Peer reviewed article

Randomised comparison of complications from three different permanent central venous access systems

Riccardo E. Vandoni[a], *Adriano Guerra*[a], *Piero Sanna*[b], *Marcel Bogen*[a], *Franco Cavalli*[b], *Philippe Gertsch*[a]

Servizio di Chirurgia, Ospedale San Giovanni[a], and Istituto Oncologico della Svizzera Italiana[b], Bellinzona, Switzerland

Summary

Principles: We present a prospective randomised trial comparing complications from three different permanent central venous access systems (PCVAS).

Methods: The PCVAS trial groups were I, polyurethane ChemoSite® (AutoSuture®); II, polyurethane Port-a-Cath® (Pharmacia-Upjohn®); and III, silicone Port-a-Cath®. The PCVAS were inserted under local anaesthesia by direct puncture of the subclavian vein, using the Seldinger technique. Every complication and its evolution was recorded and analysed. The follow-up period was closed five years after the last PCVAS was implanted, and interrupted when for any reason the device was removed.

Results: Over a period of 45 months, we included 228 patients (96 men, 132 women, average age 58 yr). Patients were followed from six days to 103 mo (median 14.7 mo). We observed 10 pneumothorax (4.3%), seven of them requiring drainage. Out of 10 infected ports (4.3%), eight were removed. We observed 46 complications (20.1%) related to the device (rupture, displacement, disconnection, and occlusion of the catheter). Most of the thirteen ruptures (5.7%) occurred in the space between the clavicle and the first rib. Catheters of group I ruptured more often than those of groups II and III ($p < 0.05$). Polyurethane catheters ruptured more often than silicone catheters ($p < 0.01$).

Conclusion: The polyurethane catheters that ruptured more often had a larger diameter and a thicker wall than the other polyurethane catheters, and were probably subjected to greater shearing between the clavicle and the first rib. Silicone catheters, although thicker and of larger diameter than the two other catheters, seemed more resistant to shearing.

Key words: complications; central venous device; rupture; silicone; polyurethane

Introduction

Permanent central venous access systems (PCVAS) have been used with increasing frequency since the mid-nineteen-eighties, principally in patients with tumoral diseases. These devices facilitate prolonged courses of chemotherapy by sparing the patients' venous integrity, which can be compromised by the drugs' toxicity [1–3]. Parenteral nutrition, blood transfusion, and blood sampling are also performed via PCVAS [2–5].

The complications associated with PCVAS are rare, but may be severe and life-threatening. During implantation of the device, haemorrhage and pneumothorax may occur. Long-term complications include thrombosis of the subclavian vein, infection of the implanted material, extravasation of chemotherapeutic agents, and rupture or dislocation of the catheter [1–12]. These complications were defined as the primary outcomes of our trial.

We prospectively compared long-term complications occurring with three different PCVAS models available on the Swiss and international markets. We always inserted PCVAS by direct puncture of the subclavian vein, and assumed that the complications during implantation are likely to be the same, regardless of the model of PCVAS, because they depend more on the technique than on the device. Long-term complications may be related to the model of PCVAS.

To the best of our knowledge this is the first study that prospectively compares the long-term complications of different types of PVCAS built with different materials.

This study was supported by Pharmacia & Upjohn®, Switzerland and Autosuture®, Switzerland, who provided the permanent central venous access systems.

Patients and methods

The local ethical committee accepted the study protocol and informed consent was obtained from all patients. The industry provided all the devices we implanted, and thus we were able to include 228 consecutive patients in our study, from March 1st 1998 to December 31st 2001. We did not exclude any patient from this trial. The mean age of our patients, 96 men and 132 women, was 58 yr (±12 yr).

All patients requiring a PCVAS, whatever the indication, were randomised into three groups. A different model of PCVAS was assigned to each group. A randomisation list was generated using internet website "www.randomization.com" and envelopes were accordingly prepared and sealed by one of the authors before recruitment began. The envelopes were opaque and sequentially numbered. It was not possible to read the allocation without opening the envelope.

All the PCVAS were implanted by one of the five senior surgeons of the hospital staff, each with 10 or more years' surgical experience.

The three groups were similar in age, sex, pathology, and distribution between groups of solid tumours and haematological diseases. Three patients had a PCVAS implanted for parenteral liquid or nutritional support. Details are listed in table 1. Two foreign patients went back to their countries of origin and were lost to follow-up. The other patients (99.2%) were followed for a mean period of 29.5 mo (± 29 mo). There was no statistical difference of mean follow-up duration between the three groups (Group I = 32 mo, Group II = 27 mo, Group III = 32 mo, p = 0.80).

Group I received polyurethane ChemoSite® (Auto-Suture® Schweiz, Switzerland). Group II received a polyurethane Port-a-Cath® (Pharmacia & Upjohn®, Switzerland). Group III received a silicone Port-a-Cath® (Pharmacia & Upjohn®, Switzerland). These three PCVAS are different in construction. Table 2 reports their specifications.

PCVAS were implanted by direct puncture of the subclavian vein using the Seldinger technique. Implantations were done under local anaesthesia and mild sedation (95% of cases), or general anaesthesia if the PCVAS was implanted during another operation. The correct position of the tip of the catheter in the upper vena cava was checked by fluoroscopy, and the reservoir was implanted in the right side prepectoral subcutaneous space in 88% of cases. The system was then flushed and connected to a perfusion of a 0.5% solution of heparin (5000 IU/l – 42 ml/h) for 24 hours. Routine administration of preoperative antibiotic was not prescribed. Chest radiographs were obtained after the operation for all patients. The PCVAS was used for its initial purpose (e.g., chemotherapy, parenteral nutrition, hydration) starting on the day after surgery.

The follow-up schedule was determined by the chemotherapeutic regimen, but patients underwent clinical examination at least once a month. Radiological investigations were performed only if specified as necessary by clinical evaluation and/or the oncological follow-up schedule. No routine radiological control of the devices was scheduled. Samples for bacterial culture were obtained only if there was a clinical suspicion of infection. The patients and oncologists following them were blinded to assigned catheter.

Each patient received a card specifying the phone numbers of the physicians and institutions they could call at any time should a problem occur between their routine appointments. Follow-up was interrupted when the device was removed, either due to a complication or where the patient was considered to be cured. The follow-up period was arbitrarily closed on December 31, 2006, five years after the last PCVAS was implanted. Every complication and its evolution was recorded and analysed.

The commercial software JMP® (version 7.0.2, SAS Institute Inc., Cary, NC, USA) was used for statistical analysis. This analysis consisted of paired t-tests, analysis of variance, Chi-square analysis or Fisher's exact test when appropriate. Results were considered to be statistically significant when $p \leq 0.05$. We did not perform a power analysis since we received the devices from the industry and decided to close the study after inserting all the devices.

Table 1

Patients' demographic data and related disease information.

	Group I 78 patients	Group II 76 patients	Group III 74 patients
Sex (M / F)	29 / 49	33 / 43	34 / 40
Mean age (yr) ± SD (yr)	57 (±12.8)	59 (±12.3)	58 (±11.1)
Number of patients with solid tumours			
Breast	17	18	12
Gynaecological	6	3	2
Gastrointestinal	20	20	19
ORL	4	7	6
Lung	3	5	9
Urologic	3	4	6
Other	9	2	5
Number of patients with haematological disease			
Non-Hodgkin lymphoma	10	10	9
Leukaemia	1	3	3
Hodgkin disease	2	1	2
Multiple myeloma	2	2	0
NON TUMOUR	1	1	1

Table 2

Technical specifications of the PCVAS.

		Group I	Group II	Group III
		Polyurethane ChemoSite®	Polyurethane Port-a-Cath®	Silicone Port-a-Cath®
Reservoir	Material	Titanium with plastic outer chamber	Titanium	Titanium
	Capacity	0.5 mL	0.3 mL	0.47 mL
Catheter	Material	Polyurethane	Polyurethane	Silicone
	External diameter	2.0 mm	1.9 mm	2.8 mm
	Internal diameter	1.0 mm	1.0 mm	1.0 mm

Results

The distribution of complications between the three groups is listed in table 3. The mean intervals between implantation of the device and the occurrence of a complication were similar in the three groups (Group I = 128 d ± 30, Group II = 116 d ± 59, Group III = 78 ± 14).

We observed no complications related to inadvertent arterial puncture during the insertion of the PCVAS.

Chest X-rays were performed in all patients a few hours after the implantations of the PCVAS. Pneumothorax was detected in 10 cases (4.3%). Drainage was necessary in seven of these patients.

Infection of the device was defined as induration, tenderness, and erythema near the reservoir, with a positive bacterial culture. Ten ports (4.3%) presented a local infection according to this definition. Two patients were successfully treated with antibiotics. However, eight ports had to be removed. The microorganisms identified were *Staphylococcus aureus* (six times), *Streptococcus species* (three times), and *Stenotrophomonas maltophilia* (once). When we suspected an infection a bacteriological sample was obtained either by culture of the devices that had to be removed or by culture of a skin smear for the two patients who were treated successfully by antibiotics. The median time between the implantation of PCVAS and the diagnosis of infection was 28 d (range 10 d–238 d). Patients suffering from solid tumours had significantly lower infection rates than patients with haematological disease (2.8% vs 10.4%, p = 0.03). There was no significant difference in infection rate between the three groups of PCVAS (see table 3).

Catheter rupture, obstruction, displacement, or disconnection was always confirmed by chest x-ray with, if needed, injection of contrast medium into the reservoir. All ruptures were suspected by the nursing staff and confirmed before chemotherapeutic agents were injected. We did not observe any complications due to cytostatic extravasation in the subcutaneous space.

We observed 46 (20.1%) late complications related to the catheters: thirteen ruptures (5.7%), nine displacements (3.9%), one disconnection (0.4%) and thirteen occlusions (5.7%). These complications required PCVAS substitution (15 times), repair (4 times) or removal (16 times). Device occlusion was successfully treated without reoperation in the remaining ten patients by injection and flushing of urokinase into the reservoir.

Out of the thirteen ruptures, 10 occurred in the space between the clavicle and the first rib. The other three catheters ruptured near their connections to the reservoirs, but were not disconnected. Three ruptured catheters, one in each PCVAS group, migrated into the right atrium and were removed by endovascular techniques. Catheters in Group I ruptured more frequently than those in Groups II and III ($p < 0.05$). Polyurethane catheters ruptured more frequently than silicone catheters ($p < 0.01$).

Comparison of other device-related complications (i.e., catheter obstruction, displacement, or disconnection) showed no significant differences between groups. Thrombosis of the subclavian vein was never observed in our patients, either as a unique complication or in association with another complication.

Table 3

Complications in each patient group.

	Total	Group I	Group II	Group III	p*
	228 patients	78 patients	76 patients	74 patients	
General					
Infections	10 (4.3%)	6 (7.7%)	1 (1.3%)	3 (4.0%)	0.06
Pneumothorax	10 (4.3%)	2 (2.6%)	4 (5.1%)	4 (5.4%)	0.59
Material					
Catheter rupture	13 (5.7%)	9 (9.9%)	3 (3.9%)	1 (1.3%)	0.02
Group I + II vs Group III			12	1	< 0.01
Catheter obstruction	13 (5.7%)	4 (5.1%)	7 (9.2%)	2 (2.7%)	0.3
Catheter displacement	9 (3.9%)	6 (7.7%)	1 (1.3%)	2 (2.7%)	0.11
Catheter disconnection	1 (0.4%)	1 (1.3%)	0	0	0.99

* Chi-square test or Fisher's exact test where applicable

Discussion

Since the early eighties the advantages of PCVAS for patients with oncological diseases undergoing intravenous chemotherapy has been clearly demonstrated [2, 3, 5, 8, 9, 11]. Indications for implantation of percutaneous tunnelled catheters, such as those of Hickman and Broviac, are now rare [5, 9, 11].

Implantation of PCVAS, when indicated, should be performed as soon as possible, to take full advantage of the device and spare the patient's

venous capital. In our study the patients who died during the follow-up period (82% of the total) had a median survival of 11.7 mo (6 d to 102 mo) after implantation of the PCVAS. None of the patients included in our study died of a complication related to the insertion of a PCVAS.

In our study, the rate of pneumothorax was similar to that published by others, who also introduced the catheter by direct puncture of the subclavian vein [3, 11]. Introducing the catheter into the cephalic vein by the direct approach appears to reduce the complication rate [8].

Some authors have reported a higher infection rate by PCVAS in patients with haematological malignancies than in patients with solid tumours [3, 9, 11], and our study confirmed this difference. This supports the hypothesis that a compromised immune defence, induced by the primary disease or by aggressive therapy, may be related to the higher infection rate [11].

Catheter rupture was a rare event. Rupture of catheters most frequently occurred under the clavicle. The mechanical forces acting on the catheter between the clavicle and the first rib have been described as the "pinch-off" syndrome [10].

Implantation by direct puncture of the subclavian vein may explain why our catheter rupture rate was higher than in other publications. In the other published series the silicone catheters were inserted in the cephalic vein [11, 12]. When the catheter is implanted via the cephalic vein, the shearing effect on the catheter is less marked. The reduction of shearing explains this difference.

The significant difference in catheter rupture rates observed between groups may be explained by the more important shearing between the clavicle and the first rib. Indeed, the polyurethane catheter that ruptured more often (Group I) had a larger diameter and thicker wall than the other polyurethane catheter (Group II). Because the silicone catheter (Group III) has the largest external diameter (2.8 mm) and the thickest wall, it seems possible that, in spite of an increased shearing effect due to a larger diameter, the higher resistance of the material resulted in less frequent rupture.

This study resulted in a change in our practice. We no longer implant polyurethane catheters and routinely use only silicone catheters.

To the best of our knowledge this is the first report of a difference in rupture rate related to materials used in the manufacture of PCVAS. Hence our data suggest that silicone catheters should be given preference to polyurethane catheters. However, the use of thinner catheters is sometimes mandatory in small patients, and it appears that industry should manufacture thinner catheters in silicone.

We are indebted to Mrs. Sabine Van den Bosch for her contribution to data collection and to Prof Costanzo Limoni, biostatistician, for reviewing the statistical analysis.

Correspondence:
Dr. med. Riccardo E. Vandoni
Capo-Servizio, Servizio di Chirurgia
Ospedale San Giovanni
CH-6500 Bellinzona
Switzerland
E-Mail: riccardo.vandoni@bluewin.ch

References

1 Vescia S, Baumgärtner AK, Jacobs VR, Kiechle-Bahat M, Rody A, Loibl S, et al. Management of venous port systems in oncology: a review of current evidence. Ann Oncol. 2008;19(1):9–15.
2 Bow EJ, Kilpatrick MG, Clinch JJ. Totally implantable venous access ports systems for patients receiving chemotherapy for solid tissue malignancies: A randomized controlled clinical trial examining the safety, efficacy, costs and impact on quality of life. J Clin Oncol. 1999;17(4):1267–73.
3 Groebli Y, Wutrich P, Safa M, Tschantz P, Callewaert G, Piguet D. Utility and complications of permanent venous access devices (PVAD) in oncological treatments. Follow-up of 100 cases. Panminerva Med. 1999(2);41:89–92.
4 Boersma RS, Jie KSG, Verbon A, van Pampus ECM, Schouten HC. Thrombotic and infectious complications of central venous catheters in patients with haematological malignancies. Ann Oncol. 2008;19(3):433–42.
5 Biffi R. Totally implantable central venous access ports for long-term chemotherapy. A prospective study analyzing complications and costs of 333 devices with a minimum follow-up of 180 days. Ann Oncol. 1998;9(7):767–73.
6 Bach F, Videbaek C, Holst-Christensen J, Boesby S. Cytostatic extravasation. A serious complication of long-term venous access. Cancer. 1991;68(3):538–9.
7 Carr ME Jr. Catheter embolization from implanted venous access devices: case reports. Angiology. 1989;40:319–23.
8 Di Carlo I, Cordio S, La Greca G, Privitera G, Russello D, Puleo S, et al. Totally implanted venous access devices implanted surgically. A retrospective study on early and late complications. Arch Surg. 2001(9);136:1050–3.
9 Groeger JS, Lucas AB, Thaler HT, Friedlander-Klar H, Brown AE, Kiehn TE, et al. Infectious morbidity associated with long-term use of venous access devices in patients with cancer. Ann Intern Med. 1993;119(12):1168–74.
10 Hinke DH, Zandt-Stasny DA, Goodmann LR, Quebbeman EJ, Krzywda EA, Andris DA. Pinch-off syndrome: a complication of implantable subclavian venous access devices. Radiology. 1990;177(11):353–6.
11 Kock HJ, Pietsch M, Krause U, Wilke H, Eigler FW. Implantable vascular access systems: experience in 1500 patients with totally implanted central venous port systems. World J Surg. 1998;22(1):12–6.
12 Stein M, Wagner RH. Komplikationen zentralvenöser Portsysteme: Erfahrungsbericht über 2359 Implantationen. Dtsch Med Wochenschr. 2005;130:1129–30.