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Catheter-Related Infection and Thrombosis: A Proven Relationship

A Review of New Technology to Reduce Catheter-Related Infection and Thrombosis

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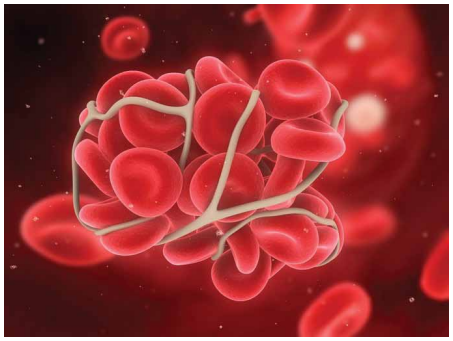
Introduction

The two most serious complications associated with peripherally inserted central catheters (PICCs) are infection and thrombosis. While infection rates with PICCs are similar to those of non-tunneled central venous catheters (CVCs),[1] reported rates of thrombosis are higher with PICCs, especially those that are a larger diameter.[2] Various preventive programs help to avert central line-associated bloodstream infections (CLABSI), but few address the issue of thrombosis.



Fibrin, a thread-like protein, lumps blood cells together resulting in a thrombus.

Defining the Problem

When thrombosis occurs in association with a PICC, concerns involve short-term and long-term sequelae with increased morbidity, mortality and cost. The presence of an indwelling CVC is the strongest independent predictive factor for thrombosis in the arm[3] and is considered the main risk factor for occurrence of upper extremity deep vein thrombosis (UEDVT).[4]

Little is reported in the literature regarding the impact and possible loss of vein access related to thrombosis. What we do know is morbidity and mortality ranges are 15-50% and are statistically equivalent to lower extremity deep vein thrombosis.[5,6] Post-thrombotic syndrome occurrence with DVT of the arm may be as high as one out of every three patients.[7]

The prevalence of CVC-associated UEDVT verified by venogram is 27-66%.[8] Veins most commonly affected are the basilic, brachial, axillary, subclavian, internal jugular and the innominant / brachiocephalic veins. Other risk factors are malposition, malignancy, obesity, two or more insertion attempts, a second CVC and the absence of heparinization.[9]

Radiographic studies show that up to 90% of cellular deposits form on the surface of the catheter, creating a fibrin sheath within the first 24 hours after insertion.[10] Upper extremity thrombosis associated with PICCs is becoming more common with the increased use of triple lumen catheters.[2] **Cancer patients with a CVC have an 1100-fold increased risk of developing UEDVT in the arm.[11]**

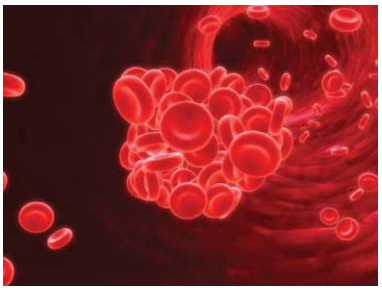
Symptoms

Symptoms most common to PICC-induced UEDVT include swelling, discomfort, functional impairment and pain to the arm.[12] Other symptoms are the occurrence of pulmonary embolus (36%), chest pain, cough, syncope and dyspnea.[13,14] Those patients who progress to post-thrombotic syndrome have significant functional disabilities and a reduced quality

of life,[15] which may translate into greater liability risk for hospitals. According to Baskin, et al. (2009), the mere presence of catheter thrombosis can set the stage for catheter-related infection.[16]

Infection and Thrombosis

The relationship between thrombosis and infection has been established with significant colonization in areas of clot, and higher rates of catheter-related sepsis and catheter-related septicemia when thrombosis is present. In animal studies, fibrin sheath formation around central venous catheters significantly promoted colonization, catheter-related infection and persistent bacteremia.[17,18] **Colonization rates are almost double in catheters with thrombosis (32% vs. 19.4%); catheter sepsis rates are more than double (19% vs. 7%); and septicemia rates are more than triple (11.6% vs. 3.6%) when thrombosis is present.[9]**



Embolization occurs when the thrombus breaks free from the vascular wall and becomes mobile.

According to the American College of Chest Physicians (ACCP Guidance, 2012), for most patients with UEDVT, catheter removal is not recommended if the device is functional and there is continued need for use. The damage associated with thrombosis is already done, but concerns over greater risk for infection remain. The rate of recurrence of upper extremity thrombosis if the catheter is removed and immediately placed into another site may be as high as 86%.[19]

The instances when a catheter should be removed are:

1. If there is active line sepsis
2. If the thrombosis is greater than one week old
3. If the thrombosis measures more than 2 cm
4. If the patient is unable to receive anticoagulants[20,21]

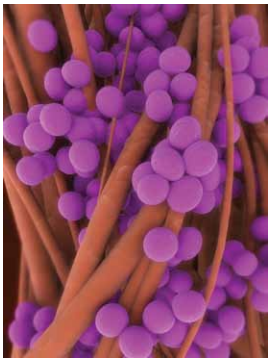
Functional catheter problems occur in 58% of all reported complications affecting 28-33% of all central venous catheters.[22,23,24] With high rates of fibrin formation on every catheter and significant incidence of thrombosis plaguing our central venous catheters, we have cause to worry about the impact on patient health.

Clinical Implications and Prevention

Even a small percentage occurrence of thrombosis or infection is significant to patient morbidity and increased cost, given that there are more than six million CVCs inserted each year in the United States alone, and that two million of those are PICCs. “There appears to be a close association between catheter-related thrombosis and catheter-related infection, and as such, it behooves the nurse to utilize strategies to prevent both,” says Nadine Nakazawa, former President of the Association of Vascular Access.[25] In the Oncology patient, the risk of infection and thrombosis is even more pronounced, as observed in the following statements:

- “CVC-related thrombosis and infections are frequently occurring complications … in patients with hematological malignancies … and can therefore not be seen as separate entities”[26]
  -Dr. R.S. Boersma
- “…measures for preventing arm DVT in patients with cancer should be considered as a first-line aim for Oncologists”[27] - *Dr. FJ Munoz*

A multi-level approach should be applied that focuses on education about guidelines, evidence, measurement of practice compliance and application of proven catheter technology. This has to happen if we are to reach goals such as those set by the Association of Practitioners in Infection Control and Epidemiology (APIC) in “Targeting Zero” campaign (www.apic.org/About-APIC/Vision-and-Mission). Organizations such as the Centers for Disease Control and Prevention (CDC), the Society of Healthcare Epidemiology of America (SHEA) and the Institute for Healthcare Improvement (IHI) have led the way to better practices and improved outcomes by establishing evidence-based directives. Other groups such as the Joint Commission, through its National Patient Safety Goals (NPSG), have sought to improve infection prevention practices by requiring education, monitoring and the use of certain technologies to reduce preventable negative outcomes. The NPSG, along with the SHEA Strategies, direct hospitals to institute education regarding CVC management and infection prevention for medical and nursing staff, upon hiring and at least annually.



Staphylococcus aureus, a common pathogen associated with catheter-related infection.

Optimized Education

Research demonstrates that patient outcomes can be improved through implementation of basic prevention practice educational programs. It has also been shown that subsequent infections can be reduced with each repetition of infection prevention programs.[28,29] According to researchers in the Coopersmith study, the most cost-effective means to reduce infection is through education of nurses and physicians, but specifically intensive care (ICU) nurses.[28] This educational intervention study conducted at Barnes Jewish Hospital with the Washington School of Medicine resulted in a three-fold reduction of CVC infections. Cost savings reported in the study were estimated to be $185,000-$2.8 million. Clearly, education has a tremendous impact on improving practices, which translates into better patient outcomes.

The goal of education is to improve practice and as such, warrants repetition to achieve the desired results. Education should include:

1. Specific need and indications for vascular access
2. Aseptic insertion procedures
3. Maintenance practices
4. Understanding levels of risk
5. General infection prevention strategies

Education must be a constant process involving training, evaluation and retraining, each with a focus on the key points of infection prevention including follow-up with patient care units, physicians and insertion personnel, along with consistent education for each new staff member. This approach to preventing thrombosis formation and catheter-related infection should be part of the management and care training strategy. Consistent education using various modalities (online, self-study, group training and product training from manufacturers) can be effective in reducing both complications and costs.

Measurement of Practice Compliance

Effectiveness of this educational process should be established through evaluation of staff compliance and patient outcomes. Infection prevention practices with the central line bundle are measured through completion of the central line insertion checklist that should accompany every CVC insertion. Other measures of policy compliance, along with statistics on complications and negative outcomes, help to paint a picture of the needs within any healthcare institution.

Compliance with certain key practices promotes higher-quality patient care. These practices should include:

KEY PRACTICES TO REDUCE INFECTIOUS COMPLICATIONS
1. Bundle applications for hand hygiene, chlorhexidine disinfection of skin and maximum barriers with insertion
2. Insert CVCs with ultrasound
3. Review of continued need and necessity for the CVC performed during daily rounds
4. Meticulous disinfection of access ports and hubs
5. Assess dressing daily for adherence and changes; use an antimicrobial sponge under dressing
6. Consider use of an anti-infective Central Vascular Access Device (Non-tunneled, PICC, Tunneled, Implanted Port) with expected dwell of greater than five days

KEY PRACTICES TO REDUCE THROMBOTIC COMPLICATIONS
1. Assess for risks of catheter related venous thrombosis as per Virchow's Triad: hypercoagulable conditions, venous stasis and endothelial damage
2. Place the catheter tip in the lower 1/3 of the superior vena cava near the cavoatrial junction
3. Assure that the vessel can accommodate the size of the catheter by maintaining an optimal catheter to vessel ratio
4. Choose the smallest sized catheter with the least number of lumens required to deliver the therapy required
5. Avoid trauma to the vessel by minimizing the number of attempts or inserting into area of a previous central catheter
6. Avoid left sided insertions if possible, due to the tortuous vessel pathway

Above and beyond the central line bundle, additional best practice measures are implemented with the purpose of improving patient care.[30] The challenge is to understand the basis and evidence of current best practices, so that each practice can be considered for priority and value to the overall result of promoting the highest level of safety for the patient.

Once the top best practices are chosen for any given facility, the next step is implementation of the practices through a structured educational process. Through a structured process, the facility creates a means to evaluate the level of compliance with each practice. Understanding and application of evidence-based best practices helps to achieve the goal of eliminating infections and reducing overall complications.

Application of Technology and Evidence for Better Health

Many hospitals have realized significant reductions in infection and complications through the application of technology designed to increase patient safety. Specific safety practices were instituted more than a decade ago by Dr. Issam Raad, MD and his team of clinicians at MD Anderson Cancer Center.[18] Dr. Raad was one of the first to begin using maximal sterile barriers and antimicrobial catheters for CVC insertions resulting in a reduction of infection. Recent improvements in technology have included antimicrobial caps for access ports, antimicrobial dressings and antimicrobial CVC catheters to reduce bacterial growth.

Chlorhexidine, as a broad-spectrum antibacterial agent, has demonstrated excellent effectiveness in reducing growth of bacteria on skin, around the insertion site and on catheters. Further, an unparalleled chlorhexidine PICC has been shown to significantly reduce microbial colonization of bacteria and fungal pathogens, while also reducing fibrin sheath formation on surfaces of the PICC (ARROW® PICC with Chlorag+ard® Technology). This performance has been documented in intravascular, *in vivo* studies.

Biofilm is a slimy, polymeric substance produced from microorganisms that have attached to the catheter surface during contamination. Dr. Raad, in his early studies at MD Anderson Cancer Center, verified that biofilm virtually covers the inner and outer surfaces of all CVCs.[18] When blood cell and bacterial attachment are inhibited, no biofilm is produced.

Without the aid of coatings that provide the combined benefit of antimicrobial and antithrombogenic protection, biofilm creates an environment that allows the growth of more dangerous microorganisms, which require higher concentrations of antibiotics to kill the bacteria. In the past, microorganisms were irreversibly attached to the catheter's external and internal surfaces, causing contamination.

Chlorag+ard® Technology Provides Antimicrobial and Antithrombogenic Protection

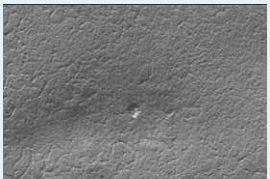
Study: In an *In Vivo* Intravascular Animal Model, Three Different Catheters Were Challenged with *Staphylococcus Aureus.*[31]

Results:

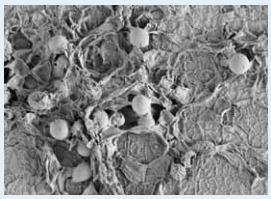
Unprotected PICC (control catheter 2: 31 days)
Highly infected tissue and significant thrombus formation

Unprotected PICC (control catheter 1: 7 days)
Infection present in tissue with significant thrombus formation

Antimicrobial / Antithrombogenic PICC: 31 days (ARROW® PICC with Chlorag+ard® Technology)
Shows no biofilm, and only minimal thrombin of fibrin development



Electron microscopy of ARROW® PICC with Chlorag+ard® Technology without bacteria following removal from host



Electron microscopy of control catheter surface showing S. aureus attached to the intraliminal surface

Infection on inserted medical devices is a significant clinical problem caused by the adhesion of bacteria to the biomaterial surface followed by biofilm formation and recruitment of other cells such as blood platelets, leading to thrombosis and thrombo-embolisms. By eliminating this bacterial and blood buildup, tremendous advancements may be possible in avoiding infection and catheter dysfunctions. The most common causes of catheter dysfunction and failure are biofilm formation, the development of a fibrin sheath, infection, and thrombus formation.[32,33] There is a strong correlation between failed blood aspiration and significant colonization of the catheter lumen.[34] The creation of a catheter that reduces microbial colonization and thrombus accumulation may very well become the most significant break-through in thrombosis/infection prevention in this century.

To this point, research conducted by Marcia Ryder, PhD, MS, RN and colleagues provides evidence of the antimicrobial and antithrombogenic effectiveness of a chlorhexidine treatment on catheter surfaces (ARROW® PICC with Chlorag+ard® Technology). During a presentation at the SHEA 2012 Conference, Dr. Ryder described the results depicted in the photos above which show that few cells, bacteria or blood adhered to the antimicrobial/antithrombogenic catheter.

The Ideal Catheter

Clinicians have long discussed and envisioned the ideal central venous catheter, describing it as a device that resists infection, thrombosis and provides long dwell times without significant impact on vessel health. According to S. Galloway the ideal catheter is chemically inert, non-thrombogenic, flexible, radiopaque and transparent.[35]

It is my opinion, with new technologies in surface treatments now available, other features of an ideal device desired by those who use central venous catheters daily are:

- Reduction of microbial colonization, a known precursor to catheter related infection[36]
- Intraluminal and extraluminal protection against a broad range of microbial pathogens with protection from tip to hub
- Reduction of thrombus accumulation on internal and external catheter surfaces with the ability to reduce occlusion and maintain blood return
- Catheter protection lasting at least 30 days

In studies performed, the ARROW® PICC with Chlorag+ard® Technology was cleared by the FDA with the features listed above.[37,31]

In Conclusion

Leading the charge to improve clinical outcomes requires research, an ability to understand the numerous results and application of those results to clinical practice. The ability to recognize a solution that will greatly affect patient outcomes is part of the decision process with any catheter. Patient safety is based on more than an opinion; it is based on evidence from research with application to practice.

As noted in antimicrobial catheter reviews by Drs. Christopher J. Crnich and Dennis G. Maki, there is a large body of randomized trials and research performed over the past 30 years that demonstrates a consistent reduction in CVC-related bloodstream infections with clear-cut cost-effectiveness.[38] Reduction of microbial colonization is a known precursor to catheter-related infection.[36] Veenstra and colleagues stated it in terms of cost savings. Antimicrobial catheters decrease catheter related infections, reduce death and even more than a decade ago achieved a savings of $68-$391 per patient.[39] This group concluded that antimicrobial catheters should be considered a part of a comprehensive nosocomial infection control program. Coupled with the fact that upper-extremity thrombosis occurs at a rate of up to 61.9% (asymptomatic)[40] and 3.0%–7.8% (symptomatic),[41,42] and an average cost per event of $11,957,[43] and the value of an antimicrobial/antithrombogenic PICC designed to help fight catheter-related infection and thrombosis becomes clear.

The question to you is this: Are these characteristics your idea of the perfect PICC, and if so, how will you apply this evidence in your practice? If we are truly about safeguarding patients, then action is necessary when the evidence is clear.

Clinical Advancements in Practice

Early Outcomes Using the Antimicrobial / Antithrombogenic PICC

Case Study 1:

In a preliminary report of a recent 12-month trial at a Southern California medical center, the rate of CLABSI fell more than 88% after the institution of the antimicrobial / antithrombogenic catheter. The change reflected a PICC CLABSI reduction from 4.17/1000 catheter days to 0.47/1000 catheter days. That substantial reduction in CLABSI enabled this hospital to move from a status in the lower 25% of all California hospitals to one that was in the highest ratings and better than national benchmark levels of 1.3/1000 catheter days. This hospital demonstrated that even though it had already applied all the basic infection prevention measures, it could still achieve an eight-fold improvement in infection reduction through the application of this new PICC.

Case Study 2:

Glenda Dennis, RN, CCRN at McKenzie Willamette Medical Center in Oregon, describes the preliminary results observed with use of the antimicrobial/antithrombogenic PICC (ARROW® PICC with Chlorag+ard® Technology). Glenda has 34 years of experience as a nurse in intensive care, radiology and has been the leader of the vascular access team for 12 years. She began researching antimicrobial PICCs to use in the hospital's inpatient and large outpatient PICC population, aiming to be in compliance with Infusion Nurses Society Standards that specify use of an antimicrobial catheter for patients requiring CVCs for longer than five days.[44] She wanted to be sure to maintain protection for the patient at home when she was not able to perform daily assessment.

She explains her experience prior to implementation of ARROW® PICC with Chlorag+ard® Technology as requiring frequent catheter declotting and occlusion management. But with the antimicrobial/antithrombogenic PICC, rarely does a catheter need intervention. The PICC team identified frequent upper-extremity deep vein thrombosis with previous PICCs. These UEDVTs are now rarely seen, if at all, with use of the antimicrobial/antithrombogenic PICC. Insertion of this catheter has been described as easy to advance to the correct position without any reported malpositions to date. Since beginning use of the new ARROW® PICC with Chlorag+ard® and institution of a split septum end cap, there have been no reported cases of central line-associated bloodstream infections (CLABSIs) to date. The goal of McKenzie Willamette Medical Center is to prevent both CLABSIs and UEDVT with their use of PICCs. According to Glenda, the antimicrobial/antithrombotic PICC is performing as the ideal catheter.

Author Information

Nancy Moureau is a Vascular Access Consultant with PICC Excellence, Inc., educator, and PRN clinician and is a paid consultant for Teleflex. She is the founder and CEO of PICC Excellence, Inc., a corporation established for training, education and consulting with PICCs and vascular access devices. A pioneer in multimedia education for PICCs, PICC Excellence developed many forms of training including many courses of online vascular access education. Having trained thousands of nurses and other medical professionals in PICC placement, Nancy is a speaker, is active in research and publishes on various issues related to vascular access and central venous catheters. As a resource for PICC information, Nancy is happy to receive questions and can be reached through nancy@piccexcellence.com or www.piccexcellence.com

About Teleflex Incorporated

Teleflex is a global provider of medical devices used in critical care and surgery. It serves healthcare providers in more than 130 countries with specialty devices for vascular access, general and regional anesthesia, urology, respiratory care, cardiac care and surgery. ARROW® PICC with Chlorag+ard® Technology is a product of ARROW International, Inc., a subsidiary of Teleflex. Teleflex also provides products and services for device manufacturers.

For more information, visit www.chloragard.com or speak with your Teleflex representative.

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