**Original Research Article**

**Evaluation of post-operative venous thromboembolism in patients undergoing abdominal surgery for malignancy- A cross sectional study**

**Abstract:**

**Background:** Abdominal malignancy is a well-known cause of death worldwide. Treatment of abdominal malignancy (AM) includes surgery, adjuvant and neoadjuvant chemo-radiotherapy depending on the extent and stage of cancer. Like all surgeries, AM surgery carries several complications. Among them venous thromboembolism (VTE) is a particular serious one having an incidence 16% to as high as 38% globally.

**Methods and materials:** This was a prospective cross sectional study conducted at a tertiary medical college and hospital of Dhaka, Bangladesh from January 2021 to December 2023.There was no institutional guideline for VTE prophylaxis. None of the patient received any standard VTE prophylaxis in the perioperative period. Statistical analysis was performed using IBM SPSS version 26.0. A p-value of < 0.05 was considered statistically significant. Multivariable analysis using a binary logistic regression model was used to verify the independent risk factors for VTE in the post-operative patients. Variables identified as having a potential association (p < 0.05) in a univariate analysis were entered into each multivariable analysis model.

**Results:** A total of 113 patients who underwent surgery for AM were included in the study. These patients were divided into two groups: VTE and non-VTE group. Among 113 patients, 11(9.73%) patients presented with DVT. Additionally, three patients (2.6%) had pulmonary embolism and all of them died in the post-operative period. Advanced age, prolong duration of surgery, advanced stage of disease, low albumin level, colorectal and gynecological surgery, elevated D-dimer level and high Caprini scores were independent predictors of post-surgical VTE.

**Conclusion:** According to the current study, post-operative VTE is a serious consequence following surgery for abdominal malignancy. In AM patients, several factors were responsible for the development of post-operative VTE. In order to determine the predictors of post-surgical VTE, more extensive multicenter research should be carried out.

Key words:*incidence, risk factors, venous thromboembolism, post-surgery*

**Introduction:**

Abdominal malignancy is a well-known cause of death worldwide. Treatment of abdominal malignancy (AM) includes surgery, adjuvant and neoadjuvant chemo-radiotherapy according to the disease extend and stage of the disease.1 Radical surgery is the mainstay of treatment of AM especially in resectable cases.2 Like all surgeries, AM surgery carries many complications. Among these venous thromboembolism (VTE) is a most critical one having an incidence 16% to as high as 38% globally.3

In general, VTE is the second most frequent cause of death in cancer patients undergoing medicinal and surgical treatment.4 VTE includes deep vein thrombosis (DVT) and its potentially fatal consequence, pulmonary embolism (PE).. Because cancer patients are more likely to experience bleeding and recurrent thrombosis, treating venous thromboembolism can be challenging.5 Surgery is also believed to have a pro-inflammatory effect on the incidence of VTE. Venous blood pooling, vascular wall injury, and the patient's hypercoagulable state are all likely to occur during the surgery. Tissue factor exposure at the surgical site is another important component that contributes to the development of VTE after surgery.6

Radical surgery for abdominal cancer patients increases the risk of VTE.7 Both VTE and PE can lead to limb swelling, ulceration, and discomfort (post thrombotic syndrome) or even death.8 Without preventative measures, the rate of perioperative DVT after general surgery is 10–40% while the risk of thrombosis after abdominal surgery is 15–40%.9 The incidence of DVT is doubled after any malignant surgery, and the risk of PE is three times higher than after any other abdominal surgery.10 According to multiple published studies, surgery itself is a risk factor for the development of VTE.11,12

Postoperative VTE can be a serious complication following AM surgery. Never the less, VTE also has a major impact on surgical patients' prognosis and negatively affect their quality of life. During the first post-operative month, VTE is the leading cause of death for individuals undergoing oncological surgery. About one-third of patients with DVT will develop post-thrombotic syndrome (PTS) in the long run, and thirty percent of patients with VTE will experience a recurrence within eight years following surgery.13 There are several known factors that raise the likelihood of a postoperative VTE. Having experienced VTE in the past, cancer, inflammatory bowel disease, thrombophilia, advanced age, obesity, smoking, acute sickness, wound infection, and prolonged immobility are among them, in addition to the actual surgical procedure.14 Consequently, there is interest in more accurately describing the specific risk factors for a VTE, especially PE, in patients undergoing abdominal surgery for malignancy. The aim of this study is to estimate the incidence of post-operative VTE in patients undergoing major abdominal cancer surgery as well as to identify the risk factors associated with VTE.

**Materials and methods:**

This was a prospective cross sectional study conducted at a tertiary medical college and hospital of Dhaka, Bangladesh from January 2021 to December 2023. At the time of study, there was no institutional guidelines for VTE prophylaxis. None of the patient received any standard VTE prophylaxis in the perioperative period. The inclusion criteria were as follows:

1. Patient age>18 years

2. Patient underwent surgery for routine cases

3. Patient diagnosed with DVT within 30 days after operation

Following patients were excluded from study

2. Past history of venous thromboembolism (VTE)

3. Incomplete medical records

5. Emergency surgery

DVT was diagnosed according to the clinical examination findings like unilateral swollen limb with pain and erythema of lower extremity aided ultrasonography, performed by certified ultrasound specialist. DVT was defined based on the following ultrasonic findings:

• Heterogeneous thrombus was present inside any of the screened veins on B-mode

• Presence of a non-compressible segment

• Flow impairment on color Doppler imaging.

PE was identified with lung ventilation/perfusion scans or chest computed tomography.

Demographic variables including age, sex, BMI, history of smoking, co-morbidities (hypertension, diabetes, coronary heart disease) were obtained. Laboratory data like complete blood count, serum albumin, C-reactive protein (CRP), blood glucose level and post-operative d-dimer were collected. Disease profile like stage of malignancy, histopathological type, location, history of chemotherapy and radiotherapy were also included in the study. Operative data like type of surgery, mode of surgery (open vs laparoscopic) duration of surgery, amount of blood transfusion were also identified. Caprini risk assessment model (RAM) score of VTE was also calculated. Originally developed for surgical patients, the Caprini RAM facilitates the derivation of VTE risk by summing individual risk factors so as to place patients into four categories: “low risk” (0-1 points), “moderate risk” (2 points), “high risk” (3-4 points), and “highest risk” (≥5 points). Post-operative data including rate of infection (wound infection, pneumonia, urinary tract infection) anastomotic leak, early mobilization, hospital mortality and length of hospital stay were also observed.

Data were collected in a preformed questionnaire. Incidence of VTE among the patients who underwent surgery for colorectal cancer (CRC) was investigated up to 90 days after surgery. Then, the clinical characteristics and laboratory results were compared between those with and without VTE. Statistical analysis was performed using IBM SPSS version 26.0. Continuous variables were analyzed in the form of the means with standard deviations (Mean ± SD). Categorical variables were shown as numbers and proportions. Continuous data were analyzed using the independent samples t-test. Categorical data were analyzed using the chi-squared test. Statistical significance was defined as a p-value of < 0.05. Multivariable analysis using a binary logistic regression model was used to verify the independent risk factors for VTE in the post-operative patients. Variables identified as having a potential association (p < 0.05) in a univariate analysis were entered into each multivariable analysis model.

**Results:**

A total of 113 patients who underwent surgery for AM were included in the study. These patients were divided into two groups: those who developed VTE group and those who did not (non-VTE group).. Among the 113 patients, 11(9.73%) patients presented with DVT. Additionally, three patients (2.6%) experinced pulmonary embolism and all of them died in the post-operative period. The general characteristics of the patients are demonstrated in Table -1. There was no significant difference in BMI, smoking, comorbidities, between the two groups. Patients with VTE were older than those without VTE (65.7 ± 8.6 vs. 42.5 ± 12.9 years, p < 0.05). Females were more affected by VTE (72.72% vs. 30.39%, p<0.05).Caprini score was more in VTE group (8±2.32 vs 3±1.4,p<0.05)

Table-1 showing demographic characteristics of patients

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics | Non-VTE(n=102) | VTE(n=11) | P-value |
|  Age (years) | 42.5 ± 12.9 | 65.7 ± 8.6 | 0.001 |
|  Male n (%) | 71(69.61%) | 3(27.27%) | 0.067 |
|  Female n (%) | 31(30.39 %) | 8(72.72%) | 0.002 |
| BMI (kg/m2) | 21±1.2 | 25±5.2 | 0.137 |
| Smoking, n (%) | 28(27.45%) | 2(18.18%) | 0.076 |
| Comorbidities |  |  |  |
| Hypertension, n (%) | 25(24.67%) | 4(36.36%) | 0.125 |
| Hyperlipidemia,n(%) | 28(28.57%) | 5(45.45%) | 0.132 |
| Diabetes, n (%) | 30(29.87%) | 5(45.45%) | 0.098 |
| Coronary heart disease n(%) | 18(17.64%) | 3(27.27%) | 0.436 |
| Caprini RAM score | 3±1.4 | 8±2.32 | 0.001 |

Table-2 Showing Disease profile of study population

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | VTE(n=11) | Non-VTE(n=102) | P value |
| Stage of malignancy |  |  |  |
| Stage-I | 0 | 9(8.88%) |  |
| Stage-II | 1(9.1%) | 40(39.21%) | 0.075 |
| Stage-III | 2(18.18%) | 37(36.27%) | 0.083 |
| Stage-IV | 8(72.72%) | 17(16.67%) | 0.004 |
| location |  |  |  |
| colon | 2(18.18%) | 11(12.11%) | 0.214 |
| Stomach | 1(9.0 %%) | 16(15.68%) | 0.543 |
| Rectum | 3(27.27%) | 16(15.68%) | 0.08 |
| Gall bladder | 0(0.0%) | 10(9.80%) | 0.234 |
| Liver  | 0(0.0%) | 6(5.77%) | 0.176 |
| Pancreas | 1(9.0%) | 16(15.68%) | 0.07 |
| Kidney | 0(0.0%) | 8(7.84%) | 0.087 |
| Bile duct | 0(0.0%) | 4(3.9%) | 0.367 |
| Small intestine | 0(0.0%) | 2(2.12%) | 0.094 |
| Ovary | 0(0.0%) | 4(3.9%) | 0.437 |
| Uterus | 4(36.36%) | 5(4.76%) | 0.002 |
| Retroperitoneum | 0(0.0%) | 3(2.94%) | 0.652 |
| Others | 0(0.0%) | 1(0.9%) | 0.885 |
| Histopathological Grade |  |  |  |
| Poorly DifferentiatedModerately differentiatedWell Differentiated | 7(66.63%)1(9.0%)3(27.27%) | 21(20.58%)13(12.74%)68(66.67%) | 0.0030.1260.063 |
| New adjuvant chemo-radiotherapy | 7(63.63 %.) | 35(36.31%) | 0.001 |

Table-3 showing laboratory variables of the patients

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **VTE** | **Without VTE** | **p-value** |
| WBC (10*∧*9/L) | 8.8 *±* 2.8 | 6.7 *±* 4.2 | 0.143 |
| Hb(gm/dl) | 11*±*2.3 | 10*±*1.4 | 0.983 |
| Platelet(10∧3 /L) | 463*±*31 | 336*±*41 | 0.097 |
| Alb (g/L) | 26.3 *±* 4.2 | 34.5 *±* 3.8 | 0.02 |
| Random Blood glucose (mmol/L) | 7.68 *±* 2.4 | 7.45 *±* 5.2 | 0.612 |
| CRP | 18±4.3 | 12±1.3 | 0.08 |
| D-dimer (ug/mL) | 4.2 ± 2.8 | 0.64 ± 2.1 | 0.004 |
| FDP | 14.3 *±* 1.4 | 5.0 *±* 1.3 | 0.083 |

Table 3 shows the results of laboratory factors in patients with VTE vs. those without VTE. In the VTE group, the level of D-dimer was significantly higher than that in the non- DVT group (4.2 ± 2.8 vs. 0.64 ± 2.1, p < 0.05) and low serum albumin level (26.3 *±* 4.2 vs 34.5 *±* 3.8) were observed in VTE group which was statistically significant (p<0.05).

Table-4 showing per-operative variables of the patients

|  |  |  |  |
| --- | --- | --- | --- |
|  | VTE(n=11) | Non VTE(n=102) | P- value |
| Type of surgery Hepatobiliary surgeryUpper GI surgeryColorectal surgeryUrologicalGynecologicalOthers  | 1(0.9%)0(0.0%)4(36.36%)1(9.0%)5(45.45%) | 20(20.77%)23(23.37%)30(29.87%)13(12.98%)13(12.98%)3(2.9%) | 0.1280.3420.4370.1670.0840.164 |
| Mode of surgery open laparoscopic | 8(72.72%)3(27.27%) | 67(66.23%)35(34.31%) | 0.1920.427 |
| Duration of surgery(hrs) | 4*±*3.6 | 2*±*1.5 | 0.001 |
| Amount of blood Transfusion(ml) | 650±65 | 345±72 | 0.004 |

Table-3 shows increased duration of surgery (4*±*3.6hrs vs 2*±*1.5hrs) and increased per-operative blood transfusion (650±65 ml vs 345±72 ml) was significantly associated with post-operative VTE(p<0.05)

Table-5 showing Multivariate logistic regression model correlated to VTE

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Odd ratio** | **95% Cl** | **P value** |
| Age | 1.281 | 1.276–1.298 | 0.004 |
| Female sex | 0.654 | 0.517–0.692 | 0.071 |
| D dimer | 1.374 | 1.358–1.449 | 0.004 |
| Duration of surgery(Hrs) | 1.436 | 1.376-1.467 | 0.001 |
| Amount of blood Transfusion(ml) | 0.654 | 0.632-0.731 | 0.312 |
| Serum Albumin | 1.476 | 1.413-1.534 | 0.002 |
| Caprini RAM score | 1.568 | 1.150-1.96 | 0.001 |
| New adjuvant chemo-radiotherapy | 0.065 | 0.054-0.71 | 0.189 |
| Stage –IV malignancy | 1.216 | 1.17-1.313 | 0.001 |
| Poorly differentiated malignancy | 0.113 | 0.110-0.124 | 0.834 |
| Gynecological Surgery | 1.524 | 1.489-1.621 | 0.001 |
| Colorectal surgery | 1.834 | 1.765-1.912 | 0.002 |
| Malignancy in uterus | 1.245 | 1.221-1.310 | 0.002 |

Advanced age, elevated D-dimer levels, and high Caprini scores were identified as independent predictors of postoperative venous thromboembolism (VTE), with odds ratios (OR) of 1.281 (95% CI: 1.276–1.298, *p* = 0.004), 1.374 (95% CI: 1.358–1.449, *p* = 0.004), and 1.568 (95% CI: 1.150–1.960, *p* = 0.001), respectively.. Besides advanced stage of disease (stage-IV), Gynecological Surgery, colorectal surgery, malignancy in uterus and prolong duration of surgery were also independent predictors of postoperative VTE (P<0.05) for patients under surgery for AM.

**Discussion:**

One of the most common complications among cancer patients is venous thromboembolism (VTE), which comprises of deep vein thrombosis (DVT) or pulmonary embolism (PE). Compared to non-cancer patients following similar treatments, cancer patients are at least twice as likely to develop postoperative DVT or PE.15 Approximately 30% of patients who did not get thromboembolic prophylaxis are at risk to develop DVT after abdominal surgery, and 1% of these patients will die from PE.16 In the current study, 2.6% of the participants experienced PE, while 9.73% developed DVT.

Post-operative VTE was more likely to occur in female patients and elderly individuals. According to a recent study, age was a risk factor for PE and DVT on its own.17 For both DVT and PE, age was an independent risk factor in our analysis (OR=1.281, 95% Cl1.276–1.298,p<0.05. According to a recent study, it is found that women were more likely to get pulmonary embolism (PE) or deep vein thrombosis (DVT) than males.18 Three patients in our study had PE, and two of them were females. Both of them passed away during the postoperative phase.

Low albumin levels are known to have an elevated propensity to clot that enhance a patient's risk of thrombosis.19 Low albumin levels have been linked to venous thromboembolism (VTE) in a number of earlier investigations.19,20 In this study, we found a significant association between postoperative VTE and a lower serum albumin level. In addition, a p-value of 0.002 from the logistic regression analysis showed a strong correlation between DVT and serum albumin.

In the current analysis, a higher incidence of VTE was linked to somewhat longer procedures (> 4 hours) (OR =1.436, 95%CI1.376-1.467, p=0.001). In a case series, Tran et al. also discovered that procedures that lasted more than three hours were associated with a higher risk of VTE (OR = 4.36, 95% CI 3.02‒6.30, p < 0.001).21 In another study by Bertelsen shown that post-operative VTE was substantially (p<0.05) linked with longer surgeries.22

the Caprini RAM score a well-recognized tool for assessing the risk of post-operative VTE is.23Our results (OR-1.568,95% CI 1.150-1.96,p<0.05)are consistent with a previous retrospective study in Europe that examined the Caprini RAM in patients who had VTE and found a strong correlation between Caprini RAM score and post-surgical DVT.24 Increased D-dimer levels are also a recognized risk factor for DVT. Previous studies showed that elevated D-dimer levels have a 25–50% specificity and an 85–95% sensitivity range for identifying post-operative VTE.25 Similar results were also found in our study where elevated D-dimer was an independent predictor of post-surgical VTE.(OR-1.374,95% CI1.358–1.449,p=0.004)).

Colorectal surgery is linked to an increased risk of postoperative thromboembolic events, including pulmonary embolism (PE) and deep vein thrombosis (DVT), in comparison to general surgery. Two well-known risk factors for venous thromboembolism (VTE) among colorectal diseases are colorectal cancer (CRC) and inflammatory bowel disease (IBD). The estimated incidence of VTE in patients with CRC ranges from 2.75 to 8.9%.26 In our study we found similar results where OR for colorectal surgery was 1.834(1.765-1.912,p=0.002) which was statistically significant.

Gynecological surgical patients have high risks for developing deep venous thrombosis because they experience hypercoagulable states, immobility and vascular injuries during the course of their surgeries. In a prospective clinical study of 141 cases treated using gynecological surgery, Liu and colleagues reported 22 cases suffered from DVT and the incidence was 15.6%.27 In our research we also found gynecological abdominal surgery was an independent risk factor for post-operative VTE. Besides uterine malignancy has more chance of developing VTE as it requires extensive pelvic dissection for cancer clearance. We also observed uterine malignancy was significantly associated with post-operative VTE (p<0.05).

There were some limitations in the present study. There were only few patients in this single-center trial. Nevertheless, the center lacked a comprehensive strategy for VTE prophylaxis, therefore the findings of this study might not accurately represent the VTE burden of patients having AM surgery.

**Conclusion:**

This study demonstrates that the post-operative VTE is a serious complication following malignant abdominal surgery, according to the current study. Post-operative VTE was independently predicted by longer surgical length, advanced disease stage, high Caprini RAM score, colorectal and gynecological surgery, elevated post-operative D-dimer, and advanced age. Therefore, it is essential for all centers to implement a standardized VTE prophylaxis protocol.

**CONSENT:**

Patient’s informed written consent was taken to publish her/his case for academic purpose.

**ETHICAL APPROVAL:**

As per international standards or university standards written ethical approval has been collected from Institutional ethical committee and preserved by the authors.

**DISCALIMER (ARTIFICIAL INTELLEGENCE):**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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