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ORIGINAL ARTICLE – PERITONEAL SURFACE MALIGNANCY

Incidence, Risk Factors, and Prevention Strategies for Venous Thromboembolism after Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

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ABSTRACT

Background. The risk factors and incidence of venous thromboembolism (VTE) are not well defined in patients undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC). We sought to characterize the incidence, risk factors, and pharmacothromboprophylaxis strategies for VTE after CRS/HIPEC.

Patients and Methods. We performed a retrospective study of CRS/HIPEC procedures at our institution from 8/2007 to 11/2017, examining the 60-day VTE incidence. Baseline, potential risk factor, and prevention strategy data were collected. Univariate and multivariate regression analysis was used to determine risk factors associated with 60-day VTEs.

Results. We identified 25 60-day VTEs among 447 CRS/HIPEC procedures (5.6%). VTEs were discovered on median postoperative day 20 (range 2–59); pulmonary emboli (68%) were the most common type of VTE. The 60-day VTE rate was 10.2% before versus 4.9% after initiation of a policy to discharge patients on pharmacothromboprophylaxis ($p = 0.10$). Patients with 60-day VTEs had longer average length of stay (14 vs. 11 days, $p = 0.01$) and higher 60-day mortality rate (4% vs. 0.2%, $p = 0.02$) than those without VTEs. Caprini score (odds ratio [OR] 1.53, 95% confidence interval [CI] 1.10–2.15, $p = 0.01$), preoperative serum albumin level (OR 0.40, 95% CI 0.16–1.00, $p = 0.05$), and 60-day non-VTE serious morbidity (OR 3.45, 95% CI 1.25–9.51, $p = 0.02$) were risk factors associated with 60-day VTEs on multivariate analysis.

Conclusions. VTEs are relatively common after CRS/HIPEC and are associated with high Caprini scores, low serum albumin levels, and additional inpatient comorbidities. They result in longer length of stay and higher mortality rate. Compliance with current guidelines for extended postoperative thromboprophylaxis was likely associated with reduced VTE rate.

Surgery is a major risk factor for venous thromboembolisms (VTEs).[1,2] Malignancy and extensive cancer surgery further increase the risk of VTEs by two to three times compared with noncancer surgery[3,4] due to the prothrombotic pathways engendered by malignancy and the hypercoagulability induced by surgery.[5] Despite thromboprophylaxis, the risk of VTEs after cancer surgery remains 1–7%.[3,4,6]

Cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) involves removal of peritoneal metastases and intraperitoneal perfusion with heated chemotherapy. This procedure often involves extensive resection of the tumor burden—a known risk factor for VTEs.[7–9] CRS/HIPEC is performed for various malignancies, including mesothelioma and peritoneal metastases from appendiceal and colorectal cancer, and is associated with a 30–50% VTE risk in the absence of prophylaxis.[10,11]

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There are established guidelines regarding perioperative pharmacological and mechanical thromboprophylaxis for cancer surgery.[12] However, there continues to be inconsistent compliance with these guidelines, with as few as 2.1% of surgical oncology patients receiving preoperative subcutaneous heparin.[13]

There are few studies characterizing VTEs and their risk factors in patients post-CRS/HIPEC. Small studies have reported PE incidence of up to 4.4%[14] and overall VTE incidence of 10–13.5%.[7,15] Risk factors previously identified include disease burden, blood transfusion, and extent of surgery.[15] These studies were limited by small sample size and nonstandard thromboprophylaxis measures. Hence, we sought to study the incidence, risk factors, and impact of consistent perioperative pharmacothromboprophylaxis on VTE rates in a larger sample size of this population within 60 days to capture only events associated with surgery.

PATIENTS AND METHODS

Design and Eligibility

This was an IRB-approved, retrospective, single-institution, case–control study of patients undergoing CRS/HIPEC at our institution from August 2007 to November 2017, to determine the incidence, prevention strategies, management, and risk factors associated with VTEs within 60 days of surgery. Patients who: (1) were on therapeutic anticoagulation at time of surgery, (2) had existing VTE at time of surgery, (3) were discharged with anticoagulation for a non-VTE reason, or (4) had a non-VTE-related inpatient mortality were excluded.

Operative Details

All patients underwent CRS followed immediately by HIPEC per the standardized technique performed at our institution.[16] The extent of peritoneal metastases was assessed at time of surgery and recorded according to the Peritoneal Cancer Index (PCI).[17] The completeness of cytoreduction score (CC score) was used after cytoreduction to assess residual, unresected disease.[18] HIPEC was subsequently performed using a closed-abdomen perfusion technique with 3–6 L warmed perfusate and intraperitoneal chemoperfusion for 90 min with goal intraperitoneal hyperthermia of 42 °C. Patients with appendiceal, colorectal, and small bowel primary tumors were given 10 mg/L perfusate of intraperitoneal mitomycin C. Patients with mesothelioma and ovarian cancer were dosed with 50 mg/m^2 cisplatin and 15 mg/m^2 doxorubicin. Visceral resections were defined as colon resection, small bowel resection, appendectomy, anatomic hepatic resection (segmentectomy or lobectomy), pancreatectomy, cholecystectomy, hysterectomy and/or oophorectomy, partial or total gastrectomy, or splenectomy.

Perioperative Pharmacothromboprophylaxis Administration

Patients generally received subcutaneous heparin preoperatively and were started on pharmacothromboprophylaxis on postoperative day 1 unless there were contraindications to this (i.e., bleeding or significant concern for bleeding). Pharmacothromboprophylaxis consisted of either low-molecular-weight heparin (enoxaparin 30 mg twice daily or 40 mg once daily), unfractionated heparin, or fondaparinux based on the patient's renal function or concern for heparin-induced thrombocytopenia (HIT) and was continued daily unless an interruption was clinically indicated (i.e., concern for bleeding or additional procedures). Upon discharge, some patients in the cohort were prescribed 14 additional days of pharmacothromboprophylaxis.

Data Collection

Patient data were obtained by review of physical and electronic medical records, including demographic data and preoperative, operative, and postoperative variables. VTEs were defined as any deep venous thrombosis (DVT), pulmonary embolus (PE), or portal–splenic–mesenteric vein thrombosis (PSMVT) within 60 days of surgery. These were discovered due to presentation of symptoms or incidentally on imaging performed for other reasons. Superficial vein thrombi were not included as VTEs. Additional VTE-associated variables were collected, including preoperative subcutaneous heparin (SQH) administration, discharge on pharmacothromboprophylaxis, presence and timing of VTE, method of VTE diagnosis, and VTE treatment. Caprini scores were calculated using the 2005 Caprini Risk Assessment Model.[19] In addition, a year-matched analysis was done to compare dosing and duration of inpatient pharmacothromboprophylaxis administration in VTE and non-VTE patients.

Statistics

Baseline demographic, preoperative, intraoperative, and postoperative details were compared between patients sustaining VTEs and those who did not using univariate and multivariate regression models. Variables with p value < 0.20 on univariate analysis were included in multivariate models. Receiver operating characteristic (ROC) curves were created for continuous variables

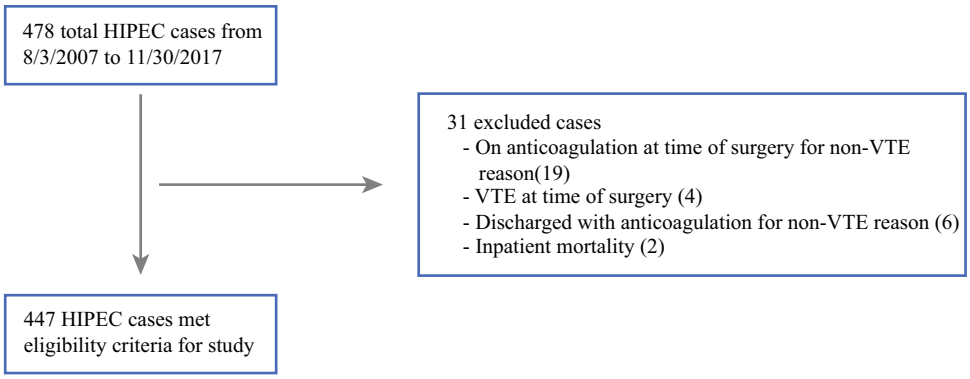

FIG. 1 Study eligibility flow diagram

significant on multivariate analysis; the Youden index was used to identify a cutoff to convert to dichotomous variables. Univariate analysis was used to compare year-matched pharmacothromboprophylaxis administration. Additional comparisons of dichotomous variables were performed using Chi squared analyses, and Student's *t* test was used to compare continuous variables. All statistical analyses were performed using SPSS Statistics version 25.0 (IBM, Armonk, New York).

RESULTS

Enrollment and Demographic Data

A total of 478 CRS/HIPEC cases were performed at our institution within the study period. Of these, 447 were included based on eligibility criteria (Fig. 1). Table 1 lists demographic details for the entire cohort.

Of 394 CRS/HIPEC cases, 393 (99.7%) were given pharmacothromboprophylaxis postoperatively: 390 (99%) were given low-molecular-weight heparin and 3 (1%) were given subcutaneous heparin, while 1 (0.3%) refused pharmacothromboprophylaxis. Postoperative prophylactic details were missing in 53 (11.9%) patients.

Pharmacothromboprophylaxis and Venous Thromboembolism

Of the 447 CRS/HIPEC procedures, there were 25 cases (5.6%) of venous thromboembolism within 60 days of surgery; 17 (68%) of these occurred within 30 days. VTEs were diagnosed on median postoperative day 20 (range 2–59). Nine (36%) VTEs occurred during the inpatient admission, on median postoperative day 8 (range 2–17), while 16 (64%) occurred in patients after discharge and were diagnosed on median postoperative day 28 (range 9–59). VTE by type included 17 (68%) with PE, 5 (20%) with DVT, and 3 (12%) with PSMVT. Nineteen (76%) were diagnosed due to symptoms: 14 (56%) on computed tomography (CT) with PE protocol, 4 (16%) on Doppler ultrasound, and 1 (4%) on CT of abdomen/pelvis. Five (20%) were found incidentally on non-PE CT, and one (4%) was found on autopsy. Of the incidentally found VTEs, two were PEs and two were portal–splenic–mesenteric vein thromboses (PSMVT). Patients with VTEs had longer length of stay (mean postoperative day 14 vs. 11, $p = 0.01$) and higher 60-day mortality rate (4% vs. 0.2%, $p = 0.02$) than those without VTEs. The mortality in the VTE group was a result of the VTE.

A policy change was made in February 2010 to discharge all patients post-CRS/HIPEC with 14 days of additional pharmacothromboprophylaxis, which consisted of low-molecular-weight heparin in 327 of 447 (73%) cases (Supplemental Figure). The 60-day VTE rate decreased from 10.2 to 4.9% after this policy was instituted ($p = 0.10$, Fig. 2).

Excluding nine patients with inpatient VTEs, patients discharged with pharmacothromboprophylaxis had lower 60-day VTE rates than those not discharged with pharmacothromboprophylaxis (2.4% vs. 8.2%, respectively, $p = 0.01$). Of the 16 patients who developed VTE after discharge, 8 were not discharged with pharmacothromboprophylaxis and developed a VTE a median of 9 days after discharge (range 2–35 days), compared with a median of 29.5 days after discharge (range 7–46 days) among those patients discharged with pharmacothromboprophylaxis ($p = 0.03$). Four of 339 (1.2%) patients discharged with pharmacothromboprophylaxis were readmitted for bleeding versus none of 99 patients who were not discharged on pharmacothromboprophylaxis ($p = 0.28$).

There was a lower rate of discharge on pharmacothromboprophylaxis in patients with VTE after discharge compared with non-VTE patients (50% vs. 78%; $p = 0.01$) after excluding those patients discharged on therapeutic anticoagulation for VTEs sustained during their admission.

TABLE 1 Patient baseline data

Characteristic	*n* (%) or median (range)
Gender	
Male	200 (45%)
Female	247 (55%)
Age (years)	54 (20–86)
BMI (kg/m^2)	26 (17–56)
Serum albumin (g/dL)	4.3 (2.4–5.2)
Caprini score	8 (6–13)
Preoperative chemotherapy/biologic therapy[1]	56 (13%)
Yes	109 (24%)
No	332 (74%)
Unknown	6 (1%)
Primary tumor site	
Appendix	295 (66%)
Colon/rectum	91 (20%)
Peritoneum (mesothelioma)	39 (9%)
Ovary	5 (1%)
Small bowel	6 (1%)
Gastric	5 (1%)
Other	4 (1%)
Unknown	2 (0.5%)
PCI	
0–9	146 (33%)
10–19	215 (48%)
20–29	81 (18%)
30–39	4 (1%)
Unknown	1 (0.2%)
CC score	
0	339 (76%)
1	88 (20%)
2	19 (4%)
3	1 (0.2%)
No. viscera resected	2 (0–10)
No. anastomoses	1 (0–6)
EBL (cc)	150 (0–3000)
Operative time (min)	420 (194–935)

BMI body mass index; *PCI* peritoneal carcinomatosis index; *CC* completeness of cytoreduction; *EBL* estimated blood loss

[1]Within 3 months prior to surgery

Risk Factors Associated with Postoperative Venous Thromboembolism

Univariate and multivariate logistic regression analyses were performed to determine potential risk factors associated with 60-day VTEs (Table 2). On univariate analysis, remote history of VTE (OR 3.70, 95% CI 0.99–13.73, $p = 0.05$), Caprini score (OR 1.46, 95% CI 1.10–1.94, $p = 0.01$), preoperative serum albumin (OR 0.41 for albumin level as continuous variable, 95% CI 0.18–0.96, $p = 0.04$), operative time > 420 min (OR 2.77, 95% CI 1.14–6.78, $p = 0.03$), and 60-day non-VTE Clavien–Dindo morbidity (OR 2.69, 95% CI 1.07–6.75, $p = 0.04$) were significantly associated with VTE. On multivariate analysis, Caprini score (OR 1.53, 95% CI 1.10–2.15, $p = 0.01$), serum albumin (OR 0.40, 95% CI 0.16–1.00, $p = 0.05$), and 60-day non-VTE Clavien–Dindo morbidity grade ≥ 3 (OR 3.45, 95% CI 1.25–9.51, $p = 0.02$) were associated with VTE. Remote history of VTE was not included in the multivariate model as it is included in the Caprini score.

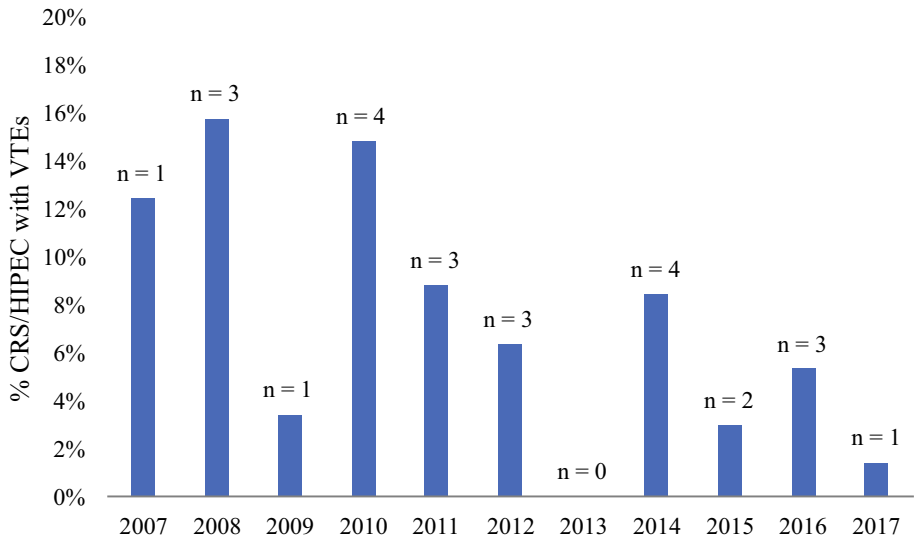

FIG. 2 Rate of venous thromboembolism after CRS/HIPEC

Albumin levels < 4.2 g/dL had a markedly increased VTE rate compared with those ≥ 4.2 g/dL (OR 2.75, 95% CI 1.12–6.70, $p = 0.03$), and Caprini scores greater than 9 also increased risk of VTE (OR 2.53, 95% CI 1.05–6.11, $p = 0.04$) based on ROC curve analysis. A more refined multivariate model was constructed using these variables (Table 3); Caprini score > 9 (OR 2.86, 95% CI 1.07–7.64, $p = 0.04$), serum albumin < 4.2 g/dL (OR 2.99, 95% CI 1.20–7.45, $p = 0.02$), and 60-day non-VTE Clavien–Dindo morbidity ≥ 3 (OR 4.24, 95% CI 1.56–11.50, $p = 0.01$) were significantly associated with VTE. BMI ≥ 25 kg/m^2 (OR 2.32, 95% CI 0.91–5.93, $p = 0.08$) or obesity with BMI ≥ 30 kg/m^2 (OR 1.83, 95% CI 0.78–4.27, $p = 0.16$) did not reach statistical significance for risk of VTE.

We further explored the relationship of serious (grade ≥ 3) Clavien–Dindo non-VTE morbidities in cases with VTEs and found that six of seven (86%) of them had the non-VTE complication *prior to* diagnosis of the VTE. These non-VTE Clavien morbidities consisted of small bowel perforation, small bowel obstruction, abscess or fluid collection requiring percutaneous drainage, gastric perforation, and infection.

Risk Factors Associated with Pharmacothromboprophylaxis

Patients with VTEs had no different rates of missed or delayed inpatient pharmacothromboprophylaxis administration than 25 non-VTE year-matched patients (60% vs. 56%, $p = 0.26$, and 16% vs. 12%, $p = 0.58$, respectively). Additionally, the type of pharmacothromboprophylaxis (i.e., enoxaparin, SQH, or fondaparinux) on which patients were discharged was not associated with VTE risk.

DISCUSSION

Patients undergoing cancer surgery have high risk of venous thromboembolism. However, the incidence of VTE and associated risk factors are not well defined for patients undergoing CRS/HIPEC. Our study shows a 5.6% 60-day postoperative VTE rate in this population, similar to reports of a 1–7% rate for other surgical oncologic procedures.[4,6] Given the added risk factors of high tumor burden and extensive surgery in patients undergoing CRS/HIPEC, one might expect the VTE rates to be higher in this population. In fact, prior studies have found a 10–13.5% VTE rate after CRS/HIPEC.[7,15]

The rates we report may be lower than those previously reported because of different inclusion criteria (i.e., other studies had an undefined postoperative period during which VTEs were considered) or longer interval of pharmacothromboprophylaxis. We limited VTE incidence to 60 days after surgery, as longer follow-up time may capture underlying malignancy or subsequent systemic therapy-related VTEs rather than those related to surgery. Another difference in our study from prior reports involves the type of VTE discovered. Portal–splenic–mesenteric vein thromboses (PSMVT) were the most common type of VTE in previous studies, whereas PE was most common in our study.[7,15] PSMVTs are often associated with intraabdominal complications, which were relatively uncommon in our cohort.[20]

Despite the relatively low rate of VTE in our study, postoperative VTE was associated with a 4% 60-day mortality rate—nearly 20-fold higher than in those without VTE. This highlights the importance of mitigation strategies to reduce the VTE rate as much as possible. The introduction of a policy to discharge patients on pharmacothromboprophylaxis significantly impacted the 60-day

TABLE 2 Univariate and multivariate logistic regression of potential VTE risk factors

Patient variable (*n*)	60-Day VTE *n* (%)	Univariate analysis		Multivariate analysis	
		OR (95% CI)	*p* value	OR (95% CI)	*p* value
Gender					
Male (200)	10 (5.0)	1.23 (0.54, 2.80)	0.62		
Female (247)	15 (6.1)				
Age (years)		1.01 (0.98, 1.05)	0.43		
BMI (kg/m^2)[1]		1.05 (0.99, 1.12)	0.09		
Current smoker					
Yes (13)	1 (7.7)	1.42 (0.18, 11.4)	0.74		
No (432)	24 (5.6)				
Unknown (2)	0				
ASA class		0.62 (0.19, 2.04)	0.43		
II (49)	3 (6.1)				
III (303)	13 (4.3)				
IV (8)	0				
Unknown (87)	9 (10.3)				
CCI = 0					
Yes (75)	3 (4.0)	0.66 (0.19, 2.27)	0.51		
No (372)	22 (5.9)				
Remote VTE[2]					
Yes (18)	3 (16.7)	3.70 (0.99, 13.73)	0.05		
No (429)	22 (5.1)				
Caprini score		1.46 (1.10, 1.94)	0.01	1.53 (1.10, 2.15)	0.01
Primary tumor site		0.78 (0.49, 1.23)	0.28		
Appendix (295)	18 (6.1)				
Colorectal (91)	5 (5.5)				
Peritoneum (mesothelioma) (39)	1 (2.6)				
Ovary (5)	1 (20)				
Small bowel (6)	0				
Gastric (5)	0				
Other (4)	0				
Unknown (2)	0				
Serum albumin (g/dL)		0.41 (0.18, 0.96)	0.04	0.40 (0.16, 1.00)	0.05
Prior resection					
Yes (328)	21 (6.4)	1.95 (0.66, 5.80)	0.23		
No (118)	4 (3.4)				
Unknown (1)	0				
Prior CRS/HIPEC					
Yes (25)	1 (4)	0.70 (0.09, 5.43)	0.74		
No (411)	23 (5.6)				
Unknown (11)	1 (9.1)				
Preoperative chemotherapy/biologic therapy[3]					
Yes (109)	6 (5.5)	1.02 (0.39, 2.63)	0.97		
No (332)	18 (5.4)				
Unknown (6)	1 (16.7)				
Preoperative SQH					
Yes (407)	21 (5.2)	0.49 (0.16, 1.50)	0.21		

TABLE 2 continued

Patient variable (*n*)	60-Day VTE *n* (%)	Univariate analysis		Multivariate analysis	
		OR (95% CI)	*p* value	OR (95% CI)	*p* value
No (40)	4 (10)				
PCI		1.39 (0.81, 2.39)	0.24		
0–9 (146)	5 (3.4)				
10–19 (215)	16 (7.4)				
20–29 (81)	2 (2.5)				
30–39 (4)	2 (50)				
Unknown (1)	0				
EBL > 150 cc					
Yes (259)	15 (5.8)	1.73 (0.76, 3.94)	0.19	0.90 (0.30, 2.68)	0.85
No (188)	10 (5.3)				
Operative time > 420 min					
Yes (221)	18 (8.1)	2.77 (1.14, 6.78)	0.03	2.58 (0.82, 8.15)	0.11
No (226)	7 (3.1)				
Intraoperative transfusion					
Yes (49)	2 (4.1)	1.01 (0.22, 4.60)	0.99		
No (320)	13 (4.1)				
Unknown (78)	10 (12.8)				
No. viscera resected		1.28 (0.99, 1.66)	0.06	1.00 (0.70, 1.44)	0.98
No. anastomoses		1.00 (0.65, 1.56)	0.99		
60-Day non-VTE CD Gr. 3–4					
Yes (60)	7 (11.7)	2.69 (1.07, 6.75)	0.04	3.45 (1.25, 9.51)	0.02
No (385)	18 (4.7)				
Unknown (2)	0				

VTE venous thromboembolism; *OR* odds ratio; *CI* confidence interval; *BMI* body mass index; *CCI* Charlson comorbidity index; *SQH* subcutaneous heparin; *PCI* peritoneal carcinomatosis index; *EBL* estimated blood loss; *CD* Clavien–Dindo complication

[1]BMI not included in multivariate analysis due to its inclusion in calculating the Caprini score itself

[2]Greater than 1 month prior to and no longer present at time of surgery. Not included in multivariate model as it is incorporated in the Caprini score

[3]Within 3 months prior to surgery

VTE rate, decreasing it from 10 to 4.9% after utilization of this policy. This policy was initiated in 2010 after some instances of postdischarge VTE in our CRS/HIPEC patients. This policy is in accordance with established guidelines indicating the need for a total of 4 weeks of pharmacothromboprophylaxis in high-risk patients after abdominal or pelvic surgery for cancer.[2,21] Given that patients have an average length of stay of nearly 2 weeks, discharging them on 14 days of pharmacothromboprophylaxis fulfills this duration. Hence, the efficacy and safety of this approach in the current study could indicate this duration as the recommended regimen after CRS/HIPEC. Our current protocol is shown in Supplemental Table 1.

However, we did not include discharge on pharmacothromboprophylaxis as a variable in our models, as in 36% of patients with VTEs, it occurred as an inpatient, and these patients were discharged on therapeutic anticoagulation. Discharging patients with pharmacothromboprophylactic agents did have a significant effect on reducing the rate of postoperative VTEs after discharge (8.2% 60-day VTE rate without outpatient pharmacothromboprophylaxis vs. 2.4% with), and those patients not discharged with pharmacothromboprophylaxis sustained their VTE much sooner after discharge (median of 9 days) than those on pharmacothromboprophylaxis (median of 29.5 days). Only 11 of 25 (44%) VTEs in our study occurred while the patients were receiving pharmacothromboprophylaxis, of whom 8 had at least one significant risk factor. This could indicate the need for more active VTE surveillance, i.e., screening ultrasound examinations or low threshold for other diagnostic testing in these patients.

TABLE 3 Revised univariate and multivariate logistic regression of potential VTE risk factors

Patient variable (*n*)	60-Day VTE *n* (%)	Univariate analysis		Multivariate analysis	
		OR (95% CI)	*p* value	OR (95% CI)	*p* value
Caprini score > 9					
Yes (72)	7 (9.7)	2.53 (1.05, 6.11)	0.04	2.86 (1.07, 7.64)	0.04
No (338)	14 (4.1)				
Serum albumin < 4.2 *g/dL*					
Yes (139)	12 (8.6)	2.75 (1.12, 6.70)	0.03	2.99 (1.20, 7.45)	0.02
No (271)	9 (3.3)				
60-Day non-VTE CD Gr. 3–4					
Yes (57)	7 (12.3)	3.39 (1.31, 8.81)	0.01	4.24 (1.56, 11.50)	0.01
No (353)	14 (4.0)				

Patients with missing values removed

VTE venous thromboembolism; *OR* odds ratio; *CI* confidence interval; *CD* Clavien–Dindo complication

We found no significant increase in bleeding complications in those discharged on anticoagulants, further supporting its safety as well as efficacy in preventing VTEs. Our finding of a reduced postoperative VTE rate with discharge on pharmacothromboprophylaxis is concordant with published prospective studies.[20,22]

Inpatient VTEs occurred on median postoperative day 8 (range 2–17) versus those that happened after discharge on median postoperative day 28 (range 9–59). Given that postoperative pharmacothromboprophylaxis is prescribed for 14 days and the median length of stay for all patients is 9 days (range 2–36 days), perhaps there is a temporal association of hypercoagulability with pharmacothromboprophylaxis discontinuation which could indicate the need for prolonging postoperative pharmacothromboprophylaxis in patients with identified risk factors.

Decreased serum albumin was a significant risk factor associated with VTEs upon univariate analysis. Serum albumin is correlated with overall poor health and a hyperinflammatory state that could contribute to the hypercoagulability observed in patients with otherwise no signs of nephrotic protein wasting.[23] After cancer surgery, it has been shown to be a risk factor for postoperative complications[24] and poor prognosis. In the general population, studies have shown an association with decreased serum albumin and increased risk of VTEs as well as overall mortality.[25]

Having a serious non-VTE Clavien–Dindo complication within 60 days of surgery was significantly associated with VTEs upon univariate analysis. We found that most non-VTE serious complications occurred prior to the VTE, suggesting a causal relationship, but this would have to be further studied.

The Caprini score was also significantly associated with VTE; patients with VTEs had a median Caprini score of 9 (range 7–12) compared with 8 (range 6–13) in non-VTE patients. Previous studies have shown the Caprini score to be significantly associated with VTEs after abdominal cancer surgery.[20] The Caprini score was originally based on a sample of general, vascular, and urological surgery patients and later validated in plastic surgery patients, suggesting that it might underestimate the risk after abdominal/pelvic cancer surgery.[2,19,26] There are no prior studies showing this association between Caprini score and CRS/HIPEC. All patients after CRS/HIPEC in our study were already at high risk at baseline (Caprini score $\geq$ 5). Previous studies have shown that Caprini score > 8 puts patients at "superhigh" risk with a 11.3% VTE risk.[2,27] We found a significantly increased risk of VTE in patients with Caprini score > 9 with a 11% VTE rate. Our study supports use of this risk assessment model in the post-CRS/HIPEC population of patients.

When comparing year-matched VTE and non-VTE patients, there were no significant differences in the administration of pharmacothromboprophylaxis. Hence, delaying the start day of pharmacothromboprophylaxis or skipping a dose due to anticipated procedure (e.g., epidural removal) did not appear to increase the risk of VTE in this study, although we did not examine this in the entire cohort.

Limitations of this study include its retrospective nature. This is of particular significance when calculating Caprini scores, which have been shown to be underestimated when calculated by medical record.[28] We also had imbalanced sample sizes; the non-VTE group was significantly larger than the VTE group due to the relative rarity of VTE, which can affect multivariate and predictive models. Also, VTE screening was not performed in all patients in our study, which may explain the relatively low VTE rate found. However, we feel this likely excluded non-clinically significant VTEs.

CONCLUSIONS

Discharging patients on pharmacothromboprophylaxis is associated with reduced postoperative VTE rates after CRS/HIPEC. Caprini score, serum albumin, and 60-day non-VTE serious morbidity are possible risk factors for VTE in this population, and they may be useful in predicting this potentially fatal complication.

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DISCLOSURE None.

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