## UC Davis UC Davis Previously Published Works

## Title

Vena Cava Filter Use in Cancer Patients with Acute Venous Thromboembolism in California

**Permalink** https://escholarship.org/uc/item/71p7s9f6

**Journal** Thrombosis Research, 135(5)

**ISSN** 0049-3848

## **Authors**

Ho, Gwendolyn Brunson, Ann White, Richard <u>et al.</u>

Publication Date 2015-05-01

## DOI

10.1016/j.thromres.2015.02.002

Peer reviewed

Contents lists available at ScienceDirect

## Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

# Vena Cava Filter Use in Cancer Patients with Acute Venous Thromboembolism in California $\stackrel{\leftrightarrow}{\sim}$

### Gwendolyn Ho<sup>a</sup>, Ann Brunson<sup>a</sup>, Richard White<sup>b</sup>, Ted Wun<sup>a,c,\*</sup>

<sup>a</sup> Division of Hematology Oncology, Department of Internal Medicine, University of California, Davis School of Medicine, USA

<sup>b</sup> Division of General Internal Medicine, Department of Internal Medicine, University of California, Davis School of Medicine, USA

<sup>c</sup> Section of Hematology Oncology, VA Northern California Health Care System, USA

#### ARTICLE INFO

Article history: Received 26 November 2014 Received in revised form 7 January 2015 Accepted 2 February 2015 Available online 7 February 2015

Keywords: Cancer and thrombosis Vena cava filter Venous thrombosis Deep venous thrombosis Pulmonary embolism

#### ABSTRACT

*Background:* Few studies have evaluated the use of vena cava filters (VCF) in cancer patients with acute venous thromboembolism (VTE).

*Methods:* Hospital discharge records of patients who were admitted with a principal diagnosis of lower extremity deep-vein thrombosis or pulmonary embolism and cancer in California between January 1, 2005 and December 31, 2009 were analyzed. Multivariable logistic regression analysis was used to identify variables associated with VCF use.

*Results:* A VCF was placed in 2747 (19.6%) of 14,000 cancer patients. The percentage of patients treated with a VCF varied widely across hospitals, from 0% to 52% (mean = 19.2%, median = 17.2%), and by cancer type, ranging from 8% for lip/oral to 43% for brain. Using multivariable analysis, the strongest predictors of VCF use were a diagnosis of brain cancer (OR = 4.6, CI: 3.7 -5.6), undergoing major surgery (OR = 4.9, CI: 3.9 -6.1), and bleeding (OR = 2.7, CI: 2.0-3.5). Other factors significantly associated with VCF insertion included hospital characteristics (larger, urban and private), and greater severity-of-illness at the time of admission. Only 1083 (7.7%) of patients had an absolute contraindication to anticoagulation (bleeding or surgery).

*Conclusions:* A VCF was deployed in approximately 20% of acute VTE patients with cancer, but use varied widely between hospitals and cancer types. The strongest risk factors were undergoing surgery, active bleeding, and having brain cancer. Only 21% of VCF treated cancer patients had a strict contraindication to anticoagulation therapy. Further research is needed to determine if VCF use is of any benefit in cancer patients with acute VTE. Published by Elsevier Ltd.

#### Introduction

Acute venous thromboembolism (VTE) is a common cause of morbidity and mortality in cancer patients [1]. Cancer patients have a 4 to 6 fold higher risk of developing incident VTE compared to matched non-cancer patients [2,3], they have a higher risk of recurrent VTE [4,5], and development of VTE in cancer patients is associated with higher mortality [6–8]. The management of acute VTE in cancer patients may be challenging because they have an increased risk of developing major bleeding during anticoagulation therapy [4]. The frequency of vena caval filter (VCF) use in the management of patients with acute VTE has expanded exponentially, with one study showing a 20-fold increase between 1979-1999 [9]. The use of VCFs has emerged as a particularly common therapeutic modality in patients with cancer in

E-mail address: Ted.wun@ucmdc.ucdavis.edu (T. Wun).

the United States although the clinical benefit in this setting remains controversial [10,11].

The American College of Chest Physicians 2012 guidelines recommend against the use of VCFs in patients with acute VTE except in patients who have a contraindication to therapeutic anticoagulation, such as patients with active bleeding or patients who require surgery [12]. Nevertheless recent studies have documented great variation in use of VCFs among hospitals in the United States. In a population-based study from Worcester Massachusetts, VCFs were placed in 13% of 1547 patients hospitalized for acute VTE, but by consensus of three experts, the use of VCF was appropriate in only 51% of the cases [13]. Another large retrospective study found a striking variation in the frequency of VCF placement in patients hospitalized for acute VTE, with a range of from 0 to 39%. This study found that cancer patients had 70% higher odds of VCF use compared to patients without cancer [14].

Although VCF placement in cancer patients appears to be common, there have been no studies that have determined the factors associated with more frequent use of VCFs in patients with cancer. The objective of this study was to determine the clinical, demographic and hospital characteristics associated with VCF use in cancer patients. We



**Regular** Article



HROMBOSI: Research

 $<sup>\</sup>stackrel{\scriptscriptstyle{\scriptsize\rm theta}}{\longrightarrow}$  Financial Disclosures: The authors have no relevant financial disclosures.

<sup>\*</sup> Corresponding author at: Division of Hematology Oncology, UC Davis Comprehensive Cancer Center, 4501 X Street, Sacramento, CA 95817. Tel.: +1 916 734 5959.

hypothesized the use of VCFs would be higher in those patients with a contraindication to anticoagulation as well as in those with cancers that were perceived to have a high bleeding risk.

#### Methods

This was retrospective observational study that was designed to determine factors associated with VCF use in patients who required hospitalization specifically for acute lower extremity deep-vein-thrombosis (DVT) or pulmonary embolism (PE) and had cancer. We restricted the analysis to patients admitted to a hospital in California between Jan 1, 2005 and Dec 31, 2009. This study was approved by the California Health and Welfare Agency Committee for the Protection of Human Subjects, and the University of California, Davis Institutional Review Board.

#### Databases

The California Patient Discharge Database (PDD) contains information about all patients hospitalized in the state, except patients admitted to one of 14 Federal hospitals (12 Veterans Affairs hospitals and two military hospitals). Serial records from a single person can be linked using an encrypted form of the social-security number, called the record linkage number (RLN) [15,16]. All PDD records include demographic information, insurance status (e.g. self-pay, Medicare, insurance, etc.), a principal medical diagnosis, up to 24 additional 'secondary' diagnoses, and a principal and up to 20 secondary procedures coded using International Classification of Diseases, 9th Revision, Clinical Modification codes (ICD-9-CM). Since 1996 all medical diagnoses in the PDD required a present-on-admission (POA) indicator. The database also includes a hospital identifier with the ability to link to hospital characteristics (e.g. public, academic, for-profit, etc.) and location (rural vs. urban).

#### Acute -VTE

All cases admitted with a principal diagnosis of either acute DVT in the lower extremity or acute PE between Jan 1, 2005 and Dec 31, 2009 were first identified (see Supplemental Appendix for ICD-9-CM codes). Cases diagnosed with hospital-acquired acute VTE only were identified by the presence of a secondary diagnosis code for acute VTE coupled with a POA indicator of no (POA = N). Hospital-acquired VTE cases were excluded to ensure that VTE occurred prior to filter placement. For each linked record, we selected only the first hospitalization for acute-VTE during the study period.

#### Cancer Cases

Cases were categorized as having cancer based on the presence of a cancer diagnosis code (see Appendix) at the time of admission or within a 6 month time period prior to the index hospitalization. Cases with unknown cancer primary site were excluded from the cohort. Cancer type was categorized by "perceived" bleeding risk (high bleed risk-brain, high bleed risk-acute leukemia, moderate bleed risk-urinary and kidney, and low bleed risk-all others). The within-hospital frequency of VCF placement in cases with and without cancer was also compared.

#### Vena Cava Filter Use

All cases hospitalized for acute VTE with cancer that had a VCF placed were identified by procedure code 38.7 (interruption of the vena cava). Although this procedure code is also used for vena cava plication, ligation or other interruption, these other procedures are rarely performed [17,18]. All of the cases with acute VTE that had a VCF placed any time prior to Jan 1, 2005 (back to Jan, 1991) were excluded. The frequency of VCF use was calculated as the number of hospitalizations that

included VCF placement divided by the corresponding total number of hospitalizations for acute VTE.

#### Hospitals

Optimally the frequency of VCF use should be compared only among hospitals that admitted at least a minimal number of VTE cases. We targeted hospitals that admitted a minimum of 55 or more acute VTE hospitalizations over the 6-year study period in our previous analysis of non-cancer cases, the current study required the same but there was no minimal number of cancer cases. This cut-off of 55 hospitalizations was chosen in order ensure that there were a sufficient number of "opportunities" for VCF placement to guarantee that the 95% confidence limits on the calculated frequency of VCF use was not wider than 10%, assuming that the average frequency of VCF use was 15%. The within hospital VCF use correlation between cancer and noncancer patients was restricted to hospitals with at least 55 acute VTE cases, and 15 or more acute VTE cancer patients (223 hospitals) as well in order to improve the reliability of this calculation.

#### Active Bleeding

Cases with bleeding were identified using ATRIA Study identified set of ICD-9-CM codes [19,20]. Cases were classified as having intracranial bleeding, gastrointestinal bleeding, or "other" bleeding. Hematuria alone and epistaxis were included only if the patient also received a blood transfusion. Bleeding was categorized as either present at the time of admission or that developed during the hospital stay using the POA flag (Y/W = on admission, N/U = during the hospitalization). Having active bleeding was considered a contraindication to anticoagulation.

#### Surgery

Major operating room procedures were identified using a set of ICD-9-CM codes used by the Centers for Medicare and Medicaid Services. This list was modified by excluding relatively minor operating room procedures such as cosmetic surgery, and endoscopic procedures commonly performed outside of the operating room, such as upper gastrointestinal endoscopy, colonoscopy and cystoscopy. Vascular procedures commonly performed in conjunction with either thrombolysis, venous stenting or placements of a VCF were analyzed separately.

Major surgery was defined as undergoing a major operation during the index hospitalization. Prior surgery was defined as undergoing surgery within 7 days prior to the index hospitalization. Insertion of VCF was not counted as a major surgery. Undergoing surgery was considered a contraindication to anticoagulation.

#### Co-morbidity and Severity-of-illness

Chronic co-morbid conditions (up to 26) were defined using the Elixhauser co-morbidity software (see Supplemental Appendix) [21,22]. Cancer was not counted as a co-morbidity in this analysis. Cases with cancer were classified as having metastatic cancer (ICD-9-CM 196.0-199.9) or non-metastatic cancer (ICD-9-CM 140.0-195.9, 200.0-209.9). Proprietary software from 3M<sup>™</sup> (APR-DRG grouper, V-24) was applied to every record to determine the severity-of-illness (SOI) at the time of admission, which was classified as mild, moderate, major or extreme [23].

#### Statistical Analysis

Categorical data were analyzed using Chi-square testing. Univariate models were used to determine differences in VCF use between groups. Multivariable logistic regression modeling was used to model potential predictive factors for VCF use, which included age, sex, metastatic disease, perceived bleeding risk of cancer type and other clinical characteristics, race/ethnicity and insurance status as socioeconomic factors, and hospital-specific characteristics (size by number of beds, location and type). Kaiser Foundation hospitals were compared to other private and teaching hospitals because they uniquely reflect the care provided by a large, highly penetrant and vertically integrated health maintenance organization.

Analyses were performed using SAS® (9.3 and 9.4) and a two-sided p-value less than 0.05 was considered statistically significant.

#### Results

A total of 87,150 cases were identified with a principal diagnosis code of VTE, either pulmonary embolism or lower extremity deep venous thromboembolism. We excluded cases with no active cancer (N = 71,996) or cancer with unknown primary site (N = 1090). We also excluded cases from hospitals with less than 55 acute VTE cases (N = 64). Our final cohort included a total of 14,000 patients admitted with acute VTE and cancer, but without any prior record of having a VCF placed (Fig. 1). Bleeding occurred in 5.6% of all cases and a major surgery was noted in 2.6%. A VCF was inserted in 19.6% of the cancer cases. The frequency of VCF use varied widely between hospitals with a range of 0% to 52% among 223 hospitals that had more than 55 acute VTE hospitalizations and 15 or more of these in patients with cancer.

There were 7,194 filters placed amongst 64,348 acute VTE cases that did not have cancer (11.2%). Fig. 2 shows the correlation between the frequency of filter use in the cancer and non-cancer cases. For most hospitals, the use of VCFs was greater in cancer patients with acute VTE compared to non-cancer patients. There was a high correlation in the frequency of VCF use in non-cancer and cancer patients within a hospital (r = 0.71,  $R^2 = 0.51$ ).

The frequency distribution of VCF use, and proportions of patients with VCF placement that had bleeding and surgery, by cancer type is shown is Fig. 3. Cases with brain cancer had the highest frequency of VCF use (43%) whereas it was much lower in patients with lymphoma (13%), leukemia (13%), breast (12%) and lip/oral cancer (8%). Of note, in the cases with brain cancer and VTE that had a VCF placed, only 9%



Fig. 2. Correlation of VCF Placement for Acute VTE in Cancer vs. Non-Cancer Patients in California Hospitals. Excludes hospitals with <15 cancer/acute VTE cases.

had bleeding and 9% surgery (some had both). As shown in Fig. 3, the proportion of patients within each tumor type with contraindication to anticoagulation (bleeding or surgery) also greatly varied.

The bivariate frequency of VCF use based on clinical/demographic, socioeconomic, and hospital-characteristics is shown in Table 1. There was no significant difference in VCF use based on race/ethnicity, insurance status or type of facility. Among these cases with acute VTE, the frequency of VCF placement was higher in the cases with active bleeding (47.0%), brain cancer (43.0%), major surgery (58.4%), cases with meta-static cancer (22.0%) and cases with a greater number of comorbid conditions or increasing severity of illness at the time of admission. The use of VCFs was low in hospitals with fewer than 100 beds (7.5%) but similar in hospitals with 100-200 beds (17.4%) and those with over 200 beds (20.8%). Use of VCFs was only 14.1% in Kaiser hospitals. Use in rural hospitals was quite low, 6.5% compared to urban hospitals (20.2%).



Fig. 1. Cohort Diagram.



Fig. 3. Frequency of VCF placement, Bleeding and Surgery by Cancer Type. Bleeding include those that had bleeding at the time of admission and/or during the index hospitalization. Surgery includes those that underwent a major operation during hospitalization or 7 days prior.

The multivariable logistic regression model analyzing predictors of VCF use is shown in Table 2. The strongest clinical predictors of VCF use were having brain cancer (OR = 4.6, 95% CI: 3.7-5.6), major surgery during the hospitalization (OR = 4.9, 95% CI: 3.9-6.1), bleeding at the time of admission (OR = 2.7, 95% CI: 2.1-3.5), bleeding during the hospitalization (OR = 2.7, 95% CI: 1.9-3.9); major severity-of-illness (OR = 1.9, 95%CI: 1.5-2.4), extreme severity-of-illness (OR = 1.8, 95%CI: 1.4-2.4) and metastatic cancer (OR = 1.5, 95%CI: 1.3-1.6). There was no significant difference in the odds of VCF use when comparing acute leukemia or moderate perceived bleeding risk-bladder and kidney cancers to low perceived bleeding risk cancers.

Differences by hospital characteristics found on univariable analysis were confirmed in the adjusted multivariable model. Smaller and rural hospitals were less likely to place VCF in patients with cancer and acute VTE: fewer than 100 licensed beds (OR = 0.4; 95%CI 0.3-0.5; 100-199 licensed beds (OR = 0.9, 95%CI: 0.8-1.0); and rural location versus urban (OR = 0.4; 95%CI: 0.3-0.5). Private hospitals had significantly greater odds of using a VCF compared to non-teaching Kaiser Foundation hospitals. There was no significant difference in the odds of VCF use when profit and not-for- profit hospitals were compared. This logistic model had a c-statistic of 0.702.

#### Discussion

In a previous analysis we reported that cancer patients with acute VTE were more likely to have VCF placement compared to non-cancer patients with acute VTE. The major findings of the present study was the wide variation in frequency of VCF use in cancer patients among California hospitals with significant variation depending on the underlying type, metastatic status, and perceived bleed risk of cancer. The frequency of VCF use in cancer patients also differed depending on hospital and clinical characteristics.

In a previous study, the frequency of VCF placement for all patients with acute VTE varied among 263 California hospitals from 0 to 39%. In the present study, we found an even wider variation in the frequency of VCF use in the cancer patients with acute VTE, from 0-52%. Even after adjusting for important factors that might influence the decision to use a VCF, such as bleeding, undergoing surgery, metastases, severity-of-illness, and the number of chronic comorbidities, hospital characteristics were still significantly predictive of VCF use. Admission to a larger, urban and private hospital was associated with greater odds of having a vena caval filter placed. There was also a strong correlation between

VCF insertion between cancer and non-cancer patients. This finding suggests that local culture and practice pattern within a hospital affects the use of VCFs. We also speculate that larger private and teaching hospitals may have greater availability of specialists who are skilled in placing VCFs.

The variation in the frequency of VCF placement between cancer types was quite striking, with a very high percentage of cases with brain cancer receiving a VCF, but also frequent use in patients with melanoma and cancer involving the pancreas, female genital tract, colon and urinary tract. However, variable proportions of cases had a clear contraindication for anticoagulation (surgery, active bleeding), despite the high frequency of VCF placement (Fig. 3). In certain malignancies such as lip/oral and urinary tract, the use of VCFs occurred primarily in those patients undergoing surgery or having active bleeding. However, in other cancers including melanoma, leukemia and brain, VCF placement occurred despite the lack of a clear contraindication to anticoagulation. We hypothesized that part of this variation would be due to a perceived higher risk of bleeding in certain cancer types. Indeed in the adjusted model, having brain cancer was associated with an over 4-fold increased odds of VCF placement. However, having other malignancies often perceived to be associated with higher risk of bleeding such as acute leukemia, bladder and kidney cancer were not significant predictors of VCF placement when adjusted for other covariables. The high rate of VCF placement in melanoma patients was also unexpected, but may be due to a perception that melanoma has a high bleeding risk as a highly vascular malignancy and/or the presence of brain metastases.

Literature on the use of VCFs in patients with brain cancer is limited and inconclusive. In this study, we found that almost half of all brain cancer patients had a VCF placed but only 9 % of these patients had active bleeding and 9 % had major surgery at the time of the index hospitalization or prior 7 days. The high frequency of VCF placement in these patients, despite lack of contraindication to anticoagulation in most, may reflect an overall perception that brain tumors have a higher propensity for intracranial hemorrhage while on anticoagulation. While brain tumors are highly vascular, retrospective studies have suggested the actual risk of intracranial bleeding while on anticoagulation in patients with primary brain tumors is not significantly increased [24–26]. Several studies have also revealed high rates of complications with VCF use in brain tumor patients [27,28]. One study found that in 42 patients treated with VCFs, 62% developed complications including recurrent PE and DVT, filter thrombosis and post-thrombophlebitis

#### Table 1

Characteristics of Cancer Patients Hospitalized for Acute VTE.

Variables	All Filter		P-Value		
		N	Ν	%	
Total		14,000	2,747	19.6%	
Age	Age < 50	1,539	259	16.8%	0.0423
	50-59	2,334	456	19.5%	
	60-69	3,500	694	19.8%	
	70-79	3,811	755	19.8%	
	80+	2,816	583	20.7%	
Gender	Male	6,903	1,438	20.8%	0.0004
	Female	7,097	1,309	18.4%	
Cancer Type - Perceived Bleed Risk	High- Brain	530	228	43.0%	< 0.0001
	High- Acute Leukemia	89	12	13.5%	
	Mid- Bladder, Kidney	738	164	22.2%	
	Low- everything else	12,643	2,343	18.5%	
Metastatic	Yes	6,100	1,344	22.0%	< 0.0001
	No	7,900	1,403	17.8%	
Bleeding	POA Yes	575	265	46.1%	< 0.0001
	POA No	215	106	49.3%	
	No Bleeding	13,210	2,376	18.0%	
Bleeding Category	ICH	43	27	62.8%	0.0047
	GI	424	212	50.0%	
	Other/Transfusion	323	132	40.9%	
Thrombolytic RX	Yes	253	82	32.4%	< 0.0001
	No	13,747	2,665	19.4%	
Major Surgery	Yes	361	211	58.4%	< 0.0001
	No	13,639	2,536	18.6%	
Vascular Surgery	Yes	193	73	37.8%	< 0.0001
	No	13,807	2,674	19.4%	
Comorbidities	None	1,919	258	13.4%	< 0.0001
	1-2	6,291	1,124	17.9%	
	3+	5,790	1,365	23.6%	0.0001
VIE lype	PE(+/-DVI)	7,999	1,380	17.3%	<0.0001
	Proximal DVI	3,967	886	22.3%	
Constant of Marcon	Distal DVI	2,034	481	23.6%	.0.0001
Severity of miness	SOI-Million	1,194	1 091	10.0%	< 0.0001
	SOI-Moderate	5,508	1,081	10.0%	
	SOI-IVIAJOI	5,429	1,310	24.2%	
Eacility Cizo	SOI-EXTREME 0.00 Pada	809	231	20.0%	<0.0001
Facility Size	100, 100 Pada	269	44	17.3%	< 0.0001
	$200 \perp \text{Pode}$	2,343	2 250	20.9%	
Facility Tumo	200 + Beds Kaisor	2 275	2,235	20.8%	<0.0001
racinty Type	Tooching	2,275	202	14.1%	<0.0001
	Drivato	2,021	2042	15.0%	
Facility Location	Rural	5,704	2,045	6.5%	<0.0001
Facility LUCATION	Kuidi Urban	J02 13/18	2 700	0.3%	<0.0001
Kind of Facility	Non-Profit	10,410	2,705	10.0%	01174
King of Facility	For-Profit	3 3/0	674	19.9%	0.11/4
	101-110110	3,340	024	10.7/0	

NH = Non-Hispanic PE = Pulmonary Embolism DVT = Deep Vein Thrombosis.

syndrome. Interesting, none of the patients who received both anticoagulation and VCF had hemorrhagic complications in this report [29]. Despite the overall evidence showing a low rate of intracranial hemorrhage and a high risk of complications related to VCF use, the present study reveals VCFs are frequently used in brain cancer patients.

The use of VCFs to treat VTE in patients, both in those with cancer and without cancer, continues to be controversial. A few single center studies have found that VCFs are safe and highly effective in preventing PE-related deaths in patients with both hematological and solid tumors [11,30]. However, other studies found increased rates of VCF-related complications in cancer patients including new vena caval thrombosis, retroperitoneal hemorrhage, recurrent VTE and mal-deployed filters, and have questioned the benefit of VCF placement in patients with advanced malignancy [10,11,26,31]. Several studies have also reported that in patients with stage III and IV malignant disease, VCF placement conferred no survival benefit compared to treatment with anticoagulation therapy [31,32]. The cost-effectiveness of VCFs in cancer patients has also been questioned [33,34].

Despite uncertain benefit, cancer patients hospitalized with acute VTE are almost two times more likely to have a VCF placed in comparison to non-cancer patients [14]. The clinical variables most

strongly associated with VCF placement in cancer patients were active bleeding, undergoing a major operation, presence of metastatic disease, greater severity-of-illness at the time of admission, and presence of comorbidities. However, overall only 21% of those who had a VCF placed had active bleeding or underwent major surgery. Therefore, only a minority of the cancer patients with VCF had a clear contraindication to anticoagulation.

There are a number of limitations to this observational study. There was minimal information on cancer stage (other than metastatic cancer) or cancer therapy. Future studies may determine the effect of these clinical variables on the frequency of VCF placement. There was not reliable data on whether retrievable VCFs were used, and if so whether the filter was retrieved. While it is possible that hospitals that place VCFs in a large proportion of cancer patients with acute VTE do actually remove the VCF within a short period of time, current literature suggests that only a small proportion of retrievable VCFs are actually retrieved [35,36]. Due to the retrospective nature of the study, it is possible that more patients may have had a contraindication to anticoagulation than observed. While we could not identify the specific clinical indication for placement of each VCF, we did adjust for contraindications to anticoagulation, such as bleeding and undergoing surgery

#### Table 2

Multi-variable Model to Predict Use of VCF Among. Cancer Patients with Acute VTE.

Variables	OR	(95% CL)	P-Value
Gender (vs. Male)			
Female	0.9	(0.79, 0.95)	0.0020
Race/Ethnicity (vs. NH White)			
African American	1.0	(0.85, 1.16)	0.9654
Hispanic	0.9	(0.82, 1.09)	0.4208
Asian/PI	1.0	(0.81, 1.22)	0.9279
Other/Unknown	0.9	(0.67, 1.21)	0.4726
Age (continuous, 10 year increase)	1.1	(1.01, 1.11)	0.0107
Insurance Coverage (vs. Medicare)			
Medi-Cal	0.9	(0.77, 1.11)	0.4071
Private	1.2	(1.03, 1.33)	0.0130
Self-Pay Other/Unknown	0.6	(0.32, 1.14)	0.1224
Other/Onknown	0.9	(0.27, 2.72)	0.7960
Cancer Type-Perceived Bleeding Risk			
High Bleed Risk-Brain	4.6	(3.74, 5.55)	< 0.0001
High Bleed Risk-Acute Leukemia Mid Bloed Pick Kidnov/Bladdor	0.9	(0.46, 1.61) (0.85, 1.26)	0.6401
Metastatic Disease (vs. No)	1.0	(0.85, 1.20) (1.34, 1.62)	< 0.7449
Wetustutie Discuse (Vs. 100)	1.5	(1.54, 1.62)	<0.0001
Severity of Illness (vs. Minor)			
Moderate	1.4	(1.13, 1.72)	0.0020
Major Extreme	1.9	(1.53, 2.37) (1.41, 2.41)	< 0.0001
Extreme	1.0	(1.41, 2.41)	<0.0001
Bleeding (vs. None)			
Present on Admission	2.7	(2.09, 3.50)	< 0.0001
Hospital Acquired	2.7	(1.94, 3.88)	< 0.0001
Bleeding Type (vs. Other/Transfusion)			
ICH	2.2	(1.09, 4.51)	0.0285
Gl Thrombolistic Acoust (viz. None)	1.5	(1.09, 2.03)	0.0123
Major Surgery (vs. None)	1.4	(1.01, 2.02) (3.89, 6.14)	< 0.0452
Major Surgery (VS. None)	4.5	(5.65, 6.14)	<0.0001
Prior Surgery (vs. None)			
Prior Surgery- <7 days	0.8	(0.52, 1.26)	0.3587
Vascular Surgery (vs None)	1.0	(0.87, 1.12) (1.00, 2.15)	0.8248
vascular surgery (vs None)	1.5	(1.00, 2.15)	0.0324
Comorbidities (vs. None)			
1-2 Comorbidity	1.2	(1.04, 1.42)	0.0126
3 + Comorbidities	1.5	(1.25, 1.74)	<0.0001
Proximal DVT	1.4	(1.28, 1.57)	< 0.0001
Distal DVT	1.5	(1.33, 1.71)	< 0.0001
Facility Size (vs. $200 + \text{ beds})$	0.4	(0.26, 0.50)	< 0.0001
100-199 beds	0.4	(0.20, 0.50) (0.76, 0.98)	0.0280
	010	(01/0,0100)	010200
Type of Facility (vs. Kaiser)	1.0	(1 50 2 10)	-0.0001
riivate Teaching	1.ð 1.5	(1.39, 2.10) (1.24, 1.76)	< 0.000 I < 0.0001
reaching	1.5	(1.27, 1.70)	~0.0001
Location of Facility (vs. Urban)	o :	(0.05.0.50)	0.000
Kural	0.4	(0.25, 0.52)	< 0.0001
Kind of Facility (vs Non-Profit)			
For Profit	0.9	(0.81, 1.01)	0.0791

NH = Non-Hispanic PE = Pulmonary Embolism DVT = Deep Vein Thrombosis.

during the hospitalization. While we could not directly determine whether bleeding occurred prior to filter placement, we included both those with bleeding on admission and during the hospitalization in our study cohort. This may mean that even fewer patients actually had active bleeding and a true contraindication to anticoagulation requiring filter placement when initially diagnosed with VTE. We could not identify specific attending physicians or their specialty. There may be as much between-physician variation in VCF use within each hospital as there is variation between hospitals. Thus, the observed degree of variation in VCF use among hospitals may underestimate even larger variations among physician-groups both within and between hospitals. In conclusion, we observed large variation between hospitals and cancer types in the frequency of VCF use in patients with cancer. Most patients with cancer that had VCF placement did not have clear contraindications to anticoagulation. Further studies are needed to determine if VCF use improves outcomes in cancer patients hospitalized for acute VTE.

#### **Conflict of Interest Statement**

All authors report no conflict of interest.

#### Acknowledgements

G.H. was supported by an HONORS Award from the American Society of Hematology; R.W. by the Hibbard Williams Endowment; T.W. by UL0000012 from NCATS/NIH.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx. doi.org/10.1016/j.thromres.2015.02.002.

#### References

- [1] Debourdeau P, Farge D, Beckers M, Baglin C, Bauersachs RM, Brenner B, et al. International clinical practice guidelines for the treatment and prophylaxis of thrombosis associated with central venous catheters in patients with cancer. J Thromb Haemost 2013;11:71–80.
- [2] Blom JW, Doggen CJ, Osanto S, Rosendaal FR. Malignancies, prothrombotic mutations, and the risk of venous thrombosis. JAMA 2005;293:715–22.
- [3] Walker AJ, Card TR, West J, Crooks C, Grainge MJ. Incidence of venous thromboembolism in patients with cancer - a cohort study using linked United Kingdom databases. Eur J Cancer 2013;49:1404–13.
- [4] Prandoni P, Lensing AW, Piccioli A, Bernardi E, Simioni P, Girolami B, et al. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. Blood 2002;100:3484–8.
- [5] Levitan N, Dowlati A, Remick SC, Tahsildar HI, Sivinski LD, Beyth R, et al. Rates of initial and recurrent thromboembolic disease among patients with malignancy versus those without malignancy. Risk analysis using Medicare claims data. Medicine 1999; 78:285–91.
- [6] Gussoni G, Frasson S, La Regina M, Di Micco P, Monreal M. Three-month mortality rate and clinical predictors in patients with venous thromboembolism and cancer. Findings from the RIETE registry. Thromb Res 2013;131:24–30.
- [7] Monreal M, Falga C, Valdes M, Suarez C, Gabriel F, Tolosa C, et al. Fatal pulmonary embolism and fatal bleeding in cancer patients with venous thromboembolism: findings from the RIETE registry. J Thromb Haemost 2006;4:1950–6.
- [8] Chew HK, Wun T, Harvey D, Zhou H, White RH. Incidence of venous thromboenbolism and its effect on survival among patients with common cancers. Arch Intern Med 2006;166:458–64.
- [9] Stein PD, Kayali F, Olson RE. Twenty-one-year trends in the use of inferior vena cava filters. Arch Intern Med 2004;164:1541–5.
- [10] Barginear MF, Lesser M, Akerman ML, Strakhan M, Shapira I, Bradley T, et al. Need for inferior vena cava filters in cancer patients: a surrogate marker for poor outcome. Clinical and applied thrombosis/hemostasis : official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis 2009;15:263–9.
- [11] Wallace MJ, Jean JL, Gupta S, Eapen GA, Johnson MM, Ahrar K, et al. Use of inferior vena caval filters and survival in patients with malignancy. Cancer 2004;101: 1902–7.
- [12] Kearon C, Akl EA, Comerota AJ, Prandoni P, Bounameaux H, Goldhaber SZ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141 [e419S-e494S].
- [13] Spencer FA, Bates SM, Goldberg RJ, Lessard D, Emery C, Glushchenko A, et al. A population-based study of inferior vena cava filters in patients with acute venous thromboembolism. Arch Intern Med 2010;170:1456–62.
- [14] White RH, Geraghty EM, Brunson A, Murine S, Wun T, Spencer F, et al. High Variation Between Hospitals in Vena Cava Filter Use for Venous Thromboembolism. JAMA Intern Med 2013;173:506–12.
- [15] Grannis SJ JMO, McDonald CJ. Analysis of identifier performance using a deterministic linkage algorithm. Proc Amia Symp 2002:305–9.
- [16] Hser Y, Evans E. Cross-system data linkage for treatment outcome evaluation: lessons learned from the California Treatment Outcome Project. Eval Program Plann 2008;2.
- [17] Athanasoulis CA, Kaufman JA, Halpern EF, Waltman AC, Geller SC, Fan C-M. Inferior Vena Caval Filters: Review of a 26-year Single-Center Clinical Experience1. Radiology 2000;216:54–66.
- [18] Stein PD, Matta F, Hull RD. Increasing Use of Vena Cava Filters for Prevention of Pulmonary Embolism. Am J Med 2011;124:655–61.

- [19] Fang MC, Go AS, Chang Y, Borowsky LH, Pomernacki NK, Udaltsova N, et al. A new risk scheme to predict warfarin-associated hemorrhage: The ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) Study. J Am Coll Cardiol 2011;58:395–401.
- [20] Singer DE, Chang Y, Fang MC, Borowsky LH, Pomernacki NK, Udaltsova N, et al. The net clinical benefit of warfarin anticoagulation in atrial fibrillation. Ann Intern Med 2009;151:297–305.
- [21] Elixhauser. Comorbidity software. In: HCUP, editor; 2011.
- [22] Schoenman JA, Sutton JP, Elixhauser A, Love D. Understanding and Enhancing the Value of Hospital Discharge Data. Med Care Res Rev 2007;64:449–68.
- [23] Lavernia CJ, Laoruengthana A, Contreras JS, Rossi MD. All-Patient Refined Diagnosis-Related Groups in Primary Arthroplasty. J Arthroplasty 2009;24:19–23.
- [24] Choucair AK, Silver P, Levin VA. Risk of intracranial hemorrhage in glioma patients receiving anticoagulant therapy for venous thromboembolism. J Neurosurg 1987; 66:357–8.
- [25] Altschuler EM, Jungreis CA, Sekhar LN, Jannetta PJ, Sheptak PE. Operative treatment of intracranial epidermoid cysts and cholesterol granulomas: report of 21 cases. Neurosurgery 1990;26:606–13 [discussion 14].
- [26] Olin JW, Young JR, Graor RA, Ruschhaupt WF, Beven EG, Bay JW. Treatment of deep vein thrombosis and pulmonary emboli in patients with primary and metastatic brain tumors. Anticoagulants or inferior vena cava filter? Arch Intern Med 1987; 147:2177–9.
- [27] Lee AY, Levine MN. Management of venous thromboembolism in cancer patients. Oncology (Williston Park) 2000;14:409–17 [21; discussion 22, 25-6.].
- [28] Schwarz RE, Marrero AM, Conlon KC, Burt M. Inferior vena cava filters in cancer patients: indications and outcome. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 1996;14:652–7.

- [29] Levin JM, Schiff D, Loeffler JS, Fine HA, Black PM, Wen PY. Complications of therapy for venous thromboembolic disease in patients with brain tumors. Neurology 1993; 43:1111–4.
- [30] Athanasoulis CA, Kaufman JA, Halpern EF, Waltman AC, Geller SC, Fan CM. Inferior vena caval filters: review of a 26-year single-center clinical experience. Radiology 2000;216:54–66.
- [31] Schunn C, Schunn GB, Hobbs G, Vona-Davis LC, Waheed U. Inferior vena cava filter placement in late-stage cancer. Vasc Endovascular Surg 2006;40:287–94.
- [32] Ihnat DM, Mills JL, Hughes JD, Gentile AT, Berman SS, Westerband A. Treatment of patients with venous thromboembolism and malignant disease: should vena cava filter placement be routine? J Vasc Surg 1998;28:800–7.
- [33] Jarrett BP, Dougherty MJ, Calligaro KD. Inferior vena cava filters in malignant disease. J Vasc Surg 2002;36:704–7.
- [34] Chau Q, Cantor SB, Caramel E, Hicks M, Kurtin D, Grover T, et al. Cost-effectiveness of the bird's nest filter for preventing pulmonary embolism among patients with malignant brain tumors and deep venous thrombosis of the lower extremities. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 2003;11:795–9.
- [35] Administration UFaD. Removing Retrievable Inferior Vena Cava Filters: Initial Communication; 2010.
- [36] Duszak Jr R, Parker L, Levin DC, Rao VM. Placement and Removal of Inferior Vena Cava Filters: National Trends in the Medicare Population. J Am Coll Radiol 2011;8: 483–9.