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Identifying the impact of the Zone Insertion Method™ (ZIM™): A randomized controlled trial

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Abstract

Background: In 2011, Dawson proposed the Zone Insertion Method™ (ZIM™) to identify the optimal peripherally inserted central catheters (PICCs) insertion site in the upper arm. However, data on the effectiveness and safety of the ZIM™ in guiding PICC placement in Chinese population is limited.

Methods: In this randomized controlled trial, 120 cancer patients were randomly assigned to the upper portion of the red zone (RZ), the green zone (GZ) and the lower portion of the yellow zone (YZ) groups (at a 1:1:1 ratio). The aim was to compare the degree of patient comfort and the incidence of major PICC complications among the three insertion zones based on the ZIM™ in a Chinese Cancer Center. (Clinical Trials. Gov number, ChiCTR1900024111)

Results: A total of 118 catheters were inserted in 118 patients (2 patients were lost to follow-up). After the 1-month follow-up, patients randomly assigned to the YZ group had a higher degree of comfort with a lower score than those assigned to the other two zone groups: 30.21±3.16 in the YZ group versus 31.65±2.51 in the RZ group and 31.59±2.92 in the GZ group (P=.046). The incidence of thrombosis (10/40, 25%) and occlusion (4/40, 10%) in the RZ, which were significantly higher than those in the other two zone groups (χ^2 =7.368, P=.02; χ^2 =5.778, P =.03), whereas the risk in the GZ group was similar to that in the YZ group. The incidence of contact dermatitis in the GZ group was significantly higher than that of the other two zone groups (χ^2=12.873, P=.001).

Conclusions: This study found that the lower portion of YZ seems to be another suitable PICC insertion site for a higher degree of comfort and a lower risk of occlusion and thrombosis, which broadens the choice of PICC insertion sites in the upper arm for clinical practice.

Keywords

Zone Insertion Method™ (ZIM™), Peripherally Inserted Central Catheters, Cancer, Randomized controlled trial, Complications

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Background

Peripherally inserted central venous catheters (PICCs) are applied in a wide range of patient groups for longer-term treatment and infusion of irritating medications, such as chemotherapy,[1] extended antibiotic therapy[2] or total parenteral nutrition.[3] According to the previous studies, upper arm is a recommended peripheral catheter insertion location to reduce the incidence of intravascular Catheter-related Infections (CRIs) and thrombosis.[4,5] However, this guideline did not identify the exact insertion site of the upper extremity.

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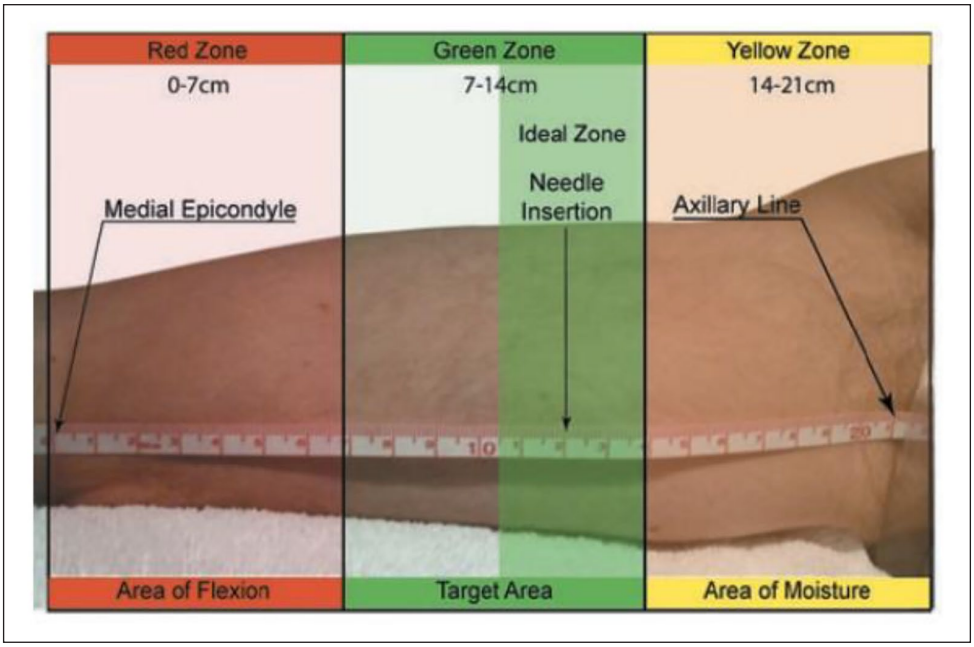

Figure 1. Zone insertion Method (ZIM).
Reprinted with permission from Dawson RB. PICC Zone Insertion Method™(ZIM™): a systematic approach to determine the ideal insertion site for PICCs in the upper arm. Journal of the Association for Vascular Access. 2011;16(3):156-65. © Robert B Dawson 2021.

In 2011, Dawson[6] proposed a systematic method, ZIM™, which uses ultrasound guidance to identify the optimal PICC insertion site in the upper arm. This new method divided the upper arm into three color zones, red, green and yellow, based on the anatomical characteristics of the musculoskeletal tissue, lymph, nerves, skin and vessels.[6] Dawson[6] found that this method greatly reduces the incidence of thrombosis. However, in this observational study, the sample was small, and there was no indication of the client group or whether any higher-risk cancer patients were included. In addition to catheter-related thrombosis, infection,[7] arterial puncture[8] and even CVAD-associated skin impairment (CASI)[9] are the most common and severe complications associated with PICCs. Simultaneously, there is a wide variance in the vessel diameter for peripherally inserted catheter insertion in the upper arms of different groups of people, such as those from the United States,[10] Sweden[11] and China.[12]

Of note, the potential for major PICC complications (e.g., CRI, CLABSI, and CASI) might be associated with the degree of patient comfort. PICCs may cause fear and discomfort, and patients look forward to removing their PICCs as a symbol of the coming freedom.[13]

To date, few studies have investigated the effectiveness and safety of ZIM™ in improving the degree of patient comfort by decreasing PICC complications in the Chinese population. Therefore, the authors performed a randomized controlled study to compare the degree of comfort and the incidence of PICC complications among the three PICC placement sites of the upper arm based on ZIM™ in a Chinese cancer center.

Methods

Participants

Participants were selected between March 1, 2019, and April 31, 2019, and were cancer patients over 18 years of age with a life expectancy of more than four months. Patients who needed to undergo chemotherapy and require a PICC for therapy were eligible for inclusion. Ongoing severe systemic infection, clinically significant upper extremity/central deep venous thrombosis (DVT), superior vena cava compression syndrome, severe coagulopathy, the inability to communicate, an imminent need for a dialysis fistula, and cardiac disease were exclusion criteria. This study was approved by the ethics committees at Sun Yat-sen University Cancer Centre (ClinicalTrials. Gov number, ChiCTR1900024111).

Insertion and maintenance

To control the insertion technique, a modified Seldinger technique under ultrasound and EKG guidance was used to guide PICC insertion by the vascular access nursing team. The lower third of the superior vena cava or Cavo-atrial junction was considered the optimal tip position, which was confirmed by an interventional radiologist. ZIM™ dividing the medial upper arm into three main color zones of red, green and yellow, was applied to select the PICC insertion site[6] (Figure 1). The Red Zone (RZ) starts at the medial epicondyle (MEC) and extends one-third the distance to the axillary line. The green zone (GZ) is located in

the middle third of the upper arm. The Yellow Zone (YZ) is the upper zone or the most proximal third of the upper arm. In this study, the upper portion of the RZ, the lower portion of the YZ and the GZ were considered suitable for catheter placement. PICC placement was performed at the upper portion of the RZ to avoid the elbow triangle and the upper portion of YZ to away from axilla and shoulder. The catheterization site was assigned to participants using a 1:1:1 randomization scheme. 4-Fr silicon single lumen PICCs (Bard Access Systems, Inc., UT, USA and Cathicord™, Shandong Branden Medical Devices Co., Ltd., China) were used in this study.

Postinsertion care and maintenance were standardized with 3M Tegaderm Diamond Pattern Film Dressing 1679 (3M Health Care, St. Paul, MN, USA), needleless connectors (BD Switzerland Sàrl®; Eysin, Switzerland) and StatLock™ PICC Plus Stabilization Device (Bard Access Systems, Inc., UT, USA). Follow-up maintenance was performed weekly or as required if the dressing lifted. Furthermore, 0.9% sodium chloride was already introduced as a locking and flushing solution.

Outcomes and definition

A primary outcome evaluated by Li et al.[14] was the degree of patient comfort and was assessed using a specifically developed questionnaire. According to Li et al.[14] the questionnaire's valid content rate (VCR) was 0.8, and its Cronbach's α was 0.62. Patients' degree of comfort was measured during PICC placement by Questionnaire 1 and 1 month after PICC placement by Questionnaire 2 (Appendix 1). The second outcome was the PICC complications, including thrombosis, infection, occlusion, contact dermatitis and so on. Complications (Appendix 2) were identified and monitored by the vascular access nursing team until the PICC was removed.

Study design

A prospective randomized controlled study was conducted to compare cancer patients' degree of comfort and the incidence of catheter complications among three different insertion sites based on ZIM™[6]. Patients were randomly assigned to groups using a 1:1:1 allocation ratio.

Sample size and randomization

The calculation formula of the multisampling rate comparison in the group design with a two-tailed α of 0.05 and a power of 0.80 was used. The sample ratio of the groups was 1:1:1. The trial was designed to compare the degree of patient comfort and the incidence of catheter complications among the three groups. Previous literature reports[15,16] estimated that the comfort levels of patients in the three insertion zones were 45% in the RZ, 80% in the GZ and 40% in the YZ. To allow for a 20% dropout rate after randomization, we aimed to include 40 patients in each group.

Patients were recruited for eligibility by the nursing staff in intravenous therapy clinics. Eligible patients were subsequently informed and included by a PICC specialized nurse at the intravenous therapy clinic. The randomization sequence was computer-generated and prepared by an independent statistician using a block size of three. Data at the time of randomization, during catheter placement, and at follow-up after 1 month were collected and registered by the staff in the clinical trial unit.

Data collection

Patient data were retrieved from the hospital information system. The following variables were recorded: demographic and background data, the patients' degree of comfort (during PICC placement and 1 month after PICC placement), insertion characteristics and PICC complications. Clinical parameters, including BMI, white blood cell count and red blood cell count, within the first 24 hours of PICC placement were also recorded. All patients were followed until PICC removal, and major PICC complications were recorded. All outcomes were ascertained by medical record review, telephone follow-up, or both after PICC placement.

Statistical analysis

Continuous variables are expressed as means (SD), and qualitative variables are presented as frequencies (n) and percentages (%). Comparisons of the three groups were performed with the χ^2 test, ANOVA or Kruskal-Wallis test, depending on whether the data were discrete or continuous and whether the distributions were normal. The χ^2 test was used to compare categorical variables, and ANOVA or the Kruskal-Wallis test were used for continuous variables. All significant variables associated with the degree of patient comfort and catheter-related complications were assessed using the Wilcoxon rank-sum test with the use of the Kruskal-Wallis procedure. A two-tailed p-value of less than 0.05 was considered statistically significant. The data were managed and analyzed using IBM SPSS Statistics for Mac Version 25.0 (IBM Corp., Armonk, NY, USA).

Result

Baseline characteristics

Of the participants recruited, only 2 out of 120 patients were lost to follow-up. The study population retained for analysis included 118 patients; and over a 3-month period, the 118 patients with 118 PICCs (40 RZ, 39 GZ and 39 YZ) (Figure 2) were reviewed over 12,855 catheter days. Many PICCs remaining in situ were removed due to the completion of treatment (115, 97.5%), and 3

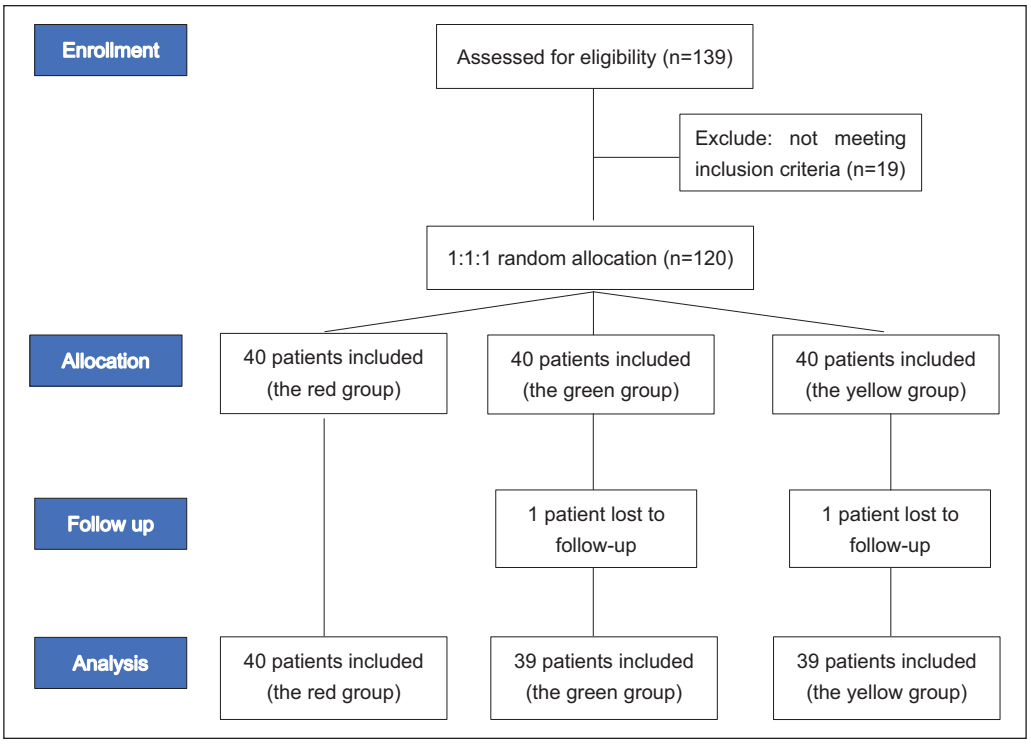

Figure 2. Screening and Randomization of Catheter Insertions.

PICCs (2.5%) were removed due to complications (e.g., infection, occlusion, and thrombosis). In the overall population, the male-to-female ratio was approximately 2:1. PICC insertion was most commonly conducted in patients with nasopharyngeal carcinoma (55, 46.6%), lymphoma (20, 16.9%), genitourinary tumors (15, 12.7%) and other tumors (28, 23.7%). This difference was not statistically significant ($P = .43$). In the three groups, chemotherapy was the main purpose of PICC placement. Except for the RBC count, the baseline characteristics between the three groups were balanced, as shown in Table 1.

Data related to PICC placement

Table 2 presents the data related to PICC placement. Vein diameter was significantly larger in the YZ at 3.0 (2.9-3.4) mm versus 2.9 (2.8-3.0) mm in the RZ and 2.9 (2.8-3.1) mm in the GZ ($P = .003$). The amount of bleeding was significantly different between the three groups (Table 2). The amount of bleeding in patients randomly assigned to the RZ was significantly lower than that for patients with PICC placements in the green and yellow insertion zones ($Z = 10.170$, $P = .006$). The catheter insertion length was longest in the RZ, 41.4 ± 2.9 cm versus 38.8 ± 2.9 cm in the GZ and 35.5 ± 2.8 cm in the YZ ($P < .001$). The distance from the medial epicondyle was significantly different among the three insertion zones ($P < .001$).

Patients' degree of comfort

There were two questionnaires to assess patients' degree of comfort (Questionnaire 1 with 6 items to assess patients' degree of comfort during the PICC placement procedure and Questionnaire 2 with 14 items to assess patients' degree of comfort after 1 month of PICC placement using a 5-point Likert scale (Appendix 1)). The total score ranged from 6 to 30 in Questionnaire 1 and from 14 to 70 in Questionnaire 2, and a higher score indicated a lower degree of comfort. The patients' degree of comfort during PICC placement among the three insertion zones was not statistically significantly different ($P = .97$) (Table 3). One month after follow-up, patients randomly assigned to the YZ had a higher degree of comfort with a lower score than the other two insertion zones with 30.21 ± 3.16 in the yellow group versus 31.65 ± 2.51 in the red group and 31.59 ± 2.92 in the green group ($P = .046$). In particular, the items "I often feel that the skin covered with dressing is very itchy and unbearable" ($P = .048$) and "I feel that the PICCs affects my appearance" were significantly different among the three groups" ($P = .01$) (Table 4).

Incidence of catheter-related complications

Although many complications were observed during the study, the overall incidence of complications between the three insertion zones was not significantly different ($\chi^{2=}1.071$, $P = .60$). Among the zones, 53.9% (21/39) of

Table 1. Demographic data of the three groups.

Items	Red group (n = 40)	Green group (n = 39)	Yellow group (n = 39)	*P*-value
Age, y	48 ± 14	48 ± 10	51 ± 12	.31
Sex, female n (%)	13 (32.5)	14 (35.9)	17 (43.6)	.59
Marital status n (%)				.87
Married/Divorced	37 (92.5)	37 (94.9)	38 (97.4)	
Single	3 (7.5)	2 (5.1)	1 (2.6)	
Levels of education n (%)				.75
Primary education	7 (17.5)	9 (23.1)	8 (20.5)	
Secondary education	15 (37.5)	16 (41.0)	12 (30.8)	
High school diploma	11 (27.5)	6 (12.8)	10 (25.6)	
Bachelor's or above	7 (17.5)	9 (23.1)	9 (23.1)	
Work schedules n (%)				.48
Full-time	24 (60)	23 (59.0)	22 (56.4)	
Part-time	1 (2.5)	4 (10.3)	1 (2.6)	
Unemployment	15 (37.5)	12 (30.8)	16 (41.0)	
Treatments for cancer n (%)				.52
Radio and chemotherapy	25 (62.5)	27 (69.2)	17 (43.6)	
Radio or chemotherapy	15 (37.5)	12 (30.8)	22 (56.4)	
Diagnosis n (%)				.43
Nasopharyngeal carcinoma	19 (47.5)	21 (53.8)	15 (38.5)	
Lymphoma	6 (15.0)	4 (10.3)	10 (25.6)	
Genitourinary tumors	4 (10.0)	4 (10.3)	7 (17.9)	
Other types of tumors	11 (27.5)	10 (25.6)	7 (17.9)	
Comorbidities n (%)	5 (12.5)	5 (12.8)	5 (12.8)	1.00
BMI	22.3 ± 3.8	23.5 ± 2.8	22.9 ± 3.2	.28
WBC	6.8 ± 2.8	7.6 ± 3.1	6.6 ± 2.3	.23
RBC	4.6 ± 0.7	5.0 ± 0.8	4.5 ± 0.60	.02

the catheters had at least one complication in the GZ, followed by the YZ (19/39, 48.7%) and RZ (19/40, 47.5%). The most common complications in the RZ were thrombosis (10/40,25%) and occlusion (4/40,10%), which were significantly higher than those in the other two insertion zones (χ^2 =7.368, *P*=.02; χ^2 =5.778, *P*=.03), whereas the risk in the GZ was similar to that in the YZ. The incidence of catheter dislodgement/migration was highest in the YZ (10/39, 25.6%) compared to four cases in the RZ and six cases in the GZ, but no statistically significant difference was detected (*P*=.20). Contact dermatitis was the most common complication in the GZ (10/39, 25.6%), which was significantly higher than the numbers in the red and yellow insertion zones (χ^2=12.873, *P*<.001). There were no significant differences in the incidence of infection and lymphatic leakage among the three insertion zones. Table 5 details the incidence of individual complications noted during the study.

Discussion

Although the GZ is a commonly recommended PICC insertion site,[6] patients with PICC placement in the YZ felt more comfortable despite the overall incidence of catheter-related complications not differing among the three insertion zones in this study. Notably, catheterization in the RZ was associated with a significantly higher risk of the combined outcome of catheter-related thrombosis and occlusion, and affected patients' appearance. Simultaneously, the GZ was associated with an increased risk of contact dermatitis.

Degree of Patient comfort

Surprisingly, in the results of the patients' comfort questionnaire, this study found that the patients with PICC placement in the YZ felt more comfortable than patients with PICC placement in the other insertion zones after 1 month of PICC placement. In item of 13, more patients with PICC placement in the RZ felt that PICC placement affected their appearance. It is well accepted that placement of the PICC in the red insertion area is more difficult to cover with a sleeve, especially in the summer, because the PICC is located close to the inner side of the medial epicondyle (MEC).

Additionally, in item of 8, more patients with PICC placement in the GZ felt that the skin covered with the dressing was very itchy and unbearable. In the current

Table 2. Insertion Characteristics (n = 118).

Items	Red group (n = 40)	Green group (n = 39)	Yellow group (n = 39)	χ2/F/Z	*P*-value
Brand of PICC line n (%)				0.458	.94
Cathicord ™	6 (15.0)	4 (10.3)	5 (12.8)		
BARD	34 (85.0)	35 (89.7)	34 (87.2)		
Insertion arm n (%)				0.143	.97
Left	24 (60)	24 (61.5)	25 (64.1)		
Right	16 (40)	15 (38.5)	14 (35.9)		
Insertion vein n (%)				1.241	.54
Basilar	36 (90)	36 (92.3)	33 (84.6)		
Brachial	4 (10)	3 (7.7)	6 (15.4)		
Arm circumference (cm)	26.6 ± 3.7	27.9 ± 2.7	28.8 ± 3.0	5.100	.008
The length of the upper arm (cm)	21.7 ± 1.4	21.2 ± 1.1	21.6 ± 1.3	1.975	.14
Vessel depth (cm)	0.5 ± 0.3	0.6 ± 0.3	0.6 ± 0.2	0.601	.55
Distance from the medial epicondyle (cm)				189.590	<.001
< 7	39 (97.5)	1 (2.5)	0 (0.0)		
8-14	1 (2.6)	38 (97.4)	6 (15.4)		
>14	0 (0.0)	0 (0.0)	33 (84.6)		
Length of PICC insertion (cm)	41.4 ± 2.9	38.8 ± 2.9	35.5 ± 2.8	41.669	<.001
Blood vessel diameter, median (IQR), mm	2.9 (2.8-3.0)	2.9 (2.8-3.1)	3.0 (2.9-3.4)	11.955	.003
Puncture attempts (n, %)				4.223	.07
Once	40 (100.0)	39 (100.0)	36 (92.7)		
Over twice	0 (0.0)	0 (0.0)	3 (7.7)		
Amount of blood loss, median (IQR), g	0.8 (0.6-1.1)	1.0 (0.6-1.5)	1.3 (0.8-2.2)	10.170	.006
Duration of catheter use (days)	110 ± 37	112 ± 54	103 ± 50	0.354	.70

Table 3. Degree of patient comfort during PICC placement (n = 118).

Items	Red group (n = 40)	Green group (n = 39)	Yellow group (n = 39)	*P*-value
The pain at the puncture point is unbearable during puncture.	2.05 ± 0.32	2.03 ± 0.16	2.15 ± 0.49	.23
I understand the nurses' instructions and cooperate with the nurses to complete PICC catheterization.	3.83 ± 0.39	3.87 ± 0.41	3.72 ± 0.51	.29
It is unbearable to insist on completing the entire PICC placement procedure.	2.00 ± 0.01	1.95 ± 0.22	2.00 ± 0.01	.13
Maintaining the posture of the arm during PICC placement is very uncomfortable.	3.98 ± 0.16	4.03 ± 0.16	4.00 ± 0.01	.23
Repeated punctures after failure of the first puncture causes suffering.	2.00 ± 0.01	2.05 ± 0.32	2.00 ± 0.01	.34
It is difficult to get my chin close to the collarbone during PICC placement.	2.00 ± 0.01	2.03 ± 0.16	2.00 ± 0.01	.37
Total score	13.90 ± 55	13.87 ± 57	13.87 ± 66	.97

study, 12.7% of the included patients developed CAVD-associated contact dermatitis, and 66.7% of the cases of contact dermatitis were found in the GZ. This overall incidence of contact dermatitis in this study agreed with previous studies,[17,18] which demonstrated that approximately 9.3% to 14.8% of patients develop CVAD-associated contact dermatitis. In the current study, the GZ tended to have a higher incidence of contact dermatitis than the other insertion zones. This result may be explained by the frictional irritancy caused by the sleeve of a short sleeve T-shirt for the observational period in summer. As in previous studies, chemicals were the main cause of contact dermatitis, and frictional irritancy (e.g., clothes, footwear, N95 respirator mask) is often one of several factors contributing to dermatitis and is underrecognized.[19,20]

Currently, multiple factors are involved in contact dermatitis caused by CVAD, including population differences, aging, skin conditions, dressing products, poor dressing integrity and treatment characteristics (e.g., chemotherapy characteristics).[17,21] It is undeniable that contract dermatitis in patients with cancer is associated with reduced health-related quality of life.[13] This is because

Table 4. Degree of patient comfort 1 month after PICC placement (n = 118).

Items	Red group (n = 40)	Green group (n = 39)	Yellow group (n = 39)	*P*-value
1. I am afraid of the catheter being pressed and being unable to sleep well.	2.00 ± 0.45	2.00 ± 0.40	1.87 ± 0.57	.40
2. I often worry about the puncture site oozing.	2.00 ± 0.39	2.05 ± 0.39	2.08 ± 0.53	.74
3. I am afraid that the PICC will cause serious complications.	2.03 ± 0.58	2.03 ± 0.63	2.21 ± 0.77	.38
4. The catheter will not make my daily life inconvenient.	2.95 ± 1.01	2.82 ± 1.00	2.69 ± 0.95	.51
5. The catheter remaining in place will influence my movement.	2.58 ± 0.90	2.79 ± 0.98	2.38 ± 0.78	.13
6. I often feel rheumatic jerks in the arm where the PICC was inserted.	2.17 ± 0.55	2.13 ± 0.41	2.05 ± 0.22	.42
7. When I move the arm with the PICC, I feel pulling.	2.05 ± 0.32	2.05 ± 0.32	2.10 ± 0.45	.77
8. I often feel that the skin covered with the PICC transparent dressing is very itchy and unbearable.	2.13 ± 0.56	2.23 ± 0.58	1.95 ± 0.32	.048
9. I often feel pain at the PICC puncture site.	2.10 ± 0.44	1.97 ± 0.16	2.00 ± 0.00	.10
10. I always feel numbness in the finger on the PICC placement side.	1.98 ± 0.16	2.00 ± 0.23	2.10 ± 0.45	.15
11. I feel tired because I am afraid of bending the catheter and try to keep my arm straight.	1.65 ± 0.63	1.56 ± 0.55	1.87 ± 0.70	.09
12. The maintenance of PICC every 7 days takes too much time.	2.17 ± 0.55	2.28 ± 0.69	2.10 ± 0.50	.40
13. I feel that the PICC line affects my appearance.	3.15 ± 0.98	3.08 ± 1.01	2.54 ± 0.88	.01
14. I am afraid that others will see the PICC and feel embarrassed.	2.70 ± 0.97	2.59 ± 0.91	2.2.6 ± 0.677	.06
Total score	31.65 ± 2.51	31.59 ± 2.92	30.21 ± 3.16	.046

Table 5. Incidence of complications and comparison of the two groups (n = 118).

Items (n)%	Red group (n = 40)	Green group (n = 39)	Yellow group (n = 39)	Overall (n = 118)	$\chi 2$	*P*-value
Overall complications during PICC procedure	1 (2.5)	1 (2.6)	2 (5.1)	4 (3.4)	0.702	.85
Overall complications after PICC placement	19 (47.5)	21 (53.9)	19 (48.7)	59 (50)	1.071	.60
Occlusion	4 (10.0)	0 (0.0)	0 (0.0)	4 (3.4)	5.778	.03
Infection	0 (0.0)	2 (5.0)	1 (2.6)	3 (2.5)	1.921	.32
Thrombosis	10 (25.0)	2 (5.1)	3 (7.7)	15 (12.7)	7.368	.02
Contact dermatitis	0 (0.0)	10 (25.6)	5 (12.8)	15 (12.7)	12.873	.001
Lymphatic leakage	1 (2.5)	1 (2.6)	0 (0.0)	2 (1.7)	1.243	1.00
Catheter dislodgment or migration	4 (10.0)	6 (15.4)	10 (25.6)	20 (16.9)	3.360	.19

contact dermatitis may involve other distressing and uncomfortable symptoms, including stinging or itching. Consequently, contact dermatitis cannot be overemphasized, and the clinician must concurrently address patient comfort.

Incidence of catheter-related complications

Thrombosis is a serious complication of PICCs and seems to be higher in critically ill patients and those with malignant cancer.[22] In the current study, the incidence of thrombosis was 12.7%, and the majority, 65% (10/15), was found in the RZ (the upper portion of the RZ). The higher incidence of thrombosis occurring in the RZ is consistent with the study conducted by Dawson.[6] This is because the compression of tissue and muscle in this area with elbow joint flexion can lead to catheter movement, bleeding, ecchymosis, and vein irritation.[6] In the current study, PICC placement was performed at the upper portion of the RZ to avoid the elbow triangle. Despite this, RZ insertion still had a higher incidence of thrombosis. A possible explanation for this might be that the vessel diameter of the RZ was generally smaller than those of the other two zones in the current study. According to the previous studies,[23,24] the catheter-to-vein ratio (CVR) is 1:3, which is an important dependent factor associated with thrombosis. Alternatively, more proximal venipuncture (e.g., brachial and basilic veins ascending toward the axilla) can provide larger blood vessels and reduce the incidence of DVT.[24,25]

Additionally, the incidence of occlusion (10%) was also higher in the RZ than in the other two insertion zones in the current study. Furthermore, there were four patients with catheter obstruction in the red group, and three of them suffered from CRT. There are three types of catheter occlusions, including mechanical obstruction, obstruction related to drug or parenteral nutrition, and thrombotic obstruction.[26] The reported incidence of catheter occlusion in prospective patients has ranged from 2.3 to 35%.[27,28] However, catheter occlusion was found in over 60 percent

of pediatric patients with malignant cancer and those undergoing antineoplastic chemotherapy.[29] Stephens et al.[30] also highlighted that thrombotic catheter occlusion accounted for 60% of all catheter occlusions. This is because catheters can also become occluded secondary to a thrombotic process, such as a fibrin sheath around the catheter tip, an intraluminal blood clot, or venous thrombosis, which can occur separately or in combination.[26]

Another possible explanation for this is that the longer length of the catheter might increase the resistance to flushing and produce more reflux in the catheter as the body moves.[31,32] As previously mentioned, the length of PICC placement in the RZ was generally longer than those in the other two zones in this study, which might increase the incidence of catheter occlusion. Catheter occlusion is one of the most common complications of PICCs, which cause the accidental removal of the catheter and delay or interrupt infusion therapy.[33–35] In general, these data highlight the importance and relevance of catheter occlusion related to catheter-related venous thrombosis for clinicians or the vascular access nursing team when choosing the optimal insertion zone for PICC placement.

Limitations

This study has potential limitations. First, the sample size of this study might be insufficient, and this study was conducted in a single center. However, the center is the major oncology and teaching hospital in the region with a wide range of specialties. For this reason, the patient population is likely to be representative of similar hospitals. Second, irritant contact dermatitis (ICD) and allergic contact dermatitis (ACD) were not distinguished in the current study, because it is virtually impossible to distinguish ICD from ACD clinically.

Third, this research did not distinguish upper GZ as the proposed ideal zone for insertion by Dawson.[6] Although GZ may be more acceptable as proposed by Dawson,[6] this research identified the upper RZ and the lower YZ to explore a more specific proposed insertion zone and find the lower YZ was the most comfortable zone. Fourth, The CVR recommended by the most vascular access experts is 1:3,[23,24] although a study by Sharp et al.[25] explained that $<45\%$ was a risk prevention strategy. Thus, according to the 1:3 rule as above, using 4Fr PICCs in veins less than 4mm in the current study did not satisfy this rule and might influence the incidence of thrombosis. The future studies should accurately measure an appropriately sized vessel prior to device insertion to help reduce the risk of thrombosis.

Last, the physiological change of the tip position will move up 2 cm or down 2 cm during the arm movement,[36] especially the PICC insertion in the lower RZ close to the medial epicondyle (MEC). In order to stay away from MEC, the upper RZ was selected in this study to avoid risk factors related to RZ characteristics.

Conclusions

In conclusion, PICC-related complications were associated with the degree of patient comfort. This study found that patients who receive PICC placement in the lower portion of the YZ had a higher degree of comfort because of the lower incidence of contact dermatitis and less influence on patient appearance. In addition, the risk of occlusion and thrombosis in the lower portion of YZ was lower than the upper portion of RZ, but similar to the risk of GZ. Consequently, the lower portion of YZ seems to be another suitable PICC insertion site in the upper arm, which broadens the choice of PICC insertion sites for clinical practice.

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Author involvement

CLH and ZMW were the primary authors responsible for the design of this study, acquisition of data, analysis and interpret work data, critically revised important knowledge content, and the writing of the manuscript. Both authors also accountable for the final approval of the version to be published. WHH, XHZ, XLL, JLL, and LHL were responsible for the PICC insertion and maintenance, assessing the patients' degree of comfort, and collecting data. JL is corresponding author responsible for communicating with journals during the manuscript submission, peer review, and publication process, responding to editors' inquiries and comments on the work, and cooperating with journals' requests for data or other information when there are questions about the paper after publication.

Declaration of conflicting interests

The authors declare that there is no conflict of interest..

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Ethical statement

Ethical approval was given by the clinical research ethics committee of Sun Yat-sen University Cancer Center with the following reference number: B2019-078-01.

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Supplemental material

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