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Complications and Costs of Peripherally Inserted Central Venous Catheters Compared With Implantable Port Catheters for Cancer Patients

A Meta-analysis

KEY WORDS

Central venous access
Cost analysis
Meta-analysis
Neoplasms
Safety

Background: Peripherally inserted central catheters (PICCs) and implantable port catheters (IPCs) are 2 most common central venous access for cancer patients receiving chemotherapy. However, no specific evidence exists to guide practitioners on safety and less cost. **Objective:** To compare the differences of complications and costs of PICC and IPC in the treatment of cancer patients with chemotherapy and to provide a basis for better clinical decision making. **Methods:** All the cohort studies were searched in the Cochrane Library, JBI, PubMed, Elsevier, Web of Science, CINAHL, CBM, and CNKI from inception to July 2018. Two reviewers screened and selected trials, evaluated quality, and extracted data. Meta-analysis and description of the outcomes were performed by using the RevMan 5.3 software. **Results:** A total of 761 articles were retrieved, with 15 articles meeting eligibility criteria. Outcome analysis showed no difference in 1-puncture success rate. Peripherally inserted central catheter use was associated with

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Research funding was provided by the National Natural Science Foundation of China (71804073).

The authors have no conflicts of interest to disclose.

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Accepted for publication June 7, 2019.

DOI: 10.1097/NCC.0000000000000742

higher complication rates than IPC, including occlusion, infection, malposition, catheter-related thrombosis, extravasation, phlebitis, and accidental removal rate. The life span of IPC was longer than that of PICC, and the costs of IPC were lower.

Conclusions: Implantable port catheter has advantages over PICC in reducing cancer patients' complications and less cost in terms of long-term cancer chemotherapy.

Implications for Practice: In terms of safety, the results provide evidence for practitioners to choose which type of central venous catheters is better for cancer chemotherapy patients. In terms of costs, practitioners need to make decisions about which type of central venous catheters has less cost.

Cancer has become the second leading cause of death in the world. There are more than 6 million new-onset cancer diagnoses every year in China.¹ As the environment and lifestyle change, the population of cancer patients is expected to grow in the coming decades.² Chemotherapy is a common treatment for cancer patients that can prolong the survival of metastatic malignancies.³ Many chemotherapies are infused through intravenous access and may damage peripheral blood vessels.⁴ Further, repeated venipuncture is an unpleasant experience for patients, which makes the central vascular access superior to the peripheral vascular access.⁵⁻⁷

Central venous access provides a greater guarantee of safety and comfort during chemotherapy to cancer patients. Peripherally inserted central venous catheters (PICCs) and implantable port catheters (IPCs) are 2 common infusion pathways for chemotherapy.⁸ In the 1970s, the PICC was introduced as a central venous catheter (CVC) placed into the brachial, basilic, and cephalic vein.⁹ Development of the IPC followed in the 1980s, and IPC was placed in the subclavian vein as a port for intravenous access without the need for external catheter lines.¹⁰ The introduction of PICC and IPC represents one of the most important advances in nursing technologies for cancer patients. They form a necessary reliable route through which patients can receive nutritional support, chemotherapy, long-term infusions, and repeated blood tests. Thus, the contrastive analysis of these 2 pathways has been a popular issue for nurses.^{3,11}

Today is an era that focuses on patient safety and raising cost awareness. The safety and costs comparisons of these 2 common infusion catheters have become a frequent focus of research.¹² Medical decision makers hope to have more evidence to fully evaluate the complications of these 2 procedures and cost benefits. However, there is no clear or conclusive evidence of which type of CVC is preferred in terms of safety and costs. The extent of use of these 2 catheters varies from country to country, with the practitioners in China being more likely to recommend PICC for their patients. This may be due to a perception of non-inferiority of complication rates of PICC compared with IPC, as well as lower costs of implantation with PICC compared with IPC.¹³ However, other studies have shown that the weekly maintenance costs of PICC mean costs in the long run may be even higher than IPC.¹⁴ It has been reported in a study that the incidence of complications of PICC (32.8% of 351 patients) is higher than that of IPC,¹⁵ whereas in another observational

study, the incidence of complications during 106 intravenous catheterizations was not different between the 2 methods.¹⁶

The most common catheter complications of PICC and IPC are occlusion, infection, malposition, catheter breakage, catheter-related thrombosis, extravasation, phlebitis, accidental removal rate, and pneumothorax.^{17,18} There is a lack of good evidence to guide practitioners and patients in the optimal choice between the 2 catheters currently, especially based on balancing complications and costs. In addition, because existing works originate from different countries and healthcare economies, the cost accounting methods and currencies reported vary, making it more difficult to integrate information. Thus, this meta-analysis aims to compare the differences in complication rates and costs of PICC and IPC in the treatment of cancer patients with chemotherapy, to provide a basis for better clinical decision making.

■ Methods

This study was undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines.¹⁹ Operational definitions were detailed prior to search initiation based on recommendations from the *Cochrane Handbook for Systematic Reviews of Interventions*.²⁰

Selection Criteria

Only Cohort studies assessing the effects of different central venous access devices in cancers were included. Further, these studies met the following inclusion criteria: (1) patients being treated for solid or hematological malignant tumors by chemotherapy through central venous access devices; (2) studies that compared 2 devices (PICC and IPC); (3) primary outcomes included the incidence of device-related complications (occlusion, infection, malposition, catheter-related thrombosis, extravasation, phlebitis, and accidental removal rate) and costs; other related outcomes such as 1-puncture success rate and catheter life span were also included; and (4) studies using English or Chinese that all the authors could review.

Search Strategy

Electronic databases search included Cochrane Library, JBI, PubMed, Elsevier, Web of Science, CINAHL, CBM, and

China National Knowledge Infrastructure, from 1966 to July 2018. Selected medical subject headings were combined with free text terms following MeSH (Medical Subject Headings) terms relating to PICC (peripherally inserted CVC, peripheral intravenous catheter, peripherally inserted central cannula), IPC (implantable port catheter, Port A, TIVAD, implantable access port, subcutaneous central venous port, totally implanted venous access device, totally implantable access port, central venous port access system), cancer (tumor, neoplasms, sarcoma, lymphoma, carcinoma), and chemotherapy (chemical, chemo, chemotherapeutant, chemotherapeutic), in PubMed. This was adjusted for use in other databases using appropriate search symbols and Boolean operators (Table 1). Meanwhile, cited reference retrievals were also performed. Reference lists of all relevant systematic reviews and studies were checked for additional potentially relevant studies.

Study Selection and Data Extraction

Two reviewers (Y.-L.P. and Z.-S.L.) independently read and eliminated duplicate and irrelevant studies from the title and abstract. The remaining full text was obtained and critically reviewed by both authors independently for inclusion. Any discrepancies in data extraction or study selection were discussed by both reviewers and adjudicated by a third reviewer. Two reviewers then independently extracted data into a predesigned form recording the following: (1) author and country; (2) publication year; (3) date collection time; (4) characteristics of the subjects, including age and gender features; (5) details of observation group and control group, including catheters' placement and maintenance; (6) type of cancer; and (7) type of outcomes.

Quality Appraisal

All the cohort studies were assessed independently by 2 reviewers for risk of bias using the Newcastle-Ottawa Scale.²¹ This scale involves 8 items with a full score of 9. Articles scoring between 6 and 9 points are rated grade A (low risk of bias), whereas those scoring less than 6 points or that involve significant differences

in age and gender between the 2 groups are rated grade B (high risk of bias).

Data Analysis

Meta-analysis of outcomes data was performed using the Cochrane Collaboration RevMan V.5.3 software.²² Meta-analyses for continuous variables (catheter life span) were performed using a fixed-effects model from the mean difference and SD of the mean difference, between the intervention and control groups. As for count data (1-puncture success event, accidental removal event, and complications of occlusion, infection, malposition, catheter-related thrombosis, extravasation, phlebitis), differences in total event numbers were used to evaluate any effect.

We used χ^2 test and I^2 statistic to determine whether there was heterogeneity between each study.²³ Relative ratios (RRs) were used to calculate binary variables, and continuous data were analyzed using the weighted mean difference; 95% confidence intervals (CIs) were calculated for all analyses. If there are more than 10 studies in each outcome, we conducted the funnel plots to assess publication bias.

Results

Search Process

A total of 761 studies were identified through our search (Figure 1). After removing duplicates, the remaining 445 articles were screened by titles and abstracts. After screening, 40 articles were obtained for full text reading, following which 15 cohort studies^{11,12,24-36} involving 8006 patients met our inclusion criteria and quality assessment and were included in our study.

Quality Appraisal

The risk of bias in the included 15 cohort studies^{11,12,24-36} was summarized (Table 2). All included studies had good baseline comparability of groups and were grade A quality (low risk of bias).

 **Table 1 • PubMed Search Strategy**

ID	Search Terms	Results
1	Search (“catheterization, peripheral” [MeSH]) OR (“PICC”) OR (“peripherally inserted central venous catheter*”) OR (“peripherally inserted central catheter*”) OR (“peripherally inserted central cannula”)	1658
2	Search (“Port-A”) OR (“Port-A-Cath”) OR (“TIVAD*”) OR (“TIVAS”) OR (“TICVP”) OR (“implantable port catheter*”) OR (“implant* venous-access port”) OR (“implant* access port”) OR (“implantable port systems”) OR (“venous port access”) OR (“central venous port access system”) OR (“subcutaneously implanted port catheter*”) OR (“subcutaneous central venous ports”) OR (“subcutaneously implanted port-chamber catheter*”) OR (“totally implantable access port”) OR (“totally implanted venous access device*”) OR (“totally implantable venous access system”)	7366
3	Search (“neoplasms” [MeSH]) OR (“cancer”) OR (“tumor”) OR (“sarcoma”) OR (“lymphoma”) OR (“carcino*”)	3 698 130
4	Search (“chemo*”) OR (“chemotherapy”) OR (“chemical”) OR (“chemotherapeutic”) OR (“chemotherapeutant”)	3 121 730
5	Search #1 AND #2 AND #3 AND #4	133

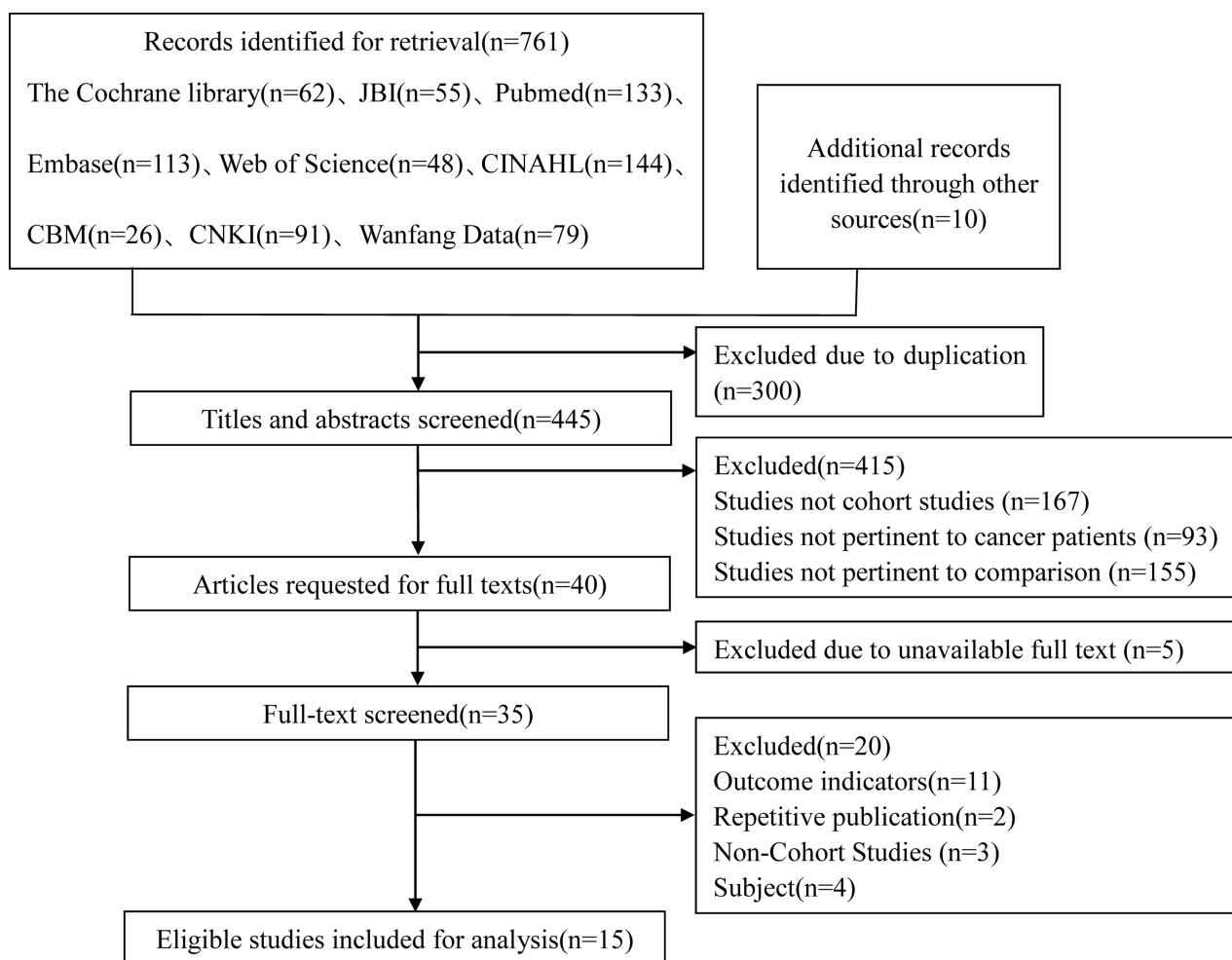


Figure 1. Study flow diagram.

Table 2 • Quality Evaluation of 15 Cohort Studies										
First Author	Selection				Comparability	Outcome			Total Score	Quality Level
	①	②	③	④	⑤	⑥	⑦	⑧		
Karin ²⁴	1	1	1	1	2	0	1	1	8	A
Martella ¹¹	1	1	1	1	1	0	1	0	6	A
Jain ²⁵	1	1	1	1	2	0	1	1	8	A
Verboom ²⁶	1	1	1	1	2	0	1	0	7	A
Viart ²⁷	1	1	1	1	2	0	0	0	6	A
Fang ²⁸	1	1	1	1	2	1	1	1	9	A
Wang ²⁹	1	1	1	1	2	0	1	0	7	A
Bratton ³⁰	1	1	1	1	2	0	1	0	7	A
Rotzinger ¹²	1	1	1	1	2	0	1	0	7	A
Lefebvre ³¹	1	1	1	1	2	0	1	1	8	A
Revel-Vilk ³²	1	1	1	1	2	0	1	1	8	A
Kim ³³	1	1	1	1	2	0	1	1	8	A
Lu ³⁴	1	1	1	1	2	0	0	0	6	A
Tang ³⁵	1	1	1	1	2	0	1	0	7	A
Liu ³⁶	1	1	1	1	2	0	1	1	8	A

① Representativeness of the exposed cohort; ② selection of the non-exposed cohort; ③ ascertainment of exposure; ④ demonstration that outcome of interest was not present at start of study; ⑤ comparability of cohorts on the basis of the design or analysis; ⑥ assessment of outcome; ⑦ follow-up long enough for outcomes to occur; ⑧ adequacy of follow-up of cohorts.

Table 3 • Characteristics of Included Studies

Authors, Country	Year	Date Collection		Subjects	① Observation Group and ② Control Group		Disease	Outcome
		Time	Time		①	②		
Karin et al, ²⁴ United Kingdom	2015	From January 2011 until August 2013	55 Adult cancer patients with an average age of 53.9 y, women accounted for 54.5%	① 4F polyurethane single-lumen PICC catheters; inserted into the brachial veins under local anesthesia with ultrasound; flushed weekly when not in use (n = 9) ② Central venous access ports (VAPs); inserted into the right internal jugular veins under local anesthesia with ultrasound; flushed monthly when not in use (n = 30)	① PICC; inserted under general anesthesia; weekly dressing changes (n = 45) ② Subcutaneously implanted port-chamber catheters; inserted under general anesthesia; monthly dressing changes (n = 57)	Solid tumors (colorectal, breast, ovarian, anus, esophagus, glioblastoma multiforme, sarcoma)	B, C, D, E	
Martella et al, ¹¹ Italy	2015	From November 2009 until March 2013	102 Adult cancer patients with an average age of 54.3 y, women accounted for 96%	① PICC; inserted under general anesthesia; weekly dressing changes (n = 45) ② Subcutaneously implanted port-chamber catheters; inserted under general anesthesia; monthly dressing changes (n = 57)	① PICC; inserted under general anesthesia; weekly dressing changes (n = 45) ② Subcutaneously implanted port-chamber catheters; inserted under general anesthesia; monthly dressing changes (n = 57)	Malignant tumors (20 with sarcoma, 80 with ovarian cancer, and 2 with cervical cancer)	C, D, F, H, J	
Jain et al, ²⁵ India	2013	From August 2010 until July 2011	213 Cancer patients (pediatric patients, n = 112; adult patients, n = 101) with an average age of 4 and 40 y, respectively	① PICC; flushed daily with heparin solution (n = 98) ② Port-a-Cath; inserted under general anesthesia; flushed every 2 wk (n = 25)	① PICC; flushed daily with heparin solution (n = 98) ② Port-a-Cath; inserted under general anesthesia; flushed every 2 wk (n = 25)	Malignant tumors (81 with solid malignancy, 132 with hematological malignancy)	B, C, F	
Verboom et al, ²⁶ the Netherlands	2017	From 1999 until 2014	127 Adult cancer patients with an average age of 54.3 y, women accounted for 52%	① PICC; inserted under general anesthesia (n = 10) ② VAPs; inserted under general anesthesia (n = 102)	① PICC; inserted under general anesthesia (n = 10) ② VAPs; inserted under general anesthesia (n = 102)	Soft tissue sarcoma (52 with leiomyosarcoma, 33 with liposarcoma, 16 with synovial sarcoma, and 26 with various others)	D, F, G	
Viart et al, ²⁷ France	2015	From January 2014 until December 2014	27 Adult cancer patients; no statistical difference in age and sex	① PICC; inserted under general anesthesia with ultrasound (n = 10) ② Port-A-Cath; inserted under general anesthesia with ultrasound (n = 17)	① PICC; inserted under general anesthesia with ultrasound (n = 10) ② Port-A-Cath; inserted under general anesthesia with ultrasound (n = 17)	Malignant tumors	J	
Fang et al, ²⁸ China	2017	From March 2014 until December 2016	145 Adult cancer patients with an average age of 52.1 y, women accounted for 59.3%	① 4F single-lumen Bard Groshong PICC; inserted into the basilic vein under local anesthesia; flushed after each use and once a week between chemotherapy (n = 60) ② 7F single-lumen Bard Groshong Port; inserted into the jugular veins under local anesthesia; flushed every 4 wk when not in use (n = 45)	① 4F single-lumen Bard Groshong PICC; inserted into the basilic vein under local anesthesia; flushed after each use and once a week between chemotherapy (n = 60) ② 7F single-lumen Bard Groshong Port; inserted into the jugular veins under local anesthesia; flushed every 4 wk when not in use (n = 45)	Malignant tumors (56 with breast cancer, 42 with lung cancer, 38 with gastrointestinal cancer, 9 with other cancer)	A, B, C, D, F, H, I, J	
Wang et al, ²⁹ China	2016	From January 2015 until January 2016	110 Breast cancer patients, no significant difference in age, family monthly income, payment methods, tumor staging, and other indicators	① PICC; inserted into the basilic vein under local anesthesia; nurse conducts catheter maintenance weekly (n = 60) ② IPC; inserted into the right jugular vein under local anesthesia puncture; nurse conducts catheter maintenance monthly (n = 50)	① PICC; inserted into the basilic vein under local anesthesia; nurse conducts catheter maintenance weekly (n = 60) ② IPC; inserted into the right jugular vein under local anesthesia puncture; nurse conducts catheter maintenance monthly (n = 50)	Breast cancer	A, D, F, I, J	

(continues)

Table 3 • Characteristics of Included Studies

Authors, Country	Year	Date Collection		Subjects	① Observation Group and ② Control Group		Disease	Outcome
		Time	Time		①	②		
Bratton et al, ³⁰ United States	2014	From September 9, 2004, until October 23, 2012	178 Pediatric cancer patients, age 1–10 y old accounted for 94.1%, females accounted for 45.9%	① PICC; inserted under general anesthesia; flushed with 5 mL normal saline (NS) each daily treatment (n = 34) ② Port-a-Cath; inserted under general anesthesia; flushed with 10 mL NS each daily (n = 110)	① PICC; inserted under local anesthesia with ultrasound (n = 791) ② Central venous port catheters; inserted under local anesthesia with ultrasound (n = 1777)	Malignant tumors (131 with brain tumor; 19 with rhabdomyosarcoma, 4 with Ewing sarcoma, 16 with other cancer)	C, D, E, G, H, I	
Rotzinger et al, ¹² Switzerland	2017	From January 2011 until December 2013	145 Adult cancer patients with an average age of 60.8 y, women accounted for 53.4%	① PICC; inserted under local anesthesia with ultrasound (n = 110)	① 4F single-lumen polyurethane PICC catheters; inserted into the basilica vein under local anesthesia with ultrasound; a weekly maintenance with dressing change and saline wash (n = 158) ② Port catheter; inserted into the internal jugular vein under local anesthesia with ultrasound; no maintenance was required for port catheter (n = 290)	Malignant tumors (pancreatic carcinoma, lung carcinoma, ovarian cancer, lymphoma, breast cancer, cervical cancer, leukemia, etc) HER2-negative early breast cancer	D, J	
Lefebvre et al, ³¹ France	2015	From January 2011 until December 2013	448 Female cancer patients, age ≥60 y accounted for 35.9%, body mass index ≥30 kg/m ² accounted for 20.9%	① 4F single-lumen polyurethane PICC catheters; inserted into the basilica vein under local anesthesia with ultrasound; a weekly maintenance with dressing change and saline wash (n = 158) ② Port catheter; inserted into the internal jugular vein under local anesthesia with ultrasound; no maintenance was required for port catheter (n = 290)	① PICC; inserted under general anesthesia (n = 188) ② Port-a-Cath; inserted under general anesthesia (n = 126)	Malignant tumors (73 with acute lymphoblastic leukemia, 48 with sarcoma, 36 with lymphoma, 32 with myeloid leukemia, 25 with brain tumor, 15 with neuroblastoma, 6 with bone marrow transplantation, 27 with other diagnosis)	C	
Revel-Vilk et al, ³² Israel	2010	From June 2006 until January 2009	262 Pediatric cancer patients with an average age of 7.4 y	① PICC; inserted under general anesthesia (n = 188) ② Port-a-Cath; inserted under general anesthesia (n = 126)	① 5F polyurethane single-lumen PICC catheters; inserted into the antecubital, basilic, brachial, or cephalic vein under with radiological guidance; flushed weekly when not in use (n = 24) ② Central venous ports; a single lumen; inserted into the vein under fluoroscopic guidance; flushed monthly when not in use (n = 72)	Malignant tumors (breast, bone, pediatric, gynecologic, hematological, gastrointestinal)	D	
Kim et al, ³³ Korea	2010	From March 2007 to March 2009	116 Adult cancer patients with an average age of 61 y; women accounted for 48.3%	① 3-Directional valvular PICC; inserted into the basilic vein under local anesthesia; nurse conducts catheter maintenance weekly (n = 214) ② 6F or 7F 3-valve infusion port; inserted into the right jugular vein under local anesthesia with ultrasound; nurse conducts catheter maintenance monthly (n = 336)	① 5F polyurethane single-lumen PICC catheters; inserted into the antecubital, basilic, brachial, or cephalic vein under with radiological guidance; flushed weekly when not in use (n = 24) ② Central venous ports; a single lumen; inserted into the vein under fluoroscopic guidance; flushed monthly when not in use (n = 72)	Malignant tumors	D	
Lu et al, ³⁴ China	2017	From January 2015 until December 2015	550 Breast cancer patients, all female	① PICC; inserted under general anesthesia; flushed with 5 mL normal saline (NS) each daily treatment (n = 34) ② Port-a-Cath; inserted under general anesthesia; flushed with 10 mL NS each daily (n = 110)	① PICC; inserted under local anesthesia with ultrasound (n = 791) ② Central venous port catheters; inserted under local anesthesia with ultrasound (n = 1777)	Malignant tumors (131 with brain tumor; 19 with rhabdomyosarcoma, 4 with Ewing sarcoma, 16 with other cancer)	C, D, E, G, H, I	

(continues)

Table 3 • Characteristics of Included Studies

Authors, Country	Year	Date Collection Time	Subjects	① Observation Group and ② Control Group		Disease	Outcome
				①	②		
Tang et al, ³⁵ China	2014	From January 2012 until December 2012	2970 Cancer patients with chemotherapy	① 4F-5F 3-way valve PICC catheter; inserted into the basilic vein under the local anesthesia; nurse conducted catheter maintenance weekly (n = 1509)	② 5F-7F venous port access; inserted into the right jugular vein under local anesthesia; nurse conducted catheter maintenance monthly (n = 1461)	Malignant tumors	C, D, F, H
Liu et al, ³⁶ China	2017	From August 2013 until January 2015	298 Adult breast cancer patients with an average age of 55.2 y, women accounted for 100%.	① 4F 3-directional valvular PICC; inserted into the basilic vein under local anesthesia; follow-up for 12 mo (n = 120)	② 6F-7F 3-valve infusion port; inserted into the internal jugular veins under local anesthesia; follow-up for 12 mo (n = 178)	Breast cancer	C, D, E, G

Abbreviations: (Outcome) A, 1-puncture success rate; B, catheter life span; C, occlusion; D, infection; E, malposition; F, catheter-related thrombosis; G, extravasation; H, phlebitis; I, accidental removal rate; J, costs.

Study Characteristics

In total, 15 cohort studies were considered eligible, information from which is listed in Table 3. Overall, the included studies originated from China (n = 5),^{28,29,34–36} United States (n = 1),³⁰ United Kingdom (n = 1),²⁴ Italy (n = 1),¹¹ India (n = 1),²⁵ the Netherlands (n = 1),²⁶ France (n = 2),^{27,31} Switzerland (n = 1),¹² Israel (n = 1),³² and Korea (n = 1),³³ respectively. The 15 studies included 8006 cancer patients with CVC, among which 3330 patients used PICC, and 4676 patients used IPC. Among them, catheterization was performed under ultrasound guidance in 4 studies.^{12,24,31,34} Four studies included women with breast cancer.^{29,31,34,36} Three studies included patients with childhood cancer.^{25,30,32}

Quantitative Synthesis (Meta-analysis)

COMPLICATIONS

Occlusion

Eight studies^{11,24,25,28,30,32,35,36} reported line occlusion in patients with PICC and IPC (Figure 2). The results showed that the incidence of occlusion complications in the PICC group was significantly higher than that in the IPC group (RR, 5.41; 95% CI, 2.56–11.43; $P < .05$). There was no statistical heterogeneity between the studies ($I^2 = 0\%$, $P = .63$), and the fixed-effect model was selected for meta-analysis.

Infection

Twelve studies^{11,12,24,26,28–31,33–36} reported the effects of PICC and IPC on infection rates (Figure 3). The results showed that the incidence of infectious complications in the PICC groups was significantly higher than that in the IPC groups (RR, 3.43; 95% CI, 2.58–4.56; $P < .05$). There was no statistical heterogeneity among these studies ($I^2 = 0\%$, $P = .58$). Subgroup analysis showed the incidence of local infection of punctures and catheter-related infection in PICC was significantly higher than in IPC (RR, 3.28 [95% CI, 2.39–4.51; $P < .05$]; RR, 4.10 [95% CI, 2.16–7.77; $P < .05$], respectively) without significant heterogeneity ($I^2 = 39\%$ [$P = .18$], $I^2 = 0\%$ [$P = .75$], respectively). Funnel plot was used to assess the possible publication bias of studies. As shown in Figure 4, distribution of data points in funnel plot showed that the symmetry was not good enough to exclude publication bias, suggesting that our meta-analysis results may be unstable.

Malposition

Three studies^{24,30,36} reported the effects of PICC and IPC on malposition (Figure 5). The incidence of malposition complications in PICC was higher than in IPC (RR, 11.93; 95% CI, 2.89–49.18; $P < .05$), without significant heterogeneity ($I^2 = 0\%$, $P = .62$).

Catheter-Related Thrombosis

Eight studies^{11,25,26,28,29,31,35,36} reported the effects of PICC and IPC on the catheter-related thrombosis (Figure 6). The results showed that the incidence of catheter-related thrombosis in PICC was higher than in IPC (RR, 5.01; 95% CI, 2.71–9.25; $P < .05$) with minimal heterogeneity ($I^2 = 22\%$, $P = .25$).

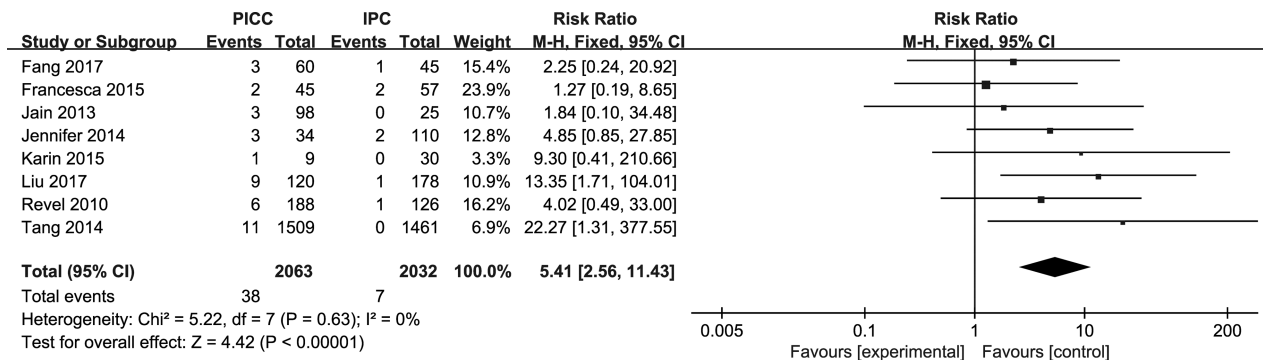


Figure 2. Forest plot of meta-analysis comparing the occlusion complications between PICC and IPC.

Extravasation

Four studies^{26,30,31,36} reported the effects of PICC and IPC on extravasation (Figure 7). The results showed that the incidence of extravasation complications in PICC was statistically significantly higher than in IPC (RR, 5.32; 95% CI, 1.72–16.38; $P < .05$), with no heterogeneity between studies ($I^2 = 0\%$, $P = .72$).

Phlebitis

Six studies^{11,12,28,31,34,35} reported the effects of PICC and IPC on phlebitis rates (Figure 8). The results showed that the incidence of phlebitis complications in PICC was statistically significantly higher than in IPC (RR, 13.11; 95% CI, 4.12–41.67; $P < .05$), with no heterogeneity between studies ($I^2 = 0\%$, $P = .69$).

ACCIDENTAL REMOVAL RATE

Four studies^{11,12,25,26} reported the effects of PICC and IPC on the accidental removal rate (Figure 9). There was no statistical heterogeneity among the studies ($I^2 = 0\%$, $P = .89$). The results showed that the accidental removal rate in PICC was statistically

significantly higher than in IPC (RR, 6.66; 95% CI, 2.67–16.59; $P < .05$).

ONE PUNCTURE SUCCESS

Three studies^{28,29,34} reported the effect of PICC and IPC on the 1-puncture success rate (Figure 10). The statistical heterogeneity between the studies was low ($I^2 = 16\%$, $P = .30$), and results showed that the 1-puncture success rate did not differ significantly between the 2 methods (RR, 0.99; 95% CI, 0.97–1.01; $P = .45$).

CATHETER LIFE SPAN

Three studies^{24,25,28} reported the effect of PICC and IPC on catheter life span (Figure 11). An obvious statistical heterogeneity was apparent between the 3 studies initially ($P < .001$, $I^2 = 97\%$). Exclusion method was used to eliminate the heterogeneity, which was found to come from Jain and colleagues²⁵ study. After elimination, statistical heterogeneity was reduced ($I^2 = 12\%$, $P = .29$), and results showed that IPC's life span was statistically

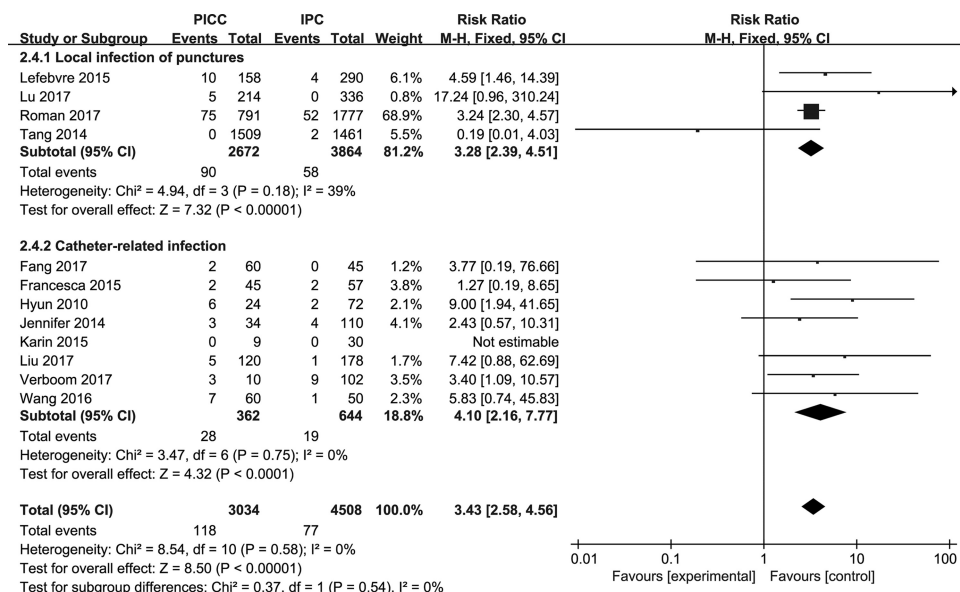


Figure 3. Forest plot of meta-analysis comparing the infection complications between PICC and IPC.

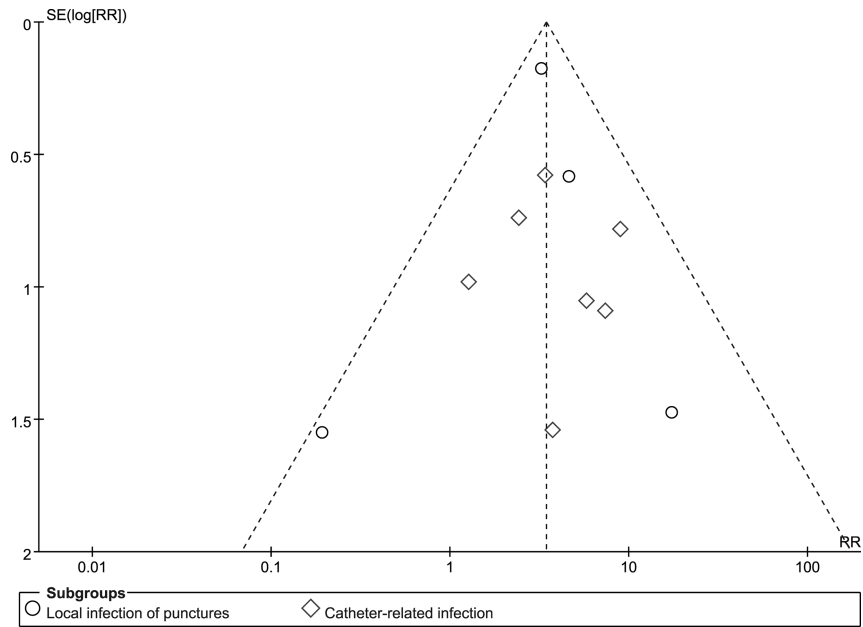


Figure 4. Funnel plot comparing the incidence of infection between PICC and IPC.

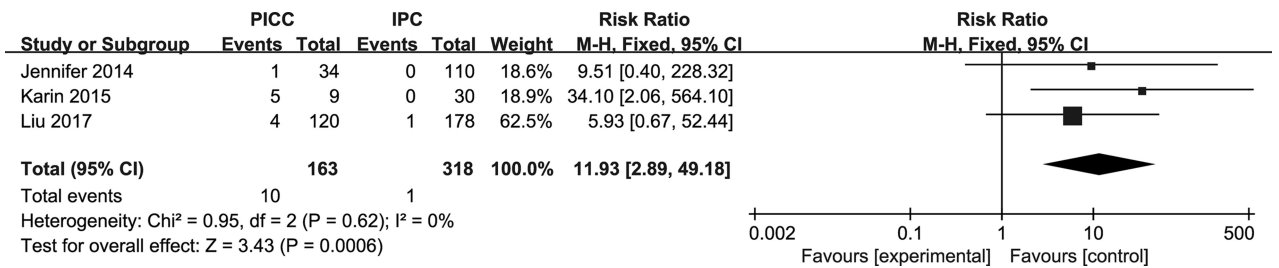


Figure 5. Forest plot of meta-analysis comparing the malposition complications between PICC and IPC.

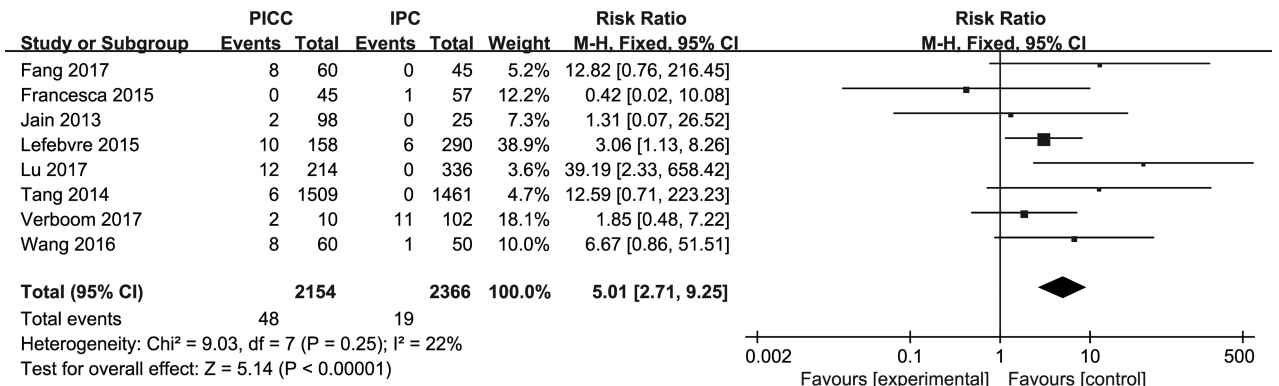


Figure 6. Forest plot of meta-analysis comparing the catheter-related thrombosis between PICC and IPC.

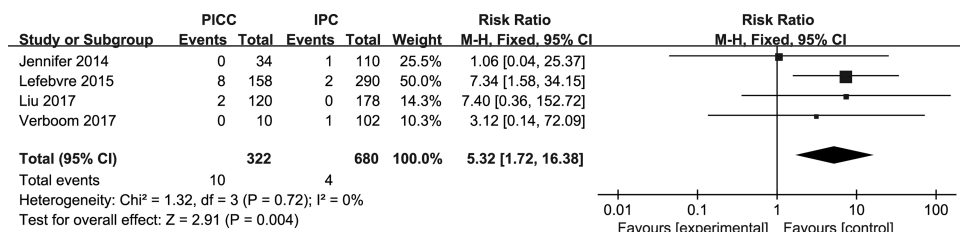


Figure 7. Forest plot of meta-analysis comparing the extravasation complications between PICC and IPC.

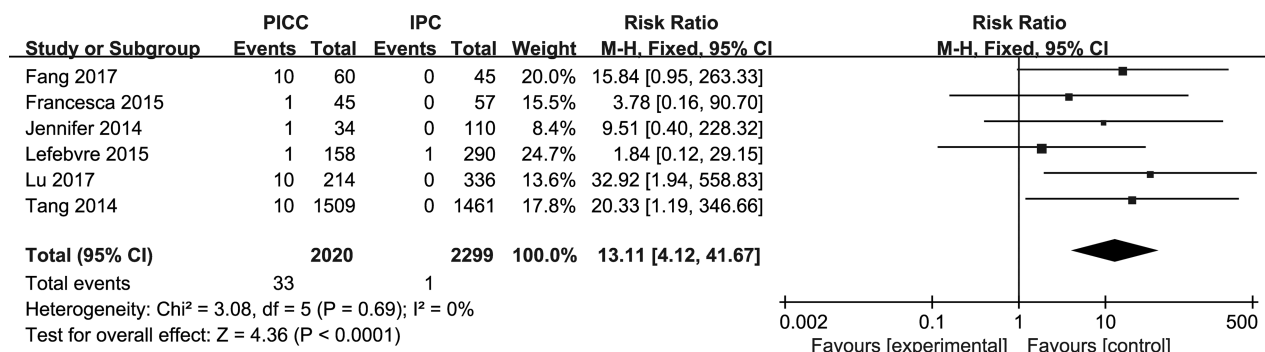


Figure 8. Forest plot of meta-analysis comparing the phlebitis complications between PICC and IPC.

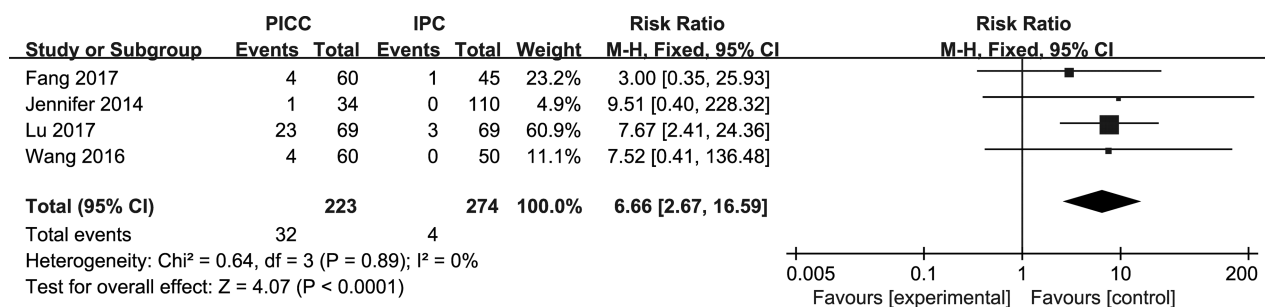


Figure 9. Forest plot of meta-analysis comparing the accidental removal rate between PICC and IPC.

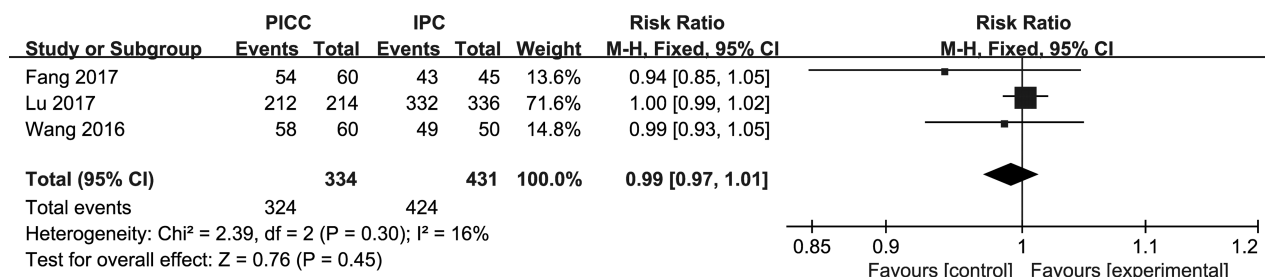


Figure 10. Forest plot of meta-analysis comparing the 1-puncture success rate between PICC and IPC.

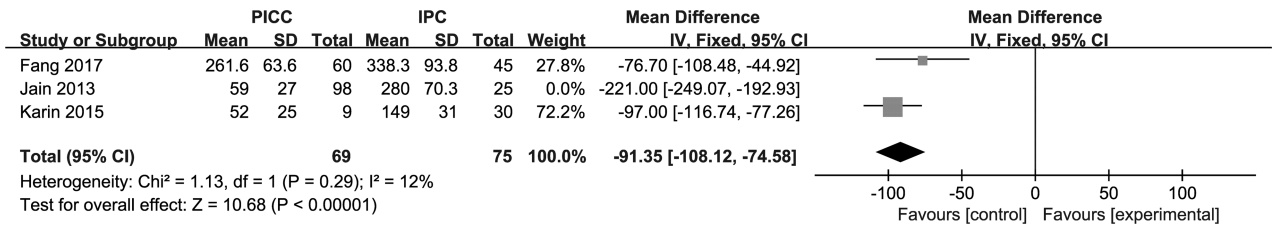


Figure 11. Forest plot of meta-analysis comparing the catheter life span between PICC and IPC.

longer than that of PICC (weighted mean difference = -91.35; 95% CI, -108.12 to -74.58; *P* < .05).

COSTS

The costs of PICC and IPC were reported at different time frames: 1, 6, and 12 months after catheterization. Because of the variability in health economics and cost estimation methods across studies, pooled meta-analysis was not possible. However, 6 studies^{11,12,27–29,34} reported on cost differences at these time points. All 6 studies^{11,12,27–29,34} reported 1-month costs of PICC to be lower than those of IPC. Further, 4 studies^{11,28,29,34} reported costs at 6 months and also reported lower costs with PICC than with IPC. However, these same 4 studies also reported costs at 12 months, by which time the costs of PICC have become greater than those of IPC.

Discussion

Summary of Main Findings

After a comprehensive literature review, 15 cohort studies involving more than 8000 cancer patients receiving chemotherapy were included in this study. Study quality was high (grade A), and recording of outcomes (complications) was relatively complete, consistent with previous systematic review studies.^{37,38}

Practitioners should select the suitable type of catheter according to the patient’s physical conditions, 1-puncture success rate, catheter life span, complication rates, cost, and other factors.³³ Higher complication rates associate with PICC, and the higher accidental removal rate compared with IPC may have been responsible for the shorter life span of the PICC compared with IPC.³⁹ As indicated in the INS “Infusion Therapy Standards of Practice” in 2016, a PICC’s duration of placement should be from several months to 1 year.⁴⁰ However, several studies have shown that an IPC can be used for 19.2 to 38.5 years if nurses follow maintenance procedures.⁴¹ Furthermore, for patients who have treatment for more than 1 year, the use of IPC can avoid the pain caused by repeated puncture.

The overall incidence of all 7 complications included in this study was higher with PICC compared with IPC. Malignancy itself and the chemotherapies that are infused through the CVCs increase the risk of thrombosis and vessel or line occlusion.⁴² This meta-analysis demonstrated a higher incidence of PICC thrombosis and occlusion than that of IPC. Another systematic review of catheter-related thrombosis risk factors in cancer patients obtained similar results.⁴³ Possible explanations may be

that the IPC has a short route into the blood vessels and thus delivers relatively little stimulation to the vessel walls, whereas vessel entry in PICC patients involves a longer length of catheter. The resultant mechanical stimulation to vascular endothelial cells by a foreign material may promote the activation of thrombotic factors, inducing occlusion of the vessels.

This study also showed the incidence of IPC malposition, extravasation, phlebitis, and accidental removal was lower than that of PICC. It may be that the IPC base, fixed into the chest wall, provides a sturdier access point that rarely moves as the upper limbs move. In contrast, the PICC puncture point is often located in the arm and is more prone to movement during upper limb exertion, strenuous exercise, or even mobilizing.

Incidence of PICC infection was higher than that of IPC, which is consistent with the results of the subgroup analysis. Bouza et al⁴⁴ have shown that infections are most likely to come from the skin (65%), catheter or catheter joints (30%), or other pathways (15%). The puncture seat and catheter of IPC are implanted completely under the skin without any device in vitro, whereas the PICC includes an external section, through which microbes in the skin may migrate to enter the subcutaneous portions, or importantly the blood, increasing the likelihood of infection.

This study compared the total cost of 2 CVCs. The descriptive results showed that IPC cost was higher than PICC cost at 1 and 6 months, whereas IPC cost was lower than PICC cost by 12 months. Cancer patients need to pay for the CVC in 2 aspects, one is the necessary cost of catheterization, including material cost, site cost, and medical staff remuneration. The other is the cost of post-catheter maintenance, including the cost of materials for catheter maintenance and the cost of labor compensation, transportation, and management of catheter complications. Because the price of IPC is much higher than that of PICC, the cost of IPC is also higher than that of PICC at the beginning of catheterization. However, IPC patients generally need to be maintained only once every 4 weeks in the hospital, whereas PICC patients need to be maintained once a week in the hospital, which greatly increases the maintenance cost of PICC patients. In addition, PICC complications appear greater than IPC, leading to higher complication treatment costs. Thus, is it easier to see how longer-term costs of IPC are lower than those of PICC, which is consistent with the cost analysis results of a randomized controlled trial carried out by Patel et al.⁴⁵

Limitations

Variations in cancer type, patient age, and gender among participants in the cohort studies often influence clinician’s decisions

regarding the type of CVC to be used. In combination with insufficient information reporting on the severity of the disease and complications, there is likely to have been a failure to effectively control for such confounding factors, potentially leading to bias with the results. Further, variations in the specific methods of catheterization, the particular devices used, catheter material, starting time, catheter maintenance method, and frequency mean that these confounders may also have not been controlled for. Outcome measure reporting may have been incomplete, and subjective indicators such as patient satisfaction and quality of life were not included. This study did not investigate complications such as the incidence of arterial puncture and pneumothorax; however, there are reports^{46,47} that the incidence of such complications is lower when using PICC compared with IPC. Finally, there may be publication bias caused by incomplete literature collection because only published Chinese and English documents have been retrieved. Thus, the conclusions of this meta-analysis should be interpreted with caution.

■ Conclusions

With the continuous improvements in medical technology, it is possible for cancer patients to survive with their illnesses for many years, making the application of CVCs more and more pertinent. According to this meta-analysis, IPC was superior to PICC in terms of catheter life span, incidence of complications, and long-term costs. Researchers also found that health education is needed in future practice before catheterization to help patients realize the benefit of implementing IPC. Therefore, we recommended that practitioners consider IPC placement for cancer patients needing long-term chemotherapy where technology is available. In addition, we suggest local government departments include IPC in the reimbursement system of medical insurance, to further reduce the medical expenses of patients.

ACKNOWLEDGMENTS

The authors thank Dr Shi-Zheng Du of the School of Nursing, Nanjing University of Chinese Medicine, for his guidance on meta-analysis. They also thank Chun-Li Liu of PICC catheterization room, Jiangu Cancer Hospital, for her experience in catheters.

References

1. Melaku YA, Appleton SL, Gill TK, et al. Incidence, prevalence, mortality, disability-adjusted life years and risk factors of cancer in Australia and comparison with OECD countries, 1990–2015: findings from the Global Burden of Disease Study 2015. *Cancer Epidemiol.* 2018;52:43–54.
2. Gandhi J, Davidson C, Hall C, et al. Population-based study demonstrating an increase in colorectal cancer in young patients. *Br J Surg.* 2017;104(8):1063–1068.
3. Ang P, Chia KH, Teoh MK, Wong KK. Use of a peripherally implanted subcutaneous permanent central venous access device for chemotherapy—the Singapore General Hospital experience. *Aust N Z J Med.* 2000;30(4):470–474.
4. Skaff ER, Doucette S, McDiarmid S, Huebsch L, Sabloff M. Vascular access devices in leukemia: a retrospective review amongst patients treated at the

- Ottawa Hospital with induction chemotherapy for acute leukemia. *Leuk Lymphoma.* 2012;53(6):1090–1095.
5. Masoorli S. Nerve injuries related to vascular access insertion and assessment. *J Infus Nurs.* 2007;30(6):346–350.
6. Silvestri V, Nerini L, Missio G, et al. Levels of anxiety and pain during chemotherapy with peripheral versus central vascular access: an experimental evaluation. *J Vasc Access.* 2004;5(4):147–153.
7. Goossens GA, Vrebos M, Stas M, De Wever I, Frederickx L. Central vascular access devices in oncology and hematology considered from a different point of view: how do patients experience their vascular access ports? *J Infus Nurs.* 2005;28(1):61–67.
8. Johansson E, Hammarskjöld F, Lundberg D, Arnlind MH. Advantages and disadvantages of peripherally inserted central venous catheters (PICC) compared to other central venous lines: a systematic review of the literature. *Acta Oncol.* 2013;52(5):886–892.
9. Kelly L. A practical guide to safe PICC placement. *Br J Nurs.* 2013;22(8):S13–S14, S16, S18–S19.
10. Gonda SJ, Li R. Principles of subcutaneous port placement. *Tech Vasc Interv Radiol.* 2011;14(4):198–203.
11. Martella F, Salutati V, Marchetti C, et al. A retrospective analysis of trabectedin infusion by peripherally inserted central venous catheters: a multicentric Italian experience. *Anticancer Drugs.* 2015;26(9):990–994.
12. Rotzinger R, Gebauer B, Schnapauff D et al. Placement of central venous port catheters and peripherally inserted central catheters in the routine clinical setting of a radiology department: analysis of costs and intervention duration learning curve. *Acta Radiol.* 2017;58(12):1468–1475.
13. Tan J, Liu L, Xie J, Hu L, Yang Q, Wang H. Cost-effectiveness analysis of ultrasound-guided Seldinger peripherally inserted central catheters (PICC). *Springerplus.* 2016;5(1):2051.
14. O'Brien J, Paquet F, Lindsay R, Valenti D. Insertion of PICCs with minimum number of lumens reduces complications and costs. *J Am Coll Radiol.* 2013;10(11):864–868.
15. Walshe LJ, Malak SF, Eagan J, Sepkowitz KA. Complication rates among cancer patients with peripherally inserted central catheters. *J Clin Oncol.* 2002;20:3276–3281.
16. Worth LJ, Seymour JF, Slavin MA. Infective and thrombotic complications of central venous catheters in patients with hematological malignancy: prospective evaluation of no tunneled devices. *Support Care Cancer.* 2009;17:811–818.
17. Chan RJ, Northfield S, Larsen E, et al. Central venous access device securement and dressing effectiveness for peripherally inserted central catheters in adult acute hospital patients (CASCADE): a pilot randomised controlled trial. *Trials.* 2017;18(1):458.
18. Dasgupta N, Patel MN, Racadio JM, Johnson ND, Lungren MP. Comparison of complications between pediatric peripherally inserted central catheter placement techniques. *Pediatr Radiol.* 2016;46(10):1439–1443.
19. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-analyses: the PRISMA statement. *Int J Surg.* 2010;8(5):336–341.
20. Higgins J, Green S. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0.* The Cochrane Collaboration; 2011. <http://handbook.cochrane.org/>. Accessed August 2018.
21. Wells G, Shea B, Connell D. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. <http://www.ohri.ca/programs/clinical-epidemiology/oxford.asp>. Accessed August 2018.
22. Department CIKM. RevMan 5 Download and Installation. <http://tech.cochrane.org/revman/download>. Accessed September 15, 2016.
23. Thorlund K, Imberger G, Johnston BC, et al. Evolution of heterogeneity (I^2) estimates and their 95% confidence intervals in large meta-analyses. *PLoS One.* 2012;7(7):e39471.
24. Karin C, Mohammed A, David S, Kenningham RR, Ahmed S. A comparison of infections and complications in central venous catheters in adults with solid tumors. *J Vasc Access.* 2015;16(1):38–41.

25. Jain SA, Shukla SN, Talati SS, et al. A retrospective study of central venous catheters GCRI experience. *Indian J Med Paediatr Oncol.* 2013;34(4): 238–241.
26. Verboom MC, Ouwerkerk J, Steeghs N, et al. Central venous access related adverse events after trabectedin infusions in soft tissue sarcoma patients; experience and management in a nationwide multi-center study. *Clin Sarcoma Res.* 2017;7(2).
27. Viart H, Combe C, Martinelli T, Thomas J, Hida H. Comparison between implantation costs of peripherally inserted central catheter and implanted subcutaneous ports. *Ann Pharm Fr.* 2015;73(3):239–244.
28. Fang S, Yang J, Song L, Jiang Y, Liu Y. Comparison of three types of central venous catheters in patients with malignant tumor receiving chemotherapy. *Patient Prefer Adherence.* 2017;11:1197–1204.
29. Wang N, Dong Y, Zhang B, Gao YJ, Fu H. Comparison of the application of IVPA and PICC in breast cancer patients. *Med Philos B.* 2016;37(7): 36–38.
30. Bratton J, Johnstone PA, McMullen KP. Outpatient management of vascular access devices in children receiving radiotherapy: complications and morbidity. *Pediatr Blood Cancer.* 2014;61(3):499–501.
31. Lefebvre L, Noyon E, Georgescu D, et al. Port catheter versus peripherally inserted central catheter for postoperative chemotherapy in early breast cancer: a retrospective analysis of 448 patients. *Support Care Cancer.* 2016;24(3):1397–1403.
32. Revel-Vilk S, Yacobovich J, Tamary H, et al. Risk factors for central venous catheter thrombotic complications in children and adolescents with cancer. *Cancer.* 2010;116(17):4197–4205.
33. Kim HJ, Yun J, Kim HJ, et al. Safety and effectiveness of central venous catheterization in patients with cancer: prospective observational study. *J Korean Med Sci.* 2010;25(12):1748–1753.
34. Lu XT, Gao RF, Zhang YF. Clinical use of ultrasound-guided implantable venous access port versus PICC in chemotherapy of breast cancer. *Chin Remedies Clin.* 2017;17(1):13–16.
35. Tang PL, Chen LF, Cheng SZ, Zhou XM, Wang HY, Hou QX. The maintenance comparison of applying PICC and VPA among cancer patients undergoing chemotherapy. *Chin Nurs Manage.* 2014;14(4):420–422.
36. Liu Y. Comparison of implanted vascular access ports and PICC in breast cancer patients. *Chin J Prac Nurs.* 2017;10(18):1413–1416.
37. Sun DH, Zhang L, Chu J. Clinical effect of venous-access ports and PICC in patients with tumor chemotherapy: a systematic evaluation. *Chin Nurs Res.* 2018;32(9):1407–1414.
38. Sun YY, Gao W, Cui Y, et al. A systematic review on the effects of venous access port and PICC in cancer patients undergoing chemotherapy. *J Shandong Univ (Health Sci).* 2015;53(10):73–81.
39. Kabsy Y, Baudin G, Vinti H, et al. Peripherally inserted central catheters (PICC) in onco-hematology. PICC line in onco-hematology. *Bull Cancer.* 2010;97(9):1067–1071.
40. Infusion Nurses Society. Infusion therapy standards of practice. *J Infus Nurs.* 2016;39(1S):S8. S93–S94
41. 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):12–16.
42. Singh G, Rathi AK, Singh K, Sharma D. Venous thromboembolism in cancer patients—magnitude of problem, approach, and management. *Indian J Cancer.* 2017;54(1):308–312.
43. Saber W, Moua T, Williams EC, et al. Risk factors for catheter related thrombosis (CRT) in cancer patients: a patient level data (IPD) meta-analysis of clinical trials and prospective studies. *J Thromb Haemost.* 2011; 9(2):312319.
44. Bouza E, Burillo A, Munoz P. Catheter related infections: diagnosis and intravascular treatment. *Clin Microbiol Infect.* 2002;8(5):265274.
45. Patel GS, Jain K, Kumar R, et al. Comparison of peripherally inserted central venous catheters (PICC) versus subcutaneously implanted port-chamber catheters by complication and cost for patients receiving chemotherapy for non-hematological malignancies. *Support Care Cancer.* 2014;22(1): 121–128.
46. Narducci F, Jean-Laurent M, Boulanger L, et al. Totally implantable venous access port systems and risk factors for complications: a one-year prospective study in a cancer centre. *Eur J Surg Oncol.* 2011;37(10):913–918.
47. Chang YF, Lo AC, Tsai CH, et al. Higher complication risk of totally implantable venous access port systems in patients with advanced cancer—a single institution retrospective analysis. *Palliat Med.* 2013;27(2):185–191.