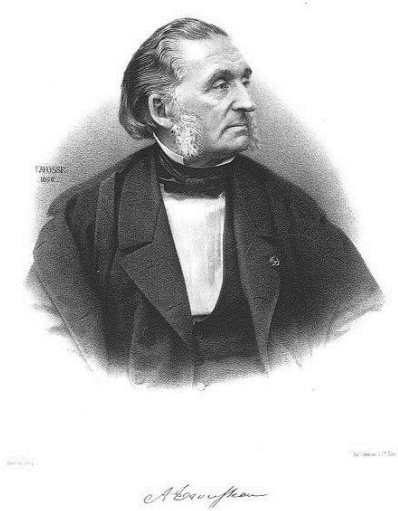
ΘΡΟΜΒΟΕΜΒΟΛΙΚΗ ΝΟΣΟΣ ΣΤΗ ΝΕΟΠΛΑΣΙΑ

ΚΩΝΣΤΑΝΤΙΝΟΣ ΣΠΑΝΟΣ , M.D., M.Sc.
ΕΙΔΙΚΕΥΟΜΕΝΟΣ ΑΓΓΕΙΟΧΕΙΡΟΥΡΓΙΚΗΣ Π.Π.Γ.Ν.ΛΑΡΙΣΑΣ
ΔΙΕΥΘΥΝΤΗΣ ΚΛΙΝΙΚΗΣ,ΚΑΘΗΓΗΤΗΣ, ΑΘ.ΓΙΑΝΝΟΥΚΑΣ , M.D., M.Sc., PhD, FEBVS

•ΠΡΩΤΟΣ ΣΥΣΧΕΤΙΣΜΟΣ ΤΟ 1865 ΑΠΌ ΤΟΝ ARMAND TROUSSEAU



• In his 95th lecture in a series on clinical medicine (delivered at the Hôtel Dieu in Paris noted:

'I have long been struck with the frequency with which cancerous patients are affected with painful edema in the superior or inferior extremities, whether or not either was the seat of cancer.'[1]

1.Trousseau, thrombosis and cancer: A history consult.November ACP Hospitalist, *copyright* © 2011 *by the American College of Physicians*

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association.

Venous Thromboembolism and Cancer: Risks and Outcomes

Agnes Y.Y. Lee and Mark N. Levine

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ΣΤΟ ΓΕΝΙΚΟ ΠΛΗΘΥΣΜΟ 117/100000 ΠΡΩΤΟ ΕΠΕΙΣΟΔΙΟ ΕΒΦΘ/ΠΕ

ΕΤΗΣΙΑ ΠΙΘΑΝΟΤΗΤΑ Θ.Ν. **1/200** ΚΑΡΚΙΝΟΠΑΘΕΙΣ

ΤΟ 20% ΤΩΝ ΑΣΘΕΝΩΝ ΜΕ ΘΝ ΑΦΟΡΟΥΝ ΑΣΘΕΝΕΙΣ ΜΕ ΚΑΚΟΗΘΕΙΑ

ΤΟ 20% ΤΩΝ ΑΣΘΕΝΩΝ ΜΕ ΚΑΚΟΗΘΕΙΑ ΘΑ ΠΡΟΣΒΛΗΘΟΥΝ ΑΠΌ ΤΗ ΘΝ

Agnes et al,Venous Thromboembolism And Cancer:Risks and Outcomes,Circulation.2003;107I-17-I21.

Review Article

Venous Thromboembolism in the Patient With Cancer

Focus on Burden of Disease and Benefits of Thromboprophylaxis

Gary H. Lyman, MD, MPH

Venous thromboembolism (VTE) is a significant cause of morbidity and mortality in patients with cancer. The risk of VTE varies over the natural history of cancer, with the highest risk occurring during hospitalization and after disease recurrence. Patient and disease characteristics are associated with further increased risk of VTE in this setting. Specific factors include cancer type (eg, pancreatic cancer, brain cancer, lymphoma) and the presence of metastatic disease at the time of diagnosis. VTE is a significant predictor of increased mortality during the first year among all types and stages of cancer, with metastatic disease reported to be the strongest predictor of mortality. VTE is also associated with early death in ambulatory patients with cancer. These data highlight the need for close monitoring, prompt treatment, and appropriate preventive strategies for VTE in patients with cancer. The American Society of Clinical Oncology and the National Comprehensive Cancer Network have issued guidelines regarding the prophylaxis and treatment of patients with cancer. This review summarizes the impact of VTE on patients with cancer, the effects of VTE on clinical outcomes, the importance of thromboprophylaxis in this population, relevant ongoing clinical trials examining the prevention of VTE, and new pharmacologic treatment options. ***Cancer*** **2011;117:1334–49.** *© 2010 American Cancer Society.*

KEYWORDS: venous thromboembolism (VTE), cancer, thromboprophylaxis, anticoagulant, chemotherapy, low molecular weight heparin (LMWH).

Table 2. Risk Factors for VTE in Patients With Cancer

Category	Risk Factor
Patient characteristics	● Advanced age ● Gender ● Ethnicity ○ African American, higher ○ Asian, lower
Cancer-related factors	● Cancer site ○ Brain ○ Pancreas ○ Kidney ○ Stomach ○ Bladder ○ Gynecologic ○ Lung ○ Blood ● Advanced stage ● Initial period after diagnosis
Biomarkers	● Increased platelet count prior to chemotherapy ● D-dimer ● Tissue factor expression in tumor cells
Treatment-related factors	● Major surgery ● Hospitalization ● Cancer therapy ● Chemotherapy or hormonal therapy ● Antiangiogenic and immunomodulatory agents ○ Bevacizumab ○ Thalidomide and lenalidomide ● Erythropoiesis-stimulating agents

VTE indicates venous thromboembolism.

Reprinted from Khorana AA, Rao MV. Approaches to risk-stratifying cancer patients for venous thromboembolism. *Thromb Res.* 2007;120(suppl 2):S41-S50. Copyright © 2007, with permission from Elsevier.[14]

J Natl Compr Canc Netw. 2011 Jul 1;9(7):789-97.

Risk assessment and prophylaxis for VTE in cancer patients.

Khorana AA.

Source
James P. Wilmot Cancer Center, and the Department of Medicine,
University of Rochester, New York, USA. alok_khorana@urmc.rochester.edu

KHORANA CRITERIA

Table 2. Predictive model for chemotherapy-associated VTE[16]

Patient characteristics	Risk score
Site of cancer	
Very high risk: stomach, pancreas	2
High risk: lung, lymphoma, gynecologic, bladder, testicular	1
Prechemotherapy platelet count 350 000/mm^3 or more	1
Prechemotherapy hemoglobin level $<$ 10 g/dL and/or planned use of erythropoiesis-stimulating agents	1
Prechemotherapy leukocyte count $>$ 11 000/mm^3	1
Body mass index 35 kg/m^2 or more	1

High-risk score, $\geq$ 3; intermediate-risk score, 1-2; low-risk score, 0.

ΣΗΜΑΝΤΙΚΟ ΡΟΛΟ ΠΑΙΖΟΥΝ:

- ΤΟ ΣΤΑΔΙΟ ΤΗΣ ΝΟΣΟΥ
- ΧΗΜΕΙΟΘΕΡΑΠΕΙΑ
- ΤΟ ΕΙΔΟΣ ΤΗΣ ΚΑΚΟΗΘΕΙΑΣ

➢**B14 KAI B20 TRIALS**

ΚΑΡΚΙΝΟΣ ΣΤΗΘΟΥΣ :

•ΧΩΡΙΣ ΛΕΜΦΑΔΕΝΕΣ

PLACEBO+TAMOXIFEN VS TAMOXIFEN+CHEMO

0.9% VS 4.2

•ΜΕ (+) ΛΕΜΦΑΔΕΝΕΣ

PLACEBO+TAMOXIFEN VS TAMOXIFEN+CHEMO

1% VS 10%

•ΜΕΤΑΣΤΑΣΕΙΣ 4.5%-17.5%

Clin Trials. 2013 Apr;10(2):280-91. doi: 10.1177/1740774512470315. Epub 2013 Jan 18.
National Surgical Adjuvant Breast and Bowel Project Study of Tamoxifen and Raloxifene trial: advancing the science of recruitment and breast cancer risk assessment in minority communities.
McCaskill-Stevens W

➢ΧΗΜΕΙΟΘΕΡΑΠΕΙΑ ΑΥΞΑΝΕΙ 6.5-fold risk

➢ΣΥΝΔΙΑΣΜΟΣ ΑΝΤΙΝΕΟΠΛΑΣΜΑΤΙΚΩΝ ΦΑΡΜΑΚΩΝ ΑΥΞΑΝΕΙ ΤΗΝ ΠΙΘΑΝΟΤΗΤΑ ΘΝ 2-fold risk

Barni et al.Journal of Translational Medicine 2001,9:179

ΠΙΘΑΝΟΣ ΠΑΘΟΦΥΣΙΟΛΟΓΙΚΟΣ ΜΗΧΑΝΙΣΜΟΣ :

•ΔΥΣΛΕΙΤΟΥΡΓΙΑ ΤΟΥ ΕΝΔΟΘΗΛΙΟΥ

•ΑΛΛΑΓΗ ΣΤΟ ΕΠΙΠΕΔΟ ΤΩΝ ΠΡΟ- ΚΑΙ ΑΝΤΙΠΗΚΤΙΚΩΝ ΠΡΩΤΕΙΝΩΝ

•ΜΕΙΩΣΗ ΤΗΣ ΔΡΑΣΗΣ ΤΩΝ ΚΥΤΟΚΙΝΩΝ

Agnes et al,Venous Thromboembolism And Cancer:Risks and Outcomes, Circulation.2003;107I-17-I21.

➢ΤΟ ΕΙΔΟΣ ΤΗΣ ΕΝΤΟΠΙΣΗΣ ΤΗΣ ΚΑΚΟΗΘΕΙΑΣ:

ΠΑΚΡΕΑΣ	8.1%	ΝΕΦΡΟΙ	5.6%
ΩΟΘΗΚΕΣ	5,6%	ΠΝΕΥΜΟΝΕΣ	5.1%
ΣΤΟΜΑΧ I	4.9%	ΠΟΛ.ΜΥΕΛΩΜΑ	5%
Non-HODGIN ΛΕΜΦ.	4.8%	HODGIN DIS.	4.6%

Freesia et al.Risk of Venous Thromboembolism in patients with cancer:
A systematic review and meta-analysis.Plos Medicine.2012 July,Vol.9.Issue7

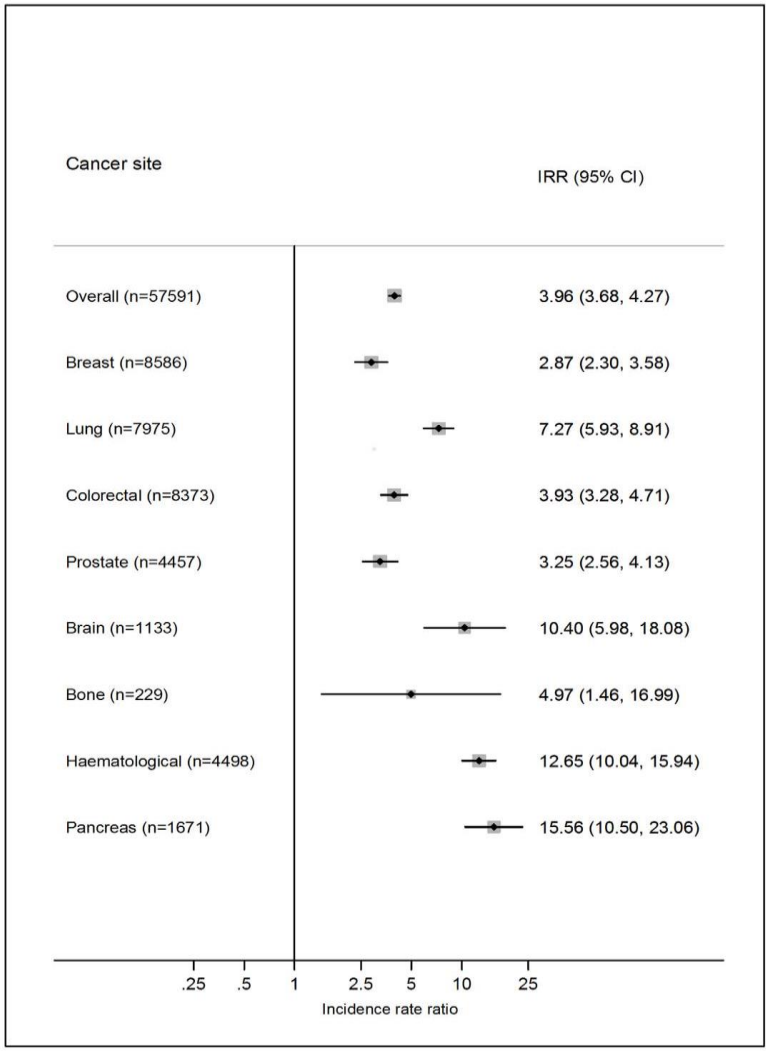


Figure 11. Relative risks of venous thromboembolism in cancer patients compared with in the general population. Results for selected cancer types obtained from Cronin-Fenton et al. [36]. IRR, incidence rate ratio.
doi:10.1371/journal.pmed.1001275.g011

ΣΥΣΧΕΤΙΣΜΟΣ ΘΝ ΚΑΙ ΥΠΟΚΛΙΝΙΚΟΥ ΚΑΡΚΙΝΟΥ

ΙΔΙΟΠΑΘΗΣ ΘΝ > ΔΕΥΤΕΡΟΠΑΘΗΣ ΘΝ
4.8-FOLD higher RISK ΓΙΑ ΚΑΚΟΗΘΕΙΑ

- 10% ΑΣΘΕΝΩΝ ΜΕ ΙΔΙΟΠΑΘΗ ΘΝ ΔΙΑΓΙΓΝΩΣΚΕΤΑΙ ΚΑΡΚΙΝΟΣ **ΣΤΑ 5-10 ΕΤΗ**

- ΑΠΟ ΑΥΤΟΥΣ 75% ΘΑ ΔΙΑΓΝΩΣΤΕΙ ΣΤΟ **ΠΡΩΤΟ** ΕΤΟΣ ΜΕΤΑ ΤΟ ΕΠΕΙΣΟΔΙΟ ΤΗΣ ΘΝ.

ΣΤΟ **40%**ΤΩΝ ΑΣΘΕΝΩΝ ΠΟΥ ΑΝΕΥΡΕΘΗΣΑΝ ΌΤΙ ΠΑΣΧΟΥΝ ΑΠΌ ΚΑΚΟΗΘΕΙΑ ,Η ΟΠΟΙΑ ΔΙΑΓΙΓΝΩΣΤΗΚΕ ΜΕΤΑ ΤΟ ΠΡΩΤΟ ΤΟΥΣ ΕΠΕΙΣΟΔΙΟ ΘΝ, ΑΝΕΥΡΕΘΗΣΑΝ ΚΑΙ ΜΕΤΑΣΤΑΣΕΙΣ.

LITTLE EVIDENCE IF IT IS COST EFFECTIVE OR IF IT WILL IMPROVE DIAGNOSIS

Sørensen HT, Johnsen SP, Nørgård B, Zacharski LR, **Baron** JA. **Cancer** and **venous thromboembolism**: a multidisciplinary approach.Clin Lab. 2003;49(11-12):615-23. Review

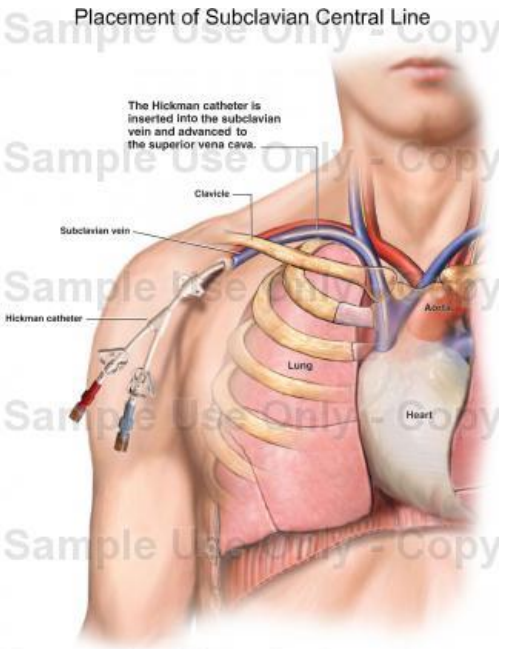
ΘΝ ΣΤΟΥΣ ΚΑΡΚΙΝΟΠΑΘΕΙΣ ΠΟΥ ΣΥΣΧΕΤΙΖΕΤΑΙ ΜΕ ΤΗ ΧΡΗΣΗ ΚΕΝΤΡΙΚΩΝ ΚΑΘΕΤΗΡΩΝ

•ΞΕΝΟ ΣΩΜΑ ΣΕ ΕΠΙΡΡΕΠΕΙΣ ΑΣΘΕΝΕΙΣ

•ΧΗΜΟΘΕΡΑΠΕΥΤΙΚΟΙ ΠΑΡΑΓΟΝΤΕΣ ΧΟΡΗΓΟΥΝΤΑΙ ΑΠΟ ΤΗΝ ΠΕΡΙΟΧΗ ΑΥΤΉ

•ΤΟΠΙΚΗ ΑΚΤΙΝΟΒΟΛΙΑ

ΕΩΣ 14% ΘΝ



Agnes et al,Venous Thromboembolism And Cancer:Risks and Outcomes,Circulation.2003;107I-17-I21.

ΘΕΡΑΠΕΙΑ

Table 4. Recent Studies of Pharmacologic Anticoagulants in Medical Patients With Cancer

Study	Patient Population	Treatments	Primary Outcome	Result	Significance Level	Bleeding Rates	Significance Level	Length of Treatment	Setting
Hull 2010[31]	Acutely ill medical patients	Enoxaparin, 40 mg QD or placebo	VTE	Enoxaparin, 2.5% (45/1818); Placebo, 4.2% (78/1867)	$P < .042$	Major bleeding: enoxaparin, 0.8%; placebo, 0.3%	$P < .05$	28 d	Prophylaxis
De Cicco 2009[32]	Cancer patients with a central vein catheter	Acenocumarine, 1 mg QD or dalteparin, 5000 IU QD or no anticoagulant therapy	Central vein catheter-related thrombosis	Acenocumarine, 21.9% (25/114); dalteparin, 40.0% (48/120); no treatment, 52.6% (60/114)	Acenocumarine vs no treatment: $P < .01$; dalteparin vs no treatment: $P = .05$; acenocumarine vs dalteparin: $P = .01$	Major bleeding: none observed	NR	Acenocumarine: 11 d; dalteparin, 8 d	Prophylaxis
Young 2009[33]	Cancer patients receiving chemotherapy via central venous catheters	Fixed-dose warfarin, 1 mg QD or INR-adjusted warfarin QD or no warfarin	Catheter-related thrombotic events	Fixed-dose warfarin, 7% (34/471); INR-adjusted warfarin, 3% (13/473); no warfarin, 6% (24/404)	Warfarin vs no warfarin: $P = .98$; fixed-dose warfarin vs INR-adjusted warfarin: $P = .002$	Major bleeding: fixed-dose warfarin, 1%; INR-adjusted warfarin, 3%; no warfarin, <1%	Warfarin vs no warfarin: $P = .07$; INR-adjusted warfarin vs fixed-dose warfarin: $P = .09$	Treatment continued until catheter removal or occurrence of thrombosis	Prophylaxis
Weber 2008[34]	Terminal cancer	Nadroparin, 2850–3800 IU/kg QD or no treatment	VTE	Nadroparin, 10% (1/10); no treatment, 0% (0/10)	$P = 1.00$	Major bleeding: nadroparin, 10%; no treatment, 0%	$P = 1.00$	Treatment continued until death	Prophylaxis
Robins 2008[35]	Glioblastoma multiforme	Dalteparin, 5000 IU QD with conventional radiotherapy vs control cohort	Survival time	Median survival time in dalteparin-treated patients: 11.9 mo	$P = .47$ vs control cohort	Major bleeding: none reported	NR	≤24 mo	Prophylaxis
Niers 2007[36]	Hematologic malignancy	Nadroparin, 2850 IU QD vs placebo	Catheter-related thrombosis	Nadroparin, 17% (7/41); placebo, 9% (4/46)	$P = .49$	Major bleeding: none reported	NR	3 wk	Prophylaxis
Meister 2008[37]	Acute lymphoblastic leukemia	Antithrombin alone vs antithrombin plus enoxaparin, 0.75–1.2 mg/kg QD	VTE	Antithrombin alone, 12.7% (9/71); antithrombin plus enoxaparin, 0%	$P = .02$	Major bleeding: none reported	NR	1–2 wk during chemotherapy induction and reinduction phases	Prophylaxis
Icli 2007[38]	Advanced pancreatic cancer	Combination chemotherapy plus nadroparin, 2850 IU QD vs combination chemotherapy alone	Treatment response rate; survival	Response rate: nadroparin, 58.8% (20/34); no nadroparin, 12.1% (4/33). Median overall survival time: nadroparin, 13.0 mo; no nadroparin, 5.5 mo	Response rate: $P = .0001$; survival time: $P = .0001$	Treatment-related bleeding: none reported	NR	Until disease progression	Prophylaxis
Miller 2006[39]	Patients with multiple myeloma or chronic lymphocytic leukemia treated with thalidomide-based therapies	Warfarin 1 or 2 mg QD vs historical studies with similar chemotherapy regimens	VTE	Warfarin, 5.9% (4/68); thalidomide plus doxorubicin, 27%; thalidomide plus epirubicin, 26%	Warfarin regimen vs thalidomide plus doxorubicin: $P = .034$; warfarin regimen vs thalidomide plus epirubicin: $P = .009$	Treatment-related bleeding: none reported	NR	4 mo	Prophylaxis

(Continued)

Table 4. (Continued)

Study	Patient Population	Treatments	Primary Outcome	Result	Significance Level	Bleeding Rates	Significance Level	Length of Treatment	Setting
Deitcher 2006[40]	Patients with active cancer and acute VTE	Enoxaparin, 1 mg/kg BID × 5 d, then 1 mg/kg QD thereafter *or* enoxaparin, 1 mg/kg BID × 5 d, then 1.5 mg/kg QD thereafter vs enoxaparin, 1 mg/kg BID × 5 d or until INR target achieved, then INR-adjusted warfarin thereafter	Recurrent VTE	Enoxaparin at 1 mg/kg, 3.4% (1/29); enoxaparin at 1.5 mg/kg, 3.1% (1/32); warfarin, 6.7% (2/30)	NR	Major bleeding: enoxaparin at 1 mg/kg, 6.5%; enoxaparin at 1.5 mg/kg, 11.1%; warfarin, 2.9%	NR	180 d	Treatment
Ruud 2006[41]	Children with active cancer and central venous lines	INR-adjusted warfarin QD vs no prophylaxis	Central vein catheter-related VTE	Warfarin, 48% (14/29); no prophylaxis, 36% (12/33)	$P = .44$	Bleeding rates NR	NR	6 mo	Prophylaxis
Ikhlaque 2006[42]	Patients receiving thalidomide therapy	Low-dose warfarin (1–2 mg/d) or high-dose warfarin (adjusted to INR 2–3) vs no prophylaxis	DVT	Low-dose warfarin, 2.7% (1/37); high-dose warfarin, 11.1% (2/18); no warfarin, 23.7% (18/76)	$P = .01$ for any dose of warfarin vs no warfarin	Clinical bleeding: low-dose warfarin, 0%; high-dose warfarin, 22.2%; no warfarin, 0%	NR	≤14 mo	Prophylaxis
Baz 2005[43]	Multiple myeloma	Aspirin, 81 mg QD initiated at the start of chemotherapy or aspirin, 81 mg QD initiated after the start of chemotherapy vs no aspirin	VTE	Aspirin initiated at the start of chemotherapy, 19% (11/58); aspirin initiated after the start of chemotherapy, 15% (4/26); no aspirin, 58% (11/19)	$P \leq .002$ for both aspirin groups vs no aspirin	Significant bleeding complications: none reported	NR	Median, 2 y	Prophylaxis
Karthaus 2006[44]	Cancer patients with central venous catheters	Dalteparin, 5000 IU QD vs placebo	Catheter-related complications	Dalteparin, 3.7% (11/294); placebo, 3.4% (5/145)	$P = .88$	Any bleeding event: dalteparin, 17.5%; placebo, 15%	NR	16 wk	Prophylaxis
Verso 2005[45]	Cancer patients with central venous catheters	Enoxaparin, 40 mg QD vs placebo	DVT or clinically overt PE	DVT: enoxaparin, 14.1% (22/155); placebo, 18.0% (28/155)	$P = .35$	Major bleeding: none reported	NR	6 wk	Prophylaxis
Couban 2005[46]	Cancer patients with central venous catheters	Warfarin, 1 mg QD vs placebo	Central venous catheter-related thrombosis	Warfarin, 4.6% (6/130); placebo, 4.0% (5/125)	HR 1.20 (95% CI, 0.37–3.94)	Major bleeding: warfarin, 0%; placebo, 2%	$P = .07$	Until catheter removal, death, or catheter-related thrombosis	Prophylaxis

QD indicates every day; VTE, venous thromboembolism; NR, not reported; INR, international normalized ratio; BID, twice daily; DVT, deep vein thrombosis; PE, pulmonary embolism; HR, hazard ratio; 95% CI, 95% confidence interval.

Table 3 Randomized clinical trials testing the effect of LMWHs on survival of cancer patients

Study	Cancer type	Control	LMWH (regimen)	Effect on survival[a]
Altinbas et al[76]	SCLC	None	Dalteparin (5000 IU/day, 18 weeks)	+
FAMOUS[75]	Advanced cancer	Placebo	Dalteparin (5000 IU/day, 1 year)	+/– (+ patient with better prognosis)
MALT[77]	Metastasized and advanced cancer	Placebo	Nadroparin (therapeutic dose 2 weeks + half dose 4 weeks)	+/– (+ patient with better prognosis)
Sideras et al[78]	Advanced cancer	None	Dalteparin (5000 IU/day, 2 years)	+
INPACT[82]	NSCLC, prostate, pancreatic	None	Nadroparin (therapeutic dose 2 weeks + half dose 4 weeks, weight adjusted, followed by up to six cycles)	None
ABEL[94]	Limited SCLC	None	Bemiparin (3500 IU/day, 26 weeks)	+
TILT (ongoing, NCT 004775098)	NSCLC	Placebo	Tinzaparin (100 IU/kg once-daily, 12 weeks)	N/A

Notes: [a]+, positive effect of LMWH on survival; N/A, results not yet available; +/–, inconclusive.
Abbreviations: LMWH, low-molecular-weight heparin; NCT, National Clinical Trial; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer.

Table 4 In vitro studies exploring the effect of LMWH on tumor-induced endothelial cell angiogenesis

LMWH	Experimental model	Anti-angiogenic effect	LMWH mechanism proposed	Reference
Dalteparin	TCM-stimulated HMEC-1 and HUVEC	Inhibition of endothelial cell tube formation	Interference with bFGF and VEGF binding to their receptors	Marchetti et al[85]
	bFGF-stimulated HUVEC	Inhibition of endothelial cell tube formation and proliferation	Interference with bFGF binding to its receptor	Khorana et al[86]
Enoxaparin	bFGF-stimulated HUVEC	Inhibition of endothelial cell tube formation and proliferation	Interference with bFGF binding to its receptor	Khorana et al[86]
Tinzaparin	bFGF and TF/FVIIa stimulated HUVEC	Inhibition of endothelial cell tube formation	Increased release of TFPI	Mousa and Mohamed[88]
	bFGF-stimulated HUVEC	Inhibition of endothelial cell tube formation and proliferation	Interference with bFGF binding to its receptor	Khorana et al[86]
Bemiparin	TCM-stimulated HMEC-1	Inhibition of endothelial cell tube formation, proliferation, and wound healing	Interference with angiogenic factor binding to their receptor, increased released of TFPI	Vignoli et al[87]
Nadroparin	–	–	–	N/A
Certoparin	–	–	–	N/A

Note: Selected works from the literature on the commercially available LMWH cited in the article.
Abbreviations: bFGF, basic fibroblast growth factor; HMEC-1, human microvascular endothelial cell line-1; HUVEC, human umbilical vein endothelial cells; LMWH, low-molecular-weight heparin; N/A, not applicable; TCM, tumor-conditioned medium; TF, tissue factor; FVIIa, activated coagulation factor VII; TFPI, tissue factor pathway inhibitor; VEGF, vascular endothelial growth factor.

Table 1: Summary of guidelines for prevention and treatment of venous thromboembolism in cancer [5–8].

Guidelines and pharmacologic prophylaxis		VKA	UFH	LMWH	FXa-I
American College of Chest Physicians (ACCP) (Prevention in cancer patients (medical and surgical))		No	Yes (SQ)	Yes	Yes
Duration of prevention: (1) For medical oncology cancer patients who have acute medical illness or who are bedridden for the duration of hospitalization. (2) For surgical cancer patients (pelvic, abdominal, orthopedic) duration of prophylaxis up to 4 weeks. (3) In the presence of contraindications or high risk of bleeding, mechanical methods may be temporarily substituted and pharmacologic prophylaxis should resume after risk of bleeding subsides.					
American College of Chest Physician(ACCP)	Acute	No	No	Yes	Not addressed
(Treatment in cancer patients)	Long term	Yes	No	Yes	No
Duration of treatment: At least 3 months of treatment with LMWH, followed by treatment with either LMWH or VKA.					
American Society of Clinical Oncology (ASCO) (Prevention in cancer patients)		No	Yes (SQ)	Yes	Yes
Duration of prevention: (1) For as long as the patient is hospitalized (due to surgery or acute medical illness) or until the patient is ambulatory. (2) In the presence of contraindication or high risk of bleeding, mechanical methods may be temporarily substituted and pharmacologic prophylaxis should resume after risk of bleeding subsides. (3) In certain multiple myeloma patients receiving thrombogenic chemotherapy (lenalidomide or thalidomide with dexamethasone), low-dose VKA (INR~1.5) or enoxaparin (40 mg) may be considered.					
American Society of Clinical Oncology (ASCO)	Acute 5–10 days	No	Yes (IV)	Yes	Yes
(Treatment in cancer patients)	Long term	Yes	No	Yes	Not addressed
Duration of treatment: LMWH is preferred for 5–10 days, then LMWH for at least 6 months. VKA may be substituted if LMWH is not accessible. After 6 months of treatment, indefinite treatment duration for cancer patients with metastasis or those actively receiving chemotherapy.					
National Comprehensive Cancer Network (NCCN) (Prevention in cancer patients)		Yes	Yes (SQ)	Yes	Yes
Duration of prevention: (1) For the duration of hospitalization for medical illness and up to 4 weeks in surgical cancer patients. (2) In the presence of contraindication, use mechanical prophylaxis until bleeding risk subsides. (3) In certain high-risk medical oncology patients (i.e., aggressive tumor such as pancreatic, gastric, lymphoma, or in cases of obesity or prior VTE), longer prophylaxis is recommended. (4) In certain multiple myeloma patients receiving thrombogenic chemotherapy (lenalidomide or thalidomide with dexamethasone), VKA (INR of 2-3) or aspirin (81–325 mg) may be considered.					
National Comprehensive Cancer Network (NCCN)	Acute 5–10 days	No	Yes (IV)	Yes	Yes
(Treatment in cancer patients)	Long term	Yes	No	Yes	Not addressed
Duration of treatment: (1) LMWH is preferred for the first 3–6 months in DVT and 6–12 months in PE. (2) VKA can be considered if LMWH is not accessible.					

VKA: vitamin K antagonist; UHF: unfractionated heparin; LMWH: low-molecular-weight heparin; FXa-I: direct factor-Xa inhibitor; SQ: subcutaneous; IV: intravenous; INR: international normalized ratio; DTV: deep vein thrombosis.

Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Gary H. Lyman, Alok A. Khorana, Nicole M. Kuderer, Agnes Y. Lee, Juan Ignacio Arcelus, Edward P. Balaban, Jeffrey M. Clarke, Christopher R. Flowers, Charles W. Francis, Leigh E. Gates, Ajay K. Kakkar, Nigel S. Key, Mark N. Levine, Howard A. Liebman, Margaret A. Tempero, Sandra L. Wong, Ann Alexis Prestrud, and Anna Falanga

A B S T R A C T

Purpose
To provide recommendations about prophylaxis and treatment of venous thromboembolism (VTE) in patients with cancer. Prophylaxis in the outpatient, inpatient, and perioperative settings was considered, as were treatment and use of anticoagulation as a cancer-directed therapy.

Methods
A systematic review of the literature published from December 2007 to December 2012 was completed in MEDLINE and the Cochrane Collaboration Library. An Update Committee reviewed evidence to determine which recommendations required revision.

Results
Forty-two publications met eligibility criteria, including 16 systematic reviews and 24 randomized controlled trials.

Recommendations
Most hospitalized patients with cancer require thromboprophylaxis throughout hospitalization. Thromboprophylaxis is not routinely recommended for outpatients with cancer. It may be considered for selected high-risk patients. Patients with multiple myeloma receiving antiangiogenesis agents with chemotherapy and/or dexamethasone should receive prophylaxis with either low–molecular weight heparin (LMWH) or low-dose aspirin. Patients undergoing major cancer surgery should receive prophylaxis, starting before surgery and continuing for at least 7 to 10 days. Extending prophylaxis up to 4 weeks should be considered in those with high-risk features. LMWH is recommended for the initial 5 to 10 days of treatment for deep vein thrombosis and pulmonary embolism as well as for long-term (6 months) secondary prophylaxis. Use of novel oral anticoagulants is not currently recommended for patients with malignancy and VTE. Anticoagulation should not be used for cancer treatment in the absence of other indications. Patients with cancer should be periodically assessed for VTE risk. Oncology professionals should provide patient education about the signs and symptoms of VTE.

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J Thromb Haemost. 2013 Jan;11(1):56-70. doi: 10.1111/jth.12070.

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Source Assistance Publique-Hôpitaux de Paris, Internal Medicine and Vascular Disease Unit, Saint-Louis Hospital, Paris, France.

➢ΣΤΗ ΜΕΘ ΣΤΟΥΣ ΚΑΡΚΙΝΟΠΑΘΕΙΣ ΑΣΘΕΝΕΙΣ ΣΕ ΚΡΙΣΙΜΗ ΚΑΤΑΣΤΑΣΗ

ΕΒΦΘ 5.1-5.8% VS ΑΙΜΟΡΡΑΓΙΑ 13%
ΠΕ 1.2-2.3%

(Η ΦΑΡΜΑΚΟΚΙΝΗΤΙΚΗ ΕΠΗΡΕΑΖΕΤΑΙ ΛΟΓΩ ΜΕΙΩΜΕΝΟΥ ΗΠΑΤΙΚΟΥ ΜΕΤΑΒΟΛΙΣΜΟΥ, ΜΕΙΩΜΕΝΗΣ ΝΕΦΡΙΚΗΣ ΛΕΙΤΟΥΡΓΕΙΑΣ, ΑΤΡΟΦΙΑΣ ΓΑΣΤΡΕΝΤΕΡΙΚΟΥ ΣΩΛΗΝΑ, ΜΕΙΩΣΗΣ Η ΑΥΞΗΣΗΣ ΠΡΟΣΛΗΨΗΣ ΥΓΡΩΝ ΣΤΟ ΕΞΩΑΓΓΕΙΑΚΟ ΧΩΡΟ, ΚΑΚΗ ΙΣΤΙΚΗ ΔΙΑΠΕΡΑΤΟΤΗΤΑ, ΜΕΙΩΣΗΣ ΠΡΩΤΕΙΝΩΝ ΠΟΥ ΣΥΝΔΕΟΝΤΑΙ ΜΕ ΤΙΣ ΦΑΡΜΑΚΕΥΤΙΚΕΣ ΟΥΣΙΕΣ.)

Ο ΑΝΑΣΤΟΛΕΑΣ FXa-1 ΧΩΡΙΣ ΕΠΕΙΣΟΔΙΑ ΘΝ ΚΑΙ ΕΛΑΧΙΣΤΑ ΑΙΜΟΡΡΑΓΙΚΑ ΕΠΕΙΣΟΔΙΑ.

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NCCN GUIDELINES AS AN UNLABELED USE

ΠΡΟΓΝΩΣΗ ΤΩΝ ΑΣΘΕΝΩΝ ΜΕ ΝΕΟΠΛΑΣΙΑ ΚΑΙ ΘΝ

•ΟΙ ΑΣΘΕΝΕΙΣ ΜΕ ΘΝ ΕΧΟΥΝ **4- ΜΕ 8- ΦΟΡΕΣ** **ΥΨΗΛΟΤΕΡΗ ΘΝΗΤΟΤΗΤΑ** ΜΕΤΑ ΑΠΟ ΕΝΑ ΟΞΥ ΕΠΕΙΣΟΔΙΟ ΘΡΟΜΒΩΣΗΣ

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•ΔΙΠΛΑΣΙΕΣ ΠΙΘΑΝΟΤΗΤΕΣ ΝΑ ΠΡΟΚΑΛΕΣΕΙ ΑΙΜΟΡΡΑΓΙΑ Η ΑΝΤΙΠΗΚΤΙΚΗ ΑΓΩΓΗ

•ΔΙΠΛΑΣΙΟ ΤΟ ΚΟΣΤΟΣ ΓΙΑ ΤΗΝ ΑΝΤΙΜΕΤΩΠΙΣΗ ΤΗΣ ΘΝ ΣΤΟΥΣ ΚΑΡΚΙΝΟΠΑΘΕΙΣ **20.065$ VS 7.7712-10.804$**

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- Η ΝΟΣΟΚΟΜΕΙΑΚΗ ΘΝΗΣΙΜΟΤΗΤΑ ΕΙΝΑΙ **2-5 ΦΟΡΕΣ ΥΨΗΛΟΤΕΡΗ** ΣΤΟΥΣ ΚΑΡΚΙΝΟΠΑΘΕΙΣ ΜΕ ΘΝ ΣΕ ΣΧΕΣΗ ΜΕ ΑΥΤΟΥΣ ΧΩΡΙΣ ΘΝ

- ΤΟ **9.2%** ΤΩΝ ΝΟΣΟΚΟΜΕΙΑΚΩΝ ΘΑΝΑΤΩΝ ΤΩΝ ΑΣΘΕΝΩΝ ΜΕ ΚΑΡΚΙΝΟ ΟΦΕΙΛΕΤΑΙ ΣΤΗ ΘΝ

- 1-YEAR SURVIVAL RATE

  12% ΜΕ ΘΝ VS **36%** ΧΩΡΙΣ

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BMC Medical Informatics & Decision Making

RESEARCH ARTICLE Open Access

Diagnosis and management of people with venous thromboembolism and advanced cancer: how do doctors decide? a qualitative study

Miriam J Johnson[1,2*], Laura Sheard[2], Anthony Maraveyas[2,3], Simon Noble[4], Hayley Prout[4], Ian Watt[1,2] and Dawn Dowding[5]

Abstract

Background: The treatment of cancer associated thrombosis (CAT) is well established, with level 1A evidence to support the recommendation of a low molecular weight heparin (LMWH) by daily injection for 3–6 months. However, registry data suggest compliance to clinical guidelines is poor. Clinicians face particular challenges in treating CAT in advanced cancer patients due to shorter life expectancy, increased bleeding risk and concerns that self injection may be too burdensome. For these reasons decision making around the diagnosis and management of CAT in people with advanced cancer, can be complex, and should focus on its likely net benefit for the patient. We explored factors that influence doctors' decision making in this situation and sought to gain an understanding of the barriers and facilitators to the application of best practice.

Methods: Think aloud exercises using standardised case scenarios, and individual in depth interviews were conducted. All were transcribed. The think aloud exercises were analysed using Protocol Analysis and the interviews using Framework Analysis.
Participants: 46 participants took part in the think aloud exercises and 45 participants were interviewed in depth. Each group included oncologists, palliative physicians and general practitioners and included both senior doctors and those in training.
Setting: Two Strategic Health Authority regions, one in the north of England and one in Wales.

Results: The following key issues arose from the data synthesis: the importance of patient prognosis; the concept of "appropriateness"; "benefits and burdens" of diagnosis and treatment; LMWH or warfarin for treatment and sources of information which changed practice. Although interlinked, they do describe distinct aspects of the factors that influence doctors in their decisions in this area.

Conclusions: The above factors are issues doctors take into account when deciding whether to send a patient to hospital for investigation or to anticoagulate a patient with confirmed or suspected VTE. Many factors interweave and are themselves influenced by and dependent on each other. It is only after all are taken into account that the doctor arrives at the point of referring the patient for investigation. Some factors including logistic and organisational issues appeared to influence whether a patient would be investigated or treated with LMWH for a confirmed VTE. It is important that services are optimised to ensure that these do not hinder the appropriate investigation and management of individual patients.

Keywords: Venous thromboembolism, Cancer, Palliative, Clinical decision making

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