Editorial

JVA The Journal of Vascular Access

In defense of the use of peripherally inserted central catheters in pediatric patients

The Journal of Vascular Access
1–4

DOI: 10.1177/1129729820936411
journals.sagepub.com/home/jva
SAGE

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Abstract

Central venous access devices have revolutioned the care of children affected by malignancies, facilitating management of complex and prolonged infusive therapies, reducing pain and discomfort related to repeated blood samples and indiscriminate venipunctures, thus reducing also psychological stress of both patients and families. In this respect, peripherally inserted central catheters have been disseminated for use, even in pediatric oncology patients, for their many advantages: easy and non-invasive placement with no risk of insertion-related complications, as well as easy removal; reduced need for general anesthesia both for insertion and removal; adequate prolonged performance also for challenging therapies (e.g. stem cell transplantation); and low rate of late complications. Nonetheless, concerns have been recently raised about use of such devices in children with cancer, especially regarding a presumed (but not demonstrated) high risk of catheter-related venous thrombosis. Are we facing a new witch (or peripherally inserted central catheter) hunt? The choice of the central venous access device—particularly in oncologic children—should be based on an evaluation of clinical advantages and risks, as provided by appropriate and scientifically accurate clinical studies.

Keywords

Peripherally inserted central catheters, children, cancer, pediatric oncology, central venous catheters, catheter-related thrombosis

Date received: 13 March 2020; accepted: 27 April 2020

Central vascular access devices (CVADs) are vital in managing and treating pediatric cancer, providing for long-term delivery of prolonged courses of chemotherapy as well as for infusion of parenteral nutrition, blood products, intravenous fluids, antibiotics, pain medications, and other therapeutic agents. Furthermore, they are precious for repeated blood sampling. Over the years, different CVADs have been used, with different features and indications according to patients needing as well as to therapy length, intensity, and regimen.

Although CVADs have greatly improved the quality of care in pediatric oncology patients, still these devices are not without risk for complications, both early (pneumothorax, hemothorax, arterial injury, air embolism, nerve injury, catheter malposition) and late (infection, lumen occlusion, venous thrombosis). These events have

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different incidence and outcome depending on type and length of treatment, technique of CVAD placement and, of course CVAD type. In this respect, peripherally inserted central catheters (PICCs) have steadily gained popularity in the last decade, because of their advantages in terms of easy and uneventful insertion/removal without anesthesia, easy handling especially in adolescent patients, and clinical performance similar and even better if compared to centrally inserted central catheters (CICCs).[1,2] The concepts of minimal invasiveness and maximal safety at insertion have strongly pushed the utilization of PICCs, tunneled PICCs and PICC ports as an attractive alternative to CICC, tunneled CICCs, and chest ports. However, concerns regarding use of those devices in children with malignancies have been recently raised, due an alleged increased risk of catheter-related thrombosis (CRT) and subsequent thromboembolism.[3]

In 1692, in the city of Salem, Massachusetts, some children began to suffer strange symptoms. "These children were bitten and pinched by invisible agents; their arms, necks, and backs turned this way and that way, and returned back again, so it was impossible for them to do of themselves."[4] That was the beginning of the (in)famous "Salem Witch Trial": 144 people were prosecuted for witchcraft, and 19 of them were sentenced to death and executed. Only after decades they were pardoned from their charges.

With all due proportions, the Salem Witch Trial event parallels with some current surprising statements about PICCs in children with cancer . . . not far to trigger a "PICC hunt," rather than a "witch hunt."

We acknowledge the importance of central venous catheters in pediatric population and the subsequent, necessary, high-level, and evidence-based standard of care required for such devices in order to avoid potentially life-threatening complications. This concept is summarized, with special regard about children, in the Infusion Nursing Society (INS) Standards of Care:[5]

> To ensure patient safety, the clinician providing infusion therapy for special populations (neonatal, pediatric, pregnant, and older adult populations) is competent in clinical management of such populations, including knowledge of anatomical and physiological differences, safety considerations, implications for CVADs planning and management, and infusion administration.

The concept of "patient safety" must be a necessary prerequisite and must include also "knowledge" and "competence" as cornerstones of vascular access common practice, especially considering prevention of serious complications such as thrombosis or infection.

In particular, prevention of thrombosis must include the following:

- Correct indication to the device for each single patient;
- Adequate match between vein and catheter, as the catheter caliber should not exceed 33% of the diameter of the target vessel;[5,6]
- Mandatory use of ultrasound guidance during venipuncture, so to reduce cannulation attempts and minimize endothelial damage;[7]
- Accurate tip location, to be checked during the procedure and prior to use the device, so to avoid infusion-related damage;[5]
- Catheter securement with appropriate device (sutureless devices and/or subcutaneously anchored securement devices), to avoid both dislodgment and endothelial damage.[5]

Recently, Jaffray et al.[3] published a prospective, multicenter, cohort study in which they analyzed the risk of CRT, central line–associated bloodstream infection (CLABSI), and catheter malfunction associated with PICCs in pediatric patients. The authors reported a higher risk of complications with the use of PICCs compared to tunneled CICCs and ports, both in terms of thrombosis and infection. In particular, the authors' conclusion that PICCs may be associated with a 9% risk of CRT may have a significant impact in the daily clinical practice. Their results appear to be clear and strong in the abstract of their paper, but things look different at a closer examination of their work:

1. First, there is some confusion about the devices Jaffray and coworkers are talking about. In their study, the eligible patients were "children aged 6 months to less than 18 years with a newly placed PICC or tunneled lines (TL)." In table 1, the authors shows that children from 0.5 to 5 years represented 40% of PICC population (n = 499), with an impressive number of PICCs (101) inserted in children aged from 6 months to 1 year, that equals to 20% of patients under 5 years of age. Obviously, in their analysis, the authors did not differentiate PICCs from epicutaneo-caval catheters (ECC). ECCs are commonly used in neonatal intensive care, and they are sometimes considered as "PICCs" since their insertion is performed through a peripheral vein and the tip is (or should be) in either the superior or the inferior vena cava. However, ECCs are absolutely different from PICCs in terms of technique insertion and use, if compared to PICCs, and they are notoriously characterized by high risk of local thrombosis. In clinical practice, ECC and PICCs are devices with completely different characteristic in terms of caliber and material; they are used in different populations of patients (neonates vs children), with different technique of insertion (blind percutaneous vs ultrasound guided), in different veins (superficial vs deep veins); they have

different performance and different incidence of complications.[8–10] In other words, ECC in neonates/infants and PICC in children are two devices that should never be pooled together in the same analysis.

2. Another issue is related to technique of insertion. Considering that the technique of PICC insertion is of paramount importance to minimize the risk of thrombosis,[7] it is noteworthy than Jaffray et al.[3] did not report any information about the insertion technique, such as the ratio between catheter caliber and vein diameter, the use of ultrasound-guided insertion versus blind insertion of PICC at mid arm, or the adoption of a proper intraprocedural method of tip location. The reported incidence of 9% of catheter-related venous thrombosis may be simply the result of "inappropriate" techniques of insertion, that is, techniques unaware of the current evidence-based recommendations for reducing CRT. The use of large-bore catheters that occupy more than 45% of the vein diameter, and/or the adoption of "blind" percutaneous venipuncture in the antecubital fossa, and/or an inaccurate tip location are all independently associated with an increased risk of CRT.[6]
3. Last but not least, the authors' conclusions about the risk of infection are also inconsistent. The data they report go in opposite direction to previously published data.[11–13] We believe that in this study the comparison between devices was inappropriate and unfair. In fact, the authors report a higher incidence of CLABSI in patients with PICCs than in patients with "TL." They also clearly state that more than 70% of the "TL" are totally implanted ports: while the definition of ports as "TL" is somehow inappropriate, ports notoriously have a low rate of infective complications.[2,6,14–19] However, in our opinion, a comparison between ports and PICCs has little clinical sense, since these devices have different indications (intermittent long-term use for ports vs continuous short- to medium-term use for PICCs), as clearly stated in the INS standards of practice.[5] Moreover, 30% of "TL" in the study were tunneled CICCs. It is widely known that tunneling is a factor that independently reduces the risk of extraluminal contamination.[19] As a matter of fact, in many institutions, PICCs are tunneled so to reduce this risk: We believe a fair and acceptable comparison would have been between tunneled CVADs (tunneled PICC and/or tunneled CICC) versus non-tunneled CVADs (non-tunneled CICC and/or non-tunneled PICC). In conclusion, it makes no sense to compare tunneled CICC versus non-tunneled PICC: the resulting difference will be obviously related to the presence of the tunnel and not to the type of device.

The worldwide diffusion of the paper by Jaffray et al.[3] may have some dangerous side effects in clinical practice. An acritical acceptance of the conclusions of their study may start another "witch hunt" against PICCs. We have seen all this once before. In 2013, a paper published in *The Lancet*[20] suggested that in adult patients PICCs might be associated with a high risk of venous thrombosis; this contention was supported by a "systematic review" and by a "meta-analysis" of the studies available at that time. Interestingly, that analysis had the same limitations of the study by Jaffray et al.:[3] the authors had pooled many different clinical studies on PICCs, without differentiating between ultrasound-guided PICCs and PICCs inserted "blindly" in the antecubital fossa; asymptomatic and symptomatic thrombosis had been considered together as similar events; most of the studies included in the analysis did not report any detail about the insertion technique, in terms of match of the catheter caliber with catheter size, tip location method, and so on. In other words, the authors' conclusions were inappropriate and inconsistent because of an inaccurate pooling of different clinical situations. Unfortunately, their final clinical "messages"—though quite incorrect and definitely misleading—were automatically accepted by many key opinion leaders and even included in some guidelines[5] and in some consensus documents.[21] In particular, the dogma that PICC may be dangerously associated with venous thrombosis, especially in intensive care and in oncologic patients, though highly questionable, became quite popular in the world of venous access. Since 2013, many clinical studies have shown that the risk of PICC-related thrombosis is similar to the risk of CICC-related thrombosis, when the insertion technique follows the current recommendation of good clinical practice.[4,7,22–24] Still, some negative effect of that "witch hunt" still linger on. There is no need to witness a new unreasonable campaign against PICCs. It is no time for a witch hunt; it is time for good research, and for evidence-based data.

A recent paper published on this Journal[7,25] has clearly discussed this issue, focusing on the current need for appropriate methodology both in clinical studies and in meta-analysis, so to avoid inaccurate interpretations of the data, which is a phenomenon unfortunately becoming quite frequent in the area of venous access.

In conclusion, at present, there is no evidence that an ultrasound-guided PICC inserted according to the current recommendations may have more risk of CRT or of CLABSI if compared to other non-tunneled central venous access devices, neither in adults nor in children. On the other hand, vascular access experts and pediatric healthcare providers must be aware that in pediatric patients, PICCs have a very low risk of relevant insertion-related complications, while the insertion of a CICC is associated with a little but not irrelevant incidence of severe complications.

Author contributions

All authors discussed and contributed to the final manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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