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The use of peripherally inserted central catheter reduced the incidence of phlebitis in heart failure patients: A randomized trial

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Abstract

Background: During decompensated heart failure, the use of intravenous inotropes can be necessary. With peripheral venous access, prolonged inotrope infusion can cause phlebitis. However, traditional central venous catheters have possible complications. Peripherally inserted central catheters (PICCs) may be an alternative to traditional catheters.

Aim: Our objective was to compare the incidence of phlebitis between patients with PICC and those with peripheral venous access catheter indwelling.

Methods: In a randomized clinical trial, the patients were randomized to PICC and control groups, with 40 patients in each group. The inclusion criteria were hospitalized patients with advanced heart failure, ejection fraction of <0.45, and platelet count of $>50{,}000/mm^3$ and current use of continuous intravenous infusion of dobutamine. The patients were randomly assigned to receive a PICC or keep their peripheral venous access. The primary end point was the occurrence of phlebitis.

Results: The PICC and control groups included 40 patients each. The median age was 61.5 years; ejection fraction, 0.24; and dobutamine dose, 7.73 μg/(kg min). Phlebitis occurred in 1 patient (2.5%) in the PICC group and in 38 patients (95.0%) in the control group, with an odds ratio of 0.10% (95% confidence interval: 0.01%–1.60%, $p < 0.001$).

Conclusion: In conclusion, in severe heart failure patients who received intravenous dobutamine, PICC use reduced the incidence of phlebitis when compared to patients with peripheral venous access. Therefore, the PICC use should considered over peripheral venous access for prolonged intravenous therapy in heart failure patients.

Keywords

Catheter, phlebitis, congestive heart failure, dobutamine

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Introduction

For hospitalized patients with decompensated heart failure, peripherally inserted central catheter (PICC) is an alternative to peripheral venous catheter to avoid its frequent complications. The PICC is widely known to be recommended in cancer therapy.[1] Moreover, the PICC is safely inserted in a peripheral vein of the arm that needs local anesthesia. Besides its long-term permanency advantage, PICC reduces the risk of injury to the peripheral vein because it delivers irritating drugs into the large central vein. The occurrence of phlebitis with peripheral venous access for continuous infusions is reported in >30% of patients.[2] The central catheter is used to solve this problem. However the centrally inserted central catheter can be associated with complications, like hemothorax or pneumothorax.[3] The PICC is an alternative for the centrally inserted central catheter and it is usually inserted with

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ultrasonography guidance.[4] Infections related to PICC are uncommon in clinical practice.[5]

Frequently, patients with severe advanced heart failure experience decompensation due to pulmonary congestion, low cardiac output, or both. For this life-threatening situation, intravenous inotropics can be necessary. These patients may sometimes become dependent on intravenous inotropics, which require a long-term central venous access line.

The objective of the present study was to assess the effects of PICC indwelling on the incidence of phlebitis in patients with heart failure who have prolonged intravenous inotrope infusion.

Methods

Study design

To evaluate the incidence of phlebitis after PICC insertion in comparison with that after peripheral venous access, an open-label randomized clinical trial was conducted between December 7, 2012 and October 2, 2014 in the adult cardiology department of a university hospital. The patients were randomized into two groups by using permuted blocks of 4. The sequence of randomization was designed with random allocation blocks of 4 using random number tables. The randomization sequence was generated through an online site (www.randomization.com) by M.E.O.; sealed envelopes were prepared by K.R.N.V.; and the participants were assigned to the groups by E.V.C.S.

Population

Patients who were admitted with decompensated congestive heart failure and treated with intravenous inotropic agents through a peripheral venous access were screened to participate in this study. The inclusion criteria were the following: advanced congestive heart failure, use of intravenous vasoactive drugs, left ventricular ejection fraction of <0.45, an upper limb venous system capable of catheter insertion, and peripherally inserted central catheter insertion. The exclusion criteria were as follows: age of <18 years, cardiac pacemaker or defibrillator, uncontrolled or untreated active systemic infection, platelet count of $<50{,}000\,mm^3$, skin injury in the cubital region, and presence of a central catheter. The researcher nurse (E.V.C.S.) assessed and selected all the patients for study inclusion.

Sample size calculation

On the basis of the pilot study data, we estimated the incidence of phlebitis to be 20% in the PICC group and 80% in the control group. To obtain a statistical power of 80% and an α-error of 5%, the necessary sample size was estimated to be 39 patients in each group. For a more conservative estimation, we decided to include 40 patients in each group (80 patients total) to achieve the statistical power if the incidence of phlebitis was 60% in the control group and 20% in the PICC group. In total, 172 patients were evaluated, of whom 86 did not meet the inclusion criteria, and 6 did not agree to participate.

Ethical considerations

Eligible patients were invited to participate and received written information about the study objectives and procedures. After receiving detailed explanations of the study, the patients signed an informed consent form if they agreed to participate. The study protocol was approved by the local ethics committee, and the study was conducted in accordance with the principles of the Declaration of Helsinki (1989). This study was registered at https://clinicaltrials.gov/ct2/show/NCT02854254. There is no conflict of interest.

Intervention and endpoints

The patients were divided into two groups, the PICC and control groups (peripheral venous access). The patients in the PICC group underwent catheter insertion by the researcher under ultrasonography guidance.[4] The PICC was a 4-French, single-lumen catheter with a length of 65 cm (PowerPICC, Bard Access System, https://www.bardaccess.com/products/ir/powerpiccsolo). The researcher (E.V.C.S.) is a nurse well trained in this experimental procedure.

In the control group, the patients were maintained with peripheral venous access with a flexible peripheral intravenous device and evaluated similarly to the PICC group.

The concentration of dobutamine solution was 2 mg/ml, obtained with two ampoules of 20 ml, 250 mg of dobutamine each, diluted in saline solution 0.9% 210 ml (500 mg/250 ml). The studied line, PICC or peripheral access, was used exclusively for dobutamine infusion. Other intravenous drugs were infused through other intravenous access. The dobutamine dose and remaining drug therapy were prescribed by a cardiologist.

The primary endpoint was the occurrence of phlebitis. The researcher evaluated the insertion site daily. The degree of phlebitis was scored according to the Infusion Nurses Society phlebitis scale.[6] Briefly, phlebitis Grade 1 is erythema at access site with or without pain; phlebitis Grade 2 is pain at access site with erythema and/or edema; phlebitis Grade 3 is pain at access site with erythema and/or edema, streak formation, palpable venous cord; phlebitis Grade 4 is pain at access site with erythema and/or edema, streak formation, palpable venous cord >1 inch in length, purulent drainage. Photographs of all the catheters and insertion sites were obtained daily. The patients were followed up to the time of phlebitis occurrence; in the absence of phlebitis, they were followed for 10 consecutive days. The standard management based on Infusion Nursing Society recommendation was adopted in case of phlebitis occurrence.

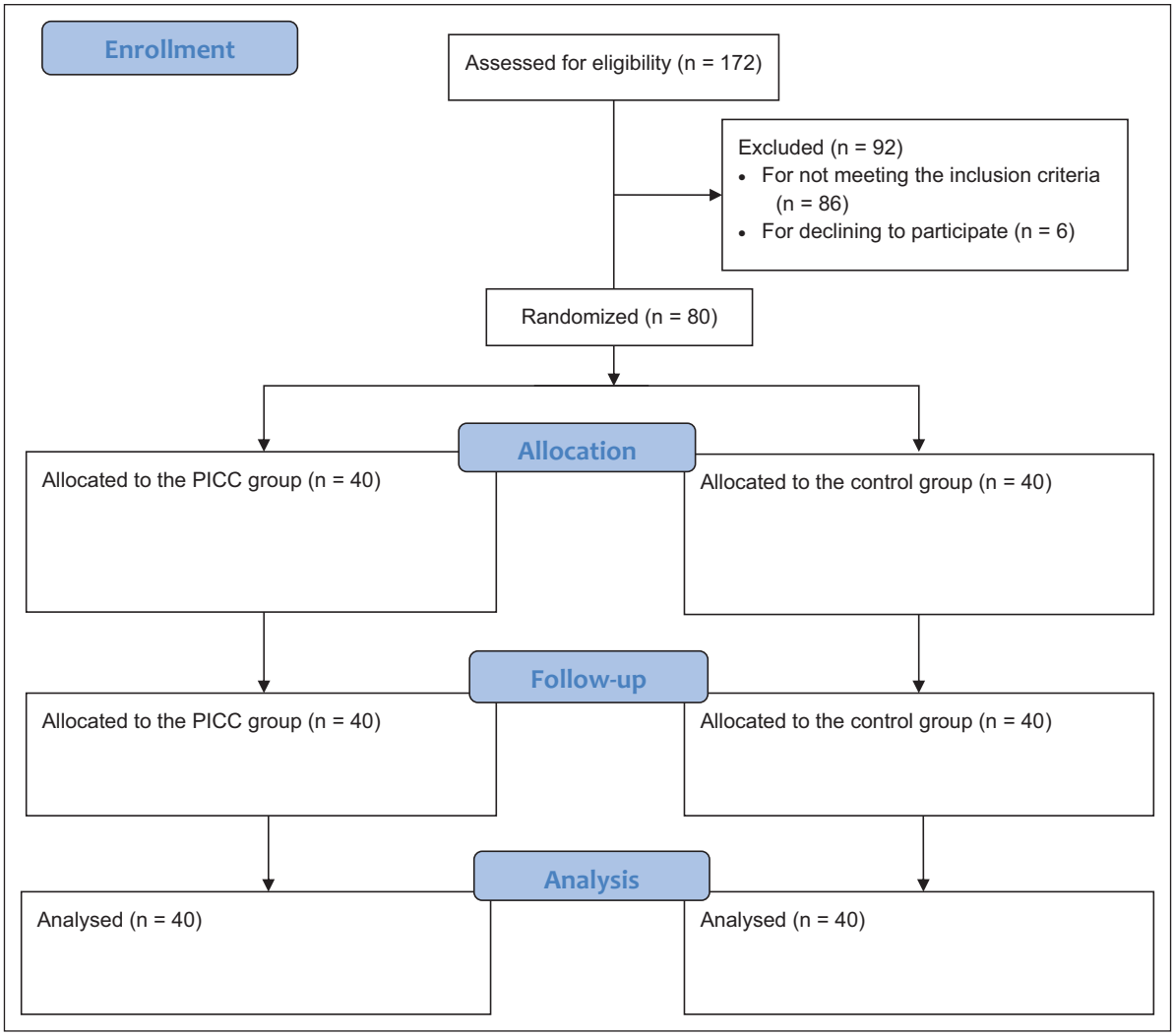

Figure 1. Flow diagram of the study. PICC: peripherally inserted central catheter.

Statistical analyses

Categorical variables were expressed as numbers and percentage and were compared between the groups using chi-square test (χ^2) or Fisher exact test. Continuous variables were expressed as means, standard deviations, and variances and were compared between the groups using a Student *t* test. A Kaplan-Meier time-to event curve was generated for each group.[7] A logistic regression analysis was used to examine the predictive value of the PICC group and other variables for the occurrence of phlebitis, determining the odds ratio, and its 95% confidence interval.[8] The results were considered statistically significant if they had a p value of <0.05. All the randomized patients were included in the intent-to-treat analysis.

Results

Between December 7, 2012 and October 2, 2014, 172 patients were evaluated. Patients who were admitted with decompensated congestive heart failure and using intravenous inotropic agents were screened for eligibility to participate in this study. The study included 80 patients, divided into PICC and control groups, with 40 patients in each group (Figure 1).The study was stopped after it reached the expected sample size.

Most patients (72.5%) were men. The median (IQR) age was 61.5 (16)years; and 72.5% of the patients were Caucasian. The most frequent etiologies of heart disease in the PICC and control groups, respectively, were ischemia (18 (45%) and 11 (27.5%)), hypertension (11 (27.5%) and 17 (42.5%)), and Chagas disease (6 (15%) and 11 (27.5%)). When clinically rating the patients, most patients showed a C profile (PICC group, 37 (92.5%); control group, 26 (90%)), while three patients (7.5%) in the PICC group and four (10%) patients in the control group showed an L profile.

The baseline clinical characteristics (Table 1) included age, ethnicity, etiology, clinical hemodynamic profile, left ventricular ejection fraction, and vasoactive drug (dobutamine) dose.

Table 1. Baseline characteristics of the patients.

	PICC ($n=40$)	Control ($n=40$)
Men, *n* (%)	30 (75)	28 (70)
Age, years, median (IQR)	61.1 (14)	60.5 (23)
Caucasian, *n* (%)	29 (72.5)	29 (72.5)
Etiology		
Ischemia, *n* (%)	18 (45)	11 (27.5)
Hypertension, *n* (%)	11 (27.5)	17 (42.5)
Chagas disease, *n* (%)	6 (15)	11 (27.5)
Clinical hemodynamic profile		
Profile C, *n* (%)	37 (92.5)	36 (90)
Profile L, *n* (%)	3 (7.5)	4 (10)
Ejection fraction, mean (SD)	24.0 (8.0)	28 (8.8)
Dobutamine dose μg/(kg min), mean (SD)	9.16 (7.31)	6.41 (4.00)
Betablockers, *n* (%)	29 (73)	30 (75)
ACEI or ARB *n* (%)	19 (48)	24 (60)
Aspirin, *n* (%)	15 (38)	11 (28)
Furosemide, *n* (%)	30 (75)	31 (78)
Heparin, *n* (%)	31 (78)	29 (73)
Hydralazine, *n* (%)	17 (43)	14 (35)
Nitrates, *n* (%)	14 (43)	20 (50)

PICC: peripherally inserted central catheter; IQR: interquartile range; SD: standard deviation; ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker.

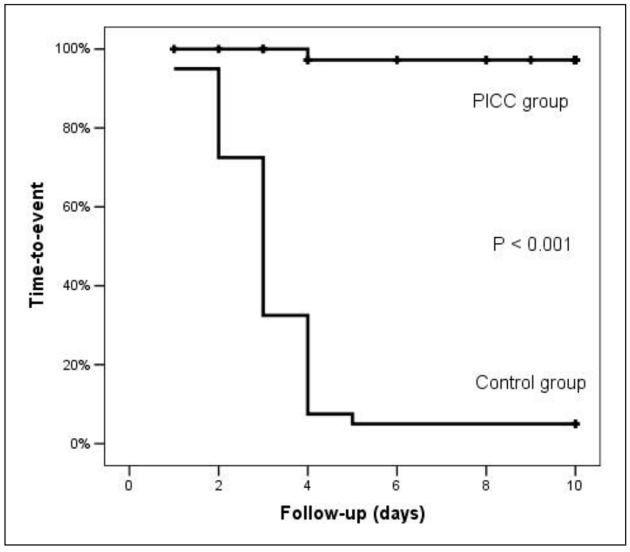

Figure 2. Incidence of phlebitis in the peripherally inserted central catheter (PICC) and control groups.

The primary study outcome, the occurrence of phlebitis, was present in 38 patients (95%) in the control group and 1 patient (2.5%) in the PICC group (Figure 2). The odds ratio was 0.10% (95% confidence interval: 0.01%–1.60%; $p < 0.001$; Table 2). One patient had a bloodstream infection with a positive blood culture. Another patient had a suspected venous thrombosis in the upper limb, but this diagnosis was not confirmed on ultrasonography. No other adverse events were related to the use of a PICC.

Table 2. Main outcomes in the PICC and control groups.

		PICC ($n=40$)	Control ($n=40$)	Hazard ratio (95% confidence interval)
Phlebitis		1 (2.5%)	38 (95%)	0.1% (0.0%–1.6%)
None	0	39	2	
Degree	1	0	10	
	2	0	21	
	3	1	6	
	4	0	1	

The median hospitalization duration was 32 days (interquartile range (IQR), 30 days) in the PICC group and 37 days (IQR, 36 days) in the control group ($p=0.946$). The in-hospital total mortality was 41.3% (all patients), 35% (PICC group), and 47.5% (control group); $p=0.171$.

Discussion

We found that PICC use reduced the incidence of phlebitis by 99.9% as compared with peripheral venous access in the patients with severe heart failure who required prolonged use of dobutamine. To the best of our knowledge, this is the first study to show this benefit of PICC use in a very select group of patients in a specific clinical situation, which included prolonged use of dobutamine.

The current guidelines recommend PICC use when patients should receive drugs that could cause injury to the venous endothelium.[9] Chemotherapy and prolonged antibiotic therapy are widely accepted as indications for PICC.[1] The pathophysiology of phlebitis associated with peripheral venous access is related to drug delivery in the small veins and, consequently, direct injury of the endothelium. Drug delivery in the central great veins, where bloodstream velocity is high, can avoid endothelial damage.

Chemotherapy and prolonged antibiotic therapy are well known to provoke phlebitis when they are infused via a peripheral venous catheter.[10] The physical characteristics (mainly pH) of these drugs are responsible for endothelial irritation and, consequently, phlebitis.[11–17] Similarly, the dobutamine solution has a low pH and consequently causes a high incidence of phlebitis in the peripheral vein of patients with heart failure. To create a pharmacological stress during echocardiography, dobutamine is infused via the peripheral vein, but the infusion duration is short, around 30 min.[18]

Dobutamine has a class IIb recommendation for patients with heart failure in low cardiac output states.[19] Dobutamine is an adrenergic agonist that stimulates myocardial contraction, resulting in inotropic and chronotropic effects. Dobutamine's pH is between 2.5 and 5.5[20] which can cause

direct damage to the endothelium and consequently cause an inflammatory process, resulting in phlebitis.[21]

In addition to direct injury, dobutamine can cause phlebitis through an immune-mediated process.[22] This type of complication ranges from complaints of pain around the catheter insertion site to even more serious injuries, such as blisters, purulent secretion, and skin necrosis. This complication may be worse in patients with a history of previous allergies or hypersensitivities.

In our control group, the incidence of phlebitis was higher (95%) than that in previous published studies without a specific drug. An observational study by Cicolini et al.,[23] which included 427 patients who were receiving infusions through a peripheral venous access revealed a phlebitis incidence of 64.6%. Cicolini et al.[24] found an increased incidence of phlebitis (23.6%) with increasing catheter duration. It seems that continuous intravenous infusion of dobutamine is particularly related to phlebitis.

Poletti et al.[25] studied 137 patients who were admitted to cardiac intensive care and were submitted to implant of PICC. Among them 41.6% had heart failure and 24.8% were in use of dopamine or dobutamine. Catheter-related blood stream infection was diagnosed in one patient. This finding is compatible to our results. Paquet et al.[26] studied 202 patients in randomized trial e found an incidence of 1% of insertion site infection and 2% of central line associated blood stream infection.

Haglund et al.[27] retrospectively evaluated 149 patients with advanced heart failure, receiving continuous intravenous milrinone through a PICC. In this study, PICC complications occurred in 35 patients (27%) and included 48 infections and 4 thromboses. The median duration of PICC use was 63 days. In this study, the incidence of adverse effects and the follow-up duration were greater than those in our study. Milrinone has a low pH, similarly to dobutamine.

Study limitations

The phlebitis was defined by only one researcher. The type of intervention (PICC or peripheral venous access) required an open-label trial design, which might be a source of bias. This sample size was not powered to measure clinical major outcomes.

The occurrence of phlebitis requires a change of the intravenous access site, local care, antibiotics or anticoagulants, resulting in an additional hospital stay. Our study is not a cost-benefit study; however, the prevention of phlebitis using PICC is probably more advantageous than managing phlebitis in peripheral venous access.

In conclusion, in severe heart failure patients who received intravenous dobutamine, PICC use reduced the incidence of phlebitis when compared to patients with peripheral venous access. Therefore, the PICC use should considered over peripheral venous access for prolonged intravenous therapy in heart failure patients.

Author's note

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Author contributions

Eunice Vieira Cavalcante Silva designed the study, recruited the patients, performed PICC insertion, collected and analyzed the data, and wrote the manuscript; Marcelo Eidi Ochiai designed the study, recruited the patients, collected and analyzed the data, and wrote the manuscript; Kelly Regina Novaes Vieira designed the study, conducted the pilot study, and generated the randomization sequence; and Antonio Carlos Pereira Barretto supervised and approved the 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.

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