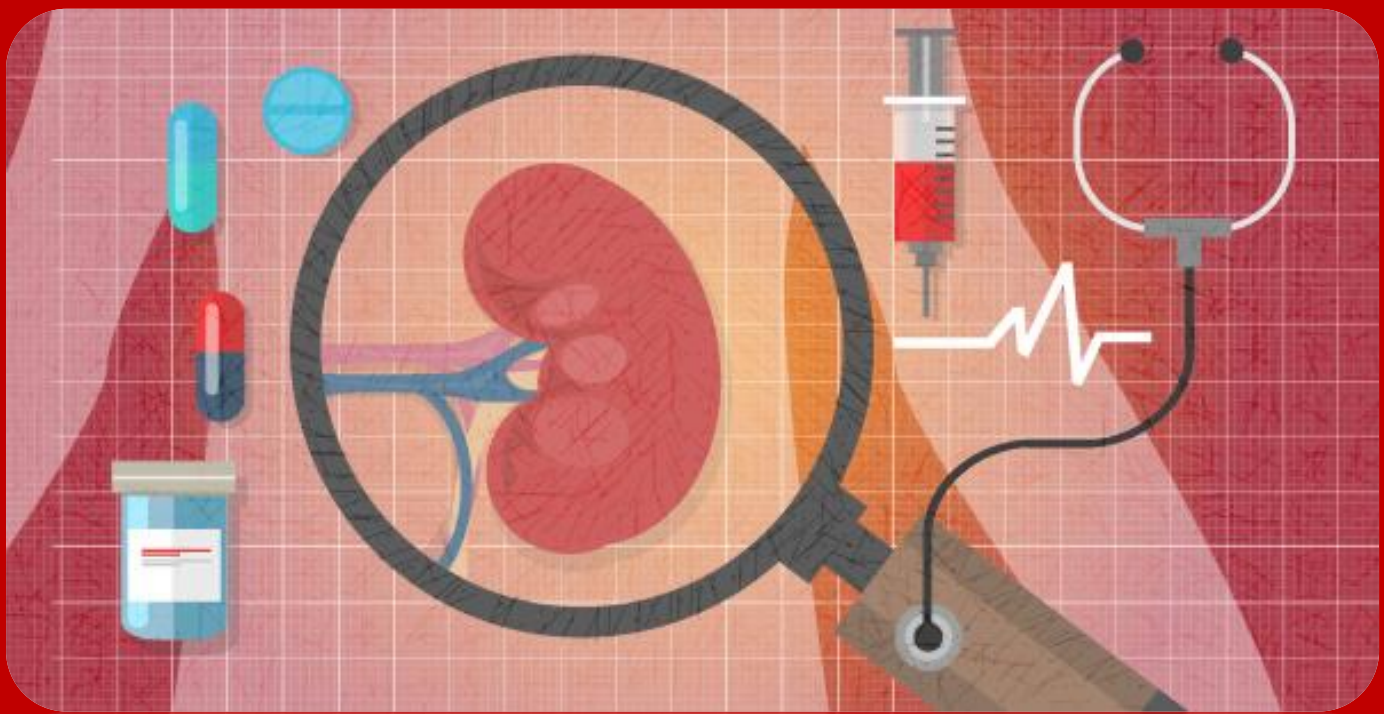
Role of Thrombolytics in Vascular Access Dysfunction



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Background and Objective of the Survey

Thrombolytics play a significant role in managing vascular access dysfunction, particularly in the context of hemodialysis and central venous catheters. Vascular access dysfunction, such as thrombosis or stenosis, is a common complication in patients requiring long-term vascular access for hemodialysis or intravenous therapy.

In hemodialysis patients, thrombolytics are often used to treat thrombotic occlusions of arteriovenous fistulas (AVFs) or grafts (AVGs), which are the preferred vascular access options for hemodialysis. Prompt administration of thrombolytics can salvage the access site, allowing for continued hemodialysis without the need for invasive interventions such as angioplasty or surgical revision.

Similarly, thrombolytics are utilized in managing central venous catheter dysfunction, where thrombotic occlusions can compromise vascular access for intravenous therapies or hemodialysis. Thrombolytic therapy can restore patency to the catheter, avoiding the need for catheter replacement and minimizing patient discomfort and inconvenience.

However, the use of thrombolytics in vascular access dysfunction requires careful consideration of factors such as the location and extent of the thrombus, the patient's bleeding risk, and the underlying cause of vascular access dysfunction.

Survey objective:

To evaluate the role of thrombolytics in vascular access dysfunction

Methodology of the Survey

A survey was conducted to evaluate the role of thrombolytics in vascular access dysfunction. A total of 150 doctors from India participated in the survey.

Step 1: A literature search was done on the topic. Below topics were covered in the literature search

- Introduction
- Prevalence Rate Of Different Types Of VA
- Arteriovenous Fistula (AVF)
- Arteriovenous Graft (AVG)
- Graft Materials
- AVG Complications
- Central Venous Catheters (Cvcs)
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- Femoral Vein
- Subclavian Vein
- CVC Complications
- Temporary And Permanent Dialysis Catheter
- Mortality And Morbidity Of Vascular Access
- Tenecteplase for the improvement of blood flow rate in dysfunctional hemodialysis catheters
- A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of Tenecteplase for Improvement of Hemodialysis Catheter Function: TROPICS 3

Step 2: A survey questionnaire was prepared based on the literature search. The survey form was shared through the digital medium with physicians across India.

Step 3: Their responses were analyzed and the findings are provided in this survey analysis booklet.

Literature Review

Introduction[1]

The number of patients with end-stage chronic kidney disease (CKD) requiring renal replacement therapy has increased progressively worldwide. Permanent vascular access (VA) is the life-line for the majority of these patients when hemodialysis (HD) is the treatment of choice. Thus, the successful creation of permanent VA and the appropriate management to decrease the complications is mandatory. A good functional access is also vital in order to deliver adequate HD therapy in end-stage renal disease (ESRD) patients. Despite the advances that have taken place in the field of nephrology and particularly in dialysis, few things have changed in recent years with regards to VA, mainly the introduction of the polytetrafluoroethylene graft and the cuffed double lumen silicone catheter. However, the cost of VA related care was found to be more than five-fold higher for patients with arteriovenous graft (AVG) compared to patients with a functioning arteriovenous fistula (AVF). It seems that the native AVF that Brescia and Cimino described in 1966 still remains the first choice for VA. Thereafter, VA still remains the "Achilles' heel" of the procedure and HD VA dysfunction is one of the most important causes of morbidity in this population. It has been estimated that VA dysfunction is responsible for 20% of all hospitalizations; the annual cost of placing and looking after dialysis VA in the United States exceeds 1 billion dollars per year. Nowadays, three types of permanent VA are being used: AVF, AVG and cuffed central venous catheters (CVC). They all have to be able to provide enough blood flow to deliver adequate HD, to have a long use life and a low rate of complications. The native forearm AVF has the longest survival and requires the fewest interventions. For this reason, the forearm AVF is the first choice, followed by the upper-arm AVF, the AVG and the cuffed CVC as the final step.

The history of HD VA is closely associated with the history of dialysis. Haas performed the first HD treatment in humans using glass cannulae to acquire blood from the radial artery and reverting it to the cubital vein in 1924. In 1943, venepuncture needles were used by Kolff or blood acquisition from the femoral artery and its reinfusion to the patient by vein puncture. Quinton et al developed the arteriovenous Teflon shunt in the 60s. In 1966, Brescia, Cimino, Appel and Hurwich published their paper about AVF. In 1968 Röhl et al published thirty radial-artery-side-to-vein-end anastomoses. Today, the artery-side-to-vein-end anastomosis has

become a standard procedure. In 1976, Baker et al presented the first results with expanded PTFE grafts in 72 HD patients.

Prevalence Rate Of Different Types Of VA[1]

There are many differences worldwide in the most common type of VA being used. In Australia among adults patients on HD, separated into incident (< 150 d since first dialysis) and prevalent cohorts (≥ 150 d), AVF was present in 61% *vs* 77%, AVG was present in 11% *vs* 19%, and CVC was present in 28% *vs* 4% in the incident and prevalent cohorts, respectively. A direct broad-based comparison of VA use and survival in Europe (EUR) and the United States was reported in a representative study [Dialysis outcomes and practice patterns study, (DOPPS) which used the same data collection protocol for more than 6400 HD patients to compare VA use at 145 United States dialysis units and 101 units in five European countries (France, Germany, Italy, Spain and the United Kingdom). AVF was used by 80% of European and 24% of United States prevalent patients and was significantly associated with younger age, male gender, lower body mass index, non-diabetic status, lack of peripheral vascular disease and no angina. After adjusting for these factors, AVF *vs* graft use was still much higher in Europe than United States (AVF use 83% *vs* 21%). For patients who were new to HD, access use was: 66% AVF in Europe *vs* 15% in United States, 31% catheters in Europe *vs* 60% in United States, and 2% grafts in Europe *vs* 24% in United States. In addition, 25% of European and 46% of United States incident patients did not have a permanent access placed prior to starting HD. In Europe, 84% of new HD patients had seen a nephrologist for more than 30 d prior to ESRD compared with 74% in the United States; pre-ESRD care was associated with increased odds of AVF *vs* graft use. AVF and grafts each displayed better survival if used when initiating HD compared with being used after patients began dialysis with a catheter.

According to the study by Ethier et al which was based on data from DOPPS, from more than 300 HD units from 12 countries and more than 35 000 patients, international trends in VA use and trends in patient characteristics and practices associated with VA use from 1996 to 2007 were examined. Since 2005, a native AVF was used by 67%-91% of prevalent patients in Japan, Italy, Germany, France, Spain, the UK, Australia and New Zealand, and 50%-59% in Belgium, Sweden and Canada. From 1996 to 2007, AVF use rose from 24% to 47% in the United States but declined in Italy, Germany and Spain. Moreover, graft use fell by 50% in the United States from 58% use in 1996 to 28% by 2007. Across three phases of data collection, patients consistently were less likely to use an AVF *vs* other VA types if female, of older age, having greater body mass index, diabetes, peripheral vascular disease or recurrent cellulitis/gangrene.

In addition, countries with a greater prevalence of diabetes in HD patients had a significantly lower percentage of patients using an AVF. Despite poorer outcomes for central vein catheters, catheter use rose 1.5 to 3-fold among prevalent patients in many countries from 1996 to 2007, even among 18-70 years old non-diabetic patients. Furthermore, 58%-73% of patients new to ESRD used a catheter for the initiation of HD in five countries, despite 60%-79% of patients having been seen by a nephrologist > 4 mo prior to ESRD. Compared to patients using an AVF, patients with a catheter displayed significantly lower mean Kt/V levels. A secondary analysis of the Membrane Permeability Outcome (MPO) study by Martin-Malo et al grouped participating countries according to geographical location; thus study centers in France, Greece, Italy, Portugal and Spain were allocated to southern Europe (n = 499), and those in all other countries (Belgium, Germany, Poland and Sweden) to northern Europe (n = 148). In patients from the northern European countries, a higher prevalence of diabetes mellitus and cardiovascular disease was observed than in those from southern Europe (diabetes 35.1% *vs* 21.0%; cardiovascular disease 40.5% *vs* 22.8%). In northern Europe, 23% of patients started HD with a catheter for VA, while in southern European centers, only 13% did so. According to a nationwide statistical survey of 4081 dialysis facilities in Japan at the end of 2008, the number of patients undergoing dialysis was determined to be 283 421. Regarding the type of VA in patients treated by facility dialysis, in 89.7% of patients an AVF was used and in 7.1% an AVG was use. According to a single center study in China by Yu et al of 376 maintenance HD patients, 97.87% had native AVFs, 1.33% had AVG and only 0.80% had cuff catheter. Swarnalatha et al, in their study from a tertiary care center in India with 237 new HD patients in a three year period, report that AVF was secured in 29.95% of patients at presentation and internal jugular catheter was the most common form of VA at initiation of HD, taking into account that 65.40% of patients had emergency HD.

Arteriovenous Fistula (AVF) [2]

The AVF needs to be planned at least one or two months before starting HD, a time required for the proper maturation of the VA. A correct flow-chart should include a preoperative phase, an operative phase, and a postoperative one.

Clinical and instrumental evaluation is necessary to decide the type of VA, the technical approach, and the correct follow-up to handle complications as early as possible. To preserve the vascular system, it is important to avoid blood withdrawals or intravenous infusions from the arm and forearm, and to use the veins of the hands for these purposes.

The preoperative phase of AVF includes accurate collection of medical history, physical examination, and instrumental evaluation. Anamnestic collection should investigate about heart diseases, to assess any alteration in cardiac output. Indeed, as a consequence of AVF, there may be changes in blood flow, pulmonary pressure, and cardiac output, especially when the blood flow of the AVF is greater than 2,000 mL/min. Previous arterial and/or venous catheterization needs to be investigated for the high risk of central vein stenosis with consequent reduced venous output of the future VA. It is important to identify the dominant limb in order to avoid a limitation of the patient's quality of life.

The physical examination is aimed to investigate arterial and venous system functioning and therefore exclude the presence of any edema, surgical scars, radial, ulnar and brachial pulses, and superficial venous circles. The Allen test should be performed to evaluate an abnormal vascularization of the palmar arch.

The gold standard to decide on the type and location of VA is the duplex ultrasound scan. It allows the assessment of the arterial and venous diameters; a vein diameter >2 mm and an artery diameter >1.6 mm are considered adequate. These two parameters are predictive of AVF maturation.

According to the guidelines of the National Kidney Foundation (NKF-K/DOQI), the site order for the surgical intervention of AVF for HD is the following: forearm (radio–cephalic or distal AVF), elbow (brachio–cephalic or proximal AVF), arm (brachial–basilic AVF with transposition or proximal AVF).

The AVF directly on the wrist is considered the gold standard for VA. It is relatively simple to create, and since there is a low incidence of complications, the long-term patency rates are excellent and do not preclude the possibility of future access. Different types of arteriovenous anastomoses are possible: side-to-end of the vein on the artery, latero-lateral, terminalized side-to-side, side-to-end of the artery on the vein, and end-to-end. The most common is the anastomosis of the vein side-to-end of the artery.

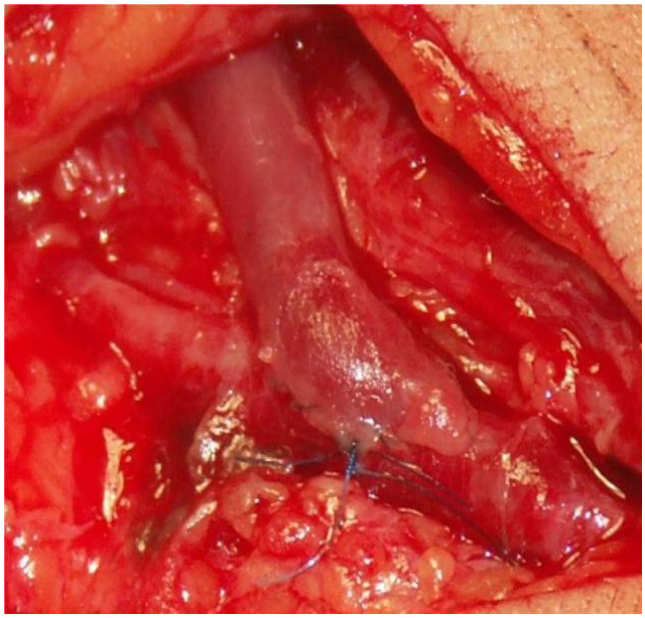


Figure 1. Native radio-cephalic arteriovenous fistula for hemodialysis, with latero-terminal anastomosis

The patency rate for distal access at 1 year, reported in the literature, varies from 56% to 79%. The second treatment option is represented by the proximal AVF. It has the advantage of employing major caliber autologous material, which facilitates both the making up of the access and the subsequent venous cannulation for the use of access, as well as a higher patency rate compared with distal ones. However, it is characterized by a higher rate of complications such as steal syndrome and arterial alterations in cardiac output.

The brachio-basilic AVF also requires an additional technical procedure; that is, the superficialization of the basilic vein. This can be done in two stages, with the advantage of handling a vein which is already "arterialized" and therefore more resistant, but with the drawback of a more delayed use of the access.

One-year patency rate for proximal accesses reported in the literature varies from 70% to 84%. Before starting to use the AVF, a waiting time is needed in order to obtain structural modifications of the vein wall which consist of "arterialization" as a result of the turbulent flow. According to the guidelines NKF-K/DOQI 2006, an access can be defined functional when the flow is >600 mL/min, the vein has a minimum diameter of 0.6 cm and does not exceed the depth of 0.6 cm, and the margins are clearly identifiable. The timing related to the achievement of these characteristics ranges from 1 to 3 months from surgical intervention of AVF. To evaluate the abovementioned parameters, a careful clinical and instrumental monitoring is required. In particular, the flow measurement method would be useful.

The most frequent complications related to AVFs are insufficient maturation of the AVF, stenosis, thrombosis, infection, aneurysm, “steal syndrome” due to ischemia, and high-rate flow AVF.

The failure of AVF can be related to stenosis of the artery of vein. Such a complication can be corrected by means of endovascular or surgical procedure, so short stenotic segments can be treated by means of percutaneous transluminal angioplasty, whilst surgical replacement is the gold standard for more extensive stenotic segments.

Nowadays, an increasing proportion of people who start dialysis are 75 years or older, with three-quarters of them having five or more comorbidities, and 90% having cardiovascular disease. Indeed, when the radio–cephalic fistula was described in 1966 by Cimino and Brescia, the patients’ average age was 43 years, almost all had chronic glomerulonephritis. A preoperative, clinical prediction ruled to determine fistulas that are likely to fail to mature showed the relevance of older age as a risk category for “fail to mature”. For this reason, placement of unnecessary AVF in elderly patients with low life expectancy is not recommended.

However, in order to have tools to predict AVF maturation/failure or successful use, an ongoing multicenter clinical trial, “The Hemodialysis Fistula Maturation (HFM) Study”, has been designed to elucidate clinical and biological factors associated with fistula maturation outcomes.

Arteriovenous Graft (AVG) [2]

This type of VA consists of an AVF made with prosthetic interposition between an artery and a vein, with two purposes: the first is to be able to link two vessels which would not be possible to connect due to their distance, and the second is to interpose between an artery and a vein a high capacity prosthetic segment that can also be used for the insertion of HD catheters.

AVG is the second step of treatment, following the AVF made with native vessels. In selected cases, an AVG is indicated as the first line of treatment, such as in cases of paucity of autologous material and/or for a short predictable period of hemodialytic treatment (children), or in patients with short obese limbs, where the superficial veins are deep in the subcutaneous tissue, and finally in patients with extreme vascular fragility (thrombocytopenic purpura), where the simple venous puncture produces wounds and serious hematomas.

The prosthetic AV access has been the most common access for dialysis in the US. This is related to several reasons and to a nihilistic attitude on the part of access surgeons that contributes to the underutilization of autogenous access sites.– However, there are many efforts

in the US and Canada to reverse this trend, as several studies suggest greater morbidity of AVG compared with autogenous access.–

For optimal AVG planning, a clinical evaluation of the upper limb is necessary. Skin integrity, presence of superficial veins, which imply a central vein occlusion, and the presence of peripheral pulses should be evaluated. The second step for optimal planning is the duplex ultrasound exam. Vessel mapping is very important to reduce secondary surgical or endovascular procedures.

Duplex ultrasound provides indications on upper limb artery patency and on the presence of stenosis or occlusions that could be treated before restoring an adequate flow. Outflow study is needed to evaluate vessel patency and diameter, which are predictive factors of failure.

Silva et al applied preoperative duplex ultrasound of both arterial inflow and venous outflow and concluded that a minimal vein diameter of 4 mm was required for a successful polytetrafluoroethylene-vein anastomosis.

Graft Materials[2]

Prosthetic AV grafts are classified as either biological or synthetic. In general, biological prostheses are of limited availability, expensive, and of variable size and quantity. Benedetto et al described a technique to rescue surgery of autologous AVF using bovine mesenteric vein, with good results. These can be placed in the forearm, the arm, and the thigh, and can have a straight, curved, or loop configuration.

Table 1. Graft materials

Type	Material	Characteristic
Biological	Denatured homologous vein allograft	
	Cryopreserved saphenous vein	Caution should be exercised in patients at high risk for infection.
	Bovine heterografts – typified by SGVG 100	Safe alternative for patients with a history of multiple failed synthetic grafts.
	Human umbilical vein	
	Sheep collagen grafts	
Synthetic	Dacron® (E.I. du Pont de Nemours and Company, Wilmington, DE, USA)	

	PTFE	This fluorocarbon polymer has become the prosthetic graft of choice. Stretch ePTFE is preferable to standard ePTFE.
	Procol® (Hancock, Jaffe, Laboratories, Irvine, CA, USA) bovine mesenteric vein graft, which closely resembles the human saphenous vein	Higher graft survival for the bioprosthesis versus ePTFE (82% versus 50%; $P<0.04$) over a period of 20 months.

Abbreviations: ePTFE, expanded PTFE; PTFE, polytetrafluoroethylene; SGVG 100, SynerGraft Vascular Graft Model 100.

Although insertion sites in the upper limb are preferred because of the lower risk of associated sepsis, when the upper-limb sites are exhausted, the thigh is the next favored site., Slater and Raftery reported a cumulative graft patency of 80.5% at 2 years, with no graft loss due to sepsis, in a series of 22 thigh grafts inserted in 21 patients. However, Englesbe et al reported a less favorable experience: 27% of the femoral AV grafts were lost for sepsis, with an overall secondary patency rate of 26% at 2 years. When implanted in the thigh, the graft can have a straight, looped, or curved configuration.

Forearm grafts with loop configuration yield greater overall patency rates and require fewer revisions than forearm grafts with straight configuration. Axillary loop grafts are indicated when more distal options for VA are exhausted or when the risk of steal syndrome is extremely high.

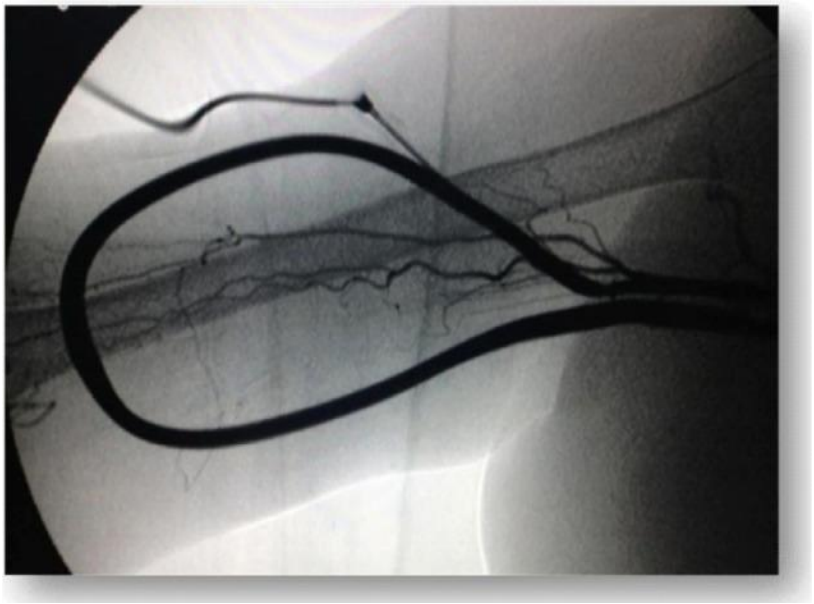


Figure 2. Synthetic axillo–axillary graft in polytetrafluoroethylene material

AVG Complications[2]

Functional survival of AVG is much shorter than with AVF. The natural course of AVG is thrombosis due to venous stenosis caused by neointimal hyperplasia. The increased production of smooth muscle cells, myofibroblasts, and vascularization within the neointima is the main cause of thrombosis. There is also angiogenesis and numerous macrophages in the tissue around the graft.

Growth factors such as platelet derived, vascular endothelial, and basic fibroblast growth factors are present within the neointimal lesion. Thrombosis of an AVG is usually the result of multiple factors, such as stenosis, hypotension, and excessive compression for hemostasis. The risk for thrombosis increases with decreasing blood flow. The influence of the anastomotic angle upon hemodynamics has been investigated using a porcine aortic model with 8 mm polyurethane interposition grafts and an end-to-side configuration. Distal anastomoses were created, with angles of either 90°, 45°, or 15°. Both the 90° and 45° configurations displayed a zone of recirculation at the anastomosis, while the 15° anastomosis displayed no flow disturbance.

To reduce the risk of graft thrombosis, the use of dypiridamole, sulfinpyrazone, ticlopidina, and combined aspirin and dipyridamole has been proposed. Although these agents showed a low rate of serious bleeding in dialysis patients, there is no definitive evidence of their efficacy. The effect of fish oil on synthetic HD graft patency was studied in a recent clinical trial. The authors showed that daily fish oil ingestion failed to reach the primary outcome since

it did not decrease the proportion of grafts with loss of native patency within 12 months. However, other secondary outcomes such as graft patency, rates of thrombosis, and interventions, were improved.

AVP infections are serious complications and are the second leading cause of dialysis access loss. The incidence of HD-related bacteremia is more than tenfold higher in AVGs than AVFs: 2.5 episodes per 1,000 dialysis procedures versus 0.2. Patients must be more careful about their hygiene because it seems to be the most important modifiable risk factor.

The critical issues in the management of AV graft infection are the need to eradicate infection and to achieve HD with reduced morbidity. Treatment involves intravenous antibiotics and total graft excision in septic patients or when the graft is bathed in pus; subtotal, when all of the graft is removed except an oversewn small cuff of prosthetic material on an underlying patent vessel; and partial, when a limited portion of AVG is removed and a new graft is inserted through adjacent sterile tissue.

Pseudoaneurysms should be referred to a surgeon for resection when they are >2 times wider than the graft or rapidly increasing in size or when the overlying skin appears under duress.

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 be distinguished. Endovascular treatment with stent grafts in complicated access, in AVFs as well as in AVGs, is a simple, safe, and rapid ambulatory procedure that enables treatment of both the aneurysm and its accompanying draining vein stenosis. It enables continued cannulation of the existing access and avoids the use of central catheters.,

Central Venous Catheters (CVCS) [2]

CVC represents a good choice, especially when urgent or emergent HD is required either at the time of initiation of renal replacement therapy or when a permanent access becomes dysfunctional. These devices are universally available, can be inserted into different sites of the body, and maturation time is not required, allowing immediate HD.

Preferable locations for insertion are the internal jugular and femoral veins, and in the third instance, the subclavian vein. Ultrasonography accurately locates the target vein and also provides information about venous pressure and the presence of intravascular thrombi. Its use should therefore be an integral part of central venous catheterization.

Table 2. Central vein approaches for dialysis catheters

Priority	Vein	Advantages	Disadvantages or complications
First choice	Internal jugular vein	Best with ultrasound	Medium infection risk
		Right side gives more chance to correct blind catheter tip placement	Medium bleeding risk
			Uncomfortable when not tunneled
Second choice	Femoral vein	Lower bleeding risk	Higher infection risk
		No need for radiological control after insertion	Higher thrombosis risk
			Poor catheter performance when patient sits up
Third choice (avoid proximal or terminal arteriovenous fistula in the same side)	Subclavian vein	Lower infection risk	Higher bleeding risk
		Suitability for subcutaneous tunneling and port access	Higher pneumothorax risk
			Higher thrombosis risk
			"Blind" procedure that cannot be guided with ultrasound

Internal Jugular Vein (IJV) [2]

The IJV represents the first choice for CVC insertion for several reasons. First of all, it is a large superficial vein that has easy ultrasound visualization. Moreover, the straight course into the superior vena cava or right atrium, without any corners, reduces the requirement for screening during insertion and allows high blood flow for HD. The lower part of the IJV lies behind a triangle formed by the junction of the sternal and clavicular insertions of the sternomastoid muscle and the clavicle. This triangle is used as a surface landmark

Normally, the vein lays anterolaterally to the artery, but in a small percentage of patients, the vein is immediately anterior to the artery or even medial to it. Therefore, for the significant anatomical variation in the vein and its course, percutaneous ultrasound-guided technique for IJV access has become the standard practice.

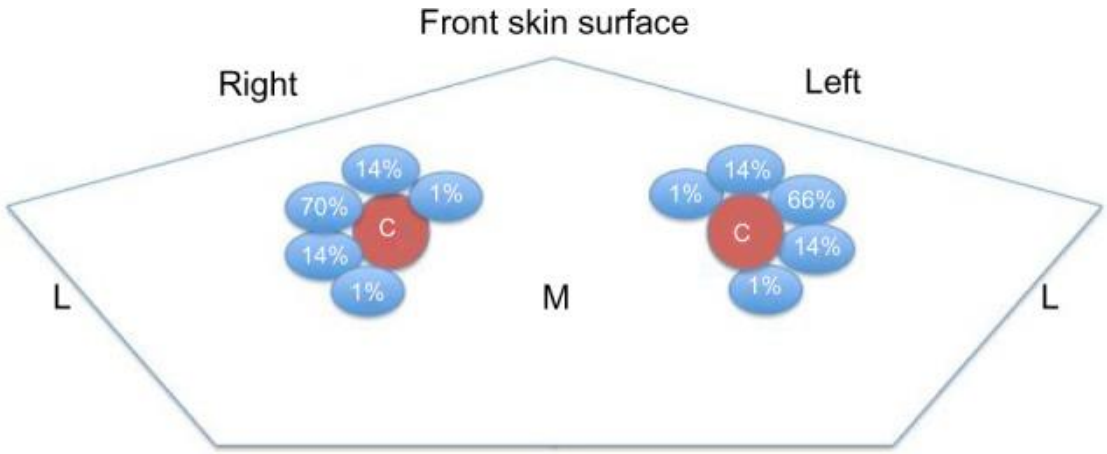


Figure 3. Percentage of variation in anatomical relations between the right and left internal jugular vein (in blue) and common carotid artery (C).

Traditionally, the vein has been located by the landmark technique; however, ultrasound guidance is now recommended as the preferred method for insertion of CVCs into the IJV in adults and children in elective situations. For the insertion of a CVC into the IJV, the patient should be optimally positioned, with a 10° head-down tilt (Trendelenburg position) to help distend the vein and reduce the risk of air embolism.

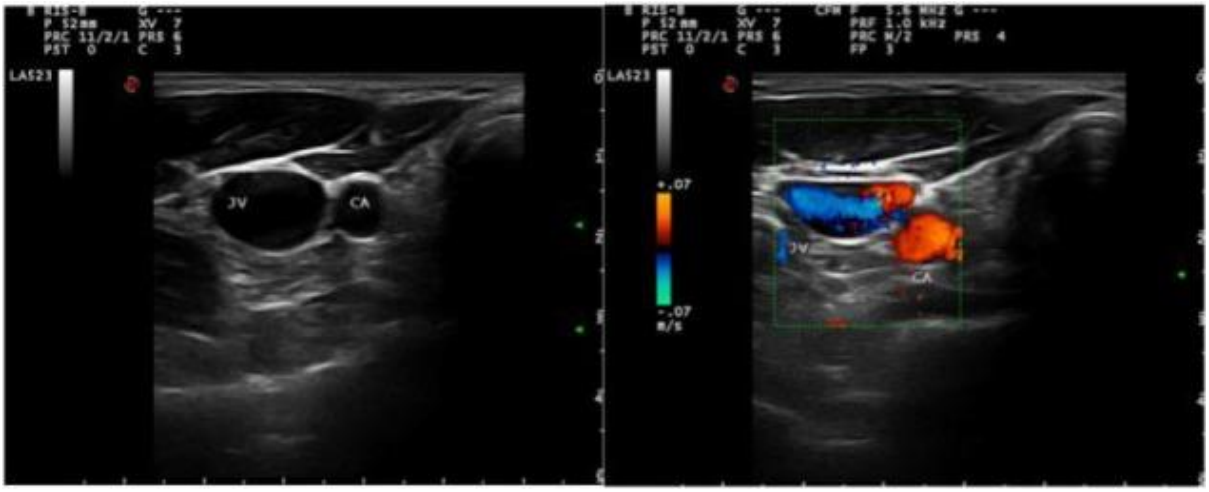


Figure 4. Ultrasound cross-sectional (left) and Doppler ultrasound (right) image of right internal jugular vein (IJV) and carotid artery (CA)

Note: Both vessels are very superficial since they are in a range of depth of field between 1 and 2.5 cm.

It may be safer if the patient's head is in the neutral position. Furthermore, the vein can lie directly above the carotid artery, increasing the risk of arterial puncture. A very modest degree of rotation of the head away from the side to be cannulated may be necessary, but extreme

rotation is best avoided as it may reduce vein diameter. Indeed, head rotation can cause the IJV to move laterally in relation to surface landmarks and become more difficult to locate.

There are two different main approaches, according to the visualization of the needle during its entry into the vein, using ultrasound guidance: in-plane and out-of-plane, placing the probe on the vein long axis or short axis. Recently, it has been shown that the lateral short axis in-plane technique has virtually no limitations, ensuring most benefits, and for this reason, it should be considered as the first-line technique for IJV cannulation.

The common method for direct insertion into the great veins is the Seldinger technique, using a guidewire over the needle. With this technique after the vein is entered, the guidewire is advanced into the vein and the needle is removed. Once the guidewire has been passed, it is important not to insert too far. Indeed, it may irritate the right atrium and cause arrhythmias, most commonly atrial ectopics. Then, before inserting the catheter, a dilator needs to be passed over the guidewire, using care to not cause vein trauma.

The length of the catheter inserted via the right IJV is typically 15 cm, whilst it should be 17 cm via the left IJV. Ideally, for temporary catheters, the tip should lie outside the right atrium, and its position should be checked during the procedure with electrocardiography, or on a post-procedure chest radiograph, before starting HD. For tunneled cuffed catheter, one of the two tips should lie inside the right atrium, whilst the other tip should lie 1 cm above, outside the right atrium.

Femoral Vein[2]

The femoral vein is considered the second approach for inserting temporary dialysis catheters in inpatients. The advantage is lower bleeding risk, and moreover, radiological control after insertion is not required. However, X-ray verification may be useful for longer-term access to ensure that there is no kinking and that the catheter tip has not entered lumbar vein or other branches. The landmark technique was described for the first time by Hohn and Lambert in 1966. The patient is in a supine position and abducts and externally rotates the thigh. The point of needle insertion into the femoral vein is situated below the inguinal ligament (approximately 2 cm) and medially to the beating of the femoral artery. The needle is inserted cephalad at an angle of 10°–15° dorsally in relation to the frontal plane and slightly medially in relation to the sagittal plane, and it is usually entered at about 2–4 cm deep. The abovementioned Seldinger technique is used also for the femoral vein.

The Valsalva maneuver is used to increase femoral vein diameter. The optimal location of the distal tip of catheters inserted through the iliac veins should be the inferior vena cava or the

right atrium. However, the majority of standard catheters (20 cm long) reach the iliac veins, and this position of the tip can cause increased blood recirculation. It should be taken into consideration that longer catheters increase the resistance of blood flow. For the permanent CVCs in femoral veins, a possible alternative is the external abdomen location of a cuffed catheter, as a variant of the normal external leg location.

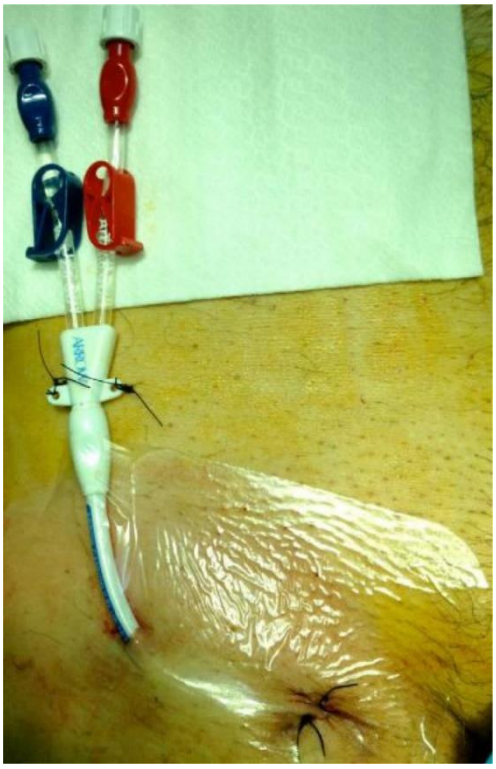


Figure 5. External abdomen location of cuffed tunneled central venous catheters in femoral vein, as a variant of the normal external leg location

Subclavian Vein[2]

The subclavian insertion of the catheter is considered the third choice because of the high risk of subclavian thrombosis with complication to create a VA in the ipsilateral arm. Historically, the supraclavicular subclavian catheterization was realized by Yoffa. The objective of this technique is to puncture the subclavian vein in its superior aspect just as it joins the IJV. The correct identification of the clavisternomastoid angle formed by the junction of the lateral head of the sternocleidomastoid muscle and the clavicle is mandatory. Active raising of the patient's head may make this landmark more apparent. The needle is inserted 1 cm lateral to the lateral head of the sternocleidomastoid muscle and 1 cm posterior to the clavicle and directed at a 45° angle to the sagittal and transverse planes and 15° below the coronal plane, aiming toward the contralateral nipple. The needle bisects the clavisternomastoid angle as it is advanced in an

avascular plane, away from the subclavian artery and the dome of the pleura, entering the junction of the subclavian vein and IJV. The right side is preferred because of the lower pleural dome, more direct route to the superior vena cava, and absence of thoracic duct. The Trendelenburg position is recommended to decrease risk of air embolism and to potentially help to distend the vein, as the subclavian vein is not bound by fascia on its superior aspect. To further minimize complications, the needle bevel should be facing down prior to insertion, attempts should cease after 2–3 unsuccessful tries, and most importantly, the clavisternomastoid angle must be clearly identified prior to insertion. The main disadvantages are higher bleeding and pneumothorax and thrombosis risk. Moreover, a "blind" procedure cannot be guided with ultrasound.

CVC Complications[2]

Caution needs to be used in implanting and management of CVCs, since their use is associated with a high risk of complications. Complications associated with CVC insertion range from 5% to 19%., Insertion complications include vascular injury (arterial puncture, pseudoaneurysm, and AVF), hematoma, air embolism, pneumothorax, and malposition. Generally, all these complications are limited to accidental arterial puncture when ultrasound guidance is used.,

Arterial puncture is a common risk during vein cannulation, since veins run alongside arteries. Even if the risk is higher for femoral than for jugular and subclavian veins, the complications of subclavian arterial puncture are much more severe, as the vessels cannot be compressed manually from the outside of the body because they lie under the clavicle, and this leads to hemothorax in severe cases.

The risk of pneumothorax is greatest in the subclavian area due to the proximity of the pleura to the vein, with an incidence rate of 2%–3% with this approach.

Indwelling complications are infection, thrombosis, catheter pinching/kinking, and fracture with possible embolization. Infections are discussed elsewhere. The risk of thrombosis is lower in the IJV, slightly higher in the subclavian vein, and still higher in the femoral vein. Classically, thrombosis is more likely where there is the combination of low blood flow, turbulence, and increased coagulopathy. The severity of thrombosis depends on the sites of location. Indeed, thrombosis of superficial veins in the forearm causes mild morbidity, whereas femoral venous thrombosis may cause life-threatening pulmonary embolism.

Another complication is stenosis of veins that may occur over a period of time, after damage to the vein wall due to infection or mechanical stress. The risk of stenosis is reduced if the

catheter lies in the center of a big vein with a high blood flow away from junctions with other veins.

Puncture of the carotid artery during attempted IJV cannulation can cause emboli of atherosclerotic tissue into the brain, with the severe consequences of a stroke. Arterial emboli from the subclavian and femoral regions are less dangerous to the patient.

Infections are more common in the femoral region due to the proximity of the perineum, whilst the subclavian vein probably causes less infection than the IJV.

Since an increasing number of patients have implanted pacemakers and defibrillators, usually inserted via the subclavian veins and superior vena cava into the right heart, a careful assessment of risks and benefits should be taken. The access site should be on the opposite side to where the implanted device lies wherever possible. However, there is a risk of superior vena cava syndrome due to thrombosis of the vessel secondary to placement of CVCs or pacemakers.

Temporary And Permanent Dialysis Catheter[2]

CVCs for HD are essentially of two types: acute (non-tunneled) catheters and chronic (tunneled) catheters. The choice between placement of an acute/temporary or a chronic/permanent catheter should be based on several factors: duration of use, bacteremia, and patient conditions.

Acute dialysis catheters are non-cuffed, non-tunneled catheters used for immediate VA. They are primarily used for acute renal failure in bed-bound patients, and for short-term use in patients with malfunction of permanent access. Long-term use of acute catheters is not recommended, but does occur, with acceptable infection rates, in dialysis centers where tunneled, cuffed catheters are not available. Most acute catheters are made of polyurethane, available with larger lumen sizes and capable of delivering blood flow rates over 300 mL/min following NKF-K/DOQI guidelines.

Concerning the indwelling time for catheter access, the acute catheter lacks a subcutaneous cuff, and it should be restricted to the first 1 or 2 weeks of HD, knowing that beyond 1 week, the infection rate increases exponentially. Moreover, guidelines recommend that temporary catheters should remain in place no longer than 5 days at the femoral vein.

A chronic catheter has a subcutaneous cuff which is placed in the subcutaneous tissue near the insertion site of a tunneled catheter and allows for fibrous sealing of its skin entry; this provides a barrier against infection by preventing migration of bacteria down the outer surface of the catheter, and the catheter can potentially be used for months to years. Insertion of a cuffed,

tunneled catheter is recommended as soon as it is known that prolonged renal replacement therapy (more than 2 weeks of HD) is needed.

Catheter materials[2]

Materials play an important role in terms of indwelling time of the catheter. During the past decade, there has been an emergence of technological advancements in the design of dialysis catheters in an attempt to reduce catheter malfunction, decrease infection rates, and improve their long-term efficiency. The availability of plastic polymers such as polyethylene, polypropylene, polyvinyl chloride, and fluorocarbons (polytetrafluoroethylene) provided tubing that began to meet many of the properties required for intravascular implantation. These materials are relatively thrombogenic by present day standards and also quite rigid, contributing to endothelial injury.

Polyvinyl chloride may be rendered more flexible by adding plasticizers, but these compounds elute into blood, with the possibility of unwanted biological effects and progressive hardening of the catheter. In the early 1940s the development of silicone polymers provided materials that offered greater biocompatibility and stability for long-term implantation, particularly due to reduced thrombogenicity.

By the early 1960s, medical grade silicone tubing had become commercially available – a significant advance in the evolution of clinical and experimental vascular catheters. More recently, developments in biocompatible polyurethane materials have provided catheter materials with physical properties superior to silicones.

Today, the most important materials used for CVCs are silicon and polyurethane, both of which are biocompatible and durable. There is no significant difference in the overall duration of function between silicone and polyurethane catheters; however, it has been observed that the infection rates were 3.6 per 1,000 catheter-days for silicone catheters and 3.5 per 1,000 catheter-days for polyurethane catheters.

The main difference between these materials is that polyurethane has a higher tensile strength than silicone, which allows catheters to be manufactured with a higher inner lumen and same outer diameter, improving in that way the overall catheter flow rate. Perhaps, due to the thinner walls, polyurethane catheters are more prone to kinking, although industry has already overcome this problem, offering kink-resistant double-lumen polyurethane catheters with flows greater than 400 mL/min.

One strategy aimed at reducing infection rates in acute catheters was the addition of an antimicrobial coating effective against pathogens. A study by Rupp et al demonstrated a

protective effect in the prevention of bacterial colonization when comparing protected with unprotected catheters. Protected catheters were able to reduce bacterial colonization of the catheter by 44% and catheter-related bacteremia by 79%.,

Currently, many new dialysis catheters are being developed in an effort to decrease thrombosis and infection rates and to prolong the long-term outcome of catheterization. Thrombosis has long been a problem with dialysis catheters. One way this problem has been addressed is by the evolution of material technology. A transition has been made using polyurethane rather than silicone because it allows for better catheter resistance and softness, while still maintaining a large internal diameter.

Recirculation is another important issue with chronic HD catheters. Correct tip positioning and design are two key points to reduce or prevent recirculation.

In our experience, retrograde tunneling improves the ability to ideally position the catheter tip, cuff and hub, and split-tip design, with both lumens placed in the right atrium. Retrograde tunneling has always been a good option to provide high blood flow with less recirculation, overcoming limits of some step-tip catheters, mainly due to the distance between arterial and venous port.

Recently, the latest technology has been able to provide a unique tip design, featuring ports that are reversed with respect to conventional step-tip (or staggered-tip) catheters. In fact, the arterial intake port, which is located at the distal tip of the catheter, is positioned in the lower right atrium and the venous outflow port is 6 cm proximal to the arterial port. The positioning of the arterial port directly above the inferior vena cava, in combination with the port spacing, minimizes recirculation, maintaining the advantages of the correct tip positioning of a retrograde catheter.

Mortality And Morbidity Of Vascular Access[1]

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. Additionally, patients who had a catheter as first VA had more complications and higher mortality. Patients who initiate HD with a TC or an AVG have a heightened state of inflammation, which may contribute to the excess 90 d mortality after HD initiation. The CHOICE study examined mortality based on access type in 616 HD patients for up to 3 years of follow-up. CVCs and AVGs were associated with approximately 50% and 26% increased mortality respectively, compared with AVFs with prevalence in men and elderly patients. Despite these findings and the K/DOQI recommendations, dialysis access data from 2002-2003 showed that only 33% of

prevalent HD patients in the United States were being dialyzed *via* AVFs. On the other hand, in Europe and Canada, the majority of patients (74% and 53% respectively) were being dialyzed *via* AVFs. Pisoni et al, in a facility-based analyses of DOPPS in order to diminish treatment-by-indication bias, suggest that less catheter and graft use improves patient survival. The high mortality associated at the beginning of HD with CVC (RR: 3.68), independently of other factors, make the decrease in the use of this VA an objective of the first order.

Additionally, Wasse et al report that levels of self-care and leg effort activity were higher among incident HD patients using an AVF compared to those using a CVC. They also found that compared with persistent CVC use, early persistent AVF use is associated with the perception of improved health status and quality of life among patients with ESRD. The elderly diabetic population with peripheral arteriosclerotic obstructive disease is particularly prone to angio-access induced hand ischemia. In our previous work with 149 HD patients who had undergone 202 VA procedures (177 Cimino-Brescia fistulae and 25 PTFE grafts), we found that the Cimino-Brescia fistula was used as the first choice of VA 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. The only reason for technique failure was vascular thrombosis in both groups. Similar reports have been published by Swindlehurst et al, according to which the creation of permanent HD 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. Desilva et al state that, while specific subgroups in the HD population exist where use of fistulas and grafts at time of dialysis initiation is not of proven statistical benefit to survival, elderly HD patients with comorbidities still appear to benefit from the use of fistulas and grafts. Therefore, it is clear that a primary fistula strategy in incident elderly ESRD is feasible and does not result in inferior outcomes. Age should therefore not be a determinant for primary fistula creation. Saxena et a state that significantly higher persistent MSSA and MRSA nasal carriage rates among ESRD patients over 75 years of age are suggestive of an elevated risk of potentially serious S. aureus-related complications among the very elderly during long-term HD. These findings might be helpful in the identification of elderly HD patients as a high-risk group for S. aureus-linked VA-related septicemia and to evolve appropriate preventive strategies. However, elderly patients should be considered for angioaccess as first line of venous access. The study by Morsy et al showed a successful first dialysis with angioaccess with failure and patency rates comparable to other age groups.

Recently, our data are different than what we published in 1998. We found in 189 patients that females were more likely to start HD with a double lumen catheter than males and patients

with heart failure were independent of gender. Female patients had PTFE grafts as first VA and the elderly patients had more complications and more VA procedures. Martinez-Gallardo et al reported that acute decompensated CHF episodes are common in pre-dialysis CKD patients. In addition to classical risk factors, pre-emptive AVF placement was strongly associated with the development of CHF.

However, Di Iorio et al in their cohort study demonstrate that in chronic dialysis patients, CVC choice is associated with significantly increased hospitalization, mortality rate and relative risk of death compared to AVF patients; differences disappeared after correction for comorbidity. Therefore, these data suggest that CVC use *per se* is not associated with increased mortality risks with respect to AVF.

Nephrologists must bear in mind that every VA in the upper limb, lower limb or body wall needs a run-in and a run-off: currently, thrombosis of the central vessels due to the excessive widespread use of CVCs emerge as a substantial cause of HD morbidity and mortality. Gadallah et al have presented an unusual case of marked breast enlargement secondary to HD AVF and subclavian vein occlusion proximal to the junction of the mammary vein. A similar case but without subclavian vein occlusion has been presented by Ruiz-Valverde et a. Chan et al report that obesity was not associated with increased AVF or AVG revision rates or failure and was only associated with poorer AVF maturity at the highest BMI quartile, so it should not preclude placement of AVF as VA of choice, except in the very obese where assessment should be individually based.

In the 2010 USRDS Annual Data Report, hospitalization in 2008 increased again, to a point 46% above their 1993 level. In 2007-2008, women treated with HD were 16% more likely to be hospitalized overall than men. They also had a greater risk than men of cardiovascular, infectious and VA hospitalizations, 11%, 14% and 29% greater, respectively.

There are also causes of morbidity common in all kind of VAs as bacterial spondylodiscitis must be suspected whenever a patient on HD is admitted with fever and/or back pain. The presence of a CVC and a history of multiple vascular accesses may be important risk factors. Prolonged antibiotic therapy with initial broad-spectrum coverage seems to be the best therapeutic approach. Infective endocarditis should be suspected when HD patients suffer from long-term fever, for which prompt blood culture and transthoracic echocardiography confirmation could be performed. Transesophageal echocardiography could be considered even when transthoracic echocardiography produces negative findings. With catheters removed, a full course of appropriate sensitive antibiotics and surgery, if indicated, could improve the outcome of chronic HD patients complicated by infective endocarditis.

Tenecteplase for the improvement of blood flow rate in dysfunctional hemodialysis catheters[3]

Background: We evaluated the efficacy and safety of the thrombolytic agent tenecteplase for the treatment of dysfunctional hemodialysis (HD) catheters.

Methods: Data were pooled from 2 Phase III clinical studies: the randomized, placebo-controlled TROPICS 3 trial and the open-label TROPICS 4 trial. Eligible patients received either an initial dose of tenecteplase (2 mg/lumen) or placebo (TROPICS 3 only) for a 1-h intracatheter dwell. Treatment success was defined as blood flow rate (BFR) ≥ 300 ml/min and a ≥ 25 ml/min increase from baseline BFR, without line reversal, 30 min before and at the end of HD. All TROPICS 4 patients and the TROPICS 3 patients enrolled after the final protocol amendment without treatment success received an instillation of tenecteplase at the end of the initial visit for an extended dwell of up to 72 h.

Results: A total of 372 patients with dysfunctional catheters were enrolled in the 2 studies. Of the 297 patients treated with tenecteplase at the initial visit, 31% achieved treatment success, with a mean (SD) change from baseline BFR of 73 (120) ml/min. Among the 179 patients who received a 1-h dwell of study drug followed by extended-dwell tenecteplase, 46% had treatment success at the end of the next HD session. Six catheter-related bloodstream infections and 2 thromboses were reported in patients following tenecteplase exposure.

Conclusion: Tenecteplase, administered as a 1-h dwell or a 1-h dwell followed by an extended dwell, was associated with improved BFR in dysfunctional HD catheters in the TROPICS 3 and 4 clinical trials.

A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of Tenecteplase for Improvement of Hemodialysis Catheter Function: TROPICS 3[4]

Background and objectives: Despite widespread use of tunneled hemodialysis (HD) catheters, their utility is limited by the development of thrombotic complications. To address this problem, this study investigated whether the thrombolytic agent tenecteplase can restore blood flow rates (BFRs) in dysfunctional HD catheters.

Design, setting, participants, & measurements: In this randomized, double-blind study, patients with dysfunctional tunneled HD catheters, defined as a BFR <300 ml/min at −250

mmHg pressure in the arterial line, received 1-hour intracatheter dwell with tenecteplase (2 mg) or placebo. The primary endpoint was the percentage of patients with BFR ≥300 ml/min and an increase of ≥25 ml/min above baseline 30 minutes before and at the end of HD. Safety endpoints included the incidence of hemorrhagic, thrombotic, and infectious complications.

Results: Eligible patients (*n* = 149) were treated with tenecteplase (*n* = 74) or placebo (*n* = 75). Mean baseline BFR was similar for the tenecteplase and placebo groups at 151 and 137 ml/min, respectively. After a 1-hour dwell, 22% of patients in the tenecteplase group had functional catheters compared with 5% among placebo controls (*P* = 0.004). At the end of dialysis, mean change in BFR was 47 ml/min in the tenecteplase group *versus* 12 ml/min in the placebo group (*P* = 0.008). Four catheter-related bloodstream infections (one tenecteplase, three placebo) and one thrombosis (tenecteplase) were observed. There were no reports of intracranial hemorrhage, major bleeding, embolic events, or catheter-related complications.

Conclusions: Tenecteplase improved HD catheter function and had a favorable safety profile compared with placebo.

References:

1. Pantelias K, Grapsa E. Vascular access today. *World J Nephrol*. 2012;1(3):69-78.
2. Santoro D, Benedetto F, Mondello P, et al. Vascular access for hemodialysis: current perspectives. *Int J Nephrol Renovasc Dis*. 2014;7:281-294.
3. Goldman J, Fishbane S, Oliver MJ, Blaney M, Jacobs JR, Begelman SM. Tenecteplase for the improvement of blood flow rate in dysfunctional hemodialysis catheters. *Clin Nephrol*. 2012;77(1):55-61.
4. Tumlin J, Goldman J, Spiegel DM, et al. A phase III, randomized, double-blind, placebo-controlled study of tenecteplase for improvement of hemodialysis catheter function: TROPICS 3. *Clin J Am Soc Nephrol*. 2010;5(4):631-636.

Survey Form

1) In your clinical practice, what % of haemodialysis patients present with AV fistula dysfunction?

a. <5%
b. 5-10%
c. 11-20%
d. 21-30%
e. 31-40%
f. 41-50%
g. 50%

2) In your clinical practice, what % of haemodialysis patients present with catheter dysfunction?

a. <5%
b. 5-10%
c. 11-20%
d. 21-30%
e. 31-40%
f. 41-50%
g. 50%

3) How do you manage patients presenting with AV fistula dysfunction?

a. Use thrombolytic agent
b. Refer to vascular surgeon

4) Out of ten patients presenting with AV fistula, how many patients do you manage with thrombolytic agent?

a. 2
b. 4
c. 6
d. 8

5) If you have used thrombolytic drug in such patients, do you find efficacy satisfactory?

a. Yes
b. No

6) How do you manage patients presenting with Catheter dysfunction?

a. Always replace the catheter
b. Use thrombolytic agent
c. Use thrombolytic agent first and replace catheter in case of failure only

7) In which of the following settings you prefer using thrombolytic agent?

a. For the treatment of thrombosis in catheter dysfunction
b. Prevention of Catheter Lumen Occlusion
c. Both for prevention and treatments of thrombosis

8) What is your most preferred type of thrombolytic agent in haemodialysis patients having catheter dysfunction?

a. Alteplase
b. Tenecteplase
c. Urokinase
d. Reteplase

9) What are the important parameters that you consider while choosing the thrombolytic agent in vascular access dysfunction?

a. Efficacy
b. Availability
c. Cost
d. Safety

10) What are the clinical parameters basis which you opt for thrombolytic agent in catheter dysfunction?

a. Catheter Blood Flow
b. Arterial pressure
c. Both A & B

11) Have you ever used tenecteplase in your patients having AV fistula dysfunction?

a. Yes
b. No

12) If yes, how would you rate your experience using tenecteplase (in terms of safety and efficacy) on a scale of 1-10 (1 being worst, 10 being best) in AV fistula dysfunction?

a. 1
b. 2
c. 3
d. 4
e. 5
f. 6
g. 7
h. 8
i. 9
j. 10

13) Have you ever used tenecteplase in your patients having catheter dysfunction?

a. Yes
b. No

14) If yes, how would you rate your experience using tenecteplase (in terms of safety and efficacy) on a scale of 1-10 (1 being worst, 10 being best) in catheter dysfunction?

a. 1
b. 2
c. 3
d. 4
e. 5
f. 6
g. 7
h. 8
i. 9
j. 10

15) Do you experience availability issues with Urokianse in your region?

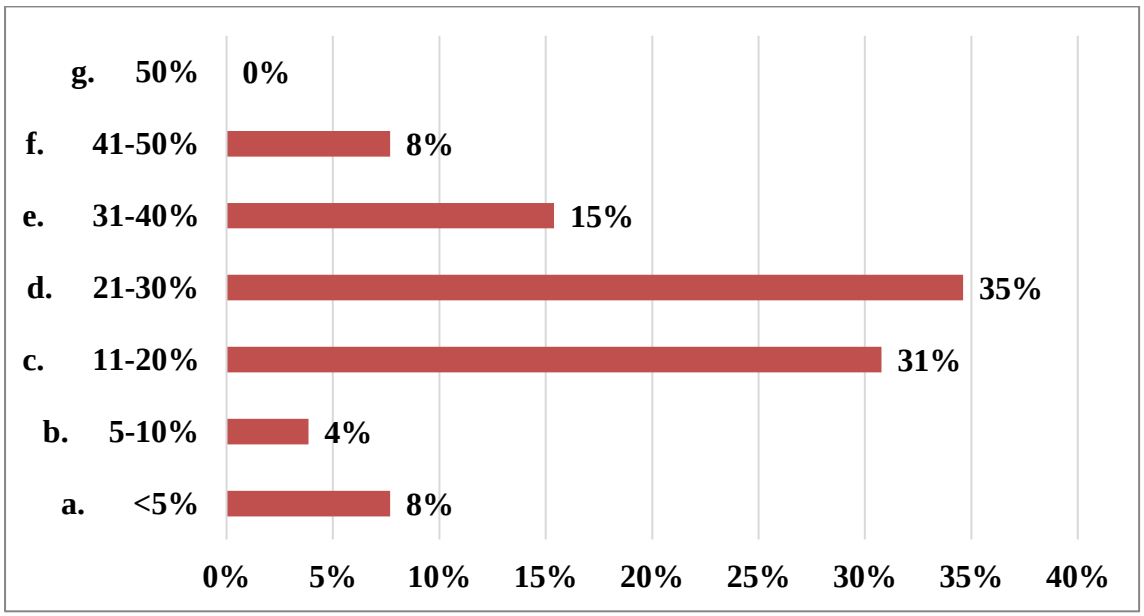
a. Yes

b. No

Survey Findings

1) In your clinical practice, what % of haemodialysis patients present with AV fistula dysfunction?

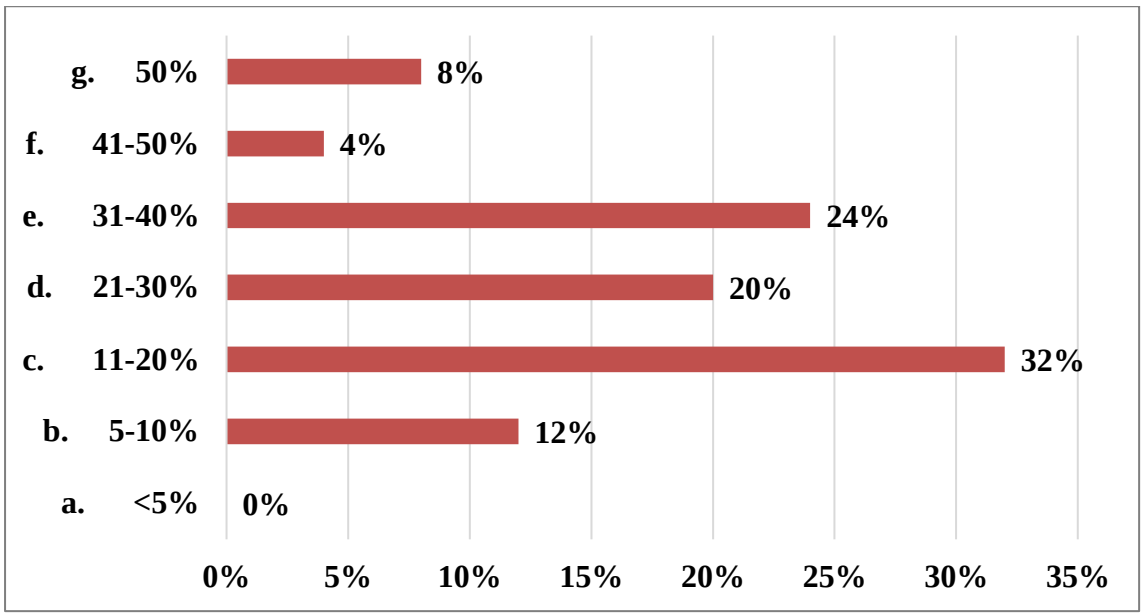
a. <5%
b. 5-10%
c. 11-20%
d. 21-30%
e. 31-40%
f. 41-50%
g. 50%



In the clinical experience of 35% of doctors, 21-30% of haemodialysis patients present with AV fistula dysfunction.

2) In your clinical practice, what % of haemodialysis patients present with catheter dysfunction?

a. <5%
b. 5-10%
c. 11-20%
d. 21-30%
e. 31-40%
f. 41-50%
g. 50%

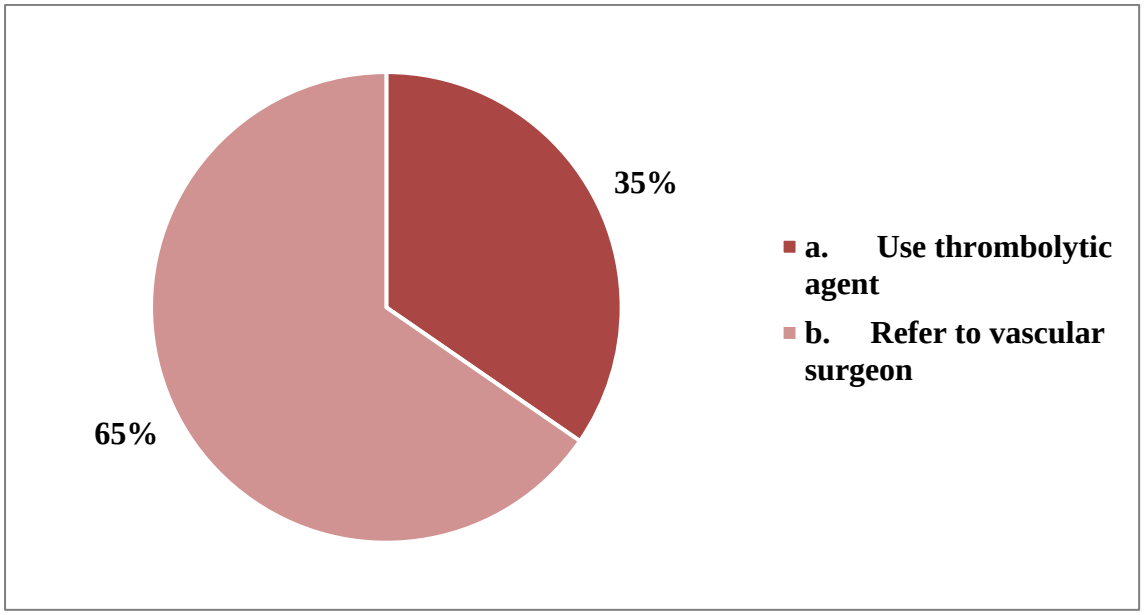


According to 32% of doctors, 11-20% of haemodialysis patients present with catheter dysfunction.

3) How do you manage patients presenting with AV fistula dysfunction?

a. Use thrombolytic agent

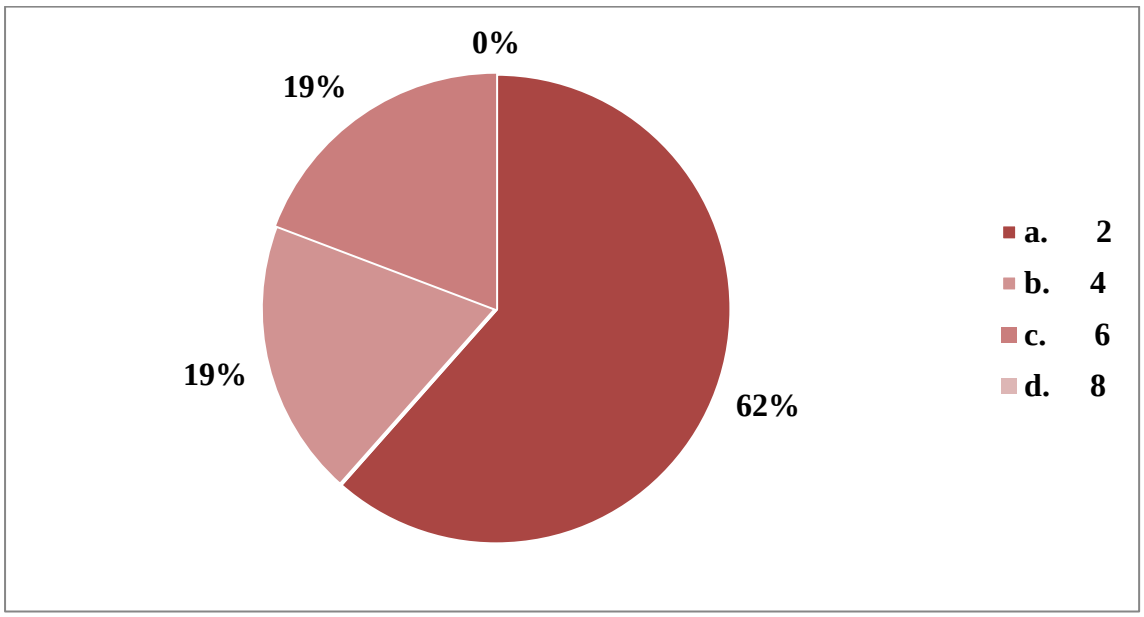
b. Refer to vascular surgeon



According to 65% of doctors, they manage patients presenting with AV fistula Dysfunction by refering to vascular surgeon.

4) Out of ten patients presenting with AV fistula, how many patients do you manage with thrombolytic agent?

a. 2
b. 4
c. 6
d. 8

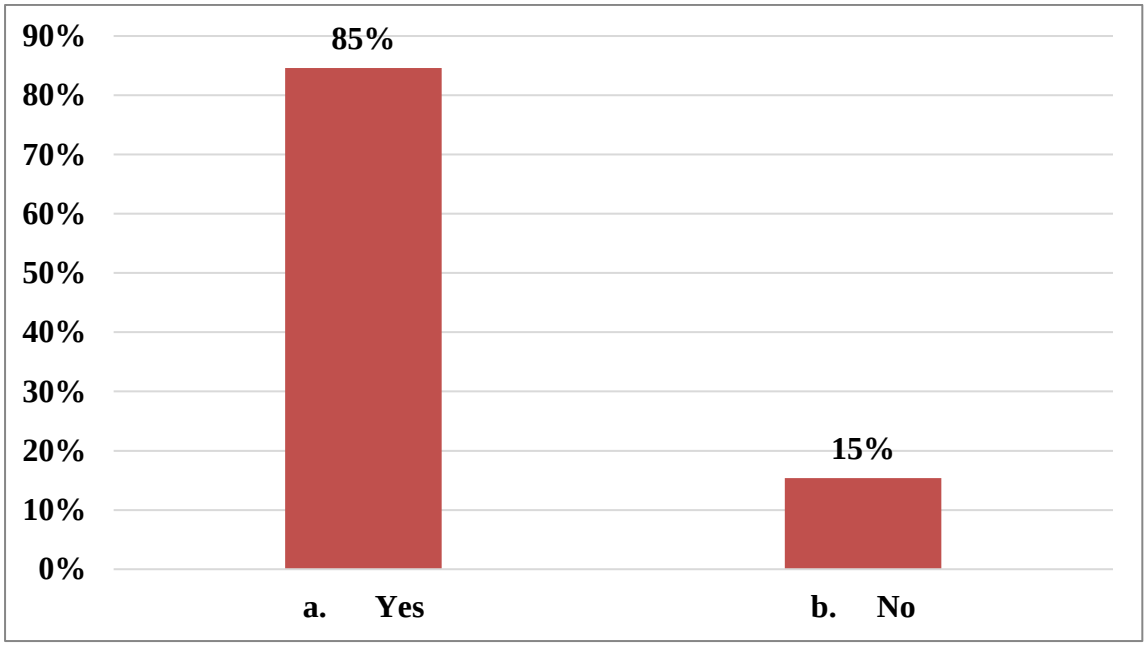


According to 62% of doctors, out of ten patients presenting with AV fistula, they manage 2 patients with thrombolytic agent.

5) If you have used thrombolytic drug in such patients, do you find efficacy satisfactory?

a. Yes

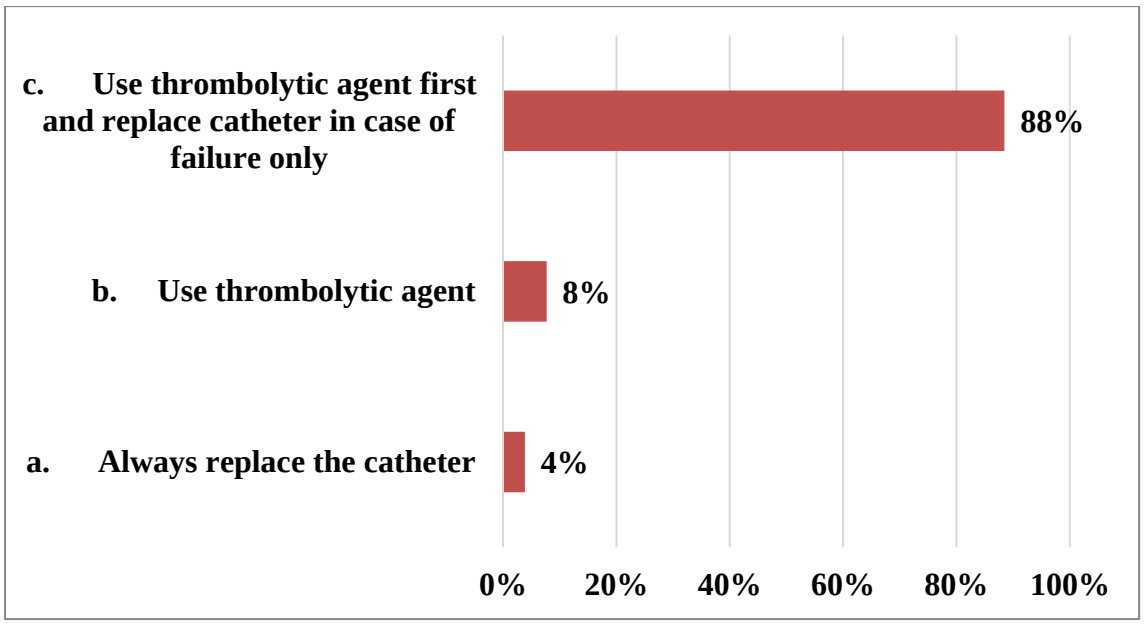
b. No



According to majority of doctors, 85%, they have used thrombolytic drug in such patients with satisfactory efficacy.

6) How do you manage patients presenting with Catheter dysfunction?

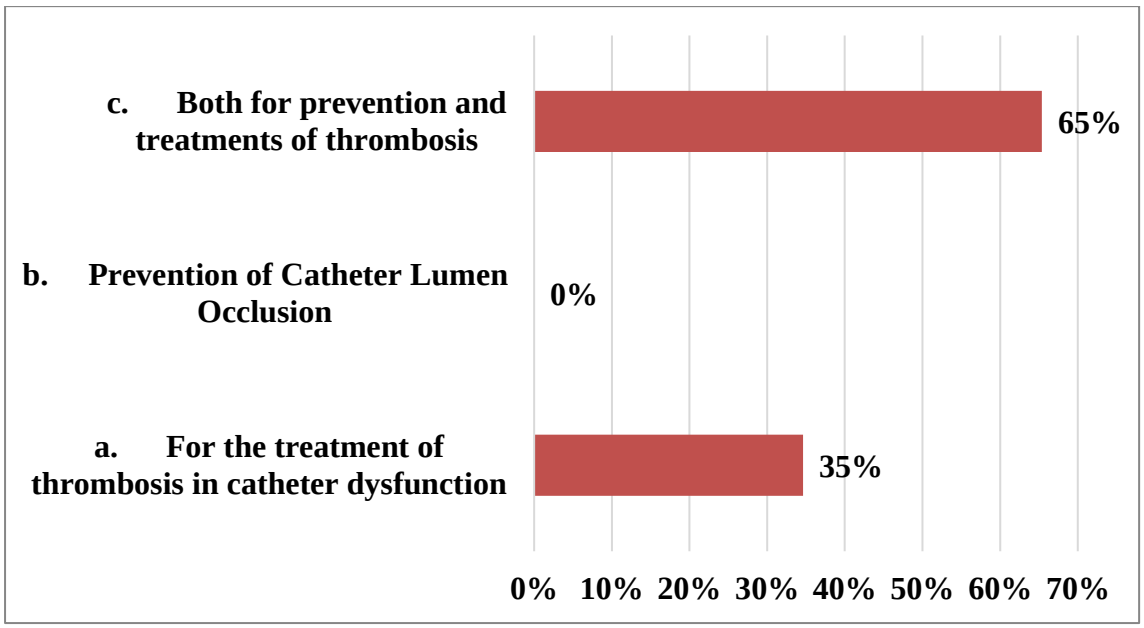
a. Always replace the catheter
b. Use thrombolytic agent
c. Use thrombolytic agent first and replace catheter in case of failure only



Majority of doctors, 88%, they manage patients presenting with Catheter dysfunction by using thrombolytic agent first and replace catheter in case of failure only.

7) In which of the following settings you prefer using thrombolytic agent?

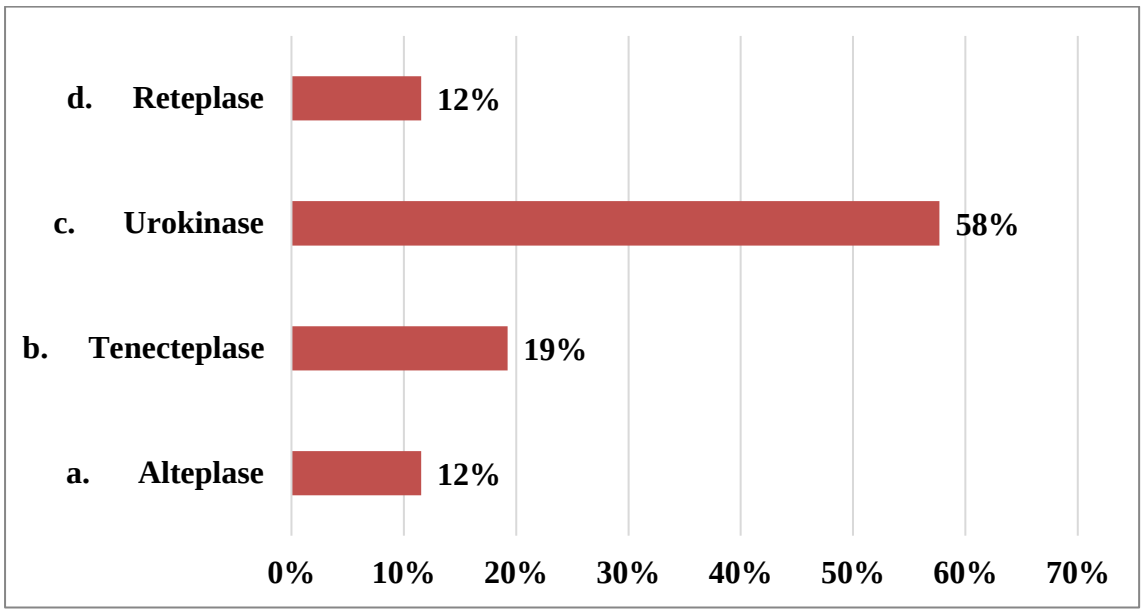
a. For the treatment of thrombosis in catheter dysfunction
b. Prevention of Catheter Lumen Occlusion
c. Both for prevention and treatments of thrombosis



65% of doctors prefer using thrombolytic agent both for prevention and treatments of thrombosis.

8) What is your most preferred type of thrombolytic agent in haemodialysis patients having catheter dysfunction?

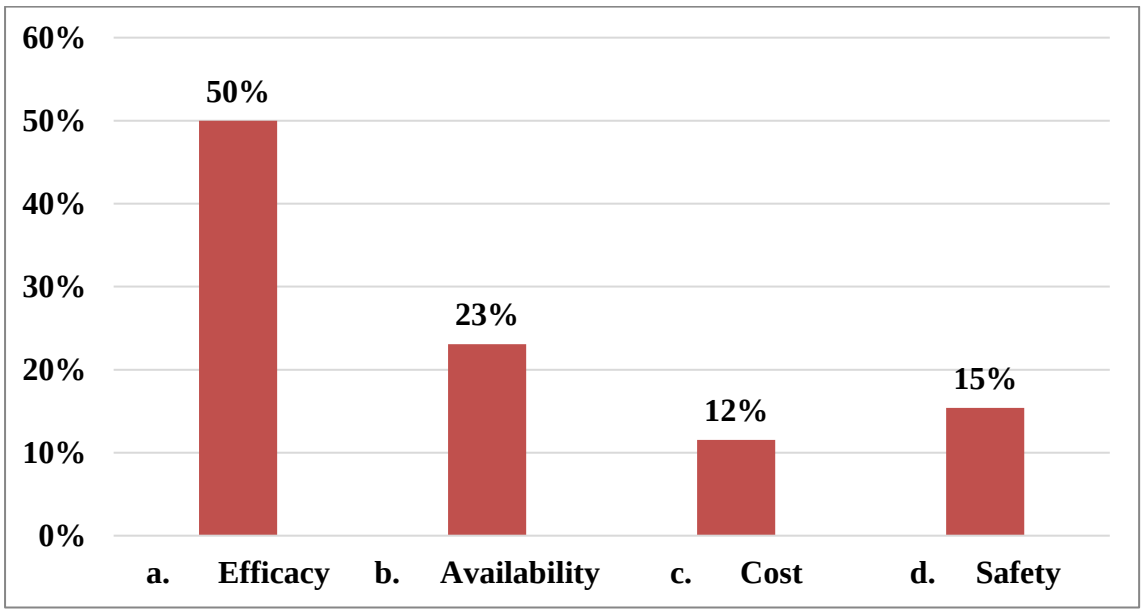
a. Alteplase
b. Tenecteplase
c. Urokinase
d. Reteplase



According to 58% of doctors, their most preferred type of thrombolytic agent in haemodialysis patients having catheter dysfunction is Urokinase.

9) What are the important parameters that you consider while choosing the thrombolytic agent in vascular access dysfunction?

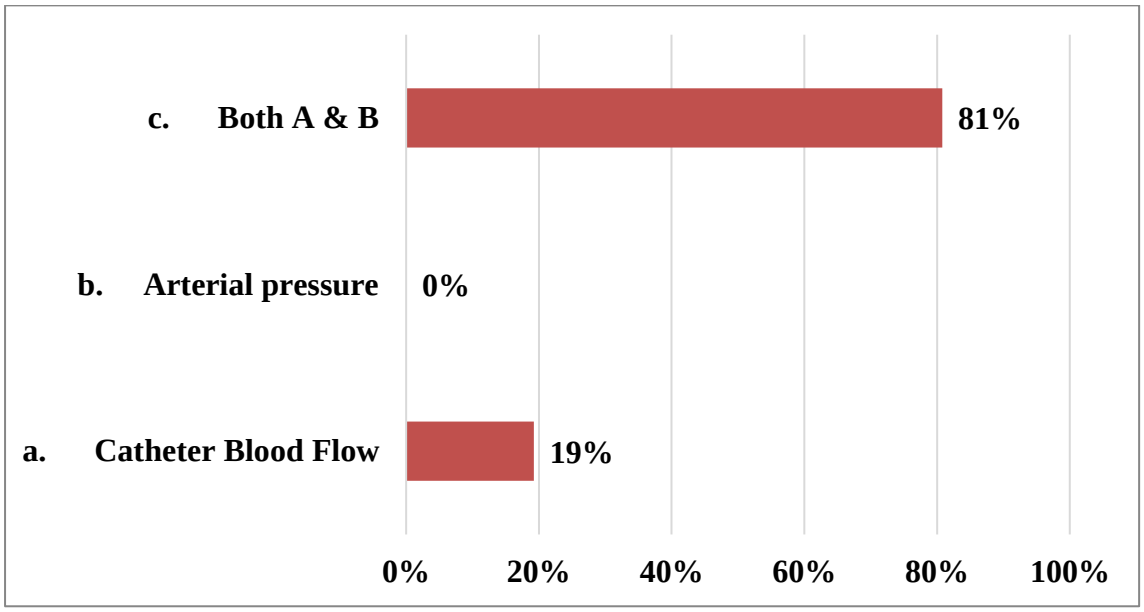
a. Efficacy
b. Availability
c. Cost
d. Safety



According to 50% of doctors consider efficacy an important parameter while choosing the thrombolytic agent in vascular access dysfunction.

10) What are the clinical parameters basis which you opt for thrombolytic agent in catheter dysfunction?

a. Catheter Blood Flow
b. Arterial pressure
c. Both A & B

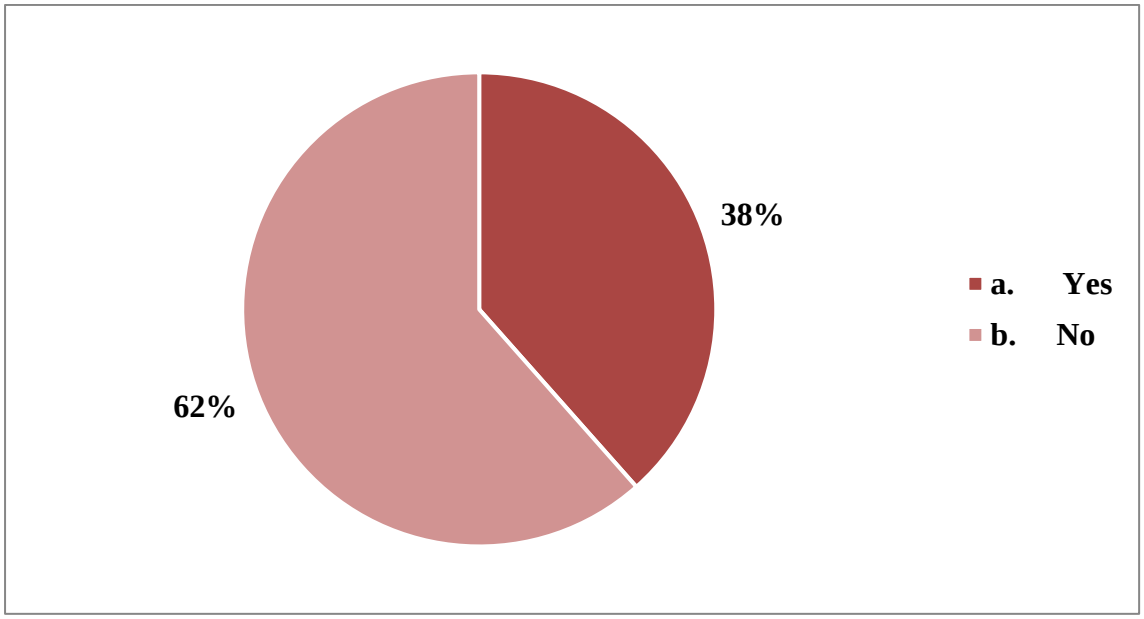


Majority of doctors, 81%, opt for the clinical parameters of Catheter Blood Flow and Arterial pressure for thrombolytic agent in catheter dysfunction.

11) Have you ever used tenecteplase in your patients having AV fistula dysfunction?

a. Yes

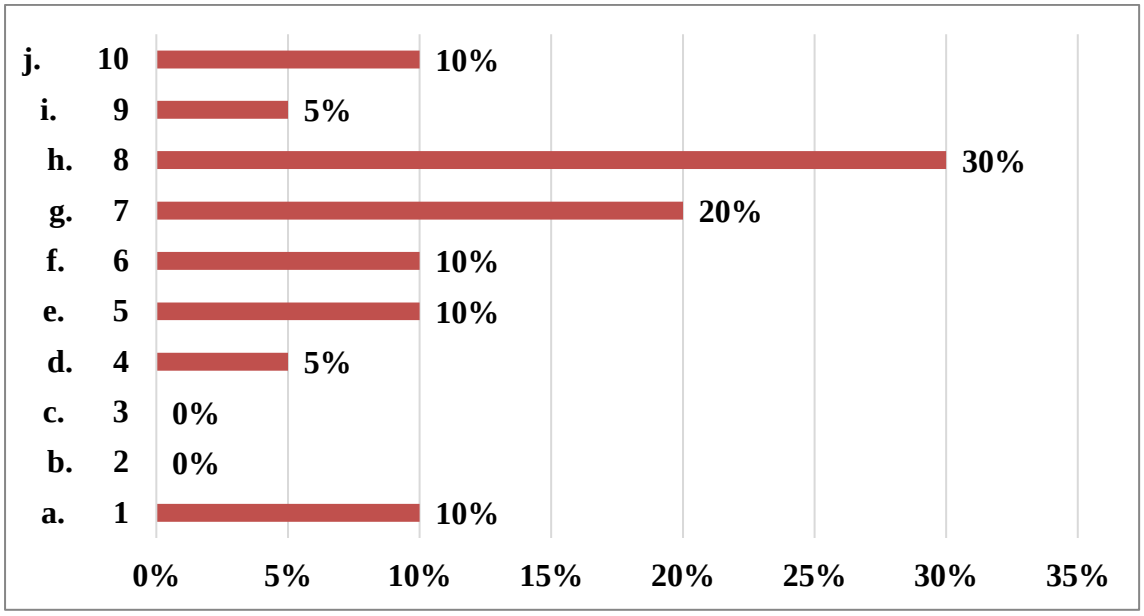
b. No



Majority of doctors, 62% have not used tenecteplase in their patients having AV fistula dysfunction.

12) If yes, how would you rate your experience using tenecteplase (in terms of safety and efficacy) on a scale of 1-10 (1 being worst, 10 being best) in AV fistula dysfunction?

a. 1
b. 2
c. 3
d. 4
e. 5
f. 6
g. 7
h. 8
i. 9
j. 10

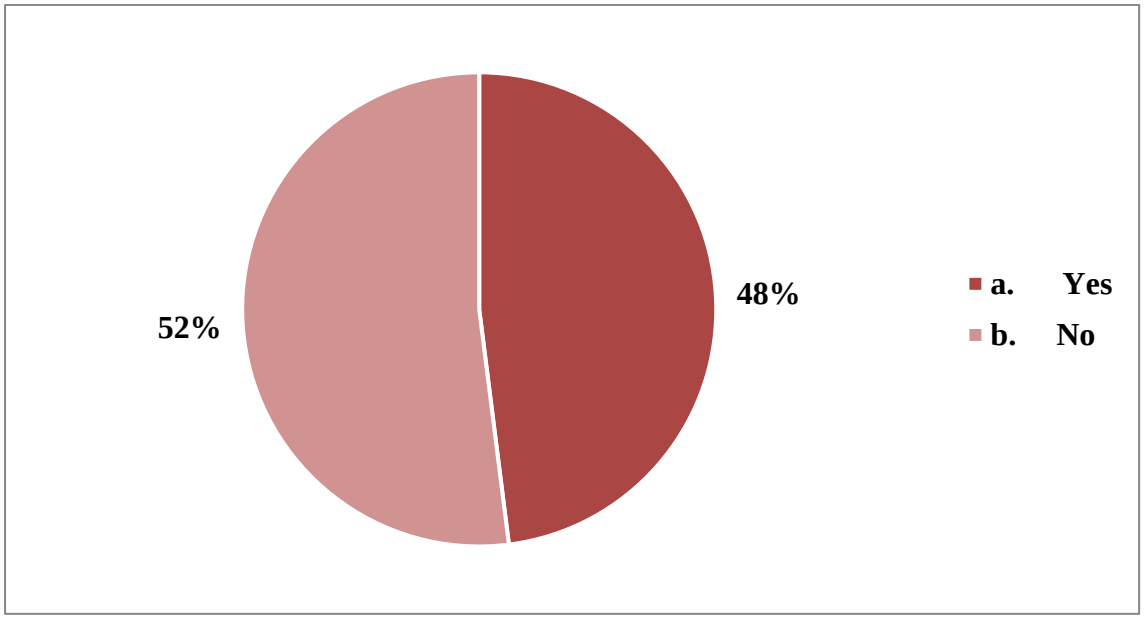


30% of doctors who have used Tenecteplase rate their experience using tenecteplase (in terms of safety and efficacy) on a scale of 1-10 (1 being worst, 10 being best) in AV fistula dysfunction as 8.

13) Have you ever used tenecteplase in your patients having catheter dysfunction?

a. Yes

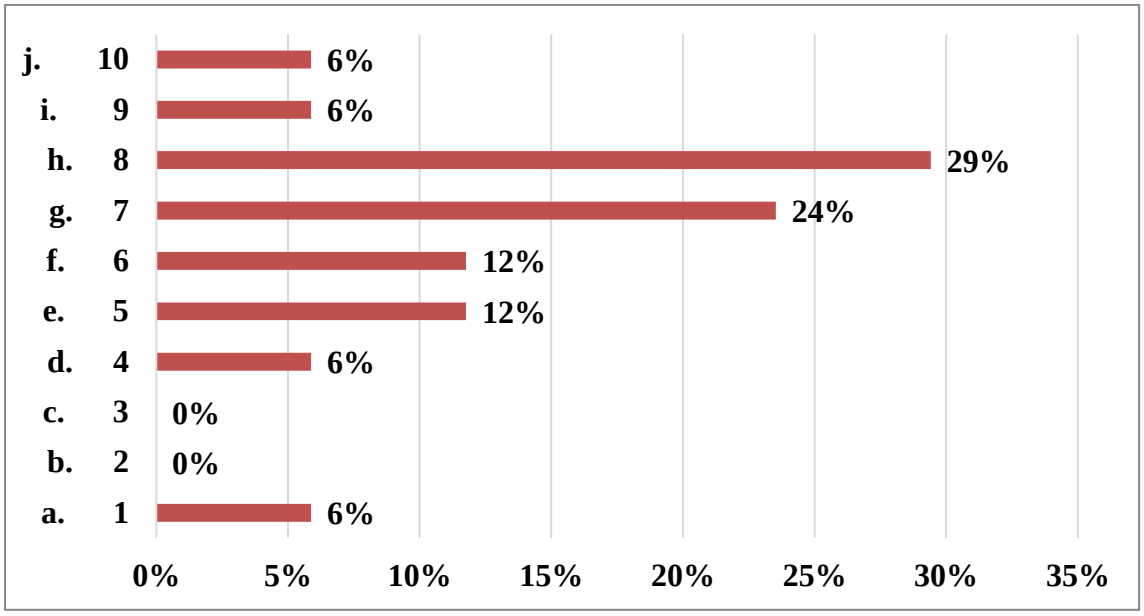
b. No



52% of doctors have never used tenecteplase in their patients having catheter dysfunction.

14) If yes, how would you rate your experience using tenecteplase (in terms of safety and efficacy) on a scale of 1-10 (1 being worst, 10 being best) in catheter dysfunction?

a. 1
b. 2
c. 3
d. 4
e. 5
f. 6
g. 7
h. 8
i. 9
j. 10

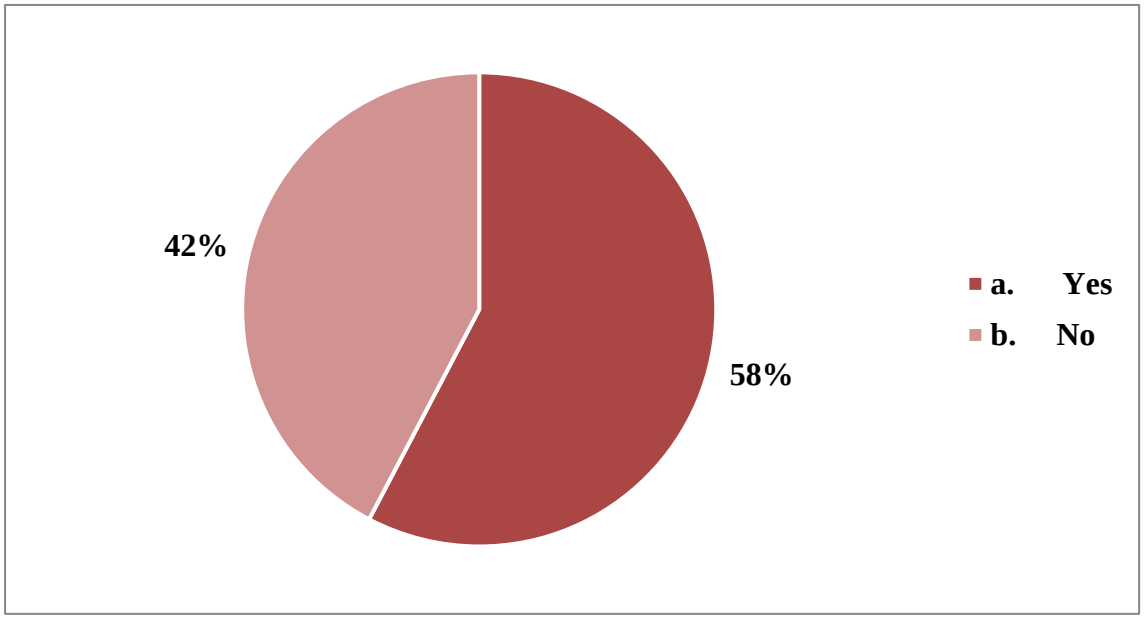


29% of doctors rate their experience using tenecteplase (in terms of safety and efficacy) on a scale of 1-10 as 8.

15) Do you experience availability issues with Urokianse in your region?

a. Yes

b. No



58% of doctors experience availability issues with Urokianse in their region.

Summary

- In the clinical experience of 35% of doctors, 21-30% of haemodialysis patients present with AV fistula dysfunction.
- According to 32% of doctors, 11-20% of haemodialysis patients present with catheter dysfunction.
- According to 65% of doctors, they manage patients presenting with AV fistula dysfunction by referring to vascular surgeon.
- According to 62% of doctors, out of ten patients presenting with AV fistula, they manage 2 patients with thrombolytic agent.
- According to majority of doctors, 85%, they have used thrombolytic drug in such patients with satisfactory efficacy.
- Majority of doctors, 88%, they manage patients presenting with Catheter dysfunction by using thrombolytic agent first and replace catheter in case of failure only.
- 65% of doctors prefer using thrombolytic agent both for prevention and treatments of thrombosis.
- According to 58% of doctors, their most preferred type of thrombolytic agent in haemodialysis patients having catheter dysfunction is Urokinase.
- According to 50% of doctors consider efficacy an important parameter while choosing the thrombolytic agent in vascular access dysfunction.
- Majority of doctors, 81%, opt for the clinical parameters of Catheter Blood Flow and Arterial pressure for thrombolytic agent in catheter dysfunction.
- Majority of doctors, 62% have not used tenecteplase in their patients having AV fistula dysfunction.
- 30% of doctors who have used Tenecteplase rate their experience using tenecteplase (in terms of safety and efficacy) on a scale of 1-10 (1 being worst, 10 being best) in AV fistula dysfunction as 8.
- 52% of doctors have never used tenecteplase in their patients having catheter dysfunction.
- 29% of doctors rate their experience using tenecteplase (in terms of safety and efficacy) on a scale of 1-10 as 8.
- 58% of doctors experience availability issues with Urokianse in their region.

Consultant Opinion

Based on the survey analysis regarding the management of AV fistula and catheter dysfunction in hemodialysis patients, here are some recommendations and opportunities for improving patient care and potential strategies for pharmaceutical companies:

Market Opportunities:
Recognize the high prevalence of AV fistula and catheter dysfunction in hemodialysis patients as an opportunity for pharmaceutical companies to develop and market specialized thrombolytic agents tailored to the needs of this patient population.

Value for Healthcare Professionals:
Provide healthcare professionals with comprehensive education and training on the management of AV fistula and catheter dysfunction, including the use of thrombolytic agents, referral criteria, and treatment algorithms.

Adverse Effect Management:
Conduct further research and development to minimize the occurrence of adverse effects associated with thrombolytic agents used in hemodialysis patients, ensuring safety and tolerability.

Withdrawal Management:
Develop guidelines and protocols for the appropriate use of thrombolytic agents in the management of AV fistula and catheter dysfunction, including dosing, administration routes, and monitoring parameters.

Market Positioning:
Position thrombolytic agents as essential components of the treatment armamentarium for AV fistula and catheter dysfunction, highlighting their efficacy in restoring vascular access patency and preventing thrombosis-related complications.

Personalized Treatment Decisions:
Encourage healthcare providers to individualize treatment decisions for hemodialysis patients based on factors such as the type of vascular access dysfunction, patient comorbidities, and response to thrombolytic therapy, ensuring tailored and optimized care.

Improving Patient Outcomes:

Collaborate with healthcare providers to optimize patient outcomes in hemodialysis by integrating thrombolytic therapy into comprehensive management strategies, aiming to reduce the incidence of access-related complications and improve long-term vascular access patency.

Innovation and Research:

Invest in ongoing research and development to explore novel thrombolytic agents with improved efficacy, safety, and pharmacokinetic profiles for the management of AV fistula and catheter dysfunction in hemodialysis patients.

By addressing these aspects, both healthcare professionals and pharmaceutical companies can work together to optimize the management of AV fistula and catheter dysfunction in hemodialysis patients, ultimately improving patient outcomes and enhancing the overall quality of care in this population.

NOTES

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Developed by:

Weston Medical Education Foundation of India

CTS-77, Shop No.11, Swapna Siddhi CHS LTD, Akurli Road Near Malad Sahakari Bank
Kandivali (E), Mumbai - 400101. M: 9322615653 I W: www.wmefi.co.in