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Eight-week interval in flushing and locking port-a-cath in cancer patients: A single-institution experience and systematic review

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Abstract

Port-a-cath (PAC) system is one of the most frequently employed venous accesses for administration of chemotherapy and supportive care. To prevent late complications, the latest guidelines recommend flushing/locking procedures every four weeks. In this retrospective study, we evaluate the frequencies of late complications with a eight-week flushing/locking procedure compared to the standard one. This study retrospectively compares the frequency of complications occurred using standard versus delayed flushing schedules. We performed a systematic review of the published studies about PAC complications associated with longer flushing intervals. Three hundred and ninety fully available patients were enrolled. One hundred and six patients had their PAC flushed/locked every month, 347 patients performed the flushing/locking procedures every eight weeks, 63 patients switched from the four to the eight-week schedule. No difference was seen in the number of occlusions, infections and mechanical dysfunctions between the two patient groups. The systematic literature review confirmed, in a total of 1,347 patients, the absence of an increased proportion of complications with delayed schedules. PAC flushing and locking every eight weeks are feasible and safe. This delayed schedule may improve patients' quality of life and decrease both nursing workload and costs for the national health system.

KEYWORDS

cancer patients, complications, flushing, PAC, timing, venous access

1 | INTRODUCTION

Central venous catheters play an important role in the management of cancer patients. Their introduction in the routine clinical practice has facilitated the vascular access, and their use is not limited to the safe administration of chemotherapeutic drugs, but also for prolonged endovascular administration of supportive care (D'Souza, 2014; Vescia et al., 2008; Zohu et al., 2014).

The port-a-cath (PAC) system is one of the most frequently employed venous access types. It is a totally implantable venous access device in which a conventional central venous catheter is connected to a reservoir that is implanted into a surgically created pocket on the

chest wall or upper arm (Lambert, Chadwick, McMahon, & Scarife, 1988). A non-coring (Huber) needle should be used to access PACs (Kelley, 2008). It is inserted through the skin to the septum of the port to access the reservoir. The advantages of this type of catheter are as follows: reduced risk of infection, less frequent flushing and less interference with daily activities.

Although the PAC implantation is a simple surgical operation, it can be associated with early and late complications. The early complications, such as pneumothorax, haemothorax, injury of large blood vessels, cardiac arrhythmia, air emboli and malposition of the catheter, are related to the surgery procedure. The late complications are due to the presence of a foreign catheter in the body. The most frequently reported late events are occlusions (thrombosis), infections and mechanical dysfunctions with a prevalence of about 6%–7%, 8%–9% and 3%–7% respectively (Bassi, Giri, Pattanayak, Abraham, & Pandey, 2012; Kefeli et al., 2009). Flushing and locking of PACs are essential in the prevention of these complications.

The aim of the flushing is to clean the catheter, and the procedure consists of a manual injection of 0.9% sodium chloride. The catheter is immediately locked after flushing in order to prevent intraluminal occlusions and/or catheter colonisation. Traditionally, an anticoagulant, such as diluted heparin, is added to a limited volume of a liquid (Goossens, 2015; Schiffer et al., 2013).

According to the latest guidelines, PACs not being accessed should be flushed and locked every 4 weeks (Guideline for Totally Implantable Central Venous Access Port, 2013). However, this frequent timing is not very well accepted neither by the patients nor by the nursing staff. This is the reason why literature reports several attempts to delay the flushing and locking processes (Diaz et al., 2017; Solinas et al., 2017).

Since 2009, a 8-week flushing and locking schedule was adopted at the Medical Oncology Unit of ASST Spedali Civili in Brescia. The aim of this study was to retrospectively evaluate the frequencies of the most common complications (infective, obstructive and mechanical) of PACs with this delayed schedule and compare them to the standard flushing schedule (4 weeks), initially used. To reinforce the final results, we also performed a systematic review of the literature of papers employing a delayed schedule than 4 weeks.

2 | METHODS

PAC system was adopted from 2005 onwards at the Medical Oncology Unit of Spedali Civili of Brescia. From 2005 to October 2009, the standard procedure of PAC flushing and locking every 4 weeks was employed, while from November 2009 to January 2014,

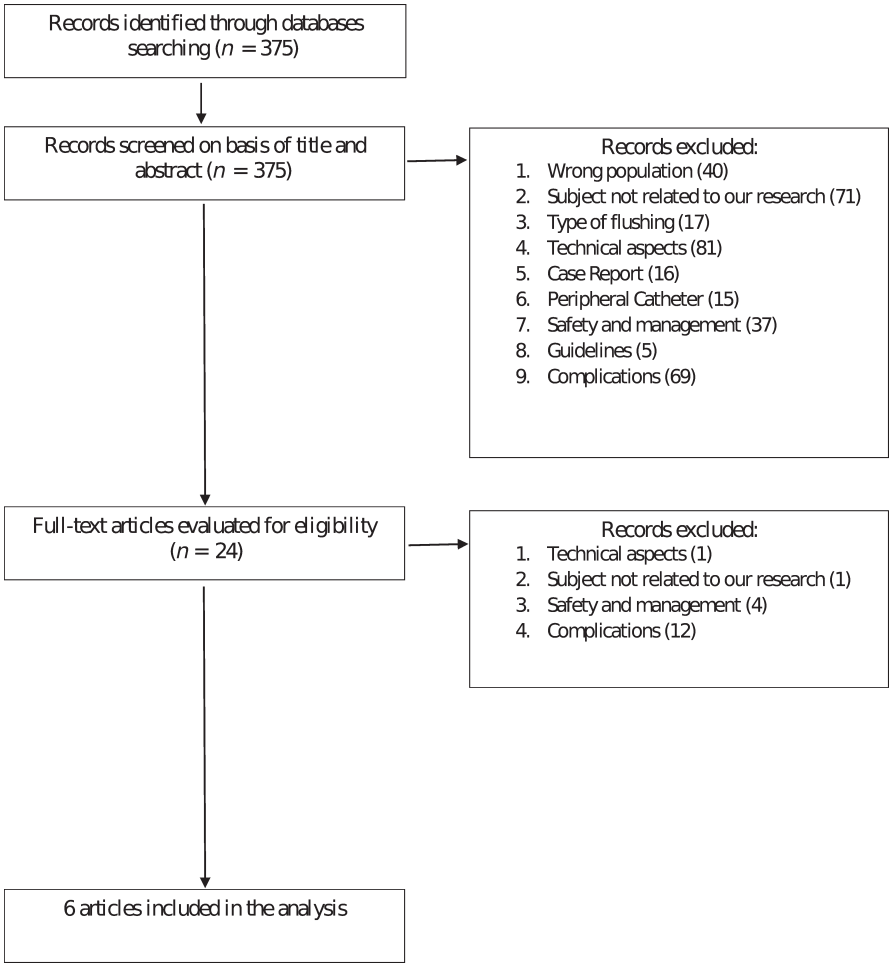

FIGURE 1 Flow-chart summarizing the strategy used to identify eligible studies (PRISMA)

the periodic flushing was performed every 8 weeks. Flushing and locking were performed using 10 cc of normal saline solution followed by 5 cc of heparin solution (4 ml heparin/100 ml of normal saline solution). Patients enrolled were followed up to December 2017.

In this study, we retrospectively compared the frequency of complications occurred using the standard timing (every 4 weeks) versus the delayed schedule (every 8 weeks). In particular, the number of infections, obstructions and mechanical complications were recorded and compared. Only patients with a cancer diagnosis who underwent at least two consecutive flushing/locking procedures were considered.

Descriptive statistics were used to summarise patients' characteristics. Differences between categorical variables were assessed by a chi-square. Statistical significance was set up at $p < 0.05$. Epi Info software was used for statistical analyses.

The retrospective collection and analyses of data were submitted to the Ethical Review Board of the Spedali Civili Hospital, Brescia, Italy.

We also performed a systematic review of published studies reporting the frequencies of PAC complications adopting a longer flushing interval than the standard 4 weeks. PubMed was used to conduct the article search. The following keywords were introduced as follows: ([(port a cath AND flushing)] OR (port[Title/Abstract] AND flushing[Title/Abstract] AND interval[Title/Abstract])) OR (port[Title/Abstract] AND implantable[Title/Abstract] AND venous access[Title/Abstract]). PRISMA flow diagram was made to summarise the findings (Figure 1). Three hundred and seventy-five articles were screened in this research. Six studies adopting more than 4-week flushing intervals and reporting relative complications were found.

3 | RESULTS

3.1 | Patients

Four hundred and twelve consecutive patients meeting the inclusion criteria had a PAC positioned at our Institution from 2009 to 2014. Complete data were available for 390 patients (Figure 2). Patients' characteristics are reported in Table 1.

3.2 | Frequency of catheter complications

One hundred and six consecutive patients observed between 2005 and 2009 had their PAC flushed and/or locked every 4 weeks, the subsequent 347 patients observed from 2009 to January 2014 performed the flushing/locking procedures every 8 weeks. In addition, 63 patients initially observed between 2005 and 2009 switched from one schedule to the other one in 2009 and they were therefore considered twice. A total of 5,194 catheter flushings were performed as follows: 2,286 between 2005 and 2009 and 2,908 from 2009 to the last follow-up visit, death or port removal. The median follow-up was 30 months (range 1–131). Each patient was followed for at least 24 months.

A total of 12 patients (11%) and 31 patients (8.9%) had complications in 4- and 8-week flushing group respectively ($p = 0.54$). Results are summarised in Figure 3.

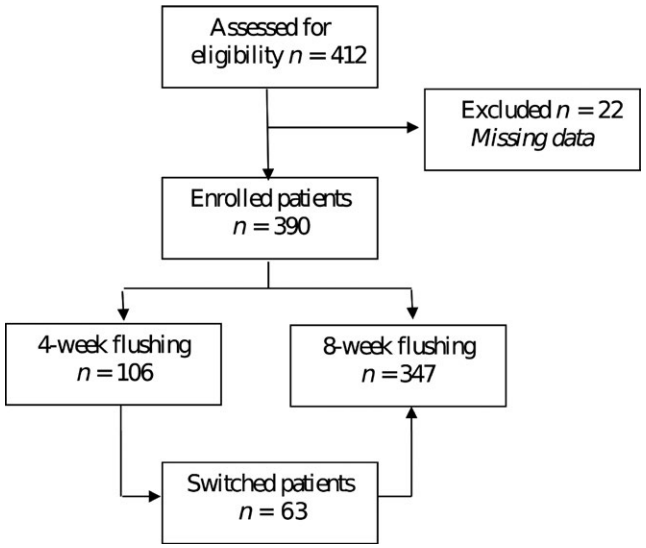

FIGURE 2 Study design

TABLE 1 Patients' characteristics

Patients' characteristics		
N		390
Median age (range)		56 (18–80)
Sex	Male	168 (43%)
	Female	222 (57%)
Primary histology	Colorectal carcinoma	211 (54%)
	Breast cancer	72 (18%)
	Gastric cancer	59 (15%)
	Sarcoma	17 (4%)
	Pancreas and biliary tract carcinoma	12 (3%)
	Other malignancies	19 (5%)

Mechanical complications, including reservoir dislocation and extravasation, occurred in 18 patients (4.6%), 6 patients (5.7%) in the 4-week group and 12 patients (3.5%) in the 8-week group respectively ($p = 0.31$) (Table 2).

Infections, mainly caused by *Staphylococcus Epidermidis* and *Saprophyticus*, had a whole prevalence of 3.9% (10 patients). It was observed in 2 patients (1.9%) in the 4-week flushing group and 8 patients (2.3%) in the 8-week flushing group respectively ($p = 0.80$).

Occlusions were found in 15 patients (3.8%): 4 patients in the first group (3.8%) and 11 patients (3.2%) in the second one ($p = 0.76$).

3.3 | Systematic literature review

In 4 single-arm studies (Bassi et al., 2012; Biffi et al., 2004; Diaz et al., 2017; Solinas et al., 2017), PACs were flushed every 6 or 12 weeks.

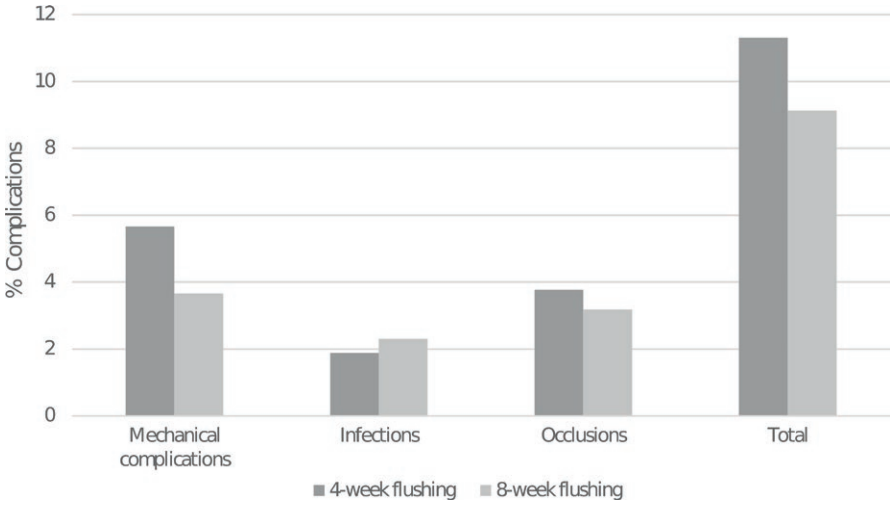

FIGURE 3 Results: percentage of complications in 4-week flushing group and 8-week flushing group

TABLE 2 Mechanical complications

Mechanical complications	4-week flushing (*n*)	8-week flushing (*n*)
Reservoir dislocation	1	2
Extravasation	1	3
Bleeding	1	1
Catheter dysfunction	0	3
Rupture	1	0
Other (oedema, arterial puncture, etc)	2	3

A total of 925 patients were included, the frequencies of complications were 1.6%, 1.0% and 2.7% for infections, occlusions and mechanical complications respectively (Table 3).

In 2 studies (Ignatov et al., 2010; Kuo et al., 2005), a non-randomised comparison between the standard (4 weeks) and longer interval procedures was performed. Table 4 summarises the results of these studies in addition to those of the present article. A total of 812 patients were considered, and the standard flushing scheme was used in 260, whereas a prolonged interval was performed in 615 patients. Patients of our study who switched from the 4-week schedule to the 8-week one were considered in both groups. The proportions of complications (infections, occlusions and mechanical dysfunctions) were 8.1% and 7.3% respectively (p value = 0.70).

4 | DISCUSSION

PACs are essential devices in the oncological clinical practice for the safe administration of chemotherapeutic drugs and supportive therapies. International guidelines have been implemented to provide recommendations on their insertion, use and management. According to the latest guidelines published in 2013, PACs not being accessed should be flushed and locked every 4 weeks in order to prevent infective, obstructive and mechanical complications.

In this retrospective non-randomised study, the prevalence of PAC complications in patients receiving flushing/locking procedures according to the standard 4-week schedule was compared with that of patients receiving PAC flushing every 8 weeks.

The data showed a frequency of infections, occlusions and other mechanical complications that were similar in the two series of patients. Moreover, the proportion of PAC complications of the two groups of patients included in the present study was comparable to those observed in the literature with the standard 4-week interval of flushing. Our data suggest that an 8-week schedule of PAC flushing is feasible and not associated with an increased risk of complications.

To confirm our results, a systematic review was performed. From the analysis of six published studies, no significant difference between standard and prolonged flushing schedule was observed in terms of complications.

The data of this study could have positive impacts for patients and the nursing staff. The need of a monthly timing of PAC flushing is time-consuming for a patient who has finished oncologic treatment

TABLE 3 Single-arm studies on complications after the adoption of longer flushing schedules than standard 4-week schedule

Authors	Patients (*n*°)	Timing (weeks)	Infection	Occlusion	Mechanical
Bassi et al. (2012)	81	4–6	8 (8.6%)	5 (6.2%)	3 (3.6%)
Biffi et al. (2004)	376	12	5 (1.3%)	4 (4.2%)	1 (2.7%)
Diaz et al., (2017)	87	12	0 (0%)	0 (0%)	10 (11.5%)
Solinas et al. (2017)	381	12	2 (0.5%)	0 (0%)	11 (3.1%)
Total	925		15 (1.6%)	9 (1.0%)	25 (2.7%)

TABLE 4 Studies comparing standard versus longer flushing intervals and on the relevant complications

Authors	Total no of patients	Timing (weeks)	Patients no	Infection	Occlusion	Mechanical	Total no of complications
Kuo et al. (2005)	73	3–6	14 (19%)	na	2 (14%)	na	2 (14%)
		6–8.5	28(39%)		2 (7.2%)		2 (7.2%)
		8.5–11.5	11 (15%)		1 (9.1%)		1 (9.1%)
		>11.5	20 (27%)		2 (10%)		2 (10%)
Ignatov et al. (2010)	349	1–4	140 (40.1%)	na	na	na	7 (5%)
		5–8	87 (24.9%)				6 (6.9%)
		9–12	30 (8.6%)				0 (0%)
		>13	26 (7.5%)				2 (7.7%)
		Switched from 1–4 to>12	66 (18.9%)				1 (1.5%)
Present study	390	4	106 (27.2%)	2 (1.9%)	4 (3.8%)	6 (5.7%)	12 (11.4%)
		8	347 (89.0%)	8 (2.3%)	11 (3.2%)	12 (3.5%)	31 (9.0%)
Total	812	Standard I		na	6/120 (5%)	na	21/260 (8.1%)
		Longer I			16/406 (3.9%)		45/615 (7.3%)
					p-value = 0.61		*p*-value = 0.70

Notes:. I = interval, na = not available

and leads to the patient perception of frequent hospital needs. The longer schedule would reduce the patient discomfort and the nurse workload. In addition, a longer schedule reduces the costs. Given the cost of every single-flushing procedure of about 12 € and considering that about 530 flushing are performed every year, we have estimated a saving of 6,500 €/year with the delayed flushing schedule (excluding the nursing time) as compared to the standard schedule.

In conclusion, this study shows that PAC flushing and locking every 8 weeks is feasible and safe, with benefits for both patients and nursing staff. A prospective phase III study is warranted to provide a formal demonstration of efficacy.

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CONFLICT OF INTEREST

None.

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