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Venous thromboembolism in common laparoscopic abdominal surgical operations

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A b s t r a c t

Background: Venous thromboembolism (VTE) is potentially a serious postoperative complication. We examined the incidence and outcome of VTE among different laparoscopic abdominal surgical operations for benign diseases.

Methods: The National Surgical Quality Improvement Program database was utilized to evaluate all patients with benign disease who underwent laparoscopic abdominal operations including colorectal surgery, bariatric surgery, cholecystectomy, esophageal surgery, abdominal wall hernia repair, and appendectomy from 2005 to 2014. Multivariate logistic regression analysis was performed.

Results: 750,159 patients were studied and the overall incidence of VTE was 0.32% within 30 days of operation. Colorectal surgery had the highest incidence of VTE (734/65512, 1.12%) with significantly longest length of stay and operative time. Patients who developed VTE had higher mortality and worse outcomes compared to non-VTE patients.

Conclusions: Laparoscopic colorectal operations for benign disease is at higher risk for development of VTE compared to other laparoscopic abdominal operations. Further studies should be performed to elucidate the underlying mechanisms for our finding.

1. Introduction

Postoperative venous thromboembolism (VTE) is one of the most common post-surgical complications, which may have disastrous impacts on surgical outcomes.¹ VTE includes deep vein thrombosis (DVT) and pulmonary embolism (PE) and is one of the leading causes of morbidity and prolonged hospitalization in surgical patients,^{2,3} and it has been accounted for 5-10% of all in-hospital deaths in US.^{4,5}

Although, several VTE preventative guidelines and recommendation have been issued from different surgical societies,^{6,7} recent publications demonstrated that there is an incremental trend for VTE occurrences.⁸ This increase of incidences is most likely related to the proliferation of higher risk patients who undergo surgical procedures, varied outcomes, and low rates of compliance with VTE preventative guidelines.^{9,10}

Since the introduction of laparoscopy, minimally invasive techniques have been adopted across multiple surgical disciplines and is now the preferred surgical approach of choice for most common abdominal operations.¹¹ Certain factors associated with laparoscopy may contribute to a higher risk for VTE, such as the use of pneumoperitoneum, reverse Trendelenburg positioning, and prolonged operative times; however, recent published studies revealed that laparoscopic surgery is associated with a lower incidence of VTE compared with that of open surgery in several

commonly performed gastrointestinal procedures.^{12,13} The aim of this study was to determine the incidence of VTE rates among different laparoscopic abdominal surgical procedures. Since malignancy has been well shown to be an independent risk factor for VTE,^{14,15} we select our patient population that underwent abdominal surgery specifically for benign diseases to avoid malignancy being a confounding variable.

2. Materials and methods

The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database is the first nationally validated, outcomes-based program designed for improving surgical quality of care. It is comprised of more than 500 hospitals that collect hospital-level data on preoperative risk factors, intraoperative variables, and 30-day morbidity and mortality after inpatient and outpatient surgical procedures. A trained surgical clinical reviewer is used at participating hospitals to standardize data capture and ensure reliability.¹⁶

The 2005 to 2014 ACS-NSQIP database was retrospectively reviewed to identify patients who underwent laparoscopic abdominal operations. Approval for the use of the NSQIP patient level data in this study was obtained from the institutional review board of the University of California, Irvine Medical Center and NSQIP.

We examined all patients who underwent laparoscopic abdominal operations based on the following Current Procedural Terminology (CPT) codes: cholecystectomy (47562, 47563, 47564), esophageal surgery (gastroesophageal reflux: 43279, 43280, 43283, paraesophageal hernia: 43281, 43282), bariatric surgery (43644, 43645, 43659, 43770, 43771, 43772, 43773, 43774, 43775), colorectal surgery (colectomy: 44204, 44205, 44206, 44207, 44208, 44210, 44211, 44212, proctectomy: 45395, 45397, 45400, 45402, 45499), hernia repair (inguinal hernia: 49650, 49651, incisional hernia: 49652, 49653, 49654, 49655, 49656, 49657), and appendectomy (44970, 44979). Patients who had malignant diseases and patients younger than 18 years were excluded from this study.

All the patients with VTE were identified and divided into six groups based on sub-specialty: colorectal surgery, bariatric surgery, cholecystectomy, esophageal surgery, hernia repair, and appendectomy. In our subset analysis, patients were divided into VTE vs. non-VTE groups. Postoperative VTE was defined according to NSQIP original variables of deep vein thrombosis (DVT) and pulmonary embolism (PE). Variables used in the analysis were provided by the NSQIP database and included demographic data (age, race, and gender), comorbidities, operation length, type of procedures, type of admission (emergent vs. non-emergent), length of stay, and postoperative complications.

The outcomes evaluated were 30-day mortality, superficial surgical site infection (SSI), organ space SSI, deep incisional SSI, wound disruption, pneumonia, unplanned intubation, ventilator dependency more than 48 h, urinary tract infection, acute renal failure, renal insufficiency, postoperative sepsis, postoperative septic shock, and bleeding disorders. Risk adjusted analysis was performed to identify predictors of VTE.

2.1. Statistical analysis

Statistical analyses were conducted using SPSS software, Version 23 (SPSS Inc., Chicago, IL). The main analysis method was multivariate analysis using logistic regression model to explore the

independent association between perioperative factors and complications of VTE. In order to report risk adjusted data, adjustments were made for all the variables of the study. For each variable, the adjusted odds ratio (AOR) with a 95% confidence interval was calculated. Statistical significance was set at *P* values greater than 0.05.

3. Results

A total of 750,159 laparoscopic abdominal operations were performed with 2424 (0.32%) patients diagnosed with VTE within 30 days of operation. Of these, the VTE rate was highest for colorectal surgery at 1.12% (734 of 65,512) and lowest following appendectomy at 0.16% (276 of 168,963). The VTE rate was 0.5% following esophageal surgery (171 of 31,511), 0.35% following bariatric surgery (539 of 153,552), 0.2% following cholecystectomy (489 of 239,499), and 0.24% following incisional and inguinal hernia repair (215 of 91,122) (Fig. 1). The median age of patients with VTE was 59 years for colorectal surgery; 48 years for bariatric surgery; 63 years for cholecystectomy; 68 years for esophageal surgery; 61 years for incisional and inguinal hernia repair; and 51 years for appendectomy.

Patient demographics and comorbidities for patients with VTE according to different laparoscopic abdominal operation are listed in Table 1. For patients with VTE, mean length of stay (13 ± 11.5 days) and operative time (209 ± 111 min) were longer for colorectal operations compared to other abdominal operations (Table 1).

In the subset analysis, patients with VTE and non-VTE were studied. Patient demographics and comorbidities of patients with VTE vs. non-VTE are listed in Table 2. Mean length of hospitalization was significantly longer in patients with vs. without VTE (8.4 ± 11 vs. 2 ± 6 days, respectively, $P < 0.0001$). Mean operation time in patients with and without VTE were 140 ± 99 and 85 ± 62 , respectively ($P < 0.0001$) (Table 2).

Risk adjusted analysis of top four factors associated with VTE includes chronic steroid use (AOR 2.71, $P < 0.01$), preoperative blood transfusion (AOR 2.70, $P < 0.01$), Black or African American ethnicity (AOR 2.69, $P < 0.01$), and preoperative sepsis (AOR 2.55, $P < 0.01$) (Table 3).

The unadjusted mortality rates in patients with and without VTE were 3.3 and 0.2%, respectively. After adjusting for comorbidities, risk of mortality was higher in patients with VTE (AOR 4.54, CI 3.40e6.05, $P < 0.0001$). Patients with VTE following colorectal had the highest risk for mortality compared to other procedures (AOR 2.36, CI 1.89e2.94, $P < 0.0001$). Multivariate analysis also confirmed the association of VTE with worse patient outcomes. Ventilator dependency (AOR 10.51, CI 8.22e12.52, $P < 0.0001$), unplanned reintubation (AOR 9.76, CI 8.07e11.80, $P < 0.0001$), renal insufficiency (AOR 8.17, CI 6.0e11.13, $P < 0.0001$), pneumonia (AOR 8.22, CI 6.86e9.84, $P < 0.0001$), and septic shock (AOR 7.46, CI 5.90e9.42, $P < 0.0001$) were the most significantly increased post-surgical outcomes (Table 4).

Finally, on multivariate analysis, a comparison of the likelihood of developing VTE following several laparoscopic abdominal procedures demonstrated the odds of developing VTE following cholecystectomy (AOR: 0.94; 95% CI: 0.75e1.17; p 0.60) and hernia repair (AOR: 1.0; 95% CI: 0.80e1.26; p 0.95) were not significantly different from the baseline of appendectomy. However, odds were significantly higher in patients undergoing colorectal surgery (4.99; 3.99e6.24; $p < 0.0001$), bariatric surgery (1.36; 1.01e1.82; $p < 0.037$), and esophageal surgery (1.80; 1.31e2.47; $p < 0.0001$) (Fig. 2).

4. Discussion

There are a variety of risk factors for development of VTE in surgical patients. Some of these factors include the type of surgical procedure, the degree of invasiveness, type of anesthesia, and extended period of immobilization.^{17,18} With significant growth of minimally invasive surgery in last few decades, laparoscopic surgery is the procedure of choice for most abdominal procedures. The risk for VTE complications after laparoscopic surgery has been considered potentially higher than that of open surgery because of the use of pneumoperitoneum, altered patient positioning and possibly a prolonged operative time during the learning curve of the laparoscopic procedure.¹⁹⁻²¹ However, recent studies have demonstrated that the overall incidence of VTE is actually lower after laparoscopic operation compared with open operation.^{12,13,22} In the current study, we examined the incidence of VTE among six laparoscopic abdominal surgical procedures and found that colorectal surgery have the highest incidence of postoperative VTE. The

Fig. 1. Overall incidence of VTE in patients who underwent different laparoscopic abdominal operations. Colorectal surgery showed highest incidence of VTE and appendectomy showed lowest VTE rate.

top factors predictive of VTE include the type of procedure (colorectal surgery), chronic steroid use, preoperative blood transfusion, African-American ethnicity, and preoperative sepsis. Additionally, patients with VTE had significantly higher morbidity and mortality compared to non-VTE patients.

Table 1

Unadjusted Demographics and Comorbidities of patients with VTE who underwent laparoscopic abdominal operations in the United States, 2005-2014.

Patients Characteristics		Colorectal (734)	Bariatric (539)	Cholecystectomy (489)	Appendectomy (276)	Hernia (215)	Esophageal (171)
Age	Mean $\pm$ SD (year)	57 $\pm$ 18	48 $\pm$ 12	61 $\pm$ 18	50 $\pm$ 17.6	60 $\pm$ 15	66 $\pm$ 14.41
	Median, year	59	48	63	51	61	68
Sex	Male	340 (46.3%)	166 (30.8%)	174 (35.6%)	152 (55.1%)	121 (56.3%)	53 (31%)
Race	White	598 (88.4%)	364 (76.5%)	364 (86.9%)	196 (85.6%)	170 (85.9%)	137 (91.3%)
	African American	73 (10.8%)	109 (22.9%)	47 (11.3%)	27 (11.8%)	27 (13.6%)	10 (6.7%)
	Asian	3 (0.5%)	1 (0.2%)	4 (0.9%)	5 (2.2%)	1 (0.5%)	1 (0.6%)
	Other	2 (0.3%)	2 (0.4%)	4 (0.9%)	1 (0.4%)	0 (0%)	2 (1.2%)
BMI ^a	Mean $\pm$ SD	29 $\pm$ 7	47 $\pm$ 11	31.2 $\pm$ 7.5	30.2 $\pm$ 8	34.7 $\pm$ 10.5	30.2 $\pm$ 6.4
	<18.5	30 (4.2%)	2 (0.4%)	5 (1%)	4 (1.6%)	3 (1.4%)	2 (1.2%)
	18.5-24.9	184 (26%)	12 (2.2%)	79 (16.8%)	52 (20.9%)	22 (10.5%)	32 (19%)
	25-29.9	224 (31.5%)	13 (2.4%)	123 (26%)	82 (32.9%)	48 (23%)	52 (31%)
	30-34.9	222 (31.3%)	90 (16.8%)	199 (42.2%)	86 (34.5%)	88 (42.1%)	73 (43.5%)
	>35	50 (7%)	421 (78.2%)	66 (14%)	25 (10.1%)	48 (23%)	9 (5.3%)
Other Variables	ASA Score > Two	369 (50.2%)	407 (75.5%)	267 (54.5%)	97 (35.1%)	119 (55.3%)	105 (61.4%)
	Hypertension	322 (43.9%)	313 (58.1%)	267 (54.6%)	80 (29%)	119 (55.3%)	104 (60.8%)
	Smoke	91 (12.4%)	65 (12.1%)	64 (13.1%)	49 (17.8%)	22 (10.2%)	596 (20.3%)
	Weight loss	34 (4.6%)	3 (0.6%)	17 (3.5%)	0 (0%)	0 (0%)	7 (4.1%)
	Dyspnea	65 (8.9%)	109 (20.2%)	44 (9%)	19 (6.9%)	34 (15.8%)	34 (19.9%)
	COPD ^c	43 (5.9%)	17 (3.2%)	38 (7.8%)	8 (2.9%)	17 (7.9%)	20 (11.7%)
	Diabetes Mellitus	82 (11.3%)	132 (25.6%)	75 (15.8%)	17 (6.3%)	37 (17.5%)	15 (8.9%)
	Ventilator Dependency	5 (0.7%)	3 (0.6%)	5 (1%)	3 (1.1%)	0 (0%)	1 (0.6%)
	Steroid use	183 (24.9%)	17 (3.2%)	31 (6.3%)	6 (2.2%)	7 (3.3%)	14 (8.2%)
	Ascites	4 (0.5%)	1 (0.2%)	3 (0.6%)	3 (1.1%)	0 (0%)	0 (0.0%)
	Congestive Heart Failure	7 (1%)	3 (0.6%)	14 (2.9%)	3 (1.1%)	2 (0.9%)	1 (0.6%)
	Preoperative Bleeding Disorder	45 (6.1%)	17 (3.2%)	45 (9.2%)	14 (5.1%)	12 (5.6%)	12 (7%)
	Preoperative Blood Transfusion	38 (5.2%)	1 (0.2%)	7 (1.4%)	3 (1.1%)	3 (1.4%)	3 (1.8%)
	Dialysis	4 (0.5%)	5 (0.9%)	10 (2%)	3 (1.1%)	2 (0.9%)	1 (0.6%)
	Preoperative Acute Renal Failure	3 (0.4%)	1 (0.2%)	5 (1%)	3 (1.1%)	2 (0.9%)	1 (0.6%)
	Wound Infections	15 (2%)	10 (1.9%)	11 (2.2%)	6 (2.2%)	2 (0.9%)	1 (0.6%)
	Sepsis	31 (4.2%)	2 (0.4%)	27 (5.5%)	60 (21.7%)	1 (0.5%)	5 (2.9%)
	Septic Shock	5 (0.7%)	1 (0.2%)	5 (1%)	8 (2.9%)	0 (0%)	1 (0.6%)
	Hypoalbuminemia ^d	424 (57.8%)	210 (39%)	282 (57.7%)	112 (40.6%)	139 (64.7%)	95 (55.6%)
Type of admission	Emergent	74 (10.1%)	9 (1.7%)	75 (15.3%)	185 (67%)	12 (5.6%)	13 (7.6%)
	Elective	(50.4%)	330 (61.2%)	144 (29.4%)	13 (4.7%)	140 (65.1%)	79 (46.2%)
Other factors	Mean length of Stay (Days $\pm$ SD)	13 $\pm$ 11.5	5 $\pm$ 8	7 $\pm$ 10	7 $\pm$ 10	5 $\pm$ 9	5 $\pm$ 4
	Mean Operative duration (Minutes $\pm$ SD)	209 $\pm$ 111	136 $\pm$ 76	83 $\pm$ 49	60 $\pm$ 33	107 $\pm$ 79	186 $\pm$ 85

^a Body Mass Index.

^b American Society of Anesthesiologists.

^c Chronic Obstructive Pulmonary Disease.

^d Serum albumin level lower than 3.5 g/dL.

Table 2

Demographics and Comorbidities of patients who underwent laparoscopic abdominal operations in the United States, 2005e2014 (VTE vs. Non-VTE).

Patients Characteristics		Non-VTE (747,735)	VTE (2424)	P-value
		Reference		
Age	Mean $\pm$ SD (year)	48 $\pm$ 17	56 $\pm$ 17.3	<0.0001
	Median, year	47	56	0.012
Sex	Male	286337 (38.3%)	1006 (41.5%)	0.002
Race	White	499296 (85%)	1829 (85.1%)	0.03
	African American	63047 (10.7%)	293 (13.6%)	0.001
	Asian	17430 (2.3%)	15 (0.7%)	0.24
	Other	7755 (1%)	11 (0.5%)	0.18
BMI ^a	Mean $\pm$ SD	33 $\pm$ 11.5	34 $\pm$ 11.1	e
	≤18.5	8231 (1.1%)	46 (2%)	0.16
	18.5e24.9	140990 (19.7%)	381 (16.2%)	0.39
	25≤ <30	186314 (26%)	542 (23.1%)	0.004
	30≤ <40	218405 (30.7%)	758 (32.3%)	0.49
	≥40	160429 (22.5%)	619 (26.4%)	0.01
Other Variables	ASA Score > Two	249772 (33.4%)	1362 (56.2%)	<0.0001
	Hypertension	264726 (35.4%)	1205 (49.7%)	0.09
	Smoke	127123 (17%)	302 (12.5%)	0.01
	Weight loss	5723 (0.8%)	61 (2.5%)	0.006
	Dyspnea	53431 (7.1%)	305 (12.6%)	0.003
	COPD ^c	16702 (2.2%)	143 (5.9%)	0.11
	Diabetes Mellitus	76457 (10.5%)	358 (14.8%)	0.11
	Ventilator Dependency	371 (0.04%)	17 (0.7%)	0.004
	Steroid use	17512 (2.3%)	258 (10.6%)	<0.0001
	Ascites	1485 (0.2%)	11 (0.5%)	0.56
	Congestive Heart Failure	2148 (0.3%)	30 (1.2%)	0.53
	Preoperative Bleeding Disorder	15629 (2.1%)	145 (6%)	<0.0001
	Preoperative Blood Transfusion	1421 (0.2%)	55 (2.3%)	<0.0001
	Dialysis	2819 (0.4%)	25 (1%)	0.69
	Preoperative Acute Renal Failure	752 (0.1%)	15 (0.6%)	0.31
	Wound Infections	3555 (0.5%)	45 (1.9%)	0.004
	Sepsis	15300 (2%)	126 (5.2%)	<0.0001
	Septic Shock	663 (0.1%)	20 (0.8%)	0.06
	Hypoalbuminemia ^d	329976 (44.1%)	1262 (52.1%)	<0.0001
Type of admission	Emergent	151671 (20.3%)	362 (15.2%)	0.04
	Elective	298819 (40%)	1076 (44.4%)	Reference
Other factors	Mean length of Stay (Days $\pm$ SD)	2 $\pm$ 6	8.4 $\pm$ 11	<0.0001
	Mean Operative duration (Minutes $\pm$ SD)	85 $\pm$ 62	140 $\pm$ 99	<0.0001

^a Body Mass Index.

^b American Society of Anesthesiologists.

^c Chronic Obstructive Pulmonary Disease.

^d Serum albumin level lower than 3.5 g/dL.

In our study, colorectal operations had higher risk for VTE compared to other abdominal operations. Other studies,^{23,24} similarly showed that colorectal operations have significantly higher odds for VTE development compared to other major abdominal operations. Some possible explanations include the use of the lithotomy position, long operation time, and prolonged hospitalization during these cases.^{13,22} Beside the procedural type, other risk

Table 3

Risk-adjusted analysis of VTE predictors of patients who underwent laparoscopic abdominal operations.

	AOR	95% CI	P Value
Age	1.02	1.0e1.02	<0.01
Male	1.02	1.09e1.31	<0.01
Comorbidities			
Chronic Steroid use	2.71	2.34e3.13	<0.01
Preoperative blood transfusion	2.70	2.0e3.66	<0.01
African American Ethnicity	2.69	1.47e4.93	<0.01
Preoperative sepsis	2.55	2.06e3.16	<0.01
Ventilator dependency	2.47	1.33e4.59	<0.01
Preoperative wound infections	1.61	1.16e2.22	<0.01
Preoperative bleeding disorders	1.49	1.22e1.81	<0.01
Hypoalbuminemia ^a	1.20	1.09e1.31	<0.01
BMI more than 40	1.15	0.82e1.62	<0.01

^a Serum albumin level lower than 3.5 g/dL.

factors for VTE development included older age, higher BMI, preoperative weight loss more than 10%, higher ASA score (>2), male gender, preoperative blood transfusion, steroid use, sepsis, bleeding disorders, wound infections, hypoalbumenia, and ventilator dependency.

We found the overall incidence of VTE to be 0.3% which is similar to a previous study on the VTE rate in laparoscopic abdominal operations for benign disease.¹² In this study, patients with VTE had 10 times higher in-hospital mortality than patients without VTE (3.3% vs 0.2%). This significantly higher mortality rate caused by VTE was similarly reflected in each of the six specific abdominal operations.

There are several limitations in this study. The limitation of data from administrative databases are the accuracy in coding and input of data. The wide variation in hospital setting, hospital quality, and surgeons' expertise in a nationwide database can be confounders for this study. The NSQIP database only extends to 30 days postoperatively, therefore, long-term VTE complications were not captured in this study. Also, NSQIP database doesn't provide the information regarding the use and method of prophylactic regimens for VTE as well as the duration of VTE prophylaxis. Therefore, VTE incidence in this study may be underestimated the associations between the examined factors and postoperative VTE occurrences.

Table 4

Risk-adjusted analysis of postoperative outcomes of patients who underwent laparoscopic abdominal operations in the United States, 2005-2014 (VTE vs. Non-VTE).

Complications	Non-VTE (747735)	VTE (2424)	AOR	95% CI	P Value
In-Hospital Mortality	1489 (0.2%)	79 (3.3%)	4.54	3.40e6.05	<0.0001
Acute Renal Failure	680 (0.1%)	39 (1.6%)	6.36	4.31e9.33	<0.0001
Renal Insufficiency	862 (0.1%)	55 (2.3%)	8.17	6.0e11.13	<0.0001
Urinary Tract Infection	5594 (0.7%)	96 (4%)	2.86	2.27e3.60	<0.0001
Unplanned Intubation	2477 (0.3%)	168 (6.9%)	9.76	8.07e11.80	<0.0001
Ventilator Dependency	1949 (0.3%)	156 (6.4%)	10.51	8.22e12.52	<0.0001
Pneumonia	3429 (0.5%)	182 (7.5%)	8.22	6.86e9.84	<0.0001
Superficial SSI ^a	8850 (1.2%)	85 (3.5%)	1.74	1.37e2.20	<0.0001
Deep SSI	1394 (0.2%)	22 (0.9%)	1.75	1.07e2.86	0.02
Organ Space SSI	7204 (1%)	241 (9.9%)	6.0	5.12e7.03	<0.0001
Wound Dehiscence	876 (0.1%)	23 (0.9%)	2.94	1.87e4.62	<0.0001
Any SSI	17085 (2.3%)	336 (13.9%)	3.77	3.29e4.32	<0.0001
Bleeding Disorders	5210 (0.7%)	152 (6.3%)	2.83	2.31e3.45	<0.0001
Sepsis	7495 (1%)	213 (8.8%)	4.52	3.77e5.40	<0.0001
Septic Shock	1840 (0.2%)	115 (4.7%)	7.46	5.90e9.42	<0.0001

^a SSI: Surgical Site Infections.

Fig. 2. Adjusted Odds of developing VTE by surgical procedure relative to appendectomy. Odds were significantly higher in patients undergoing colorectal surgery, bariatric surgery, and esophageal surgery ($P < 0.05$).

There is also lack of information about the physiologic status of the patient and history for VTE. Despite these limitations, our study is one of the largest samples of the VTE incidences among the common laparoscopic general surgery procedures in patients with benign disease.

In conclusions, laparoscopic colorectal operations for benign disease is at higher risk for development of VTE compared to other laparoscopic abdominal operations. Further studies should be performed to elucidate the underlying mechanisms for this finding.

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Abbreviations: VTE, Venous thromboembolism; DVT, Deep vein thrombosis; PE, Pulmonary embolism; NSQIP, National Surgical Quality Improvement Program; SSI, Superficial surgical site infection; AOR, Adjusted odds ratio; CI, Confidence interval.

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