Deep Vein Thrombosis in Indian Cancer Patients Undergoing Major Thoracic and Abdomino-Pelvic Surgery

Ashish Jakhetiya¹ · Nootan Kumar Shukla¹ · S V Suryanarayana Deo¹ ·
Pankaj Kumar Garg^{1,2} · Sanjay Thulkar³

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Abstract The aim of the study was to determine the incidence of postoperative deep vein thrombosis (DVT) in Indian patients undergoing surgery for thoracic and abdomino-pelvic malignancies.

A prospective observational study was conducted in a tertiary care cancer centre in North India. Two hundred and fifty consecutive patients who underwent curative surgery for thoracic and abdomino-pelvic malignancies during the period March 2014 to March 2015 were enrolled in the study. Perioperative pharmacological antithrombotic prophylaxis was not prescribed to any of the patient as per the institutional protocol. All the patients underwent colour duplex ultrasound of the bilateral lower limbs – preoperatively to determine the baseline status, and on 7th and 28th day postoperatively to look for presence of DVT. None of the patient in the study cohort showed clinical or radiological evidence of lower limb deep vein thrombosis. Our study suggests very low incidence of deep vein thrombosis in Indian patients undergoing surgery for thoracic and abdomino-pelvic malignancy.

Keywords Surgery · Cancer · Venous thromboembolism · Deep vein thrombosis

Introduction

Though the relationship between thrombosis and malignancy has been well documented, pathophysiological mechanisms remains poorly understood. Studies have shown that malignancy increases the risk of venous thromboembolism (VTE) by two to four times [1, 2]. There is growing evidence to suggest the role of prothrombotic pathways and various cytokines responsible for high incidence of VTE in malignancy [3]. VTE events that may occur perioperatively include deep vein thrombosis (DVT) and pulmonary embolism (PE). Postoperative DVT is a well-studied complication of major oncological surgeries. The presence of malignant disease doubles the risk of DVT, with reported incidences of asymptomatic calf vein thrombi at 40 %–80 %, proximal vein thrombi 10 %–20 %, PE 4 %–10 % and fatal PE 1 %–5 % without perioperative prophylaxis [4]. VTE is reported to be the most common cause of death at 30 days follow-up period among cancer patients undergoing surgery [5]. The risk for thromboembolic complications in cancer surgery may have altered over the years. Refinement in surgical techniques, advanced perioperative care, early postoperative recovery and ambulation may have reduced the risk of VTE [5].

Though DVT is considered a major postoperative complication in western population, studies support that Asians have low prevalence of DVT [6]. There is scarcity of published literature related to incidence of postoperative DVT in cancer patients in India. A few studies have reported conflicting results about the incidence of DVT in Indian patients [7–9]; this has resulted in marked variation in DVT prophylaxis policies across the centres in India. We designed a prospective study to determine incidence of postoperative DVT in cancer patients undergoing thoracic and abdomino-pelvic surgery.

✉ Ashish Jakhetiya
ashish_jakhetiya@yahoo.com

¹ Department of Surgical Oncology, Dr BRA Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi 110029, India

² Department of Surgery, University College of Medical Sciences and Guru Teg Bahadur Hospital, University of Delhi, Delhi 110095, India

³ Department of Radiodiagnosis, Dr BRA Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi 110029, India

Methods

This prospective observational study was done in a tertiary care centre in North India. The study was approved by the institutional ethics committee for human research. Two hundred and fifty consecutive patients, aged 18–75 years, who underwent curative surgery for thoracic and abdominopelvic malignancies during the period March 2014 to March 2015 were included. All the patients gave their informed consent prior to participation into the study. Patients who underwent emergency surgery or were found to have disseminated malignancy on exploration were not included in the study. Also the patients with past history of DVT or on anti-coagulant treatment including aspirin were excluded.

Preoperative duplex colour ultrasonography (USG) of bilateral lower limbs was performed in all patients to rule out chronic DVT; examination of common femoral, superficial femoral, popliteal, anterior and posterior tibial veins was performed. Each patient's demographic details, body mass index (BMI), tumour related features (stage, histology, prior chemotherapy and/or radiotherapy, prior surgeries), indwelling central venous catheter, nature and duration of surgery, type of anaesthesia and post-operative recovery risk factors (time to full ambulation) were recorded. Perioperative pharmacological antithrombotic prophylaxis was not prescribed to any of the patient as per the institutional protocol. Early post-operative mobilization and ambulation was performed in all patients in accordance with a routine protocol. All the patients were examined for clinical

signs of VTE. They also underwent colour duplex USG of the bilateral lower limbs –on 7th and 28th day postoperatively to look for presence of DVT.

All the colour duplex USG studies were performed or directly supervised by same radiologist. Presence of DVT was defined as the constant intraluminal defect or a non-compressible venous segment; thrombosis was classified as distal if it involves the calf veins and as proximal if it involves the popliteal or more proximal veins. Patients with involvement of both calf and proximal veins were classified as proximal thrombosis. Isolated muscular or superficial thrombosis was not considered as DVT.

Results

Two hundred and fifty patients were included in the study. Mean age of study population was 48.92 (SD, 13.0) years and 54 % were females. Almost 90 % of the patients were residents of North India. Mean BMI was 24.65 (SD, 4.78) kg/m²; 11 % were obese (>30 kg/m²) and 9 % were undernourished (<18.5 kg/m²). Majority (80 %) of the patients belonged to Eastern Cooperative Oncology Group (ECOG) performance status 1. Pre-existing medical illnesses were recorded in 9.2 % patients while 15.6 % patients had history of smoking. Common cancer sites were lung (14 %), rectum (12.8 %) and colon (11.2 %). Common histopathological diagnoses were adenocarcinoma (53 %), squamous cell

Table 1 Distribution of cancer sites in the patient cohort (*n* = 250)

No	Diagnosis	Frequency	Percentage
1	Carcinoma stomach	23	9.20
2	Carcinoma esophagus	25	10.00
3	Carcinoma colon	28	11.20
4	Carcinoma rectum	32	12.80
5	Carcinoma anal canal	2	0.80
6	Carcinoma cervix	10	4.00
7	Carcinoma endometrium	4	1.60
8	Carcinoma lung	35	14.00
9	Carcinoma jejunum	1	0.40
10	Carcinoma gall bladder	22	8.80
11	Carcinoma ovary	24	9.60
12	Carcinoma kidney	9	3.60
13	Carcinoma pancreas	10	4.00
14	Periampullary carcinoma	3	1.20
15	Cholangiocarcinoma	4	1.60
16	Carcinoma testies	4	1.60
17	Chest wall sarcoma	2	0.80
18	Retroperitoneal sarcoma	5	2.00
19	Thymoma	3	1.20
20	Others (Pelvic GIST, leiomyoma, peritoneal meothelioma)	4	1.60

Table 2 Distribution of various surgical procedures in the patient cohort ($n = 250$)

No	Procedure	Number	Frequency (%)
1	Colo-rectal resections	60	24
	(a) Abdominoperineal resection	22	8.8
	(b) Low anterior resection	10	4
	(c) Right hemicolectomy	18	7.2
	(d) Left hemicolectomy	8	3.2
	(e) Total colectomy	2	0.8
2	Lung resections	34	13.6
	(a) Pneumonectomy	17	6.8
	(b) Lobectomy	17	6.8
3	Esophageal resections	24	9.6
4	Pancreaticoduodenectomy	13	5.2
5	Radical nephrectomy	9	3.6
6	Optimal ovarian cytoreduction	27	10.8
7	Radical cholecystectomy	23	9.2
8	Gastrectomy	23	9.2
	(a) Distal radical gastrectomy	9	3.6
	(b) Total gastrectomy	13	5.2
	© Esophagogastrectomy	1	0.4
9	Radical hysterectomy	14	5.6
10	Exploration and mass excision	9	3.6
11	Hemihepatectomy	2	0.8
12	Pelvic exenteration	3	1.2
13	Sternotomy and mass excision	3	1.2
14	RPLND	4	1.6
15	Radical chest wall resection	2	0.8

carcinoma (17 %), papillary serous adenocarcinoma (7 %), neuroendocrine tumor (3 %), and gastrointestinal stromal tumor (2 %). Different diagnosis and their distribution are depicted in Table 1. Out of 250 patients, 32(12.80 %) had history of prior incomplete surgery, 43(17.2 %) received neoadjuvant radiotherapy, and 76 (30.4 %) received neoadjuvant chemotherapy. Common surgical procedures were colo-rectal resections in 24.0 %, lung resections in 13.6 %, ovarian

cytoreduction in 10.8 %, and esophageal resections in 9.6 % patients. (Table 2) Patient position during surgery was supine in 51 % patients followed by lithotomy and thoracotomy in 25 % and 24 % patients respectively. Central venous line (internal jugular vein or subclavian vein) was inserted in 155(62 %) patients; mean duration of central line catheterization was 4.9 days (SD, 1.5). Mean duration of surgery was 229.0 min (SD 80.4, range 60–540). Postoperative mechanical ventilation was used in 5.2 % patients and mean duration of postoperative mechanical ventilation was 1.1 days (SD, 0.3). Mean duration of immobility after surgery was 1.1 days (SD, 0.3). Mean duration of hospital stay after surgery was 8.5 days (SD, 3.5). The most common postoperative complications were surgical site infection (8.8 %), pulmonary atelectasis (6.4 %) and bowel anastomosis leak (2.8 %). Table 3 displays the major post operative complications among the patients cohort. Most of the cases were of AJCC/TNM (2010) stage II and III; Table 4 displays the distribution of disease stage and pathological diagnosis in the patient cohort.

Discussion

DVT is well known postoperative complication which has significant impact in terms of morbidity and health care cost. Risk of postoperative DVT has been divided into low, moderate, high and very high risk [4, 10]. Factors specific to malignancy influencing the risk of VTE include site and type of malignancy, stage of the disease, and administration of preoperative chemotherapy [5, 11, 12].

Though majority of the patients in our study were from moderate to high risk category, yet none showed any evidence of DVT/PE. Most of the patients belonged to AJCC/TNM stage II and III, and all underwent curative resection. Two randomized controlled trials (RCTs) published from India showed negligible incidence of DVT after major abdominal and colorectal cancer surgery [13, 14]. A RCT conducted to assess the risk of DVT in North Indian patients undergoing major abdominal surgery reported that none of the 65 patients

Table 3 Major Postoperative complications

No.	Complication	Frequency, n(%)
1.	Surgical site infection	22 (8.8 %)
2.	Pulmonary atelectasis	16 (6.4 %)
3.	Bowel anastomosis leak	7 (2.8 %)
4.	Bronchopneumonia	6 (2.4 %)
5.	Intra-abdominal/pelvic abscess	5 (2 %)
6.	Sepsis	3 (1.2 %)
7.	Bleeding	2 (0.8 %)
8.	Early post operative bowel obstruction	2 (0.8 %)
9.	Postoperative death (sepsis and multi organ failure)	1 (0.4 %)

in two treatment arms developed DVT; Nadroparin prophylaxis was prescribed in 34 patients while 31 had no prophylaxis [13]. Another RCT performed at Tata Memorial Hospital was prematurely closed as none of the 99 colorectal cancer patients who underwent curative surgery (both prophylaxis and no prophylaxis group) were found to develop DVT [14]. These studies highlighted that the Indian patients have low risk of development of postoperative DVT [13–15].

The reasons for the low frequency of postoperative DVT among the Indian patients may be related to racial, genetic or rheological factors. Stein et al. showed that both incidence and mortality for DVT/PE are lower in Asian population and attributed this to low prevalence of factor V Leiden mutation and possibility of lower levels of fibrinogen, factor VIIc and factor VIIIc. They also concluded that clinical assessment of prior probability of VTE should probably be adjusted based on ethnic differences [15, 16]. There is need of further studies to clarify

the possible decreased prevalence of factor V Leiden mutation and G20210 A mutation in the Indians which may explain the relative immunity of the Indian patients for DVT [13]. Other reasons for low incidence of postoperative DVT in our patient cohort may include good preoperative performance status of the patients, resectable stage of the tumours, meticulous surgical techniques, and early post-operative ambulation.

Use of duplex colour USG as a screening modality for DVT may be considered a limitation of the study. Though it is an operator dependent investigation and may miss small calf vein thrombi, it has its own advantages. It is inexpensive, non-invasive, and widely available and bedside investigation; it, in expert hands, gives accurate results. Though venography is a gold standard investigation for DVT, yet its role as a screening modality is limited in view of its invasiveness and procedure associated morbidity.

Table 4 Distribution of disease stage and pathological diagnosis in the patient cohort

No.	Diagnosis	No of cases	Stage grouping	Histology	other
1	Carcinoma Stomach	23	I – 3 II – 14 III – 6	Adenocarcinoma – 18 NET – 2 GIST – 2 Others – 1	Proximal and mid body – 14 Distal – 9
2	Carcinoma Esophagus	25	I – 2 II – 6 III – 17	SCC – 20 Adenocarcinoma – 4 Others – 1	
3	Carcinoma colon	28	In situ – 1 I – 2 II – 11 III – 14	Adenocarcinoma – 26 Others – 2	Right – 18 Left – 8 Multiple Polyposis – 2
4	Carcinoma rectum	32	In situ – 1 I – 5 II – 11 III – 15	Adenocarcinoma – 31 Others – 1	Lower third – 22 Middle third – 10
5	Carcinoma cervix	10	I – 5 II – 4 III – 1	SCC – 9 Adenocarcinoma – 1	
6	Carcinoma lung	35	I – 4 II – 14 III – 17	Adenocarcinoma – 14 SCC – 13 NET – 3 Adenoid cystic – 2 Others – 3	
7	Carcinoma gall bladder	22	I – 5 II – 6 III – 8 IV – 3	Adenocarcinoma – 22	
8	Carcinoma ovary	24	I – 5 II – 2 III – 17	Papillary serous carcinoma – 17 Endometreoid – 3 Germ cell tumor – 1 Others – 3	
9	Renal cell carcinoma	9	I – 2 II – 3 III – 4	Clear cell carcinoma – 6 Chromophobe – 1 Others – 2	
10	Carcinoma pancreas	10	I – 5 II – 5	Adenocarcinoma – 7 NET – 3	

Conclusion

The present study reiterates the notion of low frequency of post-operative DVT in Indian patients. Further studies involving multiple regional cancer centres with large sample size will further provide accurate epidemiological data regarding the DVT in Indian patients. Analysis of underlying genetic factors may add new dimension to the etiopathogenesis. There is a need to relook the pharmacological prophylactic policy in Indian cancer patients undergoing major surgeries.

Compliance with Ethical Standards

Conflict of Interest None to declare

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