

# Low complication rates in the use of port-a-caths in oncology patients

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## ABSTRACT

**Background:** Port-a-caths (PACs) represent an important component of the care of cancer patients, in particular for administration of chemotherapy. We sought to analyse the longevity and complications of PACs in cancer patients in a large community hospital.

**Methods:** We retrospectively analysed the indications, duration of use, complications and reasons for removal of PACs in cancer patients treated in our centre from January 2005 to December 2010, and compared these with findings in patients who received a PAC in the same period for reasons not related to cancer.

**Results:** During the study period 152 cancer patients received a total of 170 PACs; in the same period, 21 patients received a total of 35 PACs for reasons unrelated to cancer. The total analysis comprised 70,919 days of PAC use. Most cancer patients had a solid tumour (97%). PACs were removed because of a complication in 25 cases in cancer patients (14.7%) vs 15 cases in non-cancer patients (42.9%,  $p < 0.01$ ). Culture-proven infection was the reason for PAC removal in 16 cases in cancer patients (23.5%) vs eight cases in non-cancer patients (42.1%;  $p = \text{NS}$ ). The total number of PAC-associated infections was 20 in cancer patients (0.35 infections per 1000 PAC days) vs 19 in non-cancer patients (1.43 infections per 1000 PAC days;  $p < 0.01$ ). No PAC-associated thrombosis was found.

**Conclusion:** In clinical practice the use of PACs in cancer patients is safe with lower complication rates when compared with PAC use in patients without malignancy.

## KEYWORDS

Cancer, chemotherapy, infection, oncology, Port-A-Cath

## INTRODUCTION

Venous access is problematic for oncology patients receiving repeated courses of cytotoxic therapy. Totally implantable ports connected to a central venous catheter were first introduced in 1982 and soon replaced subcutaneously tunnelled catheters such as Hickman, Groshong and Broviac lines.<sup>1,2</sup> These totally implantable venous access ports (TIVAPs), among which port-a-caths (PACs), now represent an important component of the regular care of cancer patients by providing a simple way of accessing the venous system for administration of chemotherapy, antibiotics, analgesics, blood products and fluids, and for the collection of blood. Although in general these devices are safe, their use can be associated with significant complications, most notably infection and thrombosis.

Previous studies have examined complication rates of PAC use in cancer patients.<sup>3-11</sup> Such knowledge is significant considering the importance of PACs for the clinical care of cancer patients and for guiding preventive measures. This in particular holds true for the main complications described in the literature: infection and thrombosis. In the current study we retrospectively analysed the indications, duration of use, complications and reasons for removal of PACs in patients with malignancies treated in our centre (a large community hospital in the Netherlands) from January 2005 to December 2010. In addition, we analysed the microbial causes of PAC-associated infections in these patients and their impact on PAC use and removal. In order to obtain insight into complications that may relate to cancer specifically, we compared findings in cancer patients with those in patients who received a PAC in the same period for reasons not related to cancer.

## MATERIALS AND METHODS

### Patients

We performed a retrospective analysis of 173 adult patients (>18 years of age) who received a total of 205 PACs in the Reinier de Graaf Hospital in Delft, the Netherlands between January 2005 and December 2010. The analysis was approved by the institutional medical ethics committee.

### Study design

PAC removals within two days after implantation were excluded since these were considered to be related to the surgical procedure. A single type of PAC was used (Deltec™, Smiths Medical). The PACs were inserted by surgeons from the Department of Vascular Surgery in the operation room under general or local anaesthesia using a standardised surgical technique. The access route was chosen according to the patient's anatomy, preferably the right subclavian or external jugular vein. Prophylactic antibiotics were not routinely administered. The PACs were accessed and cared for by trained nursing staff. Lock with heparin solution was done after every PAC access and every four weeks if the PAC was not in use. Patients did not receive routine anticoagulant therapy. PAC-associated infection was defined as 1) a positive culture of blood obtained from either a peripheral vein or from the port and 2) clinical suspicion of PAC infection as reflected by local symptoms or absence of another infectious source.<sup>12</sup> For the analysis of PAC-associated infections, multiple positive blood cultures with a single pathogen in one

clinical episode were counted as one PAC-associated infection with this pathogen.<sup>12</sup> The occurrence of a PAC-associated infection was defined as a complication; other non-infection-related complications were analysed by studying reasons for PAC removal making use of patient hospital records. Diagnostic procedures were done as ordered by the physician; systematic venographies were not performed. Minor complications such as local pain, skin irritation and/or transient inability to draw blood from the PAC were not analysed.

### Statistical analysis

Data are expressed as means, medians, interquartile range and ranges as indicated. Differences between cancer patients and non-cancer patients were analysed by the Mann-Whitney U test, Chi square test and log-rank test. A p value below 0.05 was considered to be statistically significant.

## RESULTS

### Patients

From January 2005 to December 2010, 152 patients with a malignancy received a total of 170 PACs; in the same period, 21 patients received a total of 35 PACs for reasons unrelated to cancer (*table 1*). In both groups, more women than men received a PAC (73.7% amongst cancer patients and 61.9% amongst non-cancer patients). The vast majority of patients with a malignancy suffered from a solid tumour, with breast and colorectal cancer as the

**Table 1.** Patient characteristics and indications for port-a-cath placement

	Total	Cancer patients	Non-cancer patients
Number of PACs (%)	205	170 (82.9%)	35 (17.1%)
Number of patients (%)	173	152 (87.9%)	21 (12.1%)
Female (%)	125 (72.3%)	112 (73.7%)	13 (61.9%)
Male (%)	48 (27.7%)	40 (26.3%)	8 (38.1%)
Mean age (range) at time of PAC placement	51.8 (18-80)	51.7 (26-77)	53.5 (18-80)
Diagnosis (%)		Breast cancer 72 (47.4%) Colorectal cancer 50 (32.9%) Upper GI cancer 9 (5.9%) Ovarian cancer 11 (7.3%) Lymphoma 4 (2.6%) Other 6 (3.9%)	Neuromuscular disease <sup>1</sup> 12 (57.1%) Congestive heart failure 8 (38.1%) CIVD <sup>2</sup> 1 (4.8%)
Indication			
• Chemotherapy		152 (100%)	-
• Immunotherapy <sup>3</sup>		14 (9.2%)	10 (47.6%)
• Analgesics		-	2 (9.5%)
• Dopamine		-	8 (38.1%)
• Bisphosphonate (APD)		-	1 (4.8%)
Mean (range) number of days in situ			
• Total	70.919	57.642	13.277
• Per PAC	346 (9-2064)	339 (9-2064)	379 (13-1839)

<sup>1</sup>Dystrophia (n=4), chronic inflammatory demyelinating polyneuropathy (n=6) and multiple sclerosis (n=2); <sup>2</sup>Common variable immunodeficiency; <sup>3</sup>Refers to monoclonal antibodies: in cancer patients trastuzumab (Herceptin®, antibody directed against epidermal growth factor receptor-2) or bevacizumab (Avastin®, antibody binding to the vascular endothelial growth factor preventing binding to the receptor), in non-cancer patients gammaglobulin (Gammagard®).

predominant diagnoses (47.4% and 32.9%, respectively). In non-cancer patients neuromuscular disease was the most frequent diagnosis (57.1%). The total analysis comprised 70,919 days of PAC use, of which 57,642 days in cancer patients and 13,277 days in non-cancer patients. In cancer patients all PACs were used for administration of chemotherapy. In 14 cases (9.2%) it was also used for immunotherapy. In non-cancer patients ten PACs (47.6%) were inserted for immunotherapy and eight PACs (38.1%) for chronic treatment with dopamine for heart failure (table 1).

### Longevity of PACs

Table 2 shows the longevity and reasons for removal of the inserted PACs. In cancer patients, 20% of PACs were in use at the end of follow-up, compared with 31.4% in non-cancer patients (p=NS). Figure 1 is a Kaplan-Meier plot showing that the average survival of the PACs was similar in cancer and non-cancer patients (mean time to removal 927 days vs 899 days, p=0.9 by log-rank test). The percentage of PACs removed during the follow-up period was 40% in cancer patients and 51.5% in non-cancer patients (p=NS). The mean number of days a PAC was *in situ* at the time of removal was 309 days and 500 days in cancer and non-cancer patients respectively, p=NS). In

**Table 2. Numbers and reasons for port-a-cath removal**

PACs	Total (n=205)	In cancer patients (n=170)	In non-cancer patients (n=35)
Number of PACs in situ at closure of data collection (%)	45 (22.0)	34 (20.0)	11 (31.4)
Number of PACs removed (%)	86 (41.9)	68 (40.0)	18 (51.5)
Number of days in situ <sup>1</sup>			
• Mean	353	312	500
• Median	224	215	247
• Range	6-2064	6-2064	24-1809
Number of patients with PAC removed	77	64	13
• Female	60	51	9
• Male	17	13	4
Reason for removal (% of total removed)			
• Treatment completed	46 (53.5)	43 (63.2)	3 (15.8)
• PAC infection <sup>2</sup>	24 (27.9)	16 (23.5)	8 (42.1)
• Occlusion <sup>3</sup>	4 (4.7)	2 (3.0)	2 (10.5)
• Malfunction <sup>4</sup>	9 (10.5)	4 (5.9)	5 (26.3)
• Other <sup>5</sup>	3 (3.5)	3 (4.5)	0

<sup>1</sup>p=NS for difference between patients with cancer and non-cancer patients; <sup>2</sup>PAC infection is defined as positive culture from blood obtained from the port or a peripheral vein and clinical suspicion of PAC as defined by symptoms or ruling out other foci; <sup>3</sup>Defined as inability to infuse fluids into the PAC system, confirmed by administration of radiological contrast fluid into the port; <sup>4</sup>For example nicking of the line, port moved away into deeper (breast) tissue, port turned away; <sup>5</sup>Due to progressive disease in the chest wall covering the port, necessity to insert a Levine shunt, fat necrosis around the PAC.

cancer patients, most PACs were removed because therapy was completed (63.2 vs 15.8% in non-cancer patients, p<0.01). Twenty-five (14.7%) and 15 (42.9%) of PACs were removed for complications (infectious or non-infectious) in cancer and non-cancer patients respectively (p<0.01).

### PAC-associated infections

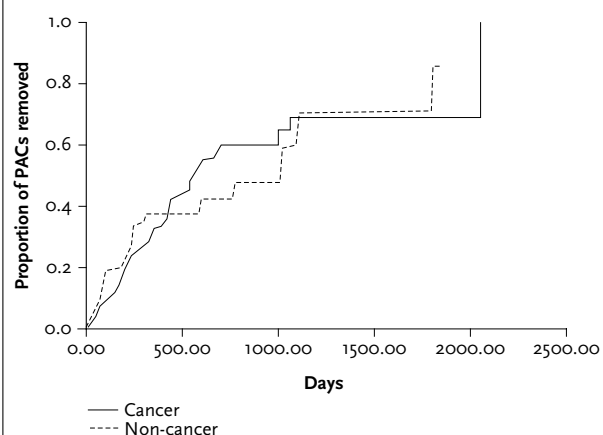
PAC-associated bloodstream infection occurred in 25 of 173 patients (14.4%) (table 3). Amongst cancer patients, 18 (11.8%) were diagnosed with PAC-associated infection during the study period, vs seven (33.3%) non-cancer patients (p=0.02). The total number of PAC-associated

**Table 3. Port-a-caths in patients with blood stream infections (BSI) and causative organisms**

	All PACs	Cancer	Non-cancer	P-value
Number of PACs inserted	205	170	35	
Number of patients with PAC and BSI	25 (14.4%)	18 (11.8%)	7 (33.3%)	0.02
Number PACs with BSI (% of total)	30 (14.6)	18 (10.6)	12 (34.3)	<0.01
Number of episodes of positive blood cultures <sup>1</sup>	39	21	18	<0.01
Number of different organism in these cultures	43	21	22	
Number of days PAC in situ prior to positive blood culture				0.01
Median	167	100	414	
IQR	55-553	36-234	125-902	
<b>Causative organisms</b>				
Gram-positive	29	14	15	NS
• <i>Staphylococcus aureus</i>	10	5	5	
• Coagulase negative staphylococci	16	7	9	
• <i>Enterococcus</i>	1	-	1	
• <i>Streptococcus pneumoniae</i>	1	1	-	
• Other streptococci	1	1	-	
Gram-negative	13	6	7	NS
• <i>Escherichia coli</i>	2	1	1	
• <i>Pseudomonas aeruginosa</i>	2	-	2	
• <i>Klebsiella oxytoca</i>	1	-	1	
• <i>Klebsiella pneumoniae</i>	1	1	-	
• <i>Serratia marcescens</i>	1	1	-	
• <i>Rhizobacteria</i>	1	-	1	
• <i>Stenotrophomonas maltophilia</i>	1	-	1	
• <i>Enterobacter</i>	2	1	1	
• <i>Acinetobacter</i>	1	1	-	
• <i>Aeromonas hydrophilia</i>	1	1	-	
Yeasts	1	1	-	-
• <i>Candida glabratum</i>	1	1	-	

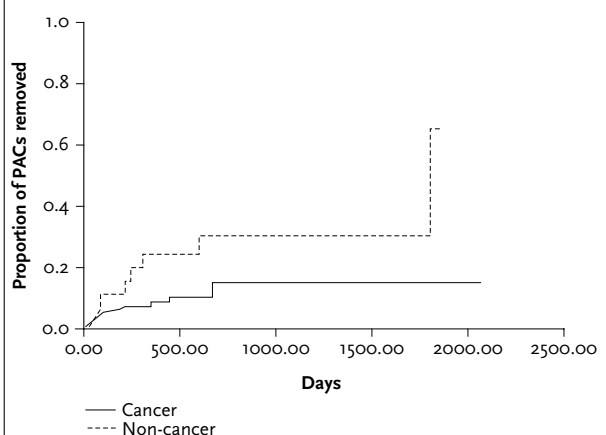
<sup>1</sup>One blood culture per episode (i.e. if four blood cultures were positive for a particular pathogen during the same infection, only one culture was counted).

**Figure 1.** Cumulative proportion of port-a-caths (PACs) removed for any reason



Cases were censored at death or end of follow-up. P=NS by log rank test for difference between PACs in patients with cancer and PACs in other patients

**Figure 2.** Proportion of port-a-caths (PACs) removed for infectious complications



P=0.03 by log-rank test for difference between PACs in patients with cancer and PACs in other patients

infections was 21 in cancer patients (0.36 infections per 1000 PAC days) vs 18 in non-cancer patients (1.4 infections per 1000 PAC days;  $p < 0.01$  vs cancer patients); Of interest, the median time that a PAC was *in situ* before a bloodstream infection occurred was shorter in cancer patients than in non-cancer patients (100 vs 414 days respectively,  $p = 0.01$ ). The cumulative proportion of PACs removed for an infectious complication is shown in figure 2. Causative organisms did not differ between cancer and non-cancer patients (table 3). In both groups, gram-positive pathogens, in particular *Staphylococcus aureus* and coagulase-negative staphylococci, were most prevalent (more than two-thirds of all bloodstream infections).

## DISCUSSION

In the last decades, much attention has been given to the achievement of an adequate means of venous access in cancer patients that is suitable for long-term use, in particular for repeated administration of chemotherapy and blood drawing for testing. Totally implantable venous access ports, such as PACs, are preferred to other approaches for many different reasons, including a reduced risk for infection and thrombosis, less visibility and fewer restrictions on daily activity.<sup>13</sup> We here report on our experience with PACs in a large community hospital in the Netherlands during a six-year period (January 2005 to December 2010), comparing indications, duration of use, complications and reasons for removal in 170 cancer patients and 35 patients without malignancy, comprising more than 70,000 days (which is almost 200 patient-years) of PAC use.

The complication rate of PACs in cancer patients in part depends on the type of malignant disease (solid tumour or haematological malignancy) and neutrophil counts in peripheral blood.<sup>13</sup> In the current analysis the vast majority of oncology patients had solid tumours, in particular breast and colorectal cancer (table 1), and only three patients had leucocytopenia at the time of PAC-associated infection (data not shown). Hence, our results predominantly apply to patients with solid tumours and normal leucocyte counts. The current study excluded early complications of PAC placements, such as pneumothorax, primary malposition and arterial perforation, since these are related to the surgical procedure. The overall rate of removal of PACs for infectious or non-infectious complications was lower in cancer patients compared with non-cancer patients. Furthermore, the risk that a PAC will be removed for infectious reasons is lower in cancer patients than in non-cancer patients. Although a definitive explanation for this difference is lacking, it may be related to a higher experience amongst oncology nurses in the management of PACs and/or differences in underlying diseases. For example, insufficient hygienic precautions, inadequate flushing of the system after the introduction of fluids or too long an interval between use of the port make the system at risk for irreversible complications. Insufficient dosing of positive pressure leading to narrowing of the lumen of the catheter due to deposits of fibrin or other substances will eventually obstruct the PAC.<sup>6</sup> Different infection rates in cancer and non-cancer patients could have been caused by differences in susceptibility for infection due to the underlying disease. However, although the most important indication for PAC use in non-cancer patients was immunotherapy in the form of infusion of gammaglobulin, this therapy was provided for neuromuscular disease in all

but one patient (who had a common variable immunodeficiency). As such, infection rates in non-cancer patients are not biased due to a large number of patients with primary immunodeficiency.

Although PACs are associated with much fewer infectious complications than other approaches to obtain prolonged access to the venous circulation, infection remains an issue of concern.<sup>7,13</sup> In clinical practice, the diagnosis of PAC-associated infection can be made with or without bacteriological confirmation.<sup>14,15</sup> In the present analysis we only included culture-proven infection: PAC-associated infection was defined as a positive culture of blood obtained from either a peripheral vein or the port and clinical suspicion of PAC infection as reflected by local symptoms or absence of another infectious source.<sup>12</sup> The incidence of PAC-associated infection amongst cancer patients found here (11.8%) is within the same range as that reported in previous studies: positive blood cultures associated with PACs have been reported to occur in 2.4 to 16.0% of patients,<sup>3,4,11</sup> representing a major cause of hospital-acquired bacteraemia and the most frequent reason for catheter removal.<sup>4,16</sup> The vast majority of PAC-associated infections were caused by coagulase-negative staphylococci and *Staphylococcus aureus*, which is in accordance with earlier investigations.<sup>11,13</sup>

There are no standard criteria for catheter removal in PACs.<sup>12,13</sup> In the presence of uncomplicated infection due to coagulase-negative staphylococci, the PAC may be retained if there is no evidence of persisting or relapsing bacteraemia. For PAC-associated infection caused by pathogens other than coagulase-negative staphylococci, some physicians would retain the port, partially depending on the patient's clinical status. In our analysis, most PAC-associated infections resulted in PAC removal in cancer patients (80% of cases), but not in patients without cancer (42%). This difference was not related to a clear difference in causative pathogens. It is conceivable that medical oncologists are reluctant to continue chemotherapy through a PAC that has been infected and that as a consequence PAC-associated infection more often leads to PAC removal in cancer patients.

The reported incidence of venous thrombosis as a PAC-associated complication varies between zero and 10%.<sup>13</sup> In our centre, thrombosis was never the cause of PAC removal during the six-year study period. Notably, since most cases of catheter-related thrombosis are asymptomatic,<sup>13</sup> this does not exclude that thrombosis did occur in our population. Data on prophylactic anticoagulant therapy are not available for the studied population, but this is not a routine policy in our hospital.

Several earlier investigations have examined the complication rate of PACs in a single-centre setting. No device-related deaths were observed and complications

as infection and thrombosis were rare for all types of patients.<sup>5,9,11</sup> In a Dutch retrospective analysis encompassing a period of 7.5 years (1992 to 1999) involving 38 PACs, the most prevalent complications were infection (two cases or 5.3%) and thrombosis (three cases or 7.9%).<sup>5</sup> Although the number of PACs studied was relatively low, these data suggest that the incidence of PAC-associated thrombosis may have decreased in more recent years, probably at least in part as a result of better preventive care by the nursing staff.

Our study has several limitations. Firstly, the study has a low sample size relative to the low incidence of PAC-related problems, which in particular is true for thrombosis. Secondly, the study groups were not comparable with respect to baseline and prognostic variables, which may hamper appropriate comparisons.

The use of PACs is widely implemented in the clinical care of patients with cancer. These devices have a high acceptance among patients, nurses and doctors. The current analysis illustrates the low rate of complications associated with the use of PACs in the setting of a large community hospital in the Netherlands.

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