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Original Contribution

Preferences of air-blood-saline sonographic microbubble contrast agents among emergency medicine resident physicians☆,☆☆

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ABSTRACT

Introduction: The placement of a central venous catheter (CVC) remains an important intervention in the care of critically ill patients in the emergency department, and bedside ultrasound can be used for procedural guidance as well as conformation of placement. Microbubble contrast-enhanced ultrasound may facilitate CVC tip position localization, and the addition of autologous blood can significantly increase its echogenicity. The purpose of this study was to describe the preferences of a group of resident physicians regarding the performance of various concentrations of air-blood-saline sonographic microbubble contrast agents.

Methods: Institutional Animal Care and Use Committee approved prospective study. A CVC was inserted into the right internal jugular vein of a 20-kg Yorkshire swine under general anesthesia. Contrast mixtures were created with air, saline, and varying amounts of blood and were injected while echocardiographic video clips were recorded and reviewed by 25 physician sonographers.

Results: All reading physicians reported increased overall echogenicity, a higher peak echogenicity, and greater personal preference for blood containing solutions. Nearly all reading physicians preferred the lower percentage blood containing mixtures over the higher percentage blood containing mixture.

Conclusion: The inclusion of 1 to 3 parts of 10 of the patient's blood in the preparation of a sonographic contrast mixture increased the echogenicity of the contrast, resulted in better visualization of both the contrast and the endocardial border and was the preferred mixture among the resident physicians studied.

1. Background

The placement of a central venous catheter (CVC) remains an important intervention in the care of critically ill patients in the emergency department, and the use of bedside ultrasound to guide placement is widely used [1-7]. Once placement of the CVC is completed, correct vessel type (arterial versus venous), catheter location, and depth of the tip must be confirmed before it can be used. Inadvertent arterial placement can lead to several serious and potentially life-threatening consequences including exsanguination, stroke, arteriovenous fistula, and dissection [8]. Most guidelines recommend that the CVC tip should sit in the inferior third of the superior vena cava (SVC) at the junction of the right atrium, as complications can occur with malposition [9,10]. If it lies more cephalad in the SVC, venous thrombosis and catheter dysfunction can occur, whereas intracardiac catheter tips can result in arrhythmias, tricuspid valve damage, and cardiac perforation leading to pericardial tamponade [9,11-13].

Traditionally, a postprocedure chest radiograph is performed to confirm the location of the catheter tip; however, it has several limitations including availability, time delays, and limited accuracy in the identification of CVC tip position, as it is unable to directly visualize the SVC–right atrial border [9,10]. As an alternative to traditional chest radiograph, bedside ultrasound is performed in real time by the treating physician and is able to visualize the right atrium directly; therefore, it may decrease or avoid these limitations [14,15].

The use of ultrasound to identify CVC tip position may be facilitated by the use of intravenous contrast enhancement. Ultrasound contrast relies on microbubbles of air, which have a markedly different acoustic impedance than fluid and are, therefore, highly sonographically reflective. Sonographic contrast can be made by mixing and hand agitating a combination of normal saline and air. Blood added to the contrast mixture has been noted to significantly increase the concentration, intensity, and stability of microbubbles in circulation [16,17].

Injection of a contrast agent through the CVC (distal port when using a triple lumen catheter) and subsequent visualization of the highly echogenic bubbles in the right heart demonstrate that the CVC is in the venous system. In addition, it can provide information about the location of the catheter tip. A CVC with its tip in the superior vena cava will result in a dense laminar flow of microbubbles seen flowing into the right atrium 1 to 2 seconds after injection; a CVC in the right atrium will result in turbulent flow that is immediately seen. Placement

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elsewhere will cause a delay in microbubble appearance (>2 seconds) with decreased echogenicity [18,19].

Various compositions of microbubble contrast have been described [20-22]; however, it remains unclear which mixture of ultrasound contrast is best suited for this application. To date, there has been no study comparing physician preference of various compositions of microbubble ultrasound contrast when injected through a CVC.

1.1. Objectives

The purpose of this study was to evaluate a group of resident physician's preferences of various air-blood-saline sonographic microbubble contrast agents with regard to their echogenicity, ability to be visualized, ability to define the borders of the right atrium and right ventricle, and overall preference for use.

2. Methods

This was a prospective study in a live anesthetized porcine model. The study was approved by the Institutional Animal Care and Use Committee. A 20-kg Yorkshire swine was placed under general anesthesia, and a triple lumen CVC was inserted into the right internal jugular vein using the Seldinger technique under dynamic ultrasound guidance, using a Sonosite M-turbo ultrasound system (Bothell, WA) with a p21x (5-1 MHz) phased array probe. Subcostal echocardiography was used to visualize the catheter tip in the superior portion of the right atrium, then, the CVC was slowly pulled back a few millimeters until the tip was no longer visualized. The CVC was secured with sutures, and several microbubble contrast mixtures were prepared (Table 1).

Contrast mixture 1 was composed of saline and air only. Blood-containing contrast mixtures were made by withdrawing the specified amount of blood from the distal port of the CVC with a 10-mL syringe, then detaching the syringe, and adding the specified amount of saline. The syringe with either saline or blood/saline and another 10-mL syringe with 1-mL room air were simultaneously attached to either side of a 3-way stopcock (Fig. 1), and the contents were flushed back and forth between the 2 syringes for 10 seconds until well mixed. Within 5 seconds of this agitation, the resulting contrast mixture was attached to the distal port of the CVC, and 5 mL was injected. The ultrasound probe was placed in the subcostal area, visualizing the right atrium and right ventricle. A 6-second video clip was recorded as soon as the plunger on the syringe was depressed. All video clips were taken at a tissue depth of 19 cm, and gain settings were not changed during the study. This procedure was performed with each of the contrast mixtures.

The apical 4-chamber view was then obtained, and the procedure was repeated for each contrast mixture with sonographic visualization in this view.

Postgraduate year (PGY) 1-3 emergency medicine (EM) residents reviewed the video clips obtained during their weekly didactic conference. Residents had varying levels of prior ultrasound experience including an introductory 1-day course at the beginning of intern year where cardiac ultrasound is reviewed and a 1-week emergency ultrasound rotation during both the PGY-1 and PGY-2 years. There are 4 dedicated ultrasound division faculty members, 89% of the full-time adult faculty are credentialed in focused cardiac ultrasound, and ultrasound is commonly incorporated into bedside teaching and patient care. To ensure that the reading physicians had an understanding of how to interpret the video clips, sample cardiac views without contrast were reviewed at the beginning of the session. Reading physicians were asked to rate the different mixtures with regard to overall echogenicity, highest peak echogenicity, ease of visualization, right-sided endocardial border definition, and overall preference. Clips of the 4 contrast mixtures were shown simultaneously for each view to allow for direct comparison. The reading physicians were aware that different mixtures of blood, air, and saline would be used in the different video clips but were blinded to the order in which the clips were taken, the contrast mixture being used, and the responses of their colleagues. This portion of the study was exempt from institutional review board review, as level of training was the only identifier collected on the data sheets.

Table 1
Composition of ultrasonographic contrast mixtures

	Air	Blood	Saline
Contrast 1	1 mL	0 mL	9 mL
Contrast 2	1 mL	1 mL	8 mL
Contrast 3	1 mL	3 mL	6 mL
Contrast 4	1 mL	5 mL	4 mL

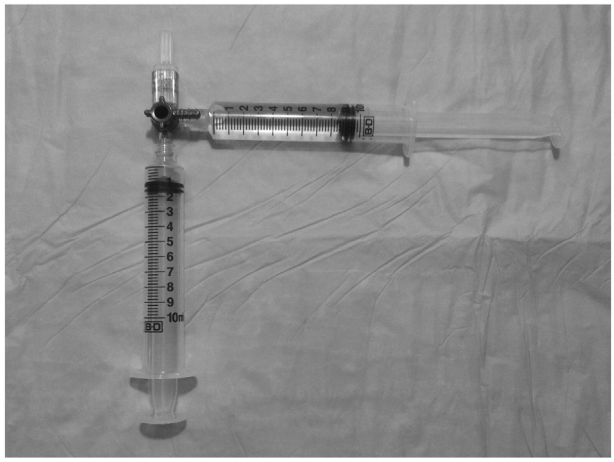

Fig. 1. A 10-mL syringe with 1-mL room air and a 10-mL syringe with 9-mL saline are attached to a 3-way stopcock. The third side will be attached to the distal port of the CVC.

3. Results

Nine PGY-1, 8 PGY-2, and 8 PGY-3 EM (total 25) residents reviewed the sonographic video clips in the subcostal (Figs. 2-5; Videos 1-4) as well as the apical 4-chamber view. The evaluations of the different mixtures by the reading physicians are summarized in Table 2. The combined evaluations of the reading physicians for bloodless and blood-containing mixtures are summarized in Table 3.

4. Discussion

Contrast-enhanced ultrasound was first described by Gramiak et al. in 1968 [23], and enhancement agents have since expanded in scope

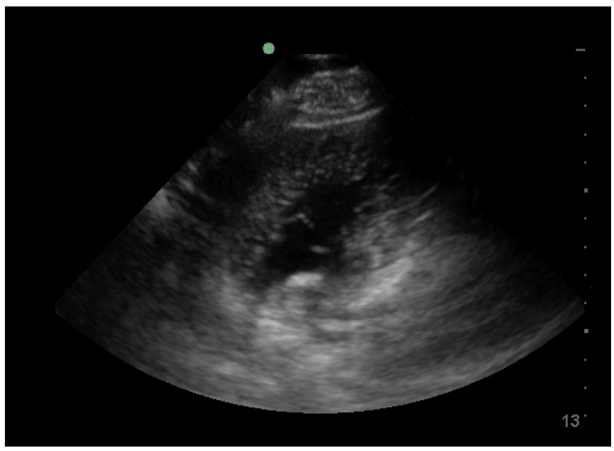

Fig. 2. Subcostal view of the heart. Microbubbles in the right atrium and ventricle after the injection of 5 mL of contrast 1.

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