

Prevalence of Deep Vein Thrombosis Following Knee Replacement Surgery in Patients with a History of Chemotherapy

Abstract

Introduction: Deep vein thrombosis (DVT) is accompanied by adverse effects after surgery and the prevalence of this complication is unknown following knee replacement surgery in patients with a history of chemotherapy. Therefore, the present study aimed to investigate the frequency of DVT after knee replacement surgery in patients with a history of chemotherapy.

Methods: This descriptive-analytical study was performed on 189 candidates for knee replacement surgery who had a history of chemotherapy during 36 months ending in March 2016 and referred to Shohada and Imam Reza hospitals affiliated to Tabriz University of Medical Sciences, Tabriz, Iran. After surgery, patients were evaluated for the incidence of DVT and the factors, influencing it based on the instrument of determining DVT and Doppler ultrasound. Statistical analysis was completed by Spearman's correlation and regression tests.

Results: The mean standard deviation of DVT score was 43.49 ± 6.66 , which indicates that after knee replacement surgery, patients with a history of chemotherapy are at high risk for DVT. The prevalence of DVT was 25.92% (N=49) and the number of chemotherapy sessions ($P=0.001$) correlated with the occurrence of DVT.

Conclusion: The prevalence of DVT following knee replacement surgery in people with a history of chemotherapy is above the normal mean reported in the literature. Consequently, further therapeutic and preventive measures are required.

Keywords: Deep vein thrombosis; Knee replacement Arthroplasty; Chemotherapy, Risk factors, knee

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Introduction

Deep vein thrombosis (DVT) is one of the rare but dangerous and fatal post-surgery complications. Several factors are involved in the emergence of DVT, including a previous history of DVT, multiple limb trauma, immobility, prolonged surgeries, cancer, and consumption of medications that affect coagulation^(1, 2). One of the most important causes of DVT is surgery and its related issues, such as surgery duration, the extent of the surgical incision, surgery type, and post-op medicines administration⁽³⁾. However, the highest DVT rates are attributed to orthopedic surgeries, especially hip, shoulder, and knee replacement, as well as femoral Kuntscher nailing⁽⁴⁾. Compared to other surgeries, DVT is highly prevalent following a knee replacement surgery (3%-4%). Despite the relatively low prevalence of DVT, the emergence of this complication is associated with high-risk sequels and a high chance of mortality. Therefore, preventive measures have always been considered by healthcare systems and physicians in this regard. Numerous factors are involved in increasing the incidence of DVT following knee replacement surgery, including a previous history of DVT, history of cardiovascular diseases, high body mass index (BMI), smoking, long duration of surgery, blood transfusion during and after surgery, history of cancer, and history of chemotherapy or radiotherapy^(5, 6).

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The impact of chemotherapeutic agents on blood cells augments the risk of DVT in cancer patients and can elevate the prevalence of DVT in combination with other factors⁽⁷⁾, one of which is knee replacement surgery. Given the increase in chemotherapy and knee replacement surgeries, several patients with a history of chemotherapy seem to be candidates for knee replacement surgery. On the other hand, the risk of DVT is higher in these individuals, compared to healthy people. The DVT might be coupled with unfavorable post-op complications and the prevalence of this condition is unclear in patients who have a history of chemotherapy and are also candidates for knee replacement surgery. With this background in mind, the present study aimed to evaluate the frequency of DVT following knee replacement surgery in patients with a history of chemotherapy.

Methods

Study Design

This analytical and descriptive study was performed in Shohada and Imam Reza hospitals affiliated to Tabriz University of Medical Sciences, Iran during 2018-2020. All participants were selected by census and based on research objectives with a sample size of 189. The inclusion criteria were a history of chemotherapy during the previous three months, being a candidate for knee replacement surgery (unilateral), the last stage of chemotherapy being in the last two weeks, age of >18 years, and consent to participate in the research project. On the other hand, the exclusion criteria entailed a history of DVT in the past six months, a history of hospitalization due to pulmonary embolism in the past six months, use of anticoagulants, a history of cardiovascular diseases, inability to walk, hospitalization for more than 10 days in the past month, metastatic cancers and a BMI>45.

Research Process

In this study, we first selected 189 patients who were candidates for knee replacement surgery over 36 months by the end of March 2021. All subjects were hospitalized one day pre-op and blood tests were performed for all of them. If the test results were normal, further consultations, including anesthesia, forensic, and internal medicine were completed. Patients were prepared for surgery in case the surgery was safe in terms of the mentioned consultations. It is noteworthy that all cases were assessed for DVT and ultrasound was performed in case of observing the risk factors. The subjects with confirmed DVT were excluded from the research. Compressing stockings were used for all patients 12 h pre-op according to the protocol of Tabriz University of Medical Sciences. After the surgery, patients were kept in the hospital for 48 h and were assessed by an orthopedic assistant every 12 h in terms of DVT. On the other hand, DVT was evaluated by ultrasound in all patients on the first and second post-op days (the process was carried out and reported by the related attendant). After discharge, the research questionnaire was filled by one of the team members once a day for one month via phone call. In case of suspicion of DVT, a quick ultrasound examination was performed by a radiologist. Following surgery, all patients were given 100 mg of aspirin (Iran Paksh, Tehran, Iran) daily for 21 days.

Research Instruments

The instrument encompassed two sections, the first of which included the demographic characteristics of patients, such as age, BMI, the number of chemotherapy sessions, smoking, alcohol use, and occupational status. The second section contained a DVT-Limb Symmetry Index (LSI). The index includes 19 one-point questions, 6 two-point questions, 8 three-point questions, and 5 six-point questions. It should be noted that the mentioned tool has been used in various studies for DVT assessment (8). The instrument was examined in the Iranian population and its validity and reliability were confirmed as 0.9 and a Cronbach's alpha of

0.78, respectively (8). The score range of the instrument is 0-85 and the participants were classified as low-, moderate-, and high-risk with scores of <10, 10-40, and >40, respectively. In addition, those who scored >10 were recommended to undergo an ultrasound procedure for DVT (8).

Ethical Considerations

The present study adhered to all the ethical considerations of medical researches. Patients were not deprived of the routine care of the ward and all of them were hospitalized based on the DVT prevention protocol of Tabriz University of Medical Sciences. Moreover, no additional costs were received from patients and written informed consent was obtained from the participants prior to the research. Furthermore, the research project was approved by the ethics committee of Tabriz University of Medical Sciences with the code of IR.TBZMED.REC.1397.1059.

Statistical Analysis

Data were described and analyzed by mean, standard deviation, percentage, and

frequency, as well as the regression test and Spearman's correlation using the SPSS software version 21. P-value < 0.05 was considered statistically significant.

Results

In this study, we assessed 189 patients, including 108 females and 81 males with a history of chemotherapy following knee replacement surgery in terms of post-op DVT. The mean age of the participants was reported to be 52.49 ± 5.66 years with the majority of cases aged 50-60 years. In addition, the mean BMI of the subjects was 24.3 ± 12.29 with the range of 18-35 indicating that most of the patients were overweight. The majority of the cases who received chemotherapy for 9-12 sessions (minimum and maximum sessions of 3 and 15, respectively) were non-smokers and employed without any history of alcohol consumption (Table 1).

Table 1. Evaluation of the individual-social characteristics of the participants

Variable		N(%)	Post-surgery DVT	
			Yes (n=26)	Yes (n=163)
Age (year) M $\pm$ SD		52.5 $\pm$ 49.66	-	-
40-50 years N (%)		N=43 (22.75%)	N=9	N=34
50-60 years N (%)		N=81 (42.85%)	N=18	N=63
Above 60 years N (%)		N=65 (34.39%)	N=22	N=43
BMI	Low weight	N=22 (17.46%)	N=5	N=28
	Normal weight	N=59 (31.21%)	N=11	N=48
	Overweight	N=66 (34.92%)	N=14	N=52
	Obese	N=31 (16.40%)	N=19	N=12
Number of chemotherapy sessions				
Three-six session N (%)		N=29 (15.36%)	N=3	N=26
Six-nine sessions N (%)		N=45 (23.80%)	N=9	N=36
9-10 sessions N (%)		N=71 (37.56%)	N=14	N=57
More than 12 sessions N (%)		N=44 (23.28%)	N=23	N=21
Smoking	Yes N (%)	N=55 (29.11%)	N=31	N=24
	No N (%)	N=134 (70.89%)	N=18	N=116
Alcohol use	Yes N (%)	N=34 (17.98%)	N=20	N=14
	No N (%)	N=155 (82.12%)	N=29	N=126
Regular exercise	Yes N (%)	N=40 (21.17%)	N=11	N=29
	No N (%)	N=149 (78.83%)	N=38	N=109
Occupational status	Housewife N (%)	N=33 (17.46%)	N=20	N=13
	Employed N (%)	N=100 (52.91%)	N=11	N=89
	Retired N (%)	N=56 (29.62%)	N=18	N=38

The mean score of DVT was reported to be 43.49 ± 6.66 , which showed that DVT risk was dangerously high in patients who underwent knee replacement surgery and had a history of chemotherapy. The DVT risk classification demonstrated that 26, 100, and 63 subjects had a weak, moderate, and high risk of DVT, respectively. In addition, we observed that the age of older than 60 years ($n=22$), being obese ($n=19$), undergoing more than 12 chemotherapy sessions ($n=23$), smoking ($n=31$), not using alcohol ($n=29$), not exercising regularly ($n=38$),

and being retired ($n=18$) were associated with the highest DVT rates.

Examination of patients with DVT by Doppler ultrasound showed that 49 individuals (25.92%) were diagnosed with this issue and needed treatment. On the other hand, evaluation of the DVT risk factors revealed a relationship between the number of chemotherapy sessions and DVT ($P=0.001$) (Table 2). In other words, the higher the number of chemotherapy sessions, the higher the risk of DVT. However, no correlation was observed between DVT and other variables..

Table 2 presents the results of the regression test and Spearman's correlation for assessing the relationships between qualitative variables and DVT

Variable	test statistics	P-value
Age (year) M $\pm$ SD	*2.229	0.39
BMI M $\pm$ SD	*1.888	0.236
Number of chemotherapy sessions	^a -0.105	0.001
Smoking	^a 0.396	0.77
Alcohol use	^a 0.508	0.36
Regular exercise	^a 0.411	0.19
Occupational status	^a 0.549	0.25
*Regression, ^a Spearman's correlation		

Discussion

The present study aimed to evaluate the frequency of DVT following knee replacement surgery in patients with a history of chemotherapy in Imam Reza and Shohada hospitals affiliated to Tabriz University of Medical Sciences. According to our results, the majority of the participants had a moderate DVT risk. The studies conducted by Chang et al. (2018) ⁽⁹⁾, Synder et al. (2017) ⁽¹⁰⁾, and Yao et al. (2018) ⁽¹¹⁾ on DVT following knee replacement surgery demonstrated that most participants had a weak risk of DVT, which is inconsistent with our findings. These controversial results might be due to different study populations. In the current research, we only focused on patients with a history of chemotherapy. In addition, the prevalence of DVT was reported as

25%. In other words, one in four people was affected by this condition. Regarding post-op DVT, only 10% of people had this complication leading to other problems. However, our findings are not in line with the results obtained by Zhang et al. (2019) ⁽¹²⁾, Wakabayashi et al. (2017) ⁽¹³⁾, and Cafri et al. (2017) (14), which could be attributed to the assessment of people with a history of chemotherapy in the present research.

According to the results of the present study, chemotherapy was identified as a risk factor for DVT occurrence. It is believed that medications used in chemotherapy elevate the risk of coagulation and DVT by affecting blood cells and arterial walls. On the other hand, cancer also leads to hypercoagulability disorders as the result of the effects of cancer cells on blood cells, which ultimately leads to an augmented

incidence of DVT. The simultaneous impact of knee replacement surgery and history of chemotherapy increases DVT, which requires specific preventive and treatment measures.

In the current study, DVT was observed in those who were receiving 100 mg/day of prophylactic aspirin. Therefore, it is recommended that future studies address the agents at diverse doses. It should be noted that the risk of bleeding in cancer patients complicates medication prescription. Consequently, further studies are suggested in this area.

Some of the major drawbacks of the present study were not assessing the medication regimens of patients during chemotherapy, not taking into consideration the type of cancer and history of the last chemotherapy session, as well as not examining blood cells, thrombin time, and international normalized ration. Therefore,

evaluation of the mentioned issues is recommended in future studies. Moreover, given the high prevalence of this condition, it is suggested to take various preventive measures to diminish the DVT incidence rate.

Conclusion

The findings of the present study demonstrated that the DVT rate following knee replacement surgery was higher in those with a history of chemotherapy. As a result, there is a higher need for preventive and treatment measures in this area.

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