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**Protocol**

# Methods for peripherally inserted central catheter measurement in neonates and children: protocol for a randomized controlled trial

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## ABSTRACT

**Background:** Peripherally inserted central catheters (PICC) are widely used in neonates and children requiring intravenous therapy due to their clinical advantages. However, incorrect catheter tip positioning remains frequent and may lead to serious complications. The conventional anatomical landmark–based measurement presents important accuracy limitations. A new approach, the Tomazoni method, has been proposed to improve tip positioning, but current evidence is limited to a small single-center study, highlighting the need for further investigation in broader populations. The objective is to describe a study protocol designed to prospectively evaluate the effectiveness of the Tomazoni measurement method for PICC insertion in neonates and children.
**Methods:** Study protocol for a pragmatic, parallel-group, double-blind randomized clinical trial. Eligible participants will be neonates and children requiring upper-limb PICC insertion. The control group will undergo the traditional measurement method, while the experimental group will receive the Tomazoni method. Data will be collected using an instrument including patient, procedure, and catheter characteristics. Analyses are planned to involve frequency distributions, association tests, and relative risk. The primary outcome will be the initial catheter tip position.
**Conclusions:** The findings are expected to contribute to the development of safer and more effective practices in PICC insertion in children and neonates' populations, supporting patient safety and quality of care in critical neonatal and pediatric environments.

**Keywords:** Neonatal nursing, Venous central catheters, Intensive care units, Neonatal, Patient safety

## INTRODUCTION

Critically ill neonates and children often require intravenous therapy (IVT) to support and restore their health, depending on their clinical condition.[1] For IVT to be safely administered, careful selection of the appropriate venous access is essential, considering the patient's clinical status and the physicochemical properties of the infused solutions.[2]

Especially among neonates, but also in children, the peripherally inserted central catheter (PICC) has become one of the main venous access devices due to its numerous advantages, including the preservation of peripheral venous networks, reduction in the number of venipunctures, and minimization of painful procedures.[3] However, despite these benefits, PICC use is also associated with risks, particularly related to catheter tip positioning, which may lead to complications such as phlebitis, extravasation, thrombosis, embolism, infection, arrhythmias, and cardiac tamponade.[2]

To minimize the occurrence of PICC-related adverse events, ensuring accurate central tip positioning is crucial.

The currently recommended strategy relies on anatomical landmark-based measurement, which involves measuring from the insertion site to the right sternoclavicular junction, and then to the right third intercostal space.[2] Nevertheless, this method presents significant accuracy challenges, especially in neonates, for whom the literature reports improper tip positioning rates exceeding 90%.[4]

A new measurement method specifically designed for neonates was proposed to address this issue. This approach, known as the "Tomazoni method", consists of measuring the distance from the insertion site to the right sternoclavicular junction.[4] Preliminary evidence from a single-center study suggested a higher likelihood of achieving central PICC tip positioning when using this method compared with the traditional measurement technique.[4]

Notably, this initial study was the first of its kind conducted in Brazil and was restricted to a single NICU, which limits the generalizability of its findings for neonatal population. In addition, the study had a small sample size and did not assess the influence of potential confounding variables, such as body weight or age, on the performance of the measurement method. Body weight has been shown to affect venous network development and vessel caliber, resulting in thinner and more fragile veins, which may influence PICC tip positioning.[2] The literature lacks measurement strategies specifically designed and validated for the pediatric population, highlighting the need for pediatric exploration.

Therefore, further studies conducted in diverse settings and including broader, more heterogeneous samples are warranted to compare existing measurement methods and to prospectively evaluate the performance of the Tomazoni method. This randomized clinical trial is designed to primarily focus on neonates, while also including children as a secondary population to expand the clinical applicability of the findings.

This paper aims to describe a study protocol designed to prospectively evaluate the effectiveness of the Tomazoni measurement method for PICC insertion in neonates as the primary population of interest, while also including children.

The specific objectives are to determine the expected prevalence of peripheral, central, and intracardiac catheter tip positions using both the traditional and Tomazoni methods are applied, and to estimate the incidence of complications associated with PICC use according to the study allocation groups.

### *Hypotheses*

The Tomazoni method for PICC measurement will be effective in achieving central positioning of the peripherally inserted central catheter in neonates and children, compared to the traditional method.

## METHODS

### *Study design*

This study consists of a protocol for a pragmatic, parallel-group, double-blind randomized clinical trial (RCT). It is designed as an exploratory and parallel RCT in which each participant will be exclusively allocated to one of the two study groups: the experimental group (EG), which will receive the proposed intervention, and the control group (CG), which will undergo the standard procedure. Group allocation will follow a 1:1 ratio.

The development and description of this protocol were guided by the template for intervention description and replication (TIDieR).[5] Additionally, the study report adheres to the criteria established by the consolidated standards of reporting trials (CONSORT) checklist and standard protocol items: recommendations for interventional trials (SPIRIT) guideline.[6,7]

No patients or members of the public were involved in the design, conduct, or reporting of this trial, which was prospectively registered in the Brazilian clinical trials registry (ReBEC) under the identifier RBR-55zwb45.

### *Study setting and sampling*

The study will be conducted in a neonatal intensive care unit (NICU) and in pediatric inpatient and intensive care units of a large public hospital located in Belo Horizonte, Minas Gerais, Brazil. The study sample will consist of PICC insertion procedures performed in neonates and children up to 12 years of age. Neonates will constitute the main study population, with children included to explore applicability beyond the neonatal setting.

To ensure adequate sample size and sufficient statistical power to detect differences between groups, a sample size calculation was undertaken.[8] For the neonatal population, the calculation was based on an estimated central positioning rate of 2.3% in the CG and 47.7% in the EG,[4] with a 95% confidence level, 80% statistical power, and a 25% minimum difference between groups. Therefore, the representative sample was estimated to include at least 44 procedures in total, accounting for a 20% loss.

Additionally, given the absence of prior studies conducted in the pediatric population, a pilot study will be carried out as an initial exploratory phase in this population. In this case, the sample size calculation was based on a minimum of 50 procedures, plus an estimated loss rate of 20%, resulting in a total sample of 64 procedures.[9]

### *Inclusion and exclusion criteria*

As an inclusion criterion, PICC insertion in upper limbs will be required, since the Tomazoni method is intended exclusively for insertions in upper limbs. The non-inclusion criteria are congenital abnormalities of the

venous system; structural malformations of the upper limbs; variations in the anatomical position of the heart; diaphragmatic hernia; and hemodynamic instability. These criteria are justified as they are factors related to the neonate or child that may influence central PICC positioning, thus potentially introducing selection bias.

***Randomization***

Randomization refers to the process of randomly allocating subjects between study groups and constitutes a methodological strategy aimed at reducing bias.[8,10] In the present study, a stratified block randomization method will be applied. Each participant will first be classified into a specific stratum, and then, each stratum will be independently listed for random allocation.[10] For the neonatal population, stratification will be based on birth weight, categorizing newborns into normal weight (≥2,500 g) and low birth weight (<2,500 g). For the pediatric population, stratification will consider three age ranges: infants (29 days to <2 years), preschool children (2 to <6 years), and school-aged children (6 to 12 years). The insertion procedures will be allocated in blocks of four, alternating between the EG and CG, ensuring balanced distribution.

These randomization lists will be prepared by an external collaborator who is not part of the research team and will be responsible for assigning the procedures to the respective groups within each defined stratum. The folders will be prepared containing opaque, tamper-proof envelopes, sequentially numbered. Each envelope will contain the group allocation designation, identified by alphabetical codes (A or B). The definition of which code corresponds to the EG and CG will be determined in advance, confidentially, also by an external collaborator, without the knowledge of the research team.

Only the nurses responsible for PICC insertion will have access to the group designation indicated in each envelope, as they must apply the method corresponding to the assigned group protocol. The identity of the groups (A or B) will remain confidential for the remaining members of the research team until completion of the statistical analysis and conclusion of the planned study. In case of a large number of peripheral positioning, noticed by the nurses responsible for the catheter insertion, the research may be suspended and unblinding procedures may be initiated for safety reasons.

***Study interventions***

The only difference between the groups will be the measurement method. The CG will undergo the traditional measurement method: from the insertion site to the sternoclavicular junction and then to the third right intercostal space.[2] The EG will be subjected to the Tomazoni measurement method: from the insertion site to the right sternoclavicular junction (Figure 1), with allocation ratio of 1:1.[4]

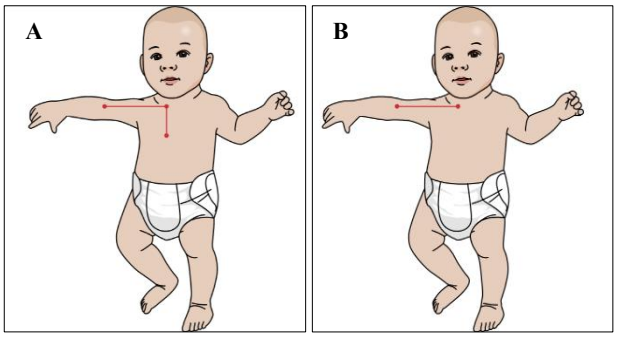


**Figure 1 (A and B): Traditional method of measurement (left) and Tomazoni method (right).**

PICC insertion procedures will follow the research protocol described below: indication for PICC by the attending team and communication to the research team, assessment of eligibility according to inclusion and non-inclusion criteria; contact with legal guardians and signing of the informed consent form, as well as the assent form; procedure randomization; measurement of the catheter length to be inserted; according to randomization group - inspect upper limbs and select potential catheterization sites, position the upper limb extended at a 90° angle in relation to the body, if CG measure the distance from the insertion point to the right sternoclavicular junction and then to the third right intercostal space, using a flexible, non-elastic, standardized measuring tape, if EG, measure the distance from the insertion point to the right sternoclavicular junction using a flexible, non-elastic, standardized measuring tape, and record potential catheterization sites and their respective insertion lengths; procedure for PICC insertion; request radiograph for tip confirmation, with patient positioned in the supine position, with arms extended in adduction; check catheter tip position; adjust catheter length by traction, if appropriate; and complete the data collection instrument.

***Study variables and outcomes***

For data collection, an instrument based on recommendations from the literature will be used, particularly the guidelines proposed by the INS, which include information on PICC insertion, maintenance, and removal procedures.[2] In addition, the instrument will collect information regarding patient characteristics and details of the insertion procedure.

The intervention variable corresponds to the PICC measurement method according to group allocation. The primary outcome variable concerns the initial location of the catheter tip: the position of the PICC tip on the first radiograph taken immediately after catheter insertion. Central positioning will be defined as placement in the superior vena cava or the cavoatrial junction.[2] Secondary outcomes will include the occurrence of catheter withdrawal after radiography; the length of the catheter withdrawn; PICC dwell time; and the reason for PICC removal.

To ensure objectivity in defining central positioning, radiographs will be analyzed by two external collaborators not involved in the study, who are nurses and/or neonatologists and pediatricians with expertise in radiographic evaluation. In cases of disagreement, a third evaluator will be consulted. All evaluators will be blinded to the randomization group allocation.

***Data collection***

The research will be carried out in stages. In the first stage, the study will be presented to the managers and coordinators of the participating units, as well as to the nurses involved.

The second stage of the study will consist of training the nurses qualified to perform PICC insertion. The training will be conducted by the research team, and the professionals will receive guidance and engage in practical exercises using both measurement methods and at different puncture sites.

The final stage will consist of the prospective implementation of the Research Protocol. The trained nurses will carry out the intervention, and the research team will be continuously available to clarify any questions that may arise.

Table 1 presents the participant timeline for the study.

As this study involves a single intervention with outcomes assessed immediately thereafter, no specific strategies to ensure protocol adherence are planned, and there is no anticipated risk of data loss.

**Table 1: Study timeline for enrolled participants.**

| Timepoint | Enrollment | Intervention allocation | Post-randomization | | | |
|---|---|---|---|---|---|---|
| | | | $t_1$ | $t_2$ | $t_3$ | $t_4$ |
| **Enrollment** | | | | | | |
| Eligibility screen | X | | | | | |
| Informed consent | X | | | | | |
| Randomization | | X | | | | |
| **Intervention/comparator** | | | | | | |
| Intervention group | | | X | | | |
| Control group | | | X | | | |
| **Assessments** | | | | | | |
| Tip position | | | | X | | |
| Catheter related complications | | | | | X | |
| Catheter removal | | | | | | X |

t1 – catheter insertion; t2 – radiography for tip location confirmation; t3 – catheter dwell time, t4 – catheter removal

***Data analysis***

The collected variables will be organized and analyzed in a database using the statistical software statistical package for the social sciences (SPSS)® version 29, with double-checking. Descriptive statistics will be performed using absolute and relative frequencies, measures of central tendency, and measures of variability, according to the type and normality of the data. The Kolmogorov-Smirnov test will be applied to assess the adherence of the variables to a normal distribution.

To assess associations between qualitative variables, association tests and measures will be applied, such as the Chi-square and risk ratio, with a 95% confidence interval and a significance level of 5%. For numerical variables with a normal distribution, the *t*-test will be used, and for asymmetric distributions, the Mann-Whitney test will be applied.

The statistician responsible for data analysis will be blinded to the assignment of procedures to the control and experimental groups.

***Ethical considerations***

The study has been approved by the Research Ethics Committee of the Federal University of Minas Gerais, under opinion number 6.746.823 and CAAE 71842123.3.0000.5149, and by the Research Ethics Committee of the Hospital, under opinion number 6.835.486 and CAAE 71842123.3.3001.5129.

At the time eligibility criteria are verified for neonate and children, consent from the legal guardians will be obtained through the signing of the informed consent form (ICF). As healthcare professionals are responsible for PICC insertion procedure, all personnel will also receive guidance and will be invited to sign the ICF should they agree to participate.

The data collected will be accessed exclusively by the researchers and will be used for the publication of scientific results, with participant anonymity fully ensured. All data will be stored in a secure location for a period of five years, after which they will be deleted and/or incinerated.

## DISCUSSION

This randomized clinical trial protocol has been developed to evaluate the effectiveness of the Tomazoni measurement method compared with the traditional anatomical landmark-based approach for determining the optimal length for PICC in neonates and children. By addressing the high prevalence of inadequate tip positioning reported in previous studies, this research aims to generate robust evidence to guide clinical decision-making and to potentially improve patient safety in neonatal and pediatric venous access.

Although the PICC is recognized for its benefits such as reducing multiple venipunctures and preserving peripheral venous integrity, its safety is largely dependent on accurate tip placement.[2-3,11] Inadequate positioning can result in serious complications, including thrombosis, extravasation, and even cardiac tamponade. The literature indicates that improper tip positioning remains a persistent challenge, highlighting the need for innovative and reproducible measurement strategies that can be easily implemented in clinical settings.[4]

The Tomazoni method has shown promising accuracy compared with the traditional measurement techniques in a previous single-center study.[4] However, as this prior research was limited to a neonatal population and conducted in a specific institutional context, the generalizability of its findings remains restricted. The present trial is designed to address these gaps by including both neonatal and pediatric populations, applying a rigorous randomization process, and ensuring blinding across all key phases of the study. These methodological strengths are expected to enhance internal validity and minimize the risk of selection and measurement bias.[8-10]

Another relevant contribution of this protocol is the use of stratified randomization, which enables balanced distribution of key confounding factors, such as age and birth weight, across groups. These variables may influence venous anatomy affecting the accuracy of tip placement. In addition, the inclusion of a pilot pediatric population represents an important step toward expanding evidence. Thus, this trial has the potential to address a significant knowledge gap and to inform the development of pediatric-specific measurement guidelines.

The intervention is designed to emphasize reproducibility and clinical feasibility, as both measurement methods require minimal resources and can be performed by trained nurses at the bedside. This pragmatic approach is expected to enhance the study's external validity, increasing its potential for translation into routine practice across diverse healthcare settings. Furthermore, the trial incorporates rigorous procedures for blinding and radiographic assessment, which are intended to strengthen the reliability of outcome evaluation.

Despite its strengths, the study may present some limitations. The single-center nature of data collection may limit the generalizability of the findings to other institutions with different organizational structures or patient profiles. Future multicenter studies may be required to further validate the results across varied clinical contexts.

As a limitation of the study, the time elapsed between the PICC insertion procedure and the performance of the X-ray will be considered, since X-rays are not done immediately after PICC insertion procedure in the institution where the study will take place.

## CONCLUSION

The findings are expected to contribute to the development of safer and more effective practices in PICC insertion in children and neonates. Furthermore, the results may support the standardization of measurement techniques across neonatal and pediatric settings. By strengthening the scientific basis for clinical procedures, this trial is expected to advance patient safety and quality of care in critical neonatal and pediatric environments.

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