

A prospective, randomized comparison of three different types of valved and non-valved peripherally inserted central catheters

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ABSTRACT

Purpose: Few randomized studies have investigated the impact of valved and non-valved power-injectable peripherally inserted central catheters (PICCs) in terms of incidence of occlusion, infection, malfunction and venous thrombosis.

Methods: We have prospectively compared three types of third-generation polyurethane PICCs. One hundred and eighty adult patients candidate to chemotherapy were randomized into three groups: power-injectable PICCs with Solo-2 proximal valve (Bard); power-injectable PICCs with PASV (Pressure Activated Safety Valve) proximal valve (Navilyst); and non-valved power-injectable PICCs (Medcomp). All PICCs were single lumen 4Fr, inserted according to a well-defined protocol - maximal barrier precautions, ultrasound guidance, intracavitary electrocardiography (IC-ECG), and so on - and managed according to the recommendations of the most recent guidelines (antisepsis with 2% chlorhexidine, transparent dressing, sutureless device, strict 'scrub the hub' policy, neutral displacement needle-free connectors and so on). All catheters were flushed with 10 ml saline before and after each infusion, or with 20 ml saline after blood sampling or infusion of blood products. No heparin was used.

Results: We detected no complications at insertion; no PICC-related bloodstream infections; no dislocations; five cases of transient occlusion and two cases of persistent withdrawal occlusion, evenly distributed among the groups; one episode of complete irreversible obstruction (group A); four episodes of asymptomatic peripheral venous thrombosis; one episode of symptomatic, severe central vein thrombosis (group B). In 31% of PICCs in group A (19/61) and in 65% of group B (39/60), difficulties with gravity infusion were reported; three PICCs of group A were complicated by rupture of the intravascular tract during pump infusion. Five PICCs were removed because of complications, four in group A (one obstruction; three ruptures) and one in group B (central venous thrombosis).

Conclusion: We found no clinical advantages of valved vs. non-valved PICCs.

Key words: Catheter rupture, Central venous catheter, Infection, Occlusion, Peripherally inserted central catheter, Power-injectable polyurethane, Valved catheters, Thrombosis

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INTRODUCTION

Peripherally inserted central catheters (PICCs) are venous access devices (VADs) commonly used in clinical practice both for intra-hospital and extra-hospital infusions. In our University Hospital, they are also used for short-medium term (<4 months) antineoplastic chemotherapy in the outpatients of our Oncology Unit. This use of PICC for short-medium term intermittent treatment is considered appropriate by most recent guidelines (1), though it is associated with some possible risk of occlusion of the VAD, as the PICC is used intermittently and remains closed for prolonged time. Thus, we have taken

in consideration the potential advantage of using valved catheters, which are marketed for the purpose of reducing the risk of occlusion. As there are no evident data in the literature demonstrating the actual advantage of valved vs non-valved PICCs and as the purchase of valved PICCs implies a higher cost, we have decided to start a randomized controlled study to verify the evidence of any significant difference between valved and non-valved PICCs in terms of occlusion, malfunction, infection and thrombosis. In accordance with the recommendations of our Hospital Management, we have restricted our investigation to power-injectable polyurethane PICCs, as our previous experience of delivering chemotherapy with

silicon PICCs was associated with several episodes of intravascular rupture of the catheter (six Groshong PICCs broke down during pump-infusion of taxols, a group of highly viscous chemotherapeutic drugs). As two different types of valved power-injectable polyurethane PICCs are currently available, we designed the study as a randomized controlled comparison between three different types of PICCs, one non-valved and two valved.

METHODS

This study was designed as a prospective, randomized, controlled trial investigating the clinical performance of three different PICCs:

1. Power PICC Solo (Bard): open-ended, power-injectable polyurethane PICC with proximal valve 'Solo-2';
2. Xcela PICC (Navilyst): open-ended, power-injectable polyurethane PICC with proximal valve 'PASV';
3. ProPICC (Medcomp): open-ended, power-injectable polyurethane PICC with no valve.

The study was designed in collaboration between the Vascular Access Team, the Oncology Unit and our Hospital Management and approved by our local Ethics Committee.

We enrolled exclusively adult oncologic patients candidate to the insertion of a 4Fr single-lumen PICC for intermittent infusion of chemotherapy drugs for a period not exceeding 4 months. Patients who had some local contraindications to PICC insertion or who refused to participate to the study were excluded.

All PICCs were 4Fr single lumen and they were inserted by specialist vascular access nurses of the Oncology Unit, adopting to the GAVeCeLT protocol for Safe Insertion of PICCs (so-called 'SIP protocol'), an insertion bundle (2) including bilateral ultrasound scan of all veins at arm and neck before the procedure; hand washing, aseptic technique and maximal barrier protection; choice of the appropriate vein at upper midarm (so that the vein diameter in mm should be at least the catheter diameter in Fr); clear identification of median nerve and brachial artery before the venipuncture; ultrasound-guided venipuncture; ultrasound scan of the internal jugular vein during the introduction of the catheter; IC-ECG method for assessing tip position; and securement of the PICC with a sutureless device.

All patients were treated as outpatients. Each PICC was exclusively used while the patient was in the Day Hospital of the Oncology Unit, by the same group of oncology nurses, strictly adopting the policies of our Hospital for dressing change, change of the needle-free connector (NFC) and flushing/locking the lumen, on a weekly basis. At each use of the catheter (every 2 or 3 weeks, depending

on the scheduled treatment), the veins of the arm carrying the PICCs were scanned by ultrasound to rule out venous thrombosis.

The flushing/locking policies consisted of the following four recommendations:

1. flush with 10 ml saline (push/pause technique) before and after each infusion;
2. flush with 20 ml saline (push/pause technique) after blood sampling or after infusion of blood products, lipids and/or contrast media;
3. use only NFC with neutral displacement (Micro-Clave, ICU Medical);
4. lock with saline only—no heparin.

The main endpoint of the study was to evaluate the incidence of occlusion and malfunction of the catheters. As the definition of these terms is sometimes ambivalent, we prepared a questionnaire for each use of each catheter, which had to be filled by the nurse caring for the PICC on that specific day. The questionnaire included questions investigating the following items:

1. Flow performance:
 - (a) blood return;
 - (b) flow by gravity infusion (with and without NFC);
 - (c) flow by pump infusion (with and without NFC);
2. Evidence of lumen occlusion:
 - (a) complete occlusion (no infusion, no withdrawal);
 - (b) partial occlusion (difficult infusion or withdrawal);
 - (c) PWO—partial withdrawal occlusion (infusion ok but no withdrawal);
 - (d) occlusions solved by flushing;
 - (e) occlusions solved by pharmacological action (urokinase);
 - (f) PICCs removed because of irreversible occlusion.

In case of difficulty in infusion and/or withdrawal, our hospital policy recommends a stepwise progression of interventions: control of the external portion of the line for possible kinking, replacement of the NFC, attempts to restore patency by saline flushing, ultrasound scan to rule out venous thrombosis, control of PICC's integrity and position by chest x-ray, pharmacological attempt to restore patency (urokinase 10,000 unit/ml). The occlusions solved by simple flushing or by urokinase were defined as 'transient'. PICC was removed only in case of 'irreversible' occlusion. According to the policies of our Hospital, we never used heparin, either for prevention or for treatment of the occlusions.

All questionnaires were collected and the results were transferred on a software-based database for statistical analysis. In the same database, the most important data regarding the patient and its PICC were also recorded. Secondary endpoints were the incidence of catheter-related

blood stream infection (CRBSI), as defined by the current international guidelines (3); the incidence of asymptomatic and symptomatic venous thrombosis, as detected by ultrasound; and mechanical complications (dislocation, 'minor', <4 cm, or 'major', >4 cm; catheter rupture). The occurrence of these complications was also reported in the database.

The statistical analysis of the data was performed by standard descriptive statistics; percentages were compared by Chi-square test. The study was designed to have 80% power to show a 20% absolute reduction in occlusion (our primary endpoint) using a 5% significance level (two-sided), which implied the recruitment of at least 100 patients per group (total of 300 patients).

RESULTS

The study was interrupted at 180 patients (approximately 60 for each group) because of three episodes of rupture of Power Solo PICCs. All three ruptures occurred in the intravascular tract, while the patients were on pump-infused chemotherapy; in two cases, the rupture was suspected by the backflow of infused solution at the exit site; in one case, the intravascular rupture was associated with damage of the axillary vein wall and extravasation of chemotherapy close to the axilla. In all cases, the ruptures were confirmed by examining the catheters after their removal.

After these events, the Hospital Management and the Ethics Committee stopped the randomized trial. Three more Power Solo PICCs not included in this protocol eventually broke down, and as all six PICCs belonged to the same lot, a defective batch of the product was postulated.

We analyzed the results from the first 180 randomized patients, which yielded quite consistent results.

Table I shows the characteristics of the three groups of patients.

The results regarding the primary endpoint are reported in Table II: the rate of occlusions was very low (eight episodes) and only one occlusion required the removal of the catheter, being resistant to saline flushing and to urokinase. Five episodes of occlusion were transient and easily overcome by manual flushing with saline. In two catheters, PWO was detected, resistant to manual flushing; as no sign of central venous thrombosis was evident at ultrasound, and as no abnormality of position was found at chest x-ray, according to our policies, both PICCs were left in place and still used for chemotherapy.

With regard to the performance of the PICCs, there was no problem with pump infusion in any group, but in 31% of PICCs with Solo-2 Valve and in 65% of PICCs with PASV, the nurses experienced some difficulties in gravity infusion. Blood return was easy in all PICCs, with

TABLE I - PATIENTS AND PICCS

	Solo valve (n=61)	PASV (n=60)	No valve (n=59)
Age (m±SD)	64 (12.1)	61 (10.1)	62 (14.5)
Sex (%male)	36%	38%	33%
Side (%right)	65%	54%	69%
Length cm (m±SD)	38.5 (5)	40.2 (4.7)	36.7 (6.1)
PICC days (m±SD)	56 (23)	64 (31)	65 (27)
Total PICC days	2780	3699	3422

TABLE II - PRIMARY ENDPOINTS

	Solo valve (n=61)	PASV (n=60)	No valve (n=59)
Irreversible occlusions	1	0	0
Transient occlusions	2	1	2
PWO	1	0	1
Difficulty with gravity infusion	19 (31%)	39 (65%)	0
Removed for occlusion	1	0	0

TABLE III - SECONDARY ENDPOINTS

	Solo valve (n=61)	PASV (n=60)	No valve (n=59)
Infection (CRBSI)	-	-	-
Symptomatic thrombosis	-	1	-
Asymptomatic thrombosis	2	1	1
Dislocation	-	-	-
Intravascular rupture	3	-	-
Removal due to rupture	3	-	-

the only exception of the two PICCs that developed a PWO.

Table III shows other complications reported in the three groups (secondary endpoints of our study). Apart from the above-mentioned intravascular ruptures of the Power Solo PICCs, we had very few complications: no infection; no dislocation; only one symptomatic thrombosis and two asymptomatic thrombosis (no thrombotic event was associated with catheter malfunction, so that all three catheters were left in place and kept in use—the symptomatic thrombosis was treated with low molecular weight heparin 100 unit/kg/12 h).

DISCUSSION

The overall incidence of lumen occlusion is usually difficult to assess, as it is extremely variable in different studies (4-12), ranging from 1% to 35% depending on the definition of occlusion, on the clinical setting and on the adoption of appropriate policies of flushing.

The incidence of occlusions was minimal in our study, most likely because all PICCs were exclusively managed by oncology nurses specifically trained in the maintenance of VADs in cancer patients, and also because our University Hospital has a well-defined policy of flushing/locking VADs for prevention of occlusion.

Saline flushing appears to play the major role in preventing VAD malfunction (1). In fact, the main mechanisms of intraluminal occlusion are development of an intraluminal clot because of inadequate flushing after blood withdrawal or infusion of blood products, or because of accidental blood reflux into the catheter while disconnecting the line; intraluminal precipitation of drugs, due to simultaneous infusion of non-compatible drugs and/or inadequate flushing in between different infusions; occlusion by lipid aggregates or by highly viscous drugs or contrast media, most likely to occur if an appropriate saline flushing is not adopted.

Thus, in most cases, flushing is the main strategy for preventing accumulation of cells, drugs or debris obstructing the lumen. The presence of a valve, either at the proximal or at the distal end of the PICC, should theoretically help to avoid blood reflux when disconnecting the line, thus acting exclusively—and only partially—on the mechanisms described in development of an intraluminal clot; it is apparent how the main role in avoiding lumen occlusion is an appropriate policy of flushing, which will be effective on all mechanisms of lumen occlusion, development of an intraluminal clot, intraluminal precipitation of drugs and occlusion by lipid aggregates or by highly viscous drugs or contrast media.

Not surprisingly, no randomized study has ever proven the clinical effectiveness of valved PICCs in reducing the risk of occlusion. In a randomized study on 362 patients (13), the Authors could not find any difference in occlusion rate comparing proximal valve PICCs and non-valved PICCs; in another study (14), the same Authors did not find any difference in occlusion rate comparing proximal vs. distal valve PICCs. In 2005, a large retrospective study (15) suggested a possible clinical efficacy of proximal valve PICCs in reducing the occlusion rate; unfortunately, the study was not exempt from criticisms under the statistical point of view, and furthermore, there was an evident conflict of interest, as the database and the statistical analysis of the data were provided by the company manufacturing and marketing the proximal valve PICCs. Two more prospective, non-randomized studies (4, 16) failed to show any effect of distal valve PICCs on the rate of occlusion. In recent years, a few prospective, randomized studies

comparing distal valve vs. no valve (326 patients) (17), proximal valve vs. no valve (53 patients) (Alport) and distal valve vs. no valve (26 patients) (18) did not report any significance difference in the rate of lumen occlusion. More recently, a well-designed randomized controlled trial, the so-called ELECTRIC study (7), compared simultaneously proximal valve vs. distal valve vs. no valve PICCs in a population of 102 Intensive Care Unit (ICU) patients: there was no difference between groups in terms of occlusion rate.

Our study further confirms that the presence of a valve has no effect on the risk of occlusion, as already suggested consistently by the literature. Our study, carried out in a very homogeneous population of cancer patients receiving chemotherapy by pump infusion, has the additional feature of comparing three types of PICCs made of the same material, power-injectable polyurethane, whereas many of the previous studies have compared silicon valved vs. polyurethane non-valved PICCs. Even removing the confounding issue of using different materials (which could be associated—at least in theory—with different risk of lumen occlusion), the clinical data are clear: the valve, either distal or proximal, has no effect on occlusion. Also, it appears to have no effect on other types of complications, such as infection or thrombosis—whose incidence was very low in this study, as already noted in other studies (5, 16) conducted using the SIP protocol.

It is also important to stress that in our study, flushing and locking were always performed with normal saline, without using heparin, in accordance with the most recent studies that have strongly questioned the actual role of heparin in preventing occlusion of VADs (19, 20).

Although the two-valved PICCs tested in our study had proximal valves with different technical features, this had no effect on the clinical endpoints. The above-mentioned ELECTRIC study (7) was interrupted after the recruitment of 102 ICU patients because of evidence of hemolysis in the group with the 'PASV' proximal valve (Navilyst). In our study, no hemolysis was reported: this might be explained by the fact that in our group of cancer patients, blood withdrawal was rather infrequent if compared with ICU patients. On the contrary, the use of valved PICCs was associated with some difficulties during infusion of intravenous (i.v.) fluids by gravity (in 31% of Power Solo PICCs and in 65% of PASV Navilyst PICCs); this was perceived by our nurses both with and without NFC. The actual clinical relevance of this finding in this group of patients is questionable, considering that all antineoplastic infusions were delivered by pump.

CONCLUSION

There were no significant advantages related to the presence of a proximal valve, either of the 'Solo' type (Bard) or of the 'PASV' type (Navilyst).

On the contrary, the presence of a proximal valve was significantly associated with some difficulties in gravity infusion, as perceived by our nurses. Although not relevant in our clinical setting, wherein all patients were receiving infusion by pumps, this finding might be of concern in other settings, such as in home care patients.

The higher cost of the valved PICCs vs. non-valved PICCs was not justified by a better clinical performance.

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