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Venous thromboembolism following colorectal resection.

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Keywords

Colorectal resection

Venous thromboembolism

Hospital Episode Statistics

Deep vein thrombosis

Pulmonary embolism

Abstract

Aim: The study investigated the rate of significant venous thromboembolism (VTE) following colorectal resection during the index admission and over one year following discharge. It identifies risk factors associated with VTE and considers the length of VTE prophylaxis required.

Method: All adult patients who underwent colorectal resections in England between April 2007 and March 2008 were identified using Hospital Episode Statistics (HES) data. They were studied during the index admission and followed for a year to identify any patients who were readmitted as an emergency with a diagnosis of deep venous thrombosis (DVT) or pulmonary embolism (PE).

Results: 35997 patients underwent colorectal resection during the period of study. The VTE rate was 2.3%. Two hundred and one (0.56%) patients developed VTE during the index admission and 571 (1.72%) were readmitted with VTE. Following discharge from the index admission, the risk of VTE in patients with cancer remained elevated for six months compared with two months in patients with benign disease. Age, postoperative stay, cancer, emergency admission, and emergency surgery for patients with inflammatory bowel disease (IBD) were all independent risk factors associated with an increased risk of VTE. Patients with ischaemic heart disease and those having elective minimal access surgery (MAS) appear to have lower levels of VTE.

Conclusion: This study adds to the benefits of MAS and demonstrates an additional risk to patients undergoing emergency surgery for IBD. The majority of VTE occurs following discharge from the index admission. Therefore, surgery for cancer, emergency surgery for IBD, and those with an extended hospital stay may benefit from extended VTE prophylaxis. This study demonstrates that a stratified approach may be required to reduce the incidence of VTE.

What does this paper add to the literature?

The risk of VTE following colorectal surgery is very well known, but it is not clear from the literature how long the risk persists. This study shows the risk of VTE following discharge remains high for up to 6 months especially in patients having elective surgery for cancer and emergency surgery for IBD

Introduction

Venous thromboembolism (VTE) is a major cause of preventable morbidity and mortality. Each year around 25000-32000 patients die in the United Kingdom as a result of VTE related to hospital admission (1). The incidence of VTE in general surgical patients has been reported to be as high as 25% in patients who did not receive prophylaxis (2). An international consensus statement recommends that all moderate and high risk general surgery patients undergoing operation should receive VTE prophylaxis.(3) The National Institute for Health and Care Excellence (NICE) in England has issued guidelines that recommend VTE prophylaxis for all patients undergoing major abdominal surgery.(4, 5) Patients undergoing colorectal surgery are considered to be at high risk of VTE.(6-8) Certain factors such as cancer and major trauma are well known to increase the risk of VTE,(9, 10) but it is not clear whether emergency surgery with colonic resection is a risk factor. Although hospitalization without surgery is a risk factor for VTE,(11) there is little evidence to show that prolonged hospital stay following surgery increases the risk of VTE. Minimal access surgery (MAS) has been suggested to increase the risk of VTE following surgery (12, 13). The increased risk of VTE following MAS may be due to prolonged operating time, increased intra-abdominal pressure from pneumoperitoneum, and reverse Trendelenburg position.(14) Conversely MAS may reduce the risk of VTE because it is associated with a shorter hospital stay and early mobilization in the setting of enhanced

recovery. Recent studies suggest a lower risk of VTE following MAS compared to open colorectal surgery, (7, 15, 16) although these studies investigated the risk during the hospital admission but not following discharge.

The risk of symptomatic VTE following surgery remains high following discharge. (17) In the case of bariatric surgery Steele et al showed the rate of cumulative VTE increases from 0.88% during a hospital admission to 2.99% at 6 months post-surgery.(18) Because the risk of VTE extends beyond the index hospital admission, recent studies(19) suggest that patients undergoing surgery for cancer should be discharged with 28 days of pharmacological VTE prophylaxis. NICE guidelines were modified in 2010 to recommend pharmacological VTE prophylaxis for 28 days postoperatively for patients having major cancer surgery involving the abdomen or pelvis.(5)

The aim of this study was to investigate the rate of VTE following colorectal resection by laparoscopic or open technique for benign and malignant disease during the index admission and for one year following discharge. The study was also used to identify risk factors associated with VTE.

Method

Hospital Episodes Statistics (HES) data were obtained from the National Health Service Information Centre (NHSIC) and imported into Microsoft 2005 SQL server for analysis. All adult patients who underwent large bowel resection in England between April 2007 and March 2008 were identified by searching all operative fields of the HES dataset using Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (4th revision) codes (OPCS-4).

Patients undergoing laparoscopic repair were identified with the operative code Y75*, converted cases using Y714 and all other patients were considered open. Pelvic surgery was defined as surgery involving the rectum and included anterior resection, abdominoperineal

resection, Hartmann's operation (H33) and panproctocolectomy (H04), whereas other operations including total colectomy (H05 and H11), subtotal colectomy (H29), right hemicolectomy (H06 and H07), transverse colectomy (H08), left colectomy (H09) and sigmoid colectomy (H10) were classified as abdominal surgery.

Patients with a malignant diagnosis of cancer were identified using the diagnostic codes ICD 10 (C18 colon, C19 rectosigmoid, C20 rectum, and C21 anal canal), while all other diagnosis were classified as benign. Patients with benign pathology were subclassified into inflammatory bowel disease (IBD) using ICD10 codes (K50 for Crohn's disease and K51 for ulcerative colitis) and other benign pathology. Patients were also classified according to surgical approach (minimal access surgery (MAS) versus open), mode of admission (elective versus emergency), gender, age, postoperative stay and co-morbidity.

The mode of method was calculated by searching the admimeth (Admission Method) field which identifies how the patient was admitted to hospital (for elective admissions number 11, 12, and 13were selected and 21, 22, 23, 24 for emergency admission). Comorbidity was identified by searching all secondary diagnostic fields for codes for ischaemic heart disease, congestive cardiac failure, hypertension, renal disease, metastatic disease, connective tissue diseases, dementia, diabetes mellitus and complications, chronic pulmonary disease, paraplegia and hemiplegia, liver disease, cerebrovascular accident and peripheral vascular disease. The codes used for comorbidity was obtained from the Dr Foster Charlson comorbidity score.(20)

VTE was identified during the index admission i.e. an admission during which a patient underwent a colorectal resection using ICD-10 codes (International Classification Disease 10th Edition) by searching the HES dataset for the codes for PE (I26*), DVT (I80.2) (thrombophelibitis of deep vessels of lower extremities), and I80.1 (thrombophelibitis of femoral vein) in any diagnostic field except the primary diagnosis.

To identify VTE occurring after the index admission, patients were then followed for a further year using HESID (the HES Patient ID (HESID) provides a way of tracking patients through the HES database without identifying them) to identify any who were readmitted to a hospital as emergency with a diagnosis of VTE in any of the first two diagnostic fields. Of course not all patients with VTE required admission, but most with a PE and suspected PE did so. Most hospitals also treat patients with extensive DVT, ileofemoral, or bilateral DVT, phlagmasia alba dolens, or phlagamsia cerulosa dolens as inpatients. Therefore, we define significant VTE as patients who presented to a hospital with VTE and required treatment as an inpatient. A flow chart of the methodology is illustrated in Figure 1.

Statistical analysis

Univariate analysis including Chi square, Mann Whitney, and independent t-test were used as appropriate. Multivariate analysis was carried out with binary logistic regression. Only factors that were statistically significant ($P<0.05$) in univariate analysis were included in the multivariate analysis. All analyses were carried out using SPSS 13.

Results

35997 adult patients underwent colorectal resection between April 2007 and March 2008. The mean age was 65 years and the male to female ratio was 1:1. The median postoperative stay was 9 (IQR 6-15) days. Two thirds (66.3%) of the patients were admitted electively and one third as an emergency. The majority of patients (86%) underwent open surgery and 14% underwent MAS. More than half the procedures were performed for colorectal cancer (56%) and the rest were for benign pathology. A pelvic operation where surgery involved the rectum was performed in 42.7% of the patients and other types of colectomy were performed in 57.3% of cases. 2710 patients (7.5%) died during the index admission.

201 (0.56%) patients were coded to have had VTE during the index admission, and 571 (1.72%) were readmitted with VTE as the primary or secondary diagnosis as an emergency within a year of the index admission giving an overall rate of VTE at one year of 2.3%, most occurring in the first six months following surgery (Figure 2).

Increasing age, prolonged postoperative stay, open surgery, cancer and emergency admission were all associated with an increased rate of VTE, whereas pelvic surgery and gender were not associated with higher rate of VTE (Table 1).
Comorbidity including congestive cardiac failure, hypertension, and renal disease were associated with an increased risk of VTE. In contrast, patients with ischaemic heart disease appeared to have a lower rate of VTE (Table 2).

Factors that were significantly associated with VTE on univariate analysis were included in the multivariate analysis (binary logistic regression). When the cohort was analysed as a whole, prolonged postoperative stay, increased age, emergency admission, and cancer were independent factors associated with a higher VTE rate whilst patients with ischaemic heart disease were less likely to develop VTE. All other factors including surgical approach were not associated with VTE as shown in Table 3.

The proportion of patients admitted as an emergency that underwent MAS was small (10%) compared with open surgery. To eliminate any discrepancy between both groups due to the type of admission, the analysis was repeated for elective cases only. This demonstrated that the surgical approach was an independent factor associated with increased risk of VTE in patients undergoing elective surgery. Open surgery increased the risk of VTE significantly compared with MAS with an odds ratio of 1.307 (1.008-1.693) as shown in Table 5.

The risk of a VTE was high during the index admission and for first few months following discharge. The risk of readmission with VTE following surgery for cancer remained high for six months following discharge, whereas the risk following surgery for benign disease reduced after two months (Figure 3).

Patients who underwent surgery for cancer as an emergency had the highest rate of readmission for VTE, followed by patients who had elective surgery for cancer regardless of the period they spend in hospital following surgery during the index admission (Figure 4). The risk of readmission with VTE for patients who underwent surgery for benign pathology (whether elective or emergency) was low if the patients spent less than a week in the hospital whereas the risk increased significantly if they spent more than a week in the hospital.

When benign pathology was subdivided into IBD and other benign disease, the former appeared to be associated with a higher rate of readmission with VTE compared with other benign disease (2.1% vs 1.7%). Most VTE in IBD patients occurred in patients who underwent emergency surgery as an (Figure 5). The length of hospital stay remained a major factor in readmission with VTE following discharge for all pathologies (cancer, IBD and benign) as shown in Figure 6. Multivariate analysis was performed for patients underwent emergency surgery for bowel resection and showed patients with IBD are significantly associated with VTE (P= 0.002 and OR 1.999 95%CI (1.353-2.952)) as shown in Table 6.

Discussion

This study showed that with a year's follow up, the overall VTE rate in England in the year 2007 to 2008 following colorectal surgery was 2.3%. The results from this study were very similar to those from previous publications.(21)

NICE guidelines for the prophylaxis of DVT were introduced in 2007 and then amended in 2010 to recommend prolonged pharmacological prophylaxis in patients undergoing resection for malignancy.(22) As we set out to examine the rates of VTE on the index admission and following discharge and since it was likely that the majority of colorectal resection patients with both benign and malignant disease had received in hospital pharmacological prophylaxis we chose to study the year 2007-2008 because prolonged pharmacological treatment in patients undergoing resection for malignancy was not yet in routine use. We cannot of course say what VTE prophylaxis this cohort of patients had, but we believe that the use of this time facilitated the comparison of the malignant and non-malignant groups.

Only a quarter of patients coded as suffering a VTE were identified on the index admission. Further because there was no facility within HES to identify when a patient had suffered a VTE then some of the patients identified as having suffered a VTE on the index admission may have suffered this historically. However, when coders found VTE in the past history taken at admission and they included it in the diagnostic code for completeness, they tended to use the 'Z (Personal history of...) Code'. Therefore, by searching for I codes only, we assumed only those with acute VTE were selected rather than those with a previous history of VTE. Another issue of the study was that other patients may have suffered a VTE many years previously that we could not identify by searching recent preceding years for an admission. We have therefore chosen to present the data in its unabridged form and acknowledge this as a concern, i.e. that the incidence of VTE on the index admission may be an overestimate. Two studies were recently published investigating the risk of VTE and surgery by linking HES data to primary care data. Humes et al(23) investigated the risk of VTE following colectomy but not rectal surgery and Bouras et al (24) investigated VTE rate following a number of operations including thyroid, breast, hernia, etc…. Both studies found similar results. The one year VTE rate was recorded to be 2.5% by the former study and the 90 days

VTE rate was 2.11% in the latter. Obesity is a known risk factor for VTE. Searching HES data for obesity codes is feasible, but we think it is significantly under recorded. Therefore, it was not included in the study.

Most VTEs occur in patients who are readmitted during the year after the index admission. We have only included readmissions if the VTE code is in the first or second field making it much more likely that VTE was the reason for the readmission. Another limitation to the present study, was it only detected patients readmitted with VTE not those who developed it in the community or who were treated in an ambulatory setting without admission to hospital. The patients who were admitted to the hospital were, however, the high risk group. Patients with significant DVT (e.g. ileofemoral DVT, phlagmasia alba dolens, or phlagamsia cerulosa dolens) and most patients with acute PE or suspected PE were normally admitted to hospital and would have been be included and were at high risk of morbidity and mortality.

Cancer and its treatment is a well-known risk factor for VTE(9) and it is no surprise that this study confirmed this finding. However, in addition, this study demonstrated that the risk of VTE remained elevated for at least six months following discharge.
Prolonged post-operative hospital stay and increasing age were also associated with an increased risk of VTE which may have been due to poor mobility of patients especially in the elderly. Patients admitted as an emergency also had an increased risk of VTE and were likely to be sicker with poorer mobility and in a poor nutritional state compared with patients undergoing elective surgery.

When the full cohort of patients was analysed, binary logistic regression did not find any difference in the rate of VTE between patients undergoing MAS and open surgery. Most patients undergoing MAS were admitted electively, however, whereas a third of open surgical operations was performed following an emergency admission. The analysis was therefore repeated for all patients who were admitted electively. In this subgroup those undergoing MAS were shown to have a lower incidence of VTE than after open surgery. This may be an additional benefit of MAS over open surgery perhaps due in part to shorter hospital stay and early mobilization due to better pain control.

Patients with ischaemic heart disease had a lower incidence of VTE (Odds ratio 0.520 and 95% CI (0.351-0.769)). These patients are routinely started on antiplatelet medication or anticoagulation which may act as a protective factor against developing VTE postoperatively.

The study has other limitations. It is a retrospective population based cohort study using data derived from Hospital Episode Statistics. HES are routinely collected by all hospitals in the NHS in England and the validity of the results therefore depends on the accuracy and depth of coding. Nevertheless, previous studies have suggested that the accuracy of recording of diagnostic and operative codes in England is high,(25) but researchers still have to recognize and account for a degree of coding inaccuracy. HES has been shown to be useful for the assessment of effectiveness, comparative audit, and equity.(26) A recent systematic review showed that coding accuracy was improving and following the introduction of payment by result programme in 2002 the accuracy of primary diagnoses had increased from 73.8% (IQR: 59.3-92.1%) to 96.0% (IQR: 89.3-96.3).(27) Another limitation of this study is that data derived from HES cannot assess whether patients received VTE chemoprophylaxis and

for how long although by choosing the time point studied we have tried to reduce the effect of this confounding factor.

In 2010 NICE recommended the use of subcutaneous heparin in patients with malignancy for 28 days following discharge after surgical resection.(5) The study showed that only a quarter of patients who developed VTE did so during index admission and the risk of VTE remained high for six months following surgery. The four week period recommended may, therefore, not be adequate. Further studies to assess the risk of VTE following the introduction of NICE guideline 2010 may be useful to assess the effect of discharging patients with VTE receiving prophylaxis for 28 days.

Patients with benign pathology had a lower rate of VTE than those for malignant disease; however in those with a prolonged stay, the rate of VTE was similar to those seen in patients with a diagnosis of cancer. We would suggest that patients with benign disease undergoing resection who have an inpatient stay for more than 15 days following surgery should therefore also be considered for prolonged thromboprophylaxis following discharge. Perhaps the NICE guidelines should be amended to reflect this.

Patients with IBD were at higher risk of developing VTE compared with healthy controls. (28) This study confirmed increased rates of VTE in IBD although elective surgery for IBD appeared to have a much lower rate of readmission with VTE compared with emergency surgery. This may in part be due to a prolonged hospital stay.

VTE is a preventable condition, hence we believe every effort should be taken to reduce or eliminate the risk. The present study clearly demonstrated that a stratified approach may be needed to reduce the incidence of postoperative VTE in patients undergoing colorectal resection. Patients with a diagnosis of cancer and those undergoing colorectal resections for

benign condition with extended hospital stay including IBD may benefit from an extended period of chemoprophylaxis.

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Factors		Total	VTE	
Age mean (SD)	VTE		67.1 years (11.9)	<0.0001
	Non- VTE		64.5 years (15.6)	
Postoperative duration Median (IQR)	VTE		12.5 days (8-23)	<0.001
	Non- VTE		9 days (7-15)	
Gender	Male	16989	367 (2.2%)	NS
	Female	16330	405 (2.5%	
Surgical approach	MAS	4982	85 (1.7%)	0.003
	Open	28391	687 (2.4%)	
Diagnosis	Benign	14273	280 (2.0%)	<0.001
	Cancer	19046	492 (2.6%)	
Site of surgery	Pelvic	14416	341 (2.4%)	NS
	Abdominal	18903	431 (2.3%)	
Mode of admission	Elective	23172	458 (2.0%)	<0.001
	Emergency	10147	314 (3.1%)	

Table 1: Factors associated with increased risk of VTE (univariate analysis)

SD = standard deviation, IQR = interquartile range, VTE = venous thromboembolism

Co-morbidity		Total (rate)	VTE (rate)	P value
Ischaemic heart disease	Yes	3352 (10%)	56 (1.7%)	0.009
	No	29967	716 (2.4%)	
Cerebrovascular accident	Yes	263 (0.8%)	8 (3%)	NS
	No	33056	764 (2.3%)	
Congestive Cardiac Failure	Yes	460 (1.4%)	18 (3.9%)	0.022
	No	32859	754 (2.3%)	
Connective Tissue disorder	Yes	423 (1.3%)	10 (2.4%)	NS
	No	32869	762 (2.3%)	
Dementia	Yes	144 (0.4%)	4 (2.8%)	NS
	No	33175	768 (2.3%)	
Diabetes Mellitus	Yes	3114 (9.4%)	63 (2%)	NS
	No	30205	709 (2.3%)	
Liver disease	Yes	487 (1.4%)	7 (1.4%)	NS
	No	32832	765 (2.3%)	
Peripheral vascular disease	Yes	675 (2.0%)	20 (3.0%)	NS
	No	32644	752 (2.3%)	
Pulmonary diseases	Yes	3393(10.2%)	83 (2.4%)	NS
	No	29926	689 (2.3%)	
Paraplegia	Yes	116 (0.4%)	5 (4.3%)	NS
	No	33203	767 (2.3%)	
Renal disease	Yes	740 (2.2%)	26 (3.5%)	0.029
	No	32579	746 (2.3%)	
Metastatic disease	Yes	3204 (9.6%)	97 (3.0%)	0.005
	No	30115	675 (2.2%)	
Hypertension	Yes	9352 (28.7%)	243 (2.6%)	0.033

Table 2: Univariate analysis. Comorbidity and venous thromboembolism (VTE).

Factors		Wald score	P value	OR (95% CI)
Ischaemic heart disease		13.721	<0.001	0.587 (0.443-0.778)
Congestive cardiac disease		2.390	NS	1.471 (0.902-2.401)
Hypertension		1.766	NS	1.116 (0.949-1.313)
Renal disease		0.135	NS	1.081 (0.714-1.636)
Metastatic disease		1.806	NS	1.166 (0.932-1.460)
Age		4.972	0.026	0.994 (0.988-0.999)
Postoperative stay		43.665	<0.001	0.990 (0.987-0.993)
Surgical approach	MAS	2.520	NS	1
	Open			1.208 (0.957-1.524)
Pathology	Benign	20.066	<0.001	1
	Cancer			1.488 (1.251-1.771)
Mode of admission	Elective	35.731	<0.001	1
	Emergency			1.632 (1.390-1.971)

Table 3: Multivariate analysis (binary logistics regression) of factors associated with VTE (all cases)

Factors		MAS	Open	P value
Age (Mean SD)Years		65.2 (50-80)	65.5 (50-80	NS
Postoperative duration (Median IQR) Days		7 (4-10)	10 (7-16)	<0.001
Pathology	Cancer	66.2%	54.3%	<0.001
	Benign	33.8%	45.7%	
Gender	Male	50.8%	50.9%	NS
	Female	49.5%	49.1%	
Site of surgery	Pelvic	40.9%	43.0%	0.004
	Abdomen	59.1%	57.0%	
Mode of admission	Elective	90.0%	62.5%	<0.001
	Emergency	10.0%	37.5%	

Table 4: Characteristics of minimal access surgery (MAS) compared with open surgery

Factors		Wald score	P value	OR (95% CI)
Ischaemic heart disease		10.722	<0.001	0.520 (0.351-0.769)
Congestive cardiac disease		1.118	NS	0.536 (1.70-1.698)
Hypertension		0.241	NS	1.054 (0.855-1.300)
Renal disease		0.412	NS	1.237 (0.646-2.367)
Metastatic disease		5.803	0.016	1.394 (1.064-1.827)
Age		1.379	NS	0.995 (0.988-1.003)
Postoperative stay		21.141	<0.001	0.990 (0.986-0.994)
Surgical approach	MAS	4.086	0.043	1
	Open			1.307 (1.008-1.693)
Pathology	Benign	8.135	0.004	1
	Cancer			1.412 (1.114-1.789)

Table 5: Multivariate analysis (binary logistics regression) of factors associated with VTE (elective cases only)

Factors		Wald score	P value	OR (95% CI)
Ischaemic heart disease		7.642	0.006	0.451 (0.257-0.793
Congestive cardiac disease		0.092	NS	1.424 (0.944-2.147)
Hypertension		2.722	NS	0.804 (0.621-1.042)
Renal disease		0.003	NS	0.984 (0.572-1.693)
Metastatic disease		1.452	NS	1.278 (0.858-1.904)
Age		5.586	0.018	1.010 (1.002-1.019)
Postoperative stay		21.718	<0.001	1.005-1.013)
Surgical approach	MAS	0.405	NS	1
	Open			1.245 (0.743-2.088)
Pathology	Benign	32.384	<0.001	1
	IBD			1.999 (1.353-2.952)
	Cancer			2.111 (1.608-2.771)

Table 6: Multivariate analysis (binary logistics regression) of factors associated with VTE (emergency cases only)

Figure 1: Flow chart of steps used in analysis of data

HESID = Hospital Episode Statistics Patient Identification

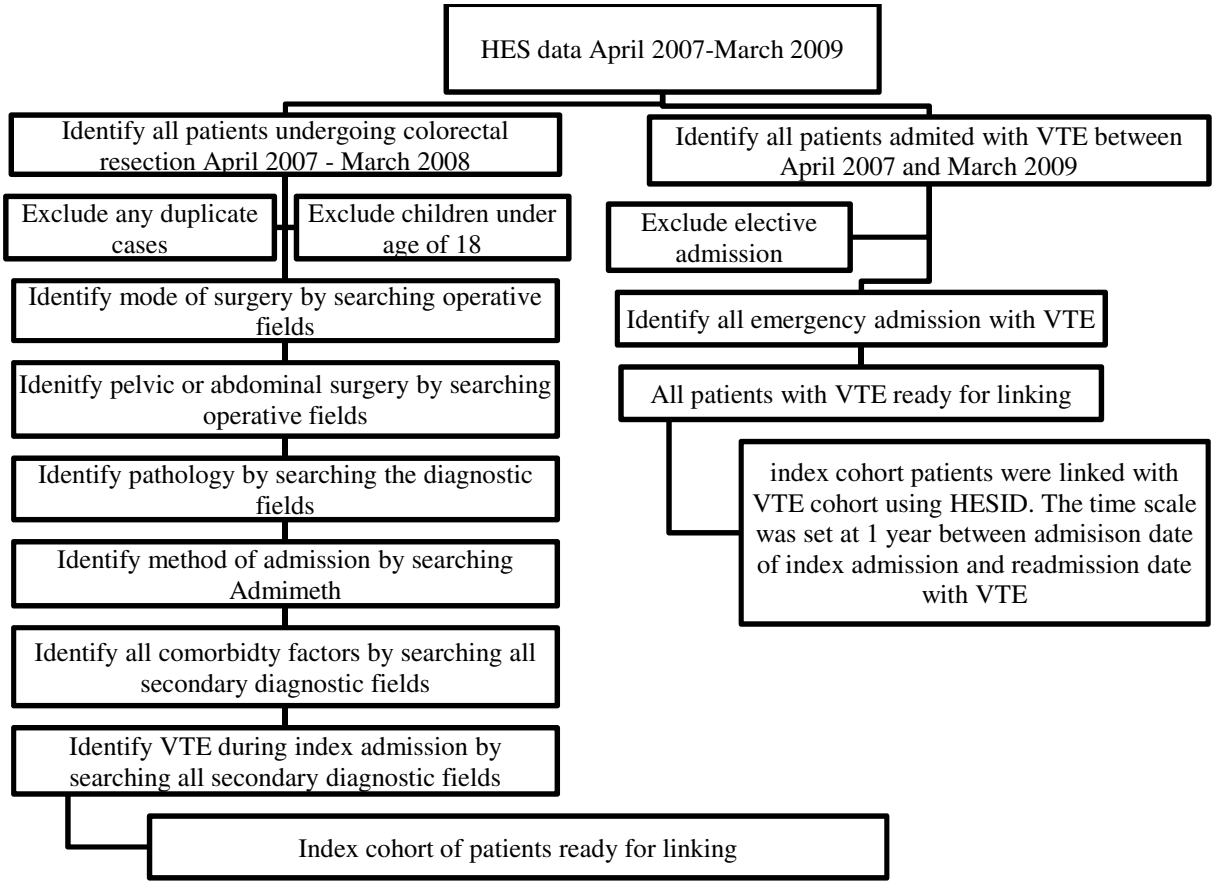

Figure 2: Interval between discharge from index admission to VTE (all cases)

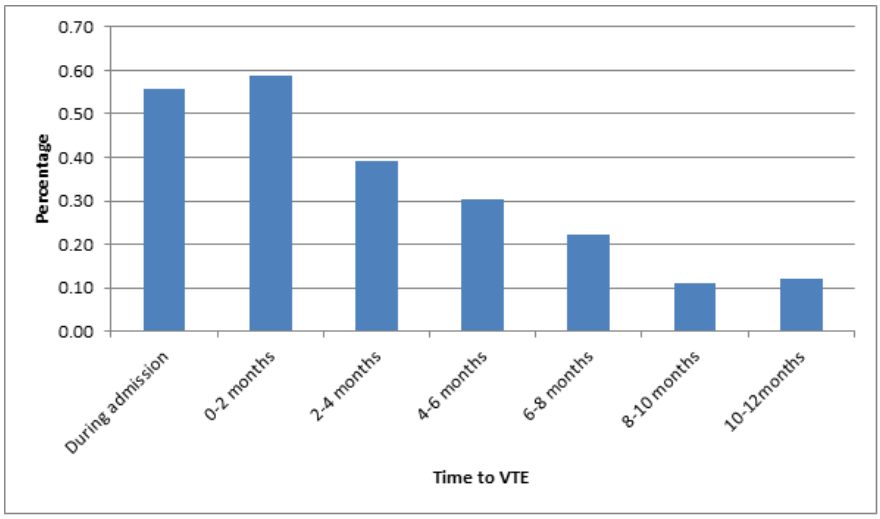

Figure 3: Interval between discharge from index admission to VTE of patients with cancer and benign pathology

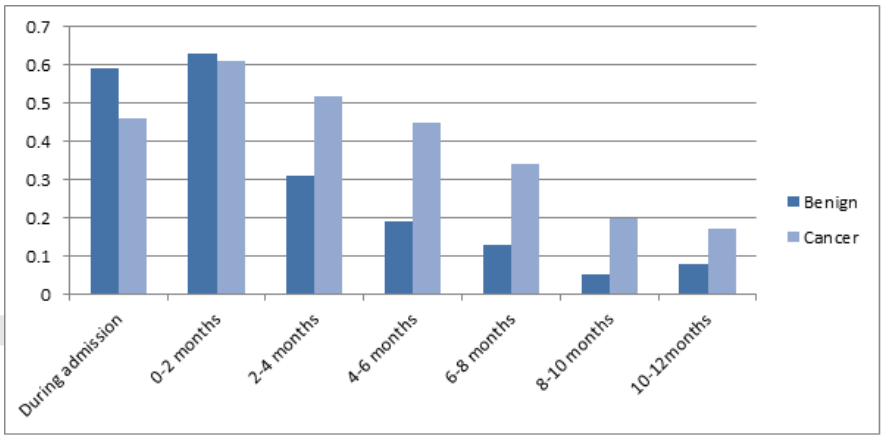

Figure 4: Readmission with VTE and the duration of postoperative stay according to pathology and elective or emergency admission

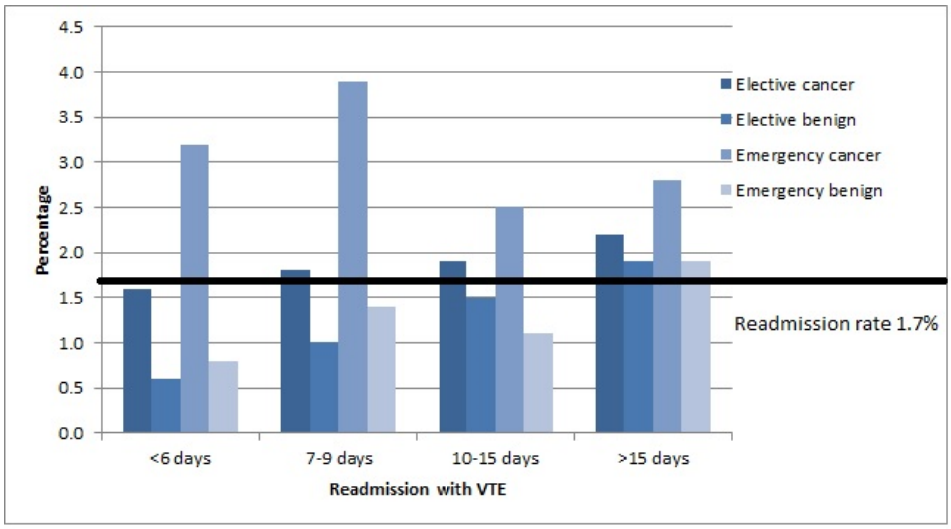

Figure 5: Readmission with VTE according to elective or emergency admission and the diagnosis of cancer, inflammatory bowel disease and other benign disease.

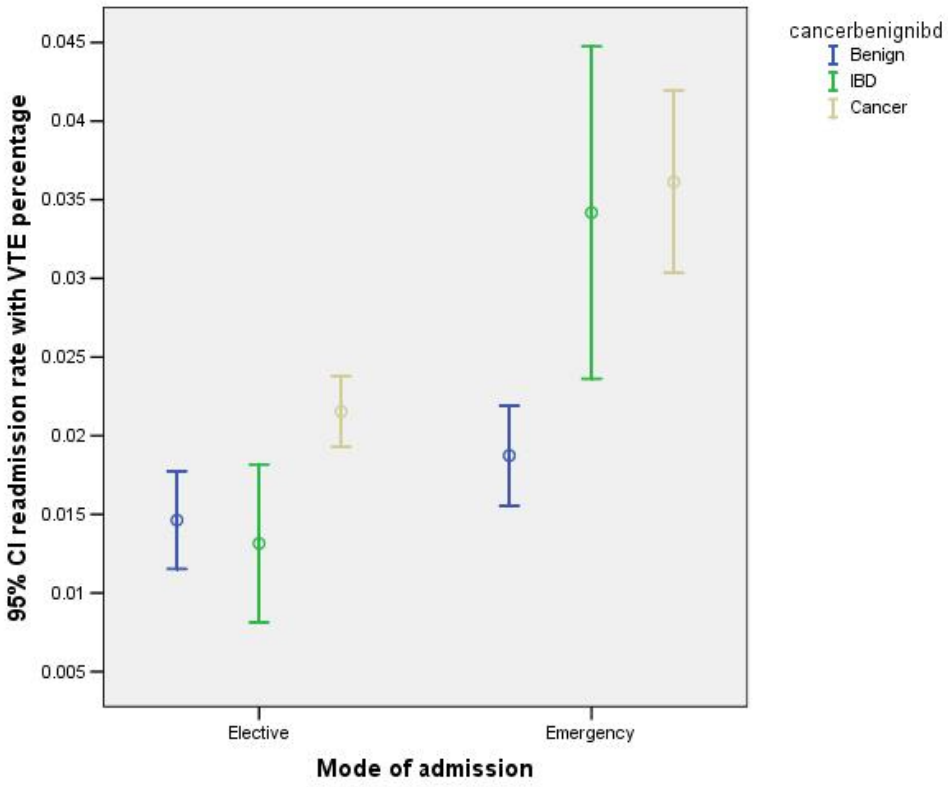

Figure 6: Readmission rate with VTE and postoperative length of stay according to the diagnosis of cancer, inflammatory bowel disease and other benign disease.