the exit site is unchanged[42]. A revision involves an incision under sterile conditions at the initial venotomy site and then a new tunnel and exit site is made[42]. They concluded that revision technique limits the risk of infection and allows any diagnostic or interventional study, including angiogram and/or angioplasty, to be performed more easily[42].

The comparisons of sheath disruption by stripping or catheter exchange with and without an angioplasty balloon do not show any one technique to be more effective than the other[43]. Catheter replacement with sheath disruption is invasive, inconvenient, costly, time--consuming and increases risk of additional complications in patients. The choice of technique should be guided by factors including cost and patient and physician preference.

Reposition is necessary when catheter tip is malpositioned in a wrong vein, as well as when it is too upward or downward in the correct vein. This procedure should ideally be performed with fluoroscopy to guide endovascular procedure, locate tip position and diagnose central veins stenosis.

■ Pharmacological

Systemic

The relative net benefit of anticoagulant therapies for prevention of catheter malfunction remains uncertain.

Some authors found that prophylactic warfarin has shown some effect in reducing thrombus formation rates in patients with a tunneled catheter, but this effect occurred only when the adequate international normalized ratio was at the correct range, 1.5 to 2.0[45-48]. It is well known that there is an increased risk of bleeding in dialysis patients due to uremia, which causes platelet dysfunction, and heparin use during dialysis, among other factors, all of which make this approach difficult. Moreover, use of warfarin in hemodialysis patients has become controversial because warfarin may promote vascular calcification[49].

Of the commonly available antiplatelet agents, none of them – whether it be acetylsalicylic acid, clopidogrel or dipyridamole have shown consistent efficacy in preventing TDC thrombosis[28].

Further high-quality randomized studies, including safety outcomes, are needed.

Lock solutions

Noninvasive local pharmacotherapy has proved to be effective in restoring catheter patency.

Regarding this type of therapy there are four main topics to summarize:

a) **The timing of the therapy**. Lock administration may be categorized according to the clinical need. An acute requirement occurs when thrombosis is already established and the catheter is nonfunctioning. In this setting, lytic therapy aims to quickly restore catheter patency to start dialysis[50]. Rescue (prophylactic) therapy attempts to salvage a malfunctioning catheter before complete thrombosis occurs[50].

b) **The type of agent**. Several agents are currently available. Anticoagulants (heparin and citrate) are preferable for prophylactic use and lytic agents are mainly used for therapeutic intention.

Heparin has been the standard agent used to prevent catheter thrombosis. Its use has been associated with systemic anticoagulation due leaking, which causes increased potential for bleeding and heparin-induced thrombocytopenia[26]. There are several studies comparing heparin with other lock solutions and a recent meta--analysis concluded that heparin hasn't been inferior regarding catheter malfunction[51].

Sodium citrate is an effective anticoagulant that chelates ionized calcium, and thereby prevents activation of calcium-dependent coagulation pathways. Several authors have shown that trisodium citrate (TSC) 4% is as effective as heparin in maintaining catheter patency and more effective in preventing catheter-related bacteremia[52,53]. This evidence led to the American Society of Diagnostic and Interventional Nephrology to recommend the use of heparin, 1000 units/ml, or 4% sodium citrate as suitable choices for catheter-lock solutions[54].

Regarding lytic agents, urokinase was the first agent studied for thrombosed CVCs but safety issues led to its withdrawal in the United States in 1999[55]. Later, both the manufacturers and the FDA warned about the risk of allergic reaction and the frequency of serious adverse events with streptokinase[55]. In 2000 the FDA approved alteplase (tPA) use[28]. Although lytic agents are currently used only after dysfunction is detected (therapy use), the Pre-CLOT study explored their role as a prophylactic tool using recombinant tPA (rtPA) (1 mg in each lumen) in the mid-week session instead of conventional lock with 5000 units/ml heparin. The authors reported a statistically significant reduction in the incidence of both catheter dysfunction and catheter--related bacteremia, as well as a comparable adverse events rate[56]. When thrombus is already formed, rtPA is currently the most common agent used, with high success rates[57]. Although reported primary patency rates are relatively short, their use allows for repeated noninvasive catheter salvage.

c) **The dose of the agent**. The amount of heparin infused is based on the luminal volume of the catheter. Heparin hemorrhagic events may be reduced by the use of low-dose heparin (1000 units/ml instead 5000 units/ml) (26, 58). Several authors already showed that low dose TSC 4% has demonstrated to be at least not inferior, when compared to heparin and 30% citrate[53]. Standard dose of lytic agent is 2mg/lumen; however, some authors found that a low dose (1mg/lumen) is as effective as 2mg and is cost saving[59].

d) **The instillation method**. There are three major methodologies: locking, push, and infusion protocols[60].

Locking method refers to an intraluminal infusion of lytic agent corresponding to the catheter lumen volume. In additionally to being anti-thrombotic purpose, the use of an interdialytic lock solution may also reduce colonization and biofilm formation, thus minimizing the risk of catheter-related bacteremia[1]. This lock can last for a few hours (short dwells) or a few days (long dwells). Although studies evaluating these two approaches are small in number and heterogeneous in the definition of outcomes, overall success is achieved in 42–97% of cases[61-66]. Long dwells allow a patient to receive the lock after one session and stays until the next day or session. This protocol does not interfere with the dialysis schedule and does not demand for more nursing care. Moreover, the success rate looks higher than short dwells, 72–100% of cases, without significantly increasing bleeding risk[61,62,66].

Push protocol starts with a lock corresponding to each catheter lumen (2mg/2ml) followed by a variable number of pushes of 0.2–0.3 ml nonsaline solution every 10–15 min, and finishing with aspiration after 30–60 min from the beginning. It allows the lock to advance toward the catheter tip and offset lytic loss through the catheter side holes but can cause some degree of systemic fibrinolysis. Once again, available data regarding this method is limited as studies are retrospective and have heterogeneous protocols and different definition of outcomes. Overall success is achieved in 59–92% of the cases[67-69]. One study found that this strategy decreased the need for repeat lytic dwells by 81%, while maintaining the proportion of successful declottings[70].

Infusion protocols include those that are delivered while the patient continues dialysis. Twardowski evaluated a high dose of urokinase infusion during a 3h dialysis session with 81% success compared to conventional heparin[71]. No studies have been published with other lytic agents like alteplase or reteplase. Infusion after dialysis sessions has already been evaluated for alteplase by some authors[57,72]. Although success rate were significantly higher, an interventional suite and careful monitoring were necessary, which is not possible in most dialysis units.

CONCLUSIONS

Although the best prophylaxis of catheter dysfunction would be the complete avoidance of catheter use, they play an important role in some groups of patients and their well-functioning is essential in delivering an efficient dialysis.

Attention to monitoring for dysfunction and infection, the two major clinical complications of catheter use, as well as prompt intervention to salvage the functionality of the indwelling catheter, are essential in preventing or minimizing potential morbidity and mortality. The revision procedure with a new tunnel and exit site looks like the best way to change a catheter. Also, instead of conventional locks, the use of small amounts of lytic agents may be a prophylactic tool in the future. Several other prophylactic methods and novel approaches have been developed to improve catheters performance but the ideal catheter remains to be found.

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