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Review

Peripherally Inserted Central Venous Catheters (PICC) versus totally implantable venous access device (PORT) for chemotherapy administration: a meta-analysis on gynecological cancer patients

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Abstract.

Background and aim: Ninety-four thousand gynecological cancer diagnoses are performed each year in the United States. The majority of these tumors require systemic adjuvant therapy. Sustained venous access was overcome by indwelling long-term central venous catheter (CVC). The best choice of which CVC to use is often arbitrary or dependent on physician confidence. This meta-analysis aims to compare PORT and peripherally inserted central catheter (PICC) outcomes during adjuvant treatment for gynecological cancer.

Methods: Meta-analysis Of Observational Studies in Epidemiology (MOOSE) and the preferred reporting items for systematic reviews and meta-analyses statement (PRISMA)were used to conduct the meta-analysis.

Results: 1320 patients were included, 794 belonging to the PORT group and 526 to the PICC group. Total complication rates were fewer in the PORT group, $p = 0.05$. CVC malfunction was less frequent in the PORT group than in the PICC group, $p < 0.01$. Finally, thrombotic events were less expressed in the PORT group than in the PICC group, $p = 0.02$. No difference was found in operative complication, migration, malposition, extravasation, infection, and complication requiring catheter removal.

Conclusions: PORT had fewer thrombotic complications and fewer malfunction problems than PICC devices. Unless specific contraindications, PORTs can be preferred for systemic treatment in gynecological cancer patients. (www.actabiomedica.it)

Keywords: Gynecological cancer; Peripherally inserted central venous catheters; PORT; Central venous catheter; Meta-analysis.

Introduction

Ninety-four thousand gynecological cancer diagnoses are performed each year in the United States(1). Of these, 90% ovarian, 35% endometrial, 60% cervical, and 65% vulvar cancers require systemic adjuvant th erapy(2,3)"PMID":"30207593","abstract":"This article provides a status report on the global burden of cancer worldwide using the GLOBOCAN 2018 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer, with a focus on geographic variability across 20 world regions. There will be an estimated 18.1 million new cancer cases (17.0 million excluding nonmelanoma skin cancer.

Most of the chemotherapies include toxic and irritating drugs and repeated venipuncture are associated with complications as local inflammation, drug infiltration, ulceration and necrosis of skin tissues, local infection, septicemia, as well as discomfort for the

patients(4). Sustained venous access was overcome by indwelling long-term central venous catheter (CVC) showing to be useful in assuring adequate access and improving quality of life(5).

There are four main CVC types: non-tunneled catheters, tunneled central catheters, fully implantable or surgically implantable catheters (PORT or port-a-caths), and peripherally inserted central catheter (PICC)(6).

The most frequently used CVCs for gynecological cancers are implanted central (eg. PORT) and PICCs. Both these CVCs are indicated for the administration of chronic therapies and are often placed into the superior vena cava(7). While the former has excellent aesthetic outcomes and allows swimming activities, the latter is less aesthetic and more frequently complicated by thrombosis(8). However, PORTs require surgical placement, while PICCs are easily inserted into an outpatient setting and do not require a platelet count before their removal(9).

Despite, a Practice Guidelines for Central Venous Access was recently published by the American Society of Anesthesiologists Task Force, the best choice of which CVC to use is often arbitrary, dependent on physician confidence, or based on patient preference(10). Furthermore, conflicting results on the complication rate have emerged from several past studies comparing PORT and PICC use (11–13).

In particular, in the subset of gynecological patients, only retrospective studies with small series have compared the PORT or PICC outcomes during adjuvant chemotherapy.

This meta-analysis aims to compare the PORT and PICC outcomes during adjuvant treatment for gynecological cancer and to provide the physician with useful information for better counseling oncological patients.

Methods

Two double-blind authors (CVA and ML) searched Pubmed, Medscience, Google Scholar, and Scopus search engines from December 2020 to February 2021. A third independent author (BR) reviewed the studies included in the first analysis. The following keywords were required: 'Central venous catheter'; 'PORT'; 'PICC'; 'Systemic adjuvant therapy'; and 'gynecology'. The Meta-analysis Of Observational Studies in Epidemiology (MOOSE)(14) and the preferred reporting items for systematic reviews and meta-analyses statement (PRISMA)(15) were used to conduct the meta-analysis. All studies comparing PORT type CVCs and PICCs during adjuvant treatment of gynecological cancers were included. Gynecological tumors falling into the inclusion criteria were ovarian, endometrial, cervical, and vulvar cancers. From each study, author, year of publication, type of study, type of tumor treated, type of CVC used, and complications during CVC placement were collected. Complications were reported as infections, thrombosis, malfunction, migration, extravasation, operative complication, complication requiring removal, and malposition. CVC malfunction meant failure to infuse drug through the catheter. CVC migration was considered as the displacement of the catheter into another large vessel. Operative complications included pneumothorax, hemothorax, air embolism, or pleural effusion. CVC malposition was considered as catheter placement in a large vessel other than that initially planned.

Case reports, studies including non-gynecological tumors, studies not reporting complications during CVC insertion and use were excluded.

Statistic analysis

All values were reported as numbers, percentages, averages, or medians. The Chi-square or Fisher exact test was used for categorical variables, while t-test and the Mann – Whitney non-parametric test were used for continuous variables. The backwardness of the studies was assessed by the I^2 test. A good level of heterogeneity of the studies was intended with an I^2 test value <50%. A random-effect model was used for all outcomes analyzed. Statistical significance was achieved for a p value <0.05. Prometa Software 3.0.0 was used for statistical analysis.

Results

Ninety-seven studies were initially analyzed. All abstracts and main text were studied if falling within the

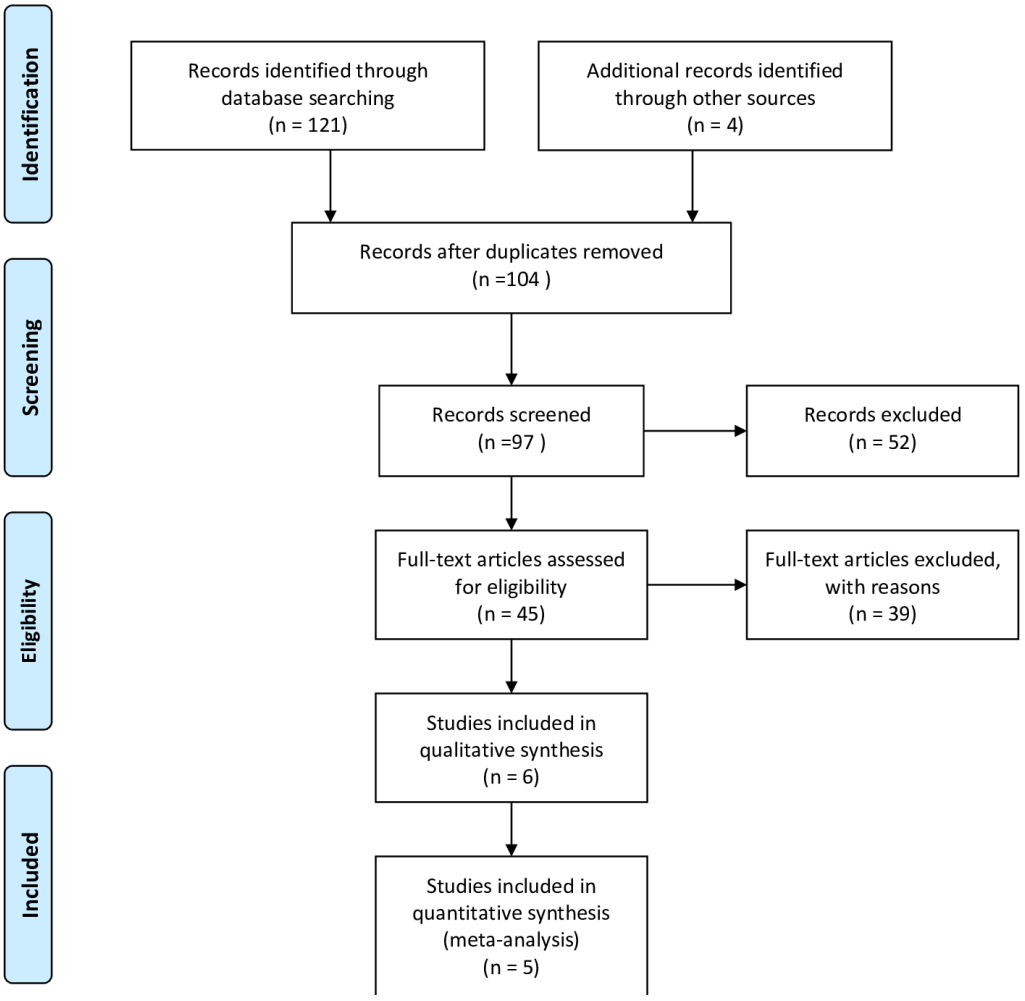

Figure 1. Prisma flow chart.

inclusion criteria of the meta-analysis. As shown in the PRISMA Flow chart (Fig. 1), 52 studies did not meet the inclusion criteria or were not relevant for the purposes of the study, 21 articles did not show useful details for the analysis, 18 case reports, and one non-English article were excluded from the analysis. Finally, 5 retrospective studies, were included in the analysis.

Overall, 1320 patients were included, 794 belonging to the PORT group and 526 to the PICC group. The median age was 56 years (range 53-61 years) and the median CVC duration was 19.3 months (range 9-78 months). Three hundred and twelve total complications were recorded, 146 (18.4%) in the PORT group and 166 (31.6%) in the PICC group. Total complication rates were fewer in the PORT group, p = 0.05, Effect Size (ES) 0.38, 95% Confidence Interval (CI) 0.14-1.02, with a large study heterogeneity I^2 = 89.9%. CVC malfunction was less frequent in the PORT group (5 cases, 0.6%) than in the PICC group (22 cases, 4.2%), p <0.01, ES 0.19, 95% CI 0.08-0.49, with heterogeneity I^2 = 0.0%. Finally, thrombotic events were less expressed in the PORT group (39 cases, 4.9%) than in the PICC group (48 cases, 9.1%), p = 0.02, ES 0.44, 95% CI 0.22-0.89, and heterogeneity I^2 = 46.7%. No difference was found in operative complication (p = 0.62), migration (p = 0.44), malposition (p = 0.44), extravasation (p = 0.33), infection (p = 0.13), and complication requiring catheter removal (p = 0.1).

The characteristics and type of complications are summarized in Table 1. The outcomes analyzed are summarized in Table 2.

Table 1. Characteristics and type of complications

Author, year	Total cases	Total Complications	Infections	Thrombosis	Malfunction	Migration	Extravasation	Operative complication	Complication requiring removal	Malposition
Ignatov, 2009										
Total	561	104	42	30	6	11	10	2	46	3
Port	292	36	15	10	2	3	4	1	20	1
Picc	269	68	27	20	4	8	6	1	26	2
Estes, 2003										
Total	116	45	24	8	8	0	0	5	29	0
Port	51	10	5	3	0	0	0	2	2	0
Picc	65	35	19	5	8	0	0	3	27	0
Martella, 2015										
Total	102	10	4	2	0	4	0	0	0	0
Port	57	5	2	1	0	2	0	0	0	0
Picc	45	5	2	1	0	2	0	0	0	0
Minassian, 2000										
Total	305	100	64	28	0	8	0	0	0	0
Port	230	80	53	20	0	7	0	0	0	0
Picc	75	20	11	8	0	1	0	0	0	0
Cohn, 2001										
Total	236	53	13	19	13	6	2	0	0	0
Port	164	15	4	5	3	2	1	0	0	0
Picc	72	38	9	14	10	4	1	0	0	0
Total	1320	**312; 23.6%**	147; 11.1%	**87; 6.6%**	**27; 2.0%**	29; 2.2%	12; 0.9%	7; 0.5%	75; 5.7%	3; 0.2%
PORT	794	146; **18.4%**	79; 9.9%	39; **4.9%**	5; **0.6%**	14; 1.8%	5; 0.6%	3; 0.4%	22; 2.8%	1; 0.1%
PICC	526	166; **31.6%**	68; 12.9%	48; **9.1%**	22; **4.2%**	15; 2.9%	7; 1.3%	4; 0.8%	53; 10.1%	2; 0.4%

Table 2. Outcomes analyzed

Outcomes	Effect Size	95% Confidence Interval	I^2 Heterogeneity	p Significance
Total Complications	0.38	0.14-1-02	89.9%	**0.05**
Thrombosis	0.44	0.22-0.89	46.7%	**0.02**
Malfunction	0.19	0.08-0-49	0.0%	**<0.001**
Complications requiring removal	0.30	0.07-1.25	56.3%	0.10
Extravasation	0.60	0.21-1.68	0.0%	0.33
Infection	0.51	0.21-1.22	74%	0.13
Malposition	0.55	0.12-2.51	0.0%	0.44
Migration	0.66	0.24-1.86	0.0%	0.44
Operative Complication	0.72	0.20-2.57	0.0%	0.61

Discussion

The choice of CVC for the chemotherapy infusion is complex, often affecting costs, complications, and not least the patient's quality of life(16).

Several studies were conducted to identify which type of CVC could be the optimal choice for oncological patients, however, almost all studies in the literature included indiscriminately all solid tumor patients in the analysis(17–19). To our best knowledge,

no studies reported the CVC complication rate in the treatment of gynecological patients.

Our study showed a lower total complication rate in the PORT than in the PICC group. Similar results have recently been suggested by Pu et al. in a meta-analysis study including solid tumors of any origin(20). The authors reported a lower complication rate and lower costs of PORTs compared to peripherally inserted catheters in a cohort of 8006 patients analyzed. Besides, a randomized trial (NCT01971021)(13) and a retrospective analysis(21) also showed a major rate of catheter-related complications with the use of PICC compared to PORT in patients with main breast and colorectal cancer.

However, since our meta-analysis showed significance at the limits ($p = 0.05$) but above all, a high rate of heterogeneity of the included studies ($I^2 = 89.9\%$), these results in the subset of gynecological patients should be considered with caution.

Then, our study showed fewer CVC-related thromboses in the PORT compared to the PICC group. In this case, the association was statistically solid, with good heterogeneity. The PICC prothrombotic effect compared to PORT has been widely observed, so that the European Society for Medical Oncology (ESMO) guidelines on central venous accesses reported thrombotic risk as to the main limitation of PICC. The pathophysiological mechanism underlying CVC-related thrombosis is multifactorial. Increased thrombin levels, protein C resistance, anti-phospholipid antibodies, as well as the underlying oncological disease have all been involved in the clot aggregation process(22). Therefore, considering the five- to seven-fold increased thrombotic risk of cancer patients with CVC(23), a careful preoperative assessment, specific calculation of thrombotic risk, and accurate management of the devices are essential for a correct functioning without complications of the PICC venous catheter.

Finally, our study reported fewer malfunctions for PORTs than for PICCs. The main cause of venous catheter malfunction is obstruction of the lumen device. The catheter may kneel on its way, the lumen may be blocked by clots, or the tip of the catheter may adhere to the inner wall of the vessel preventing the drug from passing through the catheter. Furthermore, too high concentrations of administered drugs could precipitate in the vessel lumen occluding the CVC. Ultrasound control during CVC placement has been shown to be useful in the correct functioning of the venous catheters(24). Also, patient and nurse education programs in CVC cleaning and disinfection are essential to avoid all complications arising from device mismanagement(25).

The present study has limitations related to the retrospective nature of the included studies and few case histories in the subset of patients analyzed. However, to our best knowledge, no meta-analyses had been conducted comparing PORT and PICC in patients with gynecologic cancer. Furthermore, the studies showed a good level of heterogeneity, making the meta-analysis applicable to correct counseling to be performed on the gynecological oncological patient.

Conclusion

Thorough counseling should be performed before the choice of CVC to be used for the administration of systemic adjuvant therapy in gynecological cancer patients. PORT had fewer thrombotic complications and fewer malfunction problems than PICC devices. Unless specific contraindications, PORTs may be preferred in the systemic treatment of patients with gynecological cancer.

Conflicts of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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