Review

JVA The Journal of Vascular Access

Implications for maintaining vascular access device patency and performance: Application of science to practice

The Journal of Vascular Access
1–10

DOI: 10.1177/1129729818820200
journals.sagepub.com/home/jva
SAGE

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Abstract

Introduction: Vascular access devices are commonly inserted devices that facilitate the administration of fluids and drugs, as well as blood sampling. Despite their common use in clinical settings, these devices are prone to occlusion and failure, requiring replacement and exposing the patient to ongoing discomfort/pain, local vessel inflammation and risk of infection. A range of insertion and maintenance strategies are employed to optimize device performance; however, the evidence base for many of these mechanisms is limited and the mechanisms contributing to the failure of these devices are largely unknown.
Aims/objectives: (1) To revisit existing understanding of blood, vessel physiology and biological fluid dynamics; (2) develop an understanding of the implications that different clinical practices have on vessel health, and (3) apply these understandings to vascular access device research and practice.
Method: Narrative review of biomedical and bioengineering studies related to vascular access practice.
Results/outcomes: Current vascular access device insertion and maintenance practice and policy are variable with limited clinical evidence to support the theoretical assumptions underpinning these regimens. This review demonstrates the physiological response to vascular access device insertion, flushing and infusion on the vein, blood components and blood flow. These appear to be associated with changes in intravascular fluid dynamics. Variable forces are at play that impact blood componentry and the endothelium. These may explain the mechanisms contributing to vascular access failure.
Conclusion: This review provides an update to our current knowledge and understanding of vascular physiology and the hemodynamic response, challenging some previously held assumptions regarding vascular access device maintenance, which require further investigation.

Keywords

Guidelines, intravenous, catheter, shear stress, thrombosis, venous

Date received: 20 April 2018; accepted: 20 November 2018

Background

Vascular access devices (VAD) provide vital access to the blood circulation to facilitate essential patient care and are used for diagnostic and therapeutic purposes including blood sampling, drug and fluid administration, parenteral nutrition and administering blood transfusions.[1,2] Up to 85% of hospital in-patients will require some sort of VAD during their admission, which may be inserted into the central or peripheral vasculature.[3] A range of clinical practice strategies and products exist to minimize the occlusion and thrombotic complications that arise from vascular device insertion and use. These include optimizing insertion technique, optimizing catheter-to-vein (C:V) ratio, innovative catheter material and design, systemic or localized use of anticoagulants and adequate device securement. Clinical guidelines make various recommendations

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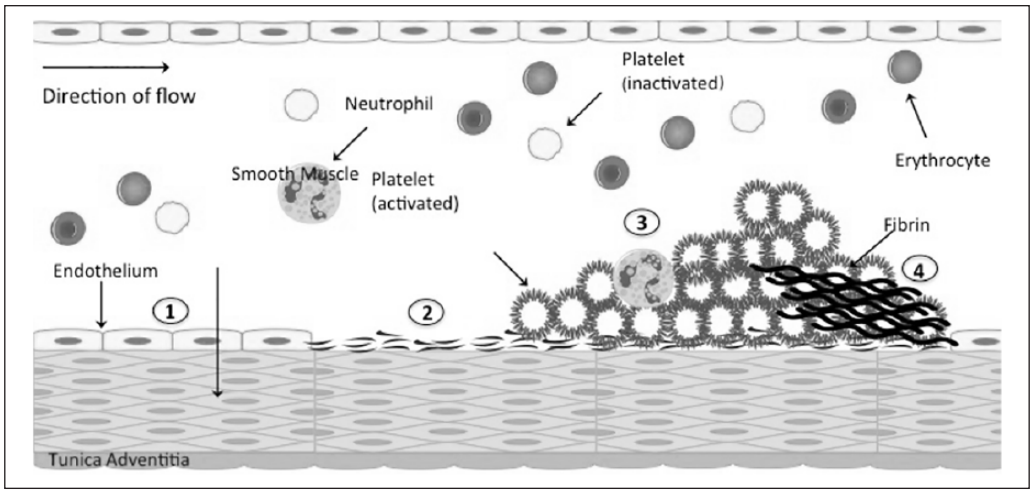

Figure 1. Hemostasis and clot formation: simplified description of the stages of clot formation: (1) vascular endothelium normally expresses an anti-thrombotic profile, which prevents platelets from binding and being activated. (2) Endothelial cells have been disturbed/damaged with collagen and extracellular matrix now exposed to the vessel lumen and blood components. (3) Activated platelets bind to the exposed collagen via vWF (not shown), in turn recruiting more platelets and other cells (e.g. neutrophils). (4) Finally, secondary hemostasis is initiated, leading to the formation of a fibrin meshwork, capturing red blood cells and forming a stable clot (thrombus).

related to these strategies with differing levels of supporting evidence.[4–6]

Some of these strategies have been developed from rigorous trial research. Other strategies have been developed that lack a rigorous evidence base or are based on assumptions and therefore may not yield their desired effect or have unwanted side effects. Complications related to VAD use persist at an unacceptable rate and it is clear other forces are at play that need to be considered. An enhanced and *contemporary* understanding of normal blood and vessel physiology and flow dynamics can be invaluable in informing practice and product development. This review will provide an up-to-date summary of vascular anatomy and physiology, blood flow and shear stress and describe their relevance to VAD patency. This may help explain and understand VAD-associated complications and failure and help to improve VAD maintenance practices and optimize patient outcomes. More specifically, this article revisits the normal physiology of the vein and blood as it pertains to intravenous (IV) insertion, use and maintenance with a view to using scientific principles and knowledge to enhance our understanding of possible causes of IV failure, which will inform future research and practice development.

Introduction to venous structure and function

Veins consist of three layers, the intima, media and adventitia. The intima, bordering the lumen of the vessel, consists of a continuous monolayer of endothelial cells resting on a basal lamina with the tunica media containing a concentric layer of smooth muscle cells which, together, serve two main functions: (1) to prevent hemostasis and (2) regulate vascular tone/diameter. In larger vessels, the intima may also contain a thin band of connective tissue beneath the endothelial basal lamina, which consists of collagen, elastin and vascular smooth muscle cells.[7]

Blood responses to vascular injury

Primary hemostasis

Blood is a two-phase fluid that comprises of red blood cells (RBCs), white blood cells (WBCs) and platelets which are suspended in an aqueous solution of plasma proteins and salts.[8] The hemostatic system maintains blood in a fluid state under normal conditions.[9] The endothelium, under normal conditions, releases thromboregulators (e.g. nitric oxide (NO)), which inhibit platelet activation and induce relaxation of vascular smooth muscle cells. However, if the endothelium is disrupted or traumatized, tissue factor (TF) is released and the highly thrombogenic subendothelial matrix, containing collagen and von Willebrand factor (vWF), is exposed.[9–11] This in turn induces the initial stages of blood clot formation known as primary hemostasis (Figure 1), where vascular spasm and platelet activation occurs. During this phase, collagen under the endothelium is exposed, activating platelets, which then secrete agents that activate neighboring platelets to self-aggregate and form a platelet plug 'sealing' the breach.[10,11]

Platelets are small (~2 μm) enucleated cell fragments derived from megakaryocytes with their primary physiological role being to recognize damaged/activated endothelium

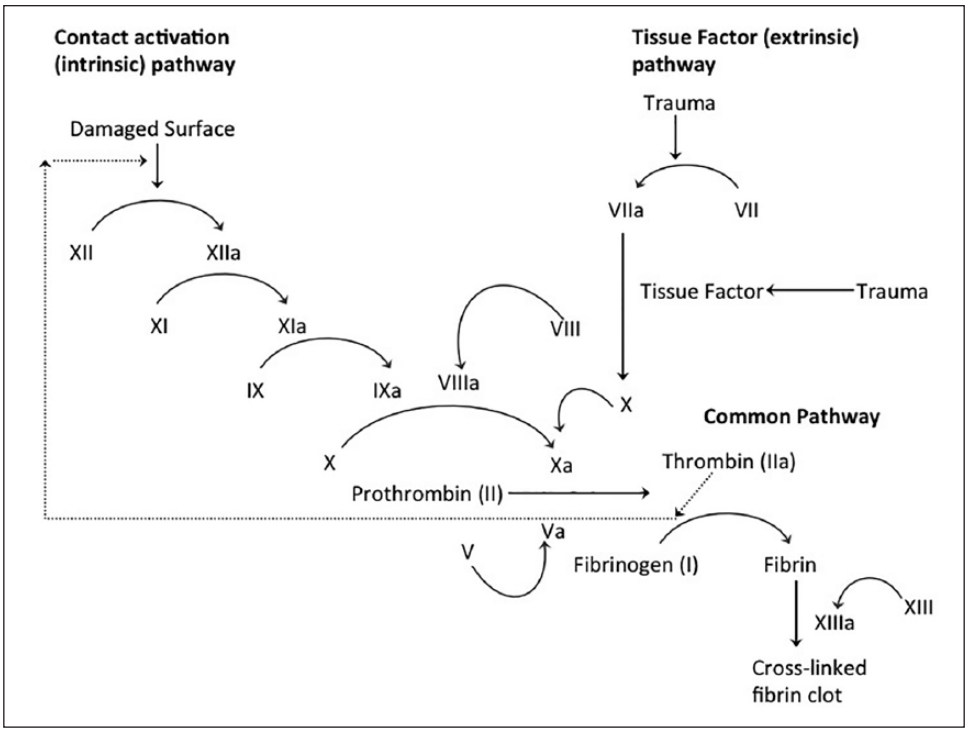

Figure 2. Coagulation cascade: the intrinsic and extrinsic pathways in the model of the coagulation cascade are outlined above. The initiation of this cascade occurs from vascular injury, each of the pathways converge at the common pathway, which generates thrombin, which in turn generates fibrin, leading to the generation of a fibrin meshwork.

and accumulate at sites of injury to prevent blood loss.[12] Circulating platelets are typically oval shaped; however, when activated, they undergo a morphological change to become stellate (star like) in shape increasing platelet surface area.[12] In response to activation, platelets increase the surface expression of a number of receptors (including P-selectin), which can encourage clotting and adherence of platelets to the endothelium and neutrophils.[12] The most important receptors include integrins that mediate the interactions between platelets and the extracellular matrix, collagen or other cells.[13]

Secondary hemostasis

Following primary hemostatic activation, the formation and stabilization of a blood clot occur by a process called secondary hemostasis. Secondary hemostatsis is associated with the initiation of blood coagulation, which occurs by the activation of the intrinsic and/or extrinsic pathways (Figure 2).[14] The intrinsic pathway is initiated when Factor XII interacts with negatively charged surfaces (e.g. phospholipids and collagen) in a process known as contact activation.[15] The activation of Factor XII is followed by the activation of Factor XI and Factor X.[15,16] Activation of Factor X (Factor X_a) occurs at a point where the intrinsic and extrinsic pathways converge (i.e. common pathway), with its role being to convert prothrombin to thrombin.[16] Thrombin (in the presence of co-factor Factor V_a) induces the formation of fibrin from fibrinogen (Factor I). Fibrin formation promotes the stabilization of the blood clot through two mechanisms (1) via its ability to capture RBCs and WBCs and (2) through its synergism with vWF, activating and promoting the adherence of additional platelets and thus supporting platelet adhesion.[17] Thrombin also interacts with the platelet receptor Protease-Activated Receptor 1 (PAR1), leading to further activation and release of platelet agonists, amplifying thrombus formation.[10,18] Platelets undergo a conformational change upon activation, promoting coagulation and supporting the production of thrombin and subsequent fibrin production, ultimately leading to the formation and stabilization of the clot.[17] The meshwork of fibrin is continuously broken down/remodelled via a mechanism known as fibrinolysis, thus preventing excessive hemostatic clot formation within the vessels and is also responsible for clot lysis once wound healing begins.[19] Activation of this system occurs simultaneously with the coagulation cascade via the activation of plasminogen, forming plasmin, which cleaves fibrin.[19]

Thrombus formation

Hemostasis is a finely regulated process, and it needs to occur only when required and for the required duration.

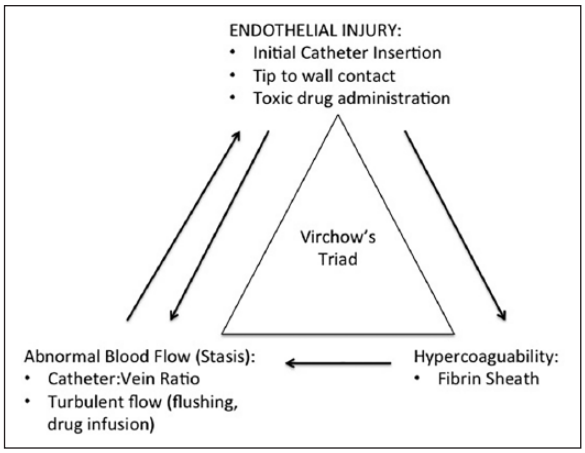

Figure 3. Virchow's triad: the three mechanisms proposed by Virchow's triad to induce thrombosis include endothelial injury, stasis and hypercoagulability. Each mechanism can independently lead to thrombus formation and each mechanism can also lead to the activation of additional mechanisms. The ways in which the insertion/maintenance of a cannula can contribute to Virchow's triad are also detailed.

However, if the regulatory mechanisms are disrupted, thrombus formation can occur, which is associated with increased morbidity and mortality. Thrombosis is pathological clot formation that results when hemostasis is inordinately and unnecessarily activated in the absence of bleeding. Both hemostasis and thrombosis share the same pathways. However, thrombosis can lead to serious vessel obstruction leading organ ischemia. The etiology of thrombosis includes hypercoagulability state, endothelial damage and turbulent blood flow which are collectively known as Virchow's Triad.[20] As such, cannulation with an IV catheter provides a suitable environment for thrombus formation. Indeed, catheter insertion induces endothelial damage, thereby releasing TF and exposing the subendothelial matrix at the site of insertion. Circulating platelets will recognize the subendothelial matrix, adhere and initiate activation process. The turbulent blood flow caused by the inserted catheter and/or injection and infusion practice can further promote thrombus formation.[21] This was illustrated in one bioengineering study using a three-dimensional (3D) computational model of a brachiocephalic vein with a peripheral intravenous catheter (PIVC) in situ. Disturbances in blood flow were observed, in particular, a recirculation region that appeared at the catheter tip and partially inside the catheter lumen.[22] Varying the flow rate (between 20, 40, and 60 mL/min) did not seem to have a significant effect on the flow field. A recirculation region in such a location can amplify local inflammatory and coagulatory processes and slowly dilute the catheter lumen with blood products that may clot and eventually block the lumen and render it non-functional.

Shear stress (and platelet activation/ inflammatory responses)

IV cannulation, and the injection and infusion of IV fluids can induce various levels of *shear stress* within vessels, which can activate blood components and blood vessels. Shear stress (in vascular access research) refers to the force applied by moving blood along the endothelial wall. This can be expressed as 'force' (dynes/cm^2 or the SI unit Pascal) or 'shear rate' (s^{-1}, calculated by $8\times$ velocity (cm/s) divided by diameter (cm)).

At normal venous flow rates, blood *likely* follows laminar flow, and the flow rate can be approximated with Poiseuille's Law, which states that the flow of fluid in a cylinder is related to the viscosity, the pressure gradient, and the length and diameter of the cylinder (vein).[23] However, when a catheter is inserted in a vein, Poiseuille's Law is no longer valid. The catheter creates a second frictional source, subsequently inducing annular (circular) flow whereby the blood flow stream surrounds the catheter while moving through the vessel.[24] Researchers have attempted to replicate this in vitro. Nifong and McDevitt[25] measured the flow rate of a blood analyte solution in glass cylinders containing steel wires that simulated the insertion of a peripherally inserted central catheter (PICC) into a central vein. Under these simulated conditions, mathematical and experimental results demonstrated that fluid flow is dramatically decreased by the insertion of a centrally located obstruction. The authors concluded that the insertion of an IV catheter may decrease flow and therefore shear stress.[25] The hypothesized reduction in blood flow along the endothelial lining would be expected to increase viscosity and potentially contribute to catheter-related thrombosis. This is congruent with the triad of Virchow (refer to Figure 3) that describes the three broad categories thought to contribute to thrombosis.[26] It should be noted that our understanding of the impact of cannulation on blood flow, shear stress, and thrombus formation within vessels is very limited and requires validation in human models.

Interestingly, Ploppa et al.'s study[27] helps us understand the blood response to low shear stress. In an effort to understand the paradoxical physiological response of leukocyte activation during sepsis, the researchers investigated WBC response using a simulated model of endothelial injury in a parallel plate flow chamber. Polymorphonuclear neutrophils (PMN) were perfused over human umbilical endothelial cells (HUVEC) under different conditions of activation and stress. Results demonstrated that PMN adhesion *increased* with *decreasing* shear stress ($<$2.0 dynes/cm^2/0.2 Pa). Furthermore, analysis of covariance (ANCOVA) showed a significant interaction between cell activation and shear stress. As soon as PMNs were activated, adhesion became increasingly dependent on shear stress.[27] This precedes the activation of

local innate inflammatory responses that accompany thrombosis and serves to amplify coagulation and removal of pathogens. This irritation and adhesion leads to the activation of WBCs and platelets, promoting inflammation and coagulation, potentially contributing to catheter failure.[27]

While it is currently understood that blood moves in a laminar or streamline flow, recent research suggests that (central) venous blood may move in a spiral pattern, similar to arterial blood flow. In arterial systems, spiral blood flow has been *suggested* as a normal physiological flow phenomenon to protect the vessel wall from damage by reducing laterally directed forces, reducing the pathology of thrombus.[28,29] Researchers reconstructed a patient-specific model based on computed tomography (CT) images and simulated the hemodynamic environment to allow assessment of the impact the VAD had on traditional parameters (wall shear stress and velocity), newer parameters (local normalized helicity (LNH), to represent the strength of helical or spiral flow) and clinical outcomes (thrombosis).[30] Results demonstrated a significant association between areas of low LNH (or loss of spiral flow) and incidence of thrombosis. The authors suggested that the presence of the VAD in the vein *may* interrupt the (spiral) pattern of blood flow. Therefore, it might be important to maintain helical flow in central veins after central venous catheter (CVC) insertion to decrease the occurrence of thrombosis.[30]

At the other end of the spectrum, because force exerted by blood flow or fluid injection changes as a result of changing blood velocity (shear rate), shear stress may also increase, potentially contributing to endothelial activation, dysfunction and injury. Endothelial injury triggers inflammation and coagulation, potentially leading to interstitial edema, thrombosis and catheter failure. Under conditions of normal physiological venous flow (5–15 cm/s) in the cephalic vein (0.6 cm diameter), shear rates are low ($<250\,s^{-1}$).[31] To assess the validity of catheter maintenance practices on inducing endothelial injury and platelet activation via increased shear, one must consider a clinical scenario of flushing a 22G PIVC at approximately 1 mL/s (e.g. 10 mL over 10 s). Saline emanating from a catheter with a 0.65 mm internal diameter (22G) generates velocities in excess of 300 cm/s and an approximate shear rate of $37{,}000\,s^{-1}$ at the ejection point. Dunkley and Harrison[32] tested the impact of exposing blood to shear rates of $\sim 5000\,s^{-1}$ for less than 1 s and showed increased platelet to leukocyte adhesion, an early and sensitive marker of platelet activation. Other research has noted that high shear rates over $10{,}000\,s^{-1}$ near the vessel wall also induces platelet adhesion to thrombogenic surfaces such as the subendothelial matrix via the interaction between platelet glycoprotein Ibα (GPIbα) receptor and plasma vWF.[33] Another simulated model experiment (cone and device) demonstrated that vWF was released from endothelial cells exposed to conditions of high shear stress (>8 dynes/cm^2 or 0.8 Pa)[34] Soluble vWF then binds to the exposed collagen to allow platelet adhesion at high shear rates. If platelets are exposed to shear rates in excess of $10{,}500\,s^{-1}$, as expected clinically, for longer than a few seconds, they become activated and can induce thrombi, if an appropriate matrix exists for them to bind (i.e. collagen). Activated platelets undergo a series of biochemical and signalling reactions that result in the release and formation of soluble platelet agonists including adenosine diphosphate (ADP), epinephrine and thrombin.[35] The release of these mediators recruit more platelets and form a platelet-rich thrombus resulting in firm adhesion and aggregation via the interaction of immobilized vWF and fibrinogen with platelet glycoprotein IIb/IIIα (GPIIb/IIIα) receptor (Figure 4).

In summary, although there is much to be learned regarding shear stress experienced by blood vessels and components, existing literature from peripheral fields supports the notion that IV catheter insertion and high pressure flushing or infusion may activate platelets and contribute to thrombus formation and inflammatory response.

Vascular access insertion and maintenance practice

A range of clinical practice strategies and products exist to minimize thrombotic complications that can arise from vascular device insertion and maintenance. These have been trialled and implemented with mixed success.

Insertion

High-quality (levels I and II) evidence has demonstrated that ultrasound-guided location and insertion can improve first insertion success and reduce complications (and related trauma) for both peripheral and central devices.[36–38] Observational studies have demonstrated the association between C:V ratio and venous thromboembolism (VTE) risk.[39,40] These suggest that a 45% C:V ratio was the optimal cut-off to reduce the risk of VTE. And in 2016, the Infusion Nurses Society (INS) Standards of Practice set a recommendation that the catheter-to-vessel ratio can increase from 33% and now take up to 45% or less of the vessel diameter.[4] However, rigorous trial evidence is required to underpin firm practice recommendations moving forward.

VAD material and design

Significant investments have been made in both production and evaluation of different catheter materials and design with the aim of reducing infection and thrombosis. However, methodological issues related to sample sizes, populations and outcome variable measurement and

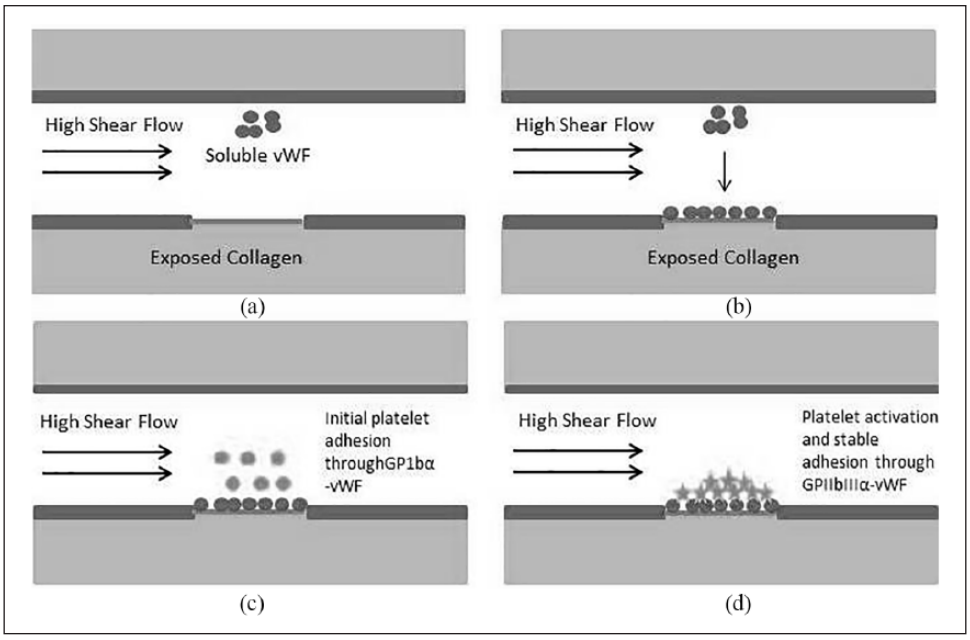

Figure 4. A summary of platelet activation and aggregation in conditions of high shear rates (i.e. during flushing). (a) Blood flows in regions with exposed collagen in high shear rates, (b) high shear conditions uncoil soluble von Willebrand Factor (vWF) which in turn stretches along the exposed collagen, (c) circulating non-activated platelets bind to the tethered vWF via glycoprotein Iba (GPIbα) and begin to activate, and (d) activated platelets release soluble agonists and vWF activating glycoprotein IIb/IIIa (αIIbβ3).

reporting have made it difficult to make conclusive recommendations about the efficacy of these interventions.[41–45] A large randomized controlled trial (RCT) of different impregnated CVCs (n=1859) in pediatrics demonstrated a reduced risk of bloodstream infection with antibiotic impregnated catheters compared to standard or heparin-bonded catheters. However, no significant effect on time to thrombosis or thrombosis risk was observed with heparin-bonded catheters.[46] A pilot RCT (n=150) in pediatrics comparing polyurethane PICC with clamp to BioFlo® PICC with antithrombogenic material (Endexo®) and pressure-activated safety valve (PASV®) demonstrated that significantly fewer patients with BioFlo® had PICC complications during use.[47] But overall, more appropriately powered, rigorous trials are required to demonstrate clinical efficacy and cost-effectiveness of different catheter materials and design.

Systemic anticoagulation

There is limited good quality data available for the systemic anticoagulation for either prevention or treatment of catheter-related thrombosis. Recommendations are therefore largely extrapolated from data from studies in patients with cancer or lower limb deep venous thrombosis (DVT).[48] A systematic review of 12 RCTs (n=2823) evaluating effect of anticoagulation for people with cancer and CVCs revealed a statistically significant reduction of symptomatic DVT with heparin and asymptomatic DVT with vitamin K antagonist (VKA) compared to no coagulation.[49] Heparin was associated with a higher risk of thrombocytopenia and asymptomatic DVT when compared with VKA. However, the findings did not rule out other clinically important benefits and harms. In lieu of further evidence, the use of systemic anticoagulation should balance the possible benefit of reduced thromboembolic complications with the possible harms and burden of anticoagulants.

Flushing and locking

Current clinical guidelines and practice recommends devices be flushed, locked and/or infused in order to maintain catheter function and patency.[4–6] The rationale for flushing and locking practice is that this will prevent accumulation of biological and exogenous material, which could otherwise contribute to occlusion and device failure.[4,50–52] The use of anticoagulant (usually heparin) to prevent occlusion of VADs has been traditionally used in the past, based on a not unreasonable suspicion of effectiveness. However, the process of in vivo catheter occlusion is complex and multi-factorial, not simply based on blood clotting or deposit of blood proteins or cells.[52] Thrombotic occlusion only accounts for only 58% of occlusions. Intraluminal occlusion can also be secondary to mechanical (e.g. kinks, pinches) and chemical (e.g. drug precipitate, lipid build-up from parenteral nutrition) causes.[53] A systematic review of 11 trials in adults (n=2392) showed that locking with heparin had little, if any effect on central venous access devices (CVAD) patency.[54] A systematic review of heparin flushing solution for CVCs in adults (six trials, n=1433) found

no conclusive evidence of important differences when heparin intermittent flushing was compared with 0.9% sodium chloride flushing for CVC maintenance in terms of efficacy or safety.[55] Notably, the dosages of heparin were significantly heterogeneous (10–5000 IU/mL) and the patient follow-up significantly variable (20–180 days) making generalisability challenging.

A systematic review of heparin for flushing of CVCs in the pediatric population highlighted the lack of high-quality evidence (three trials, n = 245) to be able to draw any firm conclusions.[56] For PIVCs, a recent cluster RCT reported reduced occlusion and phlebitis with heparin flushes.[57] However, it was a small, single-centred study, and analysis was not adjusted for the clustering design used. Overall, the lack of quality and sufficiently powered trials on the merits and safety of heparin as a flush or lock solution means that more high-quality trials are required. In addition, researchers should consider rigorous evaluation of other lock solutions (e.g. tetrasodium citrate, thrombin inhibitors, plasmin activators). Leading guideline bodies do not recommend the routine use of anticoagulant lock or flush solutions, with the exception for CVCs in pediatrics.[4,5,58] Though this recommendation again lacks a firm evidence base. Solutions recommended to clear acidic or alkaline drug precipitate and lipid residue include hydrochloric acid, sodium bicarbonate and ethanol, respectively.[4] However, there is little, no or low-level evidence to support this.

Research to date concerning IV flushing technique is limited to laboratory in vitro studies[59] and small clinical trials.[60–62] In vitro studies have demonstrated the potential benefit of flushing on rinsing the catheter or device and preventing build-up of protein and biofilm.[63–65] However, results from clinical studies indicate variable flushing practice and ongoing high failure rates.[2,61,66–71] Currently, there is no definitive evidence to advise on optimal frequency, volume or mode of maintenance strategies to reduce VAD failure. A reduction of reflux through clamping and/or use of neutral or positive displacement needleless connectors is considered good practice, but there is little definitive evidence linking this to occlusive events.[52] Previously summarized bioengineering and pre-clinical studies indicate that it may not be the flush *per se*, but rather excessive injection, infusion flow or pressures (shear force) that damage the vessel intima, by direct pressure and/or by hemodilution activating the platelets or endothelium. While we wait for vital clinical trial evidence indicating which flushing or locking practice is associated with optimal VAD function/dwell time and reduced failure, a more comprehensive understanding and application of scientific principles and physiology can inform our research and practice development. In the meantime, preclinical studies suggest that clinicians should adopt approaches to minimize supra-physiological states (where possible and if not otherwise clinically indicated), to minimize physiological stress and damage responses.

Dressing and securement

Effective dressing and securement of VADs should further prevent many complications, such as dislodgement from the vein and micromotion of the device within the vessel, which precipitate venous inflammation, occlusion, and entry of skin site bacteria into the entry site. A systematic review for dressing and securement of CVCs (22 studies, n = 7346) demonstrated the value of medication-impregnated dressing products in reducing the incidence of central VAD-related bloodstream infection relative to all other dressing types.[72] However, most of the studies were conducted in intensive care, and the impact on failure (including occlusion) was not studied. A systematic review of dressing and securement devices for peripheral venous catheters (six RCTs, n = 1539) revealed that there is no strong evidence to suggest any one dressing or securement product for preventing peripheral venous catheter failure.[73] Further, a recent large, multi-site RCT testing, four different dressing and securement products showed no significant differences in PIVC failure between the four intervention groups and highlighted the need for further innovation in dressing and securement methods.[74]

Summary of vascular access practice

In summary, many strategies, practice recommendations and products exist to reduce risk of VAD failure through occlusion and thrombosis. However, the recommendations are either not universally adopted (and desired impact not achieved); lack a rigorous evidence base, or have unwanted side effects. Complications and failure with VADs persist at an unacceptable rate and it is clear other forces are at play that need to be considered.

Revisiting our understanding of blood, vessel physiology and biological flow dynamics can help to conceptualize their response to VAD insertion and maintenance practices. This body of knowledge can assist in directing our research to improve our understanding as to why VADs fail due to thrombosis and occlusion and is therefore imperative to maximize VAD patency. A key factor in regulating the dynamics of thrombus formation and development is blood rheology (fluid/flow dynamics), with alterations in the local environment representing a critical factor to the regulation of platelet deposition and thrombus growth.[75] The insertion of a cannula into a vein would disrupt this environment and related flow through vessels, as modelled recently in the upper extremity veins.[25–27,30] An inserted catheter may decrease shear stress along the endothelium due to restricted flow, which in turn may increase blood viscosity causing further reductions in blood flow.[25] The risk of thrombosis and endothelial damage increases with the size of the catheter inserted (and thus the C:V ratio), which may be related to the risk of mechanical damage and the reduction in blood flow.[25,39,40] When venous flow rates decrease, neutrophils

can adhere to the endothelium, leading to the activation of platelets.[25,27,76] Thus, it is likely that decreased flow rates may independently contribute to thrombus formation and thrombophlebitis secondary to insertion of indwelling catheters, by facilitating platelet and leukocyte adhesion to the catheter and endothelium.[25]

Occlusion of catheters can also occur secondary to thrombosis and the formation of a fibrin sheath on the catheter surface.[77–80] Fibrin sheath formation has been associated with insertion of CVCs, which may lead to the activation of platelets and subsequent thrombus formation.[25,81,82] Fibrin deposition typically occurs in two places, the first being the area of injury (insertion site), which then propagates down the outer catheter wall. The second site is located where the tip of the catheter comes in contact with the vessel wall.[83] Thrombi obstructing the catheter lumen can be temporarily relieved when positive pressure is applied to the syringe through infusion or flushing of the catheter;[84] however, these thrombi are likely to grow over time and contribute to catheter failure. An enhanced and contemporary understanding of normal blood and vessel physiology and flow dynamics would be invaluable in informing practice and product development.

Conclusion

In summary, much of VAD insertion and maintenance practice is variable and/or is supported by a limited evidence base. The impact of these practices is based upon empirical evidence and has largely not been definitively explored and linked to clinical outcomes. Furthermore, the interaction between the VAD and the vessel and blood components has not been considered or fully explored in vivo. Therefore, studies aimed at minimizing risk of VAD failure need to explore the interaction between VAD insertion, material, design, infusion and injection, and endothelial dysfunction, platelet function and coagulopathy, and impact on biofilm. There is a definitive need to promote transdisciplinary research and collaboration to explore and understand the impact of insertion and flushing on the vein. In addition, rigorous, independent testing of different VAD maintenance strategies is required to inform policy makers and clinicians of best practice and products.

Acknowledgements

The authors acknowledge Mr. Jarod Horobin for providing advice and review concerning the assessment of shear stress and related parameters. Mr. Eugene Slaughter is also acknowledged for his editorial, proofreading and content review.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The authors are members of the Alliance for Vascular Access Teaching and Research Group (AVATAR). AVATAR research is supported by competitive government, university, hospital and professional organization research grants as well as industry unrestricted donations, investigator initiated research/educational grants and occasional consultancy payments from the following companies: 3M, Adhezion, Angiodynamics, Bard, Baxter, BBraun, Becton Dickinson, Carefusion, Centurion, Cook, Entrotech, Flomedical, Hospira, Mayo, Medtronic, ResQDevices, Smiths, Teleflex, Vygon. This manuscript is independently prepared and reflects no commercial entity nor promotes particular products unless these are supported by research data.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

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