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ORIGINAL RESEARCH

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Prolonged operative time predicts postoperative deep venous thrombosis in head and neck cancer patients who undergo free flap reconstruction

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Abstract

Objective: This study sought to quantify the deep venous thrombosis (DVT) incidence in head and neck cancer (HNC) patients undergoing free tissue transfer and to identify independent predictors of postoperative DVT.

Materials and Methods: This is a cross-sectional study of the National Surgical Quality Improvement Program database from 2010 through 2020. The sample included all HNC surgical patients treated with free flap reconstruction. The study outcome was the presence of a DVT requiring treatment within 30 days of surgery. Univariate analyses were performed using chi-squared and independent *t*-tests. A multiple logistic regression model was created using all significant univariate predictors.

Results: A total of 3954 patients were identified, of whom 53 (1.3%) experienced a postoperative DVT. The only medical comorbidity associated with DVT was COPD (RR = 2.7 [1.3, 5.4]; $p < .01$). Operative time longer than 9 hours (RR = 1.9 [1.0, 3.2]; $p = .04$) and length of stay longer than 10 days (RR = 1.9 [1.1, 3.2]; $p = .02$) were associated with greater DVT rates. In the multivariate analysis, only COPD ($p < .01$) and operative time ($p = .02$) were independently associated with DVT risk. The presence of a DVT was found to increase the relative risk of readmission (RR = 2.1 [1.2, 3.6]; $p < .01$) and non-home disposition (RR = 2.4 [1.7, 3.5]; $p < .01$).

Conclusions: The incidence of DVT in HNC free flap patients was comparable to what has been reported in the general population of HNC surgery patients. Operative time >9 h and COPD history were independent risk factors for DVT in this subset of patients. Symptomatic DVTs necessitating treatment were accompanied by poorer post-hospitalization outcomes.

Level of Evidence: Level 3.

KEYWORDS

flap physiology, head and neck, microvascular reconstruction and transplant surgery

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1 | INTRODUCTION

Venous thromboembolism (VTE) is a common nonmalignancy cause of death in cancer patients.[1] Conceptually, the prothrombotic state of malignancy combined with surgical insult and postoperative immobility makes head and neck cancer (HNC) patients particularly vulnerable to developing deep venous thrombosis (DVT).[2,3] Furthermore, head and neck reconstruction patients have been found to have a greater incidence of VTE compared with non-head and neck reconstruction patients.[4] Microvascular free tissue transfer is the standard of care for reconstructing most post-ablative HNC defects. Despite the widely accepted role of free flaps in cancer care, there is still concern that these procedures can contribute to additional risk of thrombosis.[5] Prior studies evaluating non-HNC surgical patients have shown that extended operative time is a consistent risk factor for postoperative DVT.[6–8] The longer anesthetic duration accompanying free flap reconstruction cases may therefore further exacerbate the DVT risk.

Single-center studies of VTE in HNC surgical patients have found incidence rates that range between 0.6% and 13%.[2,9,10] To our knowledge, only one prior institutional study has formally examined the incidence and risk factors for DVT exclusively among HNC patients treated with free flap reconstruction.[2] Because of the increased operative times and decreased mobility associated with free flap surgery, we suspect that this subset of HNC patients may be at heightened risk for DVT events. The purpose of this study was to use the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) dataset to determine the incidence and identify independent risk factors for postoperative DVT in HNC surgical patients treated with free flaps.

2 | MATERIALS AND METHODS

This is a cross-sectional study of the ACS-NSQIP database from 2010 to 2020. The ACS-NSQIP is a nationally validated quality improvement dataset that includes an assessment of patients' conditions 30 days after a surgical procedure. The data is recorded by clinically trained personnel at over 700 medical centers representing 49 states. All patients with a diagnosis of head and neck cancer (HNC) and a treatment that involved free flap reconstruction were included in the final study sample. HNC diagnosis was determined using the following ICD-9-CM codes (140.X–149.X) and ICD-10-CM codes (C76.0, C00.X–C14.X). Free flap reconstruction was determined using the following CPT codes: 15756, 15757, 15758, 20956, 20970, 20962, 20969, 20955, and 43496.

Study predictors were obtained from both patient and hospitalization characteristics. Patient characteristics included age, gender, BMI, ASA status, functional status, comorbidities (smoking, diabetes, CHF, COPD, disseminated cancer), and type of free flap. Free flaps were subdivided into bone or non-bone containing (muscle, skin, fascial only) flaps based on CPT taxonomy. Hospitalization characteristics included length of stay and operative time. The primary study outcome was the presence of a DVT requiring treatment as reported by hospitals to the ACS-NSQIP dataset. The secondary outcomes were the presence of an associated pulmonary embolism (PE), cardiac arrest, myocardial infarction (MI), 30-day readmission, and non-home discharge.

Descriptive statistics were calculated for all variables. Univariate comparisons were performed using chi-squared and independent sample *t*-tests between all study predictors and the incidence of DVT. A multiple logistic regression model was created to model the probability of DVT using all significant univariate predictors. A second analysis was performed to evaluate the association of DVT occurrence with other complicating events. This was performed using univariate comparisons. A $p < .05$ was considered statistically significant, and all analyses were performed with SAS 9.4 (SAS Institute, Cary, NC). As this study involved no interaction with study subjects, there were no interventions, and private, identifiable information was not being collected, this study was deemed Not Human Subjects Research under 45 CFR 46 by the Columbia University Institutional Review Board.

3 | RESULTS

A total of 3954 patients were included in the study, of whom 53 (1.3%) experienced a postoperative DVT requiring treatment. The majority of patients were Caucasian (83.8%) and male (65.7%). The mean age was 61.7 years, and the mean BMI was 26.2 kg/m^2. Approximately one-third of patients were smokers (33.4%), 13.4% were diabetics, 0.6% had CHF, and 7.1% had COPD. Most patients were ASA class 3 (72.4%) and were baseline independent with ADLs (98.4%). Few patients (5.8%) had evidence of metastatic disease at preoperative work-up. The mean operative time was 9.4 h (SD = 3.1), and the mean length of hospitalization was 9.6 days (SD = 16.3).

In the univariate analysis, the only comorbidity associated with DVT was COPD (RR = 2.7 [1.3, 5.4]; $p < .01$) (Table 1). Notably, there was no increased DVT risk with metastatic disease ($p = .97$), bony free flap ($p = .55$), and smoking status ($p = .84$). To assess the impact of operative time on DVT risk, categorical cutoffs were created using the mean values for operative times and length of stay rounded to the nearest whole number. Nine hours was the threshold of significance for the relationship between operative time and DVT rate. There were higher rates of DVT among patients who had operative times longer than 9 h (RR = 1.9 [1.0, 3.2]; $p = .04$) and lengths of stay longer than 10 days (RR = 1.9 [1.1, 3.2]; $p = .02$). The DVT rate was 1.7% when the operative time exceeded 9 h, whereas the DVT rate dropped to 0.9% with operative times less than 9 hours. The multivariate regression model for DVT events was significant ($p < .01$), and both COPD (OR = 2.7 [1.3, 5.7]; $p < .01$) and operative time longer than 9 h (OR = 1.9 [1.0, 3.5]; $p = .04$) were independent predictors of DVT (Table 2). LOS fell out of significance after controlling for other confounders. When assessing the its association with other complicating events, the presence of a DVT was found to increase the relative risk of postoperative PE (RR = 15.6 [7.2, 33.7]; $p < .01$), MI (RR = 5.1 [1.6, 16.0]; $p < .01$), readmission (RR = 2.1 [1.2, 3.6]; $p < .01$), and non-home disposition (RR = 2.4 [1.7, 3.5]; $p < .01$) (Table 3; Figure 1).

TABLE 1 Risk factors associated with postoperative DVT.

	DVT, *n* (%)	No DVT, *n* (%)	*p*-value**
Age			.16
<65 years	26 (1.1%)	2287 (98.9%)	
≥65 years	27 (1.7%)	1614 (98.4%)	
Gender			.73
Female	17 (1.3%)	1338 (98.8%)	
Male	36 (1.4%)	2562 (98.6%)	
Race			.67
White	34 (1.3%)	2597 (98.7%)	
Black	5 (2.0%)	248 (98.1%)	
Other	3 (1.2%)	248 (98.8%)	
Bone flap			.55
No	46 (1.4%)	3268 (98.6%)	
Yes	7 (1.1%)	633 (98.9%)	
Diabetes			.97
No	46 (1.3%)	3378 (98.7%)	
Yes	7 (1.3%)	523 (98.7%)	
Smoking			.84
No	36 (1.4%)	2603 (98.6%)	
Yes	17 (1.3%)	1304 (98.7%)	
Preoperative functional status			.89
Independent	52 (1.3%)	3821 (98.7%)	
Not independent	1 (1.5%)	64 (98.5%)	
COPD			<.01*
No	44 (1.2%)	3629 (98.8%)	
Yes	9 (3.2%)	272 (96.8%)	
CHF			.21
No	52 (1.3%)	3879 (98.7%)	
Yes	1 (4.4%)	22 (95.7%)	
Hypertension			.43
No	31 (1.5%)	2070 (98.5%)	
Yes	22 (1.2%)	1831 (98.8%)	
Disseminated cancer			.95
No	50 (1.3%)	3673 (98.7%)	
Yes	3 (1.3%)	228 (98.7%)	
Weight loss (>10% bodyweight in last 6 months)			.37
No	46 (1.3%)	3528 (98.7%)	
Yes	7 (1.8%)	373 (98.2%)	
ASA classification			.09
1/2	6 (0.7%)	805 (100%)	
3/4/5	47 (1.5%)	3092 (98.5%)	
LOS > 10 days			.02*
No	24 (1.0%)	2383 (99.0%)	
Yes	29 (1.9%)	1518 (98.1%)	
OR time ≥9 h			.04*
No	18 (0.9%)	1886 (99.1%)	
Yes	35 (1.7%)	2015 (98.3%)	
BMI, kg/m^2*	26.0 (6.2)	26.2 (6.5)	.83

*$p < .05$; **By the chi-squared test or independent samples *t*-test.

TABLE 2 Multiple logistic regression model for postoperative DVT requiring treatment.

	DVT	
	OR [95% CI]	*p*-value
COPD	2.71 [1.30, 5.66]	<.01*
LOS >10 days	1.60 [0.91, 2.83]	.10
OR time ≥9 h	1.91 [1.04, 3.49]	.04*

4 | DISCUSSION

The purpose of this study was to determine the incidence and risk factors for DVT in HNC patients undergoing free flap reconstruction. We found that DVT events were present in 1.3% of all admissions. Thai et al. performed a single-center retrospective cohort of 134 HNC free flap patients and reported a similar 1.4% incidence of confirmed VTE.[2] Sinha et al. found a DVT incidence of 1.7% in their institutional cohort ($n = 384$), and when they compared free and pedicled flap patients there were no significant differences (1.6% vs. 2.2%, $p = .28$).[11] Our findings are also congruent with DVT rates in the general population of HNC surgical patients, suggesting that free flap reconstruction may not be an independent risk factor for DVT. Hennessey et al. examined DVT/PE in all patients undergoing ablative HNC procedures using the Nationwide Inpatient Sample, and they found a 2% incidence of DVT/PE.[12]

Our most notable finding is that operative time longer than 9 h was an independent predictor of post-operative symptomatic DVT. It remains unclear whether this finding is driven by prolonged operative immobility, hemoconcentration, tissue injury, or a combination of these factors. Prolonged operative time has been shown to be a risk factor for DVT in multiple other non-HNC surgical studies,[6–8] and to our knowledge, ours is the first to show that operative time predicts post-operative DVT in HNC and free flap patients. Within the HNC literature, Clayburgh et al did not find a significant association between operative time and VTE, but their institutional study may have been underpowered for such a comparison given the low rates of DVT.[9] The presence of a DVT is known to be an independent predictor of increased patient mortality, hospitalization length, and healthcare cost.[12] We found that DVTs increase the risk of non-home discharge destination, 30-day readmission, and other cardioembolic events.

Our study also found that COPD is associated with an increased risk of post-operative DVT. DVT risk factors in the general population have been well-described; however, less is known about how these specific risk factors are reflected in our specific patient cohort (HNC patients treated with free flaps). Consistent with our findings, in a prior large-scale HNC study, cardiopulmonary diseases were shown to be the most common preexisting medical conditions in DVT patients.[12] Interestingly, our data did not find an association between the flap type, smoking status, or BMI on DVT incidence. One might expect that lower extremity donor sites may be associated with increased risk of DVT due to local inflammation from surgical

TABLE 3 Outcomes associated with postoperative DVT.

	DVT, *n* (%)	No DVT, *n* (%)	*p*-value**
Postoperative PE			<.01*
No	46 (86.8%)	3868 (99.2%)	
Yes	7 (13.2%)	33 (0.8%)	
Postoperative cardiac arrest with CPR			.06
No	51 (96.2%)	3859 (98.9%)	
Yes	2 (3.8%)	42 (1.1%)	
Postoperative MI			<.01*
No	50 (94.3%)	3858 (98.9%)	
Yes	3 (5.7%)	43 (1.1%)	
Readmission			<.01*
No	40 (78.4%)	3230 (89.8%)	
Yes	11 (21.6%)	368 (10.2%)	
Disposition			<.01*
Home	28 (60.9%)	3136 (84.0%)	
Not home	18 (39.1%)	599 (16.0%)	

*$p < .05$; **By the chi-squared test or independent samples t-test.

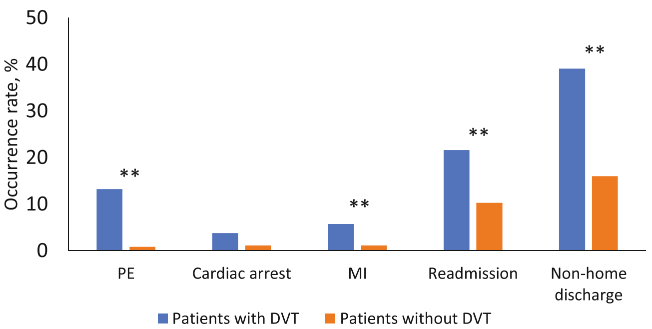

FIGURE 1 Rates of postoperative outcomes in patients with and without deep vein thrombosis (DVT). MI, myocardial infarction; PE, pulmonary embolism. ***p*-value <.01.

manipulation and increased likelihood of post-operative immobilization. While there is some evidence supporting a higher DVT risk with lower limb donor sites,[10] the limitations of the NSQIP dataset did not allow for this analysis in our cohort.

Our findings suggest that there should be a heightened awareness of the potential for DVT in free flap patients with COPD and operative times longer than 9 h. While it may be impractical to shorten operative time, patients with these risk factors may benefit from screening lower extremity Doppler to assess for occult DVT and initiation of treatment before VTE becomes symptomatic. Clayburgh et al. performed screening lower extremity Dopplers in HNC patients, of which 80% underwent free flaps, and found a high rate of occult DVT; appropriate patient selection based on risk factors may amplify the utility and cost-effectiveness of such a screening strategy and help prevent over-treatment, given the risks of systemic anticoagulation.

The strength of the study lies in its external validity and sampling of a representative nationwide population. The robust sample size also allows us to reliably investigate a relatively low-incidence event. Still, there are some limitations to this study that prior authors using similar methods have described. Because the ACS-NSQIP was developed as a surgical quality improvement initiative, the specific cancer subsites and staging information were not included. The granularity of clinical management details such as the postoperative anticoagulation regimen was also unavailable. As previously discussed, flap thromboprophylaxis protocols may have fringe benefits for reducing systemic thrombosis. CPT codes only allowed us to delineate bony and non-bony flaps, and presumably the bulk of the bony flaps were obtained from the fibula or scapula. It may have been more beneficial to stratify by lower extremity flaps given the suggestion that the flaps may be a higher risk for DVT; however, that information was unavailable to us.

5 | CONCLUSIONS

Prolonged operative time and COPD were associated with increased risk of DVT in HNC free flap patients. Although free flap reconstruction adds complexity to the care of HNC patients, our DVT rate of 1.3% was similar to that of the general HNC surgical population. The presence of a DVT was confirmed to be a predictor of other inpatient complications such as non-home discharge and 30-day readmission. Because untreated asymptomatic DVTs can progress and develop into late complications, early postoperative screening Dopplers may be considered in higher-risk HNC free flap patients such as those with COPD or those who experience extended operative time over 9 h. The healthcare value of earlier detection with screening Dopplers remains to be seen, and future studies could investigate the benefit of such prophylactic measures in HNC surgery.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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