

## ORIGINAL ARTICLE

# Randomized controlled trial of peripherally inserted central catheters vs. peripheral catheters for middle duration in-hospital intravenous therapy

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**Summary.** *Introduction:* Intravenous (i.v.) therapy may be associated with important catheter-related morbidity and discomfort. The safety, efficacy, comfort, and cost-effectiveness of peripherally inserted central catheters (PICCs) were compared to peripheral catheters (PCs) in a randomized controlled trial. *Methods:* Hospitalized patients requiring i.v. therapy  $\geq$  five days were randomized 1:1 to PICC or PC. Outcomes were incidence of major complications, minor complications, efficacy of catheters, patient satisfaction, and cost-effectiveness. *Results:* 60 patients were included. Major complications were observed in 22.6% of patients in the PICC group [six deep venous thrombosis (DVT), one insertion-site infection] and 3.4% of patients in the PC group [one DVT; risk ratio (RR) 6.6;  $P = 0.03$ ]. Superficial venous thrombosis (SVT) occurred in 29.0% of patients in the PICC group and 37.9% of patients in the PC group (RR 0.60;  $P = 0.20$ ). Patients in the PICC group required 1.16 catheters on average during the study period, compared with 1.97 in the PC group ( $P < 0.04$ ). The mean number of venipunctures (catheter insertion and blood sampling) was 1.36 in the PICC group vs. 8.25 in the PC group ( $P < 0.001$ ). Intravenous drug administration was considered very or quite satisfying by 96.8% of the patients in the PICC group, and 79.3% in the PC group. Insertion and maintenance mean cost was 690 US\$ for PICC and 237 US\$ for PC. *Discussion:* PICC is efficient and satisfying for hospitalized patients requiring i.v. therapy  $\geq$  five days. However, the risk of DVT, mostly asymptomatic, appears higher than previously reported, and should be considered before using a PICC.

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## Introduction

Intravenous (i.v.) drug infusion and catheter handling represent an important burden in in-hospital patient care and may be associated with serious catheter-related morbidity and discomfort. Peripheral catheters (PCs) are easily inserted but need frequent replacement as a result of occlusion, superficial venous thrombosis (SVT) or phlebitis [1]. Peripheral catheters cannot systematically be used for blood sampling, and therefore additional venous punctures are usually needed.

Peripherally inserted central catheters (PICCs) are inserted in the basilic or cephalic vein, with catheter extremity placed in the superior vena cava [2,3]. A peripherally inserted central catheter functions as a central catheter, allowing both drug infusion and blood sampling, and lessens the risk of central venous catheter insertion (i.e. carotid puncture, pneumothorax). Permeability of PICCs may last from weeks to months. Because of the high satisfaction of patients and caregivers with PICCs in hospital and ambulatory medicine, their use has considerably increased during the last two decades [4]. The PICC-related infectious [5–16] and thrombotic [17–21] complications seem to be low in several uncontrolled studies, but have not been evaluated in prospective trials. Therefore, we designed a randomized controlled trial of PICC vs. PC, for in-hospital intravenous therapy, focusing on multiple aspects, including safety, efficacy, patient satisfaction, and cost-effectiveness.

## Methods

### Patients

The study was a monocentric, non-blinded, randomized, controlled trial, in a tertiary care hospital. During the study

period, all consecutive patients hospitalized in the Department of Medicine were considered for inclusion if they required i.v. therapy, for an expected duration  $\geq$  five days. Exclusion criteria were serum creatinine levels  $> 160 \mu\text{mol L}^{-1}$ , high risk of bleeding, and need for central venous catheter. All patients gave informed consent and the study protocol was approved by the institution ethics committee.

#### *Catheter insertion and maintenance*

Patients were randomly assigned to either five French silicon single lumen PICCs (PICS-501-MPIS, Cook, Bloomington, IN, USA) or 18-gauge polyurethane PCs (Optiva 2, Medex, Carlsbad, CA, USA) by use of computer-generated random numbers. Allocation was kept blind until the end of the inclusion procedure. Randomization was stratified for thrombophilia, defined by known hereditary prothrombotic state or history of recurrent thromboembolic events, and for immunosuppression. Peripherally inserted central catheters were placed by four experimented interventional radiologists in the angiography suite, and were inserted in the basilic or brachial vein of the non-dominant arm. The vein was catheterized under sonographic control, in sterile conditions, a few centimeters proximal to the elbow. Catheter extremity was placed in the superior vena cava, and its position was checked by fluoroscopy to allow immediate tip repositioning. Peripherally inserted central catheters were used with an antireflow CLC2000 valve (ICU Medical, San Clemente, CA, USA) [22]. Peripheral catheters were bedside placed by nurses, in the more suitable superficial vein of the forearm. By default, they inserted 18-gauge PCs on the forearm, but size from 14- to 22-gauge were available if required. In both groups, catheter use, daily surveillance of insertion-site, and refection of the dressing followed standardized validated procedures [23,24]. Catheter-site dressings were inspected every day, and changed immediately if damp, loosened, or soiled. Alcoholic solution with 5% chlorhexidine was used for insertion site disinfection in both groups.

#### *Definition of outcomes*

The first outcome was the incidence of catheter-related major complications, defined by an adverse event requiring a specific treatment, prolongation of hospitalization or rehospitalization [25]. Assessment of major complications included systematic search of upper limb deep venous thrombosis (DVT) and a surveillance of catheter-related infection. The second outcome was the incidence of minor complications, defined by minor events requiring no treatment, no prolongation of hospitalization  $> 24$  h and no rehospitalization except for clinical evaluation. This included upper limb superficial venous thrombosis (SVT). The third outcome was the efficacy of the catheter, regarding i.v. perfusion and blood sampling. The fourth outcome was patient satisfaction regarding the strategy of i.v. access during the study period. The fifth outcome was the cost of the catheter use.

#### *Assessment of venous thrombosis*

Arm circumference, local pain, and superficial vein enlargement were assessed daily. All patients had an examination of superficial and deep veins of both upper limbs, by compression ultrasonography (CUS), before randomization and at the end of the study period, after catheter withdrawal [26]. Compression ultrasonography was performed with a 7.5 MHz linear transducer (En Visor HD, Philips Ultrasounds, Bothell, WA, USA). In addition, proximal venous flows were assessed to detect indirect signs of central venous thrombosis [27]. Catheter-related venous thrombosis was defined by the presence at the end of the study of non-compressible material in the vein lumen, which was absent at baseline [28]. Thromboses of the subclavian, axillary, and humeral veins were classified as DVT, whereas thromboses of the basilic and cephalic veins were classified as SVT.

#### *Assessment of infection*

Catheter-related infections were prospectively monitored by daily inspections of the dressing and insertion site. Body temperature was measured at least twice daily. New acute fever was investigated by culture of two blood samples (at least one drawn by venipuncture) and if the catheter was the suspected source of infection, it was removed and cultured [29]. Catheter-related soft tissue infection was diagnosed when erythema, induration, and pus were present at the site of insertion, in the presence of clinical or biological sign of infection. Very localized exit-site erythema, as often observed with PICCs or PCs, was not considered as a soft tissue infection.

#### *Assessment of efficacy*

Efficacy was assessed by the number of catheters required to complete the i.v. treatment, the number of venipunctures needed to insert catheters during the study period, and the number of new venipunctures needed to draw blood during the study period (including puncture failure).

#### *Assessment of satisfaction*

Patient satisfaction was evaluated at the end of the study period, by means of a questionnaire, developed specifically for this study. It was elaborated and validated in our institution during discussions with hospitalized patients who had experienced similar i.v. therapy durations. Three distinct important indicators were identified by patients: the frequency of venipuncture during hospital stay, the pain consecutive to these venipunctures and puncture failures, and the discomfort as a result of the catheter position on the arm. A questionnaire assessing these three points and the global satisfaction regarding i.v. therapy was created, using quality answers with four-point Likert intervals.

### Cost-effectiveness analysis

The mean cost of catheter insertion and maintenance was calculated in each group. The purpose of this analysis was to estimate the global cost of each strategy, including material and human costs. The PICC cost included the catheter tray, the sterile material for insertion, fluoroscopy, salaries of interventional radiologist, and attendance of the angiography suite. In both groups, the material used for catheter maintenance, including dressing, valve, fixation device, material for saline flush, and material for blood sampling, was prospectively recorded. The cost of nurses' salaries during catheter insertion and maintenance was also calculated.

### Statistics

The incidence of PICC-related DVT or infection could not reliably be anticipated from the literature (reported incidence of DVT from 0% to 60%) [5,21]. Therefore, a sample size of 60 patients was prespecified, with an optional additional similar group inclusion, if differences in the incidence of major complications had not reached statistical significance. Outcomes were analyzed according to the intention to treat model. Proportions of events were compared using the Fisher exact test. Responses of the questionnaire were compared between groups using the Pearson  $\chi^2$ -test. Continuous variables were compared by the Student's *t*-test or Mann-Whitney rank sum test according to normality of their distribution. Predictors of outcome were searched by bivariate regression analysis. Statistical significance was considered for *P*-values <0.05. Statistical analysis was performed using Stata 9.2 (Statacorp, College Station, TX, USA).

## Results

### Patients

The study started in August 2005 and was stopped in December 2006, because of the prespecified stopping rule, after inclusion of 60 patients (35% women, mean age  $\pm$  SD 67.0  $\pm$  16.5). Thirty-one were assigned to PICCs and 29 to PCs (Fig. 1). The clinical characteristics of the patients are presented in Table 1.

### Safety outcomes

Major complications were observed in seven patients [22.6%, 95% confidence interval (CI) 9.6–41.1] in the PICC group and in one patient (3.4%, 95% CI 0.1–17.8) in the PC group [risk ratio (RR) 6.6; *P* = 0.03; Table 2]. Six catheter-related DVTs of the subclavian or axillary veins occurred in the PICC group (19.4%, 95% CI 7.4–37.5) vs. one brachial DVT in the PC group (3.4%, 95% CI 0.1–17.8; *P* = 0.06). Localization and extension of the DVT are detailed in Table 3. Three patients in the PICC group had short axillary vein occlusion and three patients had a non-occlusive thrombosis of the axillary or

subclavian vein. All PICC-related DVTs were asymptomatic sonographic findings. Clinical signs were limited to 1.3  $\pm$  0.5 (mean  $\pm$  SD) cm arm circumference enlargement between baseline and end of study, compared to a 0.5  $\pm$  0.3 cm increase for patients without DVT. No patient with DVT had shoulder or neck pain, or superficial vein enlargement. No patient presented any symptom of pulmonary embolism (PE). Three of these six cases of DVT occurred despite therapeutic anticoagulation administered during study period, and one despite prophylactic anticoagulation. Among the six cases of PICC-induced DVT, the thrombotic risk factors were previous thrombo-embolic event (two), heart failure (two), active cancer (one), bed rest (all), and the catheter itself (Table 3). Although asymptomatic, these DVTs were treated by anticoagulation, following standard upper limb DVT management. Patients without contraindication to antithrombotic drug were treated by therapeutic anticoagulation for six weeks (two patients) or longer if they had long-term indication to antithrombotic treatment (one patients with atrial fibrillation, two patients with a prosthetic heart valve). One patient was not treated, because of a relative contraindication to antithrombotic drug. All patients were clinically evaluated at three months and had no post-thrombotic symptoms. Two patients were examined by CUS and had a complete recanalization of the thrombosed veins.

The case of DVT in the PC group was an extension of a thrombosis of cephalic vein in one brachial vein. The patient had received i.v. iron and unfractionated heparin for seven days, using two PCs. The DVT was managed by catheter retrieval without antithrombotic treatment and evolution was favorable at three-month follow-up.

There was one infection in the PICC group, which presented by a localized painful and erythematous 4.5 cm plaque around the insertion site. Blood cultures remained negative. Culture of the insertion point and the catheter tip was positive for *Staphylococcus epidermidis*. The patient was treated by catheter retrieval and oral amoxicillin-clavulanate. Evolution was rapidly favorable. There was no bloodstream infection in any group.

Superficial venous thrombosis occurred in nine (29.0%; 95% CI 14.2–48.3) patients with PICCs and in 13 (37.9%; 95% CI 20.7–57.7) patients in the PC group (RR 0.65; *P* = 0.20). The incidences of SVT were statistically different after adjustment for the catheter use duration by calculation of incidence densities (Table 2). All these SVTs were handled by catheter withdrawal and clinical surveillance. None required antithrombotic treatment, except topic heparinoids.

### Efficacy of catheters

In the PICC group, a mean number of 1.16 catheters (1.03 PICC and 0.13 PC) were used for each patient, compared to a mean of 1.97 catheters (1.97 PC and no PICC) in the PC group (*P* = 0.04). Four 16-gauge, 37 18-gauge, 12 20-gauge, and four 22-gauge PCs were inserted. In the PICC group, a mean number of 1.16 venipunctures were required for catheter insertion and

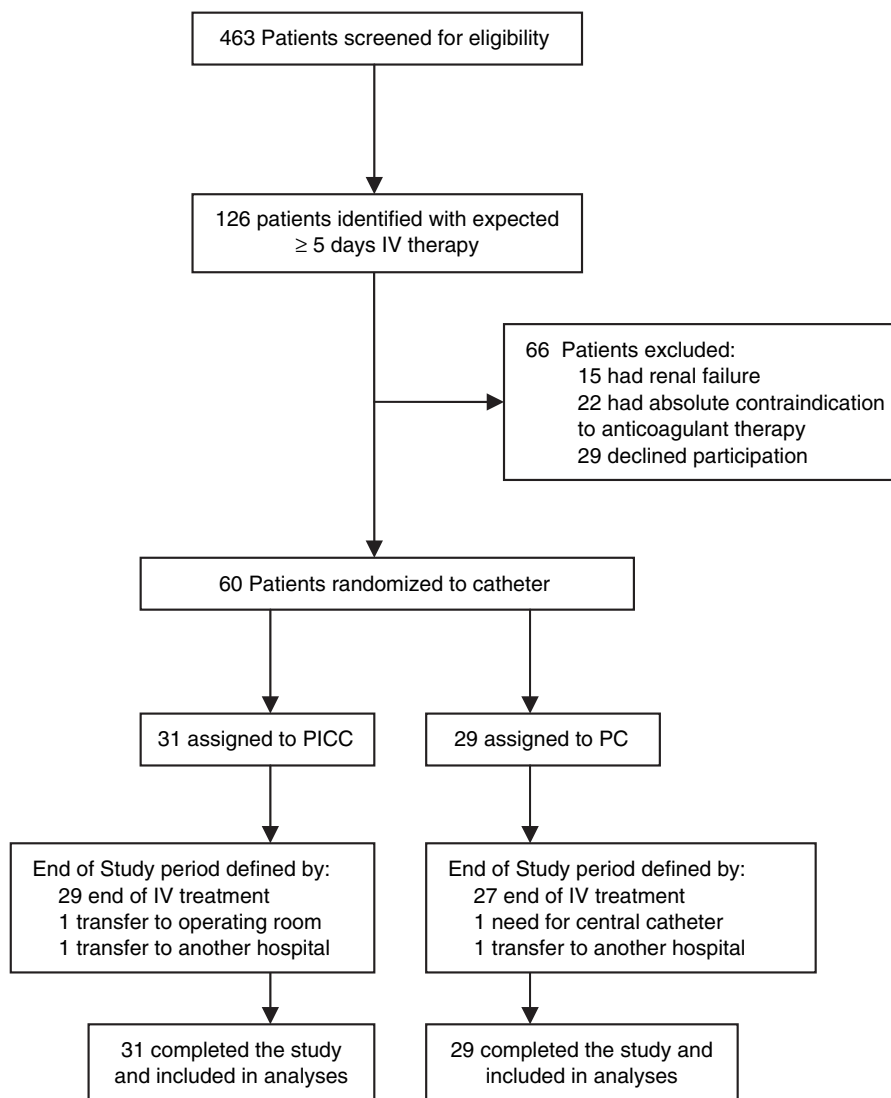


Fig. 1. Patient flow diagram from inclusion to study completion.

0.20 for blood sampling, during the study period, compared to 2.27 venipunctures for catheter insertion ( $P < 0.01$ ) and 5.98 for blood sampling ( $P < 0.001$ ) in the PC group.

#### Patient satisfaction

Satisfaction, evaluated through the questionnaire, was significantly higher in the PICC group than in the PC group (Table 4). This difference concerned the three specific questions and the global appreciation of the strategy for i.v. treatment. The i.v. drug administration and venous sampling were estimated very satisfying or quite satisfying in 96.8% of the patients in the PICC group, and 79.3% in the PC group.

#### Cost-effectiveness analysis

Overall, the cost of PICC use was evaluated at 690 US\$ per patient, whereas the cost of PC use was evaluated at 237 US\$. In

the PICC group, the price of materials required for insertion (210 US\$) and angiography suite occupancy (265 US\$) were the major contributors of the overall cost. The materials necessary for catheter maintenance were evaluated to be 27 US\$ per patient in the PICC group and 18 US\$ in the PC group. Nurses spent 4.1 h per patient for handling the PICCs and approximately 5.5 h with PCs. This represented a patient cost for nurses' salaries of 165 US\$ for PICCs and 219 US\$ for PCs.

The cost as a result of catheter complications was not included in this analysis. Management of a therapeutic anticoagulation for a catheter-related DVT usually includes five to seven days low-molecular-weight heparin, six weeks to three months oral anticoagulation and regular coagulation tests. This has an estimated cost of 300–350 US\$ for each case, which will be partially supported by the institution, the insurance company, and partially by the patient, depending on the time of diagnosis (i.e. before or after hospital discharge), and the country specific health care system.

**Table 1** Clinical characteristics of the patients

Clinical characteristics	PICC (n = 31)	PC (n = 29)
Age (median, IQR)	66 (57–77)	71 (63–80)
Male (%)	22 (70.1)	17 (58.6)
Major comorbidities (%)		
Heart failure	8 (25.8)	10 (34.5)
Coronary artery disease	11 (35.5)	8 (27.6)
Atrial fibrillation	1 (3.2)	7 (24.1)
Respiratory disease	10 (32.3)	5 (17.2)
Chronic renal failure	2 (6.5)	4 (13.8)
Active cancer	5 (16.1)	3 (10.3)
Acute infection	17 (54.4)	16 (55.2)
Venous thrombo-embolism	4 (12.9)	4 (13.8)
Diabetes mellitus	6 (19.6)	5 (17.2)
Intravenous drug users	2 (6.5)	1 (3.5)
Immunosuppression	3 (9.7)	2 (6.9)
Thrombophilia	3 (9.7)	3 (10.3)
Karnofsky score of morbidity [36] (mean ± SD)	66 ± 22	60 ± 21
Anticoagulation during study period (%)		
Prophylactic	7 (22.6)	3 (10.3)
Therapeutic	14 (45.2)	12 (41.4)
Duration of intravenous drug perfusion (mean ± SD) (days)	8.2 ± 6.0	6.8 ± 5.4*
Duration of catheter use (mean ± SD) (days)	9.4 ± 6.6	7.3 ± 5.3 <sup>†</sup>
Intravenous drugs perfused through the study catheter (%)		
Antimicrobial agent	19 (61.3)	15 (51.7)
Volume/electrolytes replacement	6 (19.4)	7 (24.1)
Unfractionated heparin	4 (12.9)	7 (24.1)
Diuretics	5 (16.1)	6 (20.7)
Other therapy	3 (7.7)	4 (13.8)

\* $P = 0.02$ ,  $^{\dagger}P = 0.01$ .

## Discussion

This study compared two different strategies of i.v. perfusion, and found a higher incidence of DVT and a lower incidence of SVT in the PICC group than in the PC group. The PICC is more efficient and provides more satisfaction to patients than the PC, but has a higher cost. The DVTs observed in the PICC group were all asymptomatic findings at ultrasonography, and their clinical evolution was favorable after handling with adequate antithrombotic treatment.

In this study the incidence of PICC-related DVT was higher than reported previously. Previous retrospective studies

reporting PICC-related complications found very low incidence of thrombosis (<2%), when complications were clinically monitored, without systematic CUS or phlebography [7–10,12–17]. These studies may have underestimated the true incidence of DVT by lack of asymptomatic DVT detection. Other retrospective studies found incidence of thrombosis up to 25% [18–20]. In these studies, the mode of inclusion was a crossing of lists of patients having had PICCs inserted and having subsequently had a phlebography. The limitation of this mode of inclusion is the lack of information on the indication to phlebography, an exam that is not routinely performed after PICC withdrawal. More recently, Abdullah *et al.* [30] prospectively searched for thrombosis by systematic phlebography after PICC withdrawal and found venous thrombosis in 38.5% of patients, mainly as a result of asymptomatic non-occluding superficial thrombosis of the basilic or cephalic veins. This incidence of thrombosis is closer to that found in our study. However, the absence of initial phlebography does not allow a definitive differentiation between new and older thromboses. Additionally, phlebography may be even more sensible than CUS to detect small non-occlusive thrombi.

The association of clinical variables and DVT was investigated by bivariate regression analysis. The variables age, gender, active cancer, heart failure, respiratory failure, renal failure, acute infection, previous thrombo-embolic disease, duration of catheter use, anticoagulation, and class of infused drug were not significantly associated with DVT. However, this analysis is limited by the small number of events. The thrombogenicity of PICCs despite anticoagulation (Table 3) may be explained by the PICC length, superficial vein narrowness, and intimal trauma by the catheter. Thrombosis localized in the subclavian vein may be a result of a proximal extension or intimal lesions consecutive to intermittent compression by clavicle. Deep venous thromboses were localized away from the superior cava vena, where the PICC tip delivers the drug. The high blood flow in this vein quickly reduces drug concentration and probably protects the venous endothelium from the drug irritant properties. Therefore, we postulate that the type of drug perfused has a limited role in the generation of DVT associated to PICC.

This study raises the question of systematic DVT screen after PICC use. There is enough evidence that symptomatic upper

**Table 2** Safety outcomes

	PICC (n = 31)	PC (n = 29)	P-value
Incidence of major complications			
All events (deep venous thrombosis, sepsis, cellulitis)	7 (22.6)	1 (3.4)	0.03
Deep venous thrombosis	6 (19.4)	1 (3.4)	0.06
Cellulitis	1 (3.2)	0	0.51
Sepsis	0	0	
Major complications per 1000 patient-days	24.0	4.7	<0.01
Incidence of minor complications			
Superficial venous thrombosis	9 (29.0)	13 (44.8)	0.20
Superficial venous thrombosis per 1000 patient-days	30.9	61.4	<0.01

Values given in parentheses are in percentages.

**Table 3** Clinical presentation and echographic findings of the seven patients with deep venous thrombosis

Age/ sex	Number of catheter and duration	Drug perfused	Prothrombotic risks factors	Antithrombotic treatment during study period	Clinical signs	Thrombosis extension					Treatment	Clinical evaluation at three months	CUS at three months	
						Sub-clavian	Axillary	Brachial	Basilic	Cephalic				
77/M	1 PICC 6 days	Antibiotics	-	Therapeutic (VKA)	Mild arm edema	+	-	-	-	-	-	VKA (three months)	No symptoms	-
68/M	1 PICC 5 days	Antibiotics, UFH	Heart failure	Therapeutic (UFH)	Mild forearm edema	-	+	++	+	-	-	VKA (three months)	No symptoms	-
70/M	1 PICC 8 days	Diuretics, potassium	Active cancer, heart failure	Prophylactic (LMWH)	None	-	+	++	+	-	-	None	No symptoms	-
44/F	1 PICC 9 days	Potassium magnesium vitamine B	-	None	Arm edema	-	+	++	++	-	-	LMWH (six weeks)	No symptoms	Complete recanalization
49/M	1 PICC 8 days	Saline, potassium, magnesium	History of DVT/EP	Therapeutic (VKA)	Mild arm edema	-	++	+	++	-	-	VKA (three months)	No symptoms	-
18/M	1 PICC 34 days	Antibiotics	History of DVT/EP	None	Arm edema	-	++	-	-	-	-	LMWH (six weeks)	No symptoms	Complete recanalization
75/F	2 PC 7 days	Iron, UFH	-	Therapeutic (UFH)	Forearm phlebitis	-	-	+	+	+	+	None	No symptoms	-

UFH, unfractionated heparin; VKA, vitamin K antagonists; LMWH, low-molecular-weight heparin; ++, occlusive thrombosis; +, non-occlusive thrombosis.

**Table 4** Patient satisfaction at the end of the study period

	PICC (31)	PC (29)	P-value
During this hospital stay, the frequency of venipunctures was			
Very acceptable	58.1	13.8	0.001
Acceptable	41.9	58.6	
Not very acceptable	0	24.1	
Unacceptable	0	3.4	
During this hospital stay, the pain consecutive to venipunctures was			
Very acceptable	67.7	24.1	0.005
Acceptable	29.0	58.0	
Not very acceptable	0	10.3	
Unacceptable	3.2	3.4	
During this hospital stay, the catheter and its position on the arm were			
Very disturbing	0	3.4	0.008
Disturbing	16.1	31.0	
Not very disturbing	45.2	62.1	
Not disturbing at all	38.7	3.4	
Overall, during this hospital stay, the intravenous drug administration was			
Very satisfying	77.4	20.7	<0.001
Satisfying	19.4	58.6	
Not very satisfying	3.2	20.7	
Not satisfying at all	0	0	

limb DVT must be appropriately confirmed and treated by antithrombotic agents in order to decrease the extension of thrombosis, the risk of post-thrombotic syndrome, and the risk of PE. This benefit is, however, less clear for asymptomatic non-occlusive catheter-related thrombosis, even more if the source of thrombosis (the catheter) can be quickly removed. It was shown that in cancer patients, longstanding central venous catheters or totally implantable catheters are complicated by up to 25% of PE [31]. In two prospective trials, 70% and 75% of these PEs were asymptomatic findings at lung scan and would probably not have been diagnosed outside a research protocol [32,33]. It is uncertain whether the systematic search of asymptomatic catheter-related PE brings any benefit. In our study, only 16.1% of patients in the PICC group had active cancer and the catheter use duration lasted a few days, before removal. No patient had symptomatic DVT and no patient had symptoms of PE. In such a population, the incidence of new PE, even asymptomatic, may be very low. Up to now, it was our policy to treat catheter-induced DVT by catheter retrieval and at least six weeks of anticoagulation. All DVTs were therefore classified as major complications in this study, even though they were asymptomatic findings. This policy may have overstaged these events as major complications. Therefore, in the setting of middle duration in-hospital PICC use, there are no strong arguments to recommend a systematic DVT screen, because there is no clear information on the prognosis of these asymptomatic DVT once the catheter is removed, and because there is no clear recommendation on the best way to manage them. Moreover, a systematic screen should include an exam before PICC insertion to avoid overdiagnosis of DVT and overtreatment. However, DVT may reach up to one-fifth of patients treated by PICCs, and present with very few clinical signs. We therefore recommend a careful

clinical surveillance and to use CUS whenever a suspicion of DVT is present clinically.

The incidence of infectious complications related to PICCs was reported in several studies, with high discrepancies. The incidences of sepsis varied from 0.4% to 25.7% of patients with PICC or from 0.01 to 80 sepsis by 10 000 days of PICC use [7,12,13]. The high variability of these results may be a result of the lack of uniformity in the definition of infectious complications, some authors reporting only clinical infections, other having reported catheter colonization [13,14]. In our study, the incidence of clinical infection related to catheters was too low to draw any conclusion.

Different studies have previously investigated the satisfaction of patients treated by PICCs, and found a higher satisfaction than with PCs [34,35]. In our study, it appears that comfort was an important point for the population included, and that comfort exceeded the fear of venous complication, especially if asymptomatic. This may be explained by the numerous comorbidities and the poor general state at inclusion, as the low Karnofsky score of morbidity shows. Multiple comorbidities usually induce the necessity of frequent blood exams, increasing the number of venipunctures. One can imagine that the perspective of a single catheter allowing all the infusions and blood sampling during a hospital stay is tempting, especially for patients previously treated with PCs.

Our analysis showed that PICCs are not as cost-effective as PCs in this setting. The difference was mainly a result of the cost of PICC insertion in the angiography suite, which was only partially compensated by the reduction of nursing time in the PICC group. Our analysis tried to include all costs related to the catheter insertion and handling, in order to perform an evaluation as complete as possible. The major PICC advantage regarding costs may be related to an early hospital discharge for patients who require central i.v. perfusion. This was not taken into account in our study. The cost difference between PICC and PC use (471 US\$ per patient) should be evaluated with caution by including the marginal cost of one hospital day, estimated to 538 US\$ in our institution.

In conclusion, this study shows that the PICC is an efficient and appreciated catheter for hospitalized patients with multiple comorbidities, requiring i.v. treatment for  $\geq$  five days. However, this study found that one-fifth of patients with PICCs developed asymptomatic DVT, whose clinical importance and prognosis are unknown. We therefore conclude that the PICC should not be used as the first choice catheter for all hospitalized patients, but it remains an interesting alternative for patients with few forearm i.v. access possibilities, for patients requiring numerous blood exams or for patients requiring prolonged i.v. access. We recommend withdrawing the PICC as soon as it is no longer used, to reduce the exposure duration to the risk of thrombosis. We also recommend the performance of a rigorous clinical surveillance for DVT and that the PICC is not used for patients with contraindication to antithrombotic treatment or for patients who may require hemodialysis.

## Disclosure of Conflict of Interests

The authors state that they have no conflict of interest.

## References

- Maki DG, Ringer M. Risk factors for infusion-related phlebitis with small peripheral venous catheters. A randomised controlled trial. *Ann Intern Med* 1991; **114**: 845–54.
- Cardella JF, Fox PS, Lawler JB. Interventional radiologic placement of peripherally inserted central catheters. *J Vasc Interv Radiol* 1993; **4**: 653–60.
- Hovsepian DM, Bonn J, Eschelmann DJ. Techniques for peripheral insertion of central venous catheters. *J Vasc Interv Radiol* 1993; **4**: 795–803.
- Horattas MC, Trupiano J, Hopkins S, Pasini D, Martino C, Murty A. Changing concepts in long-term central venous access: catheter selection and cost savings. *Am J Infect Control* 2001; **29**: 32–40.
- Cardella JF, Cardella K, Bacci N, Fox PS, Post JH. Cumulative experience with 1273 peripherally inserted central catheters at a single institution. *J Vasc Interv Radiol* 1996; **7**: 5–13.
- Last KW, Mansi JL, Oakley C. Long-term intravenous access devices: superiority of peripherally inserted central cannulae over Hickman catheters. *Ann Oncol* 1998; **9**: 142.
- Ng PK, Ault MJ, Ellrodt AG, Maldonado L. Peripherally inserted central catheters in general medicine. *Mayo Clin Proc* 1997; **72**: 225–33.
- Skiest DJ. Peripherally inserted central catheters in patients with aids are associated with a low infection rate. *Clin Infect Dis* 2000; **30**: 949–52.
- Walshe LJ, Malak SF, Eagan J, Sepkowitz KA. Complication rates among cancer patients with peripherally inserted central catheters. *J Clin Oncol* 2002; **20**: 3276–81.
- Graham DR, Keldermans MM, Klemm LW, Semenza NJ, Shafer ML. Infectious complications among patients receiving home intravenous therapy with peripheral, central or peripherally placed central venous catheters. *Am J Med* 1991; **91**(Suppl. 3B): S95–100.
- Goodwin ML, Carlson I. The peripherally inserted central catheters. A retrospective look at three years of insertions. *J Intraven Nurs* 1993; **16**: 92–103.
- Merrell SW, Peatross BG, Grossman MD, Sullivan JJ, Harker WG. Peripherally inserted central venous catheters: low risk alternatives for ongoing venous access. *West J Med* 1994; **160**: 25–30.
- Hoffer EK, Borsa J, Santulli P, Bloch R, Fontaine AB. Prospective randomized comparison of valved versus nonvalved peripherally inserted central vein catheters. *Am J Roentgenol* 1999; **173**: 1393–8.
- Cowl CT, Weinstock JV, Al-Jurf A, Ephgrave K, Murray JA, Dillon K. Complications and cost associated with parenteral nutrition delivered to hospitalised patients through either subclavian or peripherally inserted central catheters. *Clin Nutr* 2000; **19**: 237–43.
- Moureau N, Poole S, Murdock MA, Gray SM, Semba CP. Central venous catheters in home infusion care: outcome analysis in 50,470 patients. *J Vasc Interv Radiol* 2002; **13**: 1009–16.
- Cheong K, Perry D, Karapetis C, Koczwara B. High rate of complications associated with peripherally inserted central venous catheters in patients with solid tumours. *Intern Med J* 2004; **34**: 234–8.
- Smith JR, Friedell ML, Cheatham ML, Martin SP, Cohen MJ, Horowitz JD. Peripherally inserted central catheters revisited. *Am J Surg* 1998; **176**: 208–11.
- Chemaly RF, de Parres JB, Rehm SJ, Adal KA, Lisgaris MV, Katz-Scott DS, Curtas S, Gordon SM, Steiger E, Olin J, Longworth DL. Venous thrombosis associated with peripherally central catheters: a retrospective analysis of the Cleveland clinic experience. *Clin Infect Dis* 2002; **34**: 1179–83.
- Allen AW, Megargell JL, Brown DB, Lynch FC, Singh H, Singh Y, Waybill PN. Venous thrombosis associated with the placement of peripherally inserted central catheters. *J Vasc Interv Radiol* 2000; **11**: 1309–14.
- Gonsalves CF, Eschelmann DJ, Sullivan KL, DuBois N, Bonn J. Incidence of central venous stenosis and occlusion following upper extremity PICC and port placement. *Cardiovasc Intervent Radiol* 2003; **26**: 123–7.
- Kearns PJ, Coleman S, Wehner JH. Complications of long arm-catheters: a randomised trial of central vs. peripheral tip location. *J Parenter Enteral Nutr* 1996; **20**: 20–4.
- Hoffer EK, Bloch RD, Borsa JJ, Santulli P, Fontaine AB, Francoeur N. Peripherally inserted central catheter with distal versus proximal valve: prospective randomised trial. *J Vasc Interv Radiol* 2001; **12**: 1173–7.
- O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, Masur H, McCormick RD, Mermel LA, Pearson ML, Raad II, Randolph A, Weinstein RA, for the Center for Disease Control and Prevention. Guidelines for the prevention of intravascular catheter-related infections. *MMWR Recomm Rep* 2002; **51**: 1–29.
- Maki DG, Ringer M, Alvarado CJ. Prospective randomised trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous catheters. *Lancet* 1991; **338**: 339–43.
- Silberzweig JE, Sacks D, Khorsandi AS, Bakal CW. Society of Interventional Radiology Technology Assessment Committee. Reporting standards for central venous access. *J Vasc Interv Radiol* 2003; **14**: 443–52.
- Longley DG, Finlay DE, Letourneau JG. Sonography of the upper extremity and jugular veins. *Am J Roentgenol* 1993; **160**: 957–62.
- Hightower DR, Gooding GAW. Sonographic evaluation of the normal response of subclavian veins to respiratory manoeuvres. *Invest Radiol* 1985; **20**: 517–20.
- Prandoni P, Polistena P, Bernardi E, Cogo A, Casara D, Verlato F, Angelini F, Simioni P, Signorini GP, Benedetti L, Girolami A. Upper-extremity deep vein thrombosis: risk factors, diagnosis and complications. *Arch Intern Med* 1997; **157**: 357–62.
- Mermel LA, Farr BM, Sherertz RJ, Raad II, O'Grady N, Harris JS, Craven DE. Guidelines for the management of intravascular catheter-related infections. *Clin Infect Dis* 2001; **32**: 1249–72.
- Abdullah BJ, Mohammad N, Sangkar JV, Abd Aziz YF, Gan GG, Goh KY, Benedict I. Incidence of upper limb venous thrombosis associated with peripherally inserted catheters (PICC). *Br J Radiol* 2005; **78**: 596–600.
- Verso M, Agnelli G. Venous thromboembolism associated with long-term use of central venous catheters in cancer patients. *J Clin Oncol* 2003; **21**: 3665–75.
- Monreal M, Raventos A, Lerma R, Ruiz J, Lafoz E, Alastrue A, Llamazares JF. Pulmonary embolism in patients with upper extremity DVT associated to venous central lines—a prospective study. *Thromb Haemost* 1994; **72**: 548–50.
- Monreal M, Lafoz E, Ruiz J, Valls R, Alastrue A. Upper-extremity deep venous thrombosis and pulmonary embolism. A prospective study. *Chest* 1991; **99**: 280–3.
- Polak JF, Anderson D, Hagspiel K, Mungovan J. Peripherally inserted central venous catheters: factors affecting patient satisfaction. *Am J Roentgenol* 1998; **170**: 1609–11.
- Schwengel DA, McGready J, Berenholtz SM, Kozlowski LJ, Nichols DG, Yaster M. Peripherally inserted central catheters: a randomized, controlled, prospective trial in pediatric surgical patients. *Anesth Analg* 2004; **99**: 1038–43.
- Schag CC, Heinrich RL, Ganz PA. Karnofsky performance status revisited: reliability, validity, and guidelines. *J Clin Oncol* 1984; **2**: 187–93.