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Impact of distance of the catheter tip from cavo-atrial junction on bubble test (delay) time: A prospective study

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Abstract

Introduction: Correct tip positioning is a critical aspect in central vascular access devices insertion. The verification of positioning at the cavo-atrial junction is usually performed by intracavitary electrocardiography. Recently, echocardiographic techniques were proposed, including the direct visualization of the catheter or the visualization of a saline/air bolus (i.e. "bubble test"). As for the latter, a push-to-bubbles delay time below 2 s was proposed to indicate a correct positioning of the catheter tip. The aim of this study was to measure the variations of the push-to-bubbles time at increasing distance from the cavo-atrial junction, to verify if a cut-off of 1–2 s correspond to a well-positioned catheter.

Methods: We performed a prospective study including patients with clinical indication of positioning a peripherally inserted central catheter. The catheter tip was positioned at the cavo-atrial junction (P0) via intracavitary electrocardiography, and the push-to-bubbles delay time was measured. The catheter was then retracted 5 cm (P1) and 10 cm (P2), and the test was repeated at this positioning. Push-to-bubbles time measurements were performed off-line by analyzing an audio/video recording which included the echography screen and the voice signal of the operator.

Results: Forty-nine patients were included. The average push-to-bubble time when the catheter tip was in the reference position was 0.41 ± 0.21 s. Retraction of the PICC catheter of 5 and 10 cm determined a significant increase of the push-to-bubbles time: mean time difference was +0.34 (95% IC 0.25–0.43, $p < 0.001$) s between P0 and P1 (5 cm distance), and +0.77 (95% IC 0.62–0.92, $p < 0.001$) s between P0 and P2 (10 cm distance). When the catheter was at the reference position (i.e. cavo-atrial junction) only 2.1% of bubbles delay times were above 1 s.

Conclusion: The push-to-bubbles time is very low when the catheter tip is at the cavo-atrial junction. This delay increases progressively with increasing distance from the target. Push-to-bubbles delay time above 1 s might indicate a catheter not close to the cavo-atrial junction.

Keywords

Nursing, techniques and procedures, PICC, tip location, bubble test, central catheter, ultrasound

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Introduction

Central vascular access devices (CVADs) insertion is a common in-hospital procedure, with an estimate of more than 5 million CVADs positioning per year in the United States.[1] As peripherally inserted central catheters (PICCs) can be inserted through a deep vein in the upper arm, with lower risk of complications than centrally inserted central catheters (CICCs), they are often a preferred option for short, medium or long-term intravenous access.[1,2]

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As for central catheters, the tip of the PICC must be placed in the proximal third of the superior vein cava (SVC) or, better, at the junction between SVC and right atrium (RA), the so called Cavo-Atrial Junction (CAJ).[2]

The adoption of an appropriate technique to ensure correct tip location when positioning PICCs and CVADs is mandatory, as tip malposition is associated with high risk of malfunction, thrombosis, vessel damage and other complication.[2–5] Among these strategies, current literature agrees that intra-procedural techniques, compared to the post-procedural ones, as more advisable. Specifically, intracavitary electrocardiography (IC-ECG) is actually considered the first choice for the tip location,[2,3,6,7] even in specific conditions (i.e. atrial fibrillation) in which it was historically considered as not indicated.[8–10]

In the last decades, the use of ultrasounds (US) has largely expanded in the area of vascular access. Two US techniques has emerged as valuable alternatives to the IC-ECG: transthoracic echocardiography (TTE), which allows direct visualization of the catheter tip[11,12] and Contrast Enhance Ultrasound (CEUS), usually called "bubble Test."[13,14] The latter is based on a bolus of agitated saline mixed with air: the delay between saline bolus injection and bubbles visualization in the RA (i.e. "push to bubbles time"[15]) allows a rather precise indication of the distance of the tip from CAJ.[13,16–18]

Previous studies investigated the reliability of the bubble test as a technique to assess the tip location of a CVAD by comparing it with chest X-Rays,[12,14,19,20] transesophageal echocardiography,[21] transthoracic echocardiography[15] and IC-ECG.[16] Although the results of these studies do not correspond exactly, there is strong evidence suggesting a delay greater than 2 s as an indicator of catheter tip malposition.[2,13] Some authors recently suggested that a push-to-bubble time below 1 s may indicate a correct tip location.[15,17,18,22] We performed a prospective study assessing the variation of the push-to-bubbles time with progressive increasing of the distance from the CAJ by means progressive retraction of the catheter tip in SVC.

Methods

The study was approved by local Ethics Committee on December 2021 (ref. 3862, Comitato Etico Brianza). All patients expressed a written informed consent.

All patients with clinical indication of PICC positioning were considered eligible for the present study. Exclusion criteria were the following: age <18, cardiac rhythm other than sinus rhythm, impossibility to identify maximal P waves at the IC-ECG, no cardiac acoustic window.

All PICCs were inserted by Nurses of the local Vascular Access Team according to SIP protocol,[3] with the exit site in the so-called Dawson's green zone.[23] Catheters were 1 or 2 lumens (3/4 and 5 Fr, respectively) Pressure Injectable PICC (Teleflex® Medical, Dublin, Ireland), with procedural kit for maximum sterile barrier precautions. Tip location was performed by IC-ECG, and the maximal amplitude of the P waves was used as reference of correct position in CAJ.[7]

After assessing a sinus rhythm with evident P waves, a second operator looked for an acoustic window: subcostal four-chamber (longitudinal) was considered as the first choice, whereas four chamber transthoracic apical[17] and short axis left parasternal views were considered as second and third options, respectively. A 2–6 MHz sectorial probe was used. After PICC positioning in CAJ, a series of three bubble tests were performed with the following steps: "P0" test with catheter in CAJ; "P1" test with catheter pulled back 5 cm from the CAJ; "P2" test with catheter pulled back 10 cm from the CAJ. At the end of the three bubble tests, catheter was correctly repositioned under IC-ECG guide, secured and covered following internal protocol and current evidence.[2,3] Bubble tests were performed by injection of 10 ml of normal saline mixed by air (9 ml of saline and 1 ml of air).[2,13] All bubble test procedures were recorded in audio/video files, framing only the cardiac window on the US display. All flushes started simultaneously at the "G" letter of the countdown sequence ("three, two, one, Go") that each inserter had to pronounce during the recorded procedures.

Videos recorded were then analyzed by the editing video software Premiere Pro, Adobe Inc. San Josè-CA-USA, which allows to combine video stream and spectrographic analysis of audio signals, using milliseconds as unit of time measurement. The spectrographic analysis of the audio recording can be displayed in a section of the software interface and makes it possible to recognize the letter G in the countdown sequence that identifies the injection's starting (see Figure 1).

After identifying the moment of flush starting, we stopped the spectrographic analysis of the video and recorded the time (displayed as milliseconds). Then, we analyzed the video stream identifying the time point when the bubbles flush was visualized inside the RA. More precisely, in the video showing the cardiac window, three phases can be distinguished, as previously described by Meggiolaro et al.[15] (see Figure 2).

(1) Natural hypo-echogenicity can be appreciated in the right atrium (RA);
(2) The early onset of a dynamic hyperechoic flush can be visualized inside the RA;
(3) The RA and right ventricle appear totally filled by the hyperechoic flush.

At the first appearance of the hyperechoic flush (2), the video was paused and time was recorded. The push-tobubbles time (i.e. time required to reach the RA by the saline + air solution) was then calculated as the time difference between the "G" vocalization and the visualization of the hyperechoic flow in the RA. Two researchers observed all video separately and recorded push-to-bubbles times. The mean value of the two measures was then recorded for analysis.

The following variables were also recorded: gender, weight, height, side of placement, catheter intravascular

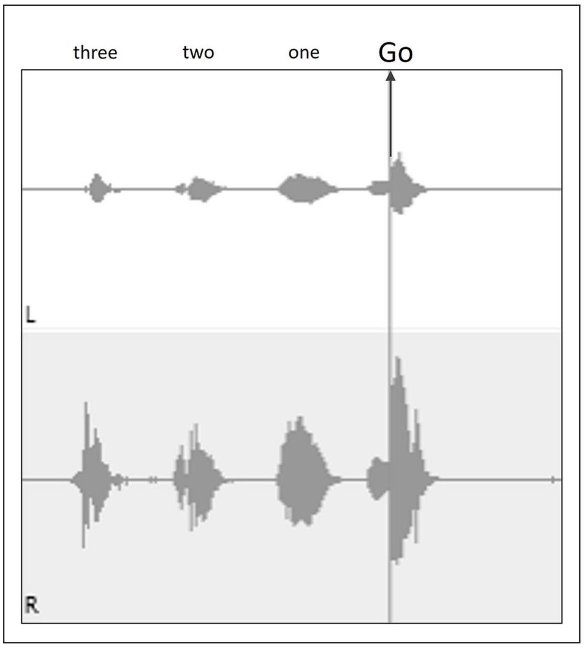

Figure 1. An example of the spectrographic analysis of the audio recording.

length, catheter diameter, P-wave visibility at IC-ECG and cardiac acoustic window availability.

Statistical analysis

Numerical data were expressed as mean and standard deviation (SD), categorical data were reported as count and proportion. Differences in push-to-bubbles delay times between the different tip positions (P0-P1-P2) were assessed by using paired Student's *t*-test, and were reported as mean differences with 95% confidence interval (95% CI). Differences of push-to-bubbles delay times between sex, different insertion sides and catheter size were assessed by Student's T test or Analysis of variance (ANOVA). Correlations between continuous variables (weight, height and intravascular length) and the push-to-bubbles delay times were explored by linear regression analysis. R^2 and *p*-values were reported. Data were analyzed by JMP 15.2 software (SAS Institute, Cary, NC).

Results

Sixty-one eligible patients were evaluated. No patient was excluded because of poor P wave visualization. An adequate cardiac acoustic window was unavailable in 12 patients, which were excluded. The remaining 49 patients were then included in the study. Twenty-seven out of 49 patients (55%) were females, the average weight and height were of 67 ± 12 kg and 166 ± 7 cm, respectively. Forty catheters were placed on the right arm and 9 on the left arm. 3 Fr.-single-lumen PICCs were used in 10% of cases, 4 Fr.-single-lumen in 65% of cases and 5 Fr.-double-lumen in the remaining 25% of cases. The mean catheter intravascular length was 37 ± 3 cm.

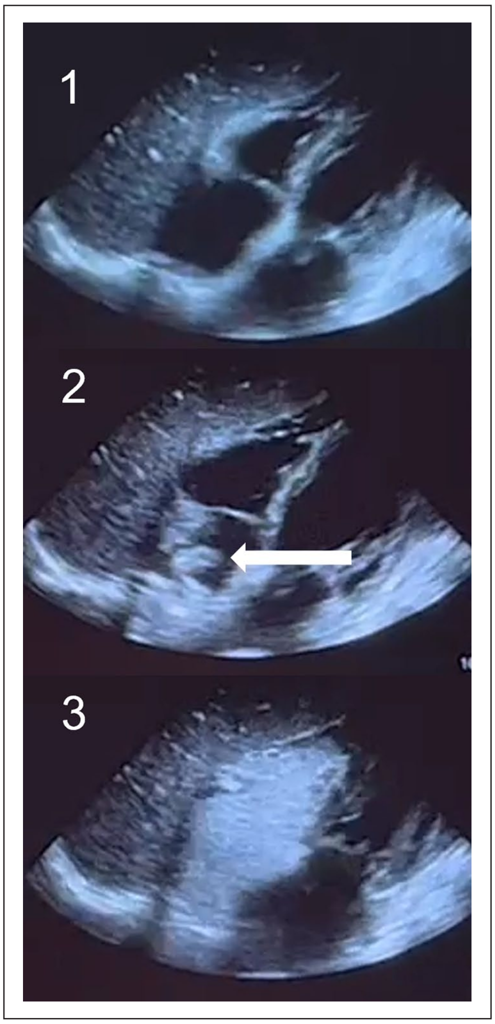

Figure 2. Bolus injection from subcostal four-chamber view.

Forty-nine videos (one for each included patient) were collected and analyzed. The subcostal four-chamber view was used in 46 patients (94%), whereas the short-axis left parasternal view and the four-chamber apical view were used in 2 (4%) and 1 (2%) patients, respectively.

Push-to-bubbles delay times at P0, P1, and P2 are summarized in Figure 3.

The average push-to-bubbles time when the catheter tip was in CAJ (P0) was 0.41 ± 0.21 s. Retraction of the PICC catheter of 5 (P1) and 10 cm (P2) determined a significant increase of the push-to-bubbles time: mean time difference between P0 and P1 was +0.34 (95% IC 0.25–0.43, $p < 0.001$) s, and was +0.77 (95% IC 0.62–0.92, $p < 0.001$) s between P0 and P2.

Figure 4 shows the proportion of push-to-bubbles times for each catheter tip position. When the catheter was at the reference position (i.e. cavo-atrial junction) 75.5% bubbles delay times were below 0.5 s, and only 2.1% of bubbles delay times were above 1 s. Contrarily, when the catheter tip was retracted 10 cm, only 4.1% of push-to-bubble delay

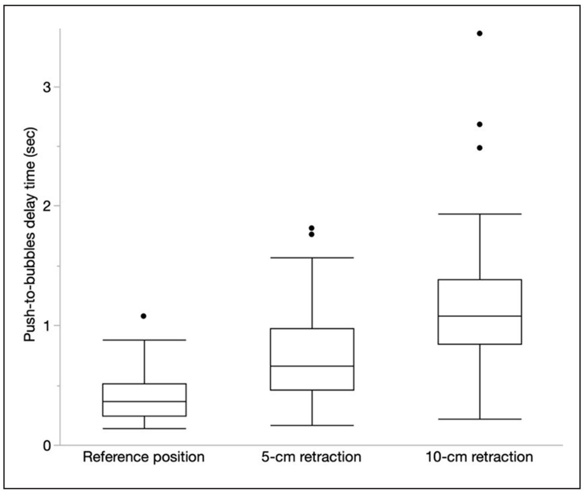

Figure 3. Push-to-bubbles delay times at the different locations. P0, cavo-atrial junction (CAJ); P1, 5-cm retraction from CAJ; P2, 10-cm retraction from CAJ.

times were below 0.5 s. When considering CAJ as the reference position (P0), the 0.5 s cutoff had a sensitivity of 75% and a specificity of 84%. When considering P0 and P1 together (i.e. the catheter tip positioned within 5 cm from the CAJ) the cutoff of 0.5 s had a sensitivity of 52% and a specificity of 98%.

No statistically significant correlation was recorded between push-to-bubbles times and weight, height and intravascular length (see Figure 5).

Side, gender, and size of the PICC catheters (3 Fr. vs 4 Fr. vs 5 Fr.) did not affect push-to-bubbles delay time (see Table 1).

Discussion

To the best of our knowledge, we reported the first study measuring the push-to-bubbles delay at increasing distance from the CAJ. We found a very low push-to-bubbles delay time when the catheter tip was in the correct position (0.41 ± 0.21 s), whereas this delay increased progressively when the catheter was retracted by 5 and 10 cm. When the catheter was at cavo-atrial junction, 75.5% bubbles delay times were below 0.5 s, and only 2.1% of bubbles delay times were above 1 s. Contrarily, when the catheter tip was retracted 10 cm, only 4.1% of push-to-bubble delay times were below 0.5 s.

A catheter tip located at a 5–10 cm distance from the CAJ is certainly intrathoracic but does not fulfill the defining criteria of a central venous access, according to current literature. Furthermore, a retracted position of the tip may also be associated with an increased risk of complications (thrombosis and malfunction).[5] For this reason, techniques aimed at identifying the correct tip position should have optimal

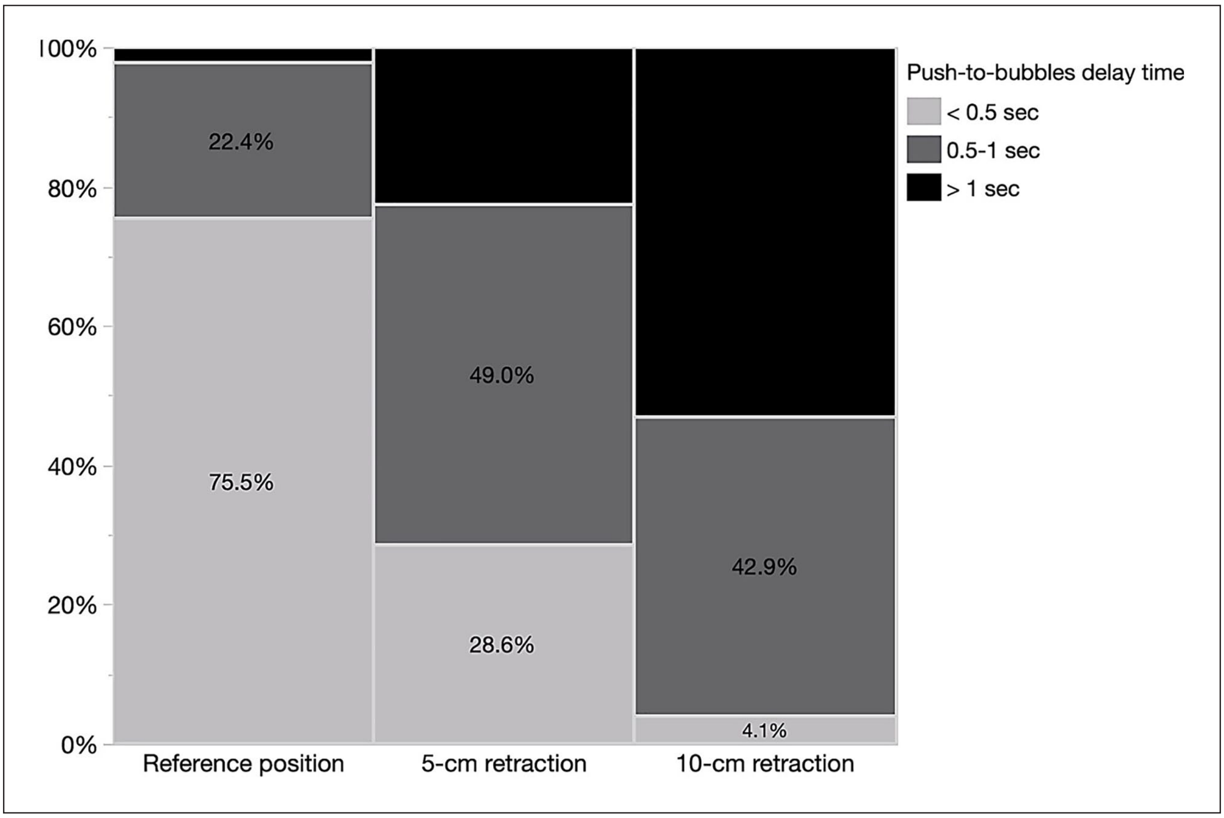

Figure 4. Distribution of push-to-bubbles times for each catheter tip position. Cavo-atrial junction, as identified by intracavitary electrocardiography, was considered as the reference position.

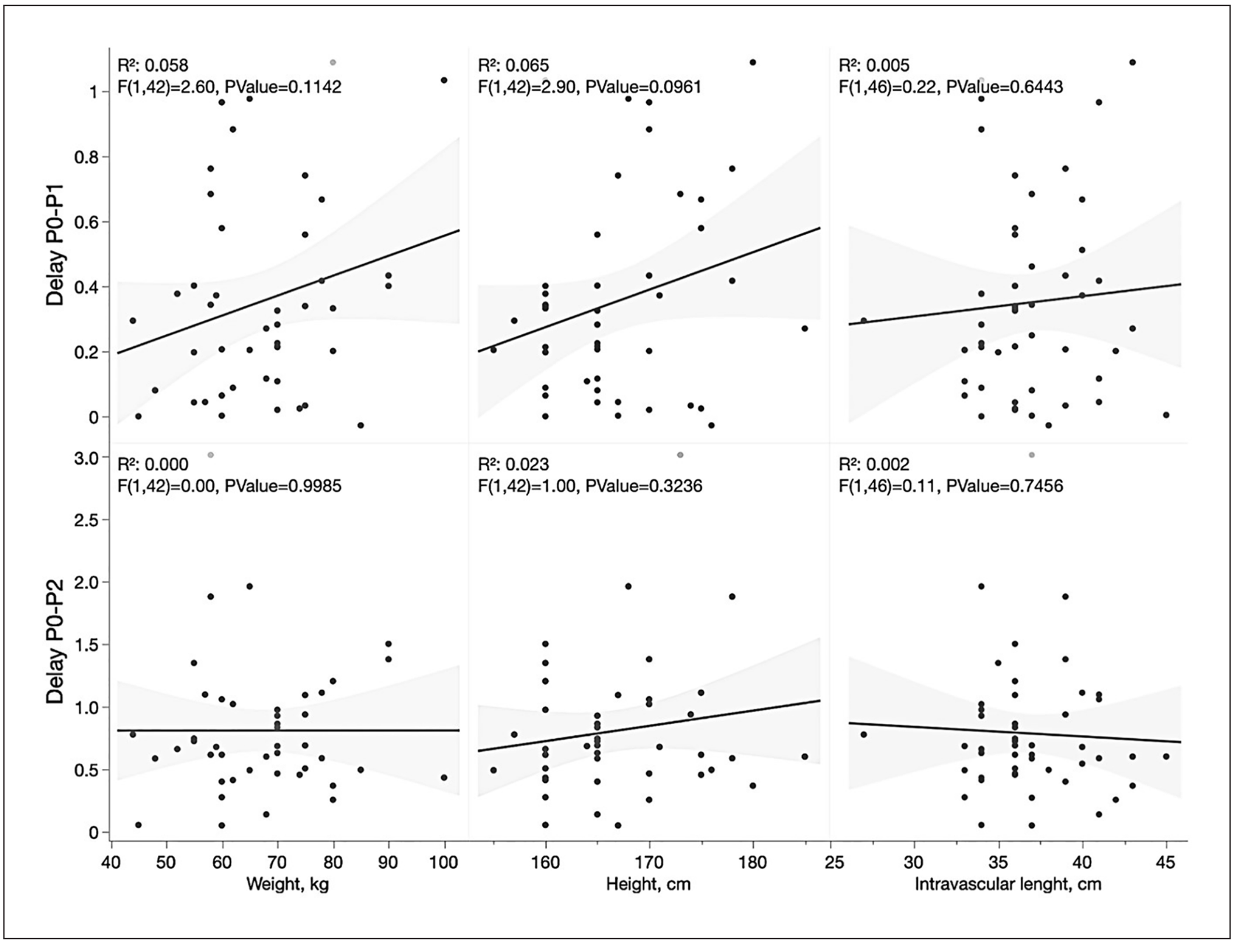

Figure 5. Correlation between weight, height, catheter intravascular length and push-to-bubbles delay times. P0, cavo-atrial junction (CAJ); P1, 5-cm retraction from CAJ; P2, 10-cm retraction from CAJ.

Table 1. Push-to-bubbles delay times stratified by sex, side of positioning and catheter size. P0, cavo-atrial junction (CAJ, reference position); P1, 5-cm retraction from CAJ; P2, 10-cm retraction from CAJ.

	Delay P0-P1		Delay P0-P2	
		p-Value		*p*-Value
Sex		0.407		0.324
Male	0.38 ± 0.32		0.69 ± 0.42	
Female	0.30 ± 0.31		0.83 ± 0.61	
Side		0.310		0.579
Right	0.32 ± 0.28		0.75 ± 0.43	
Left	0.47 ± 0.39		0.92 ± 0.85	
Catheter		0.068		0.171
3 Fr – single lumen	0.68 ± 0.34		1.1 ± 0.59	
4 Fr – single lumen	0.33 ± 0.31		0.7 ± 0.39	
5 Fr – dual lumen	0.28 ± 0.24		0.66 ± 0.41	

accuracy. The 2 s cut off, originally proposed for the push to bubbles delay time,[20] has been progressively reduced by subsequent studies,[15,22] although it is still considered by the current literature.[2,13,17] Our findings support the fact that the best expression of the ideal push to bubbles time, to be looked for in clinical practice, might be defined by the term "immediate," as described by Greca et al. in ECHOTIP protocol.[17] The discrepancy from some previous studies could be explained considering that our measurements referred to a catheter exactly located in CAJ, with the extremely small range of tolerance allowed by the IC-ECG technique.

The size of the catheters (3 Fr. vs 4 Fr. vs 5 Fr.) did not show a significant statistical correlation with push to bubbles time. However, a non-significant trend toward increased delay times with 3 Fr. catheters was noted, probably due to the higher resistance to injection (due to the small internal size). Of note, in our 5 Fr. double lumen PICC the size of the internal lumen is smaller than in the single lumen 4 Fr PICC. This topic is worthy of further study.

This study has some limitation. First, we used an offline analysis to precisely record push-to-bubbles delay times. This allowed a precise measurement of this delay time but may not be reproducible in the everyday practice. Second, our population was relatively small, therefore a larger sample might have been required to detect statistically significant difference for some of the analyzed factors (e.g. catheter size). Third, the synchronism between "Go" vocalization and the effective push starting may be variable for different operators. Some operators could be unable to synchronize themselves so precisely, and the command "go" is often pronounced before starting the push. This may determine a low precision/accuracy when measuring the time delay, and may be an additional issue when performing the bubble test in clinical practice. Fourth, the operator's skill in finding the best cardiac window to visualize microbubbles may be a critical factor. Each Nurse involved in the study underwent basic theoretical-practical training, even if the ideal skill required for this technique is not still well defined.[17] Nonetheless, we recorded a relatively high percentage (about 20%) of "no acoustic window available." We cannot exclude that this may be caused by a suboptimal training of the operators, which should be considered a limit of this study.

Conclusion

The push-to-bubbles delay time is very low (below 0.5–0.6 s) when the catheter tip is correctly positioned in Cavo-Atrial Junction. This delay increases progressively with increasing distance from the CAJ. Push-to-bubbles delay time >1 s might indicate a catheter which is not close to the CAJ.

Author contributions

Elli Stefano: Design of the study protocol and manuscript writing. Giani Marco, Pozzi Matteo: Statistical Analysis and manuscript writing. Lucchini Alberto, Foti Giuseppe: Manuscript writing. D'amata Dario, Cavalli Silvia, Cambiaghi Gloria, Marino Francesco, Russo Mario: Data collect. Giorgianni Mariavittoria, Pozzoli Jessica: Data collect and offline time measurement.

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References

1. Furlong-Dillard J, Aljabari S and Hirshberg E. Diagnostic accuracy among trainees to safely confirm peripherally inserted central catheter (PICC) placement using bedside ultrasound. *Br J Nurs Mark Allen Publ* 2020; 29: S20–S28.
2. Gorski LA, Hadaway L, Hagle ME, et al. Infusion Therapy Standards of Practice, 8th Edition. *J Infus Nurs* 2021; 44: S1–S224.
3. Brescia F, Pittiruti M, Spencer TR, et al. The SIP protocol update: Eight strategies, incorporating rapid peripheral vein assessment (RaPeVA), to minimize complications associated with peripherally inserted central catheter insertion. *J Vasc Access* Epub ahead of print 27 May 2022; DOI: 10.1177/11297298221099838.
4. Pittiruti M, Hamilton H, Biffi R, et al. ESPEN guidelines on parenteral nutrition: central venous catheters (access, care, diagnosis and therapy of complications). *Clin Nutr Edinb Scotl* 2009; 28: 365–377.
5. Caers J, Fontaine C, Vinh-Hung V, et al. Catheter tip position as a risk factor for thrombosis associated with the use of subcutaneous infusion ports. *Support Care Cancer* 2005; 13: 325–331.
6. Chopra V, Flanders SA, Saint S, et al. The Michigan appropriateness guide for intravenous catheters (MAGIC): results from a multispecialty panel using the RAND/UCLA appropriateness method. *Ann Intern Med* 2015; 163: S1–40.
7. Pittiruti M, La Greca A and Scoppettuolo G. The electrocardiographic method for positioning the tip of central venous catheters. *J Vasc Access* 2011; 12: 280–291.
8. Albertini F, Struglia M, Faraone V, et al. Effectiveness of the ECG method in the correct positioning of PICC type central venous catheters in patients with atrial fibrillation. *Minerva Cardioangiol* 2019; 67: 207–213.
9. Calabrese M, Montini L, Arlotta G, et al. A modified intracavitary electrocardiographic method for detecting the location of the tip of central venous catheters in atrial fibrillation patients. *J Vasc Access* 2019; 20: 516–523.
10. Gao Y, Liu Y, Zhang H, et al. The safety and accuracy of ECG-guided PICC tip position verification applied in patients with atrial fibrillation. *Ther Clin Risk Manag* 2018; 14: 1075–1081.
11. Raman D, Sharma M, Moghekar A, et al. Utilization of thoracic ultrasound for confirmation of central venous catheter placement and exclusion of pneumothorax: a novel technique in real-time application. *J Intensive Care Med* 2019; 34: 594–598.
12. Zanobetti M, Coppa A, Bulletti F, et al. Verification of correct central venous catheter placement in the emergency department: comparison between ultrasonography and chest radiography. *Intern Emerg Med* 2013; 8: 173–180.
13. Lamperti M, Biasucci DG, Disma N, et al. European Society of Anaesthesiology guidelines on peri-operative use of ultrasound-guided for vascular access (PERSEUS vascular access). *Eur J Anaesthesiol* 2020; 37: 344–376.

14. Cortellaro F, Mellace L, Paglia S, et al. Contrast enhanced ultrasound vs chest x-ray to determine correct central venous catheter position. *Am J Emerg Med* 2014; 32: 78–81.
15. Meggiolaro M, Scatto A, Zorzi A, et al. Confirmation of correct central venous catheter position in the preoperative setting by echocardiographic 'bubble-test'. *Minerva Anestesiol* 2015; 81: 989–1000.
16. Gidaro A, Casella F, Cogliati C, et al. Pulsed-wave Doppler for ultrasound-based tip location using bubble test: A pilot study. *J Vasc Access*. Epub ahead of print 5 July 2022. DOI: 10.1177/112972982211096
17. Greca A, Iacobone E, Elisei D, et al. ECHOTIP: A structured protocol for ultrasound-based tip navigation and tip location during placement of central venous access devices in adult patients. *J Vasc Access*. Epub ahead of print 8 September 2021. DOI: 10.1177/11297298211044325
18. Iacobone E, Elisei D, Gattari D, et al. Transthoracic echocardiography as bedside technique to verify tip location of central venous catheters in patients with atrial arrhythmia. *J Vasc Access* 2020; 21: 861–867.
19. Ablordeppey EA, Drewry AM, Beyer AB, et al. Diagnostic accuracy of central venous catheter confirmation by bedside ultrasound versus chest radiography in critically ill patients: a systematic review and meta-analysis. *Crit Care Med* 2017; 45: 715–724.
20. Vezzani A, Brusasco C, Palermo S, et al. Ultrasound localization of central vein catheter and detection of postprocedural pneumothorax: an alternative to chest radiography. *Crit Care Med* 2010; 38: 533–538.
21. Corradi F, Guarracino F, Santori G, et al. Ultrasound localization of central vein catheter tip by contrast-enhanced transthoracic ultrasonography: a comparison study with trans-esophageal echocardiography. *Crit Care* 2022; 26: 113.
22. Weekes AJ, Johnson DA, Keller SM, et al. Central vascular catheter placement evaluation using saline flush and bedside echocardiography. *Acad Emerg Med* 2014; 21: 65–72.
23. Dawson RB. PICC Zone Insertion Method™ (ZIM™): a systematic approach to determine the ideal insertion site for PICCs in the upper arm. *JAVA* 2011; 16: 156–165.