

 Received
 : 07/05/2023

 Received in revised form
 : 08/06/2023

 Accepted
 : 20/06/2023

Keywords: Deep vein thrombosis, incidence, malignancy.

Corresponding Author: **Dr. K. Prathap,** Email: prathapkaruna1@gmail.com.

DOI: 10.47009/jamp.2023.5.4.269

Source of Support: Nil, Conflict of Interest: None declared

*Int J Acad Med Pharm* 2023; 5 (4); 1340-1344



# ASSESSMENT OF INCIDENCE OF DEEP VEIN THROMBOSIS IN PATIENTS WITH MALIGNANCY UNDERGOING SURGERY

#### K. Prathap<sup>1</sup>, B. Chitra<sup>2</sup>

<sup>1</sup>Assistant Professor, Department of Vascular Surgery, Sri Venkateshwara Medical College Hospital and Research Centre, Puducherry, India.

<sup>2</sup>PG Teacher, Department of General Surgery, Southern Railways Hospital, Chennai, Tamilnadu, India.

#### Abstract

Background: Venous thromboembolism (VTE), comprising DVT and PE, significantly impacts patient morbidity, mortality, and hospital costs. Malignancy increases the risk of DVT and PE, with cancer patients on chemotherapy having a 6.5-fold higher risk. VTE is the second leading cause of mortality in cancer patients. Despite thromboprophylaxis, cancer patients undergoing surgery have a higher risk of postoperative VTE. Aim: The study aims to study the incidence of newly developing DVT in postoperative cancer patients. Materials and Methods: This prospective observational study included cancer patients undergoing surgery at Southern Railway Headquarters Hospital, Chennai, from November 2015 to June 2017. The sample size was 133 patients, with exclusion criteria for certain conditions and lack of consent. Results: Among 133 patients, 82 were females aged 51-60, with breast carcinoma being the most common malignancy. SMART SCORE assessed DVT risk; most patients were in the moderate to high-risk group. Prophylaxis was provided postoperatively, with 60.9% receiving mechanical prophylaxis and 37.6% receiving combined mechanical and pharmacological prophylaxis. In our study, the incidence of DVT in cancer patients in the Indian population who undergo surgery was 0.8%. DVT incidence was nil in breast cancer surgery patients and low in gastric surgeries. Conclusion: The study highlights the lower incidence of DVT in Indian cancer patients undergoing surgery compared to Western populations. Breast cancer and head and neck surgeries may require only mechanical prophylaxis due to their lower extent and early mobilisation.

#### INTRODUCTION

Venous thromboembolism (VTE) is a spectrum of diseases comprising Deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE contributes substantially to patient morbidity, mortality and management cost in hospitalised patients. PE is the most common preventable cause of death in hospitalised patients.

Malignancy, being a hypercoagulable state, increases the risk of developing DVT and its dreaded sequel PE. Of all the etiological and predisposing factors for DVT, cancer alone was associated with a 4.1-fold risk of thrombosis, and this risk increases to 6.5-fold in cancer patients on chemotherapy.<sup>[1,2]</sup> There is an estimated fivefold higher annual incidence of VTE in cancer patients, with about 1 in 1,000 in the general population compared to 1 in 200 in cancer patients.<sup>[3]</sup> It is to be noted that VTE and thrombotic complications are

the second most frequent cause of mortality in patients with cancer.<sup>[4]</sup>

Cancer patients undergoing surgery have twice the risk of postoperative VTE and nonfatal pulmonary embolism and three times the risk of fatal PE, compared to patients undergoing surgery for benign disease, despite the use of thromboprophylaxis.<sup>[5-7]</sup> It is a matter of concern to note that the likelihood of death in cancer patients with VTE is greater than that of patients with cancer or VTE alone.[8-9] Moreover, in cancer patients, the possibility of complications such as anticoagulant failure, bleeding, and recurrent VTE is also higher when compared to patients without cancer.<sup>[10-13]</sup> There are various reasons for this: cancer-related surgery tends to be more extensive and often involves venous trauma, while patients tend to be immobilized for prolonged postoperative periods.

Since VTE is becoming an increasingly frequent complication in cancer patients who undergo surgery and contributes significantly to morbidity and mortality, it is important to review its various aspects.

Although there are many studies denoting the incidence of DVT in cancer patients undergoing surgery worldwide, there is very little Indian literature available. In a study conducted at Tata Memorial Hospital, Mumbai, India, where 99 colorectal cancer patients who underwent colorectal surgeries were evaluated, it was found that none of the patients developed DVT. Hence, the study was prematurely terminated due to the very low incidence of DVT.<sup>[14]</sup> A retrospective chart review study from Christian Medical College, Vellore, Tamilnadu, found that the incidence of VTE was 0.17 %, and malignancy (31%) was the most common predisposing factor.

#### Aim

This study aimed to assess the incidence of newly developing Deep Vein Thrombosis (DVT) during the postoperative period in patients with malignancy undergoing a surgical procedure.

## **MATERIALS AND METHODS**

This prospective observational study was conducted at the Department of General Surgery in Southern Railway Headquarters Hospital, Chennai. The study population comprises patients admitted to the General Surgery department with malignancy and undergoing surgical procedures. The study was conducted from November 2015 to June 2017.

Exclusion criteria include patients diagnosed with hypercoagulable status, those already on Antiplatelets and Oral Anticoagulants, and patients who do not consent to participate in the study.

Ethical considerations have been taken into account, and the institutional ethical committee of Southern Railway Headquarters Hospital, Perambur, Chennai, has approved the study.

The methodology includes using WELL's score post-operatively to identify and exclude patients with suspected DVT. Patients with suspected DVT undergo venous Doppler to confirm the diagnosis. Preoperative SMART Score was used for risk assessment of developing DVT postoperatively.

In the post-operative period, DVT prophylaxis is determined based on patient factors and the duration of post-operative immobilization. Mechanical prophylaxis is provided to all patients postoperatively in the form of TED stockings. Pharmacological prophylaxis is administered in cases expected to be immobilized for more than 48 hours, using Low molecular weight heparin starting from Postoperative day (POD) 1 for 5-8 days and extended if needed.

Postoperatively, WELL'S Score is calculated on POD 2, and Venous Doppler is conducted if the score is > 2. Subsequent Venous Doppler examinations are performed on POD 7 and POD 30 to exclude DVT. If DVT is detected during any of the Venous Doppler assessments, anticoagulant treatment is initiated.

The statistical analysis will be performed using the Statistical Package for Social Sciences (SPSS) version 20. Continuous data will be analyzed for mean, median, and standard deviation, while categorical variables will be analyzed using the chi-square test, considering a 'p-value of  $\leq 0.05$  as statistically significant.

### **RESULTS**

In this study, a total of 133 patients were included, out of which there were 51 males and 82 females. The majority of the study population fell under the age group of 51-60 years. The total study population includes 7 types of malignancy, which included Breast carcinoma, Lower GI malignancy, Upper GI malignancy, Urological malignancy, Head and Neck malignancy, Sarcomas, and Metastatic chest wall lesion.

In our study, SMART SCORE was used as a risk stratification tool for assessing the risk of developing DVT. Of the 133 patients, 83 fell under the moderate to high-risk group, and the remaining 50 were in the highest-risk group, which implied that most of the study population was at a high risk of developing DVT.

Postoperatively, all the patients were assessed with WELL'S score. Since D-Dimer was not done in this study, all the patients underwent venous Doppler of both lower limbs on post-op days 2, 7, and 30. Out of 133 patients who underwent surgery, 131 of them received DVT prophylaxis, and 2 of them underwent surgery under local anesthesia and were discharged on the same day. Hence prophylaxis was not given to them. Among the 131 patients who received prophylaxis, 81 (60.9%) patients were given only Mechanical prophylaxis. Those were the patients who were mobilized either on the same day or within 48 hours, and the remaining 50 (37.6%) patients who underwent extensive surgery and were immobilized for more than 48 hours received combined mechanical and pharmacological prophylaxis. Low molecular weight heparin was given as the Pharmacological prophylaxis, and Intermittent pneumatic compression was given as the mechanical prophylaxis.

Out of 133 cases, 125 had no complications, 4 had complications that were managed medically, 3 had complications that had to be managed surgically, and 1 expired.

Out of the 57 patients who underwent breast cancer surgery, all received only mechanical prophylaxis and were advised early mobilization with no incidence of DVT.

Out of the 20 patients who underwent gastric surgeries, all of them received combined mechanical and pharmacological prophylaxis, 1 patient developed DVT who succumbed to death. Out of the 26 colorectal surgeries and 15 urological surgery, none of them developed DVT. Similar to gastric surgery, all the patients received combined prophylaxis.

None of the patients who underwent Head and neckonco surgeries and Wide local excisions for Sarcoma developed DVT.

On comparing the incidence of DVT among patients undergoing cancer surgery vs non-cancer surgery, the incidence of DVT was found to be at an insignificant p-value of 0.827% in patients undergoing cancer surgeries.

On comparing the incidence of DVT among patients undergoing Laparoscopic GI surgery vs Open GI surgery, the incidence of DVT was found to be at an insignificant p-value of 0.13 in patients undergoing open GI surgeries compared with Laparoscopic GI surgery.

In our study, the incidence of DVT among patients with malignancy undergoing surgery was 0.8%.

		Frequency	Percentage
	40 -50 years	35	26.3%
A C	51-60 years	43	32.3%
Age Groups	61 - 70 years	36	27.1%
	$\geq$ 71 years	19	14.3%
Sex	Male	51	38.3%
	Female	82	61.7%
	Breast malignancy	57	42.9%
	Lower GI Tract malignancy	27	20.3%
Diagnosis	Upper GI Tract malignancy	23	17.3%
	Urological malignancy	15	11.3%
	Head and Neck malignancy	7	5.3%
	Sarcoma	3	2.3%
	Miscellaneous	1	0.8%

#### Table 2: Distribution of patient's clinical characteristics

		Frequency	Percentage
	1	0	0.0%
Pre-op Smart Score	2	83	62.4%
	3	50	37.6%
Post-op WELL'S Score	<2	0	0.0%
Post-op WELL'S Scole	≥2	133	100.0%
Postonoustive Prombylovic	No	2	1.5%
Postoperative Prophylaxis	Yes	131	98.5%
	Nil	2	1.5%
Type of Prophylaxis	Mechanical	81	60.9%
	Mechanical And Pharmacological	50	37.6%
	Nil	125	94.0%
Complications	Medically managed	4	3.0%
Complications	Surgically managed	3	2.3%
	Death	1	0.8%

#### Table 3: Cross-tabulation of type of procedure with DVT

Sungamy	Post DVT	P value		
Surgery	No	Yes	r value	
Lap GI	13	0	0.13	
Open GI	30	1	0.15	
Cancer	126	1	0.827	
Non-Cancer	6	0	0.827	

Table 4: Cross-tabulation of type of surgery with complications									
Surgery	Complications								
	Nil	Medically managed	Surgically managed	Death					
BREAST	56	0	1	0					
COLORECTAL	23	2	1	0					
GASTRIC	18	1	0	1					
UROLOGY	13	1	1	0					
HEAD & NECK	7	0	0	0					
SARCOMA	4	0	0	0					
MISCELLANEOUS	4	0	0	0					

Table 5: Cross-tabulation of type of surgery with other factors								
	Prophylaxis		Туре		Days		Postop DVT	
Surgery	Yes	No	Mech	Mech & Pharm	0-4	5-8	No	Yes
BREAST	57	0	57	0	57	0	57	0

1342

COLORECTAL	26	0	0	26	0	26	28	0
GASTRIC	20	0	0	20	2	18	19	1
UROLOGY	13	2	9	4	9	4	15	0
HEAD&NECK	7	0	7	0	7	0	7	0
SARCOMA	4	0	4	0	4	0	4	0
MISCELLANEOUS	4	0	4	0	4	0	4	0

## DISCUSSION

The study population mostly consisted of individuals aged 51-60, similar to the mean age (53.3) in the Tata Memorial Hospital study.<sup>[14]</sup> Females outnumbered males due to the inclusion of breast carcinoma cases.

The patients in our study population fell under 7 types of malignancies. The majority of them had breast carcinoma followed by Lower GI tract malignancy (Carcinoma colon, Rectal carcinoma, Anal canal carcinoma), Upper GI tract malignancy (Carcinoma stomach, Malignant GIST), Urological malignancy (Carcinoma Urinary bladder, Prostatic carcinoma), Head and Neck malignancies (Thyroid malignancies, Parotid carcinoma, Oral cavity malignancies), Sarcomas and 1 case of Metastatic chest wall lesion. This study included a wide range of malignancies compared to the RISTOS Project.<sup>[15]</sup> which included General, Urological and Gynaecological oncology surgeries only.

In our study, the incidence of DVT in cancer patients in the Indian population who undergo surgery was 0.8 %, sharply contrasting with many Western studies showing more incidence rates.<sup>[5-7]</sup>

SMART SCORE was utilized to predict DVT risk, categorizing all patients into moderate to high or highest-risk groups. However, only one patient developed DVT. The score's drawback is its failure to consider malignancy-specific aspects, necessitating further validation in cancer patients undergoing surgery.

Out of 133 patients, 131 received prophylaxis, except for 2 undergoing minor surgery with local anesthesia. Among them, 60.9% had mechanical prophylaxis (TED stockings) and were mobilized within 48 hours. The remaining 37.6% had mechanical and pharmacological prophylaxis (Low molecular weight heparin) due to extensive surgeries and longer immobilization, supported by studies by Dahan R et al., Samama MM et al., and Cohen AT et al.<sup>[16-18]</sup>

In our study, 57 breast cancer surgery patients received only mechanical prophylaxis, mobilized on the same day or the 1st postoperative day. DVT incidence was nil, aligning with Andtbacka et al.'s study stating that early mobilization and mechanical prophylaxis alone are effective, rendering pharmacological prophylaxis unnecessary.<sup>[19]</sup>

Out of 20 patients undergoing gastric surgeries (Gastrectomies and Excision of malignant gastric GIST), one developed DVT despite combined mechanical and pharmacological prophylaxis. Our findings align with Wada et al.'s study showing a 1.3% incidence of DVT in gastric cancer surgery patients, particularly those receiving neoadjuvant chemotherapy.<sup>[20]</sup>

However our result was lesser when compared to another study done by Kim JW et al.,21 in Korea, where the incidence of DVT in patients undergoing gastric cancer surgeries was found to be 2.4%. This study was mainly done to assess DVT in the Asian population.

Colorectal surgeries are associated with a higher DVT incidence due to factors like cancer-related hypercoagulable state and prolonged surgery duration. In our study, 26 colorectal surgeries received combined mechanical and pharmacological prophylaxis, and no DVT cases were observed, aligning with a Tata Memorial Hospital study with a very low suspected DVT incidence, leading to its premature termination.<sup>[14]</sup>

In our study, 15 urological surgeries (Radical cystectomy, Orchidectomy, and Cystoscopies) had no DVT cases, similar to the RISTOS study's 0.8% VTE incidence in cancer patients undergoing urological surgery.<sup>[16]</sup>

All 7 patients undergoing head and neck cancer surgeries received mechanical prophylaxis and had no DVT. In contrast, a study by Patrick Hennesey et al. reported a 2% incidence, but the comparison was limited due to differences in surgical procedures and sample size.<sup>[22]</sup>

When comparing DVT incidence in cancer-related laparoscopic vs. open GI surgery, a minimal increase was observed in open GI surgery, but the p-value (0.13) was not significant. No prior study directly compared laparoscopic vs. open cancer surgery, but Nguyen NT et al. found generally lower DVT incidence in laparoscopic procedures, differing from this study's findings.<sup>[23]</sup>

The incidence of DVT in patients undergoing cancer surgeries was found to be minimally higher than those undergoing non-cancer surgeries, with an insignificant p-value of 0.827 which is in sharp contrast to many studies which state that Cancer patients undergoing surgery have twice the risk of postoperative VTE, compared to patients undergoing surgery for benign disease, despite the use of thromboprophylaxis.<sup>[5-7]</sup>

#### Limitations

The study's limitations include a small sample size due to the 20-month duration, single-centre design, and lack of evaluation for all types of cancer surgeries, making it challenging to generalize the results effectively.

#### CONCLUSION

The incidence of DVT in cancer patients undergoing surgery in the Indian population is lower than in the Western population. Specific cancer surgeries like breast and head and neck surgeries, which are less extensive and allow for early mobilization, require only short mechanical prophylaxis for postoperative DVT prevention. However, the incidence of DVT among patients undergoing cancer and non-cancer surgeries and cancer-related laparoscopic and open GI surgeries could not be accurately assessed due to the limited study population.

#### REFERENCES

- Heit JA, Silverstein MD, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Risk factors for deep vein thrombosis and pulmonary embolism: a population-based case-control study. Arch Intern Med. 2000;160(6):809-15.
- Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year populationbased study. Arch Intern Med. 1998;158(6):585-93.
- Lee AY, Levine MN. Venous thromboembolism and cancer: risks and outcomes. Circulation. 2003;107(23 Suppl 1):I-17.
- Werzberger A, Kuter B, Nalin D, Wiens BL, Bohidar NR, Pigeon JG, Hess G, Clemens R, Bienzle U, Schonfeld C, Schunck B. Hepatitis A vaccination. N Engl J Med. 1998;339:705.
- Kakkar AK, Williamson RC. Prevention of venous thromboembolism in cancer patients. Semin Thromb Hemost. 1999;25(2):239-243. Copyright© 1999 by Thieme Medical Publishers, Inc.
- Hutten BA, Prins MH, Gent M, Ginsberg J, Tijssen JG, Büller HR. Incidence of recurrent thromboembolic and bleeding complications among patients with venous thromboembolism in relation to both malignancy and achieved international normalized ratio: a retrospective analysis. J Clin Oncol. 2000;18(17):3078-83.
- Prandoni P, Lensing AW, Piccioli A, Bernardi E, Simioni P, Girolami B, Marchiori A, Sabbion P, Prins MH, Noventa F, Girolami A. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. Blood. 2002;100(10):3484-8.
- Levitan N, Dowlati A, Remick SC, Tahsildar HI, Sivinski LD, Beyth R, Rimm AA. Rates of initial and recurrent thromboembolic disease among patients with malignancy versus those without malignancy: risk analysis using Medicare claims data. Medicine. 1999;78(5):285-91.
- SØrensen HT, MellemkjÆr L, Olsen JH, Baron JA. Prognosis of cancers associated with venous thromboembolism. N Engl J Med. 2000;343(25):1846-50.
- Prins MH, Hettiarachchi RJ, Lensing AW, Hirsh J. Newly diagnosed malignancy in patients with venous thromboembolism. Search or wait and see? Thromb Haemost. 1997;78(1):121-5.

- Baron JA, Gridley G, Weiderpass E, Nyrén O, Linet M. Venous thromboembolism and cancer. Lancet. 1998;351(9109):1077-80.
- Bhagya Rao B, Kalayarasan R, Kate V, Ananthakrishnan N. Venous thromboembolism in cancer patients undergoing major abdominal surgery: Prevention and management. ISRN Vasc Med 2012;2012:1–22.
- Palareti G, Legnani C, Lee A, Manotti C, Hirsh J, D'Angelo A, Pengo V, Moia M, Coccheri S. A comparison of the safety and efficacy of oral anticoagulation for the treatment of venous thromboembolic disease in patients with or without malignancy. Thromb Haemost. 2000;84(5):805-10.
- Shukla PJ, Siddachari R, Ahire S, Arya S, Ramani S, Barreto SG, Gupta S, Shrikhande SV, Jagannath P, Desouza LJ. Postoperative deep vein thrombosis in patients with colorectal cancer. Indian J Gastroenterol. 2008;27(2):71-3.
- Agnelli G, Bolis G, Capussotti L, Scarpa RM, Tonelli F, Bonizzoni E, Moia M, Parazzini F, Rossi R, Sonaglia F, Valarani B. A clinical outcome-based prospective study on venous thromboembolism after cancer surgery: the RISTOS project. Ann Surg. 2006;243(1):89-95.
- Dahan R, Houlbert D, Caulin C, Cuzin E, Viltart C, Woler M, Segrestaa JM. Prevention of deep vein thrombosis in elderly medical in-patients by a low molecular weight heparin: a randomized double-blind trial. Pathophysiol Haemost Thromb. 1986;16(2):159-64.
- Samama MM, Cohen AT, Darmon JY, Desjardins L, Eldor A, Janbon C, Leizorovicz A, Nguyen H, Olsson CG, Turpie AG, Weisslinger N. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. N Engl J Med. 1999;341(11):793-800.
- Cohen AT, Davidson BL, Gallus AS, Lassen MR, Prins MH, Tomkowski W, Turpie AG, Egberts JF, Lensing AW. Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomized placebo-controlled trial. BMJ. 2006;332(7537):325-9.
- Andtbacka RH, Babiera G, Singletary SE, Hunt KK, Meric-Bernstam F, Feig BW, Ames FC, Ross MI, Dejesus Y, Kuerer HM. Incidence and prevention of venous thromboembolism in patients undergoing breast cancer surgery and treated according to clinical pathways. Ann Surg. 2006;243(1):96-101.
- Wada T, Fujiwara H, Morita S, Fukagawa T, Katai H. Incidence of and risk factors for preoperative deep venous thrombosis in patients undergoing gastric cancer surgery. Gastric Cancer. 2017;20(1):137-43.
- 21. Kim JW, Chun EJ, Choi SI, Park DJ, Kim HH, Bang SM, Kim MJ, Lee JH, Lee MS, Lee JO, Kim YJ. A prospective study on the incidence of postoperative venous thromboembolism in Korean gastric cancer patients: an inquiry into the application of Western guidelines to Asian cancer patients. PloS One. 2013;8(4):e61968.
- Hennessey P, Semenov YR, Gourin CG. The effect of deep venous thrombosis on short-term outcomes and cost of care after head and neck cancer surgery. Laryngoscope. 2012;122(10):2199-204.
- Nguyen NT, Hinojosa MW, Fayad C, Varela E, Konyalian V, Stamos MJ, Wilson SE. Laparoscopic surgery is associated with a lower incidence of venous thromboembolism compared with open surgery. Ann Surg. 2007;246(6):1021-7.