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Full Length Article

Morbidity, mortality and costs associated with venous thromboembolism in hospitalized patients with cancer

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ABSTRACT

Background: Venous thromboembolism (VTE) represents a leading cause of morbidity and mortality among patients with cancer.

Methods: Hospitalization data reported on adult cancer patients at US medical centers between 1995 and 2012 were analyzed. Cancer diagnosis, presence of VTE, comorbidities, and infectious complications were based on ICD-9-CM codes.

Results: Nearly six million hospitalizations of 3,146,388 individual patients with cancer were reported with VTE observed in 8.4%. A single hospitalization was randomly selected for each patient with VTE diagnosed in 166,537 (5.3%) of evaluated admissions. In-hospital mortality was observed in 5.5% of patients without a VTE diagnosis and in 15.0% of those with VTE including 19.4% with a pulmonary embolism. While rates of VTE increased from 3.5% in 1995 to 6.5% in 2012, no significant reported changes in VTE imaging, length of stay (LOS) or intensive care unit (ICU) admissions were observed and mortality decreased by one-third. VTE was reported in 5.2%, 5.8% and 5.4% of patients with solid tumors, lymphoma, and leukemia, respectively. Rates of VTE were greatest among patients with pancreatic, gastric or other abdominal malignancies as well as those with ovarian, lung and esophageal cancers. The risk of VTE increased progressively from 2.3% in those with no comorbidities to over 11% in those with ≥3 major comorbidities. The strongest risk factors for VTE were infectious complications including sepsis, invasive candidiasis, pneumonia and IV line infections. Average costs per hospitalization adjusted to 2015 dollars for patients without and with VTE were $19,994 and $37,352, respectively.

Conclusions: VTE among hospitalized patients with cancer has increased significantly with a major impact on hospital mortality and costs. Patients with major medical comorbidities and infectious complications are at particularly high risk.

1. Introduction

Venous thromboembolism (VTE) is a leading cause of morbidity and mortality among hospitalized patients with cancer [1–3]. While the risk of VTE is greater in hospitalized patients and those undergoing active treatment, little is known about the impact of risk factors associated with greater mortality and costs in this setting. As much as one-fourth of VTE events are related to hospitalization and fatal pulmonary embolism is the leading cause of sudden death among hospitalized patients and contributes up to as much as 10% of hospital deaths [4,5]. Current clinical practice guidelines recommend pharmacologic thromboprophylaxis for hospitalized patients with active malignancy and acute medical illness or reduced mobility in the absence of bleeding or other contraindications [6–8]. Hospitalized patients who have active malignancy without additional risk factors may be considered for pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications [6,9,10]. Data are considered inadequate to support routine thromboprophylaxis in patients admitted for minor procedures or short chemotherapy infusion, or in patients undergoing stem cell bone marrow transplantation [6].

Much of the information on risk factors associated with VTE hospitalization in patients with cancer is extrapolated from studies of seriously ill medical patients with small subgroups of patients with cancer. Guideline recommendations have been heavily influenced by three randomized controlled trials (RCTs) of thromboprophylaxis in medically ill non-surgical (medical) inpatients [11–13]. More recent trials have attempted to address thromboprophylaxis in this setting [14–16]. Extended thromboprophylaxis was evaluated in EXCLAIM

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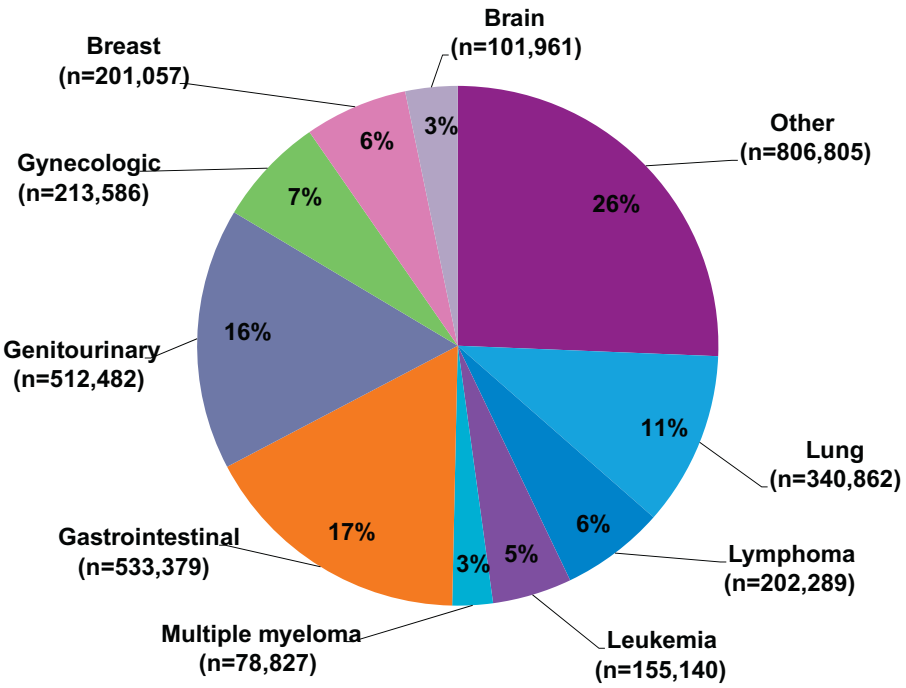

Fig. 1. Cancer type among hospitalized cancer patients, 1995–2012.

Table 1
Characteristics of hospitalized patients with cancer.

	Overall		Early years		Recent years	
	1995–2012		1995–2003		2004–2012	
	N	%	n	%	N	%
All patients	3,146,388	100.0	1,015,598		2,130,790	
Age						
18– < 40	251,940	8.0	97,940	9.6	154,000	7.2
40– < 50	374,693	11.9	136,620	13.5	238,073	11.2
50– < 60	703,940	22.4	216,772	21.3	487,168	22.9
60– < 70	821,919	26.1	248,267	24.4	573,652	26.9
70– < 80	636,482	20.2	215,001	21.2	421,481	19.8
80 or more	357,414	11.4	100,998	9.9	256,416	12.0
Gender						
Female	1,488,597	47.3	493,583	48.6	995,014	46.7
Male	1,657,736	52.7	521,991	51.4	1,135,745	53.3
Race						
White	2,254,331	71.6	725,428	71.4	1,528,903	71.8
Black	412,986	13.1	130,043	12.8	282,943	13.3
Hispanic	131,206	4.2	37,507	3.7	93,699	4.4
Asian	72,528	2.3	19,386	1.9	53,142	2.5
Other/unknown	275,337	8.8	103,234	10.2	172,103	8.1
Geographic region						
North-East	992,758	31.6	304,134	29.9	688,624	32.3
Central	968,123	30.8	322,487	31.8	645,636	30.3
West Coast	539,617	17.2	188,324	18.5	351,293	16.5
Southern	621,356	19.7	194,050	19.1	427,306	20.1
Unknown	24,534	0.8	6603	0.7	17,931	0.8
Cancer type						
Solid tumors	2,680,236	85.2	874,556	86.1	1,805,680	84.7
Lymphoma	202,289	6.4	65,376	6.4	136,913	6.4
Leukemia	155,140	4.9	46,126	4.5	109,014	5.1
Other	108,723	3.5	29,540	2.9	79,183	3.7
Number of comorbidities						
0	946,961	30.1	394,262	38.8	552,699	25.9
1	1,013,933	32.2	339,436	33.4	674,497	31.7
2	722,683	23.0	197,123	19.4	525,560	24.7
3	332,594	10.6	68,161	6.7	264,433	12.4
4+	130,217	4.1	16,616	1.6	113,601	5.3

Table 2
Venous thromboembolism, mortality, length of stay, and cost in patients with cancer.

	1995–2012	1995	2003	2012
	n = 3,146,388	n = 82,402	n = 150,063	n = 321,769
PE (% of patients)	1.8	0.8	1.6	2.3
DVT (% of patients)	4.2	3.0	3.7	5.1
VTE (% of patients)	5.3	3.5	4.7	6.5
VTE by cancer type (% with VTE)				
Solid tumors	5.2	3.5	4.6	6.5
Lymphoma	5.8	3.5	5.2	6.7
Leukemia	5.4	3.9	4.6	6.8
VTE by number of comorbidities (% with VTE)				
0	2.3	2.2	2.3	2.3
1	4.8	4.1	4.7	5.5
2	7.2	5.3	6.9	8.1
3	9.0	6.1	7.7	10.1
4 or more	11.1	5.1	8.6	12.3
Mortality (% died)				
Patients without VTE	5.5	7.3	5.4	4.3
Patients with VTE	15.0	18.1	14.5	12.9
Imaging related to VTE (% with tests)	2.6	4.7	3.0	1.9
Length of stay (days, mean)				
All patients	7.0	8.4	7.2	6.8
Patients without VTE	6.7	8.2	6.9	6.4
Patients with VTE	12.7	14.5	13.0	12.0
Total cost (2015 $$, mean)				
Patients without VTE	$19,994	$19,318	$20,568	$21,809
Patients with VTE	$37,352	$33,127	$37,727	$39,099

DVT = deep venous thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.