Peripherally Inserted Central Catheters with Distal versus Proximal Valves: Prospective Randomized Trial

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PURPOSE: To evaluate whether peripherally inserted central catheters (PICCs) with a proximal valve have any advantage compared to those with a distal valve in regard to the incidence of occlusion, infection, or malfunction.

MATERIALS AND METHODS: One hundred patients (mean age, 46 y) were randomized to receive either a distal-valved Bard Groshong catheter ($n = 48$) or a proximal-valved Catheter Innovations Pressure Activated Safety Valve catheter ($n = 52$). All catheters were 4-F, single-lumen PICCs. Catheters were placed under fluoroscopic ($n = 82$) or sonographic ($n = 18$) guidance. Most (91%) were placed for the administration of antibiotics. The placement procedure, maintenance, and weekly follow-up were the same for both catheters.

RESULTS: Percutaneous placement with the catheter tip in the central veins was successful in all patients. Mean dwell time was 36 days. There were 12 (25%) occlusive or infectious complications in the distal valve catheter group and six (11.5%) in the proximal valve group ($P = .08$). There were 25 fractures in 17 distal valve catheters (35.4%) and three (5.8%) proximal valve catheter fractures ($P < .01$).

CONCLUSION: There was a marked difference in durability between the valved catheters, in favor of the catheter with a proximal valve. There was also a trend for fewer occlusive and infectious complications with the proximal valve catheter.

RELIABLE central venous access is necessary for the management of patients who require sclerosing drugs, chemotherapeutic agents, infusion of hypertonic solutions, or prolonged antibiotic therapy (1). Peripherally inserted central catheters (PICCs) result in fewer procedural complications, lower infection rates, and decreased costs when compared with jugular or subclavian central venous catheters (1–4). The ease of placement and the avoidance of painful repetitive peripheral intravenous site puncture has broadened indications to any patient who requires venous access for longer than a week (5). Although these catheters are safe, easy to place, and cost-effective, catheter occlusion and infection continue to be common complications, with an incidence of 7%–25% (3–9). Valved catheters have been introduced in an attempt to diminish catheter occlusion by prevention of retrograde blood flow (8–13). An earlier study comparing a valved catheter directly with a clamped catheter found a lower incidence of complications with the valved design (8–10).

This study was a prospective randomized comparison of two different peripherally inserted valved catheters. The objective was to demonstrate whether the placement of the valve at the hub would demonstrate any benefit over placement of the valve at the tip of the catheter in regard to lower incidences of occlusion, infection, and other malfunction.

MATERIALS AND METHODS

Study Population

During a 5-month period, the interventional radiology service at our institution placed 285 PICCs in 211 patients. A dedicated PICC nurse reviewed the venous access request for proper long-term use indications (duration of therapy exceeding 7 d). If the patient was older than 18 and a single-lumen upper

[1] This author has disclosed the existence of a potential conflict of interest.

Table 1
Patient Demographics

	Valve Location	
	Proximal ($n = 52$)	Distal ($n = 48$)
Sex (M/F)	35/17	31/17
Age (y)		
Median	47.5	52.1
Range	18–85	18–89
Indications for catheter placement		
Antibiotics	44 (84.6)	37 (77.1)
IV access	9 (17.3)	13 (27.1)
Blood draw	0 (0)	2 (4.2)
Chemotherapy	3 (5.8)	1 (2.1)
Total parenteral nutrition	1 (1.9)	0 (0)
Hydration	0 (0)	1 (2.1)

Note.—Percentages in parentheses are of each type of catheter. Totals may exceed 100% as a result of multiple indications per patient.

extremity catheter was to be placed, the procedure and possible inclusion in the study were discussed with the patient or their representative. After signing the Institutional Review Board–approved informed consent, 98 patients were randomized from a computer-generated list to receive the 100 catheters with either proximal valves ($n = 52$) or distal valves ($n = 48$). No patients were lost to follow-up, but one continues with the catheter in use at 1 year. One PICC was placed in each of 96 patients, and two patients had two lines placed. Mean age was 48 years (95% CI of mean: 42.9–53.1 y), with a range of 18–78 years. There were no significant differences in patient demographics, underlying morbidity, or indications for PICC placement (**Tables 1,2**). The indication for access was poor peripheral access and need for intravenous antibiotic therapy in 91% of patients. Vein status was similar between groups as documented by similar numbers of women, patients requiring sonographic guidance, number of cephalic veins used, and number of attempts necessary to gain access (**Tables 1,3**).

Devices

Both catheters were 4 F in diameter with 18-gauge lumens. The Pressure Activated Safety Valve (PASV) catheters were 60 cm in length whereas the Groshong catheters were 57 cm; both were cut such that the tip was positioned at the lower superior vena cava

and the hub extended 7 cm from the skin entry site. Both catheters had valves that allowed pressure-controlled aspiration and infusion. The equipment needed to place the catheter was included with the distal valved catheter (Groshong Peripherally Inserted Central Venous Catheter set; Bard, Salt Lake City, UT), whereas the proximal valved catheter (PICC PASV Catheter; Catheter Innovations, Salt Lake City, UT) needed a micro-access kit (Peel-away Introducer Set; Cook, Inc, Bloomington, IN). The cost of the proximal valved PASV catheter was $82, and the kit that contained the access needle, guide wire and peel-away sheath was $47; the distal-valved Groshong catheter kit cost $95. Repair kits were available from the manufacturer for both catheters; each Groshong catheter came with an extra hub, and an additional repair kit cost $6.90, whereas a PASV catheter repair kit cost $70.

Procedure

Both types of catheters were placed as described previously (5,9,14). Patients with adequate peripheral veins had 20–22-gauge intravenous lines placed in a hand vein. The upper arm was cleaned and draped. Contrast material was injected and the upper arm was examined with fluoroscopy. If no hand vein was accessible or there was a history of contrast material allergy, sonography was used to identify an upper arm vein ($n = 18$).

When a suitable vein was identified, a 21-gauge needle was advanced under fluoroscopic or sonographic guidance and 1% lidocaine was administered subcutaneously for anesthesia. The vein was entered and an 0.018-inch guide wire was passed. The needle was exchanged for a 4.5-F peel-away sheath and dilator.

For the line with the proximal valve, the length of which was adjusted by trimming the distal end of the line, the wire was advanced to the junction of the superior vena cava and right atrium. The distance to the venotomy site was measured from the wire, and the PICC was cut to the appropriate length. The catheter was advanced through the vein, and the final position was documented radiographically. The outer flange was sutured to the skin, and a needleless injectable hub was affixed.

The distal valve catheter length was adjusted by cutting the proximal end. When the catheter was placed through the peel-away sheath and its tip was positioned at the desired caudal location in the superior vena cava, the guide wire was removed, the catheter was cut to the desired length, and the hub was assembled. The included plastic flange was affixed near the skin entry site by suture to the catheter, and then the flange was sutured to the skin.

The sites were dressed with 1-inch cotton gauze and covered with a clear, sterile bandage (Tegaderm; 3M, St. Paul, MN). No antibiotic ointment was used. The catheters were flushed with saline solution. The protocol for line care included a saline flush after each use or every 8 hours. Dressings were changed at 48 hours and then every 7 days or as needed.

Follow-up

Procedural parameters recorded were the vein accessed, number of attempts necessary, catheter tip position, and any immediate complications (**Table 3**). Follow-up by the PICC nurse occurred on a weekly basis as long as the line was in place. She was notified and made the initial visit if there were any in-hospital complications, such as occlusion, fracture of catheter, local inflammation, or infection. Daily care, including catheter flush, dressing change, and administration of the ap-

Table 2
Underlying Morbidity in 100 Patients

Morbidity	Valve Location	
	Proximal ($n = 52$)	Distal ($n = 48$)
Infection	43 (82.7)	40 (83.3)
Trauma	18 (34.6)	12 (25.0)
Neurologic	9 (17.3)	14 (29.1)
Diabetes	4 (7.7)	5 (10.4)
IV drug use	2 (3.8)	4 (8.3)
HIV	3 (5.8)	2 (4.2)
Cancer	4 (7.7)	3 (6.2)
Chronic renal failure	2 (3.8)	1 (2.1)
Other*	1 (1.9)	5 (10.4)

Note.—Numbers in parentheses are percentages. Totals may exceed 100% as a result of multiple categories of disease per patient.
* End-stage liver disease ($n = 2$), electroconvulsive therapy ($n = 2$), congestive heart disease ($n = 1$), burn ($n = 1$).

propriate therapeutic regimen, was performed by the ward nurse (hospital patient) or visiting nurse (home care patient). Follow-up was documented until the catheter was removed. Follow-up parameters were patient status, functional or mechanical catheter problems, reason for catheter removal, and date of removal. No patients were lost to follow-up; one catheter continues in use 1 year after implantation.

Definitions and Study Endpoints

Catheter-related infection was defined as fever or elevated white blood cell count (or both) and positive blood culture from the PICC, positive PICC tip culture, or positive peripheral blood culture with no other source and clinical improvement after catheter removal. Entry site infection was defined by purulence at the site. Phlebitis was diagnosed by local pain and a palpable cord along the vein or by positive sonographic evaluation in conjunction with erythema and edema of the extremity. Mechanical complications included catheter occlusion and fractures or leaks in the catheter.

Occlusion was defined as the inability to use the catheter for the assigned therapy, administration of antibiotics in most cases. Inability to aspirate blood did not warrant thrombolysis unless the purpose of the catheter was access for blood draws. The declotting procedure entailed injection of 2 mg recombinant tissue plasminogen activator (Activase; Genentech,

South San Francisco, CA) in 2 mL normal saline solution into the occluded catheter, which was left clamped for 30 minutes. If flow was not reestablished, a second dose was instilled and the catheter was clamped for 24 hours. If the catheter remained occluded, it was replaced. Replacement of an occluded catheter was attempted over a guide wire. If this failed or if an infected catheter was removed, the replacement catheter was placed in the contralateral arm if possible.

Catheter fractures included cracks in the external shaft or hub of the catheter that resulted in leakage of infused materials. Fractures were repaired with the manufacturer's recommended repair kits when available.

Follow-up endpoints were removal of the catheter as a result of termination of therapy, irreparable fracture or occlusion, infection, accidental removal, and patient death. Study endpoints were a significant difference in complications or mortality. Data were reviewed after each 100 patients to allow early termination of the study if there were significant findings.

Statistical Analysis

Data were collected in a vascular access computer database (Vas-Trak, Bellevue, WA) maintained by the PICC nurse and angiography nursing staff. Baseline characteristics and risk factors of the two groups and differences between treatment groups in postrandomization measures or events were com-

pared with use of the χ^2 test for discrete variables and with the Student t test for continuous variables. Sample size was calculated to demonstrate a 50% improvement in the reported complication rate (from 22% to 11%). A two-tailed test with alpha of 0.05 and beta of 0.20 required 166 patients in each group. An additional 10% were added to accommodate any loss to follow-up, which resulted in a total of 365 patients. Data are reported as means with 95% CIs and percentages are in parentheses. A P value of .05 was considered significant.

RESULTS

Catheters were successfully placed in all patients. All were placed such that their distal tip was at the caudal third of the superior vena cava. Three patients required selective catheter guidance to negotiate tortuous or partially occluded veins to reach the cavoatrial junction. There was no significant difference in procedural complications between the proximal and distal valved catheter groups (**Table 3**).

Average dwell time was 35.1 days (range, 1–211 d; 95% CI: 28.5–42.7 d) for the proximal valve catheters and 37.5 days (range, 1–306 d; 95% CI: 27.3–47.7 d) for the distal valve catheters ($P = .63$). Total catheter days were 1,980 and 1,802, respectively. Seven patients died; all deaths were expected in the course of their underlying disease and their catheters were intact (**Table 4**). Catheters were accidentally removed in five patients. Catheter malfunction caused by fracture occurred 25 times in 17 patients with the distal valve catheter; there were three proximal valve catheter fractures ($P = .0002$). Fracture most often occurred in the shaft at the point of connection to the hub. The high fracture incidence was an unexpected finding and led to the early termination of the study. Although both catheters can be repaired if broken, sometimes the nurse encountering the damaged line did not know of the repair potential and the catheter was removed.

Incidence of occlusion and infection did not differ significantly between the groups (**Table 4**). Neither the need for multiple venous puncture attempts nor the underlying morbidities of diabetes, intravenous drug use, or AIDS correlated with an increased risk of

Table 3
Procedural Data

	Valve Location	
	Proximal	Distal
Sonography-guided placement	9 (17.3)	8 (16.7)
Attempts (punctures)		
2	8 (15.4)	7 (14.6)
3	5 (9.6)	2 (4.2)
4	0 (3.8)	1 (2.0)
6	1 (1.9)	0
Arm		
Right	30 (57.7)	27 (56.2)
Left	22 (42.3)	21 (43.8)
Vein		
Basilic	36 (69.2)	34 (70.8)
Brachial	14 (26.9)	13 (27.1)
Cephalic	2 (3.8)	1 (2.1)
Tip placement		
Cavoatrial junction	48 (92.3)	46 (95.8)
Mid–superior vena cava	4 (7.7)	2 (4.2)
Complications		
Resistance encountered	2 (3.8)	1 (2.1)
Hematoma at site	1 (1.9)	0

Note.—Numbers in parentheses are percentages of total of each type of catheter.

complications (although the number of these patients was small). There were one (1.9%) and four (8.3%) suspected infections in the proximal and distal valve catheter groups, respectively ($P = .14$); zero and two (3.8%) proved positive by culture ($P = .13$). One was an exit site infection. PICCs suspected of being infected were often removed before culture results were reported.

Occlusions occurred in five (9.6%) proximal valve catheters and seven (14.6%) distal valve catheters ($P = .44$). There was no significant increase in incidence of occlusion in catheters that were difficult to place as a result of tortuous veins or stenoses. There was a high rate (75%) of successful recanalization with tissue plasminogen activator for both types of catheter. Only one proximal valved catheter and two distal valved catheters were removed because they were occluded (**Table 4**).

DISCUSSION

PICC occlusion results in delays in treatment, higher costs, and patient discomfort. Intraluminal clotted blood and fibrin may increase the risk of catheter-related sepsis. Catheter occlusion results from mechanical obstruction, either external or internal (15).

External problems such as kinks or compression of the intravenous tubing or catheter can usually be identified and rectified on examination. Internal occlusion is usually a result of clotted blood or drug precipitate. Reflux of blood into the distal catheter tip after the device is accessed or flushed allows clot to form. Alternatively, if the contents of the infusion bag run out, equalization of infusion pressure permits retrograde blood flow into the catheter (15).

Treating the occluded catheter entails additional expense. Tissue plasminogen activator is often successful; however, the drug and administration cost may be significant and repeated administration may be required (10). If unsuccessful, the catheter must be replaced. The cost of a delay in treatment is not quantified and may be most significant for an antibiotic regimen that requires continuous infusion to reach effective blood drug levels for success.

A mechanical approach to diminish catheter occlusion rates is the incorporation of a valve. Both valve designs open inward with fluid infusion pressure and outward with aspiration pressure. The valves are normally closed, which allows for direct needle-free connection and saline-only lock.

The valves also prevent bleed-back in case the material to be infused has run out.

In addition to reducing costs of tissue plasminogen activator or catheter replacement by way of its associated lower occlusion rates, the use of valved catheters results in savings from saline solution (as opposed to heparin) flushes and possible decreased nursing time demands as a result of less frequent flush requirements (10). At a cost premium of $50 per catheter, valved catheters are cost-effective if there is an improvement in the occlusion rate of 10%–20% or if the infection rate is reduced by even 1%. The disproportionate importance of the reduced infection rate is caused by the catheter-related bloodstream infection association with mortality rates of 10%, mean hospitalization of 7 days, and medical costs of as much as $6,000 (16).

The first available valved catheter was the Groshong (Bard), which has a valve at the distal end of the catheter. It opens inward with fluid infusion pressure and outward with aspiration. Studies of internal jugular or subclavian central venous Groshong catheters had mixed results. Although there were no statistically significant advantages versus conventional clamped catheters (12,13), one group reported a 50% decrease in infections (from 2.5 to 1.3 infections per 1,000 catheter days; $P = .24$) (13). In a group of high-risk patients (with cancer and neutropenia) in whom only Groshong catheters were placed, there was a low infection rate of only 0.36 per 1,000 catheter days and a 2% occlusion rate (11).

A clearer benefit has been demonstrated for the Groshong PICC. Miller and Dietrick (8) described diminished clotting complications with the Groshong system in comparison with the clamped Per-Q-Cath (Gesco International, San Antonio, TX) (3.3% vs 16% of 331 and 43 catheters, respectively). In another study, a comparison of cohorts in which the Groshong or a clamped PICC were used revealed occlusion rates of 1.7% and 27.6%, respectively ($P < .001$) (10).

The PASV PICC is a silicone catheter with a 3-way silicone valve positioned in the proximal luer hub that acts as an automatic clamp. In a randomized study that compared the PASV valved PICC with a clamped PICC, the valved catheter had fewer occlusive and infectious complications ($P = .04$) (9).

Table 4
Complications and Reason for Discontinuation of 100 PICCs

	No. of Complications		Reason for Discontinuation	
	Proximal	Distal	Proxmial	Distal
Completion of therapy (no complications)			43 (82.7)	30 (62.5)
Death from underlying disease			4 (7.7)	3 (6.2)
Ongoing			1 (1.9)	1 (2.1)
Accidental dislodgment	2	3	2 (3.8)	3 (6.2)
Catheter-related infection	1	4	1 (1.9)	4 (8.3)
Exit site infection	0	1		
Culture positive	0	1		
Catheter occlusion	5	7	1 (1.9)	2 (4.2)
Phlebitis	0	1	0	0
Catheter fracture	3	25	0	5 (10.4)
Totals	11	40	52	48

Note.—Numbers in parentheses are percentages of total of each type of catheter.

Because of the early termination of this study, the question of which valve provides more protection from occlusive incidents was not answered. The high incidence of fracture of the Groshong catheter confounded the evaluation of the valve. The additional nursing time demanded by fractures in one third of these catheters resulted in marked resistance among the nursing staff to support the continuation of the trial. One benefit of the valve location at the distal tip is that fracture of the catheter shaft does not produce bleeding or allow air embolism. This is fortunate given the incidence of fracture. The repair procedures are simple and similar for both catheters.

One other study reported significant fracture rates with Groshong catheter use (2). In a study of 209 4-F single-lumen and 5-F dual-lumen catheters with a dwell time of only 10.5 days, the fracture rate was 13.9% (2). Other trials did not demonstrate a significant fracture problem with the Groshong PICC, even though the dwell time was as long as 24 days (8). A reason for the high fracture rate in this study may be the large number of patients in our series with altered mental status, which may produce a more hostile environment for the external portion of the catheter.

PICCs continue to be compared with tunneled central venous access (2,3). The literature has demonstrated comparable infection rates, and use of valved PICCs results in comparable occlusion rates (8–10). Fluoroscopic guidance and upper arm vein access have reduced the incidence of malposition and venous thrombosis, respectively (9). This study has shown that the important advantage of a diminished occlusion rate achieved with use of a valved catheter need not be compromised by an increased fracture rate.

A deficiency of this study was the inability to blind the participants to the type of catheter used. This was not feasible as a result of the different physical appearance of the catheters. Standardization of the placement procedures and catheter care and the objective nature of the endpoints and complications minimized the effect of this bias.

This prospective randomized study was halted before a significant difference in the overall risk of catheter-related infection or occlusion could be identified between the proximal- and distal-valved PICCs. The PASV PICC complication rate was half that of the Groshong PICC ($P = .06$) and the PASV catheter had one eighth the fracture rate of the distal valved Groshong catheter ($P = .04$).

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