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Incidence of Infiltration and Phlebitis and Risk Factors Among Chemotherapy Patients: An Observational Prospective Cohort Study

Kemoterapi Alan Hastalarda İnfiltrasyon ve Flebit Görülme Sıklığı ve Risk Faktörleri: Gözlemsel Prospektif Çalışma

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ABSTRACT

Objective: This study aimed to identify the incidence rate of infiltration, phlebitis, and risk factors in chemotherapy patients.

Methods: This observational prospective cohort study was conducted in the oncology and hematology clinics of a hospital in Turkey. Peripheral intravenous catheter insertion sites (n=175) on 99 patients were monitored. Researchers monitored the peripheral intravenous catheter insertion sites for 5 days after nurses inserted them. The ethics committee approved the study.

Results: The incidence of infiltration and phlebitis was, respectively, 9.7% and 17.5%. The incidence rate of infiltration was significantly higher, respectively, in the case of vesicants and the presence of neutropenia among patients over 52 years of age. It was determined that the risk of infiltration in women was 0.21 times higher than in men. When the neutropenia value was put into the model alone, it was determined that the risk of infiltration increased 0.414 times in the case of neutropenia.

Conclusion: The patient's gender, the presence of neutropenia, and the chemotherapy drug type affect the incidence of infiltration. Regular follow-up of the catheter site will reduce the workload of the nurse by ensuring the continuation of patient care and treatment without interruption. It will also reduce the frequency of the catheterization procedure and prevent the difficulties it brings to the patient.

Keywords: Catheterization, drug therapy, nursing, phlebitis

ÖZ

Amaç: Bu çalışma, kemoterapi alan hastalarda infiltrasyon ve flebit görülme sıklığı ve risk faktörlerini belirlemek amacıyla yapılmıştır.

Yöntemler: Bu çalışma Türkiye'de bir Üniversite Hastanesinin Onkoloji ve Hematoloji Kliniklerinde gözlemsel prospektif olarak yapılmıştır. Çalışmada, periferik intravenöz kateter uygulaması yapılan 99 hastanın 175 kateter bölgesi takip edilmiştir. Çalışma kriterlerine uyan hastaların hastanede kaldıkları süre içinde tekrarlı takılan kateter bölgeleri 5 gün takip edilmiştir. Çalışmanın yapılabilmesi için etik kuruldan ve kurumdan yazılı izin alınmıştır.

Bulgular: Çalışma sonucunda periferik intravenöz kateter uygulamasının %9,7'sinde infiltrasyon, %17,7'sinde flebit görülmüştür. 52 yaş üstü, nötropenik ve vezikan ilaç kullanımının infiltrasyon riskini arttırdığı belirlenmiştir. Kadınlarda infiltrasyon riskinin erkeklere göre 0,21 kat daha fazla olduğu belirlenmiştir. Nötropeni tek başına modele alındığında nötropeni durumunda infiltrasyon riskinin 0,414 kat arttığı belirlenmiştir.

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Sonuç: Çalışma sonucunda, hastanın cinsiyeti, nötropeni ve ilaç türünün infiltrasyon durumunu etkilediği belirlenmiştir. Kateter bölgesinin düzenli takip edilmesi hasta bakımının ve tedavisinin aksamadan devamını sağlayacaktır. Ayrıca kateterizasyon işleminin sıklığını azaltacak ve hastaya getirdiği zorlukları önleyecektir.

Anahtar Kelimeler: Flebit, hemşire, ilaç uygulaması, kateterizasyon

INTRODUCTION

Intravenous (IV) chemotherapy is used most commonly for cancer treatment.[1] Intravenous chemotherapy and the proper drug treatment have numerous advantages, but IV solutions have high osmolarity and pH, damaging the vascular endothelium.[2,3] Long-term treatment, on the other hand, increases the risk of complications.[4] Most IV chemotherapy drugs are irritants causing disruption and damage to the vein structure and limiting its long-term and repeated use.[5] What is essential in peripheral intravenous catheter (PIVC) chemotherapy is the completion of the peripheral drug treatment without complications. Therefore, nurses should evaluate patients' conditions and continue to monitor and provide care to prevent complications.

Infusion of chemotherapy drugs by PIVC sometimes causes infiltration and phlebitis. Infiltration is the unintentional leakage of IV solution from the targeted vein. Mechanical or physiological problems may cause infiltration. Mechanical issues may take place during the insertion of the catheter for the first time or when the catheter is in use. At the same time, physiological problems are pre-existing or new vascular issues.[4,6] In the presence of infiltration, nurses should monitor for any signs of pain and inflammation in the insertion site and throughout the vein pathway and neurovascular changes in the extremity. They should also be able to recognize, prevent, and treat infiltration. To prevent infiltration, they should insert the PIVC correctly, choose the right size catheter, give saline from the catheter, and fix the catheter after it has been inserted. If there are any signs of infiltration, they should stop the infusion and, if necessary, establish vascular access through another site.[7,8]

Phlebitis is another complication associated with PIVC during chemotherapy and is defined as vein inflammation.[9] Phlebitis can be of mechanical, chemical, and bacterial origin.[10,11] Mechanical phlebitis is related to the catheter insertion site, size, and technique. Chemical phlebitis develops due to the administration of irritants and solutions with an osmolarity greater than 600 mOsm/L. Bacterial phlebitis may occur due to the antiseptic used to clean the catheter site or due to the material by which the catheter is fixed.[11,12] Phlebitis is more common in chemotherapy patients due to the high toxicity of drugs to the vascular endothelium.[13,14]

Nurses monitor for signs of infiltration and phlebitis because they are responsible for inserting and treating PIVCs.[11] They are also responsible for safely implementing and maintaining them, monitoring for any signs of complication, and recording them.[15] Simin et al[16] reported that infiltration and phlebitis developed in 16.3% and 44% of the catheter insertion sites they monitored. Nurses should know the risk factors for infiltration and phlebitis to prevent them before they arise.[17] They should also be able to detect early signs of PIVC-related complications of IV chemotherapy drugs and manage them effectively. To do that, they should first be informed of those early signs.[18]

Many factors affect the development of infiltration and phlebitis.[19,20] Those factors may be related to the patient or the cannula and the way it is used.[21] Patient age,[22] gender,[23] and the presence of chronic disease[24] affect the development of phlebitis. Administration, maintenance, daily monitoring of PIVCs, drug concentration, and general characteristics of the patient may increase the risk of phlebitis.[21] Daud[25] reported that the development of phlebitis was associated with gender, catheter insertion site, and drug type and that phlebitis was more common on the forearm than on the hand and the application of drugs according to fluid administration increases the incidence of phlebitis. Nurses should, therefore, take patients' age, gender, dominant hand, and the presence of neutropenia into account before inserting PIVCs. They should also ensure that the arm is below the heart level during PIVC insertion and should massage before proceeding and keep a record of the number of PIVC insertion attempts.[1] Before chemotherapy, the PIVC site should be assessed and monitored during the procedure. Phlebitis causes acute local sensitivity, redness, fever, and mild edema in the vein on the insertion site. Detecting these signs, nurses should immediately stop the infusion and apply a warm compress to the insertion site and insert the catheter into another place.[7]

There are few studies on the incidence of infiltration and phlebitis in chemotherapy patients Both Arias-Fernández et al[22] and Ozkaraman[26] reported that the incidence of phlebitis among chemotherapy patients ranged from 5% to 21%. However, PIVC chemotherapy patients suffer serious complications that reduce their quality of life. Those complications cause a delay in treatment and increased workload and care costs.[1] Therefore, nurses should be familiar with the risk factors, evaluate PIVC sites in IV chemotherapy patients, monitor their medications, and detect early signs of complications.[4,11,20] This study aimed to determine the incidence of phlebitis and infiltration and potential risk factors among chemotherapy patients and serve as a guide for nurses to that end.

METHODS

This observational prospective cohort study was conducted in the oncology and hematology clinics of a hospital in Turkey.

Study Population and Sampling Method

The study population consisted of all patients of a hospital. The sample consisted of 99 patients receiving chemotherapy in the hematology and oncology services of the hospital between September 2019 and February 2020. In total, 175 peripheral catheter interventions on 99 patients were recorded. Repeated catheter intervention attempts were also monitored.

Inclusion Criteria

- Over 18 years of age
- Receiving PIVC chemotherapy for at least 24 hours

- No 2 PIVC insertion attempts on the same arm or an interval of at least 8 hours between the 2 PIVC insertion attempts on the same arm
- Voluntary

Exclusion Criteria
- The presence of an earlier complication in the PIVC insertion site
- Central line placement for chemotherapy
- Chemotherapy was over

Power Analysis was performed to determine the sufficient number of participants necessary to detect significant differences. The result showed that a sample size of 160 would be enough with a confidence interval of 90% ($\alpha = 0.05$).

Data Collection
Data were collected using a peripheral intravenous catheter insertion monitoring form (PICIMF) developed by the researcher based on a literature review.[16,27] The PICIMF consists of 3 sections. The first section (PICIMF-1) contains patient characteristics (age, sex, dominant hand, tobacco use, vascular temperature, hemoglobin level, and presence of neutropenia, chronic disease, and diabetes). Vein status was evaluated using the 5-level vein assessment scale (grade 1: veins neither visible nor palpable; grade 2: veins visible but not palpable; grade 3: veins barely visible and palpable; grade 4: veins visible and palpable; grade 5: veins clearly visible and easily palpable).[28] The second section (PICIMF-2) contains items on the catheterization method (vein dilation, catheter vein, insertion site and angle, check with saline, number of interventions, pain status, set replacement, chemotherapy drug type, IV push medications, vein valve, and drug administration type). The third section (PICIMF-3) contains items on catheter site monitoring (infiltration and phlebitis scale and interventions for complications). The Visual Infusion Phlebitis scale was developed by the Infusion Nurses Society.[29]

Procedure
The researchers verbally informed the patients and nurses about the study, and verbal consent was obtained from those who agreed to participate.

The researcher determined the chemotherapy in patients in the clinic and completed the PICIMF-1 for those who met the inclusion criteria. For IV catheter/PIVC insertion, the insertion site was cleaned with 70% alcohol solution, the catheter was inserted and fixed with plaster by the nurse. Then, the researcher monitored catheterization and completed the PICIMF-2. The researcher evaluated the catheter site and completed the PICIMF-3 at 12, 24, 48, 72, 96, and 120 hours after the insertion of the PIVC. As per institutional policy, the nurse replaced the PIVC with a new one no more than 3 or 4 days later. The researcher monitored the insertion site and completed the PICIMF-3 for 2 days after removing the PIVC. She observed and completed the PICIMF-3 for 5 days after the PIVC was removed for any reason. She also identified and kept a record of the interventions for complications. If the catheter was inserted again into the other arm or the same site 8 hours after the first attempt, then she kept a record of it on a separate form.

Ethical Consideration
Written approvals for this study were obtained from Karadeniz Technical University Medical Faculty Scientific Research Ethics Committee (Decision No/Date: 24237859-701/ October 11. 2019). Patients and nurses were informed about the purpose and procedure of the study, and written consent was obtained from those who agreed to participate prior to data collection.

StatisticalAnalysis
Data were analyzed using the Statistical Package for Social Sciences version 22.0 (IBM SPSS Corp., Armonk, NY, USA) at a significance level of .05. Descriptive data were analyzed using number (n) and percentage (%). A chi-square (χ^2) test was used for numerical data. Logistic regression and correlation tests were performed.

RESULTS

One hundred and seventy-five catheter insertion sites were monitored for 5 days. Phlebitis was significantly more common in female patients than in males. The mean age of the patients was 50.99 ± 13.53 years. Phlebitis was more common in patients over 52 than in other age groups. Phlebitis was more common in ambidextrous and right-handed patients than in left-handed patients. Infiltration was observed in 10.4% of patients with chronic disease, and phlebitis was observed in 16.7%. Infiltration was observed in 14.3% of patients with diabetes, and phlebitis was observed in 21.1%. Infiltration was observed in 9.9% and phlebitis in 15.6% of smokers. Infiltration was observed in 10.4% of patients with a hemoglobin value below 9, and phlebitis was 23.9%. Phlebitis was more common in patients with neutropenia than in those without neutropenia. However, the variables did not affect the incidence of infiltration. The incidence of infiltration and phlebitis was 9.7% and 17.5%, respectively (n = 175) (Table 1).

Infiltration was observed in 5.7% of patients with grade 3 vein structure, and phlebitis was in 10.9%. There was no difference between using hand sanitizer and washing hands in terms of complication development ($P = .410$). Statistically significant difference was not found in clench and tap the vein ($P = .490$). Receiving massage and the forearm lower the heart level before inserting the catheter statistically significantly increased the incidence of phlebitis ($P = .080$, $P = .001$). It was determined that PIVC mainly was inserted in the anterior (47.4%) and right arms (57.7%) of the patients, but this did not affect the incidence of complications ($P = .540$, $P = .840$). It was determined that PIVC was applied at a 15°degree angle in 61% of the patients, 67.4% were given saline after PIVC insertion, 84.6% could be inserted in the first attempt, and PIVC was changed every 24 hours in 93% of them. It was determined that these features did not affect the incidence of complications ($P > .050$). It was determined that 3 or more PIVC attempts statistically increased the risk of phlebitis ($P = .010$). Vesicants statistically significantly increased the incidence of infiltration ($P = .030$) (Table 2).

A model was developed based on sex, presence of chronic disease, type of chemotherapy drug, age, and neutropenia. These risk factors causing infiltration were analyzed by logistic regression analysis, and it determined variables were not influential. The correct class rate obtained with the created model was found to be 90.3% (Table 3). As sex increases, the risk of infiltration increases 0.21 times.

A model was developed based on sex, presence of chronic disease, type of chemotherapy drug, age, and neutropenia. These risk factors causing phlebitis were analyzed by logistic regression analysis. When the neutropenia value was put into the model alone, it was determined that the risk of infiltration

Table 1. Incidence of Infiltration and Phlebitis by Demographic Characteristics

	n = 99	Infiltration (n = 175)			Phlebitis (n = 175)		
Demographic Characteristics	**n (%)**	**No, n (%)**	**Yes, n (%)**	***P*/χ^2**	**No, n (%)**	**Yes, n (%)**	***P*/χ^2**
Gender							
Male	66 (66.7)	102 (93.6)	7 (6.4)	.060	99 (90.8)	10 (9.2)	.001
Female	33 (33.3)	56 (84.8)	10 (15.2)	3.572	45 (68.2)	21 (31.8)	14.461
Age group (mean age = 50.99 ± 13.53)							
<51 years	44 (44.4)	100 (93.5)	7 (6.5)	.070	81 (88)	11 (12.0)	.040
>52 years	55 (55.6)	58 (85.3)	10 (4.7)	3.159	63 (75.9)	20 (24.1)	4.412
Chronic disease							
No	59 (59.6)	72 (91.1)	7 (8.9)	.729	64 (81)	15 (19)	.689
Yes	40 (40.4)	86 (89.6)	10 (10.4)	.120	80 (83.3)	16 (16.7)	.160
Dominant hand							
Right	71 (71.7)	112 (93.3)	8 (6.7)	.126	107 (89.2)	13 (10.8)	.001
Left	8 (8.1)	12 (85.7)	2 (14.3)	4.136	11 (78.6)	3 (21.4)	14.047
Ambidextrous	20 (20.2)	34 (82.9)	7 (17.1)		26 (63.4)	15 (36.6)	
Diabetes							
No	83 (83.8)	30 (90.9)	3 (9.1)	1.000	29 (87.9)	4 (12.1)	.350
Yes	16 (16.2)	128 (90.1)	14 (9.9)	.018	115 (81)	27 (19)	.873
Tobacco use							
No	78 (78.8)	31 (91.2)	3 (8.8)	1.00	25 (73.5)	9 (26.5)	.141
Yes	21 (21.2)	127 (90.1)	14 (9.9)	.038	119 (84.4)	22 (15.6)	2.220
Hemoglobin group (9.86 ± 2.21)							
<9	36 (36.4)	60 (89.60)	7 (10.40)	.796	51 (76.10)	16 (23.9)	.092
>9	63 (63.6)	98 (90.70)	10 (9.30)	.067	93 (86.10)	15 (13.90)	2.832
Neutropenia							
No	57 (43.4)	93 (93.9)	6 (6.1)	.060	87 (87.9)	12 (12.1)	.020
Yes	42 (76)	65 (85.5)	11 (14.5)	3.470	57 (75)	19 (25)	4.892
Total incidence	99 (100)	158 (90.3)	17 (9.7)		144 (82.3)	31 (17.7)	

increased 0.414 times in the case of neutropenia. The correct class rate obtained with the created model was found to be 81.7% (Table 3).

DISCUSSION

The acceptable rate of phlebitis by INS is 5%.[30] The incidence of phlebitis varies between 2% and 44% in the results of the studies.[16,22] In this study, phlebitis was observed in 17.7% of patients receiving PIVC chemotherapy. Arias-Fernández et al[22] found that the incidence of phlebitis in oncology, neurosurgery, and hematology patients receiving chemotherapy was 21.3%. Ozkaraman[26] reported that 5% of patients receiving chemotherapy developed phlebitis. Simin et al[16] reported phlebitis incidence as 44% patients receiving medication other than chemotherapy. Roberts et al[31] determined the incidence of phlebitis as 86% in their study with female breast cancer patients. Marsh et al[32] systematic review and meta-analysis study on PIVC-related complications in adult patients and found the phlebitis rate to be 19.3%. Larsen et al[33] found that phlebitis developed in 7.6% (n = 30) of the patients. According to Shintani et al[34], patients with hematological malignancies determined that 11% of them developed phlebitis. Santos-Costa et al[35] determined that 9% of adult oncology patients developed phlebitis. Daud[25] found that 36.1% of gynecology and orthopedic patients developed phlebitis. Urbanetto et al[27] reported phlebitis in 2.63% of patients. Atay et al[24] observed phlebitis in 31.8% of patients. Hedayatinejad et al[36] observed phlebitis grade 2 in 18.85% of intensive care and coronary patients. Study results were generally higher than this study's incidence results. This situation can be thought to be related to the nursing practices in the countries and hospitals where the studies were conducted. There are phlebitis prevention protocols in hospitals where the work was done.

The incidence of infiltration varies between 16% and 25% in the results of the studies.[16] Ozkaraman[26] found that 25% of patients with chemotherapy-related complications developed infiltration. Simin et al[16] observed infiltration in 3% of patients. Marsh et al[32], in a systematic review and meta-analysis study of PIVC-related complications in adult patients, examined the research and determined the infiltration/extravasation rate to be 13.7%. Larsen et al[33], stated that infiltration developed in 18.7%, and the most common PIVC complication was infiltration. According to Shintani et al[34], patients with hematological malignancies determined that infiltration developed in 18.4% of them. Santos-Costa et al[35] determined that 18% of adult oncology patients develop infiltration. Study results were generally higher than this study's incidence results. In this study, infiltration was observed in 9.7% of patients receiving PIVC chemotherapy. This result may be due to the difference in nurse protocols, patient characteristics,

Table 2. Characteristics of Catheterization (n = 175)

	n = 175	Infiltration (n = 175)			Phlebitis (n = 175)		
Characteristics	**Total**	**No**	**Yes**	***P*/χ^2**	**No**	**Yes**	***P*/χ^2**
Vein status							
Grade1	17 (9.7)	17 (9.7)	-	.37	14 (8.0)	3 (17.6)	.08
Grade 2	34 (19.4)	30 (17.1)	4 (2.3)	4.276	28 (16.0)	6 (3.4)	8.093
Grade 3	74 (42.3)	64 (36.6)	10 (5.7)		55 (31.4)	19 (10.9)	
Grade 4	44 (25.1)	41 (23.4)	3 (1.7)		41 (23.4)	3 (1.7)	
Grade 5	6 (3.4)	6 (3.4)	-		6 (4.2)	-	
Hand hygiene							
With soap and water	124 (70.9)	109 (87.9)	15 (12.1)	.07	101 (81.5)	23 (18.5)	.41
With antiseptics	51 (29.1)	49 (96.1)	2 (3.9)	2.754	43 (84.3)	8 (15.7)	.203
Clench and unclench the fist							
No	30 (17.1)	29 (96.7)	1 (3.3)	.312	26 (86.7)	4 (13.3)	.49
Yes	145 (82.9)	129 (89.0)	16 (11.0)	1.681	118 (81.4)	27 (18.6)	.477
Tap the vein							
No	93 (53.1)	83 (89.2)	10 (10.8)	.621	81 (87.1)	12 (12.9)	.07
Yes	82 (46.9)	75 (91.5)	7 (8.5)	.244	63 (76.8)	19 (23.2)	3.152
Massage							
No	123 (70.3)	108 (87.8)	15 (12.2)	.08	101 (82.1)	22 (17.9)	.001
Yes	52 (29.7)	50 (96.2)	2 (3.8)	2.905	43 (82.7)	9 (17.3)	.927
Forearm is lower than the heart							
No	114 (65.1)	104 (91.2)	10 (8.8)	.56	94 (82.5)	20 (17.5)	.00
Yes	61 (34.9)	54 (88.5)	7 (11.5)	.331	50 (82.0)	11 (18.0)	.936
Catheter vein							
Cephalic	103 (58.9)	88 (85.4)	15 (14.6)	7.373	86 (83.5)	17 (16.5)	.69
Basilic	44 (25.1)	43 (97.7)	1 (2.3)	.06	35 (79.5)	9 (20.5)	1.432
Cubital	11 (6.3)	10 (90.9)	1 (9.1)		8 (72.7)	3 (27.3)	
Metacarpal	17 (9.7)	17 (100.0)	-		15 (88.2)	2 (11.8)	
Catheter site							
Forearm	83 (47.4)	70 (84.3)	13 (15.7)	.08	67 (80.7)	16 (19.3)	.54
Back of the arm	40 (22.9)	39 (97.5)	1 (2.5)	8.261	36 (90.0)	4 (10.0)	3.074
Cubital	6 (3.4)	5 (83.3)	1 (16.7)		5 (83.3)	1 (16.7)	
Wrist	27 (15.4)	25 (92.6)	2 (7.4)		20 (74.1)	7 (25.9)	
Dorsal side of the hand	19 (10.9)	19 (100.0)	-		16 (84.2)	3 (15.8)	
Catheter arm							
Right	101 (57.7)	92 (91.1)	9 (8.9)	.79	84 (83.2)	17 (16.8)	.84
Left	74 (42.3)	66 (89.2)	8 (10.8)	.176	60 (81.1)	14 (18.9)	.128
Catheter insertion angle							
15	107 (61.1)	95 (88.8)	12 (11.2)	.40	87 (81.3)	20 (18.7)	.76
30	44 (25.1)	42 (95.5)	2 (4.5)	1.827	36 (81.8)	8 (18.2)	.524
45	24 (13.7)	21 (87.5)	3 (12.5)		21 (87.5)	3 (12.5)	
SF-control							
Yes	118 (67.4)	106(89.10)	13(10.90)	.431	95 (79.80)	24 (20.2)	.21
No	57 (32.6)	52 (92.90)	4 (7.10)	.621	49 (87.50)	7 (12.5)	1.536
Number of PIVC insertion attempts							
1	148 (84.6)	135 (91.2)	13 (8.80)	.068	124 (83.8)	24 (16.20)	.01
2	22 (12.6)	20 (90.90)	2 (40)	5.385	19 (86.40)	3 (13.60)	13.786
≥3	5 (2.9)	3 (60)	2 (40)		1 (20)	4 (80)	

(*Continued*)

Table 2. Characteristics of Catheterization (n = 175) (*Continued*)

	n = 175	Infiltration (n = 175)			Phlebitis (n = 175)		
Characteristics	**Total**	**No**	**Yes**	***P*/χ^2**	**No**	**Yes**	***P*/χ^2**
Set replacement							
Every 12 hours	6 (3.4)	5 (83.3)	1 (16.70)	.456	4 (66.7)	2 (33.3)	.07
24 hours	163 (93.1)	148 (90.8)	15 (9.20)	2.610	137 (84)	26 (16)	6.786
48 hours	3 (1.7)	3 (100)	-		2 (66.7)	1 (33.3)	
72 hours	3 (1.7)	2 (66.7)	1 (33)		1 (33.3)	2 (66.7)	
Push drug							
No	21 (12)	5 (83.3)	1 (16.7)	.456	20 (95.2)	1 (4.8)	.07
1	42 (24)	148 (90.8)	15 (9.2)	2.610	36 (85.7)	6 (14.3)	6.786
2	69 (39.4)	3 (100)	-		54 (78.3)	15 (21.7)	
3	43 (24.6)	2 (66.7)	1 (33.3)		34 (79.1)	-	
Chemotherapy drug type							
Irritant	44 (25.1)	98 (92.5)	8 (7.5)	.035	86 (81.1)	20 (18.9)	.336
Vesicant	80 (45.7)	14 (73.7)	5 (26.3)	6.706	14 (73.7)	5 (26.3)	2.181
Irritant and vesicant	51 (29.1)	46 (92)	4 (8)		44 (88)	6 (12)	

PIVC, peripheral intravenous catheter.

and drug treatments. Nurses should provide holistic care with a patient-centered approach in infusion therapy and focus on preventing complications.[34]

The incidence of phlebitis is affected by the patient's age and gender, catheter number, catheter insertion site, duration of catheter placement, anatomical position, medications and their doses, the nurse's experience, and the catheter material.[37] In this study, the incidence of phlebitis is related to gender and age in right and ambidextrous users and those with neutropenia ($P < .050$). However, the incidence of phlebitis is not related to chronic disease, diabetes, and tobacco use ($P > .050$). Phlebitis was significantly more common in female patients than in males. Also, gender is effective in the multivariate and univariate models for phlebitis ($P > .050$). Similarly, Abolfotouh et al[23] reported that phlebitis was more common in women than men. Nassaji-Zavareh and Ghorbani[20] found that the incidence of phlebitis in women and men was 31% and 20.7%, respectively. Infiltration was more common in female patients than in males, but not significantly ($P < .050$). Also, gender is not effective in the multivariate and univariate models for infiltration. Contrary to the findings, Liu et al[38] reported that infiltration was more common in females than men when the data were evaluated by univariate analysis. The difference in study results may be due to the different drug treatments. This situation may be related to the smaller caliber of female vessels compared to males.[39]

This study determined that phlebitis's incidence was statistically significantly higher over 52 years ($P < .050$). But age is not effective in the multivariate and univariate models for phlebitis. Similarly to this study result, Arias-Fernández et al[22] stated that the incidence of phlebitis increased with age. Hedayatinejad et al[36] reported that the development of phlebitis grade 3 in patients over 60 years of age was 25.89%. Elderly cancer patients are at higher risk of developing phlebitis because cancer significantly reduces tissue repair capacity and immune function, which also decreases with age.[1,21] Also, Roberts et al[31], in their study with female breast cancer patients, reported that younger patients had a significantly higher rate of complications. They stated that this was the application of more intensive treatments to young patients. There are studies saying that age is not a risk factor for the development of PIVC complications,[24] older age

Table 3. Logistic Regression Analyses of Incidence of Phlebitis and Infiltration by Some Variables

	Phlebitis				Infiltration			
	Multivariate		Univariate		Multivariate		Univariate	
Variables	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Sex	2.248 (0.735-6.875)	.156	2.602 (0.939-7.212)	.066	0.21 (0.084-0.523)	.001	0.216 (0.094- 0.497)	.216
Chronic disease	1.524 (0.524-4.431)	.439	0.858 (0.311-2.368)	.767	1.168 (0.499-2.734)	.72	0.83 (0.381-1.805)	.638
Type of the chemotherapy drug		.794		.995		.794		.995
Vesicant	1.278 (0.32-5.112)	.728	0.959 (0.265-3.475)	.949	1.358 (0.46-4.01)	.794	0.955 (0.366-2.49)	.924
Irritant and vesicant	1.417 (0.357-5.623)	.620	1.333 (0.351-5.066)	.673	0.99 (0.321-3.054	.579	0.964 (0.337-2.759)	.946
Age	0.999 (0.954-1.047)	.977	1 (0.96-1.042)	.208	1.025 (0.987-1.065)	.989	1.021 (0.988-1.055)	.208
Neutropenia	2.392 (0.791-7.234)	.123	2.623 (0.923-7.451)	.070	1.774 (0.745-4.225)	.205	0.414 (0.187-0.917)	.030
Constant	0.030	.012			−2.528	.195		

OR, odds ratio.

is a risk factor,[22,31] and adult patients are a risk factor.[31,40] Therefore, nurses should consider the age of PIVC chemotherapy patients and monitor for early signs of phlebitis more often. This study revealed that age is a significant risk factor in developing phlebitis. In this study, infiltration was joint in lower 51 years groups. However, age is not effective in the multivariate and univariate models for infiltration. This result differs from that of Simin et al[16], who determined that the incidence of infiltration increases with age. The reason for the difference in the study results is that apart from the individual characteristics, the disease, and the drug treatments taken, the nurse's experience is also practical.

In this study, it was determined that chronic diseases do not make effective the incidence of infiltration and phlebitis ($P > .050$). Phlebitis is ineffective in the multivariate and univariate models for infiltration and phlebitis. Contrary to the findings of Atay et al[24] stated that chronic diseases and the duration of catheterization led to an increase in the incidence of phlebitis. The risks may vary according to the types of chronic diseases. For example, diabetes causes permanent and pathological changes in the circulatory system.[21] Nassaji-Zavareh and Ghorbani[20] reported that phlebitis developed with and without diabetes. Contrary to Simin et al[16], they determined the relationship between diabetes and the incidence of phlebitis or infiltration. Rodrigues et al[14] argue that age, diabetes, chemotherapy, vein visibility, and palpability make vascular procedures difficult.[14] In this study, the incidence of phlebitis and infiltration among our patients with diabetes was 19% and 9.9%, respectively, which was not statistically significant ($P > .050$). Different study results show that diabetes alone does not carry a risk. But the duration of chronic diseases is the duration of catheterization led to an increase in the incidence of phlebitis.[21] Chronic conditions may be associated with inflammation and thrombus formation in the vascular structure and increased blood viscosity. Therefore, close follow-up of patients with comorbidities is necessary during IV treatment.[34]

In this study, there was a relationship between the presence of neutropenia and the incidence of infiltration. Also, neutropenia is not effective in the multivariate and univariate model for infiltration but is effective for phlebitis ($P > .050$). Contrary to the findings, Simin et al[16] also found no correlation between neutropenia and the incidence of infiltration or phlebitis. The difference in the study results is thought to be because it was performed with hemato-oncology patients in our study.

In this study, most catheters were inserted into the cephalic vein in the right forearm. There was no correlation between catheter insertion into the right or left arm and the incidence of phlebitis or infiltration. Infiltration was most common in cubital sites and cephalic veins, which was statistically insignificant. Phlebitis was most common in cubital veins on the wrist, which was, however, statistically insignificant. Simin et al[16] also found that the incidence of phlebitis and infiltration was significantly higher in cubital insertion sites. Arias-Fernández et al[22] reported that phlebitis was most common in the insertion sites on the forearm, while Daud[25] found that phlebitis was more common in the insertion sites in the forearm than those in the dorsal side of the hand. Ozkaraman[26] observed infiltration in 60% of patients and phlebitis in basilic vein insertion sites in all patients. Urbanetto et al[27] reported a correlation between catheters inserted into the forearm and the incidence of phlebitis. Roberts et al[31] found that using the arm alternately, 94% of patients experienced no or low-grade symptoms. This study results may be due to the difference in drug treatments. These results show that infiltration and phlebitis can develop in every site in the arm. Inserting catheters on the non-dominant arm and into large-diameter veins, such as cephalic and basilic, helps prevent complications, especially in long-term chemotherapy patients.[29] We also found that the risk of phlebitis was higher in ambidextrous patients. These results indicate that catheters should be inserted into the non-dominant arm and that the component used for drug therapy should not be moved.[2,7]

In this study, infiltration was observed in patients receiving vesicants. Vesicant-type drugs are important risk factors for the development of infiltration. It was determined that the chemotherapic drug type was not affected for phlebitis but was affected for infiltration. Chemotherapy type is ineffective in the multivariate and univariate models for infiltration and phlebitis. There is a correlation between the solution type and the phlebitis risk.[24] Chemotherapeutic drugs impair vein visibility and palpability. We observed that infiltration was most common in patients in grade 3 (barely visible and palpable veins), suggesting that warm compression or effleurage should be used to help dilate the vein before insertion of the catheter. In this study number of PIVC insertion attempts increased phlebitis risk. Most chemotherapy drugs are alkaloid agents that cause non-specific damage to normal cells and tissues while killing tumor cells. The severity of the injury is related to cytotoxicity, pH, osmotic pressure, and drug concentration. The ideal vein for PIVC insertion therapy depends on the treatment's pH, osmolarity, and duration.[1] These drugs have a low pH and high osmolarity, which damages the tunica intima layer of the vein.[24]

This study determined that clenching and unclenching the fist, tapping the vein, and lower than the client's heart to help dilate the vein before insertion of the catheter are not the risk for infiltration or phlebitis. However, massage and the number of PIVC insertion attempts increased phlebitis risk. Also, the hand hygiene of the nurse, vein status, catheter site, catheter arm, catheter insertion angle, control by saline, set replacement, and push drug are not the risk for infiltration or phlebitis. The nurse's experience performing the PIVC application is an essential factor in forming complications.[35] For this reason, there should be protocols that guide nurses in patient care from the beginning to the end of this practice in clinics.

Study Limitations

The study is limited to patients receiving chemotherapy treatment in a university's hematology and oncology services. In addition, patients' comorbidity, cancer type, and stage of chemotherapy situations constitute another limitation.

The incidence of infiltration and phlebitis was 9.7% and 17.5%, respectively, in patients receiving PIVC chemotherapy. In the female increases, the risk of infiltration increases 0.21 times. When the neutropenia value was put into the model alone, it was determined that the risk of infiltration increased 0.414 times in the case of neutropenia. The risk factors for infiltration are lowering the arm below the heart level, massage, and the high number of PIVC insertion attempts. The risk factors for phlebitis are age, gender, inserting the catheter into the dominant hand, the presence of neutropenia, and the type of chemotherapy drug. Nurses should have the knowledge and experience to start, resume, and discontinue the PIVC chemotherapy treatment.

They also play a crucial role in preventing complications.[2,3] They should be able to evaluate the characteristics of patients and IV drugs and determine the duration of treatment to provide high-quality nursing care and avoid the development of phlebitis and infiltration. Before inserting the PIVC, they should be aware of the risk factors for complications and consider the patient's characteristics to prevent them. After inserting the PIVC, they should use valid infiltration and phlebitis scales and monitor patients to avoid complications before they occur and to perform successful PIVC insertion in as few attempts as possible or on the first attempt.

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REFERENCES

1. Gao Y, Jiang T, Mei S, Zhang S, Zhu C, Sun Y. Meta-analysis of *Aloe vera* for the prevention and treatment of chemotherapy-induced phlebitis. *Int J Clin Exp Med*. 2016;9(6):9642-9650.
2. Potter PA, Perry AG, Stockert PA, et al. *Fundamentals of Nursing*. 9th ed. Missouri: Elsevier; 2017.
3. Pérez Fidalgo JA, García Fabregat L, Cervantes A, et al. Management of chemotherapy extravasation: ESMO–EONS clinical practice guidelines. *Eur J Oncol Nurs*. 2012;16(5):528-534. [CrossRef]
4. Doellman D, Hadaway L, Bowe-Geddes LA, et al. Infiltration and extravasation: update on prevention and management. *J Infus Nurs*. 2009;32(4):203-211. [CrossRef]
5. Bahçetepe N, Kutlubay Z, Engin B, Tüzün Y. Cutaneous effects of chemotherapeutic agents [in Turkish]. *Dermatoz*. 2013;4(2):69-76.
6. Dychter SS, Gold DA, Carson D, Haller M. Intravenous therapy: a review of complications and economic considerations of peripheral access. *J Infus Nurs*. 2012;35(2):84-91. [CrossRef]
7. Taylor C, Lillis C, LeMone P, et al. *Fundamentals of Nursing: The Art and Science of Nursing Care*. 8th ed. Pennsylvania: Lippincott Williams & Wilkins; 2011:1381-1413.
8. Uzun S. Intravenous fluid therapy. Atabek Aştı T, Karadağ A, eds. *Clinical Practice Skills and Methods* [in Turkish]. Adana: Nobel Kitabevi; 2011;2014:535-582.
9. Mattox EA. Complications of peripheral venous access devices: prevention, detection, and recovery strategies. *Crit Care Nurse*. 2017;37(2):1-14. [CrossRef]
10. Macklin D. Phlebitis. *Am J Nurs*. 2003;103(2):55-60. [CrossRef]
11. Webster J, McGrail M, Marsh N, Wallis MC, Ray-Barruel G, Rickard CM. Postinfusion phlebitis: incidence and risk factors. *Nurs Res Pract*. 2015:691934. [CrossRef]
12. Gunasegaran N, See MTA, Leong ST, Yuan LX, Ang SY. A randomized controlled study to evaluate the effectiveness of 2 treatment methods in reducing incidence of short peripheral catheter-related phlebitis. *J Infus Nurs*. 2018;41(2):131-137. [CrossRef]
13. Buzatto LL, Massa GP, Peterlini MAS, Whitaker IY. Factors associated with phlebitis in elderly patients with amiodarone intravenous infusion. *Acta Paul Enferm*. 2016;29(3):260-266. [CrossRef]
14. Rodrigues CC, Guilherme C, Da Costa ML, et al. Risk factors for vascular trauma during antineoplastic chemotherapy: contributions of the use of relative risk. *Acta Paul Enferm*. 2012;25(3):448-452. [CrossRef]
15. The official gazette. Regulation amending the regulation on nursing; 2011. Available at: http://www.resmigazete.gov.tr/eskiler/2011/04/20110419-5.htm. Accessed 09 February 2020.
16. Simin D, Milutinović D, Turkulov V, Brkić S. Incidence, severity and risk factors of peripheral intravenous cannula-induced complications: an observational prospective study. *J Clin Nurs*. 2019;28(9-10):1585-1599. [CrossRef]
17. Genç A. (Ed. Can G) *Ekstravazasyon (Onkoloji Hemşireliği)*. Nobel Tıp Kitabevleri, İstanbul; 2014.
18. Viale PH. Management of hypersensitivity reactions: a nursing perspective. *Oncology (Williston Park)*. 2009;23(2):26-30.
19. Uslusoy E, Mete S. Predisposing factors to phlebitis in patients with peripheral intravenous catheters: a descriptive study. *J Am Acad Nurse Pract*. 2008;20(4):172-180. [CrossRef]
20. Nassaji-Zavareh M, Ghorbani R. Peripheral intravenous catheter-related phlebitis and related risk factors. *Singapore Med J*. 2007;48(8):733-736.
21. Furtado LCdR. Incidence and predisposing factors of phlebitis in a surgery department. *Br J Nurs*. 2011;20(suppl7):S16-S25. [CrossRef]
22. Arias-Fernández L, Suérez-Mier B, del Carmen Martínez-Ortega M, et al. Incidence and risk factors of phlebitis associated to peripheral intravenous catheters. *Enfirm Clin (English Edition)*. 2017;27(2):79-86.
23. Abolfotouh MA, Salam M, Bani-Mustafa A, White D, Balkhy HH. Prospective study of incidence and predictors of peripheral intravenous catheter-induced complications. *Ther Clin Risk Manag*. 2014;10:993-1001. [CrossRef]
24. Atay S, Şen S, Cukurlu D. Phlebitis-related peripheral venous catheterization and the associated risk factors. *Niger J Clin Pract*. 2018;21(7):827-831. [CrossRef]
25. Daud A. Incidence of phlebitis among adult patients with peripheral intravenous catheter in an East Coast Hospital Malaysia. *Int J Care Scholars*. 2018;1(2):5-8. [CrossRef]
26. Ozkaraman A. *Evaluation of the Effect of Isometric Handgrip Exercise on the Peripheral Intravenous Chemotherapy Administration in Patients with Non-Hodgkin Lymphoma* [PhD Thesis]. Turkey: University of Ege; 2014.
27. Urbanetto Jde S, Peixoto CG, May TA. Incidence of phlebitis associated with the use of peripheral IV catheter and following catheter removal. *Rev Lat-Am Enferm*. 2016;24:e2746. [CrossRef]
28. Lenhardt R, Seybold T, Kimberger O, Stoiser B, Sessler DI. Local warming and insertion of peripheral venous cannulas: single blinded

prospective randomised controlled trial and single blinded randomised crossover trial. *BMJ*. 2002;325(7361):409-410. [CrossRef]
29. INS, Infusion Nurses Society. Infusion nursing standards of practice. *J Infus Nurs*. 2016;29(suppl 1):1-92.
30. Gorski L, Hadaway L, Hagle ME, et al. Infusion Nurses Society. Infusion nursing: standards of practice. *J Infus Nurs*. 2006;29:1-92.
31. Roberts R, Borley A, Hanna L, Dolan G, Ganesh S, Williams EM. Identifying risk factors for anthracycline chemotherapy-induced phlebitis in women with breast cancer: an observational study. *Clin Oncol (R Coll Radiol)*. 2021;33(4):230-240. [CrossRef].
32. Marsh N, Webster J, Ullman AJ, et al. Peripheral intravenous catheter non-infectious complications in adults: a systematic review and meta-analysis. *J Adv Nurs*. 2020;76(12):3346-3362. [CrossRef]
33. Larsen EN, Marsh N, O'Brien C, Monteagle E, Friese C, Rickard CM. Inherent and modifiable risk factors for peripheral venous catheter failure during cancer treatment: a prospective cohort study. *Support Care Cancer*. 2021;29(3):1487-1496. [CrossRef]
34. Shintani Y, Murayama R, Abe-Doi M, Sanada H. Incidence, causes, and timing of peripheral intravenous catheter failure related to insertion timing in the treatment cycle in patients with hematological malignancies: a prospective descriptive study. *Jpn J Nurs Sci*. 2022;19(4):e12484. [CrossRef]
35. Santos-Costa P, Paiva-Santos F, Sousa LB, et al. Nurses' practices in the peripheral intravenous catheterization of adult oncology patients: a mix-method study. *J Pers Med*. 2022;12(2):151. [CrossRef]
36. Hedayatinejad M, Fayazi S, Jahani S, Sakimalehi A, Hedayatinejad E. Survey of complications of peripheral venous catheterization at an intensive care unit (ICU) of Susa city. *Jentashapir J Health Res*. 2016;7(5):1-7. [CrossRef]
37. Washington GT, Barrett R. Peripheral phlebitis: a point-prevalence study. *J Infus Nurs*. 2012;35(4):252-258. [CrossRef]
38. Liu C, Chen L, Kong D, Lyu F, Luan L, Yang L. Incidence, risk factors and medical cost of peripheral intravenous catheter-related complications in hospitalised adult patients. *J Vasc Access*. 2020;10. [CrossRef]
39. Miliani K, Taravella R, Thillard D, et al. Peripheral venous catheter-related adverse events: evaluation from a multicentre epidemiological study in France (the CATHEVAL Project). *PLoS One*. 2017;12(1):e0168637. [CrossRef]
40. Wallis MC, McGrail M, Webster J, et al. Risk factors for peripheral intravenous catheter failure: a multivariate analysis of data from a randomized controlled trial. *Infect Control Hosp Epidemiol*. 2014;35(1):63-68. [CrossRef].