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Journal of Surgery

Martin B, et al. Martin B, et al.

Research Article

DOI: 10.29011/2575-9760.001277

New Era in Central Venous Access, Superiority of the PICC in the Control of Infections

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Citation: Martin B, Pomar V, Guerrero R, Cornudella E, Sánchez I, et al. (2020) New Era in Central Venous Access, Superiority of the PICC in the Control of Infections. J Surg 5: 1277. DOI: 10.29011/2575-9760.001277

Received Date: 17 January, 2020; **Accepted Date:** 27 January, 2020; **Published Date:** 30 January, 2020

Abstract

Background: Peripherally Inserted Central Catheters (PICCs) are an alternative to Central Venous Catheters (CVCs) for the administration of intravenous therapy in hospital settings. Until now, PICCs have been used in highly selected patients and without a clear indication in our hospital. Our study aims to demonstrate that the use of PICCs is associated with a lower rate of bacteremia, in addition to a lower incidence of other complications, and better quality of life.

Methods: This is a prospective, randomized single-center study whose main objective is to analyze the rate of bacteremia associated with non tunneled CVCs compared with PICCs. We also analyzed the incidence of complications during the insertion and maintenance of central venous catheters, 30-day mortality, duration of hospital stays in both arms, and perceived quality of life of patients measured using a visual analog scale for pain.

Results: Thirteen cases of catheter-associated bacteremia were diagnosed (5.4%), of which 11 (9%) cases corresponded to CVCs and 2 (1.6%) to PICCs, $p < 0.001$. The hospital stay was more prolonged in patients with CVCs who had complications during insertion or maintenance compared with patients with PICCs, $p = 0.004$ and $p = 0.04$, respectively. The CVC group also had more pain also during catheter insertion and 72 hours after insertion compared with the PICC group ($p < 0.001$ vs. $p = 0.04$).

Conclusion: In our study population, PICCs compared with CVCs were associated with fewer cases of bacteremia, less risk of insertion complications, and a better patient quality of life.

Keywords: Bacteriemia; Central venous catheter; Insertion complications catheter; Peripheral central venous catheter

Introduction

The use of Peripherally Inserted Central Catheters (PICCs) has increased in current clinical practice. The ease of insertion, numerous indications similar to those for Central Venous Catheters (CVCs) (e.g., administration of chemotherapy agents, antibiotics, blood products, parenteral nutrition, monitoring, and as venous access in difficult cases), safety, patients' perceived comfort, and the cost-benefit ratio in comparison with other CVCs account for the popularity of PICCs [1,2].

Despite these benefits, PICCs can also have mechanical and infectious complications. Catheter-related bacteremia [1-3] is currently the main cause of nosocomial bacteremia, which increases mortality and prolongs the hospital stay and costs [4-6]. Some studies suggest that PICCs are associated with a lower risk of catheter-related bacteremia compared to other devices [7-9]. Other studies find a higher risk, [10,11] although we have not found randomized studies comparing both techniques in patients

hospitalized in conventional wards. For this reason, we conducted this prospective randomized study with the primary objective of comparing the risk of bacteremia associated with PICCs compared to CVCs in adult patients in a tertiary hospital.

Material And Methods

Study Design

The study is a prospective, single-country, single-center, randomized (ratio 1:1) clinical trial approved by the ethics committee of our hospital. It was carried out during the standard practice of insertion and maintenance of central venous catheters in hospitalized patients. The study period was comprised between September 2015 and July 2017. The main objective was to compare the rate of bacteremia associated with non tunneled CVCs versus PICCs. The secondary objective was to compare the incidence of complications during the insertion and maintenance of central venous catheters, 30-day mortality, hospital stay in both arms, and the perceived quality of life of patients measured using a visual analog scale for pain.

The demographic data, rate of associated comorbidities, indications for catheter placement, causal microorganisms in bacteremia, and catheter site were collected for both groups.

Patients

Hospitalized patients older than 18 years who required at least 6 days of intravenous treatment in a conventional hospital ward were included. Patients with hematologic disease or hospitalized in the Intensive Care Unit were excluded because the baseline conditions of disease severity and immunosuppression are not comparable to those of patients in a conventional hospital ward. Patients with bacteremia or a severe clinical situation at the time of catheter insertion, outpatients, pregnant women, patients in whom peripheral venous access was not technically possible, or patients who expressly refused were also excluded. Following standard clinical practice, PICCs were inserted in the interventional radiology unit by nursing staff trained in ultrasound-guided placement. The central venous catheters were inserted in the central operating room or in the boxes of the semicritical unit by the general surgeons of the department using the standard Seldinger technique.

Systematic Review of the Literature

We searched PUBMED (including MEDLINE), MEDLINE, EmBASE, and Cochrane CENTRAL using the following keywords: "peripherally inserted central catheter", "PICC", "prospective", "central venous catheter" and "bacteremia", as well as combinations of these search terms. We restricted our search to PICCs in hospitalized patients since the objective of this article was to determine the rates of catheter-related bacteremia associated with PICCs in hospitalized patients.

Statistical Analysis

Continuous variables were expressed as the mean and Standard Deviation (SD) or median and Interquartile Interval (IQR), depending on their homogeneity. Categorical variables were expressed as absolute numbers and percentages. The Student t test or the nonparametric Mann-Whitney test were used to evaluate the continuous variables, and the Fisher exact test or the Chi square test were used for the categorical variables. Values of $p < 0.05$ were considered statistically significant. The SPSS statistical application (version 19) was used for data processing. An interim analysis was performed with 50% of the patients recruited. The research team created the database, entered the data, and conducted the statistical analysis.

Results

A total of 301 patients were analyzed, of which 45 were excluded for not meeting the inclusion criteria. Of the remaining 256 patients, 9 were excluded for the reasons detailed in Figure 1.

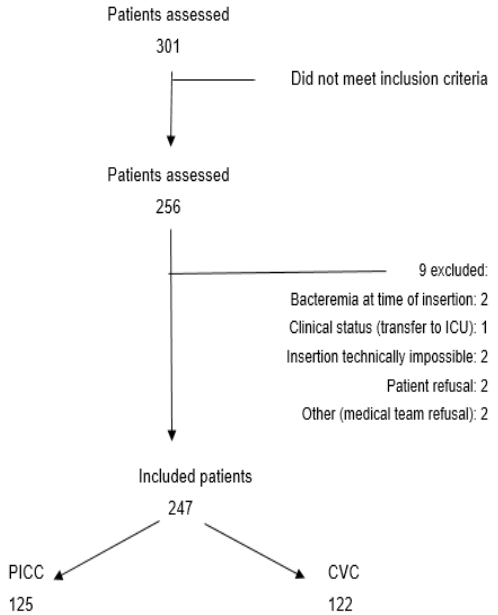

Figure 1: Patient inclusion and randomization tree.

Out of the remaining 247 patients, 125 were in the PICC arm and 122 in the CVC arm. During the study period, 247 central venous catheters were inserted: 125 PICCs and 122 CVCs. The

total population had 44% women (n = 108). In the CVC group, the median and mean ages were, respectively, 68.2 years and 69.5 years (SD 13.4), and in the PICC group, the median and mean ages were 69.6 years and 72 years (SD 14.5). In our global population, 95.5% had associated comorbidities measured according to the Charlson Comorbidity Index, of which 7.6% had high or very high values. The indication for catheter insertion was the administration of parenteral nutrition in 49% of the patients (n = 121), and the administration of antibiotic therapy in 35% (n = 87). Chemotherapy administration was not the indication for any case.

CVC insertion was mainly in the subclavian vein (105 patients, 86%) and PICC insertion was mainly in the basilic vein (113 patients, 90%) (Figure 2). During the study period, 13 (5.4%) cases of catheter-related bacteremia were diagnosed, of which 11 (9%) cases corresponded to CVCs (9 in subclavian vein and 2 in jugular vein) and 2 (1.6%) to PICCs, $p < 0.01$. The microorganism that caused the largest number of cases of bacteremia was *Staphylococcus epidermidis* (7 patients, 53.8%), followed by *Staphylococcus hominis* and *Pseudomonas aeruginosa* (each in 2 patients, 15.4%), and *Candida albicans and Enterococcus faecium* (each in 1 patient, 7.7%). Polymicrobial bacteremia did not occur in any patient. There were no significant differences in terms of the rate of bacteremia and the anatomic insertion site of the catheter: 11.8% (n = 2) jugular, 8.5% (n = 9) subclavian, 2% (n = 2) basílic, and 0% (p = 0.2) brachial and cephalic veins.

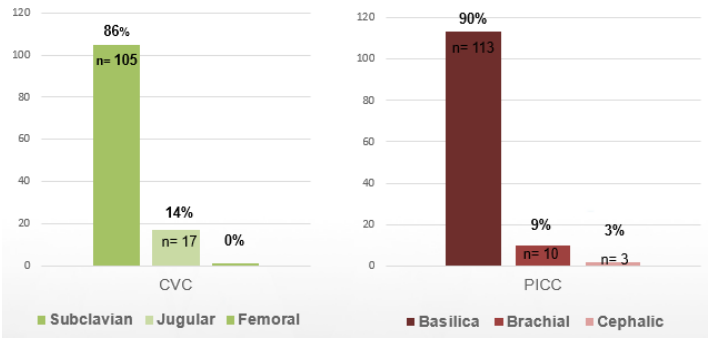

Figure 2: Catheter location.

Regarding the possible relationship between bacteremia and the place of intervention in the hospital, the global analysis showed that CVCs were associated with bacteremia significantly more often than PICCs (9%, n = 11 cases vs 1.6%, n = 2 cases, p = 0.02). However, in the CVC group we did not find significant differences in relation to the place of intervention and the occurrence of bacteremia: of 104 CVCs inserted in the operating room, 9 (8.7%) were associated with infection and of 14 CVCs inserted in the semicritical unit, 2 (14.3 %) were associated with infection (p = 0.06). Multivariate analysis of the catheter type, place of intervention, and rate of catheter-related bacteremia showed that the relationship between bacteremia and the type of inserted catheter (CVC/PICC) was more important than with the place of intervention (p = 0.02; OR 6.1; 95% CI [1.3 - 28.1]). Likewise, we did not find statistically significant differences between the indication for catheter insertion and the occurrence of bacteremia: 9 for parenteral nutrition (8%), 2 for lack of peripheral venous access (7%), and 2 for antibiotic administration (7%) (p = 0.6).

Other complications related to catheters during insertion or maintenance are listed in Table 1. Patients with more comorbidities had a greater number of complications during catheter insertion (p = 0.04). However, we did not find differences between the highest number of comorbidities and maintenance complications (p = 0.3). In the CVC group with insertion complications, we observed a significant increase in the duration of the stay, which was extended to a mean of 24 days, SD 25.1, p = 0.004 (Figure 3). In contrast, in the PICC group the mean hospital stay was not prolonged in a statistically significantly way in patients with insertion complications (20 days [SD 16.2] vs. 27 days [SD 17.9], p < 0.06) or with maintenance complications (34 days [SD 19.9] vs. 26 days [SD 17.6]) (p = 0.09) (Figure 4). The patients in the CVC arm who did not have maintenance complications had a mean hospital stay of 28 days (SD 17.2), whereas those who had maintenance complications had a hospital stay up to 17 days longer (mean stay 45 days [SD 28.5]) (p = 0.04). The quality of life of the patients in the CVC group, as measured by the pain VAS score, was a mean of 2.56 (SD 1.43) during catheter insertion and 0.62 (SD 1.46) at 72 hours, while in the PICC group the pain VAS scores were 1.72 (SD 1.23) and 0.50 (SD 0.89), respectively. During catheter insertion, the pain VAS score was ≥ 4 in 16% (n = 19) of the patients with CVCs and in 4.3% (n = 5) of the patients with PICCs (< 0.001), while at 72 hours the pain VAS score was ≥ 4 in 3.6% (n = 4) of the CVC group versus 0.9% (n = 1) of the PICC group (p = 0.04). Overall mortality at 30 days of the catheter insertion was 4.5% (n = 5) in the CVC group and 5.2% (n = 6) in the PICC (p = 0.53).

	CVC n (%) (n 122)	**PICC n (%) (n 125)**
Insertion complications		
- Venous dissection	**0**	**1 (0.4%)**
- Bruising	**2 (0.8%)**	**0**
- Arterial puncture	**6 (2.4%)**	**0**
- ≥ 2 punctures	**1 (0.4%)**	**0**
- Pneumothorax	**3 (1.2%)**	**0**
- Hemothorax	**0**	**0**
Maintenance complications		
- Catheter obstruction	**6 (2.6%)**	**7 (3.1%)**
- Phlebitis	**0**	**0**
- Upper limb edema	**1 (0.4)**	**0**
- Septic shock	**3 (1.2%)**	**0**

Table 1: Complications during catheter insertion and maintenance.

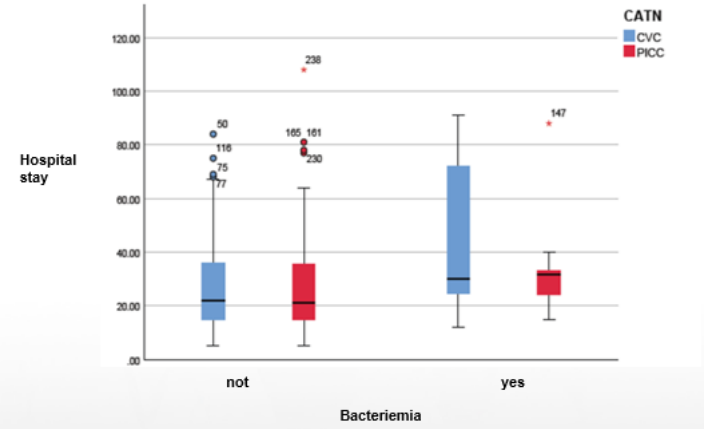

Figure 3: Effect of complications during catheter maintenance and duration of hospital stay.

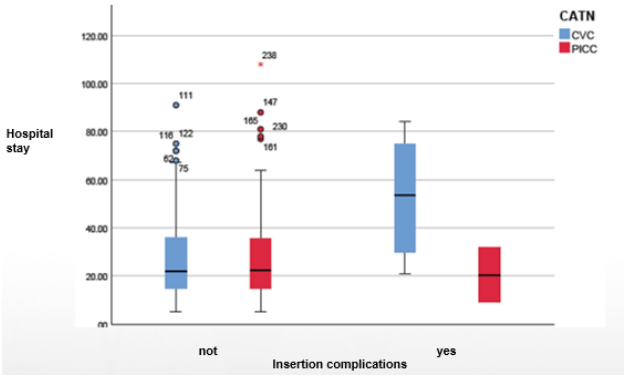

Figure 4: Effect of complications during catheter insertion and duration of hospital stay.

Discussion

Numerous studies with PICCs have suggested that they have a much lower risk of catheter-related bacteremia than conventional CVCs inserted in the internal jugular, subclavian or femoral vein, perhaps due to less dense bacterial colonization of the arm compared to the neck, upper chest, or groin [12]. However, most of these studies were retrospective and the PICCs were used exclusively or mainly in the outpatient setting, in children, or in patients in the intensive care unit [13-18]. Therefore, until now we have not had studies that analyzed and compared the rate of complications with both types of catheters in patients hospitalized in conventional wards. In our study, we found a much lower rate of bacteremia related to PICCs than to CVCs (1.6% vs. 9%, $p < 0.001$). It is notable that the rate of bacteremia related with PICCs was lower in our study than in earlier studies, [19-24] in which the rate ranged from 0 to 4.5 per 100 catheter days, although it is true that these differences could be explained in part by differences in the patient populations, the duration of catheter implantation, and the degree of catheter manipulation in these studies. This is why we excluded patients from the ICU and the Hematology Department from our study. In the prospective study by Basel Al Raly, et al. [7] which had a population similar to ours of patients hospitalized in a conventional ward in which the PICCs were inserted by radiology nurses and the CVCs were inserted in both the critical area and in the operating room, they also concluded that PICCs had a lower rate of bacteremia compared to CVCs and that infection occurred later.

Catheter-related infections can occur as a result of several different mechanisms: infection of the catheter exit site with migration of the microorganisms along the extraluminal surface, usually due to deficient aseptic technique at the time of insertion; intraluminal colonization of the catheter due to internal migration of microorganisms, usually due to incorrect manipulation of the connections and lumens; a hematogenous focus at a distance, or contamination of the fluid administered. One randomized trial found that subclavian venous catheterization was associated with a significantly lower rate of total infectious complications than femoral venous catheterization, and a trend towards a lower rate of suspected or confirmed catheter-related bloodstream infections (subclavian: 1.2 infections per 1000 catheter-days vs. femoral: 4.5 infections per 1000 catheter-days; $p = 0.07$)[12-15,25]. These results coincide with our series, in which the rate of bacteremia in relation to the anatomic insertion site was lower in the subclavian (8.5%) than in the jugular (11.8%). With regard to PICCs, other authors, such as Choppra, [26] report a higher rate of bacteremia with the basilic insertion site, which coincides with our finding of a bacteremia rate of 2% at that site compared to 0% for the rest of the insertion sites. The absence of a significant difference in our study is probably due to the number of patients included.

As reported in the literature, the most isolated microorganism in our study was *S. epidermidis (7 cases, 53.8%)*. *In* the series of Nasie Safdar and Basel Al Raly [3,7] it is noteworthy that the rate of *C. albicans* bacteremia was similar to *S. epidermidis,* whereas it was the least frequent microorganism in our study. This may be because those studies included some ICU patients with an immunosuppressive status that was very different from that of patients hospitalized in conventional wards. In the study by Choppra, [26] the risk factors associated with PICC-related bacteremia are analyzed and the number of lumens is an important factor. Double-lumen PICCs had a lower risk of bacteremia compared to triple-lumen PICCs (OR 5.21, 95% CI [2.46 - 11.04] vs. OR 10.84, 95% CI [4.38 - 26.81]). In our study, 6% of the PICCs were single-lumen and 94% were double-lumen, whereas all the CVCs were triple-lumen; this might have contributed to the higher rate of bacteremia with CVCs than with PICCs in our series.

Opilla [16,27,28] and other authors discuss the observation that parenteral nutrition solutions can favor microbial growth. Contamination during preparation and handling is rare in hospitals and in home hospitalization, but it can be difficult to control in a domestic setting. The risk of infection increases in hospitalized patients due to immunosuppression associated with malnutrition, hyperglycemia exacerbated by dextrose infusion, and microbial colonization/contamination of catheter lumens. In our study, parenteral nutrition was the most frequent indication and was associated with a rate of catheter-related bacteremia of 7.8% (n = 9), although the association was not statistically significant (p = 0.6). Our study did not have any case of deep vein thrombosis (DVT) in either arm, in contrast with other studies, [27,28] in which PICCs are associated with a greater risk of DVT (OR 2, 95% CI [55.1 - 54.3], p < 0.0001), but not of pulmonary embolism. The risk of catheter-related thrombosis may vary depending on the insertion site. In the study by Merrer, [12] CVC-related thrombosis occurred in 21.5% of patients with femoral venous catheters and in 1.9% of patients with subclavian venous catheters (P < 0.001). In another observational study, the risk of thrombosis associated with the insertion of a catheter in the internal jugular vein is approximately four times greater than the risk associated with subclavian insertion. The clinical significance of catheter-related thrombosis remains undefined, although all thromboses have the potential to release emboli [29].

In contrast, obstruction of the PICC was one of the major complications in our series (3%), coinciding with the findings of other studies such as that of Delphine, in which obstruction occurred in 8.9%. [30] In the study by David, et al. [25] mechanical complications occurred during CVC insertion. Arterial puncture was the major complication for all three venous access sites, followed by pneumothorax for the subclavian access site, coinciding with the findings in our series. Regarding quality of life in relation to the catheter type, authors such as Fang, Bortulussi or Kang, et al. [31,32] in their multicenter study in cancer patients report that PICCs provide better quality of life in terms of insertion pain (98.6%) and scant limitation of limb mobility (94.1%). The results for pain are similar to ours both during insertion and 72 hours after PICC insertion.

Limitations

Our randomized prospective study had some limitations. In the first place, it was a single-center study, so the results can only be extrapolated to similar populations after taking into account the exclusion of patients from oncohematology, intensive care, and outpatients. Secondly, the insertion of some CVCs in the semicritical unit may entail differences in sterility conditions. Finally, the number of patients included was relatively small, so some conclusions should be considered with caution.

Conclusions

In our study population, the patients with PICCs had a lower bacteremia and higher quality of life. Patients with more comorbidities had a greater number of complications during catheter insertion but not during maintenance.

The mean hospital stay was significantly longer in patients with CVCs who had complications during insertion or maintenance, compared to patients with PICCs. Therefore, we can conclude that PICCs, compared to CVCs, generally resulted in safer vascular access with less risk of mechanical and infectious complications, and a better quality of life for patients hospitalized in conventional wards.

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