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ORIGINAL ARTICLE

Routine replacement versus replacement as clinical indicated of peripheral intravenous catheters: A multisite randomised controlled trial

Jing Li RN, MSN[1] | Yanming Ding RN, MSN[1] | Qian Lu PhD[2] | Sanli Jin PhD[2] | Peiying Zhang RN, MSN[1] | Zhixia Jiang RN, PhD[3,4] | Fengxia Zhang RN[5] | Yang Lyu RN, MSN[6] | Frances Lin RN, PhD, FACCCN, SFHEA[7,8,9]

[1]Nursing Department, Peking University First Hospital, Xicheng District, Beijing, China

[2]Peking University School of Nursing, Beijing, China

[3]Guizhou Nursing Vocational College, Guiyang, China

[4]Affiliated Hospital of Zunyi Medical College, Zunyi, China

[5]Miyun Hospital, Beijing, China

[6]Beijing Chao-Yang Hospital, Beijing, China

[7]School of Nursing, Midwifery, and Paramedicine, University of the Sunshine Coast, Queensland, Australia

[8]Sunshine Coast Health Institute, Queensland, Australia

[9]School of Nursing and Midwifery, Menzies Health Institute Queensland, Griffith University, Australia

Correspondence
Jing Li and Yanming Ding, RN, MSN, Nursing Department, Peking University First Hospital, No.8, Xishiku street, Xicheng district, Beijing, 100034, China
Emails: xiaojinghaier@163.com (JL)
dingym60@126.com (YD)

Frances Lin, School of Nursing, Midwifery, and Paramedicine, University of the Sunshine Coast, 90 Sippy Downs Drive, Sippy Downs, Queensland, 4556, Australia.
Email: flin@usc.edu.au

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Abstract

Aims and objectives: To compare the safety of replacing peripheral intravenous catheter as clinically indicated versus routine replacement on patient outcomes in the Chinese context.

Background: Some evidence from developed countries recommend replacing peripheral intravenous catheter as clinically indicated; however, there is limited evidence from developing countries.

Design: A multisite randomised controlled trial.

Methods: The 3050 participants from three hospitals in China were randomly assigned to clinically indicated or routine replacement groups. Patients in the clinically indicated group had the catheters kept in situ until any of the following clinical signs appeared: phlebitis, infiltration, occlusion, displacement, local infection and diagnosed catheter-related bloodstream infection. Patients in the routine replacement group had their peripheral intravenous catheters replaced every 96 hours. The outcomes of phlebitis, infiltration, occlusion, displacement; catheter-related bloodstream infection, all-cause bloodstream infection, and local infection were compared. CONSORT checklist was used to guide the reporting of this RCT.

Results: The risk of phlebitis, phlebitis per 1000 catheter days, occlusion, dislodgement, all bloodstream infections, local infection and mortality between the two groups were not significantly different. The risk of infiltration was increased in the clinically indicated group (HR 1.29). There was no catheter-related bloodstream infection reported in either group. Patients' first peripheral intravenous catheter dwelling time and cumulative indwelling time of all peripheral intravenous catheters in the clinically indicated group were significantly longer than the routine replacement group. There was no statistical significant difference in survival times from phlebitis between the two groups.

Registration number: ChiCTRIOR17010665.

Conclusions: In the Chinese context, removing peripheral catheters as clinical indicated did not increase the risk of phlebitis, occlusion, catheter displacement and catheter infection; however, there was an increased infiltration incidence.

Relevance to clinical practice: In developing countries, removing peripheral catheters as clinical indicated is feasible, but more frequent observations of infiltration are highly recommended.

KEYWORDS
catheters, clinical indication, complications, peripheral, phlebitis, randomised controlled trial, replacement, vascular access devices

1 | INTRODUCTION

The peripheral intravenous catheter (PIVC) is an access device inserted into and reside in patients' peripheral veins. PIVC placement is a common invasive clinical procedure with up to 70% of patients admitted to hospitals require the insertion of a PIVC during their hospital stay (Alexandrou et al., 2018). The invasive nature of inserting and managing the PIVCs exposes patients to various complications including phlebitis, infection, infiltration, catheter dislodgement, occlusion, local infection and catheter-associated bloodstream infection (CRBSI), which may contribute to increased morbidity, mortality and prolonged hospital length of stay (LOS) (Lyu & Zhang, 2020; Sato et al., 2017; Simin et al., 2019).

What does this paper contribute to the wider global clinical community?

- In developing countries, removing peripheral catheters as clinical indicated does not increase the risk of phlebitis, occlusion, catheter displacement and catheter infection, but there is an increased infiltration incidence.
- More frequent observations of infiltration are highly recommended when peripheral catheters are in situ over 96h

2 | BACKGROUND

PIVCs were traditionally routinely replaced once every 3–4 days to prevent infection. In recent years, research has been conducted to test the safety of replacing PIVC when clinically indicated (Rickard et al., 2012; Vendramim et al., 2020; Xu et al., 2017). A recent Cochrane review found that there were no significant differences in bloodstream infection rates from any cause, and phlebitis rates between clinically indicated replacement and routine replacement groups (Webster et al., 2019). However, most of the published studies were conducted in developed countries such as England (Barker et al., 2004) and Australia (Rickard et al., 2012; Van Donk et al., 2009; Webster et al., 2008), with small number from developing countries (Nishanth et al., 2009; Vendramim et al., 2020).

A recent single site study conducted in China showed that there were no significant differences in the incidence of phlebitis, catheter occlusion, infiltration and accidental removal between the routine replacement group and the clinically indicated group (Xu et al., 2017). Clinical practice in PIVC management is quite different in China. For example, most hospitalised patients would have at least one PIVC inserted, and most would have an intravenous infusion (IV) infusion (Zeng et al., 2019). In China, the current National Nursing Practice Standards for Intravenous Therapy recommends that PIVCs should be routinely replaced once every 72–96 hours (National Health Commission of People's Republic of China, 2013). Anecdotal evidence suggests that the lack of high-quality research evidence on PIVC replacement in the Chinese population is making it difficult for professional organisations to adopt research evidence from other populations. To date, to our knowledge, there is limited high-quality evidence on the safety of PIVC replacement when clinically indicated in the Chinese population.

Therefore, in this multisite study, we aimed to compare the safety of replacing PIVCs as clinically indicated versus routine replacement on patient outcomes including phlebitis, infiltration, occlusion, displacement, infection and cost in the Chinese population and context. We hoped that the context-specific findings from this study will inform future policy changes on PIVC management in China and other Asian countries. It was hypothesised that there will be no difference in the risk of phlebitis between the patients whose PIVCs were routinely replaced and whose PIVCs were replaced as clinically indicated.

3 | METHODS

3.1 | Study design

This was a multisite, non-blinded, randomised equivalence trial. This trial was registered with the Chinese Clinical Trial Register (ChiCTR, www.chictr.org.cn, registration number: ChiCTRIOR17010665). Consolidated Standards of Reporting Trials (CONSORT) guidelines for reporting parallel group randomised trials checklist was used to guide the reporting of this RCT (Checklist see Supplementary File S1).

3.2 | Study setting

This study was conducted in three hospitals in China. In hospital 1, an 1835-bed tertiary hospital in Beijing, 16 wards were chosen as study sites in this study which included 6 medical wards and 10 surgical wards. Hospital 2 was a 2800-beds tertiary hospital, located in Guizhou Province, China. There were 17 wards chosen as study sites (including 8 medical wards and 9 surgical wards). Both hospitals 1 and 2 provide all range of healthcare services. Hospital 3 was a 940-bed secondary county-level hospital, located in the outskirts of Beijing. It provides primary healthcare services to populations mainly based in the county. There were 11 wards chosen as study sites in this hospital (including 8 medical wards and 3 surgical wards).

3.3 | Sample

3.3.1 | Inclusion and exclusion criteria

Patients were included if they: were aged 18 years or over; were able to give written consent from the patient or their nominated representative; and had a peripheral intravenous catheter in situ with expected intravenous therapy >4 days. Patients were excluded from the study if they: had a current bloodstream infection; had a planned removal of the catheter within 24 hours; had the PIVC in situ >72 hours at the time of screening; and had immunodeficiency diseases or were receiving immunosuppressive therapy.

3.3.2 | Sample size calculation

Sample size was calculated according to the calculation formula of the sample size of the equivalence test of the two sample rates. Published incidence of phlebitis was 11.9% in the routine replacement group and 13.7% in the clinically indicated group in a Chinese study (Xu et al., 2017). The equivalence margin was 6%, assuming a two-tailed 5% type I error rate, 90% power, plus 10% which allows for attrition. Based on this, at least 1520 samples were required for each group, totalling 3040 cases for both groups.

3.4 | Randomisation and blinding

Participants were randomised into either clinically indicated or routine replacement group using a computer-generated allocation randomised sequence (www. randomizer.org). The group allocations were concealed in opaque, sealed envelopes which were numbered consecutively. A research team member (first author) made all the opaque envelopes and distributed them to the study wards in the three hospitals. The envelopes were stored by study nurses in each study ward. An envelope was opened by the research nurse on the ward when a participant met eligibility criteria and informed consent was obtained. It was impossible to blind the participants or the bedside nurses because the catheters in the clinically indicated group were still in situ after 4 days. However, staff working in the hospital laboratory, who tested the blood samples were blinded to participant assignment as they did not have contact with patients.

3.5 | Interventions

Patients in the clinically indicated group had the PIVCs kept in situ until any of the following clinical signs appeared: phlebitis, infiltration, occlusion, displacement, local infection, and when the patient had been diagnosed as having a PIVC-related bloodstream infection.

Patients in the routine replacement group had their PIVCs replaced once every 96 hours. If any clinical indications appeared within 4 days, the catheters were removed following routine practice. Bedside nurses were responsible for inserting, maintaining, replacing and removing catheters in both groups according to the same standard operating procedures for each group.

3.6 | Outcome measurements

3.6.1 | Primary outcome

Phlebitis was assessed using the phlebitis classification definition recommended by the American Infusion Nurses Society which includes grade 0 to 4 (Infusion Nurses Society, 2016): Grade 0: no symptoms; Grade 1: erythema at access site with or without pain; Grade 2: pain at access site with erythema and/or oedema; Grade 3: pain at access site with erythema, streak formation, palpable venous cord; and Grade 4: pain at access site with erythema, streak formation, palpable venous cord >1 inch in length, and purulent drainage. Patients with Grade 1–4 were judged as having phlebitis.

3.6.2 | Secondary outcomes

We assessed six secondary outcomes including infiltration, occlusion, displacement, catheter-related bloodstream infection (CRBSI), all-cause bloodstream infection (BSI) and local infection. Infiltration means the leaking of non-blistering drug from the vein of the infusion and resulting in swelling around the insertion site. Occlusion means that the infusion does not drip, and flushing with normal saline is unsuccessful. Displacement means the accidental catheter removal. CRBSI is diagnosed when (1) there is at least one positive blood culture from a peripheral vein; (2) there are clinical signs of infection (i.e. fever with body temperature >38.5°C, hypothermia with body temperature <36.5°C, chills or hypotension (systolic blood pressure <90 mmHg)); (3) there is no other apparent source of the bloodstream infection except the intravenous catheter which is in situ within 48 hours of the bloodstream infection; and (4) the culture of intravascular catheter tip shows at least 1000 cfu/mL with the same organism (same species)

as identified in the blood. All-cause BSI is defined as any positive blood culture drawn from a peripheral vein while the PIVC is in situ or 48 hours after removal. Local infection means that there are organisms grown from purulent discharge with no evidence of associated bloodstream infection (Guenezan et al., 2019; Webster et al., 2019).

3.7 | Data collection procedure

We designed a case report form to record the following: demographic data, disease-related data, PIVC insertion-related data, PIVC usage-related data, PIVC removal/replacement-related data and PIVC complication data, such as phlebitis, CRBSI, all BSI, infiltration, occlusion, dislodgement and venous (local) infection. Data including any infusion failure, mortality, first PIVC dwelling time, cumulative indwelling time of all PIVCs, the total cost of supplies for PIVC insertion and maintenance were also included in the case report form.

Before data collection commencement at each hospital, two lead research nurses from each study ward were selected to undergo training on data collection. The research trainer (JL) conducted data collection training using a purposely developed PowerPoint presentation. The training content included data collection procedure, patient consent process, randomisation (how to use the allocations concealed in the envelopes), the standardised process of PIVC insertion and maintenance, PIVC insertion site selection and phlebitis assessment skills, and on how to complete the case report forms for each participant. Then, these lead research nurses went on to train all nurses in their ward using the training PowerPoint presentation. All nurses working in participating wards underwent training. Each nurse was assessed and given feedback after training. In addition, all hospital nurses had to routinely complete an intravenous therapy training program which was developed based on the Guidelines of Infusion by the Infusion Nurses Society (Infusion Nurses Society, 2016), and the Aseptic Non-Touch Technique (ANTT) (Stephen Rowley et al., 2010).

Data were collected between February 2018 and June 2019. The research nurses of each research ward screened patients who met the inclusion criteria daily and consented eligible patients. The research nurses observed PIVC complications daily and completed the paper case report forms. When a catheter-related bloodstream infection was suspected, blood sample was collected and sent to the laboratory for culture. If the patients were discharged from the hospital within 48 hours after the catheters were removed, the research nurses would follow-up on the phone and check if the patients had developed signs and symptoms of phlebitis. Data collection reached endpoint after PIVC was removed for 48 hours.

3.8 | Study protocol compliance audit

In each hospital, we trained two nurses who had research experience to be responsible for protocol compliance monitoring. They visited the wards that participated in the study once a week to audit study protocol compliance, including the signing of the informed consent form, randomisation (checking the opened randomisation envelops which were kept with the case report form) and the completeness of the case report forms. They communicated with the wards' research nurses on data collection progress and discussed any problems they encountered. The audit was recorded on the research quality control form.

Data entry and cleaning: data were entered by research nurses from each site into a pre-developed SPSS data file (SPSS version 22.0 for Windows (SPSS Inc., Chicago, IL, USA)). Data double checking and cleaning were conducted from August 2019 to April 2020.

3.9 | Statistical analysis

Data were analysed using SPSS. Continuous demographic and clinical variables with normal distribution were presented as mean and standard deviation (SD). Non-normally distributed variables were reported as median and interquartile range. Categorical data were presented in frequencies and percentages. Chi-square tests and t test were used to compare patients and catheter characteristics in the two groups. The intention-to-treat principle was adopted for outcome comparisons between the intervention and control groups. Survival from phlebitis was estimated using the Kaplan–Meier method, and any differences in survival were evaluated with a stratified log-rank test. Multivariable analyses with the Cox proportional hazards model were used to estimate the risk on survival from PIVC complication. A value of $p<0.05$ was considered significant.

3.10 | Ethical considerations

We obtained ethical approval from the clinical research ethics committee of Peking University First Hospital, Approved No. was 2015[1001]. Written informed consent was obtained from all patients who agreed to participate.

4 | RESULTS

A total of 3050 eligible consented patients were randomised into two groups: 1556 patients in the clinically indicated group (intervention group), and 1494 patients in the routine replacement group. Among them 1187 patients were from Hospital 1 (616 in the intervention group, 571 in the control group), 1367 patients were from Hospital 2 (705 in the intervention group, 662 in the control group), and 496 patients were from Hospital 3 (235 in the intervention group, 261 in the control group). The patients were either from medical wards (1598, 52.4%) or surgical wards (1452, 47.6%). Patient flow through the research process is shown in Figure 1.

Patient clinical characteristics are shown in Table 1. There were no significant differences between clinically indicated group and

routine replacement group in relation to age, sex, education, types of expenses, type of admission, comorbidities ($p > 0.05$).

There were a total of 4572 PIVCs in 3050 patients during the study period. Table 2 shows that there were no significant differences between the two groups in PIVC gauge, skin integrity, vein quality, anatomical location of the insertion site, treatment prescribed, types of dressing used, with or without an infusion connector, type of tapes used for external securement, materials used for auxiliary securement, whether the PIVCs were flushed when bolus medication was given during a infusion, and agents used to lock PIVC at the end of infusion.

Primary outcome analysis showed that 11.5% of patients (n = 1556) had phlebitis in the clinically indicated group, while 10% of patients had phlebitis in the routine replacement group (see Table 3). The risk of phlebitis between the two groups was not significantly different ($p = 0.193$) with an absolute risk difference (ARD) of 15.3% ($p = 0.193$). Phlebitis per 1000 catheter days was 28.4 in the clinically indicated group and 32.3 in the routine replacement group, with no statistical difference between the two groups. The per-protocol analysis showed that there was no significant difference between the clinically indicated group and the routine replacement group in the risk of phlebitis (ARD 11.9%, $p = 0.323$), and phlebitis per 1000 catheter days (HR = 0.525, $p < 0.001$).

No catheter-related bloodstream infection occurred in our study in either group. The risk of infusion failure, occlusion, dislodgement, all bloodstream infections, venous (local) infection and in-hospital mortality were all equivalent between the two groups, with no significant differences. However, infiltration was 13.9% in the clinically indicated group and 8.0% in the routine replacement group, which was statistically significant, with HR 1.29 (95% CI, 1.02 to 1.63). In the clinically indicated group, the incidence of infiltration was statistically different between different types of dressings ($\chi^2 = 28.763$, $p = 0.000$) and different PIVC insertion sites ($\chi^2 = 11.268$, $p = 0.01$), but no difference between PIVC sizes ($\chi^2 = 2.681$, $p = 0.102$). PIVCs with transparent dressings (14.8%), or located in the upper arm (28.6%) had a significantly higher incidence of infiltration. There were no other adverse events observed in either group apart from the complications reported earlier (see Table 3).

Patients' first PIVC dwelling time and cumulative indwelling time of all PIVCs in the clinically indicated group were significantly longer than the routine replacement group ($p < 0.01$). In the clinically indicated group, the longest PIVC dwelling time was 865 hours with no

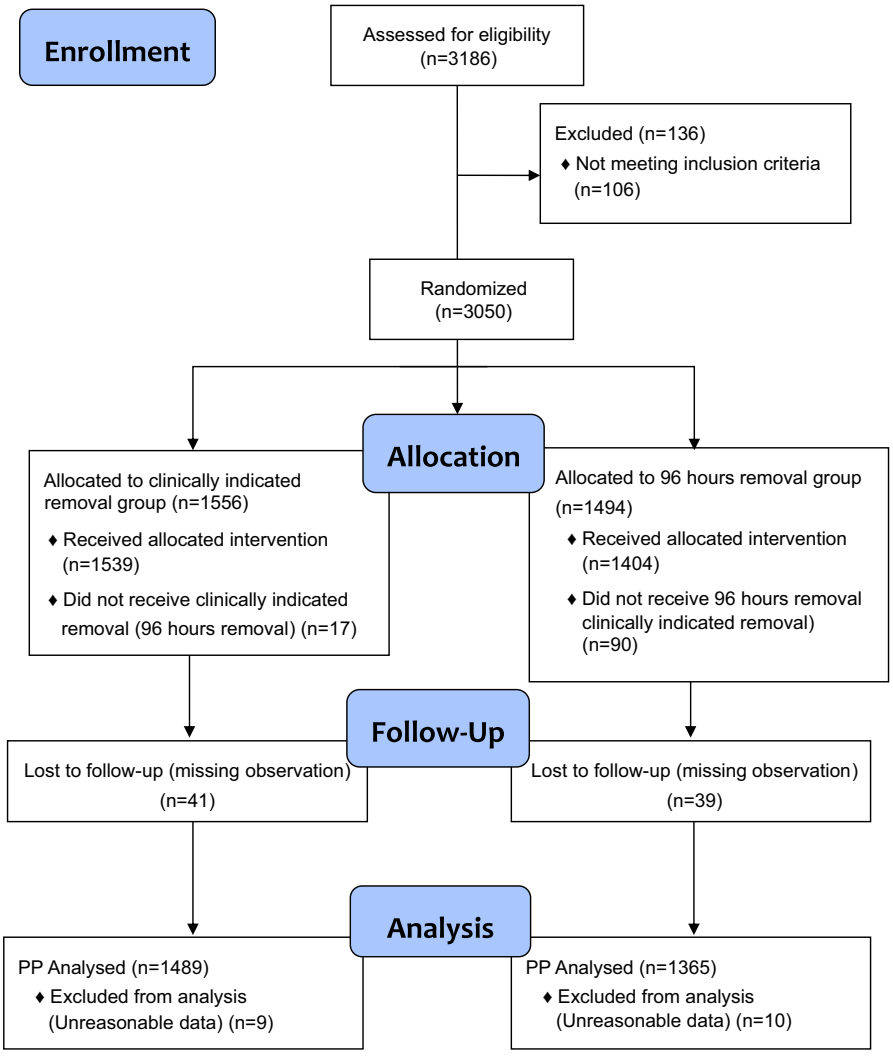


FIGURE 1 CONSORT diagram study flow [Colour figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Patient characteristics

	Clinically indicated (n = 1556) n (%)	Routine replacement (n = 1494) n (%)	p
Age (years)	58.57 (15.92)	59.06 (15.80)	.396
Sex			
Female	635 (40.81%)	622 (41.63%)	.666
Male	919 (59.06%)	872 (58.37%)	
Missing data	2 (0.12%)	0	
Education			
Primary School or below (year 6 or below)	481 (30.91%)	464 (31.06%)	.795
Middle High School (year 7–9)	576 (37.02%)	537 (35.94%)	
Senior High School (year 10–12)	208 (13.37%)	211 (14.12%)	
Diploma	90 (5.78%)	97 (6.49%)	
Undergraduate degree or higher	143 (9.19%)	126 (8.43%)	
Missing data	58 (3.73%)	59 (3.95%)	
Types of healthcare cover			
Public health services-full cover	140 (9.00%)	152 (10.17%)	.350
Own expense-no cover	173 (11.12%)	151 (10.12%)	
New rural cooperative medical system-patient co-payment cover	601 (38.62%)	574 (38.42%)	
Medical insurance-full cover	589 (37.85%)	552 (36.9%)	
Other covers	20 (1.28%)	30 (2.0%)	
Missing data	33 (2.12%)	35 (2.3%)	
Type of admission			
Medical	805 (51.74%)	793 (53.08%)	.458
Surgical	751 (48.26%)	701 (46.92%)	
Comorbidities			
None	814 (52.3 1%)	771 (51.61%)	.950
One	429 (27.57%)	440 (29.45%)	
Two or more	313 (20.12%)	283 (18.94%)	

complications occurred, which was removed at the end of the treatment. In the clinically indicated group, 723 (46.47%) catheters were in situ for more than 96 hours, of these, the average dwelling time was 139 (SD, 58.83) hours. The cost of supplies for one catheter was 80.80 RMB (US$12.30) in hospital 1, 67.25RMB (US$10.24) in hospital 2, and 75.00 RMB in hospital 3 (US$11.41). Between the two groups, there were no statistically significant differences in the overall number of PIVCs used (p=0.084) and cost of supplies (p = 0.344) (see Table 4).

The Kaplan–Meier survival curves for the dwelling time after PIVC insertion to the occurrence of phlebitis in both groups were presented in Figure 2. There was no statistical significant difference in survival times from phlebitis between the two groups (log-rank test p = 0.61).

5 | DISCUSSION

Our study found that there were no statistical significant differences in the rates of phlebitis, CRBSI, all BSI, local infection, blockage and catheter dislodgement between the clinically indicated group and routine replacement group. This supports results from previous studies conducted in Australia (Rickard et al., 2012), Brazil (Vendramim et al., 2020) and other countries ((Webster et al., 2019). With the addition of this adequately powered multi-centre study in an Asian population from an Asian country, there is now stronger evidence that replacing PIVCs as clinically indicated should be adopted in clinical practice worldwide. It is worth noting that the phlebitis rates in both groups were much higher in our sample than those reported in other countries, with Australia as 7% (Rickard et al., 2012), and Brazil as 9% (Vendramim et al., 2020). It may be related to the fact that in this study, more irritating drugs that can cause phlebitis were used. Factors contributing to these high infection rates in this population warrant further investigation, and strategies preventing phlebitis should be adopted before implementing clinically indicated replacement.

Our results also showed that there was no significant difference in survival times from phlebitis between the two groups (p = 0.61).

TABLE 2 PIVCs characteristics

	Clinically indicated (n=2294)	Routine replacement (n=2278)	X^2/Z	*p*
Catheter gauge				
≤18	5 (0.32%)	10 (0.67%)	1.997	.573
20	19 (1.22%)	20 (1.35%)		
≥22	1523 (97.87%)	1456 (97.46%)		
Skin integrity (determined according to what criteria)				
Poor	29 (1.26%)	32 (1.40%)	3.71	.156
Fair	261 (11.38%)	316 (13.87%)		
Good	1996 (87.01%)	1924 (84.13%)		
Vein quality (as above)				
Poor	130 (5.67%)	99 (4.35%)	1.891	.389
Fair	631 (27.51%)	675 (29.63%)		
Good	1524 (66.43%)	1492 (65.50%)		
Insertion bodyside				
Left side	1282 (55.89%)	1280 (56.19%)	0.106	.745
Right side	992 (43.24%)	978 (42.93%)		
Insertion site location				
Cubital fossa	17 (0.74%)	20 (0.88%)	6.601	.252
Hand	1258 (54.84%)	1284 (56.37%)		
Inner forearm	281 (12.25%)	232 (10.18%)		
Outer forearm	632 (27.55%)	645 (28.71%)		
Upper arm	21 (0.92%)	30 (1.32%)		
Other	69 (3.00%)	49 (2.15%)		
Prescribed treatment				
Intravenous antibiotic	581 (42.13%)	574 (43.58%)	202.442	.633
Intravenous crystalloid	560 (40.61%)	551 (41.84%)		
Intravenous potassium	241 (17.48%)	280 (21.26%)		
Intravenous calcium	21 (1.52%)	31 (2.35%)		
Intravenous blood products	31 (2.25%)	38 (2.89%)		
Intravenous antipyretic	58 (4.21%)	60 (4.56%)		
Intravenous vasoactive drugs	81 (5.87%)	85 (6.45%)		
Parenteral nutrition	77 (5.58%)	76 (5.77%)		
Intravenous antineoplastics	7 (0.51%)	20 (1.52%)		
Hyperosmotic drugs	174 (12.62%)	173 (13.14%)		
Intravenous cortisone	41 (2.97%)	49 (3.72%)		
Other intravenous drugs	412 (29.88%)	334 (25.36%)		
Types of dressing[a]				
Transparent polyurethane dressing	1112 (71.47%)	1063 (71.15%)	2.078	.556
Non-transparent dressing	393 (25.26%)	390 (26.10%)		
Bordered transparent polyurethane dressing	38 (2.44%)	31 (2.07%)		
Others	2 (0.12%)	5 (0.33%)		
Usage of infusion connector[a]				
Yes	1039 (66.77%)	1027 (68.74%)	0.922	.337
No	491 (31.56%)	450 (30.12%)		

(Continues)

TABLE 2 (Continued)

	Clinically indicated (n=2294)	Routine replacement (n=2278)	X^2/Z	*p*
Materials of the tape used for external fixation[a]				
Cloth	135 (8.68%)	116 (7.76%)	3.559	.469
Paper	392 (25.19%)	372 (24.90%)		
Silk	20 (1.29%)	29 (1.94%)		
Plastic	875 (56.23%)	858 (57.43%)		
None	126 (8.10%)	110 (7.36%)		
Materials used for auxiliary fixation[a]				
Splint	0 (0.0%)	2 (0.13%)	7.105	.213
Self-adhesive elastic bandage	2 (0.13%)	8 (0.54%)		
Reticular bandage	287 (18.44%)	270 (18.07%)		
Others	5 (0.33%)	4 (0.27%)		
None	1230 (82.33%)	1180 (78.98%)		
Flushing during the infusion[a]				
Yes	82 (5.27%)	83 (5.56%)	0.110	.74
No	1445 (92.87%)	1387 (92.84%)		
Agents used to lock PIVC at the end of infusion[a]				
Pre-filled flush syringes	581 (37.34%)	520 (34.81%)	2.604	.272
Self-prepared heparin saline	637 (40.94%)	627 (41.97%)		
Others	320 (20.57%)	333 (22.29%)		

Note: In some instances, total numbers are not 2294 or 2278 per group because of missing data.

[a]Clinically indicated group n = 1556, Routine replacement group n = 1494.

TABLE 3 Study outcomes by treatment group

	Clinically indicated (n=1556)	Routine replacement (n=1494)	Risk (95%CI)	*p*-value
Primary outcome, intention-to-treat analysis				
Phlebitis per patient, n (%)	179 (11.5%)	150 (10%)	RR 1.083 (0.957 to 1.226)	.193
			ARD 15.3% (12.0% to 19.2%)	
Phlebitis/1000 intravenous catheter days (95% CI)	28.4 (24.4–32.8)	32.3 (27.4–37.8)	HR: 0.696 (0.552, 0.877)	.002
Primary outcome, per-protocol analysis[a]				
Phlebitis per patient	171/1489 (11.5%)	141/1365 (10.3%)	RR 1.065 (0.937 to 1.212)	.323
			ARD 11.9% (8.7% to 15.9%)	
Phlebitis/1000 intravenous catheter days (95% CI)	27.4 (23.5–31.8)	35.0 (29.6–41.2)	HR 0.525 (0.407, 0.676)	<.001
Secondary outcomes, n (%)				
Any infusion failure	721 (46.3%)	475 (31.8%)	HR 0.94 (0.83,1.06)	.338
Infiltration	217 (13.9%)	119 (8.0%)	HR 1.29 (1.02,1.63)	.033
Occlusion	312 (20.1%)	201 (13.5%)	HR 0.91 (0.75,1.09)	.299
Dislodgement	53 (3.4%)	32 (2.1%)	HR 1.12 (0.71,1.76)	.639
CRBSI	0	0		
All BSI	3 (0.2%)	4 (0.3%)	HR 0.41 (0.08,2.00)	.270
Venous (local) infection	2 (0.1%)	2 (0.1%)	HR 0.38 (0.05,3.14)	.367
Mortality, n (%)	3 (0.2%)	3 (0.2%)	HR 0.97 (0.20,4.82)	.973

Abbreviations: ARD, absolute risk difference; BSI, bloodstream infection; CRBSI, catheter-related bloodstream infection; HR, hazard ratio; RR, relative risk.

TABLE 4 Comparison of PIVC dwelling time and costs

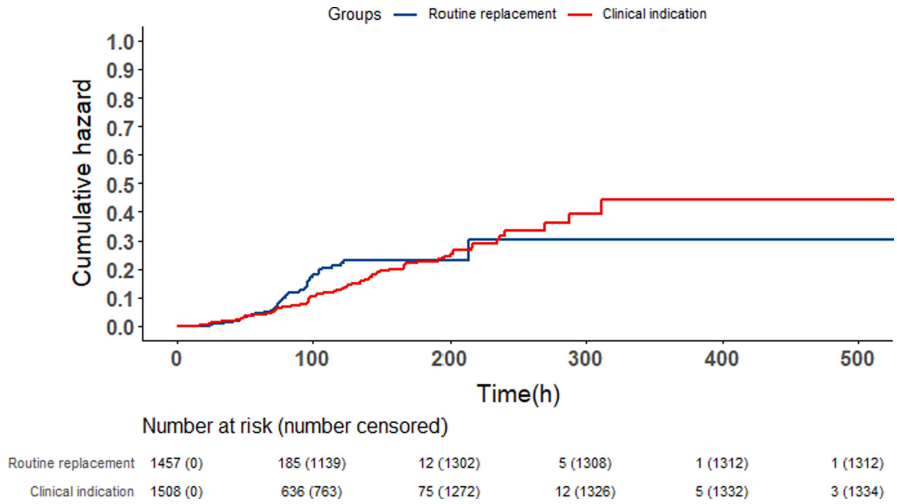
	Clinically indicated (n = 1556)	Routine replacement (n = 1494)	Difference (95% CI)	*p* value
First PIVC dwelling time (h)[a]	95.00 (55.00–126.50)	73.67 (54.96–86.50)	–	<.01
Cumulative indwelling time of all PIVCs (h)[a]	137.78 (36.33–182.18)	109.25 (36.10–239.44)	–	<.01
Total of PIVC used	1 (1,2)	1 (1,2)	0.082–0.093	.084
Cost of supplies per patient[b]	80.80 (67.25–150.00)	80.80 (67.25–150.00)	0.326–0.345	.344

Note: Data are median (IQR) or mean (SD).

[a]Per protocol.

[b]2019 cost.

FIGURE 2 Kaplan-Meier analysis of survival from phlebitis [Colour figure can be viewed at wileyonlinelibrary.com]



It confirmed that the longer PIVC dwelling time did not increase the risk of PIVC-related phlebitis. In recent years, strategies to prevent phlebitis have been continuously implemented (Ray-Barruel et al., 2019). The improvement of PIVC materials (Kus & Buyukyilmaz, 2020), the use of in-line filtration (Villa et al., 2018) and the innovation of PIVC dressing materials and more research evidence have enabled phlebitis to be preventable (Yin et al., 2020). In addition, training on preventing phlebitis has also been improved (Keogh et al., 2020). Nurses can effectively identify the risk factors for phlebitis and take preventive measures timely. Therefore, although the indwelling time of PIVCs exceeded 96 hours in our study, the risk of phlebitis did not increase.

In this study, there was no CRBSI occurred in either group, which was consistent with findings from other studies (Olivier et al., 2020; Stevens et al., 2018; Vendramim et al., 2020). Oh et al. (2020) which reported that clinically indicated PIVC replacement did not contribute to increased CRBSIs. Besides, in this study, we found that there was no increase in the risk of all BSI in the clinically indicated group compare with the routine replacement group ($p = 0.270$) and local infection ($p = 0.367$), which was consistent with previous findings (Rickard et al., 2012). PIVC-related infections were mainly caused by various bacteria invading through the insertion point (Sato et al., 2017). Adequate skin cleansing and the use of ANTT technique (Rowley & Clare, 2011) to manage PIVCs have been found to be effective in preventing bacterial infections (Nickel, 2020). In our study settings, these approaches were used when inserting and maintaining PIVCs after the training of standardised procedures for both study groups. Therefore, in the clinically indicated group, prolonged indwelling time did not increase the risk of CRBSI, all BSI or local infection.

This study showed an infiltration incidence of 13.9% in the clinically indicated group, which is significantly higher ($p = 0.033$) than the 8.0% infiltration incidence in the routine replacement group. This outcome was consistent with the study from Brazil (Vendramim et al., 2020), but different from Australia (Rickard et al., 2012). Infiltration ranked highest among complications of PIVCs with an incidence of 17.8% in a previous study conducted in China (Lyu & Zhang, 2020). The main causes may be that in Chinese hospitals, majority of hospitalised patient would have a PIVC, with one study reported that 93.1% of inpatients received intravenous infusion therapy, with average daily infusion volume being 782.67 ml per patient, (Wang et al., 2017). Consequently, the number of infusions through PIVCs in China was relatively higher, and more frequent than findings from other countries (Yuan, 2014; Zeng et al., 2019). In this study, we also found that medications with irritant or vesicant properties were administered through the PIVCs in both groups, which were not recommended by current evidence-based clinical practice guidelines (Gorski et al., 2021). These types of medications

could damage the endothelial cells of peripheral blood vessels, increased the permeability of endothelial cells, which is closely related to infiltration. In this study, the cumulative indwelling time of the catheter in the clinically indicated group was higher than previous findings from (Rickard et al., 2012). Administering these types of medications through PIVCs for a longer period can cause sustained damage to endothelial cells which could explain the reason of the higher incidence of infiltration observed in the clinically indicated group in our sample.

In addition, we found that the incidence of infiltration was statistically different between different types of dressings and different insertion sites. Marsh et al. (2018) found that additional securement products were associated with less infiltration, but the effect of transparent dressings and gauze on infiltration was unclear (Marsh et al., 2015). Liu et al reported that the risk of infiltration tripled with antecubital fossa insertion (Liu et al., 2020). Previous studies also showed that two or more attempts at cannulation, 20-gauge catheter, administration of a high-risk solutions (Simin et al., 2019), and each increase by 1 in the average number of daily PIV accesses were also associated with higher infiltration incidence (Marsh et al., 2018). Future research is needed to understand the reason of increased infiltration rate in the clinically indicated group.

Furthermore, no differences in occlusion, dislodgements and mortality were observed between the clinically indicated group and the routine replacement group, which were consistent with previous findings (Rickard et al., 2012; Vendramim et al., 2020). All three participating hospitals had rigorous PIVC management training programs in place, and regular and random audits of PIVC insertion and management were conducted as routine practice. As a result, although the indwelling time was extended in the clinically indicated group, there was no increase of catheter blockage. This study also showed that the PIVCs were secured by using dressings and tapes, a self-adhesive bandage or a mesh bandage. The continuous firm fixation of PIVCs using these securement devices observed in this study may have contributed to the results regarding dislodgements.

In terms of material use and cost, this study showed that the indwelling time of the first PIVCs and cumulative indwelling time were longer in the clinically indicated group than in the routine replacement group. This was also consistent with previous research (Rickard et al., 2012). With the acceleration of bed turnover in tertiary hospitals in China, hospital length of stay is decreasing. When the indwelling time of the PIVCs is extended, the PIVCs were likely to be used until the day of discharge, thus reducing from the need for catheter removal and replacement. This study also found that there was no statistical difference in the cost of indwelling needles per patient during the study between the groups. This was different from findings of Rickard's study (Rickard et al., 2012). This may be related to the context of the Chinese hospitals. In China, the cost of consumables is set uniformly by the government. The cost of consumables that can be paid by the medical insurance system is generally much lower than western countries (Liu et al., 2020). Therefore, in the clinical indication group, the cost reduction of indwelling PIVCs was negligible, which could explain the reason why there was no statistical difference in cost between the groups.

6 | CONCLUSION

Results from this study support other earlier studies that, comparing replacing peripheral catheters as clinical indicated with routine PIVC replacement once every 96 hours did not increase the risk of phlebitis, occlusion, catheter displacement and catheter infection. However, our study showed an increased infiltration incidence in the replacement as clinically indicated group. In addition, infiltration rates were significantly higher in patients whose PIVCs were covered with transparent dressings or were located in the upper arm. Finally, the phlebitis rates in both groups in our study were higher than those reported from other countries. Future research is needed to explore the reasons of these differences.

7 | RELEVANCE TO CLINICAL PRACTICE

In developing countries, infusion treatment plans, infusion drugs, infusion tools and the number of nurses in charge are different from those in Western countries. If the PIVCs are used more than 96 hours, more frequent observation is needed to identify complications such as infiltration timely.

7.1 | Limitations

This study was a multi-centre study, which was conducted in three hospitals that were located in different geographical locations and jurisdictions in China. These hospitals are all tertiary hospitals that provide high levels of care and are better resourced than many other hospitals located in some geographical locations. Thus, the results may not be generalised to the wider hospital population in China. In addition, it was impossible to blind the patients and research nurses. Patients in the clinically indicated group might not report pain, because they did not want to have a PIVC reinserted which could cause pain. This would affect the judgment on whether phlebitis occurred. Finally, the judgment of complications such as phlebitis and infiltration was based on subjective judgments by research nurses without using any objective evaluation tools such as B-ultrasound, so the assessment might not be accurate or consistent. However, the rigorous training on PIVC insertion site observation, and phlebitis assessment, and the rigorous quality control procedures we implemented may minimise variations.

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CONFLICT OF INTERESTS

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

Contribution to the conception and design of the study, contribution in the training of data acquisition, interpretation of data, drafting, revising and finalising, and approving the article: Jing Li; Lead all aspect of the project including conception and design of the study, data acquisition, data quality control, interpretation of data, drafting, revising, reviewing and approving the manuscript: Corresponding author Yanming Ding and Frances Lin; Contribution to the conception and design of the study, made substantial contribution in data acquisition, interpretation of data, reviewing and approving the manuscript: Qian Lu, Sanli Jin and Zhixia Jiang; Contribution in acquisition of data, data entry and verification, data analysis, interpretation of data, drafting, revising and approving the manuscript: Peiying Zhang, Fengxia Zhang and Yang Lyu.

ORCID

Jing Li https://orcid.org/0000-0001-5683-466X
Zhixia Jiang https://orcid.org/0000-0001-7044-051X
Yang Lyu https://orcid.org/0000-0002-3560-4061
Frances Lin https://orcid.org/0000-0001-8735-5469

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SUPPORTING INFORMATION

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