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Before we go too far: Ultrasound-guided central catheter placement*

One never goes so far as when one doesn't know where one is going.—Johann Wolfgang von Goethe (1749–1832)

An estimated 5 million central venous catheters (CVCs) are placed annually in the United States in a variety of settings, including intensive care units, emergency departments, operating rooms, and even outpatient settings. The frequency of mechanical complications during placement of CVC ranges from 5% to 19%, with such complications including arterial puncture, arterial cannulation, malposition, hematoma, and pneumothorax (1). In 1984, Legler and Nugent (2) published a brief report describing the use of Doppler ultrasonography to locate the internal jugular vein for cannulation. Since that time, two-dimensional ultrasound guidance has become an accepted, and now required, tool to improve success and to reduce the number of attempts required for venous cannulation. Ultrasound guidance is particularly helpful for novice operators.

In this issue of *Critical Care Medicine*, Blaivas and Adhikari (3) conducted a single-institution study to prospectively investigate the frequency of posterior wall penetration during ultrasound-guided CVC placement by emergency medicine residents with prior ultrasound training and CVC placement experience. The study protocol used a transverse approach with dynamic guidance for internal jugular cannulation on a life-size torso model (Blue Phantom, Kirkland, WA). The authors found a 64% occurrence rate of posterior venous wall puncture, a 20% occurrence rate of carotid penetration, and significant correlations with both years of training and experience using ultrasound for CVC placement (3).

This well-designed study provides four important messages. First, complications during ultrasound-guided CVC placement can occur. Second, an understanding of how these complications can occur under ultrasound guidance provides the operator with a mechanism to prevent their occurrence. Third, operator training and experience are important in determining the complications associated with this procedure. Fourth, simulations offer procedural practice that ultimately improves staff proficiency and enhances patient safety.

In regard to the first point, the rate of posterior complications in this study seems unusually high. Prior studies using real patients reported CVC complication rates of 4.6% (4). Sadler et al (5) reported a single venous wall puncture rate of 13.4% in real patients in contrast to the 64% found in simulated patients in the current study. It is our supposition that this complication, exemplified by getting a "flush of venous blood" upon withdrawal of the needle, is very common and perhaps even nearly universal in hypovolemic patients, although the clinical consequences remain entirely unclear. We expect that the number of posterior venous wall penetrations would be higher in patients who are dehydrated, are under respiratory distress, experience internal jugular vein collapse, or have a vein diameter <4–5 mm, but none of these conditions were found in the simulated procedures performed here (6). This high complication rate may be related to the inexperience of the operators (highlighting the need for additional practice), the failure to detect this complication in real life, or the simulated environment, which may in some way alter the operator's "feel" and increase the complication rate.

The second point is important particularly because these complications occurred under dynamic ultrasound guidance. One explanation for their occurrence is that the ultrasound beam is narrow (0.2–1.2 mm) and although the operator appears to be following the tip of the needle into the vessel, the tip has actually passed out of the ultrasound beam, and a cross section of the proximal part of the needle is now seen in the view (Fig. 1). In this circumstance, the tip may have already penetrated the contralateral wall of the vessel (Fig. 1). The authors discuss the benefits of using a longitudinal real-time approach for internal jugular cannulation, and this approach is also recommended by the American College of Emergency Physician (7). However, the ultrasound plane thickness compared with the needle diameter also makes it difficult to visualize the entire needle longitudinally. Partial visualization can occur and makes one vulnerable to the same phenomenon described previously for the posterior wall; namely, the operator is following the tip of the needle into the vessel, although the tip has actually passed out of the ultrasound beam, and a cross section of the proximal part of the needle is now seen in the view (Fig. 1). Only now, the lateral vessel wall has been unknowingly penetrated. Keeping the entire needle within the view is important and requires skill and practice, belaboring the procedure and causing frustration among novice and seasoned operators alike.

***See also p. 2345.**

Key Words: critical care; intensive care; central venous catheter; ultrasound guidance; bedside ultrasound; training; simulation in health care; patient safety

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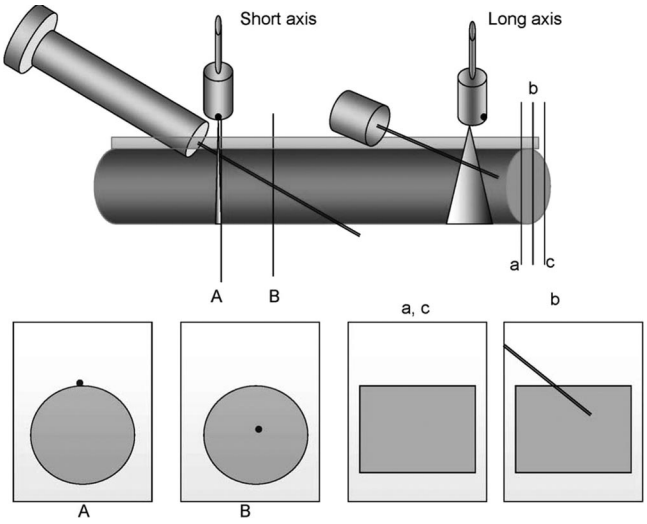

Figure 1. Difference between long- and short-axis guidance for central venous catheter placement.

Regarding the third point, multiple studies have demonstrated a negative correlation between the frequency of complications and operator experience (8). Attempts to look for new techniques to avoid those complications and to improve the efficiency and accuracy of CVC placement failed until the relatively recent introduction of ultrasound guidance. As the use of ultrasound at the bedside matures, best-practice guidelines regarding technique that are informed by well-designed studies will supplant our reliance on personal preferences. One of the most important points made by Blaivas and Adhikari (3) is the need to establish recommendations on training, competence, and proficiency in ultrasound use for diagnostic and therapeutic procedures including ultrasound-guided CVC placement. Our approach uses an educational program with three levels of competency that provides learners with the knowledge, skills, and aptitudes to effectively perform ultrasound at the bedside (9). In the absence of accepted guidelines, however, training will be highly variable and will introduce unnecessary variation into clinical practice, ultimately affecting our patients' safety. At least for now, the choice of axis for the guidance of CVC placement still depends mainly on the location of the vessel, operator experience, and personal preference.

As regards the fourth point, we appreciate the authors' use of simulation as a technique to teach and improve the skills of trainees of all different skill levels, while keeping our patients safe for high-risk procedures. Alternatives, including the possibility of performing such procedures on unembalmed, specially prepared cadavers in a manner similar to the protocol by Blaivas and Adhikari (3), will minimize patient exposure and provide the necessary information to inform and establish best-practice recommendations for ultrasound use. Pioneering efforts to validate the impact on simulation in health care, specifically CVC placement, are underway and will provide useful tools as we enhance the educational experiences of our trainees (10) and ensure adequate preparation before patient exposure.

Bedside ultrasound, as a component of the augmented physical examination, is an essential tool to improve the diagnostic and therapeutic activities in a number of venues. Its role in improving the safety and efficiency of CVC placement and other commonly performed intensive care unit procedures is increasingly being demonstrated. The contribution by Drs. Blaivas and Adhikari (3) helps us to improve our effectiveness as we establish best-practice recommendations, training requirements, and competency guidelines that will further improve safety for critically ill and injured patients.

Alexander B. Levitov, MD, FCCM, RDCS
Sameh Aziz, MD, FCCP
Anthony D. Slonim, MD, DrPH, FCCM
Carilion Clinic
Virginia Tech-Carilion School of Medicine
Roanoke, VA

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Gram-specific quantitative polymerase chain reaction for diagnosis of neonatal sepsis: Implications for clinical practice*

Sepsis in neonates, particularly those with low gestational age and birth weight, is a serious disease that is associated with high morbidity and mortality (1). The outcome of sepsis depends, to a great extent, on early identification of affected infants and rapid initiation of appropriate antimicrobial agents against causative organisms (2). The standard of care for infants suspected to have sepsis is to give combination broad-spectrum antimicrobials to cover potential pathogens at a given age or clinical setting. The type and duration of antimicrobials are usually based on results of cultures and other laboratory markers of sepsis, and the clinical condition of the affected infant. The gold standard for the microbiological diagnosis of a bloodstream infection is a positive blood culture. In small infants, the sensitivity of blood culture is low despite the presence of clinical indicators of sepsis (2–11). This may be due to intermittent seeding of bloodstream with low numbers of bacteria, suppression of bacterial growth by prior antibiotics given to the mother or infant, and insufficient volume of blood samples as is common in neonates (3).

In recent years, there have been several reports (4–13) on the use of polymerase chain reaction (PCR)-based assays for early and accurate identification of bacterial deoxyribonucleic acid (DNA) in the blood of neonates suspected or confirmed to have sepsis. These assays rely on PCR amplification of the 16S rRNA gene, a highly conserved gene present in all bacterial species, but absent in humans. As the gene has a number of divergent regions nested within it, PCR has also been targeted for species-specific detection of bacteria in clinical specimens. When compared with blood cultures, the range of the sensitivity of the PCR assays in various studies (5–7, 9, 10) was 66.7% to 100%, specificity was 87.5% to 97.85%, positive predictive value was 47% to 95.4%, and negative predictive value was 75% to 100%.

The impetus for the development of such assays is to improve the rate of microbiological diagnosis of neonates presenting with signs and symptoms of sepsis and decrease the time for identification of a pathogen. As a result, the expectation is to influence the utilization of antibiotics in such infants.

In this issue of the *Critical Care Medicine*, Chan and colleagues (14) report the results of an evaluation of a quantitative (q) PCR test for identification of Gram-negative and Gram-positive bacterial infections in 218 episodes of suspected late-onset sepsis in preterm infants. The positivity rate of blood culture was 42/176 (23.86%) and qPCR was 33/176 (18.75%). Compared with blood culture, the sensitivity and specificity of the qPCR for Gram-positive infections were 73.7% and 98.5%, and for Gram-negative infections 86.4% and 99.5%, respectively. The qPCR identified correctly the Gram-specific causative pathogens in negative blood cultures in five infants who had intra-abdominal sepsis. The results of the PCR assay were available more rapidly than blood cultures (5–29 hrs vs. 17.2–127 hrs). These results are in line with previous studies (5–7, 9, 10).

Jordan et al (5) compared the performance of a 16S rRNA gene PCR and blood cultures in 548 neonates with suspected sepsis. Twenty-five infants had positive blood cultures (4.6%) and 27 had positive PCR (4.9%). Compared with blood culture, the sensitivity, specificity, positive predictive value, and negative predictive values of the PCR were 96%, 99.4%, 88.9%, and 99.8%, respectively. The turnaround time for PCR results was around 9 hrs. In another study, Jordan et al (8) evaluated 16S rDNA PCR in 1233 near-term infants with suspected or confirmed sepsis. The blood culture positivity rate was 17/1233 (1.38%) and PCR 37/1233 (3%). Compared with culture, the sensitivity of PCR was 41.2%, specificity 97.5%, and negative predictive value of 99.2%. The low sensitivity was attributed to suboptimal sampling and preparation techniques. Shang et al (7) examined blood cultures, and 16S rRNA gene PCR amplification and microarray analysis in 172 neonates with suspected sepsis. The positivity rate of the PCR assay was significantly higher than that of blood culture (9.88% vs. 4.65%). Compared with blood culture, the sensitivity of the PCR was 100%, specificity was 97.8%, positive predictive value was 47%, and negative predictive value was 100%. The results of the PCR assay were available within 6 hrs.

Wu et al (9) studied the performance of Gram-negative stain-specific-probe-based real-time PCR representing 53 Gram-positive and Gram-negative clinically important bacterial strains in blood samples of 600 neonates with suspected sepsis. The positivity rate of the PCR assay was 50/600 (8.33%) and the blood culture 34/600 (5.67%). Compared with blood culture, the sensitivity, specificity, and index of accurate diagnosis for the PCR were 100%, 97.17%, and 0.972%, respectively. In a recent study (10) of 48 neonates with signs and symptoms of sepsis, the positivity rate of a broad range 16S-DNA PCR was 9/31 (29%), and blood culture was 6/31 (19.3%). Compared with blood culture, the sensitivity, specificity, and positive and negative predictive values of PCR were 66.7%, 87.5%, 95.4%, and 75%, respectively.

Molecular assays may be potentially useful adjunct tests in microbiological diagnosis of septic neonates. These assays (5–10, 14) have the following advantages over blood cultures: 1) they utilize smaller volumes of blood; 2) the results are available within a shorter turnaround time; 3) they can detect a small amount of bacteria; and 4) they are unlikely to be

***See also p. 2441.**

Key Words: polymerase chain reaction; quantitative polymerase chain reaction; Gram-specific quantitative polymerase chain reaction; bacterial infections; neonatal sepsis

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affected by prior antibiotic therapy. However, these assays are associated with a potential for false-positive results due to contamination from bacterial DNA, which is widespread in the environment, and false-negative results in patients who are infected with pathogens that are not targeted in the assay. Additionally, these tests are not yet readily available in all hospitals. A real-time PCR LightCycler SeptiFast Test MGRADE Kit (Roche Molecular Diagnostics, Penzberg, Germany) is available commercially in some countries (15). It detects and identifies 25 bacterial and fungal pathogens commonly associated with bloodstream infections directly in 1.5 mL of blood in <6 hrs. However, the diagnostic accuracy of this test has not been validated in neonates.

The microbiological diagnosis of infants who present with signs and symptoms of neonatal sepsis remains a challenge. Although molecular assays may improve the detection of pathogens causing sepsis, the positivity rate of PCR (range from 3% to 29%) in various studies of septic neonates is still low (5–10, 14). Further studies are needed to define the role of molecular assays in the identification of septic infants, their impact on physician management decisions regarding antibiotics, and their effect on clinical outcome.

Husn H. Frayha, MD
Section of Infectious Diseases
Department of Pediatrics
King Faisal Specialist Hospital and Research Centre
Kingdom of Saudi Arabia
Avedis Kalloghlian, MD
King Faisal Heart Institute
King Faisal Specialist Hospital and Research Center
Riyadh, Kingdom of Saudi Arabia

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