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Original Paper

Long-term, Totally Implantable Central Venous Access Ports Connected to a Groshong Catheter for Chemotherapy of Solid Tumours: Experience from 178 Cases Using a Single Type of Device

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The aim of this study was to examine the early and late complications rate of central venous access ports connected to the Groshong catheter for long-term chemotherapy delivering. All patients suffering from a neoplastic disease, who required long-term chemotherapy and underwent insertion of implantable ports during a 21-month period (1 October 1994–30 June 1996) were prospectively studied. A single type of port was used, constructed of titanium and silicone rubber (Dome Port™, Bard Inc., Salt Lake City, U.S.A.), connected to an 8 F silastic Groshong™ catheter tubing (Bard Inc.). A team of different operators (two general surgeons, one interventional radiologist and four anaesthesiologists) was involved in inserting the port. All devices were placed in the operating room under fluoroscopic control. A central venous access form was filled in by the operator after the procedure and all ports were followed prospectively for device-related and overall complications. Data from the follow-up of these patients were entered in the form and collected in a database. Follow-up continued until the device was removed, the patient died or the study was closed. 178 devices, comprising a total of 32 089 days *in situ*, were placed in 175 patients. Three patients received a second device after removal of the first. Adequate follow-up was obtained in all cases (median 180 days, range 4–559). 138 devices (77.5%) were still *in situ* when the study was closed. Early complications included six pneumothoraxes, three arterial punctures and two revisions for port and/or catheter malfunction (overall early complications in 8 patients). Late complications included 3 cases (1.68% of devices) of catheter rupture and embolisation (0.093 episodes/1000 days of use), 2 cases (1.12% of devices) of venous thrombosis (0.062 episodes/1000 days of use), 1 case (0.56% of devices) of pocket infection (0.031 episodes/1000 days of use), and 4 cases (2.24% of devices) of port-related bacteraemias (0.124 episodes/1000 days of use). Infections were caused by coagulase-negative *Staphylococcus aureus* (4 cases) and *Bacillus subtilis* (1 case); they required port removal in 3 out of 5 cases. This study represents the largest published series of patients with totally implantable access ports connected to Groshong catheters; this device is a good option for long-term access to central veins and delivery of chemotherapeutic regimens, including continuous intravenous infusions. The low incidence of major complications related to implantation and management of these devices support increased use in oncology patients. © **1997 Published by Elsevier Science Ltd.**

Key words: central venous catheters, Groshong catheter, ports, chemotherapy

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INTRODUCTION

CURRENT MANAGEMENT of many malignancies requires repeated entry into the venous system to draw blood samples and to administer cytotoxic drugs, antibiotics, blood products, fluids and nutrition. Tunnelled, cuffed silastic catheters, first described by Broviac and associates [1] and subsequently modified by Hickman and associates [2] for long-term use in outpatients, provide trouble-free function for most patients; however, catheter-related infections occur at a rate of 1.4 episodes per 1000 days of catheter use [3]. Since an obvious route of bacterial invasion in patients with Hickman catheters is the open wound maintained by the catheter's presence, efforts at reducing infection have focused on eliminating this wound. One such effort has been the development of totally implantable access ports (TIAP), and compared to those of tunnelled catheters, port infections tend to be unusual [4], although results are sometimes conflicting [5]. Most series reflect differences in the type of adopted device and patients being treated, rather than any inherent superiority of one device over another. Moreover, it is likely that patients requiring more intensive treatment, such as those with haematological malignancies, severe neutropenia or bone marrow transplant, are the ones who receive tunnelled double-lumen Hickman catheters, which allow high flows and are more easily removed. The negative role of neutropenia has been emphasised by a study of nosocomial septicaemia in cancer patients, which reported that 61% of septic episodes in patients with central venous lines occurred when the patients were neutropenic [6].

Developed in 1978, the Groshong catheter is a silicone rubber device with a unique three-position pressure-sensitive valve near the distal tip. The valve opens only with positive or negative pressure, effectively preventing spontaneous reflux of blood or inadvertent air embolism. Despite the wide use of permanent central venous access in oncology, there are surprisingly few reports describing clinical experience with the Groshong catheter and TIAP connected to such a catheter. Therefore, the purpose of this study was to present our experience in the use of TIAP connected to a Groshong catheter in cancer patients undergoing chemotherapy and to identify factors associated with overall and infectious complications. This paper deals with a prospectively studied consecutive series of unselected cancer patients, treated in a single institution using a single type of device.

PATIENTS AND METHODS

All ports placed in patients at the European Institute of Oncology in Milan during the 21-month period from 1 October 1994 to 30 June 1996 were followed prospectively for device-related and overall complications.

All devices were inserted in an operating room under fluoroscopic control (even when the patient was treated and monitored in a day-hospital setting); a single dose (2 g) of Cefazoline sodium was given intravenously (i.v.) 15 min before implant. No breaks in operative technique or instrument sterility were documented; a physician always checked the patients before discharge.

A single type of port was used, constructed of titanium and silicone rubber (Dome Port™, Bard Inc., Salt Lake City, U.S.A.) with 8 F silastic Groshong™ catheter tubing (Bard Inc.). A team of different operators (two general surgeons, one interventional radiologist and four anaesthesiologists) was involved in inserting the ports into the patients. A central venous access form was filled in by the operator after the procedure. A confirmatory chest X-ray was always obtained after the placement. Data from the follow-up of these patients were entered in the form and collected in a database. Follow-up continued until the device was removed, the patient died or the study was closed.

Complications were divided into two main categories: (1) early (intra-operative and postimplantation period to first use); and (2) late complications (occurring after the first chemotherapy course given through the device).

Blood screening for bacteraemia was not performed at regular intervals, since blood sampling for microbiology was obtained when clinically suggested (unexplained fever and/or signs of sepsis). Criteria for the diagnosis of device-related bacteraemia were defined as: (a) greater than a 10-fold increase in colony-forming units (CFU) of bacteria per ml of blood obtained through the device in comparison to peripheral blood cultures; (b) greater than 1000 CFUs of bacteria obtained through the device, in the absence of peripheral blood cultures; or (c) positive catheter tip culture upon removal in the appropriate clinical setting. Device-related bacteraemia or fungaemia was considered cured when culture results were negative at the termination of antibiotic therapy and no evidence of clinical infection occurred 2 weeks later.

Port pocket infection was defined as induration, erythema and tenderness around the port with culture-positive material aspirated from the port pocket. Cutaneous site infection was defined as induration, erythema or tenderness and exudate at the port surface needle access site. Thrombosis was identified with ultrasound and/or venography when clinically suggested by progressive arm or facial swelling.

RESULTS

One hundred and seventy-eight devices, comprising a total of 32 089 days *in situ*, were fitted in 175 patients (3 patients underwent a second port insertion after removal of the first device). All patients received at least 1 cycle of chemotherapy through the TIAP. Adequate follow-up was obtained in all the cases (median 180 days, range 4–559).

Table 1 summarises pertinent patient data and route for central venous access. Early complications of the procedure are listed in Table 2. In 6 patients, a pneumothorax was seen as a complication of the TIAP insertion, and 5 underwent a tube-thoracostomy, with no additional morbidity. Even when significant pneumothoraxes are present, patients

Table 1. Patients' characteristics

No. of ports	178
No. of patients	175
Age (years) median	50
range	15–82
Male : female ratio	70 : 105
Days *in situ* (mean)	180
Total days *in situ* (overall)	32 089
Percutaneous catheterisation*	159
Surgical venous cut-down (cephalic vein)	19

*Percutaneous subclavian vein catheterisation first described by Aubaniac [7].

Table 2. Early complications related to port insertion observed in this series

	No. of patients	% of devices
Pneumothorax	6	3.37
chest-tubes	5	
Haemothorax	0	
Arterial puncture	3	1.68
Clinically relevant haemorrhage	0	
Early revision for TIAP malfunction	2	1.12
Total	8	4.49

may have no relevant symptoms but more often have deep chest pain, dyspnoea and coughing. Our policy was to insert a chest tube when the pneumothorax was large (more than 30%) and/or symptoms were relevant. 3 patients of this series had an accidental arterial puncture during the implant procedure, which did not cause any significant complication. Arterial puncture is usually indicated by a pulsating back-bleeding from the needle; arterial entry should also be identifiable under fluoroscopy, because a wire in the thoracic arterial system will usually enter the aortic arch and pass below the diaphragm on the left side of the chest. If any doubt existed about arterial versus venous cannulation, our policy was to withdraw the wire and needle rather than risk the creation of a large hole in the artery with a dilator.

In only two cases was the implant altered, without removal, for malfunction of the catheter due to a narrowing of the lumen (one case) or dislocation into the controlateral brachio-cephalic vein (second case).

Table 3 shows the late complications. Catheter rupture and embolisation took place in 3 cases (1.68%, 0.093/1000 days of port use); 2 patients had palpitations and chest discomfort 66 ± 18 days (mean $\pm$ S.D.) after implant, during a pause between subsequent chemotherapy cycles, leading to chest X-ray and diagnosis. One patient was completely asymptomatic and incidental chest radiographic examination performed for restaging 10 months after implantation discovered the catheter embolisation. Interventional radiology techniques were very useful and more cost-effective than the operating room for retrieval of embolising catheters; it was obtained, without additional morbidity, by venous transfemoral approach using a modified Dormia device, grabbing the catheter piece and dragging it out. One patient exhibited the 'pinch-off sign' (e.g. the radiological finding of acute compression of the catheter, after subclavian placement, as it courses between the medial portion of the clavicle and the anterior extent of the first rib).

The incidence of catheter-associated venous thrombosis was 1.12% in this series (2 patients; 0.062/1000 days of port use); both patients exhibited ipsilateral arm swelling, without neurological difficulties in that extremity. The interval between implantation and the onset of clinically evident venous thrombosis was less than 30 days in both patients. Duplex ultrasonography gave a positive result, confirmed by a standard contrast venogram of the ipsilateral extremity. As the catheters were still needed, patients were treated with intravenous continuous infusion of heparin for 3 days, then oral anticoagulation and full anticoagulation was continued for 3 months. The first patient died 11 months after port insertion due to progression of her neoplastic disease, whereas the second is still alive with a stable disease 9 months after implant.

Port pocket infection, usually caused by Gram-positive cocci, suggest direct inoculation or migration of organisms along the accessing needle as the primary mechanism; it occurred in 1 case (0.56%; 0.031/1000 days of port use) and was successfully treated with the administration of appropriate intravenous antibiotics, first with empiric coverage and then targeted for the cultured organism (coagulase-negative *Staphylococcus aureus*).

Four patients suffered from port-related bacteraemia (2.24%; 0.124/1000 days of port use), leading to port removal in 3 cases (1.68%); causative agents were *Bacillus subtilis* (1 case, port removed) and coagulase-negative *Staphylococcus aureus* (3 cases, two ports removed, one retained after elimination of the clinical sepsis syndrome by antibiotic therapy). The median days ($\pm$S.D.) before infection arising were 170 ± 20. There were no TIAP-related deaths.

DISCUSSION

The first peer-reviewed article using the Groshong catheter as long-term central venous access was published in 1989, and the combined number of patients using Groshong catheters from seven series prior to our report is 426 (Table 4). Previous authors have reported insertion of the catheter alone either at the bedside or in the operating room, under fluoroscopic or ultrasound guidance. Our study represents the largest single series of patients with

Table 3. Late complications observed in this series

	No. of patients	% of devices	Per 1000 days of port use	Actions taken
Catheter rupture and embolisation	3	1.68	0.093	interventional radiology
Venous thrombosis	2	1.12	0.062	anticoagulants
Pocket infection*	1	0.56	0.031	antibiotics
Skin erosion without infection	1	0.56	0.031	replacement without removal
Port-related bacteraemia†	4	2.24	0.124	three ports removed
Total	11	6.17	0.34	
Devices still *in situ* (30 June 1996)	138	77.5		

*Infection was caused by coagulase-negative *Staphylococcus aureus*; †one infection was caused by *Bacillus subtilis* (port removed) and three infections by coagulase-negative *Staphylococcus aureus* (two ports removed).

Table 4. Groshong catheter publications

First author	Year	Number of patients	Related infections (%)	Removal for infection (%)	Mean duration of use (days)
Malviya [8]	1989	41	7.3	4.9	93
Delmore [9]	1989	72	8.3	8.3	191
Pasquale [10]	1992	55	Non-available	12.7	Non-available
Hull [11]	1992	50	6.0	2.0	30-day follow-up
Gleeson [12]	1993	67	32	11.9	68.5
Burnett [13]	1994	30	Non-available	6.7	112
Holloway [14]	1995	111	11.7	9.0	239
Present series*	1996	178	2.8	1.6	180

*Groshong catheter connected to a totally implantable access port (TIAP).

TIAP connected to Groshong catheters, all of whom underwent operating room procedure with fluoroscopy.

Early complications of subclavian venipuncture include pneumothorax, haemothorax, air embolism and arterial perforation. Pneumothorax occurs in 1–4% of subclavian line insertions [15]. Careful attention to anatomical landmarks and operator experience with the insertion of central venous catheters are most important for avoidance of this complication during subclavian vein catheterisation. Many pneumothoraxes will not become apparent in the immediate postoperative period, particularly when a small pneumothorax (<30%) has been produced; from published reports and in our experience, as many as 50% of these small pneumothoraxes can be treated conservatively, without tube thoracostomy. We did not observe a tension pneumothorax, a life-threatening situation caused by progressive accumulation of air within an emithorax, eventually compressing the vena cava and shifting the mediastinum, due to a parenchymal tear forming a one-way valve. Patients usually have hypotension, jugular venous distension and extreme anxiety; an immediate decompression of the affected side is necessary, using a large-bore catheter inserted percutaneously into the second interspace in the mid-clavicular line.

Surgical cutdown of the cephalic vein in the deltoid-pectoralis space is an effective alternative option to the percutaneous approach using the subclavian vein in patients with difficult anatomical landmarks (for example, obesity, previous surgery or irradiation in the infraclavicular region, etc.). It was adopted in 10.6% of our cases, after uneventful attempts at percutaneous incannulation. Although the success rate of 'blind' insertion of the catheter may be quite high and this approach could avoid the additional cost of ultrasound or fluoroscopy, the routine use of fluoroscopy in this series allowed us to avoid (except one case) time-consuming, patient-stressing and very expensive replacements after implant, due to an incorrect position of the catheter (most often ipsilateral internal jugular or contralateral brachiocephalic vein).

There was no significant haemorrhage related to TIAP placement in our series. Haemorrhage into the thoracic space can occur at the time of insertion from operative trauma, or after the catheter has been in place from erosion to the vein wall. The biomaterial of the catheter influences the risk of venous or cardiac perforation. Most of the reports in the literature describing these complications from catheters are more than 10 years old and reflect the use of polyethylene and other rigid polymers most frequently used in that time period. The softer silastic and polyurethane catheters now used may have a lower risk of causing these complications. Moreover, the route of insertion may be critical; unlike the subclavian vein, the left-sided internal jugular vein percutaneous approach might be dangerous, given the abrupt turn that vessel sometimes takes into the brachiocephalic vein.

Catheter-related infections have been reported in 11–45% of patients with Hickman catheters [3, 4, 10, 16, 17], 0–22% of patients with TIAP [4, 12, 16–18] and 7–32% of patients with Groshong catheters [8–12]. Device-related morbidity from the literature is difficult to compare because of varying definitions and dissimilar patient population. While several retrospective studies have noted higher infection rates for external devices compared to TIAP in select patient populations [4, 19], a prospective randomised study was unable to demonstrate a statistically significant difference in infections [16]. They appeared much higher for both Hickman catheters and ports than many other reports, probably due in part to a study population that included many patients with haematological malignancies. In a randomised study of infectious morbidity in patients with solid tumours, TIAP have been shown to be associated with fewer infections than were catheters [20]. Most often, these septic events are due to bacteraemias that develop from sites of microbial invasion remote from the catheter itself and usually respond to appropriate antibiotics without the need for catheter withdrawal [21, 22]; removal may be necessary for persistent or recurrent bacteraemia or for fungal infections.

Data from this study, derived from a prospective, but not randomised study, support the conclusions of most retrospective papers: the infectious morbidity related to TIAP is very low, even in patients undergoing cytostatic treatments for solid tumours. The mechanisms of device-related infection may explain why TIAP are less likely to be associated with infection than tunnelled catheters. Migration of skin flora through the cutaneous insertion site with catheter colonisation is supported by the finding that Gram-positive organisms, especially coagulase-negative staphylococci, are responsible for a significant percentage of the cases of device-related bacteraemia in patients with catheters. Compared with catheters, TIAP are irrigated less frequently, require no home care, and are less prone to environmental or cutaneous contamination when not accessed. All these factors may contribute to the reduced incidence of infections associated with TIAP.

In conclusion, we have demonstrated that Groshong catheters connected to totally implantable access ports are a good option for long-term access to central veins and deliv-

ery of chemotherapeutic regimens, including continuous i.v. infusions. The low incidence of major complications related to implantation and management of these devices support their increased use in oncology patients.

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