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Evidence-Based Strategies and Recommendations for Preservation of Central Venous Access in Children

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Abstract

Children with chronic illness often require prolonged or repeated venous access. They remain at high risk for venous catheter–related complications (high-risk patients), which largely derive from elective decisions during catheter insertion and continuing care. These complications result in progressive loss of the venous capital (patent and compliant venous pathways) necessary for delivery of life-preserving therapies. A nonstandardized, episodic, isolated approach to venous care in these high-need, high-cost patients is too often the norm, imposing a disproportionate burden on affected persons and escalating costs. This state-of-the-art review identifies known failure points in the current systems of venous care, details the elements of an individualized plan of care, and emphasizes a patient-centered, multidisciplinary, collaborative, and evidence-based approach to care in these vulnerable populations. These guidelines are intended to enable every practitioner in every practice to deliver better care and better outcomes to these patients through awareness of critical issues, anticipatory attention to meaningful components of care, and appropriate consultation or referral when necessary.* (*JPEN J Parenter Enteral Nutr.* 2019;00:1–24)

Keywords

central venous access complications; coordination of care; guidelines; pediatrics; shared decision-making; venous access

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Introduction

Children are particularly vulnerable to complications of chronic disease, and symptoms of severe acute complications can often be missed in these patients.[1,2] Central venous catheter (CVC)-related complications can be life-threatening, with an estimated 12.5%–25% mortality associated with catheter-related bloodstream infections (CRBSIs).[3,4] Catheter-related complications also add tens of billions of dollars to healthcare costs in the United States annually,[5] chiefly attributable to chronic (prolonged or repeated) venous access. Additional systemic complications, interruption of life-preserving therapies, and increased frequency of thrombosis and endocarditis are associated with bloodstream infections in certain high-risk populations.[6,7] Because conventional venous access routes are frequently impaired, establishing and maintaining high-quality venous access in high-risk children can be very challenging.[8]

In 2016, the VANGUARD (Venous Access: National Guideline and Registry Development) multistakeholder symposium prioritized anticipatory planning for chronic venous access, including individualized review of venous access history, to preserve central venous pathways (venous capital) and reduce complications in pediatric patients who require chronic central venous access, and thereby save lives and reduce the frequency and duration of hospitalization and associated healthcare costs.[5] A multidisciplinary panel of subject matter experts was invited to meet this charge and, based on available evidence and expert consensus, develop recommendations regarding common CVC failure points and critical components of care that anticipate the potential need for lifetime access (Table 1). The purpose of these guidelines is to help the clinical community improve the quality of CVC-related care and the quality of life for patients who require chronic central venous access.

Methodology

An in-depth Medline (PubMed) search of the relevant medical literature was performed. Peer-reviewed articles were critically reviewed with regard to study methodology, results, and conclusions. To fulfill the Institute of Medicine standards for guideline development, a subset of 5 panel members used a modified Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process to evaluate the quality of evidence for and the strength of each recommendation, similar to the classification systems used by specialty practice societies such as the American College of Cardiology and the American Heart Association.[9]

The strength of each recommendation reflects the authors' judgments about the relative strengths and weaknesses of study data, including the risks and benefits identified by the evidence and a synthesis of conflicting findings among multiple studies. The Good Practice Statement (GPS) was used for recommendations without published evidence or consensus.[10] GPS recommendations were developed from indirect literature and the experience of the expert panel and may address social, legal, and ethical questions and implementation issues not appropriate to more formal evidence grading. Details of the classification hierarchy are included with the recommendations. Where evidence was weak and expert opinions were conflicting or contradictory, a modified Delphi technique was utilized to facilitate effective decision-making.[11] Perspectives of an advisory panel of affected persons (patients, parents, families, caregivers, and support organizations) were incorporated into the document (Appendix A1).

Failure Points and Essential Components of Care

Widely advocated practices to reduce catheter-related complications in the *acute* care environment include insertion and maintenance bundles and removal of catheters that are no longer required.[12-16] For patients who require *chronic* venous access for life-preserving therapy, the situation is more complex, the opportunities for device failure and adverse events more varied, the accumulation of venous injuries more insidious, and the need for collaborative, evidence-driven care more pivotal. Compartmentalized and discontinuous clinical reasoning too often results in avoidable adverse outcomes with potentially devastating results. The following sections encourage collaborative management reasoning[17] through critical practices and precautions that facilitate optimal preservation of venous health and patency in high-risk chronic venous access patients.

Diagnostic Venous Imaging and Evaluation

Venous compromise is prevalent in patients requiring chronic access. At least 40%–50% of intestinal failure and renal failure patients have obstruction of at least 1 major venous pathway.[18,19] Vascular imaging studies should answer clinical questions and characterize the location, nature, and extent of abnormalities, directed by experts in vascular imaging and interventions. Imaging must be timely, problem centered, and task oriented for identification of relevant issues and therapeutic planning, to assess and document venous patency and outcomes of device or pathway salvage interventions.

Venous injury can be cumulative, progressing from disorganized thrombus and perivascular edema through subacute thrombus or stenosis to mature clot or vein wall fibrosis. However, even a single injury can lead to irreversible obstruction. Early recognition and aggressive intervention are necessary to preserve venous capital at risk.[20] Initial venous injuries, often subtle and occult, influence the success of

Table 1. Recommendations for Preservation of Central Venous Access in High-Risk Patients.

	Grade	Class	Strength	Recommendations
Venous imaging and evaluation				
1.1.1	C	I	Strong	In high-risk patients, venous imaging and evaluation should include review of all available and relevant prior vascular imaging studies.
Diagnostic contrast venography				
1.2.1	B	I	Strong	DIV should be used as the primary initial modality to survey the venous system for patency, obstruction, or abnormalities of the major venous pathways.
1.2.2	GPS		Strong	Baseline DIV should ideally be performed before the patient's first venous access device is removed regardless of the reason for removal and should include each pathway in which an access device has been inserted.
1.2.3	GPS		Strong	If prior history cannot be confirmed, then an initial survey of all major venous pathways should be performed.
Diagnostic venous ultrasound				
1.3.1	C	IIa	Strong	Venous ultrasound should be used as a secondary diagnostic modality to follow targeted lesions and evaluate specific clinical questions as part of a comprehensive plan to routinely survey the state of the patient's venous capital.
1.3.2	B	I	Strong	Venous ultrasound examination and its documentation should adhere to appropriate standards.
Venous access planning				
2.1.1	C	IIa	Strong	Prospective venous access planning should begin at the time the high-risk patient is first diagnosed with an indication for chronic access.
2.1.2	C	IIa	Strong	The prospective venous access plan should govern every elective venous event; no elective vein-related intervention should be undertaken outside the scope of this plan.
2.1.3	C	IIb	Strong	If an experienced multidisciplinary venous access team (see 6.1.1) does not exist within the treating institution, consultation with or referral to such a center should be considered.
2.1.4	C	I	Strong	For high-risk patients with a history of difficult access or venous access–related complications, liaison with or transfer to a pediatric tertiary care facility with expertise treating high-risk patients should be obtained as early after diagnosis as practicable.
Elective access conditions				
3.1.1	C	IIa	Strong	Venous access should be performed under the supervision of an experienced practitioner, preferably an expert in venous access and related salvage procedures in high-risk children.
3.1.2	A	I	Strong	Only individuals appropriately educated to protect the integrity of the device and access site and to prevent access-related complications should provide continuing care of venous access devices.
3.1.3	A	I	Strong	Elective venous access in high-risk patients should always be performed in a sterile environment with sterile technique, appropriate apparel, and other sterile barriers.
3.1.4	B	I	Strong	If temporary venous access (ie, a nontunneled, noncuffed central catheter or a catheter, including a midline catheter, that does not terminate near the cavoatrial junction) must be acquired for a central venous indication due to exigent clinical circumstances, it should be accompanied by a plan for removal or elective access in an appropriate theater as soon as possible thereafter.
3.1.5	A	I	Strong	For venous access, real-time ultrasound guidance for percutaneous venipuncture is preferred to the cut-down or landmark techniques.
3.1.6	A	I	Strong	Guide wire positioning and catheter delivery and positioning during CVC insertion should be performed with real-time fluoroscopic control.
Access site				
3.2.1	B	I	Strong	Conventional access sites from most to least preferred include neck veins (eg, internal or external jugular), arm veins (eg, brachial or basilic), femoral vein, and subclavian vein.
3.2.2	C	IIa	Strong	Use of upper extremity veins for access should be avoided in patients with potential future need for hemodialysis.
Catheter tip position				
3.3.1	B	I	Strong	A long-term catheter tip should be positioned in the proximal cava near the cavoatrial junction.
3.3.2	B	I	Strong	The tip(s) of a long-term hemodialysis catheter should be positioned within the right atrium.
3.3.3	C	IIa	Strong	A temporary catheter tip should be positioned in the lower SVC from above the diaphragm, or above the iliac confluence from below.
3.3.4	C	IIa	Strong	A CVC should not be used until the catheter tip position has been verified with medical imaging.
3.3.5	B	IIa	Strong	If a catheter is malpositioned, it should be promptly repositioned or replaced.
3.3.6	GPS		Strong	In a growing child, catheter tip location should be verified at least every 12 months.
Device selection				
3.4.1	C	I	Strong	Peripherally inserted or tunneled, cuffed central catheters are preferred to temporary or uncuffed catheters.
3.4.2	B	I	Strong	Subcutaneous indwelling venous ports should be reserved for chronic intermittent therapy in patients immunocompetent at the time of insertion.
3.4.3	C	I	Strong	In all cases, the smallest catheter diameter and the fewest lumens required to deliver anticipated therapy safely are recommended.
3.4.4	B	I	Strong	Antimicrobial-impregnated catheters should be considered for CVC insertion in all high-risk patients.

(*continued*)

Table 1. (continued)

	Grade	Class	Strength	Recommendations
3.4.5	B	IIb	Weak	Antimicrobial lock therapy should be considered for CVC care in all high-risk patients.
Catheter-related infection				
Documentation of suspected catheter-related infection				
4.1.1	C	I	Strong	For all high-risk patients with a venous catheter in place with signs and symptoms that suggest a bloodstream infection, diagnosis of a catheter-related infection should follow a rigorous cognitive pathway.
4.1.2	C	I	Strong	The associated elements that lead to support for or rejection of a diagnosis of catheter-related infection in each case should be clearly documented in the medical record.
4.1.3	A	I	Strong	Diagnosis should ideally be supported by central and peripheral culture, or culture from the dialysis bloodline, of an organism known to cause catheter infections with a differential latency to positivity, or by purulent discharge related to the exit site, subcutaneous tract, or port pocket, or by catheter tip culture, which grows the same microorganism as the peripheral or bloodline blood culture.
4.1.4	B	IIa	Weak	For suspected CRBSI, blood cultures should be obtained from each catheter lumen if possible.
4.1.5	A	I	Strong	If the catheter is removed under suspicion of infection, a roll-plate culture of the catheter tip should be obtained.
Catheter removal				
4.2.1	C	I	Strong	In a high-risk patient, a functioning noninfected and appropriately positioned chronic venous access device should be removed only at the end of therapy.
4.2.2	B	I	Strong	In the event of a CVC-related infection that cannot be successfully treated with the catheter in situ, including *Staphylococcus aureus*, Gram-negative enterococcus, and catheter-associated fungemia, the catheter should be removed.
4.2.3	A	I	Strong	When the patient is symptomatic of sepsis, including cardiovascular instability or end organ failure, particularly with positive blood cultures, and another focus cannot be identified, the catheter should be removed.
Catheter-related thrombosis and venous obstruction				
5.1.1	B	I	Strong	If there are signs or symptoms of deep venous obstruction, or a known history of obstruction or previous difficult access, proactive investigation should be instituted prior to attempting new access placement.
5.1.2	C	I	Strong	Diagnosis of venous obstruction or injury should be documented in the EHR, using standard nomenclature, including the nature and extent of involvement and the outcome of any related intervention.
5.1.3	GPS		Weak	If central venous obstruction is diagnosed, it should be preemptively treated.
5.1.4	C	IIa	Strong	In the event of central venous obstruction, every reasonable attempt should be made to reestablish patency for the purpose of venous access across an injured vein before accessing an uninjured vein.
5.1.5	C	IIa	Strong	Insertion of a venous stent should be avoided except as a last option to permit transplantation, alleviate risk to a vital organ, relieve intractable pain, or reduce functional impairment from venous hypertension and related inflammation and secondary lymphedema.
5.1.6	C	IIb	Weak	Consideration should be given to prophylactic anticoagulation in patients with chronic need for central venous access.
5.1.7	B	IIa	Strong	Alternate routes should be considered only if conventional venous pathways cannot be accessed or recanalized for access.
Treatment				
5.2.1	C	IIb	Weak	Vascular specialists with training and experience in difficult access and vessel and catheter salvage should perform treatment of venous obstruction, catheter salvage and venous recanalization procedures, stent insertion, and access via unconventional pathways.
Collaborative care and information management				
6.1.1	C	IIa	Strong	Each institution routinely caring for high-risk patients who require chronic central venous access should identify a CVAT.
6.1.2	C	IIa	Strong	Ideally, the CVAT should supervise continuing venous access device care and maintenance, guideline and policy development, and resolution of difficult or contentious issues regarding the maintenance of venous health and successful venous access in children at high risk for catheter-related complications.
6.1.3	C	I	Strong	To preserve venous capital and minimize risks of catheter-related dysfunction, it is strongly recommended that the CVAT develop and maintain a long-term plan for preservation of venous access for each high-risk patient.
6.1.4	C	IIa	Strong	The unified plan developed by the CVAT should be maintained as part of continuing care documentation.
6.1.5	GPS		Strong	Patient and device selection, device insertion, continuing catheter care, device and venous pathway salvage, treatment of related complications, and device removal should be considered in accordance with the existing CVAT preservation plan or in consultation with the CVAT responsible for maintaining and updating that plan.

(*continued*)

Table 1. (continued)

	Grade	Class	Strength	Recommendations
6.1.6	GPS		Strong	The CVAT should work to achieve full engagement of affected persons (patients, parents, families, caregivers, and support organizations) in the planning and process of care to ensure that patient-important outcomes are prioritized.
6.1.7	C	I	Strong	The patient-healthcare relationship should include bidirectional communication and shared decision-making, support for patient self-management, and appropriate use of eHealth technology as a complement to care.
Electronic medical record				
6.2.1	GPS		Strong	Development of a unified set of interoperable CDE specific for the venous access domain is essential.
6.2.2	GPS		Strong	A continuous electronic summary of all venous access events should be part of continuing care documentation, easily accessible to and transferable by the patient.
6.2.3	GPS		Strong	The venous access event record should be reviewed prior to any new venous intervention.
6.2.4	C	I	Strong	Active patient-reported outcomes and other patient-generated health data should be integrated with clinical data to develop real-world evidence reflective of data and issues important to the patient.

CDE, common data elements; CRBSI, catheter-related bloodstream infection; CVAT, Collaborative Venous Access Team; CVC, central venous catheter; DIV, diagnostic infusion venography; EHR, electronic health record; SVC, superior vena cava.

Grade criteria

A: Recommendation based on evidence from multiple randomized trials or meta-analyses.
B: Recommendation based on evidence from a single randomized trial or nonrandomized studies.
C: Recommendation based on expert opinion, case studies, or standards of care.
GPS: Good Practice Statement.

Class criteria

• Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.
• Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
• Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
• Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
• Class III: Conditions for which there is evidence or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.

Strength criteria

For each recommendation, an overall rating was provided:
S: Strongly recommended.
W: Weakly recommended.

subsequent efforts to maintain or restore venous patency. A baseline study of the major central veins should ideally be obtained at or before the time the high-risk patient's first CVC is removed.

Although venous ultrasound (US) is strongly recommended in some guidelines,[21] it is neither a survey modality nor adequate for diagnosis, especially in a high-risk population.[22] However, it is very useful as a secondary modality to follow targeted lesions and evaluate specific clinical questions. The use of diagnostic venous US should adhere to established guidelines.[23-25]

Conventional diagnostic infusion venography (DIV) demonstrates flow dynamics and is highly sensitive and specific with a high negative predictive value,[22] but must be directed to each vascular territory of interest. DIV is considered the reference standard to evaluate the patency of conventional central venous pathways and to document the nature and extent of anatomic abnormality or central venous obstruction.[26-29]

Computed tomography (CT) and magnetic resonance (MR) venography have technical limitations but offer useful information regarding venous obstruction.[30] Superparamagnetic iron oxide–based contrast agents may help avoid gadolinium-based MR contrast complications, such as in patients with renal failure.[31] The venous information contained in CT and MR studies, especially in delayed-phase imaging, should be reviewed and incorporated into the documented venous history.[32,33] Volumetric reconstruction may help delineate location and extent of obstruction and involvement of collateral pathways.[34] Intravascular ultrasound can also provide high-quality cross-sectional imaging of focal venous segments and may add critical information regarding pathophysiology (eg, compression, wall thickening, or perivenous fibrosis) and the response to therapeutic interventions (eg, recoil following venoplasty).[35,36]

Venous Access Planning

According to the VANGUARD Affected Persons Advisory Panel, affected persons perceive that central venous access is often treated as an incidental series of episodic events until something catastrophic happens. Although extraordinary measures can manage life-threatening complications and recanalize obstructed pathways, they are not always successful

and can incur disproportionate clinical and economic costs.[8] The anticipatory planning and preventive measures represented within these recommendations should be initiated at the time a patient is first diagnosed with a condition likely to require chronic venous access of an indeterminate period (from months to a lifetime).[37] Once initiated, such individualized planning should govern every elective venous access–related event, over time and across venues.

Elective Access Conditions

A multidisciplinary approach to venous access care in patients with chronic venous access is advised. For patients whose underlying diagnosis predicts long-term reliance on central venous access or whose venous history is already marked by difficult access or significant central obstruction, elective venous access procedures should ideally be performed at a center with advanced expertise.[8,38]

Imaging is critically important during the primary venous cannulation and catheter insertion procedure to reduce injuries that threaten venous patency and to ensure suitable location of the catheter tip. US with high-quality near-field imaging and penetration and the training and experience to use it effectively reduces the number of punctures necessary to gain access and helps to avoid injury to related vital structures. Real-time cross-sectional imaging also facilitates adaptation to local anatomic variations and identification of undiagnosed irregularities such as thrombophlebitis or venospasm.[39,40] Real-time US is the modality of choice for venous access guidance.[41-43]

Preferred sites of access include the deep veins of the neck and chest (eg, internal jugular or brachiocephalic veins) or the deep veins of the arm and shoulder (brachial, proximal basilic, and axillary),[44-46] although patient-specific factors may affect selection. Other conventional routes, including femoral,[47] subclavian, and cephalic veins, are associated with higher rates of mechanical and infectious complications. The subclavian route in particular should be avoided, especially for elective insertion of hemodiaysis catheters.[48]

Alternative routes are available. Transmediastinal access to the brachiocephalic veins or distal superior vena cava can be achieved with coronal retroclavicular US with good long-term stability.[38,49] Translumbar and transhepatic inferior vena cava access are more technically difficult. Transhepatic access is associated with greater mechanical instability, higher short-term and long-term complication rates, and risk of infection.[50-53] Hemizygos or azygos collaterals are feasible[54] albeit rarely used. Transthoracic transatrial access[51,55] is sometimes performed at the time of cardiac surgery. More invasive alternatives such as creation of an arteriovenous (AV) access[56] and use of arterial access[57] have been described, but experience in children is too limited to make a recommendation.

To date, no published studies evaluate the risk profile of catheter tip position against an anatomically validated reference standard. It is common empiric practice to intend CVC tip position near the cavoatrial junction[58] or in the case of hemodialysis catheters, within the right atrium.[59] Unambiguous methods for accurately describing catheter tip position relative to anatomic structures that are visible on a plain radiograph have been published[60,61] and integrated into quality improvement guidelines.[62]

High-quality fluoroscopy is essential for control of central venous guide wire and catheter positioning.[44] Alternative tracking technologies for tip positioning (eg, electrocardiographic and electromagnetic) are promising but have not yet been objectively validated.[63] Transthoracic echocardiography has been suggested to determine catheter tip position, but randomized, controlled trials (RCT) have not been published and expertise with the technique and equipment is not widely available.[64,65] The frequency of unsuccessful and complicated insertions without imaging (eg, at the bedside) remains unacceptably high and should not be routinely attempted in high-risk patients.[66,67] Collaboration between vascular access nurses and interventional radiologists may offer improved outcomes compared with bedside insertion.[68]

Emergent and urgent devices (ie, "temporary catheters") placed without maximum sterile barrier precautions, or catheters with tips positioned at a distance from the cavoatrial junction, should be removed as soon as possible after stabilization of the patient.[69-75] A malpositioned catheter (that was not too short initially) should be promptly evaluated with imaging and either repositioned or replaced to avoid adverse outcomes.[76,77]

For elective central venous access, device selection should be governed by specific indications documented prospectively as part of the assessment/insertion process, including the expected duration and endpoint of therapy and the intended route and tip position (Appendix A2). Affected persons should be considered shared decision makers in the selection process, especially when issues such as preference, comfort, and body image do not compromise safety and preservation of venous pathways. The smallest lumen number and diameter should be used that accomplish the clinical objectives safely and effectively.[78-80] Vesicants, including high osmolal, extreme pH, and many chemotherapeutic agents, should be administered centrally.[81,82] Chronic continuous or frequent infusions should employ a tunneled, cuffed catheter through veins of the neck, chest, or groin. There have been no RCTs evaluating midline catheters as an alternative to CVCs or evaluating their use in high-risk pediatric patients, and current evidence does not support such use.[83,84] Peripherally inserted central catheters are an acceptable alternative. However, arm veins should be avoided in patients with potential future need of hemodialysis (chronic kidney disease higher than grade G2A2 or

Table 2. Reported Central Venous Catheter Infection Rates in Pediatric Patient Populations.

Pediatric Patient Population	Infections per 1000 Catheter Days[96-98,170-173]
General population	0.2–0.9
Intensive care units	1–5
Hematology-oncology units	1–4
Hemodialysis patients	2
Intestinal failure patients	1–11
Neonatal intensive care units	11–29
Burn units	30

G3a[85]) because of the cumulative risk of thrombosis and loss of potential AV fistula sites.[26,86] For chronic intermittent access, an indwelling venous port may be placed in the veins of the chest, extremity, or groin. Ports should be used with caution in patients who are immunocompromised at the time of insertion.[87] For example, in patients with intestinal failure, ports may be relatively contraindicated prior to intestinal adaptation.[88] The port septum should be distant from contaminated sites. Chronic hemodialysis catheters are ideally tunneled, cuffed devices that should deliver adequate dialysis blood flow to achieve target dose (Kt/V at least 1.2) while arterial and venous pressures remain within acceptable parameters.[89]

Antibiotic-impregnated catheters have shown significant reduction in catheter-related infections in high-risk children[90] and have demonstrated superiority to conventional and heparin-bonded catheters in a large pediatric RCT[91] without increasing resistance to bacterial pathogens.[92] They may be especially valuable for children in the intensive care unit[91] and those with intestinal overgrowth,[93] those with active infection at the time of insertion,[4,90] immunocompromised patients, those with a history of multiple catheter-related infections, or those with deep venous obstruction of VANGUARD Class II or higher either above or below the diaphragm (Appendix 4).

Evidence for prophylactic use of antimicrobial lock solutions has been encouraging in small samples.[74,94-98] Meta-analysis suggests they reduce infection risk and can be additive to other therapies,[99,100] although support for ethanol lock therapy was equivocal in a recent double-blind, placebo-controlled RCT.[101] Similarly, evidence regarding heparin-bonded catheters in children remains too weak for a recommendation at this time.[102]

Catheter-Related Infection

The reported frequency of venous catheter–related infections is unacceptably high and still may significantly underestimate the true rate. Infection rates seem significantly higher in populations that require chronic access (Table 2), although the quality of most currently available data is low, representing retrospective review of small numbers of patients with great variability in methodology.[103,104] To know the actual rate of catheter-related infection in high-risk populations, one must know how many catheters are placed in high-risk patients; dwell time; number of culture-positive bloodstream infections, exudates, or catheter tips (if explanted); and whether there is an alternate source of primary infection.

Reliable meta-analysis of catheter-related infections is not currently available. The majority of published studies report infection rates using the surveillance definition of central line–associated bloodstream infections, which may significantly overestimate the true CRBSI rate.[105] Conversely, the influence of penalties for reporting healthcare-associated infections and the associated reluctance to obtain blood cultures (as well as the historic aversion to peripheral venous sampling in children) may account for significant underreporting of catheter infections.[5,106,107] Both strategies increase uncertainty and may result in presumptive treatment of catheter-related infection without adequate confirmation, leading to unnecessary catheter removal and other potentially harmful treatment. To better ensure appropriate recognition of catheter-related infections and to prevent inappropriate treatment and device removal, all high-risk patients with a chronic venous catheter and signs or symptoms that suggest sepsis should be rigorously evaluated for a venous catheter–related infection,[12] ideally including differential time to positivity[74,108,109] from each catheter lumen if possible,[110,111] and roll-plate culture of the catheter tip if it is removed.[4] A consensus strategy for such evaluation is provided in Infectious Disease Society of America (IDSA) guidelines (in press). It is essential that studies of catheter-related infection express results in events per 1000 catheter days. Because CRBSI significantly increases risk of mortality, especially in transplant and immunocompromised patients, it is also important that sepsis and mortality be included as key outcome measures whenever possible.[112]

Removing the source is fundamental in the treatment of infection. This creates a difficult conflict because of the need for critical catheter-dependent therapies such as parenteral nutrition and hemodialysis, the risk of loss of venous pathways, and the increased vulnerability of malnourished, immunocompromised patients to risks of catheter reinsertion and delays in therapy. It is especially problematic because proof of CRBSI has traditionally included catheter removal and culture of the tip if another source cannot be identified and because a large proportion of catheters removed for suspicion of infection lack microbiologic confirmation.[4,113]

Ideally, a functioning CVC in a high-risk patient should be removed at the end of therapy and not before. Quantitative and semiquantitative analysis has allowed more accurate in situ diagnosis of CRBSI.[114] Nevertheless, when a patient is in septic shock due to suspected or proven CRBSI

(fever with circulatory compromise or collapse), or remains symptomatic of sepsis[115-117] for >48 hours after initiation of broad-spectrum therapy, or has a complicated infection (eg, purulent discharge from the port pocket or subcutaneous tract, septic thrombosis, endocarditis, osteomyelitis), it is imperative to remove the catheter.[4] If the catheter is to be removed in the setting of septic shock, other vascular access should first be established.[118] If alternative access is difficult, the catheter may be exchanged for an antibiotic-impregnated catheter.[4]

Catheter-Related Thrombosis and Venous Obstruction

Infectious and thrombotic complications of CVCs are interrelated.[119] Since thrombus serves as a nidus of infection, there is a higher catheter-related sepsis rate in the presence of thrombosis.[120] Thrombosis and stenosis occur in children with a history of chronic central venous access with an incidence of 26%–75% in prospective and cross-sectional studies.[22,37,121] Compromise of central veins leads to increased hospital admissions for venous access–related complications and contributes to high morbidity and cost of care.[26,122-124] Thrombosis risk is significantly increased in patients who have had multiple CVCs, in patients with temporary and midline catheters, and in patients with cardiovascular implanted electronic devices.[125-127] Inherited or acquired thrombophilia should be considered in any child who develops deep vein thrombosis (DVT).[128,129]

The true incidence of DVT and stenosis in patients who require chronic access is unknown because most studies are limited to symptomatic patients[130] and reporting has been largely nonstandardized.[131] However, asymptomatic thrombosis has clearly been demonstrated in children with CVCs[37,132,133] with serious consequences including loss of venous access, infection, pulmonary embolic disease, and post-thrombotic syndrome.[134] For these reasons, at the time of CVC removal in a high-risk patient, especially with a history of prior venous compromise, venography should be performed to document patency and to treat compromising lesions before access is lost. This opportunity for vessel and catheter salvage may be invaluable to facilitate preservation of venous capital.

A variety of methods to salvage CVC complications and to recanalize obstructed pathways have been reported.[135-138] For patients with obstructive thrombus in whom thrombectomy or systemic thrombolysis fails or is unsuitable, balloon or aspiration thrombectomy or catheter-directed pharmacomechanical thrombolysis have demonstrated effectiveness in children.[139,140] For recanalization of mature thrombus or nonthrombotic obstruction, less invasive methods (eg, softer guide wires and dilators, noncompliant angioplasty balloons) should be attempted before more aggressive techniques and devices (eg, sharp recanalization, cutting balloons, stent insertion) are employed, although risk-benefit analysis and the experience of the procedural team will ultimately govern these decisions. Without long-term outcomes data for venous stents in children, they should be used with caution and restraint.[141-143]

Although evidence for high morbidity and mortality in children with venous catheter–related DVT is compelling,[8,144,145] until recently, data favoring anticoagulation for CVC-related thrombi and infection prophylaxis have been relatively weak.[146] Evidence regarding the effectiveness of a shorter duration of therapy and selective use is evolving.[147-149]

Standard nomenclature and relationships for veins commonly involved in venous access are illustrated in Appendix A3, Figure A1.[150] Following the lead of the International Small Bowel Transplant Symposium,[18] a comprehensive VANGUARD classification system for supradiaphragmatic (Appendix 4, Figures A2-A6) and infradiaphragmatic (Appendix A4, Figures A7-A11) venous obstruction is illustrated. This system is equally useful for documenting the location, extent, and nature of venous lesions, including fresh thrombus, wall thickening/fibrosis, stenosis, perivascular fibrosis, external compression, extravasation/perforation, and persistent stenotic elastic recoil. A similar framework can be used to document the location, extent, and nature of venous salvage procedures and other interventions, such as adherent catheter retrieval, catheter tip repositioning, recanalization, venoplasty, and stent insertion. As data accumulate on the relationship between patterns of venous injury, obstruction, and other critical endpoints, disease-specific analysis may prove increasingly useful.[131,151]

Collaborative Care and Information Management

Healthcare institutions that routinely care for high-risk CVC patients should have designated multidisciplinary Collaborative Venous Access Teams (CVATs).[152] Although the components of care addressed by such a team should be universal, personnel will vary from site to site but should ideally consider patient and caregiver representatives; vascular access, infusion, intestinal care, and apheresis nurses; interventional radiologists; hepatologists; surgeons; nephrologists; gastroenterologists; infectious disease physicians; intensivists; hematologists; pharmacists; and home health planning experts. Unfortunately, with the current focus on indiscriminate reduction of cost, the tendency has been to disband such teams rather than to form, strengthen, and value them.[153,154]

The existence of a multidisciplinary team does not ensure improved outcomes.[155] To be effective, the CVAT should supervise continuing CVC care and maintenance, guideline and policy development, and resolution of difficult or contentious access-related issues. CVAT leadership should have

significant experience with advanced access and salvage techniques, understand the challenges inherent in treatment of high-risk populations, and be current with the evidence base that guides relevant best practices. To preserve venous capital and minimize risks of catheter-related dysfunction, the team should develop and maintain individualized long-term plans for preservation of venous access.[156,157] Continuing care of CVCs in high-risk populations should be performed by healthcare providers with appropriate education and experience, including currency with principles of exit-site management including antimicrobial-impregnated dressings and passive disinfection caps, catheter access technique and protocols, and locking solutions or other cap-devices to reduce infection risk.[12,21,74,158-161]

Persons affected by chronic diseases experience significant disruption in their lives due to morbidity and mortality from CVC complications; frequent hospitalizations; loss of time at work, home and school; and other related costs of care. Healthcare providers often misunderstand quality of life issues for these patients, especially emotional disruption, perceptions of pain and discomfort, and impact on family.[162,163] The CVAT should pursue full engagement of affected persons in the planning and process of care to ensure that patient-important outcomes are prioritized and that patient values guide all clinical decisions.[164] The patient-healthcare relationship should include bidirectional communication and shared decision-making, support for patient self-management, appropriate use of eHealth technology as a complement to care, education on safety and access preservation, and respect for the experiences and concerns of affected persons.[165]

Through the 21st Century Cures Act, the U.S. Congress emphasized the need for interoperability, that is, the ability for health information access, use, and exchange by authorized persons "without special effort."[166] The concepts embodied in this law are timely and germane to the complex coordination-of-care needs of high-risk patients. Development of unified and unambiguous electronic vocabulary specifications is essential.[5] It is imperative that such a unified venous access vocabulary become the community standard, including electronic health record, registry, and other health information technology vendors; payers; publishers; and government and private agencies. It should also be used in structured reporting of catheter insertions and other venous access–related events.[167] Each documented event should become part of a continuous summary of venous events available to the patient and to health providers across time and venue. The summary record and multidisciplinary plan of care should be reviewed prior to any new venous intervention.

Inputs from affected persons should be integrated with clinical data to develop a body of real-world experience, accessible to the patient, to improve communication and shared decision-making. Data could also be linked through the patient's Unique Device Identifier[168] to permit coordination with national outcome tracking networks like the National Health Safety Network and other big data sources to inform guidelines, standards, reimbursement, and policy development. The needs for a robust and interoperable central venous access registry and for large-scale prospective research have been identified as national multistakeholder priorities.[5]

Conclusions

More than half of Americans have a chronic medical condition, and more than three-quarters of each healthcare dollar is spent on their care.[169] High-risk pediatric patients are by definition disproportionately vulnerable. Reliance on central venous access and the impact of related complications are particularly concentrated in this population. This paper provides recommendations that can help stakeholders improve care and quality of life for these patients. The authors recognize that the quality of evidence underlying these issues is generally weak, although the need for consistent guidance and improved communication is highly compelling. These recommendations should serve as a foundation for the carefully constructed investigations needed to provide high-quality evidence that can guide their use and modification over time.

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Statement of Authorship

K. M. Baskin contributed to the conception and design of the research and drafted the manuscript; K. M. Baskin, T. F. Saad, B. P. Modi, J. I. Vrazas, and C. M. Schaefer contributed to the acquisition and analysis of the data. All authors contributed to the interpretation of the data, critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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Appendix

A1. Collaborators

The following members of the Venous Access: National Guideline and Registry Development (VANGUARD) Initiative and the VANGUARD Affected Persons Advisory Panel are nonauthor contributors: Swapna Kakani, Emily Hoopes, Aly Becker, Kristin Huibregste, Ansley McCormick, Alaina McCormick, and Sarah Palya.

A2. Essential Data Elements of a Venous Access Record for Children at High Risk of Venous Catheter Complication

1. Diagnostic category: underlying disease, patient acuity, comorbid illness, American Society of Anesthesiologists class
2. Any contraindicating or complicating factors
   a. Coagulopathy
   b. Thrombophilia
   c. Fever, sepsis, known infection, immunodeficiency, nutrition status
   d. Venous stenosis
   e. Acute thrombosis
   f. Local skin infection
   g. Evidence of intestinal overgrowth
3. Referring service and provider; inpatient or outpatient status
4. Indication(s) for venous access placement or replacement; intended function (eg, parenteral nutrition, blood products, antibiotic administration, fluid and electrolyte therapy, dialysis, plasmapheresis/apheresis, phlebotomy, chelation, simultaneous delivery of incompatible medications)
5. Anticipated duration of and endpoint for venous access
6. Intended route and catheter tip position

7. Provider responsible for access (interventionalist, surgeon, nurse, etc)
8. Procedure location (interventional suite, operating room, bedside, etc)
9. Preprocedural or periprocedural interventions (eg, antibiotics; blood products; thrombolytic, anticoagulant or antiplatelet agents; imaging)
10. Initial access
    a. Entry side and site (eg, basilic vein, internal jugular vein, femoral vein)
    b. Method (eg, visual landmarks, fluoroscopic venography, ultrasound, cut-down)
    c. Route (eg, percutaneous, transmediastinal, paraspinal (eg, translumbar), transhepatic, endoscopically assisted[174])
    d. Device (eg, angiocatheter, single wall needle, venotomy)
    e. Number and location of unsuccessful and successful attempts
    f. Complications (eg, arterial puncture, pneumothorax)
    g. Reason for deferral, discontinuation, or failure, if insertion not completed
11. Access device and position
    a. Catheter manufacturer, description, lumen number and diameter, final internal length, composition, coating or impregnation, etc. (documentation of unique device identifier preferred)
    b. Implanted, tunneled, or direct?
    c. Cuffed or uncuffed?
    d. Tip position (for method, see Baskin et al[60]) and catheter functional status
    e. Method of catheter fixation, wound closure, and dressing
    f. Preventive therapy (eg, alcohol or antibiotic lock, heparinization, vitamin K antagonists, tissue plasminogen activator (tPA))
    g. Procedure time, radiation exposure (eg, fluoroscopy time or estimated radiation dose)
    h. Procedural complications (eg, venospasm, extravasation) and management
    i. Adjunctive therapies required (eg, papaverine, nitroglycerine, hot packs)
12. Complications, including
    a. Catheter-related infection (include dates)
        i Type (phlebitis; catheter-related sepsis; bacteremia; colonization; exit site, tunnel, or pocket infection, etc)
        ii Suspected (basis) or proven (method and results[175])
        iii Management (eg, antibiotics, catheter removal, repeat cultures)
        iv Result of catheter tip and blood cultures
        v Outcome
    b. Catheter dysfunction (include dates)
        i Type (eg, phlegmasia, extravasation or infiltration, fracture, fragment embolization, fibrin sheath formation, tip thrombus, etc)
        ii Management
        iii Outcome
    c. Vein injury or obstruction (eg, stenosis, thrombosis, fibrosis, or occlusion) (include dates)
        i Method of diagnosis or documentation
        ii Location and extent
        iii Related complications (eg, superior vena cava syndrome, post-thrombotic syndrome)
        iv Management
        v Outcome
    d. Dislodgment, migration, or malposition (include dates)
        i Method of diagnosis or documentation
        ii Site of malposition
        iii Management
        iv Outcome
    e. Other catheter-related complications
13. Catheter and venous pathway salvage procedures (include dates)
    a. In situ antibiotic therapy
    b. In situ lock therapy (eg, ethanol, antibiotic, amphotericin, echinocandins)
    c. tPA catheter thrombolysis
    d. Hydrochloric acid clearance
    e. Over-the-wire exchange
    f. Endovenous repositioning
    g. Blunt recanalization
    h. Sharp recanalization
    i. Venoplasty
    j. Stent or stent-graft insertion
14. Complications (include dates and additional details)
    a. Major (early [within 30 days of insertion] or late)
        i Admission to hospital for therapy
        ii Unplanned increase in level of care
        iii Prolonged hospitalization
        iv Permanent adverse sequelae
        v Death
    b. Minor
        i No sequelae
        ii Nominal therapy
        iii Short hospital stay (for observation)
    c. Procedurally related (within 24 hours of insertion)
15. Removal or replacement (reason and date; endpoint achieved?)

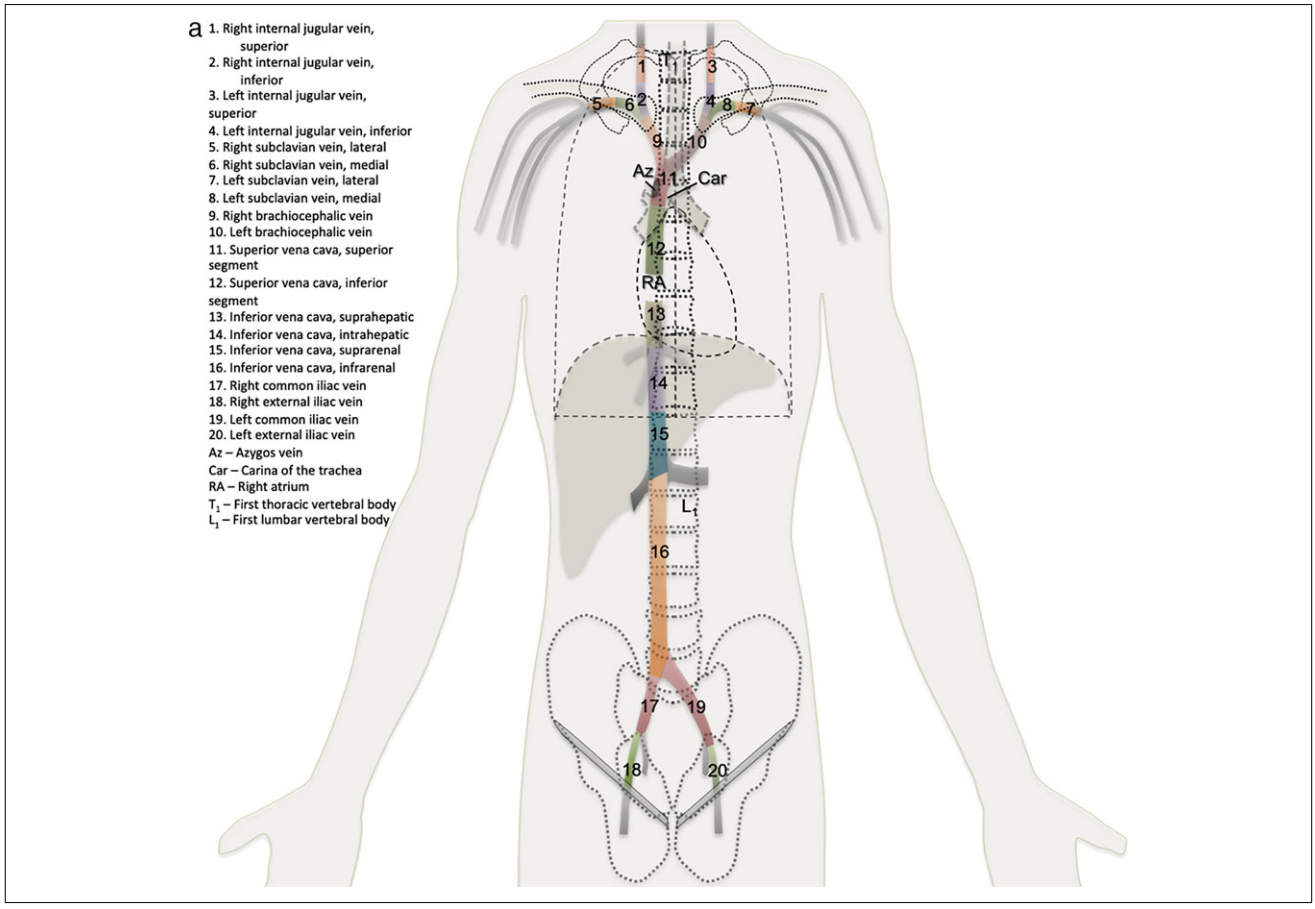

Figure A1. (a) Central venous anatomy. (b) Upper extremity venous anatomy. (c) Lower extremity venous anatomy.

Modified from Baskin, with permission. Baskin KM. *Venous Access and Related Procedures*. Temple M, Marshallack F, eds. Philadelphia, PA: Springer; 2014.

A3. Venous Anatomy

The central veins are illustrated in Figure A1A. Variant anatomy, communicating, and collateral veins are not represented. The common superficial (blue) and deep (green) veins of the extremities are illustrated in the right upper extremity in Figure A1B and the right lower extremity in Figure A1C. These are mirrored on the left. The numerous short perforating branches that pierce the superficial muscle fascia to join the superficial and deep systems are not shown. The superficial veins of the extremities form extensive and highly redundant networks, often duplicated or even triplicated, the visualizable components of which are variably expressed. The great (GSV) and small (SSV) saphenous venous trunks run within sheaths of dense perivascular connective tissue. Common branches of the superficial veins of the lower extremity may include anterior and posterior accessory saphenous veins that parallel the GSV and SSV, with their confluence near the saphenofemoral junction in the thigh and near the saphenopopliteal junction in the posterior calf. Other anterior and posterior tributary veins, sometimes only visualized when pathologically dilated, may join the saphenous veins at variable locations along their length and take their name from their position and drainage (eg, right posterior thigh tributary of the GSV, left anterior distal leg tributary of the SSV). Communicating veins may also join the GSV and SSV, the largest of which is the postero-medial communicating vein of the thigh, known as the vein of Giacomini.

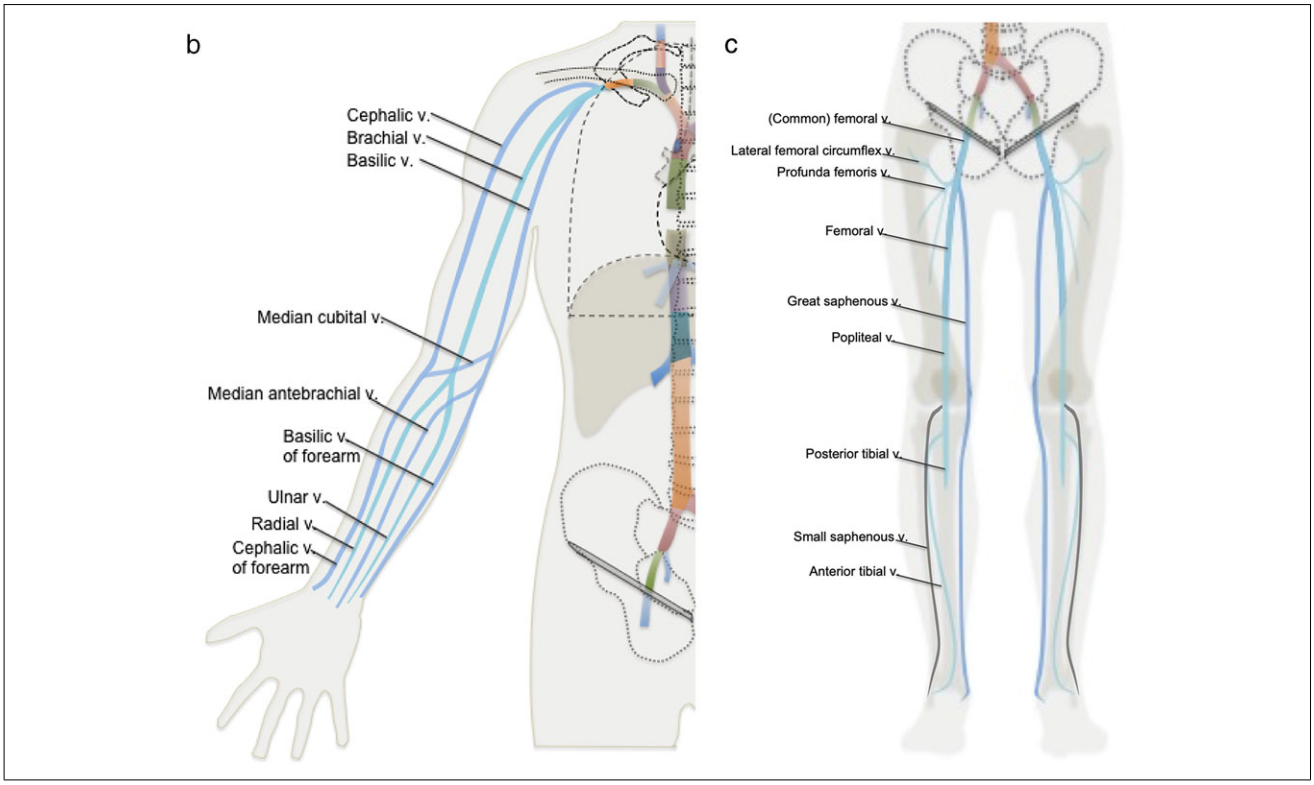

Figure A1. *Continued.*

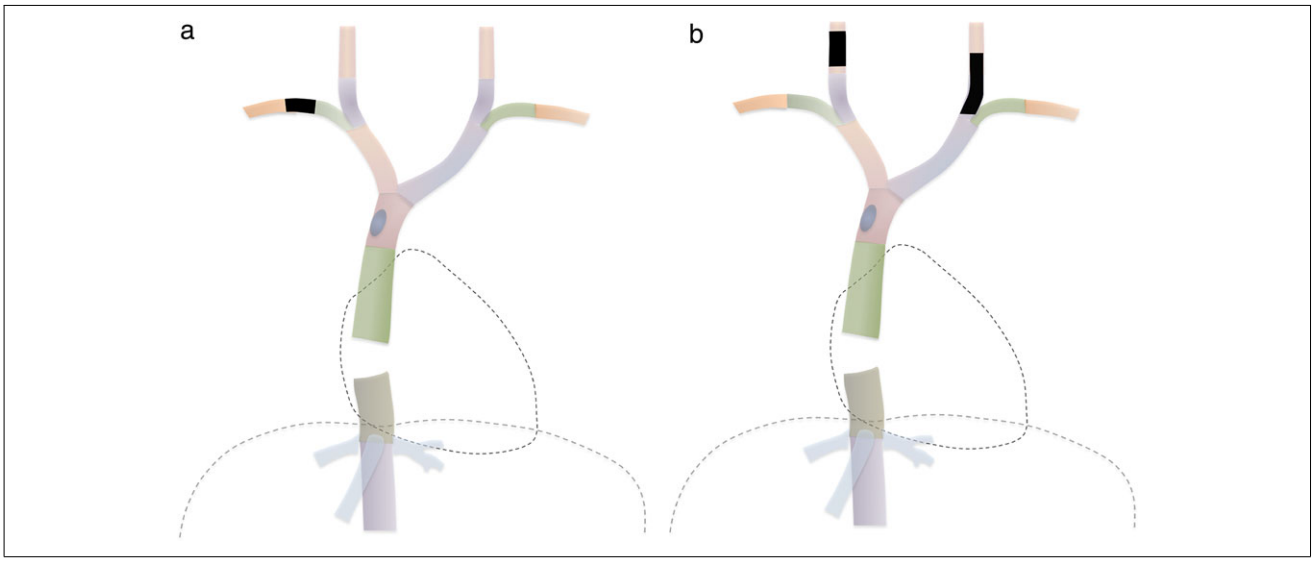

Figure A2. (a and b) SDO Class I venous obstruction: hemodynamically significant deep venous obstruction AND at least 1 preserved (uninvolved) conventional systemic venous pathway from each side.

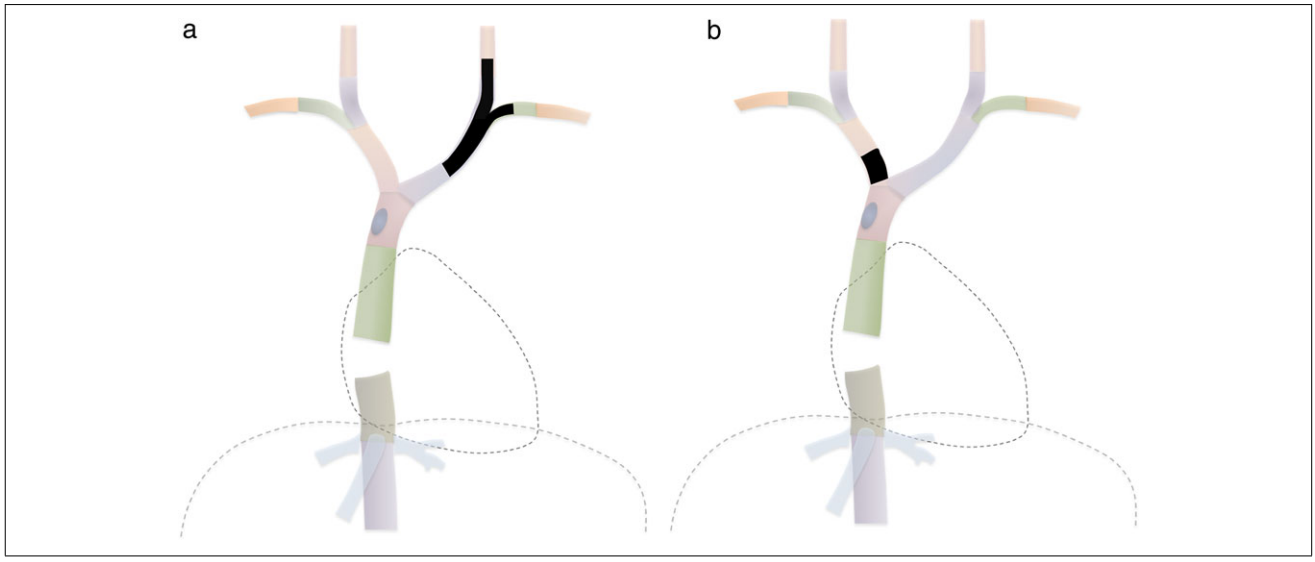

Figure A3. (a and b) SDO Class II venous obstruction: hemodynamically significant deep venous obstruction involving both pathways from 1 side, with preservation of contralateral thoracic pathways.

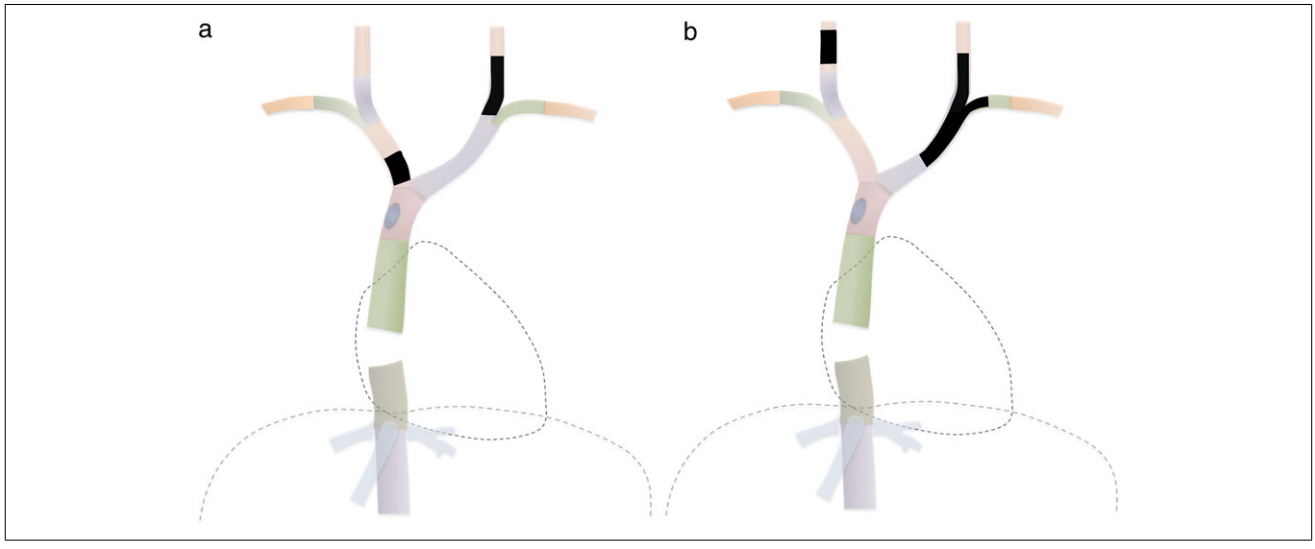

Figure A4. (a and b) SDO Class III venous obstruction: hemodynamically significant deep venous obstruction involving both pathways from 1 side, with preservation of at least 1 conventional thoracic pathway.

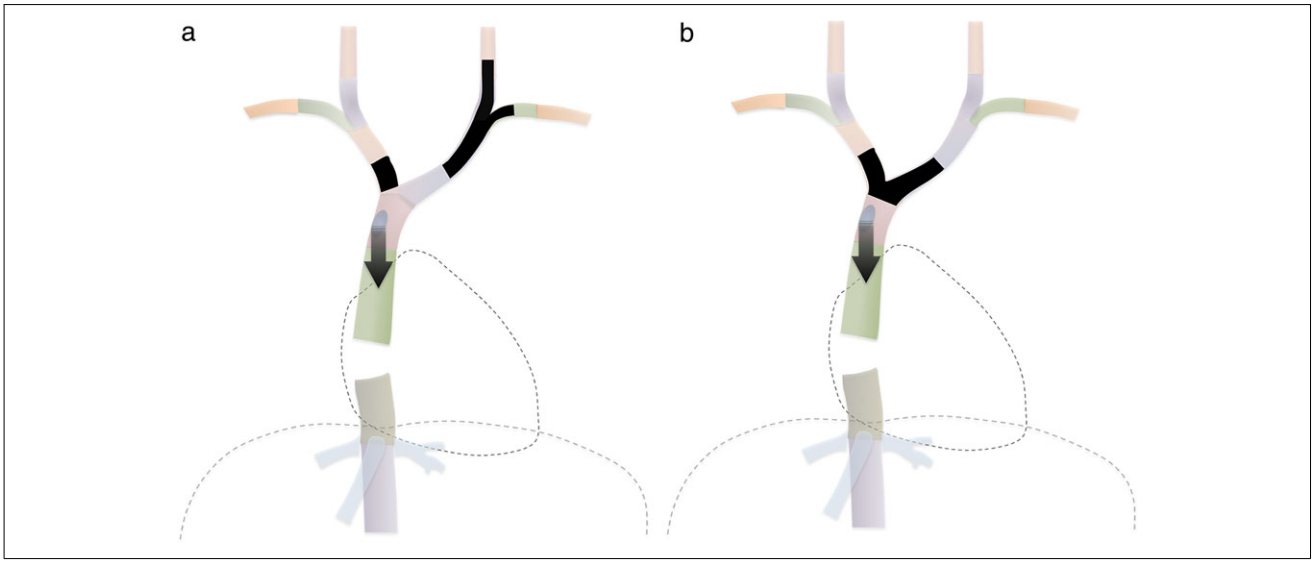

Figure A5. (a and b) SDO Class IV venous obstruction: hemodynamically significant deep venous obstruction with no patent conventional thoracic pathways, with preservation of antegrade flow from the azygos to the right atrium.

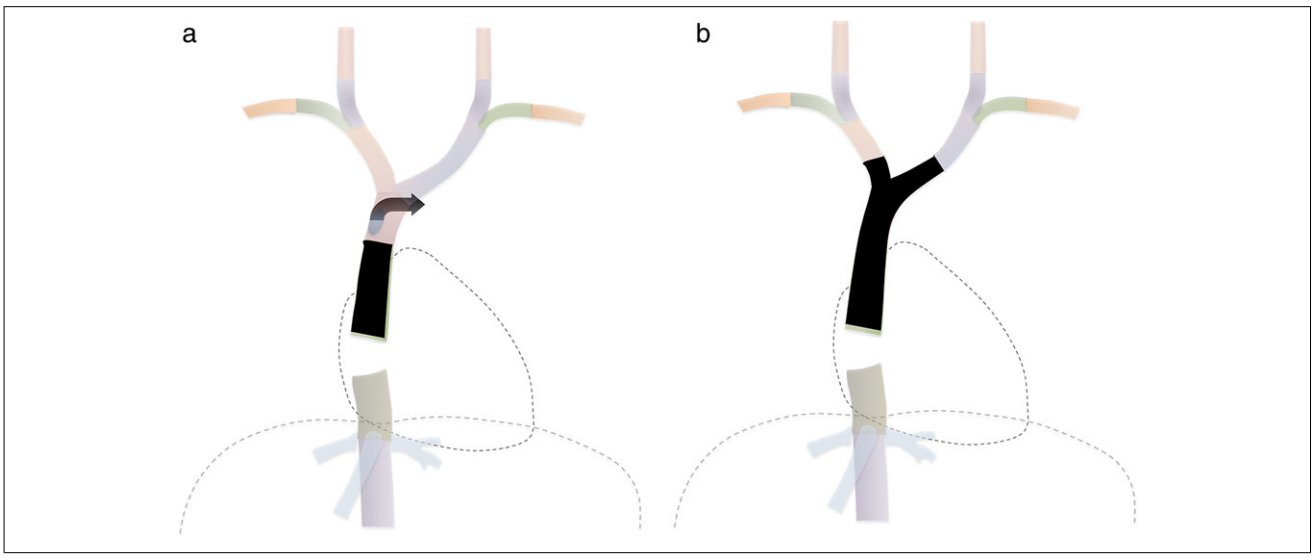

Figure A6. (a and b) SDO Class V venous obstruction: hemodynamically significant deep venous obstruction with no patent conventional thoracic pathways AND retrograde or static flow through the azygos (all blood returns to the right atrium from below the diaphragm).

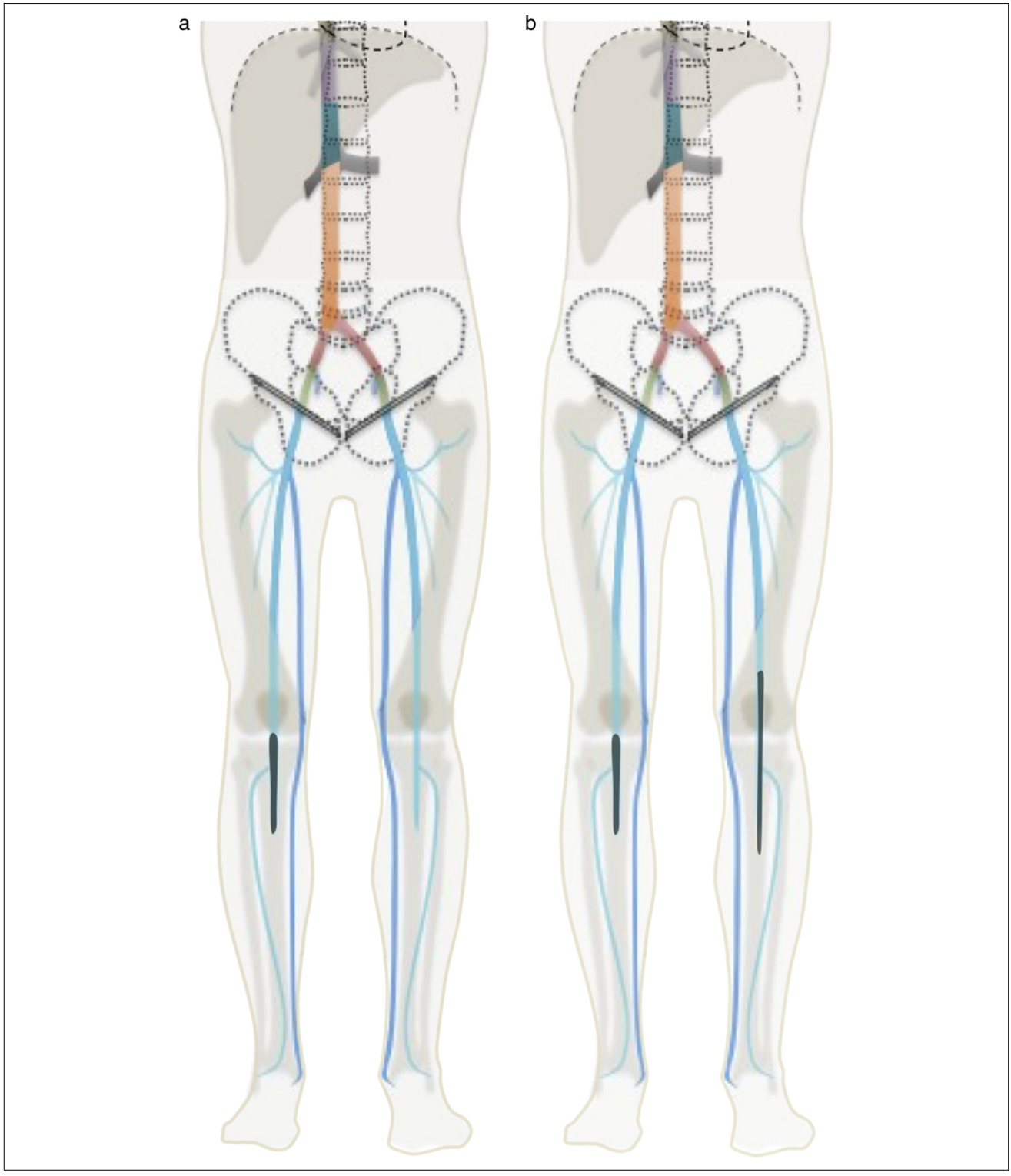

Figure A7. (a) IDO Class IA: Unilateral hemodynamically significant venous obstruction below the femoral vein without contralateral involvement. (b) IDO Class IB: Bilateral hemodynamically significant venous obstruction below the femoral veins.

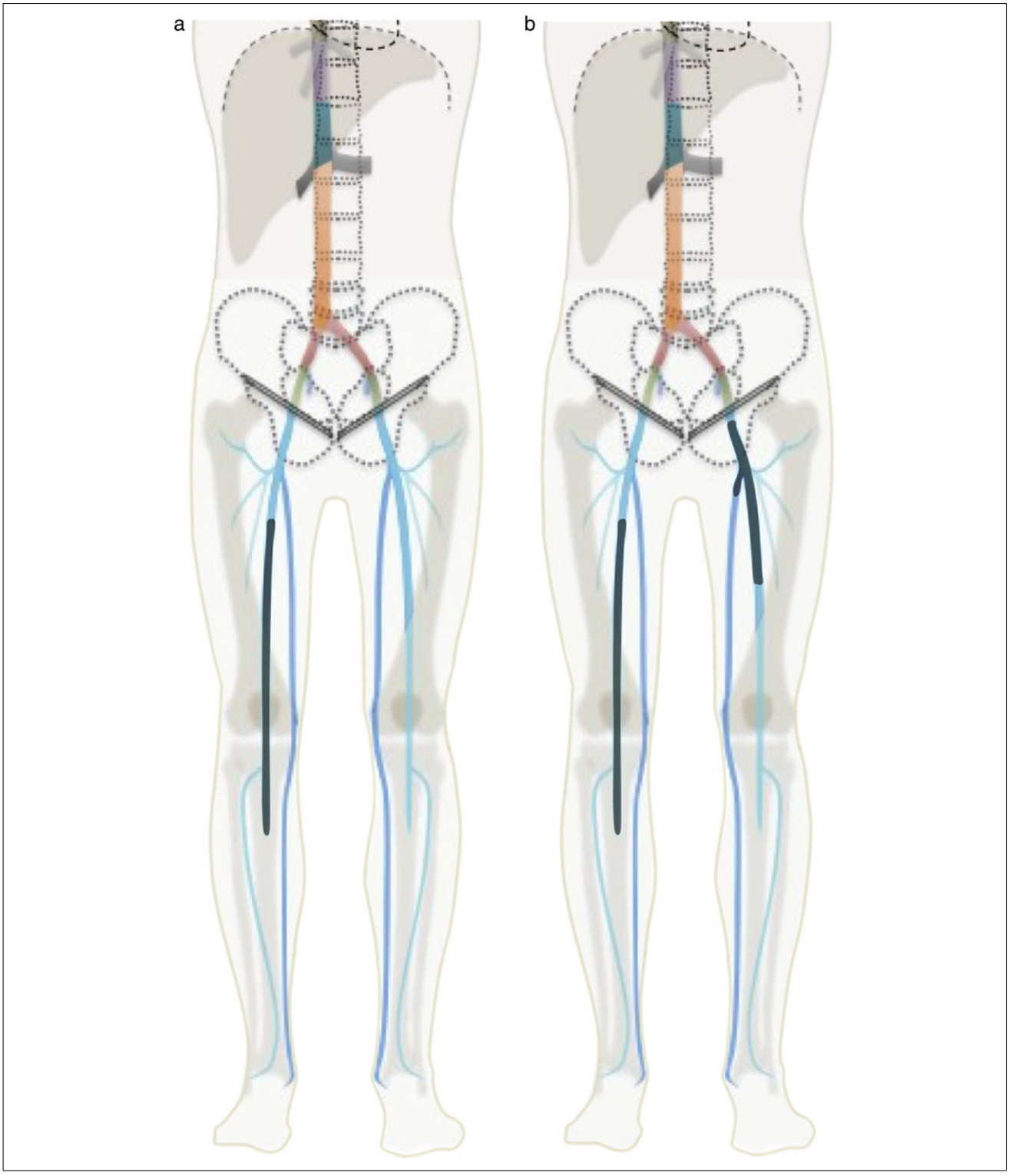

Figure A8. (a) IDO Class IIA: Unilateral hemodynamically significant obstruction between the popliteal vein and the inguinal ligament with patent contralateral flow proximal to the popliteal vein. (b) IDO Class IIB: Bilateral hemodynamically significant obstruction between the popliteal veins and the inguinal ligaments.

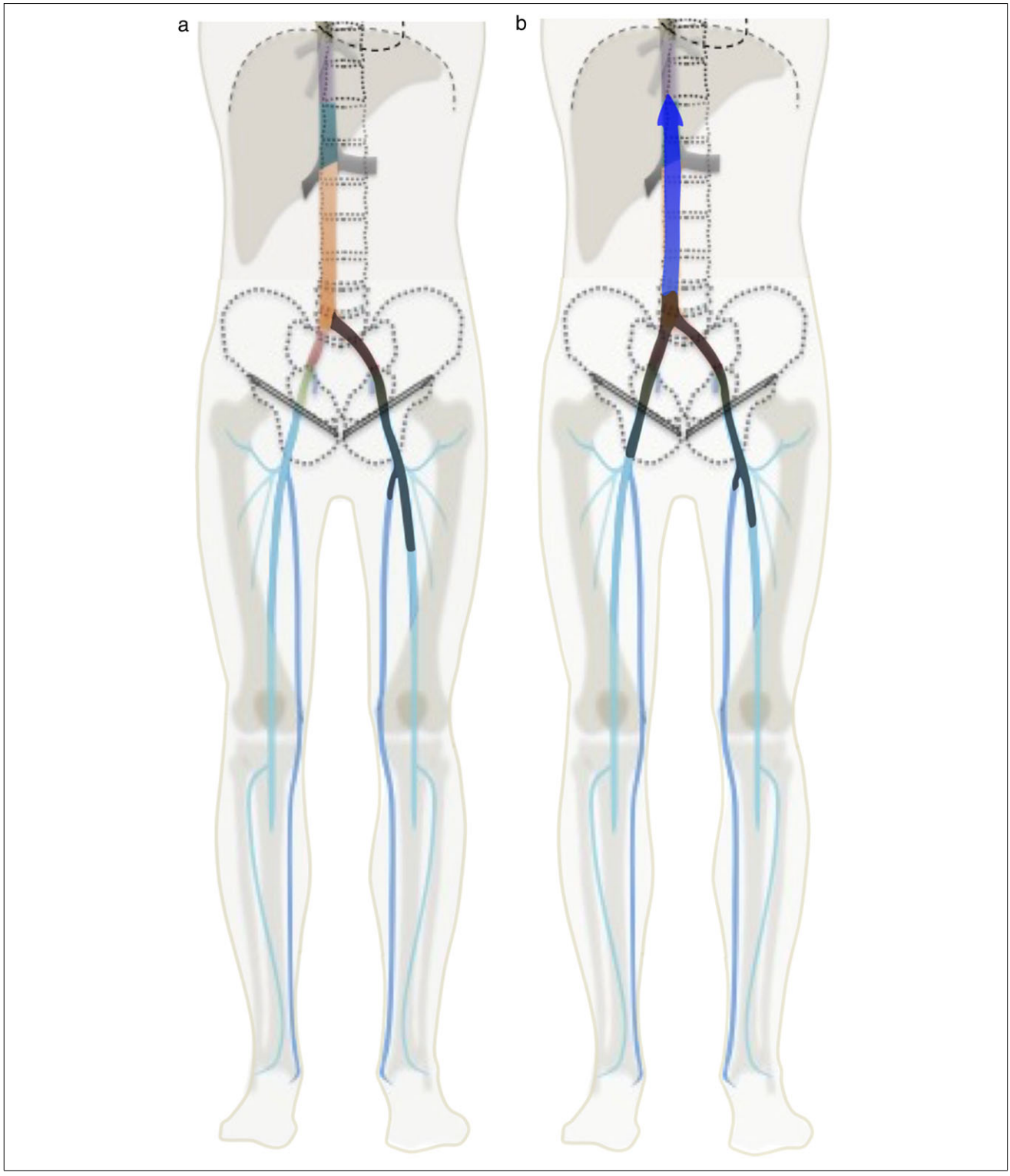

Figure A9. (a) IDO Class IIIA: Unilateral hemodynamically significant iliofemoral obstruction with patent flow proximal to the contralateral common femoral vein. (b) IDO Class IIIB: Bilateral hemodynamically significant iliofemoral obstruction with infrarenal inferior vena cava reconstitution.

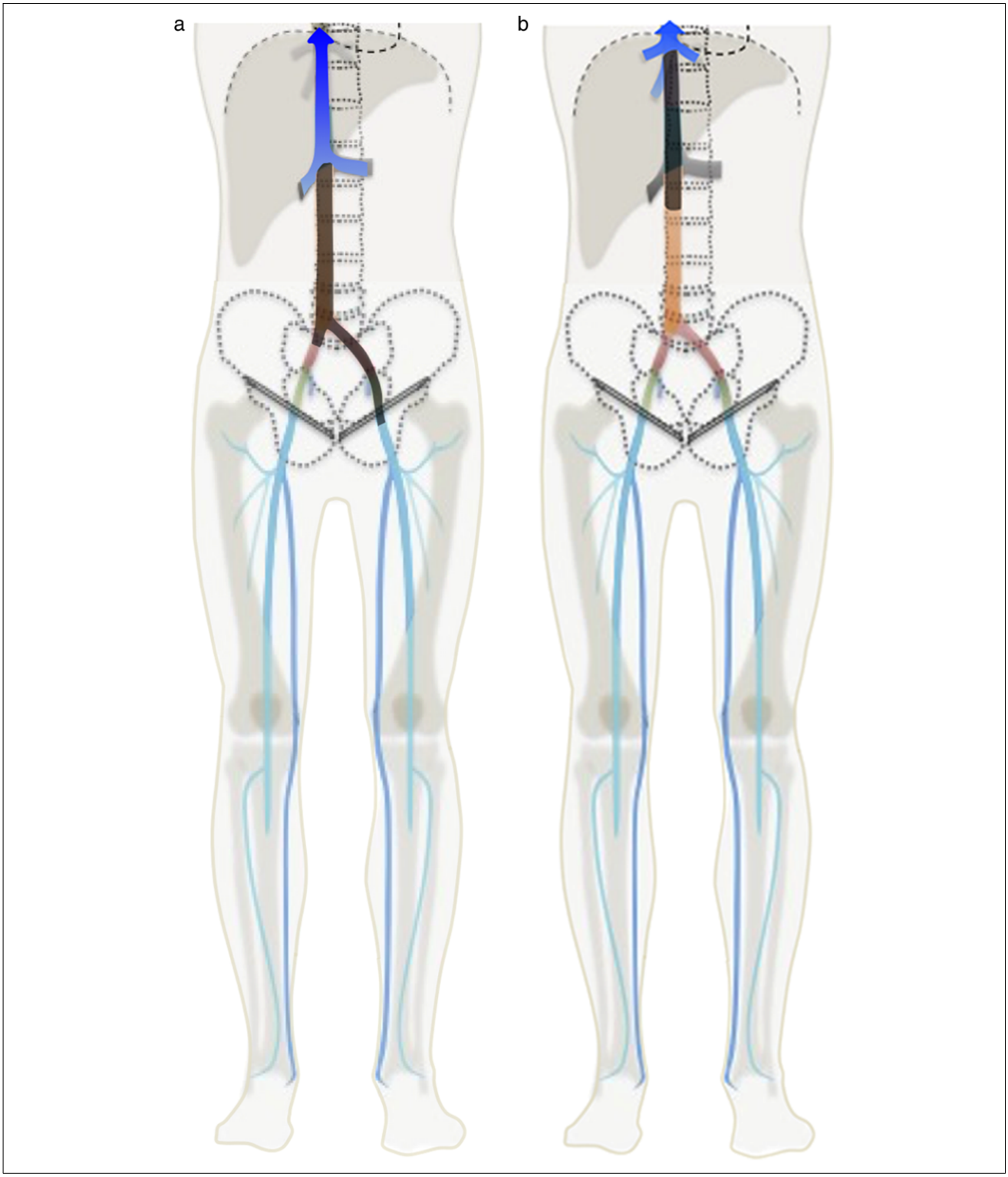

Figure A10. (a) IDO Class IVA: Hemodynamically significant infrarenal obstruction with venous return via renal capsular, portomesenteric, hepatic, and azygos/hemizygos collaterals. (b) IDO Class IVB: Hemodynamically significant suprarenal inferior vena cava obstruction with venous return via portomesenteric, hepatic, and azygos/hemizygos collaterals.

A4. VANGUARD Classification of Venous Obstruction

The obstruction of systemic central venous segments can be classified by the extent of involvement. Supra-diaphragmatic venous obstruction (SDO; Figures A2–A6) is reported separately from infra-diaphragmatic venous obstruction (IDO; Figures A7–A11).

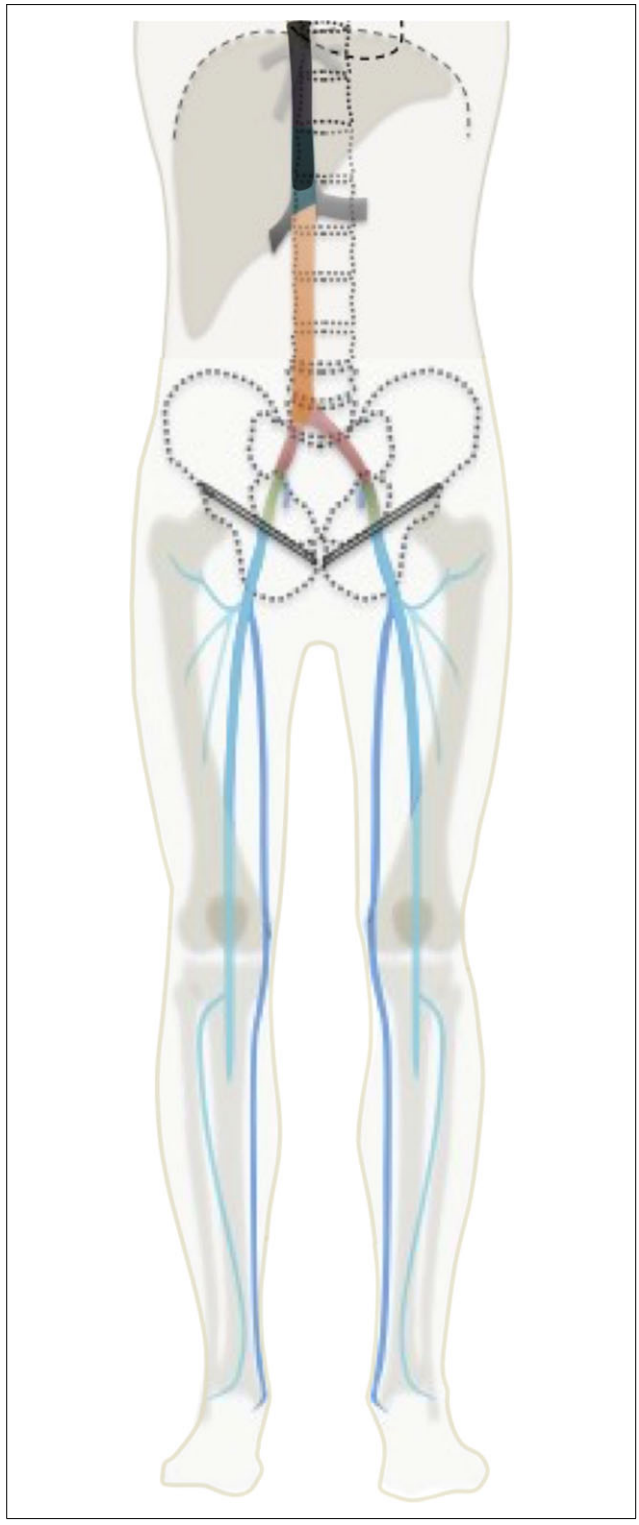

Figure A11. IDO Class V: Hemodynamically significant suprahepatic inferior vena cava obstruction with all venous return to the right atrium from above the diaphragm.