REVIEW

Implanted vascular access device options: a focused review on safety and outcomes

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Implantable vascular access devices are frequently used in patients who have poor peripheral venous access. These devices can be partially implanted as tunneled and nontunneled central catheters, or they can be fully implanted as ports. Compared with long-term catheters, implanted ports have lower infection rates and improved perceptions of quality of life, but complications still occur in 2% to 18% of patients, frequently requiring removal of the device. Since the conception of implantable vascular access device ports, numerous advances in port design, materials, and techniques for implantation and care have been developed with the goal of overcoming frequent complications. We review the evidence related to these advances and their effect on the safety profile and complications of implantable vascular access device ports.

Since the first report of a fully implantable vascular access device (IVAD) in 1982,[1] the use of these devices has grown exponentially. They consist of a reservoir cradled in the subcutaneous tissue that is connected to a catheter, with its tip terminating into a major vein. IVADs are frequently used in patients who have poor peripheral venous access and are in need of long-term administration of vesicant drugs, antimicrobials,

blood products, or parenteral nutrition.[2,3] They also are used as access for long-term therapeutic apheresis procedures.[4] Although nonimplanted, long-term catheters can be used for all of these purposes as well, the lack of an external component in IVAD ports provides multiple advantages; patients have improved perceptions of quality of life and body image and less limitation in their mobility.[5] These ports also minimize the need for maintenance care and risk of infectious complications when the IVAD is not in use.[6] These benefits of IVAD port use have also been demonstrated in pediatric cancer patients, with the added advantage of allowing the child to participate in normal activities and preserving body image.[7]

Despite the vast experience accrued over the years and the large volume of literature studying factors associated with IVAD port outcomes, early perioperative and late postoperative complications still occur (see Table 1).[8,9] Overall complication rates for IVAD ports reportedly occur in the range from 2% to 18% of all implanted devices.[10-12]

Port-related infections and venous thrombosis are particularly important, because they are associated with additional morbidity and costs and require removal of the IVAD as part of their treatment in as many as 6.5% of patients.[10] An additional complication specific to the use of IVAD ports during therapeutic apheresis is the occurrence of frequent pressure-related alarms,[13-15] which do not always result in a need to abort the procedure but can delay the duration of the treatments and require additional interventions.[13]

Here, we present a review focused on techniques, materials, and long-term management options of ports as IVAD options that have an impact on the relevant complications and overall safety profile of these devices. We also summarize the principles for the early management of some common port-related complications. Table 2 details the features of commonly used IVAD ports.

DEVICE DESIGN

In classic, open-ended IVADs, the port reservoir and catheter exist in a continuum, with no interruption to the flow of blood. The negative pressure generated during

TABLE 1. IVAD port-related complications		
Variable	Early complications	Late complications
Incidence	3.1%-18.2%[8,10]	5.4%-33.7%[6,8,10]
Cause	Due to mechanical issues related to device implantation[10]	Due to continued use and maintenance of the device[10]
Risk factors[3,7,10]	Prior catheterization attempts at the site, need for multiple needle passages during insertion, changes in the area of insertion due to radiation, BMI below 20 or above 30 kg/m^2	Initiation of chemotherapy before device implant, head and neck cancers; surgical isolation; BMI below 20 or above 30 kg/m^2
Median time to event[10]	1-30 days	20-30 weeks, infection; 60 weeks, catheter-related venous thrombosis
Common complications[6,8,10]	Pocket hematoma, cardiac arrhythmias, arterial puncture, bleeding, primary technique failure	IVAD-related infection, catheter-related venous thrombosis, catheter occlusion
Uncommon complications[6,8,10]	Sheath kinking, early pocket infection, hemothorax, pneumothorax	Catheter rupture and migration, pinch-off syndrome, catheter encrustation, erosion, extravasation

BMI = body mass index

withdrawal of the access needle promotes the influx of a blood column of up to 5 mm into the catheter tip. This can then clot, resulting in an inability to withdraw blood. The purpose of valved catheters is to minimize this unintentional "back flow" of blood into the system while still allowing either flow during aspiration with negative pressure or forward flow with positive pressure.[16] Multiple randomized trials have looked at comparisons between valved and nonvalved catheters, and all agree that there is a lack of difference in the incidence of infection or venous thrombosis with either system[16-19] but that outcomes differ in terms of clotting and withdrawal failure, which is defined as the inability to draw blood from the device under negative pressure. A 2001 trial by Biffi and colleagues evaluated titanium ports connected to Groshong catheters versus regular open-ended catheters. A Groshong catheter has a closed, rounded tip with three position valves, which allow fluids to flow in or out in response to positive or negative pressure but remain closed when not in use. The study reported a significantly higher rate of withdrawal difficulties with the valved Groshong catheter versus the open-ended catheter (12.5 vs. 2%; p < 0.001).[18] In another study, Carlo and coworkers compared IVADs with a pressure-activated safety valve at the reservoir and catheter junction with open-ended IVADs and reported more withdrawal failures with the open-ended port (11 vs. 5.8%; p = 0.02).[17] In 2014, a study done with Groshong catheters with standardized insertion technique and catheter sizes again demonstrated higher rates of withdrawal failure in the valved catheters (24 vs. 0%; p < 0.001).[16] Based on the available data, Groshong valved catheters do not appear to provide an advantage in terms of clotting or occlusion and have no significant differences in terms of other major complications, such as infection or thrombosis, compared with their nonvalved counterparts. Pressure-activated safety valves, which are direction-specific valves placed proximally rather than distally in

the catheter, may provide some advantage in terms of clotting and access; however, there is no evidence that these valves will affect the incidence of other complications, and they may require an additional upfront cost.

An advance in design is evident in power-injectable devices, which allow the injection of high-pressure volumes and can be used to perform contrasted imaging studies with a low risk of mechanical failure or catheter rupture. These catheters are generally not compatible with apheresis procedures or hemodialysis. Currently, there are minimal data in the English literature comparing outcomes with power-injectable versus regular implanted devices.

IVAD ports with particular design features that are commonly used for long-term apheresis are the Vortex port (Angiodynamics) and the Sport/Tidal port (Norfolk Medical). The Vortex has a rounded chamber with no corners or dead spaces and tangential outlets to minimize sludging, occlusions, and infection. These are available as titanium and plastic bodies with large septae, as silicone or polyurethane catheters, and as single or double lumen devices. The SportPort has a titanium or polysulfone chamber with silicone septum and spherical chamber design for lower sludging and infection risk. It has high-pressure capabilities and a septum retainer that maintains the septum in place during high-pressure use.

A major design development in April of 2017 was the US Food and Drug Administration approval of the first long-term apheresis-specific port, the PowerFlow (BARD Peripheral Vascular, Inc.). Although IVADs have been used for apheresis access since the 1990s,[20] there were frequent concerns about their long-term durability (due to potential damage of the septum with frequent access) and with the ability to reach the optimal flows and pressures needed for the apheresis procedure.[4] The PowerFlow design tries to overcome these issues and is based on the CathLink 20, a catheter initially marketed for

TABLE 2. Features of commonly used IVADs*

Device	Mfr	Power injectable	Profile†	Body material‡	Body shape§	Catheter material‡	Catheter size, Fr	Lumen	Notable features
PowerPort	Bard	Yes	F	T	Tr	P or S	P, 8; S, 9.6	Si	Option of attachable 8-Fr Groshong catheter
PowerPort VUE	Bard	Yes	F	S/T	Tr	P	6, 8	Si	
PowerPort ISP	Bard	Yes	F	T	Tr	P	6, 8	Si	Compact size, cosmetically appealing, palpation bumps for easy location; option for attachable Groshong
PowerPort slim	Bard	Yes	F	T	Tr	P	6, 8	Si	Smallest port available, good for small or petite patients; option for attachable Groshong; placement in the arm optional
PowerPort VUE MRI	Bard	Yes	F	S	Tr	P	6, 8	D	Enables suture placement around 94% of the perimeter with lower risk for dislodgement, exceptional CT marker visibility
PowerPort MRI	Bard	Yes	F	PI	Tr	P, S	P, 8; S, 9.6	Si	Option for attachable Groshong catheter, radiotranslucent
PowerPort Duo MRI	Bard	Yes	F	PI	JR	P	9.5	D	Radiotranslucent with radiopaque ring, reduced imaging artifact, large size
X-Port	Bard	No	L	T	R, Ta	P	NA	Si	Designed for arm placement with tapered body and small size, can be used for chest implant in small patients
X-Port Duo	Bard	No	F	PI	JR, Ta	P	9.5	D	Intermediate size, attachable Hickman and Groshong catheters
X-Port Inline	Bard	No	F	PI	Ca	P	9.5	D	Needs narrow pocket
X-Port ISP	Bard	No	F	PI	R, Ta	P	6, 8	Si	MRI-compatible, option of attachable 9.6-Fr Hickman or 8-Fr Groshong catheters
Slimport Dual Lumen Rosenblatt	Bard	No	L	PI	Ca	S	7	D	High-compression silicone septum with increased durability, inline design needs small incision and pocket, ideal for peripheral placement
M.R.I.	Bard	No	F	PI	R	NA	NA	Si	Radiotranslucent; ideal for MRI or radiation therapy; silicone encapsuled
M.R.I. Dual Lumen	Bard	No	I	PI	Ca	S	10, 12	D	Radiotranslucent, attachable Groshong available
M.R.I. Hard Base	Bard	No	F	PI	R	P or S	P: 8; S: 6.6, 9.6	Si	Radiotranslucent, lightweight, option for 8-Fr attachable Groshong
M.R.I. Low Profile	Bard	No	L	PI	R	NA	NA	Si	Radiotranslucent, low-profile ideal for cachectic patients
PowerFlow‖	Bard	Yes	F	T/S	F	P	9.6	Si	Catheter inner diameter approximately 2 mm; funnel accessed through a 14-G or 16-G catheter via introducer needle; high flows with adequate pressures for apheresis
Xcela Plus	Angio Dynamics	Yes	F	PI or T	R	NA	6, 8	Si	Titanium port has options with and without proximal pressure-activated valve (PASV)
BioFlo	Angio Dynamics	Yes	F	PI or T	R	P	6, 8	Si	Polyurethane catheter coated with polymer to reduce thrombogenicity; titanium port has options with and without PASV
Smart Ports	Angio Dynamics	Yes	F, L, M	T	R, Ta	P or S	7.5, 8, 9.6	Si	Round chamber with tangential outlet for flushing chamber action (vortex chamber); low-profile and mini Smart Port only available with 6.6-Fr polyurethane catheters
Vortex Ports‖	Angio Dynamics	No	F, L	PI or T	R	P or S	5, 6.6, 7.2, 7.5 8.4, 9.6 11.4	Si or D	Round chamber with tangential outlet for flushing chamber action (vortex chamber) minimizes buildup; MRI safe for plastic and conditional for

Table 2: *Continued*

Device	Mfr	Power injectable	Profile†	Body material‡	Body shape§	Catheter material‡	Catheter size, Fr	Lumen	Notable features
LifePort	Angio Dynamics	No	F, L	PI or T	R	P or S	5.7, 6.6, 8.4, 9.6, 11.4	Si or D	titanium models; large septum; options for peripheral and chest placement; average apheresis flow of 60 mL/min through 9.6-Fr catheter and 16-G needle
SportPort‖	Norfolk Medical	Yes	F	T or PI	Sph	P	9	Si	Average apheresis flow of 70 mL/min through 9-Fr catheter and 16-G needle
Polysite port series	Peruse Medical	Yes	F, L, Mi	T/PI	T base, R top	P or S	5, 6, 6.9, 8.9	Si	Designed for percutaneous approach insertion; MRI compatible; sizes shown are for polyurethane catheters; silicone catheters sizes are 5, 6.5, 7.2, and 9.5 Fr
Arrow Polysite port	Teleflex	Yes	L	T/PI	T base, R top	P	6, 7, 8	Si	MRI conditional at 1.5 and 3 Tesla (3T)
Celsite ports	Braun Interventional Systems	Yes/no	F, L	T/PI, T/epoxy	De	P or S	6.5, 8.5	Si or D	Baby port option for pediatric use with 4.5-Fr polyurethane or 6-Fr silicone catheter; also options for brachial insertion and valved catheters
Port-a-Cath II Power PAC	Smiths Medical	Yes	F, L	T/PI	R, Ta	P	6, 7, 8.5, 10	Si or D	MRI conditional up to 3T; radiopaque CT markings
Port-a-Cath Power PAC	Smiths Medical	Yes	F, L	T	R, Ta	P	6, 8.5	Si	Option of PAS port T2 power Port-a-Cath (PAC) for peripheral insertion
Chemosite	Medtronic	NA	L	L	H base, R top	S	9	Si	MRI compatible to 3T
TitaJet	PFM Medical	Yes	L	T/PI	T base, R top	P	4.8, 6.6	Si	Option for peripheral insertion; can be used in smaller patients; CT identifiable; MRI conditional
Dual-Port	PFM Medical	Yes	L	T/PI	JR	P	9	D	MRI conditional up to 3T; radiopaque; low-profile option can be used for peripheral insertion
Jetport Plus	PFM Medical	Yes/no	F, L	PI	R	P	6.6, 8	Si	MRI conditional up to 3T; radiopaque; low-profile option can be used for peripheral insertion
Portolino	PFM Medical	No	L	PI	TD	P or S	4.8	Si	Nonpower-injectable option also available
Tport contrast	PFM Medical	Yes	F, L	T	R-Ta	P	6, 8	Si	Contrivance locking mechanism; CT finder
Dignity CT port‖	Medcomp	Yes	I, L, Ped	PI	Do	P	5, 6.6, 8, 9.6	Si	Alternative for chest and arm placement
Dignity Mini	Medcomp	Yes	L, Ped	PI	Do	P	5, 6.6, 8	Si	Contrivance locking mechanism; CT finder
Dignity Titanium	Medcomp	Yes	I, L, M	T	Do	P or S	5, 6.6, 8, 9.6	Si	Contrivance locking mechanism
Pro-Fuse CT Port	Medcomp	Yes	F, L	PI	R flat base	P or S	5, 6.6, 8; 9.6	Si	Option with PASV valve technology available
Vaxcel	Navilyst	No	F, M	T or PI	R	P or S	NA	Si or D	Dual lumen available with 9.6-Fr catheter; radiopaque lettering
Xcela power injectable	Navilyst	Yes	NA	PI, T/PI, T	R	P	6.6, 8	Si or D	
Invisiport	Stealth Therapeutics	Yes	L	T/PI	B	P	6	Si	Self-deploying wing allows for small incision with adequate stability of implantation

* Information presented in this table is as provided by the manufacturers' product pages.
† Profiles: F, full profile; I, intermediate profile; L, low profile; M, mini-device; Mi, micro-device; Ped, pediatric.
‡ Materials: T, titanium; S, silicone; P, polyurethane; PI, plastic.
§ Shapes: Tr, triangular; JR, double round; R, round; Ta, tapered; Ca, capsule shape; Sph, spherical; H, hexagonal; TD, teardrop; Do, dome with concave sides; B, bullet shaped; F, funnel shaped.
‖ These devices are reported in the literature for use in therapeutic apheresis. Only the PowerFlow has been approved by the US Food and Drug Administration for this indication.
Mfr = manufacturer; NA = not available, Si = single lumen; MRI = magnetic resonance imaging; D = dual lumen; PAS = peripheral access system.

chemotherapy and hypernutrition administration but used later for apheresis in both adults and children.[14,21] The PowerFlow consists of a titanium funnel with a silicone body attached to a 9.6-French (Fr), biodurable polyurethane catheter. An over-the-needle 14-gauge (14-G) or 16-G catheter can be introduced percutaneously at a 30-degree angle through the funnel until it reaches a needle stop beyond which the introducer cannot easily be further advanced (i.e., with excessive force, smaller gauge catheters can extend beyond the acceptable seating position, which may potentially cause damage to the device). The flexible catheter can then be passed through a silicone septum, forming a seal around the catheter tip. According to the manufacturer's specifications, the PowerFlow is bench tested to endure upwards of 1000 insertions and has flow capabilities of up to 150 mL/min at low system pressure.

There are no clinical studies reporting the performance and limitations of the PowerFlow port, but retrospective studies with the CathLink 20 using an 8-Fr polyurethane catheter component had median times of port use of 36 to 45 months and adequate flows throughout the apheresis procedures with average times of 118.4 to 120.7 minutes.[14,21]

CATHETER MATERIALS

Indwelling vascular catheters are typically made of artificial elastic or polymeric materials, such as polyethylene, polyvinylchloride, Teflon, silicone, or polyurethane. For implanted ports, the more commonly used materials currently are polyurethane and silicone. A major concern with the materials used for catheters is whether they have degradation of their surface that could result in increased thrombogenicity or infection risk due to biofilm formation. A study looking at the mechanical and surface properties of silicone and polyurethane demonstrated that, even when exposed to short-term and long-term submersion in chemotherapeutic solutions, these two materials showed no significant surface degradation.[22] However, with time, both materials developed surface irregularities as a result of lost barium sulfate molecules, which are embedded in the polymer for the purpose of making the catheters radiopaque. This inhomogeneity of the surface can act as a predetermined fracture point and was significantly more pronounced in silicone catheters compared with polyurethane catheters.

A clinical study comparing polyurethane versus silicone catheters in ports implanted in the forearm showed higher rates of catheter-related bloodstream infection (hazard ratio, 3.7; 95% confidence interval, 1.3-10) and catheter lumen thrombosis (hazard ratio, 22.8; 95% confidence interval 8.4-62.2) with polyurethane catheters when directly compared with silicone catheters.[23] There were no differences in the rates of thrombophlebitis or thrombosis of the vein where the catheter was inserted. In agreement with the material data, that clinical study had a significantly higher rate of mechanical failures with silicone catheters over polyurethane catheters (2.6% vs. 0.3%; p = 0.02). The overall complication rate was 46.2% for polyurethane catheters versus 9.3% for silicone catheters (p < 0.0001). Polyurethane catheters also required removal of the device to manage catheter-related complications in 10.6% of cases compared with only 4.6% in silicone catheters. Although studies in IVADs implanted in the arm theoretically may overestimate the risk of mechanical failure due to a longer catheter course and more tensile stress points, the lower risk of infection, occlusion, and need for catheter removal with silicone catheters outweighs the risk of fracture and mechanical complications, making this material generally preferred over polyurethane. A possible exception to this may be in the use of IVADs for apheresis procedures. Although there is no literature available that directly compares silicone versus polyurethane catheters in these circumstances, many published series describe the use of predominantly polyurethane catheters based on the need for the catheters to withstand higher pressures with less risk of collapse or mechanical failure.

SURGICAL ANTIMICROBIAL PROPHYLAXIS

Recommendations against antimicrobial prophylaxis for nonimplantable catheters are widely accepted, and more weight is placed on the use of "bundles" to decrease catheter-related infections than on the use of prophylactic antimicrobials.[24] Bundles are checklists of evidence–based measures that are proven to reduce central line–associated infections and include practices like adequate hand hygiene and the use of aseptic techniques with maximal barrier precautions before insertion, skin preparation with chlorhexidine/alcohol solution, and the use of proper dressings. Despite the lack of formal guidelines recommending the use of preoperative prophylactic antimicrobials for port implantation, a 2013 survey by the American College of Surgery Fellows revealed that 88.2% of respondents routinely used antimicrobial prophylaxis in this setting.[25] A meta-analysis of 2154 patients investigated at infections related to the port within 30 days of implantation and found that, for patients who did not receive prophylactic antibiotics, the incidence of infection was 1.6% versus 1.1% in those who did receive prophylaxis.[26] With such a low rate of events at baseline and the potential implications associated with receipt of antimicrobials, promotion of resistance, alteration of the microbiome, allergic reactions, and other adverse events, the practice of antimicrobial prophylaxis seems unwarranted until adequately powered randomized studies can support it as a beneficial and safe practice.

IMPLANTATION TECHNIQUE AND SITE

IVAD port insertion options include the surgical technique (ST) with venous cut down[1] and the percutaneous technique (PT) via a Seldinger approach.[27] ST is commonly performed through the cephalic vein with use of anatomic landmarks, although other veins can be used.[28] PT is done using the internal jugular, subclavian, or cephalic veins.[12] Because of shorter implantation times and the lack of need for an operative suite,[2,12] PT has become a commonly used approach.

In the early port literature, PT reportedly had higher rates of pneumothorax and hemothorax, arterial punctures, and arrhythmias compared with ST.[12] With the introduction of ultrasound use for real-time guidance of the puncture in PT, the rate of these complications was decreased from 18.7% to only 1.5% in one study.[12] The use of ultrasound guidance is now advocated in PT over fluoroscopic or blind techniques given the reduction in complications and lack of radiation exposure.[2,29]

The main early complication with ST relates to primary failure of access, and there is virtually no incidence of pneumothorax or hemothorax.[12] The use of a modified Seldinger technique as second line for salvage after primary failure of ST improves the success rate from 80.5% to 93.9%.[30]

ST is a major predictor of complications that require removal of the IVAD.[12] However, multiple studies,[2,31] including a recent meta-analysis of 1006 patients, demonstrated no difference in the overall rate of complications (including hemothorax, pneumothorax, infection, catheter thrombosis, stenosis, kinking or extravasation, migration of the catheter or dislodging of the port reservoir, hematoma, seroma, nerve palsy, thoracic duct injury, and death) or, in particular, in the rates of infection with either technique. It is worth noting that, when the analysis was limited to a subclavian site for the PT group, there was a higher rate of catheter-related complications (thrombosis, fibrin sheath, stenosis, kinking, extravasation, migration of the catheter, or dislodgement of the reservoir) compared with ST.[32]

The decision of which technique to choose ultimately may depend on the presence of risk factors that make the patient prone to particular complications associated with a technique. In patients with severe dehydration, neutropenia, prior radiation to the area, and other factors that may increase the primary failure rate, preference should be for the use of PT with ultrasound guidance via the internal jugular or cephalic route (over the subclavian route) to minimize failure and pneumothorax incidence. The ST may be preferable in patients who have limitations to a percutaneous approach, such as obesity, scars or prior surgery at the insertion site, skeletal deformities, and lymphedema.

CATHETER MAINTENANCE

Catheter access

An important factor related to the prevention of complications in the use of vascular devices is the proper training of personnel in device maintenance and care. Knowledge and recognition of complications by health care personnel helps ensure adherence to established infection prevention protocols. The Centers for Disease Control and Prevention has issued evidence-based guidelines with a focus on intravascular catheter insertion and management to minimize catheter-related infections.[24] The following are recommendations pertaining to the maintenance of IVADs: hand hygiene with conventional soap and water or with alcohol-based hand rubs is a highly rated recommendation before palpating, accessing, or dressing an IVAD. Sterile gloves and mask should be used during access of IVADs as the equivalent for the recommended maximal barrier precautions used during the exchange or insertion of other vascular devices. The skin at the site of access must be disinfected with chlorhexidine solution or 70% alcohol and allowed to dry before access.[24] The use of noncoring needles for access of IVAD ports is recommended to prevent damage to the septum and other complications, such as plastic emboli or blood extravasation.[33,34] There are no clear recommendations regarding the length of time a needle can remain in place after access of the port or on the frequency of needle-replacement needs.

The dressings should be replaced once a week (for transparent dressings), every 2 days (for gauze dressings), or at a shorter interval if dressings are damp, soiled, or loose. There are also recommendations for the use of sterile, transparent, semipermeable dressings to cover the catheter site. Topical antibiotics at the access site are not recommended as an infection-prevention measure. The access site should be closely monitored for any signs of infection or inflammation.[24]

Catheter flushing and locking

All long-term vascular access devices are vulnerable to the formation of a protein biofilm in the internal surface of the device due to the interaction of biologic proteins with the polymeric surface of the device. These protein deposits are likely major contributors in catheter occlusion. Flushing and locking of catheters are the techniques utilized for the prevention of this complication.

Despite the existence of societal guidelines for the care of infusion devices, there are no clear recommendations for standardized flushing techniques or volumes, and these are usually determined by local practice patterns.[35] A 2012 study done in France utilized an ex vivo model of IVAD ports in which the internal surface of the catheter was coated with fibronectin and bovine albumin to emulate biologic protein film formation. The study then compared the effectiveness of single and multiple boluses

given at different time intervals, as well as continuous infusion of saline solution over time, for the removal of the protein film. The method that resulted in the recovery of approximately 90% of the protein film was a pulsed flush of a total of 10 mL saline delivered as 1-mL boluses over 0.5 seconds with an interval between boluses of 0.4 seconds. This technique resulted in turbulent flow of the saline (Reynolds number, >1000), and the results also indicated that this was favorable for the removal of adhered proteins. The use of other time intervals for bolus administration or as the interval between boluses resulted in significantly lower protein recovery. None of the catheters suffered rupture with this technique. Continuous infusion never achieves Reynolds numbers consistent with turbulent flow but, if continued over 18 to 24 hours, is capable of recovering from 70% to 77% of the bound protein. Although this was not an in vivo study, it is likely that the demonstrated interactions between volume, flow, and surface adhesion still apply in a clinical setting. Additional clinical studies using these parameters are needed, but these currently constitute the best quality evidence on flushing volume and technique.

To minimize the attachment of administered substances or blood to the internal surface of the catheter or to residual fibrin, a common recommended practice is to initially flush with normal saline, followed by the administration of drug or blood, and then finish with an additional normal saline flush (SAS acronym [saline, administration, saline]).[36]

In terms of the ideal solution for flushing IVADs, recommendations from the manufacturers for heparin or normal saline vary with catheter type. Although heparin is effective at preventing occlusions, there are concerns with its use as well as potential adverse events.[37] A survey done in intensive care unit nurses investigating flushing practices demonstrated high heterogeneity in the preferential solution used.[38] Two noninferiority randomized controlled trials compared normal saline versus heparin for the outcomes of withdrawal occlusion and total occlusion of the catheter lumen.[39,40] In a 2013 study by Goossens and colleagues, 802 patients were randomized to flushing with either saline or heparin. Devices were flushed before and after blood sampling; at the end of intravenous therapy, blood transfusions, or total parenteral nutrition; and every 8 weeks when the device was not in use. Those investigators reported rates of withdrawal occlusion for saline and heparin of 3.70% and 3.92%, respectively, with a relative risk of 0.94 and a 95% confidence interval that remained within the noninferiority margin set at 1.4. The authors concluded that normal saline was a safe and effective locking solution. No differences in the incidence of infectious complications were noted.[39] Although a 2015 study by Dal Molin and coworkers also had similar rates of occlusion in both groups (4.71% vs. 7.39% for heparin and saline, respectively), they were unable to demonstrate

noninferiority, likely due to the lack of power.[40] Some guidelines for the management of catheters in patients with cancer now endorse the use of saline as the main flushing solution over the use of anticoagulants.[41]

Current recommendations for implanted ports that are used a minimum of every 8 hours in adult patients are to flush after each drug or blood administration with 10 mL normal saline, or every 24 hours, or according to the manufacturer's recommendations.[42]

Locking is the injection of a small volume of fluid into the IVAD, which will be allowed to dwell in it for the time the catheter is not in use to prevent intraluminal clots, deposition of debris, and colonization of the catheter. The technique for locking seems to be used more uniformly and consists of withdrawal of the syringe while still applying positive pressure during the injection of the last 0.5 mL of volume. The volume used for locking will depend on the reservoir volume and catheter diameters, but average volumes approximate 2.5 mL.[36] In ports that are not actively in use, the frequency of locking/flushing recommended in the early IVAD literature was a maximum of 4 weeks. Currently, flushing/locking intervals of up to 6, 8, or even 12 weeks have been demonstrated to be safe with no significant increase in the rates of infection, occlusion, or thrombosis.[36,43,44] Formal recommendations for maintenance locking in implanted ports are to flush with 10 mL normal saline every 4 weeks in closed ports. For open implanted ports, the recommendation is to flush with 10 mL normal saline followed by 5 mL heparin every 4 weeks.[42]

PATIENT EDUCATION

Patients have an important role in ensuring adequate care of their devices. Activities performed by patients as part of their daily routine not directly linked to usual port access, such as showering or sleeping, may require additional patient instruction. Educational materials on what can or cannot be done may reduce patient anxiety and improve satisfaction. In a 2014 survey of 47 patients at a specialized cancer center, seven of 20 respondents reported never receiving education on home management of their device, and 29% of 44 respondents did not know which symptoms would be concerning for an infection in the device. Interestingly, patients were closely observant of the protocols followed by health care personnel and were able to actively correct mistakes, such as missed flushes, short cleaning times, etc.[45]

MANAGEMENT OF COMMON COMPLICATIONS

Complications related to the use of IVADs during therapeutic apheresis

Although complications observed with the general use of IVADs still apply to IVAD use in apheresis, there are

procedure-specific complications in this setting, such as pressure-related alarms and concerns with device durability due to frequent access.[14] Although the literature on apheresis-related port complications is scant, the overall complication rates appear to be significantly greater in children when compared with adults, but the types of complications reported are similar.[14,15,46] Michon and colleagues, in a study that included 186 patients who underwent a total of 1632 apheresis procedures via central catheters, noted pressure-related problems/alarms at a rate of 8% per apheresis procedure, circuit clots at a rate of 3.9% per apheresis procedure, and obstruction of the access requiring thrombolytic therapy at a rate of 6.1% per apheresis procedure. Other complications included catheter-related infection (2.1%), hematomas or bleeding after access (1.7%), thrombosis (1.7%), and air in the circuit (0.2%).[46] Although there have been no formal trials comparing complication rates in external catheters versus ports, a retrospective series by Chand and coworkers of 246 apheresis sessions in eight children reported pressure-related alarms in 16% of procedures (although all went on to be technically successful) and access difficulties in only 3% of procedures. For the management of pressure-related alarms during apheresis, recommended interventions include instillation of a tissue plasminogen activator into the IVAD before initiating the apheresis procedure,[13-15] saline flushing, needle repositioning, or reversal of needle advancement.[13] No reports of increased bleeding risk or hematoma were noted with the use of a tissue plasminogen activator for this purpose.[14]

The diagnosis and management of other early and late complications related to IVAD ports used for access in apheresis patients do not differ significantly from those of IVADs used for other purposes and are discussed below.

IVAD-related infection

Although infection is a major complication of all IVAD types, the risks vary widely, depending on the type of device utilized. In a 2006 systematic review, Maki and colleagues reported higher infection rates per 1000 device days with short-term, noncuffed, nontunneled catheters (2.7/1000 device days) compared with tunneled catheters (1.6/1000 device days and 1.7/1000 device days for cuffed and noncuffed catheters, respectively) or implantable ports (0.1/1000 device days with either peripheral or central subtypes).[47] Despite the significantly lower rates of infection with implanted ports, infection is still a major cause for premature port removal. Sets of evidence-based recommendations from the Centers for Disease Control and Prevention for the prevention of catheter-related infections have been proven to be highly efficacious in reducing the incidence of this complication and are applied universally in hospital settings (see detailed recommendations above in the "Catheter Maintenance"

section).[24] Specific situations that increase the risk of port-related infections include high frequency of access of the device, use of total parenteral nutrition, multiple punctures required at the time of port insertion, hematologic malignancy, and neutropenia.[48]

Infections related to ports can be local (access site, tunnel, or pocket) or systemic, with associated bloodstream infection.[49] Local infection of the port should be suspected if there is erythema, pain, induration, erosion, exudates, or purulence at the access site or around the pocket area. In the case of bloodstream infections, patients may or may not have local symptoms in addition to systemic symptoms, such as isolated fever, chills, or findings suggestive of severe sepsis.[48] For either of these presentations, it is necessary to obtain adequately collected, paired blood cultures from a peripheral site and the IVAD before the administration of antimicrobials.[49] For the confirmation of local infection, cultures can be obtained from the exudate at the access or pocket sites or from aseptically removed material related to the device, such as a port aspirate or culture of the IVAD hardware. Local infections with abscess or erosion of the site invariably require removal of the device and short-term antimicrobials for 7 to 10 days if there is no bloodstream infection.

IVAD-related bloodstream infection can be confirmed by differential time to positivity between the periphery and device samples or by quantitative criteria. After obtaining blood cultures, empiric antimicrobial therapy can be instituted. The first-line agent for the coverage of Gram-positive organisms is vancomycin. In neutropenic cancer patients and critically ill patients, coverage for Gram-negative organisms should be added, and consideration should be given to covering Candida infections. The final antimicrobial selection for treatment should be guided by the identified organism and reported susceptibilities.

Whenever bloodstream infection is diagnosed, a detailed patient history and examination are necessary to exclude the presence of symptoms or findings suggestive of metastatic infection (endocarditis, septic thrombophlebitis, and osteomyelitis). Their presence and the causative organism of the infection will largely determine the need for device removal and the duration of antimicrobial therapy. In patients with metastatic infection, bacteremia or fever that persists over 72 hours on antimicrobials, and *Staphylococcus aureus* or Candida species infection, removal of the device is required, and the duration of antimicrobial treatment extends to periods of 4 to 6 weeks or longer. Consultation with an infectious diseases specialist and evaluation with echocardiography are highly suggested for the management of *Staphylococcus aureus* infections.[50] For uncomplicated bloodstream infections with coagulase-negative staphylococci, enterococcus, and certain Gram-negative species, device retention with

short-term, systemic antimicrobials in combination with antibiotic lock therapy is possible.[49] Replacement of port devices after removal for infection should be delayed until confirmation of clearance of bacteremia, and a new site for placement of the device should be used.

Catheter-related thrombosis and catheter occlusion

Catheter occlusion occurs commonly and can be related to mechanical issues, such as pinch-off syndrome and needle occlusion, or to obstruction from deposition of medication or total parenteral nutrition, precipitation of incompatible drugs, formation of a fibrin or protein sheath, and from intraluminal or extraluminal clot formation.[51] Catheter occlusion is usually identified by an inability to withdraw blood on negative pressure only (withdrawal occlusion) or in combination with an inability to infuse on positive pressure (complete occlusion). The diagnostic methods used will depend on the cause of the occlusion. First, close inspection and repositioning maneuvers should be attempted to try and relieve transient mechanical occlusions. Medications should be carefully reviewed for incompatibility issues. If these issues are excluded, then the most common cause of occlusion is thrombotic obstruction. Although this can be diagnosed with contrast injections, typically, it is empirically treated with the administration of thrombolytics, such as alteplase. Alteplase to fill the IVAD volume can be administered and allowed to dwell for at least 30 minutes, with the possibility for a second dose if obstruction is not resolved. If a thrombolytic fails to clear the catheter, then mechanical options, such as guide-wire advancement or fibrin sheath stripping, are available; however, because of their invasive nature, mechanical options are rarely used or recommended.[51] More commonly, in patients who fail to respond to medical therapy, removal of the IVAD and replacement will be needed.

Patients who have nonresponsive catheter occlusions also should be considered for an evaluation for possible catheter-related venous thrombosis. Symptoms that can be present include development of collateral vessels, edema, warmth, erythema, or tenderness to palpation in the area of the clot, although the vast majority of catheter-related venous thromboses are asymptomatic. Risk factors for venous thrombosis in patients with IVADs include catheter tip malposition, prior catheter-related infection, and larger lumen sizes of the catheter. Potential complications associated with these are pulmonary embolism, post-thrombotic syndrome, and a higher risk of catheter infections. For diagnosis, ultrasonography, venography, or computed tomography venography can be used.

The management of catheter-related venous thrombosis is somewhat controversial based on the lack of prospective studies. For patients in whom the catheter is no longer needed or is nonfunctional, the recommendation from the American College of Chest Physicians is to remove the catheter and provide anticoagulation.[52,53] If the veins involved are the axillary or more proximal veins, then 3 months of anticoagulation therapy is suggested over a shorter period. In patients with a functional catheter who still require therapy, the recommendation is to maintain the catheter and continue anticoagulation for as long as the catheter is present. In patients with cancer, low-molecular-weight heparin is preferred over vitamin K antagonists and other anticoagulants. Thrombolysis is reserved for patients with a low risk of bleeding, good life expectancy, and good functional status who have persistent symptoms with a thrombus involving most of the subclavian or axillary vein.

CONCLUSIONS

IVAD port use is likely to continue growing with disease states that require long-term access based on the much lower risk of infection of ports compared with conventional CVCs and patient satisfaction. Device design and techniques for their implantation and care continue to evolve based on the need to improve device performance and safety and to minimize complications. Despite the advances made to date, adequate maintenance and care of ports continue to be paramount for the prevention of major complications like infection and occlusion. Emphasis for future research should be placed on education and standardization of techniques for maintenance care. Health care workers involved in the management of IVADs should be aware of common complications, recognition of their symptoms, and initial steps in management.

CONFLICT OF INTEREST

The author has no conflicts of interest.

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