FATTORI DI RISCHIO E SCREENING DEL PAZIENTE

ELOISE BEGGIATO

SCDU Ematologia e Terapie Cellulari -AO Mauriziano Umberto I

Clinical Questions

- Should hospitalized patients with cancer receive anticoagulation for VTE prophylaxis?
- Should ambulatory patients with cancer receive anticoagulation for VTE prophylaxis during systemic chemotherapy?
- Should patients with cancer undergoing surgery receive perioperative VTE prophylaxis?
- What is the best method for treatment of patients with cancer with established VTE to prevent recurrence?
- Should patients with cancer receive anticoagulants in the absence of established VTE to improve survival?
- What is known about risk prediction and awareness of VTE among patients with cancer?

“Costellazioni” di linee-guida

SISET

AIOM Linee Guida

The Oncologist
Symptom Management and Supportive Care

The NCCN Clinical Practice Guidelines on Venous Thromboembolic Disease: Strategies for Improving VTE Prophylaxis in Hospitalized Cancer Patients

VOLUME 25 · NUMBER 34 · DECEMBER 1 2007

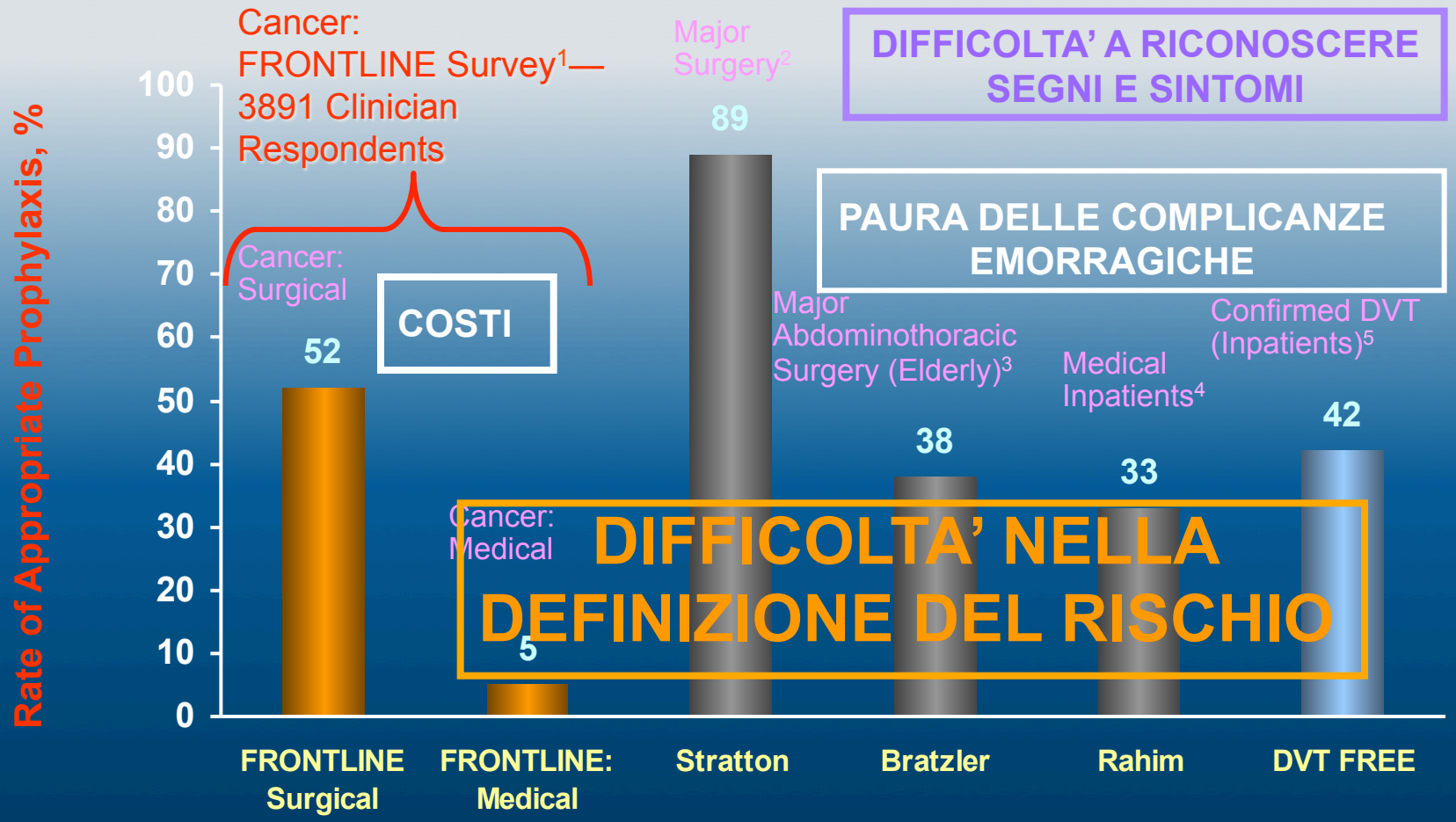
JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

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

Gary H. Lyman, Alok A. Khorana, Anna Falanga, Daniel Clerici-Pearson, Christopher Flowers, Mohammad Jahanzeb, Ajay Gakkar, Nicole M. Kuderer, Mark R. Levine, Howard Lichman, David Mendelson, Gary Raskob, Mark B. Somerfield, Paul Thadhyl, David Penn, and Charles W. Francis

VTE Prophylaxis Is Underused in Patients With Cancer

POCA ATTENZIONE AL PROBLEMA



1. Kakkar AK et al. *Oncologist*. 2003;8:381-388
2. Stratton MA et al. *Arch Intern Med*. 2000;160:334-340
3. Bratzler DW et al. *Arch Intern Med*. 1998;158:1909-1912
4. Rahim SA et al. *Thromb Res*. 2003;111:215-219
5. Goldhaber SZ et al. *Am J Cardiol*. 2004;93:259-262

Il rischio tromboembolico nel paziente oncologico

La trombosi è la seconda causa di morte nei pazienti oncologici

L'incidenza annuale combinata di trombosi venosa profonda ed embolia polmonare è stimata essere:

1: 200 pazienti con neoplasia

Il cancro da solo incrementa il rischio di TEV di circa 4 volte

La chemioterapia incrementa il rischio di TEV di circa 6.5 volte

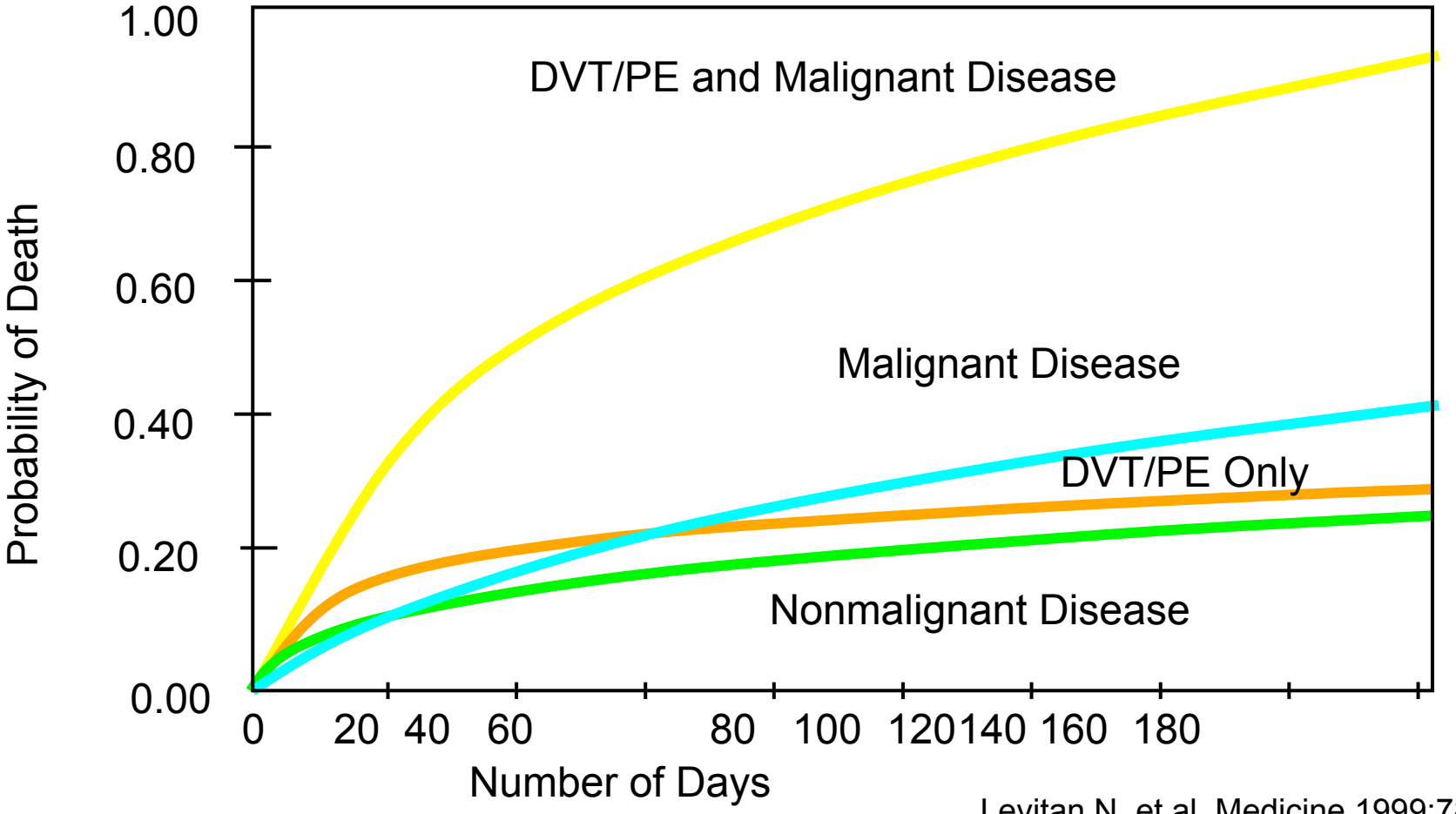
Nei pazienti che sviluppano una complicanza tromboembolica si è osservata una riduzione di un terzo della sopravvivenza ad un anno rispetto ad un gruppo comparabile che non aveva sviluppato alcun evento tromboembolico (rispettivamente 12% di sopravvivenza rispetto al 36%; p<0.001)

Heit J, Arch Intern Med 2000

Sousou T and Khorana A.Hamostaseologie 2009; 29: 121-4

Thrombosis and Survival

Likelihood of Death After Hospitalization



Levitan N, et al. Medicine 1999;78:285

AUMENTO DEL RISCHIO NEGLI ULTIMI ANNI

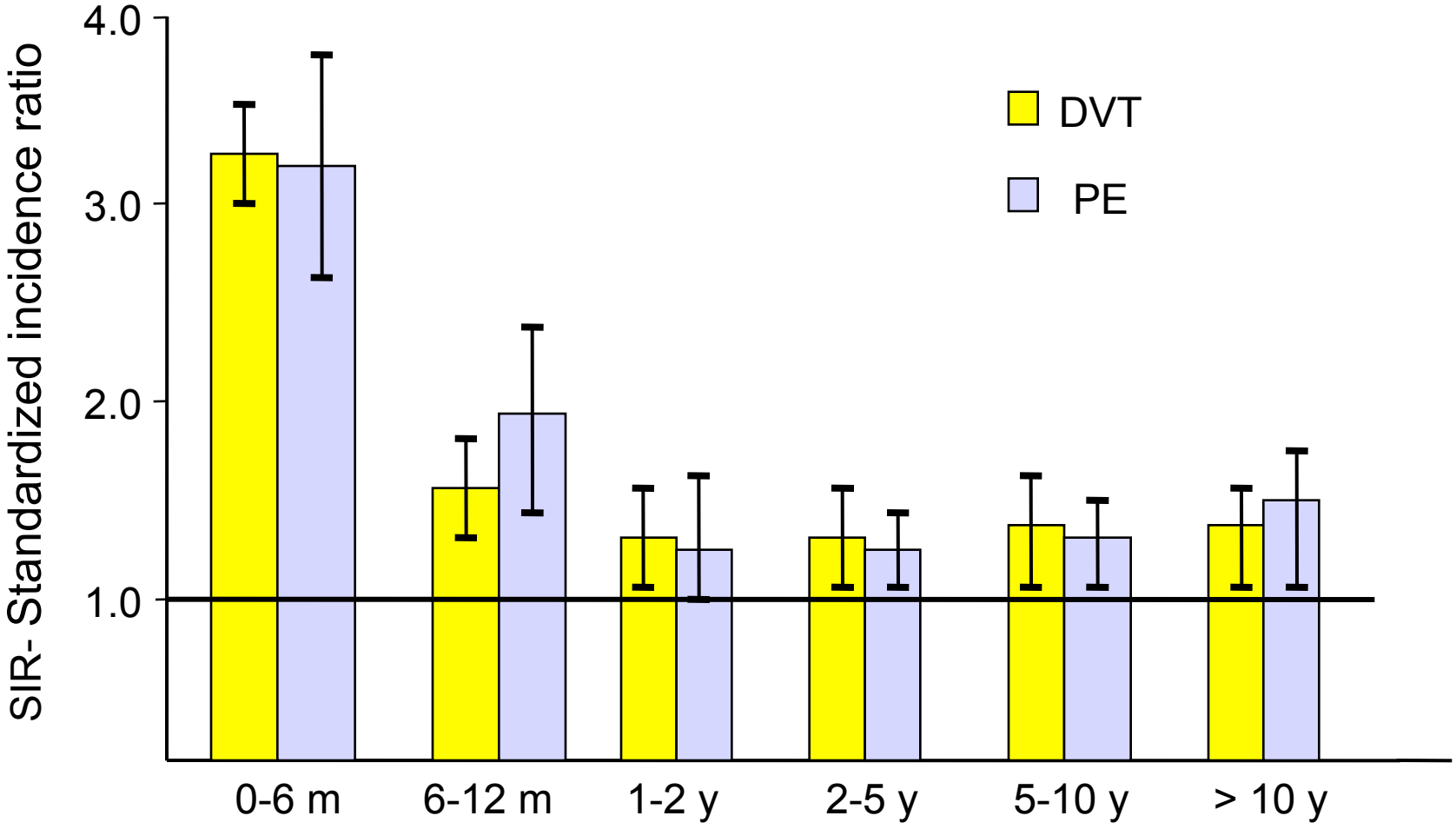
- **SISTEMI DIAGINOSTICI MIGLIORI**
- **NUOV FARMACI (antiangiogenetici..)**
- **SCHEMI DI TERAPIA AGGRESSIVI**
- **FATTORI DI CRESCITA**

TEV IDIOPATICO E TUMORE OCCULTO

- 10% pz con TEV idiopatico sviluppano un tumore entro 2 anni
- 20% pz hanno TEV recidivanti
- 25% pz anno TVP bilaterale

Bura *et. al., J Thromb Haemost* 2004;2:445-51

Risk of Cancer in Relation to Length of Time



Adapted from Sorensen et al., *NEJM* 1998;338:1169-73.

CERCARE IL TUMORE DOPO TEV IDIOPATICO

CERCARE TEV DOPO DIAGNOSI DI TUMORE

VOLUME 29 · NUMBER 17 · JUNE 10 2011

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Risk of Recurrent Venous Thromboembolism and Mortality in Patients With Cancer Incidentally Diagnosed With Pulmonary Embolism: A Comparison With Symptomatic Patients

Paul L. den Exter, Jose Hooijer, Olaf M. Dekkers, and Menno V. Huisman

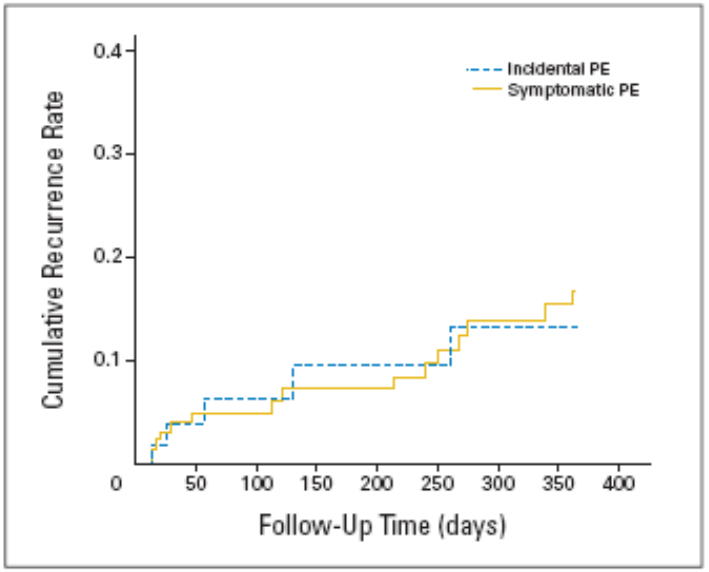


Fig 1. Cumulative risk of recurrent venous thromboembolism for patients with cancer with incidental versus symptomatic pulmonary embolism (PE; $P = .77$).

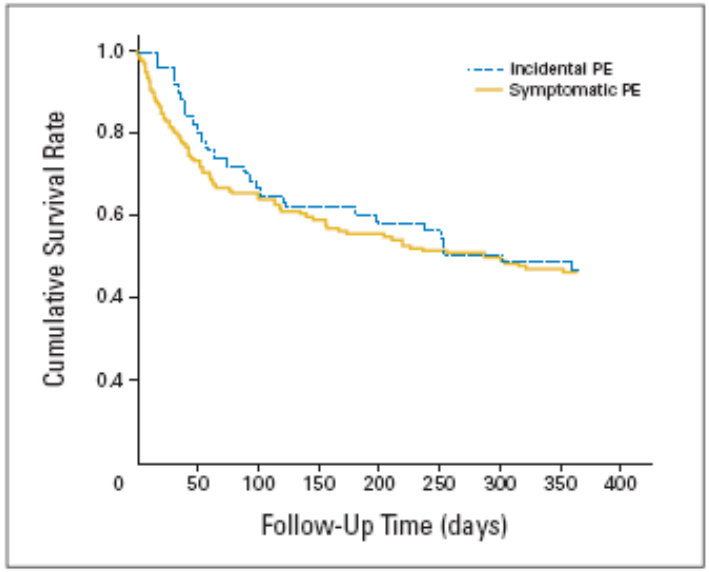


Fig 2. Kaplan-Meier cumulative survival curve until overall death for patients with cancer with incidental versus symptomatic pulmonary embolism (PE; $P = .70$).

JOURNAL OF CLINICAL ONCOLOGY ASCO SPECIAL ARTICLE

Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update 2014

Gary H. Lyman, Kari Bohlke, 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, Mark R. Somerfield, and Anna Falanga

THE BOTTOM LINE

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

Interventions

- Pharmacologic anticoagulation

Target Audience

- Medical oncologists, surgical oncologists, hospitalists, oncology nurses

Key Recommendations

- Most hospitalized patients with active cancer require thromboprophylaxis throughout hospitalization. Data are inadequate to support routine thromboprophylaxis in patients admitted for minor procedures or short chemotherapy infusion.
- Routine thromboprophylaxis is not recommended for ambulatory patients with cancer. It may be considered for highly select 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 to prevent venous thromboembolism (VTE).
- Patients undergoing major cancer surgery should receive prophylaxis starting before surgery and continuing for at least 7 to 10 days.
- Extending postoperative prophylaxis up to 4 weeks should be considered in those undergoing major abdominal or pelvic surgery with high-risk features.
- LMWH is recommended for the initial 5 to 10 days of treatment of established deep vein thrombosis and pulmonary embolism as well as for long-term secondary prophylaxis for at least 6 months.
- Use of novel oral anticoagulants is not currently recommended for patients with malignancy and VTE.
- Anticoagulation should not be used to extend survival of patients with cancer in the absence of other indications.
- Patients with cancer should be periodically assessed for VTE risk.
- Oncology professionals should educate patients about the signs and symptoms of VTE.

Methods

- An update committee was convened to determine whether previous recommendations remain valid based on an updated review of evidence from the medical literature.

Additional Information

- This guideline is published in *Journal of Clinical Oncology*. Data Supplements, including evidence tables, and clinical tools and resources can be found at www.asco.org/guidelines/vte.

- **PATIENTS WITH CANCER SHOULD BE PERIODICALLY ASSESSED FOR VTE RISK**
- **ONCOLOGY PROFESSIONAL SHOULD EDUCATE PATIENTS ABOUT SIGNS AND SYMPTOMS OF VTE**

FATTORI DI RISCHIO PER TEV

Table 2. Risk Factors for Cancer-Associated Thrombosis[24,30]

Patient-Specific Factors
Older age
Ethnicity (higher in African Americans; lower in Asian-Pacific Islanders)
Comorbid conditions (neutropenia, infection, obesity, renal disease, pulmonary disease)
Female sex
Immobilization
Heritable prothrombotic mutations (Factor V Leiden, prothrombin gene mutation)
Prior history of thromboembolism
Cancer-Specific Factors
Primary tumor site (pancreatic, ovarian, kidney, lung, gastric, brain, and hematologic)
Histologic subtype (adenocarcinoma > squamous cell carcinoma)
Locally advanced tumors/presence of distant metastases
Time from diagnosis
Treatment-Specific Risk Factors
Recent major surgery
Current hospitalization
Central venous catheters
Chemotherapy
Antiangiogenic therapy (thalidomide, lenalidomide, bevacizumab [?])
Hormonal therapy (tamoxifen)
Erythropoiesis-stimulating agents
Transfusions

BIOMARKERS

Paziente

Tumore

Terapia

Association Between Cancer Types, Cancer Treatments, and Venous Thromboembolism in Medical Oncology Patients

Michael B. Streiff, MD, FACP

FATTORI DI RISCHIO PER TEV

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FATTORI DI RISCHIO DEL TUMORE

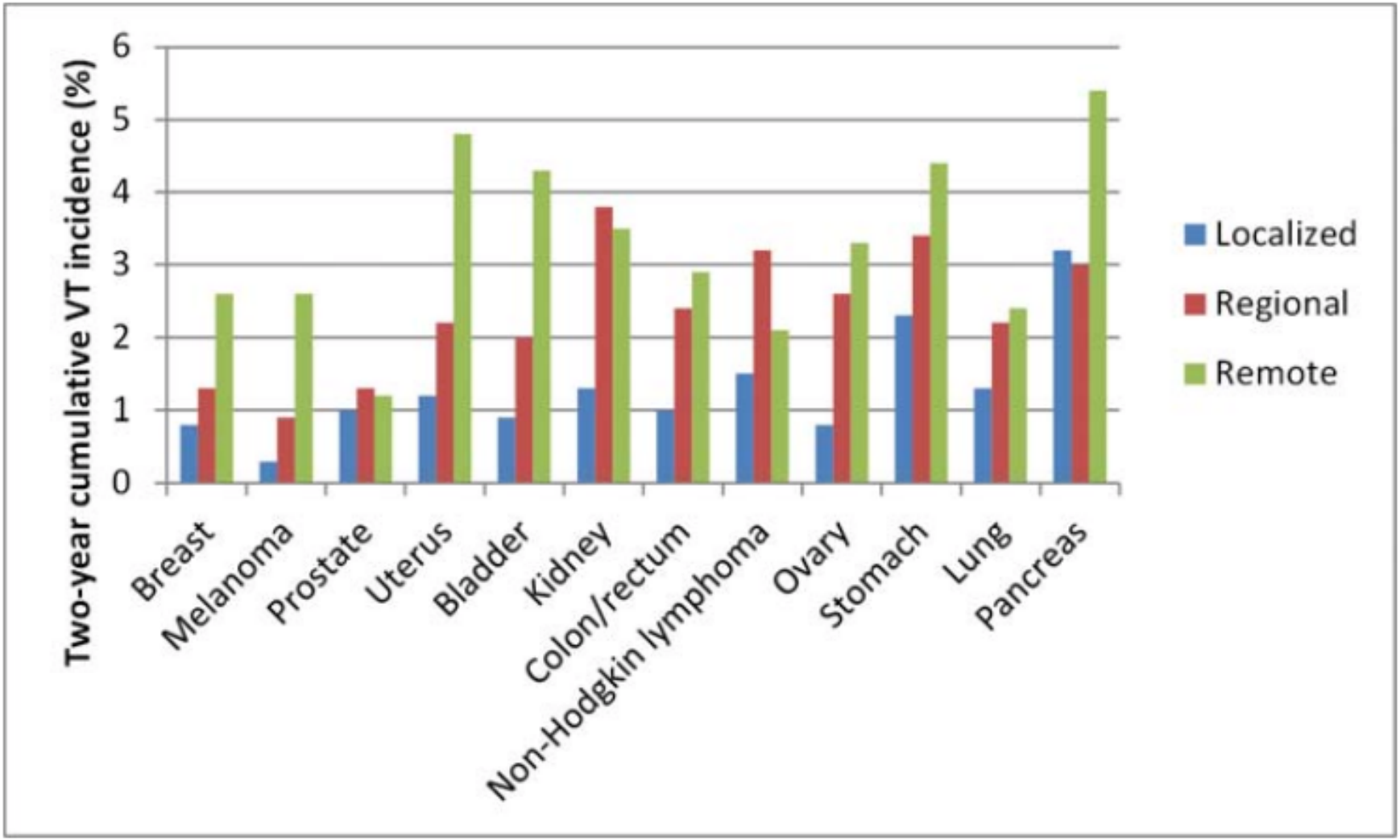
TABLE I. Selected Clinical Risk Factors and Biomarkers for Cancer-Associated Thrombosis

Cancer-associated risk factors
Primary site
Stage
Cancer histology (higher for adenocarcinoma than squamous cell)
Time after initial diagnosis (highest in first 3–6 months)

Ci sono tumori a maggior rischio?

Modified by Khorana et al, AJH 2012

CANCER RISK FACTOR
% VTE/2anni per tipo di tumore e stadio

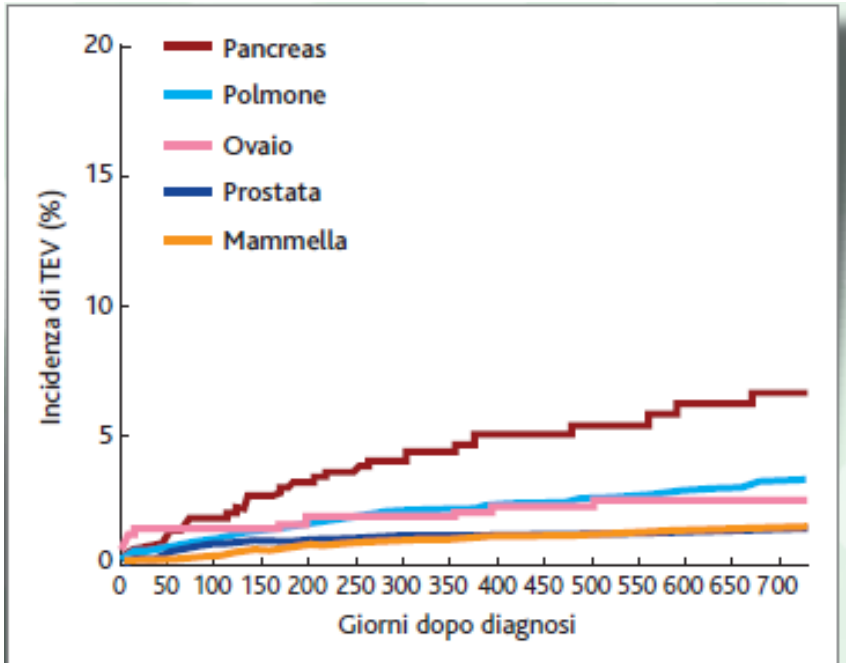


Tipo e stadio di malattia come fattori di rischio

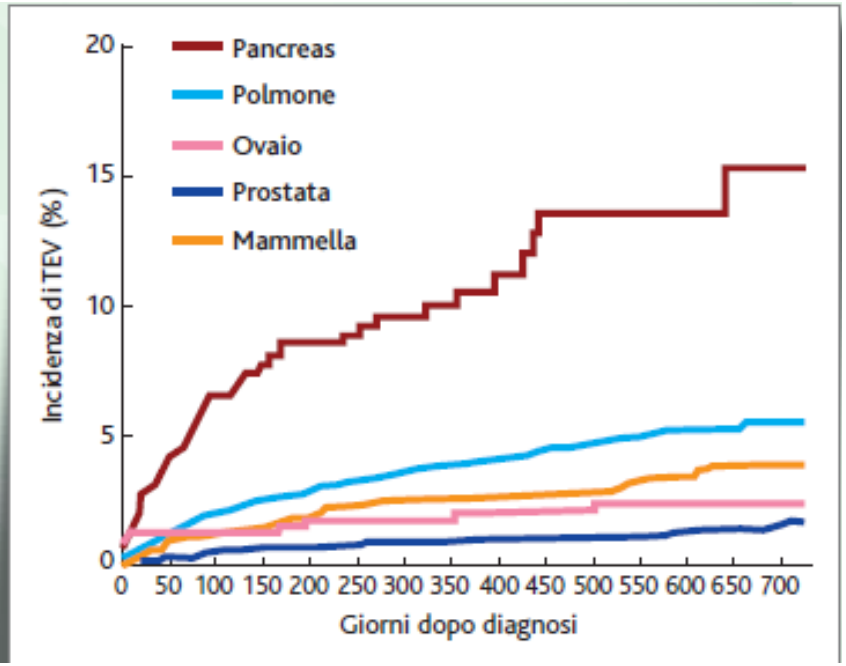
Timp et al, Blood 2013

Profilassi del TEV in oncologia

Incidenza TEV entro 2 anni dalla diagnosi di cancro localmente avanzato



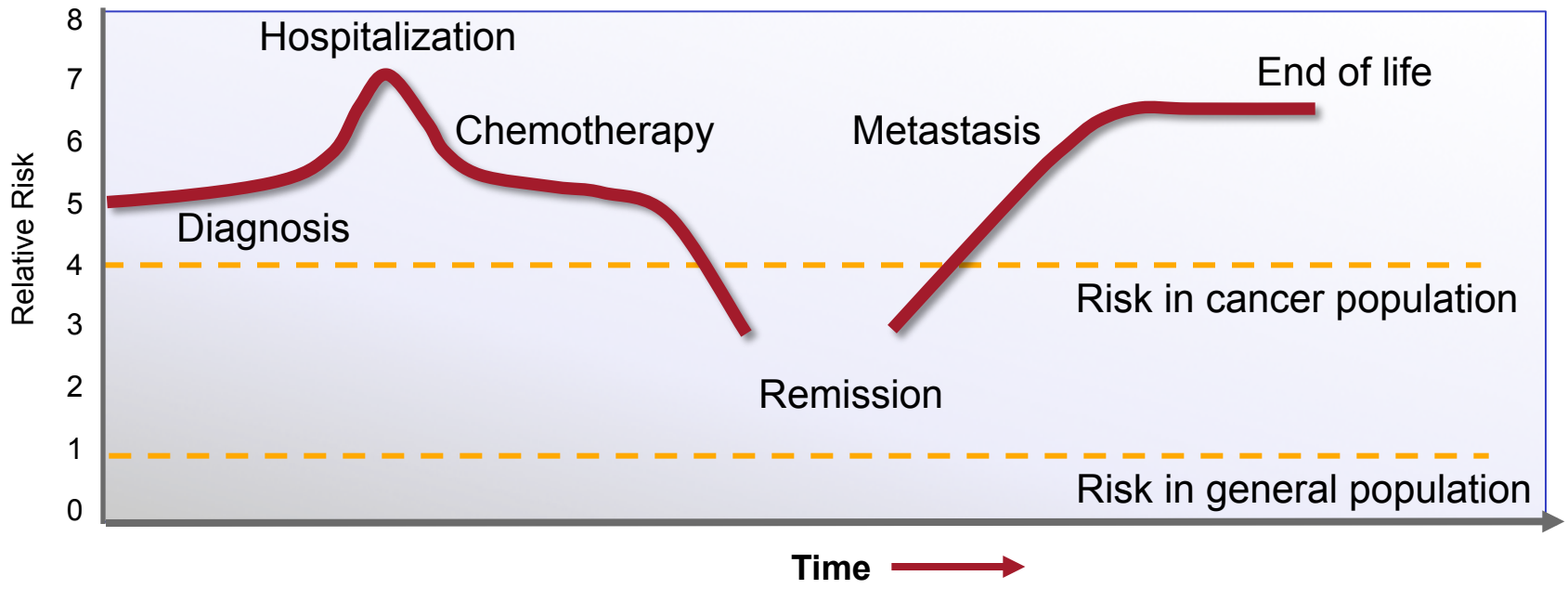
Incidenza TEV entro 2 anni dalla diagnosi di tumore metastatico



I primi mesi dopo la diagnosi (3-6 mesi) rappresentano il periodo a maggior rischio tromboembolico.

Chew HK, et al.Arch Intern Med 2006; 166: 458-64

TVE risk and cancer natural history



Rao MV, et al. In: Khorana and Francis, eds. Cancer-Associated Thrombosis; 2007

FATTORI DI RISCHIO PER TEV

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BIOMARKERS

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Association Between Cancer Types, Cancer Treatments, and Venous Thromboembolism in Medical Oncology Patients

Michael B. Streiff, MD, FACP

RISCHIO LEGATATO ALLA TERAPIA

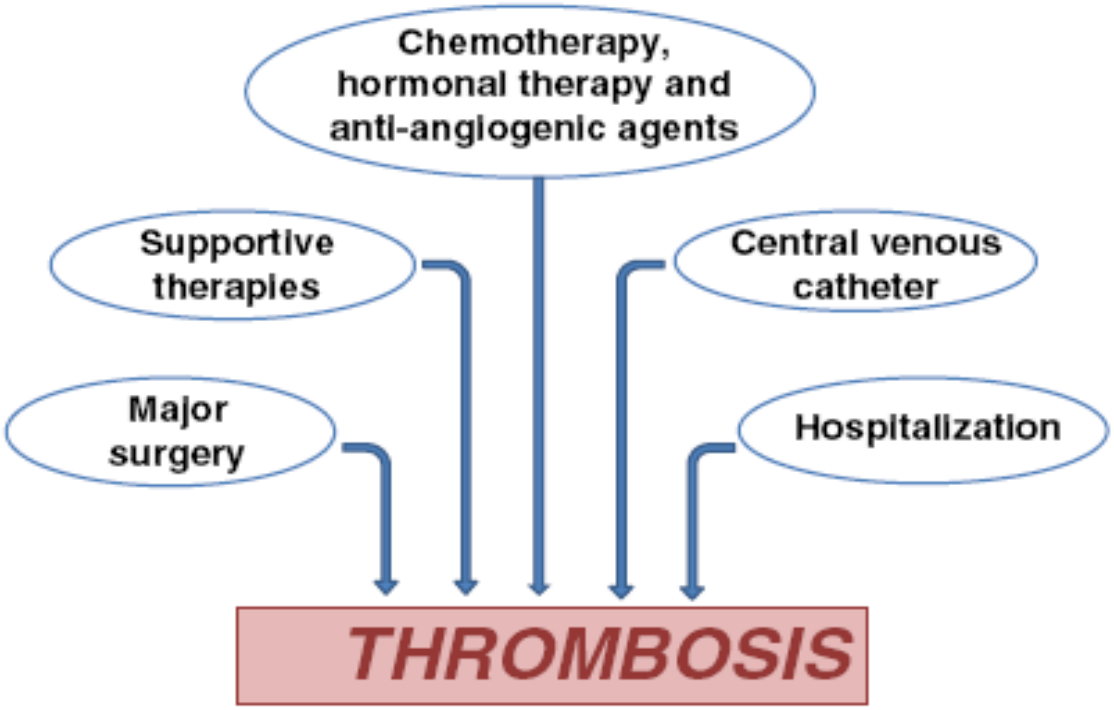
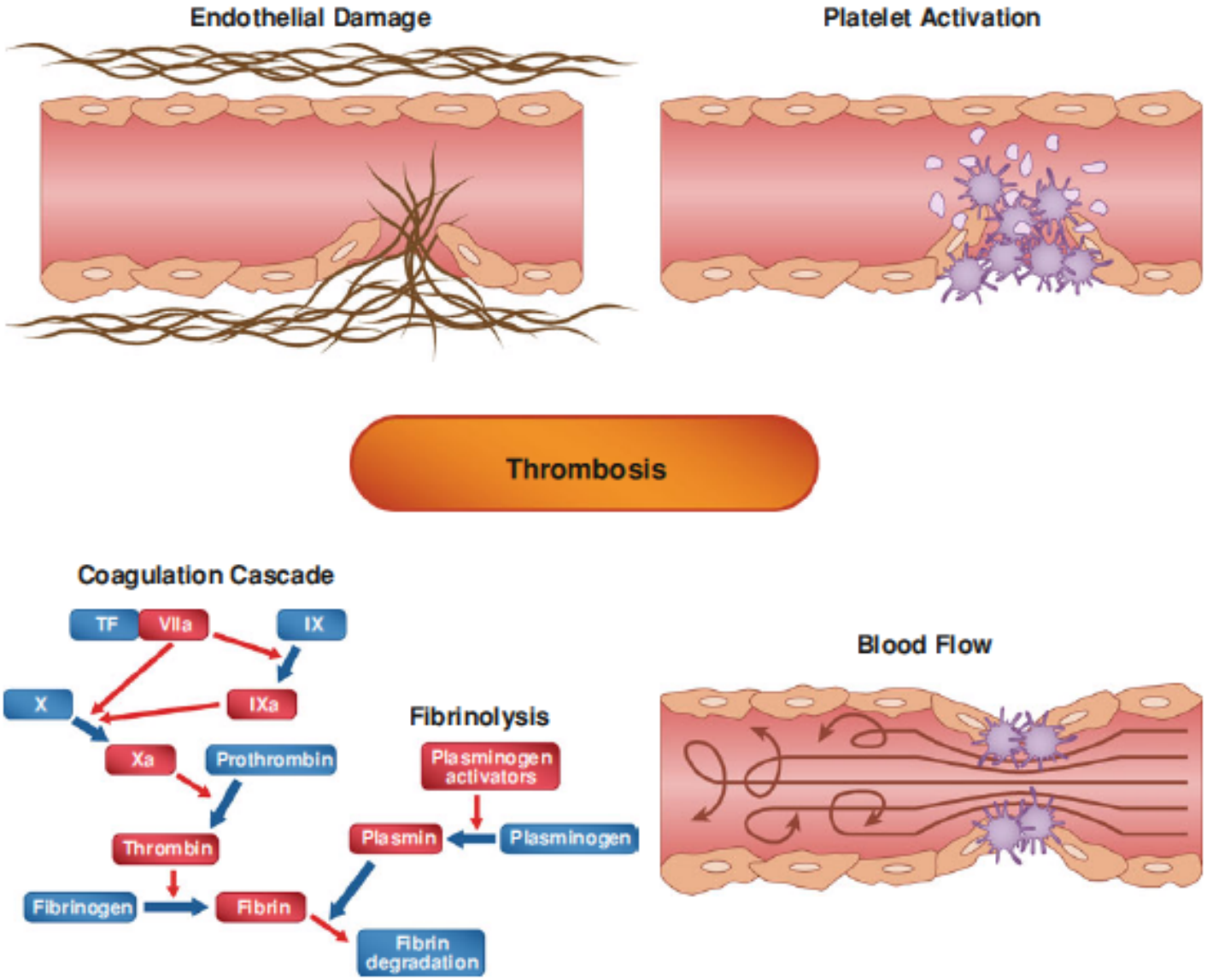


Fig. 1. Schematics of the principal anti-tumor strategies contributing to the thrombotic risk in cancer. Most of the therapeutic interventions for the cure of cancer can increase the VTE risk associated with this disease. These include major surgery, hospitalization, pharmacological anti-tumor therapies, CVC and supportive therapy (i.e. use of erythropoiesis stimulating agents).

CHEMOTHERAPY AS RISK FACTOR FOR VTE



The major components involved in the pathogenesis of thrombosis, and which can be affected by drugs. *TF* tissue factor

Ramot et al, Drug Saf 2013

La chemioterapia è un fattore di rischio indipendente per TEV

- Incidenza annua di TEV in pazienti sottoposti a chemioterapia 10,9%.

Otten H-MMB, et al. Arch Intern Med 2004; 164: 190-4

CHEMIOTERAPIA COME FATTORE DI RISCHIO TE

Type of chemotherapy	Patients	Incidental VTE	Symptomatic VTE	Overall VTE
Anthracyclines	572 (29.8)	7 (1.2)	9 (1.6)	16 (2.8)
Platin-based				
Cis- Carbo-platin	440 (23.0)	31 (7.3)	9 (2.1)	40 (9.4)
Oxaliplatin	304 (15.8)	19 (6.3)	6 (2.0)	25 (8.2)
Taxan-based	370 (19.3)	4 (1.1)	7 (1.9)	11 (3.0)
CMF	279 (14.7)	2 (0.7)	1 (0.4)	3 (1.1)
Gemcitabine	271 (14.1)	10 (3.8)	10 (3.8)	20 (7.5)
FUFA	187 (9.7)	5 (2.7)	4 (2.1)	9 (4.8)
Biologic therapy	182 (9.5)	10 (5.5)	4 (2.2)	14 (7.7)
Flour-based	129 (6.8)	3 (2.5)	4 (3.4)	7 (5.9)
Irinotecan-based	106 (5.5)	4 (3.8)	4 (3.8)	8 (7.5)
Vinorelbine	44 (2.3)	1 (2.3)	1 (2.3)	2 (4.5)
PEB	39 (2)	3 (7.7)	0	3 (7.7)
Cyclophosphamide	22 (1.1)	2 (9.0)	2 (9.0)	4 (18.8)
Topotecan	19 (1.0)	1 (5.3)	0	1 (5.3)
Ifosfamide-based	17 (0.9)	0	0	0

Di Nisio, Thromb and Haem 2010

VOLUME 29 · NUMBER 25 · SEPTEMBER 1 2011

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

High Incidence of Thromboembolic Events in Patients Treated With Cisplatin-Based Chemotherapy: A Large Retrospective Analysis

Russell A. Moore, Nelly Adel, Elyn Riedel, Manisha Bhutani, Darren R. Feldman, Nour Elise Tabbara, Gerald Soff, Rekha Parameswaran, and Hani Hassoun

Platino come agente pro-trombotico

Moore et al. JCO 2011

Table 2. Overall Incidence of Thromboembolic Events (N = 932)

Thromboembolic Event	No. of Patients	%
Thrombosis	169	18.1
Types of thromboses (n = 169)		
DVT alone	84	49.7
PE alone	43	25.4
DVT + PE	23	13.6
Arterial thrombosis alone	14	8.3
DVT + arterial thrombosis	5	3.0
Subtypes of DVTs (n = 112)		
Proximal lower extremity	22	19.6
Proximal lower and distal lower extremity	18	16.1
Proximal lower extremity and central*	5	4.4
Proximal lower extremity and central* and distal lower extremity	1	0.9
Proximal upper extremity	2	1.8
Proximal upper and distal upper extremity	3	2.7
Proximal upper and internal jugular vein and distal upper extremity	4	3.6
Internal jugular vein	5	4.4
Internal jugular vein and distal upper extremity	1	0.9
Central*	27	24.1
Distal lower extremity	20	17.9
Distal lower and distal upper extremity	1	0.9
Distal upper extremity	3	2.7
Subtypes of arterial events (n = 19)		
Central†	6	31.6
Myocardial infarction	2	10.5
Cerebrovascular accident	10	52.6
Transient ischemic attack	1	5.3
Symptomatic or incidental event (n = 169)		
Symptomatic	95	56.2
Incidental	74	43.8

Abbreviations: DVT, deep venous thrombosis; PE, pulmonary embolus.
*Central venous thromboses sites include brachiocephalic vein (n = 1), gonadal vein (n = 7), hepatic vein (n = 1), inferior vena cava (n = 5), pelvic vein (n = 4), portal vein (n = 6), renal vein (n = 4), splenic vein (n = 3), superior mesenteric vein (n = 6), and superior vena cava (n = 3).
†Central arterial thromboses sites include aortic arch (n = 1), infrarenal aorta (n = 3), internal carotid (n = 1), splenic artery (n = 1), and superior mesenteric artery (n = 1).

Eventi e Tipo di paziente

Khorana risk group		
Low	224	24.0
Intermediate	538	57.7
High	170	18.2
Cancer diagnosis		
Lung	204	21.9
Gastric/GE junction	114	12.2
Head and neck	94	10.1
Pancreatic	79	8.5
Melanoma	69	7.4
Ovarian	57	6.1
Esophageal	46	4.9
Germ cell	39	4.2
Cervical/uterine/vulvar	39	4.2
Bladder	33	3.5
Endometrial	22	2.4
Cholangiocarcinoma	18	1.9
Mesothelioma	15	1.6
Colorectal/anal/small bowel	13	1.4
Other	90	9.7

Moore et al. JCO 2011

VTE Risk with Bevacizumab in Colorectal Cancer Approaches Risk of Antiangiogenesis in Myeloma

Table 2. Incidence and Relative Risk (RR) of All-Grade Venous Thromboembolism With Bevacizumab Among Patients With Various Tumor Types

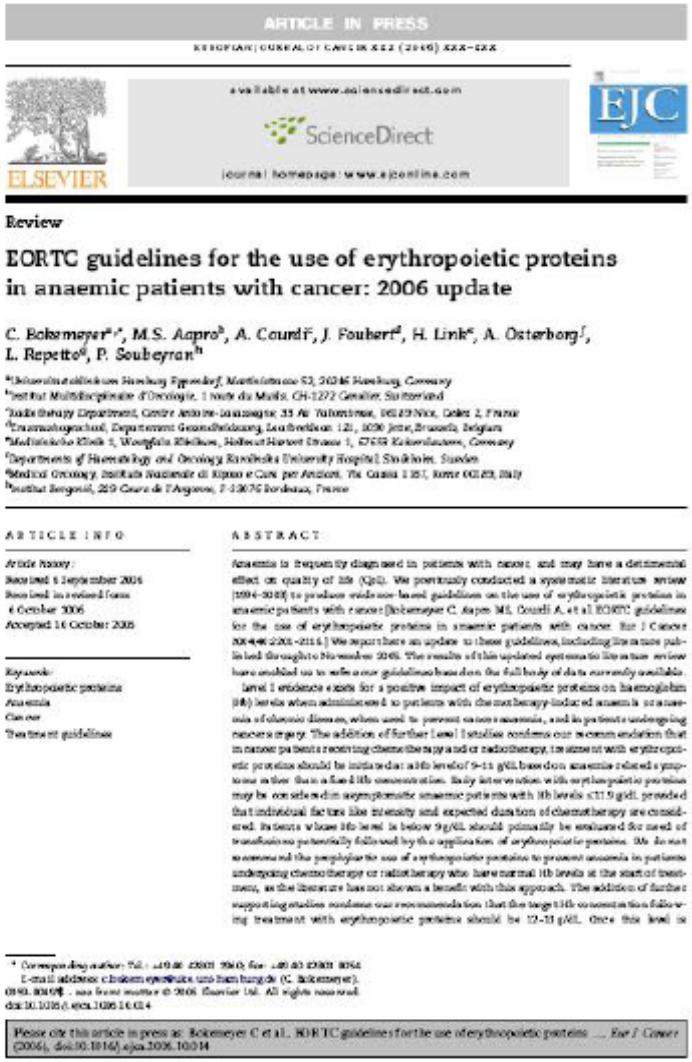
Tumor Type	No. of Studies	All-Grade Venous Thromboembolism, No./Total No.		Incidence (95% CI), %	RR (95% CI)
		Bevacizumab	Control		
Overall[a]	6	155/1196	107/1083	11.9 (6.8-19.9)	1.29 (1.03-1.63)
Colorectal cancer[a]	3	108/564	85/532	19.1 (16.1-22.6)	1.19 (0.92-1.55)
NSCLC[9,b]	1	10/66	3/32	14.9 (8.2-25.5)	1.59 (0.47-5.37)
Breast cancer[12,b]	1	17/229	12/215	7.3 (4.6-11.5)	1.30 (0.64-2.67)
Renal cell carcinoma[13,b]	1	20/337	6/304	3.0 (1.6-5.5)	3.00 (1.23-7.33)

Abbreviations: CI, confidence interval; NSCLC, non–small cell lung carcinoma.

[a]The incidence and RR were calculated from the trials included in this study by meta-analysis as described in the "Methods" section.

[b]The incidence and RR were derived from the study as listed.

Naluri SR et al. JAMA. 2008;300:2277



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Review

EORTC guidelines for the use of erythropoietic proteins in anaemic patients with cancer: 2006 update

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[g] Medical Oncology, Istituto Nazionale di Riposo e Cura per Anziani, Via Cassia 1151, Rome 00189, Italy
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ABSTRACT

Anaemia is frequently diagnosed in patients with cancer and may have a detrimental effect on quality of life (QoL). We previously conducted a systematic literature review (1994–2003) to produce evidence-based guidelines on the use of erythropoietic proteins in anaemic patients with cancer [Bokemeyer C, Aapro MS, Courdi A, et al. EORTC guidelines for the use of erythropoietic proteins in anaemic patients with cancer. Eur J Cancer 2004;40:2201–2216.] We report here an update to these guidelines, including literature published throughout November 2005. The results of this updated systematic literature review have enabled us to refine our guidelines based on the full body of data currently available.

Level 1 evidence exists for a positive impact of erythropoietic proteins on haemoglobin (Hb) levels when administered to patients with chemotherapy-induced anaemia or anaemia of chronic disease, when used to prevent severe anaemia, and in patients undergoing cancer surgery. The addition of further Level 1 studies confirms our recommendation that in cancer patients receiving chemotherapy and/or radiotherapy, treatment with erythropoietic proteins should be initiated at a Hb level of 9–11 g/dl, based on anaemia-related symptoms rather than a fixed Hb concentration. Early intervention with erythropoietic proteins may be considered in asymptomatic anaemic patients with Hb levels ≤11 g/dl, provided that individual factors like intensity and expected duration of chemotherapy are considered. Patients whose Hb level is below 9 g/dl, should primarily be evaluated for need of transfusion potentially followed by the application of erythropoietic proteins. We do not recommend the prophylactic use of erythropoietic proteins to prevent anaemia in patients undergoing chemotherapy or radiotherapy who have normal Hb levels at the start of treatment, as the literature has not shown a benefit with this approach. The addition of further supporting studies confirms our recommendation that the target Hb concentration following treatment with erythropoietic proteins should be 12–13 g/dl. Once this level is

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doi:10.1016/j.ejca.2006.10.014

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eritropoietine

- Hb < 9 g/dl:
  - valutare la necessità di trasfusioni, in aggiunta alla terapia con EPO (*C*)
- TEV RR 1.6 (*A*)

Bokemeyer C. et al. **EORTC** guidelines for the use of erythropoietic proteins in anaemic patients with cancer: 2006 update. Eur J Cancer 2007: 43; 258-70

Thrombosis Research (2006) 118, 555–568

ELSEVIER

THROMBOSIS RESEARCH

intl.elsevierhealth.com/journals/thre

REVIEW ARTICLE

Chemotherapy-induced thrombosis

Tufia C. Haddad*, Edward W. Greeno

Department of Hematology, Oncology and Transplantation, University of Minnesota Cancer Center, MMC 480, 420 Delaware Street S.E., Minneapolis, MN 55455, United States

Non esistono studi che abbiano valutato l'eventuale effetto trombogeno della radioterapia

NON CONCLUSIVI I DATI SULL'UTILIZZO DI G-CSF

CATETERE VENOSO CENTRALE

INCIDENZA DI TROMBOSI CVC RELATA VARIA TRA 0,3-28%

Risk factors of CVC-related thrombosis

Common VTE risk factors	CVC-related factors
• Age	• Material (e.g., PVC)
• Malignancy	• Multiple attempts of puncture
• Hypercoagulability	• Number of catheter lumens
• Chemotherapy	• Catheter length
• Infection	• Localisation of catheter tip
• Previous VTE	• Previous catheterisation
	• Time interval after insertion

PVC = polyvinylchloride

Linnemann B, 2012

VOLUME 31 · NUMBER 10 · APRIL 1 2013

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Central Venous Catheter Care for the Patient With Cancer: American Society of Clinical Oncology Clinical Practice Guideline

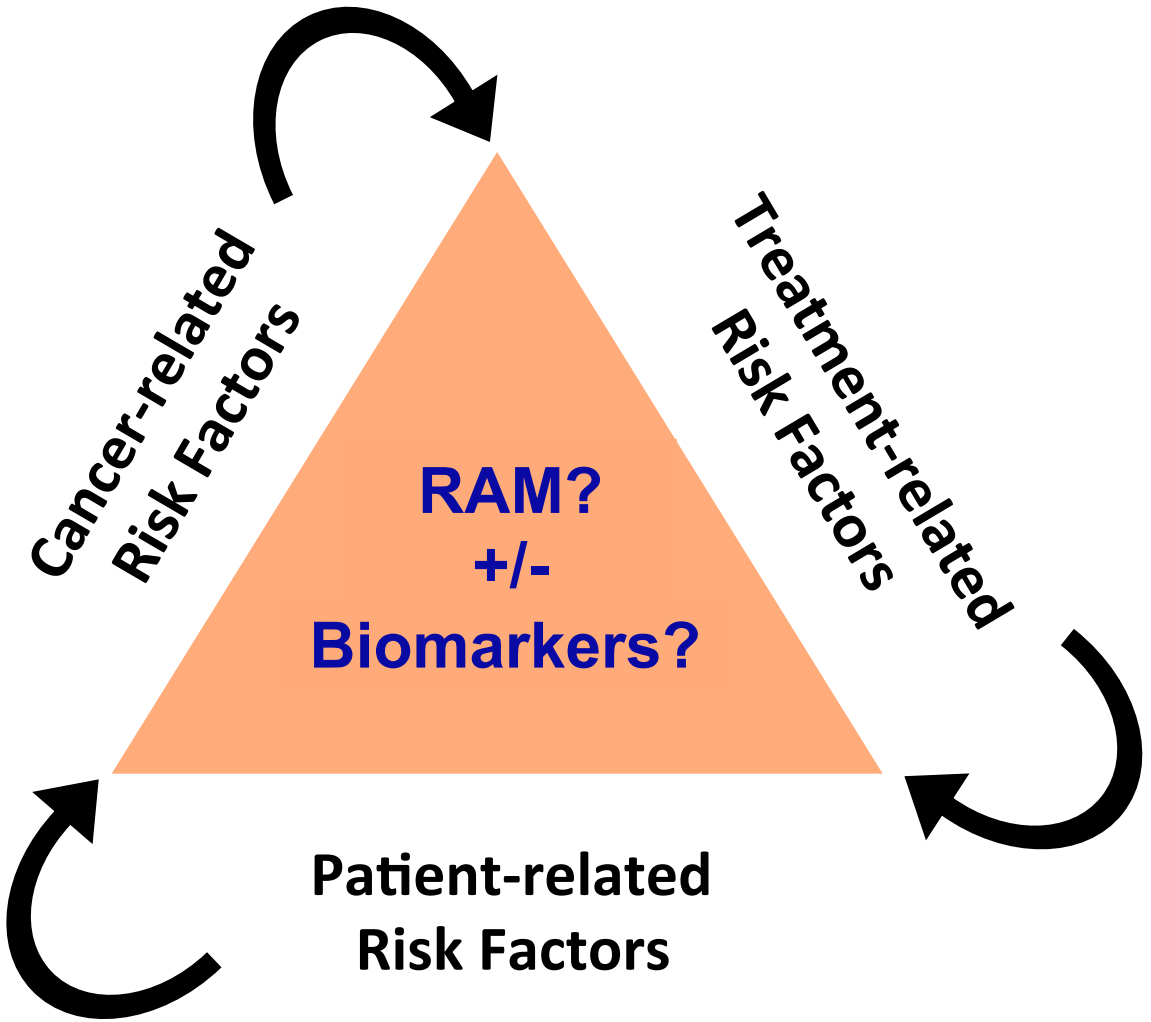
Charles A. Schiffer, Pamela B. Mangu, James C. Wade, Dawn Camp-Sorrell, Diane G. Cope, Bassel F. El-Rayes, Mark Gorman, Jennifer Ligibel, Paul Mansfield, and Mark Levine

Key Recommendations

- There is insufficient evidence to recommend a specific type of CVC or insertion site, but femoral vein insertion should be avoided, except in certain emergency situations
- CVCs should be placed by well-trained health care providers
- Use of a CVC clinical care bundle is recommended
- Use of antimicrobial/antiseptic-coated CVCs and/or heparin-impregnated CVCs has been shown to be beneficial, but the benefits and costs must be carefully considered before they can be routinely used
- Prophylactic use of systemic antibiotics is not recommended before CVC insertion
- Cultures of blood from the CVC and/or tissue at the entrance-exit sites should be obtained before initiation of antibiotic therapy; most clinically apparent exit- or entrance-site infections as well as bloodstream infections can be managed with appropriate microbial therapy, so CVC removal may not be necessary; antimicrobial agents should be optimized once the pathogens are identified; catheter removal should be considered if the infection is caused by an apparent tunnel or port-site infection, fungi, or nontuberculous mycobacteria or if there is persistent bacteremia after 48 to 72 hours of appropriate antimicrobial treatment
- Routine flushing with saline is recommended
- Prophylactic warfarin and low–molecular weight heparin have not been shown to decrease CVC-related thrombosis, so routine use is not recommended
- Tissue plasminogen activator (t-PA) is recommended to restore patency in a nonfunctioning CVC; CVC removal is recommended when the catheter is no longer needed, if there is a radiologically confirmed thrombosis that does not respond to anticoagulation therapy, or if fibrinolytic or anticoagulation therapy is contraindicated

Schiffer CA et al., 2013

Risk Stratification



The use of weighted and scored risk assessment models for venous thromboembolism

Alex C. Spyropoulos[1]; Thomas McGinn[2]; Alok A. Khorana[1]

[1]James P. Wilmot Cancer Center and Department of Medicine, University of Rochester Medical Center, Rochester, New York, USA; [2]North Shore/LIJ Health System, Department of Medicine, New York, New York, USA

Summary

Formalised risk assessment models (RAMs) for venous thromboembolism (VTE) using weighted and scored variables have only recently been widely incorporated into international antithrombotic guidelines. Scored and weighted VTE RAMs have advantages over a simplified group-specific VTE risk approach, with the potential to allow more tailored strategies for thromboprophylaxis and an improved estimation of the risk/benefit profile for a particular patient. The derivation of VTE RAMs should be based on variables that are *a priori* defined or identified in a univariate analysis and the predictive capability of each variable should be rigorously assessed for both clinical and statistical significance and internal consistency and completeness. The assessment of the RAM should include the goodness of fit of the model and construction of a prognostic index score. Any VTE RAM which has been derived must undergo validation of that model before it can be used in clinical practice. Validation of the model should be performed in a "deliberate" prospective fashion across several diverse clinical sites using pre-defined criteria using basic standards for performing model validation. We discuss the basic concepts in the derivation of recent scored and weighted VTE RAMs in hospitalised surgical and medical patients and cancer outpatients, the mechanisms for accurate external validation of the models, and implications for their use in clinical practice.

Keywords

Venous thrombosis, risk factors, epidemiological studies

PAZIENTE A RISCHIO KHORANA SCORE & VIENNA SCORE

blood

2008 111: 4902-4907
Prepublished online Jan 23, 2008;
doi:10.1182/blood-2007-10-116327

Development and validation of a predictive model for chemotherapy-associated thrombosis

Alok A. Khorana, Nicole M. Kuderer, Eva Culakova, Gary H. Lyman and Charles W. Francis

blood

Prepublished online Sep 9, 2010;
doi:10.1182/blood-2010-02-270116

Prediction of venous thromboembolism in cancer patients

Cihan Ay, Daniela Dunkler, Christine Marosi, Alexandru-Laurentiu Chiriac, Rainer Vormittag, Ralph Simanek, Peter Quehenberger, Christoph Zielinski and Ingrid Pabinger

Valutazione del paziente oncologico
PRIMA di iniziare la chemioterapia

KHORANA AND VIENNA SCORES

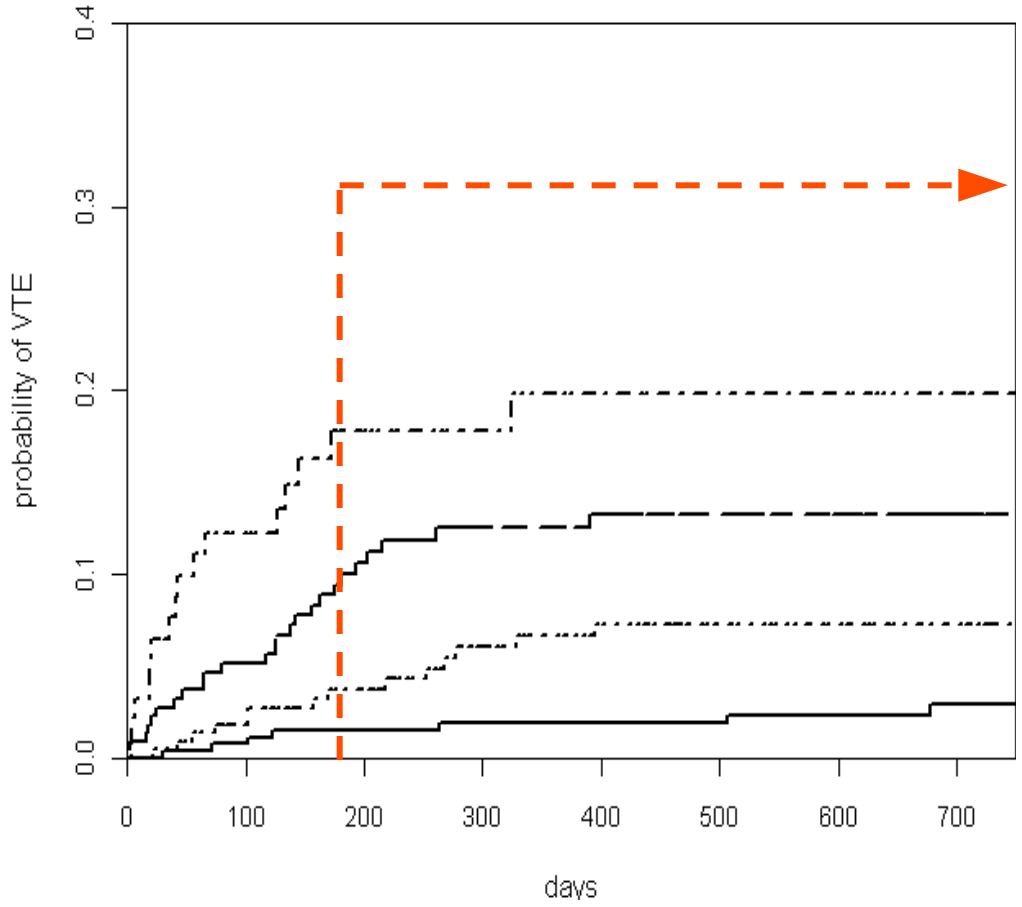
Khorana VTE Risk Assessment Score (5)			Points
Site of cancer:	very high risk:	stomach, pancreas	2
	high risk:	lung, lymphoma, gynaecologic, blader, testicular	1
Platelet count		≥ 350 x 10^9 /l	1
Hemoglobin and/or use of erythropoiesis-stimulating agents		< 10 g/dl	1
Leukocyte count		> 11 x 10^9 /l	1
Body mass index		≥ 35 kg/m^2	1
Vienna VTE Risk Assessment Score (84), addition of:			
D-Dimer		≥ 1.44 µg/ml	1
sP-selectin		≥ 53.1 mg/ml	1

Pabinger et al, Blood 2013

Khorana Model Validation

Prospective follow up of 819 patients

Median observation time/follow-up: 656 days



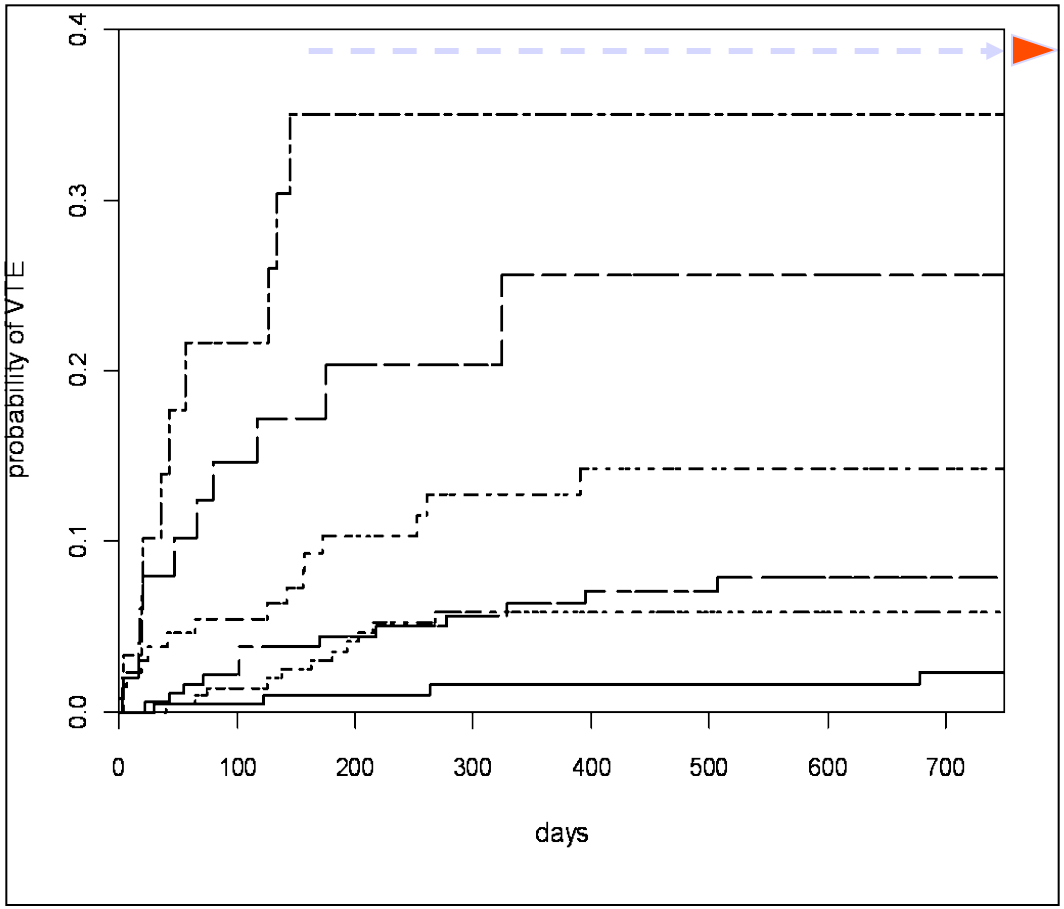
6-mo cumulative VTE rates:

	Patients n	Events %
Score ≥3	93	17.7%
Score 2	221	9.6%
Score 1	229	3.8%
Score 0	276	1.5%

Ay et al Blood 2010.

Ay Model for Outpatients

- Addition of D-dimer and soluble P-selectin to Khorana model:



6-mo cumulative VTE rates:

	Patients, n	Events,
Score>5	30	35%
Score 4	51	20.3%
Score 3	130	10.3%
Score 2	218	3.5%
Score 1	190	4.4%
Score 0	200	1.0%

Ay et al Blood 2010.

Nadroparin for the prevention of thromboembolic events in ambulatory patients with metastatic or locally advanced solid cancer receiving chemotherapy: a randomised, placebo-controlled, double-blind study

PROTECHT STUDY

Giancarlo Agnelli, Gualberto Gussoni, Carlo Bianchini, Melina Verso, Mario Mandalà, Luigi Cavanna, Sandro Barni, Roberto Labianca, Franco Buzzi, Giovanni Scambia, Rodolfo Passalacqua, Sergio Ricci, Giampietro Gasparini, Vito Lorusso, Erminio Bonizzoni, Maurizio Tonato, on behalf of the PROTECHT Investigators*

	Nadroparin (N=769)	Placebo (N=381)
Overall thromboembolic events	15 (2·0)	15 (3·9)
Deep-vein thrombosis	8 (1·0)	8 (2·1)
Pulmonary embolism	3 (0·4)	3 (0·8)
Visceral venous thrombosis	1 (0·1)	1 (0·3)
Stroke and peripheral thrombosis	3 (0·4)	3 (0·8)
Thromboembolic event by cancer site		
Lung	7/199 (3·5)	7/80 (8·8)
Gastrointestinal	4/272 (1·5)	4/148 (2·7)
Pancreas	3/36 (8·3)	1/17 (5·9)
Other	1/262 (0·4)	3/136 (2·2)

Data are n (%).

Table 3: Thromboembolic events by treatment group and cancer site

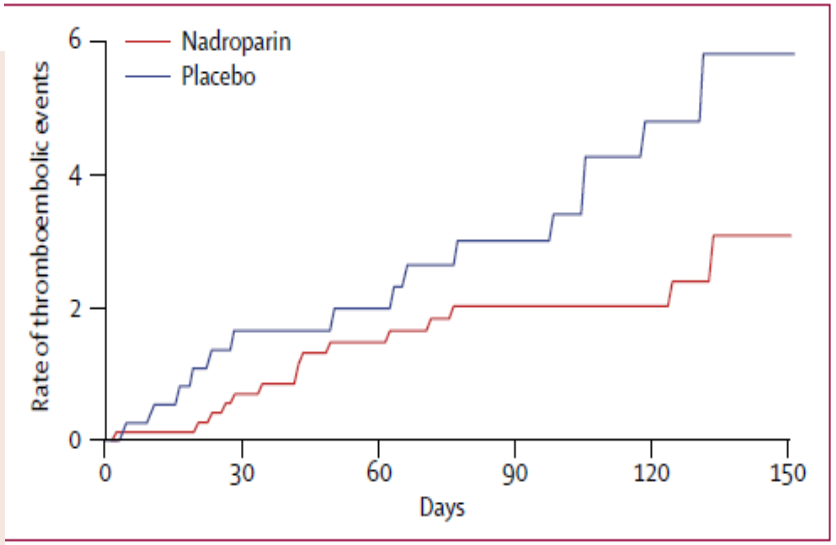


Figure 2: Cumulative hazard of thromboembolic events by treatment

Five of 769 patients in the nadroparin group (0·7%) and none in the placebo group had major bleeding (p=0·18, two-sided test).

Lancet Oncol. 2009 Oct;10(10):943-9

Nello studio PROTECHT, la nadroparina alla dose di 3.800 UI/die ha ridotto del 50% l'incidenza degli eventi tromboembolici arteriosi e venosi in pazienti con fase avanzata di malattia e sottoposti a differenti regimi di chemioterapia.

Table 4. Proportion of symptomatic TEs according to the type of chemotherapy regimen.

	% (n/N)		(95% CI)
Thromboembolic events	**Nadroparin**	**Placebo**	**Relative risk**
Overall PROTECHT population	2 (15/769)	3.9 (15/381)	0.5 (0.24-1.00)
Chemotherapy regimen containing:			
5-Fluorouracil	2.5 (7/285)	3.3 (5/151)	0.74 (0.24-2.30)
Cisplatin	2.3 (4/177)	7.0 (6/86)	0.32 (0.09-1.12)
Gemcitabine	2.6 (4/156)	8.1 (7/86)	0.32 (0.09-1.05)
Oxaliplatin	0.7 (1/143)	1.1 (1/89)	0.62 (0.04-9.83)
Docetaxel	1.4 (2/142)	4.5 (3/67)	0.31 (0.05-1.84)
Carboplatin	0.8 (1/119)	5.5 (3/55)	0.15 (0.02-1.45)
Epirubicin	0.0 (0/54)	8.3 (2/24)	ND
Adriamycin	0.0 (0/25)	5.3 (1/19)	ND
Irinotecan	3.1 (3/96)	0.0 (0/41)	ND
Vinca alkaloids	2.2 (2/90)	3.7 (1/27)	0.60 (0.06-6.36)
Capecitabine	0.0 (0/61)	3.3 (1/30)	ND
Etoposide	2.4 (1/41)	11.8 (2/17)	0.21 (0.02-2.14)
Cyclophosphamide	0.0 (0/33)	5.6 (1/18)	ND
Previous Chemotherapy			
Naïve	2.5 (10/405)	5.2 (11/213)	0.48 (0.21-1.11)
Non-naïve	1.4 (5/364)	2.4 (4/168)	0.58 (0.16-2.12)

No TE events were observed among patients receiving trastuzumab, cetuximab, bevacizumab, liposomal doxorubicin or mitomycin. Abbreviation: ND, not determinable.

Barni et al. Jour Trans Med 2011

KHORANA SCORE nei pazienti PROTECHT

KHORANA Risk Score	PROTECHT Risk Score
➢ Site of cancer ▪ Stomach, Pancreas **2p** ▪ Lung, gynaecologic, testicular **1p** ➢ Pre-chemotherapy platelet count 350 x 10^9L or more **1p** ➢ Hemoglobin level less than 100 g/L **1p** ➢ Pre-chemotherapy leukocyte count more than 11 x 10^9L **1p** ➢ BMI 35 Kg/sqm or more **1p** p:point	➢ Site of cancer ▪ Stomach, Pancreas **2p** ▪ Lung, gynaecologic, testicular **1p** ➢ Pre-chemotherapy platelet count 350 x 10^9L or more **1p** ➢ Hemoglobin level less than 100 g/L **1p** ➢ Pre-chemotherapy leukocyte count more than 11 x 10^9L **1p** ➢ BMI 35 Kg/sqm or more **1p** ➢ Chemotherapy regimen containing ▪ Cisplatin or carboplatin or gemcitabine **1p** ▪ Platinum compound plus gemcitabine **2p** p:point
No risk population (score 0): **36.8%** (139/378) Intermediate Risk Population (score 1-2): **52.1%** (197/378) High risk population (score ≥ 3): **11.1%** (42/378)	No risk population (score 0): **30.2%** (114/378) Intermediate Risk Population (score 1-2): **37%** (140/378) High risk population (score ≥ 3): **32.8%** (124/378)
33.3% (5/15) of the TEs was in the high risk population	**66.7% (10/15) of the TEs was in the high risk population**

Barni et al. MASCC 2011

Development of a Clinical Prediction Rule for Risk Stratification of Recurrent Venous Thromboembolism in Patients With Cancer-Associated Venous Thromboembolism

Martha L. Louzada, MD, MSc; Marc Carrier, MD, MSc; Alejandro Lazo-Langner, MD, MSc; Vi Dao, MD; Michael J. Kovacs, MD; Timothy O. Ramsay, PhD; Marc A. Rodger, MD, MSc; Jerry Zhang, BSc; Agnes Y.Y. Lee, MD, MSc; Guy Meyer, MD; Philip S. Wells, MD, MSc

Table 2. Ottawa Score for Recurrent VTE Risk in Cancer-Associated Thrombosis

Variable	Regression Coefficient	Points
Female	0.59	1
Lung cancer	0.94	1
Breast cancer	−0.76	−1
TNM* stage I	−1.74	−2
Previous VTE	0.40	1
Clinical probability		
Low (≤0)	. . .	−3 to 0
High (≥1)	. . .	1 to 3

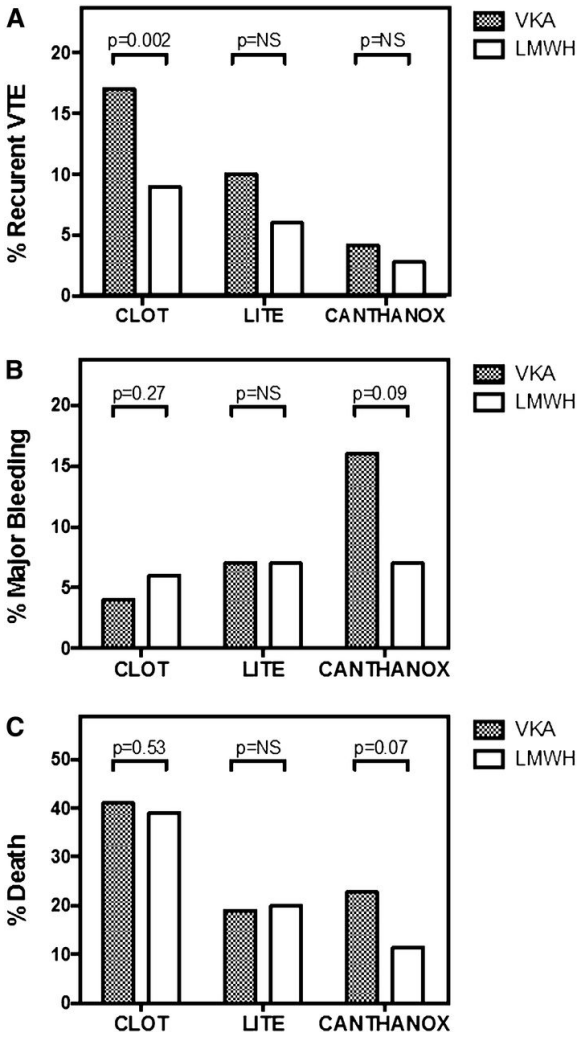
VTE indicates venous thromboembolism.
*TNM (tumor-nodes-metastasis staging system) for solid tumors only.

Treatment of cancer-associated thrombosis

by Agnes Y. Y. Lee, and Erica A. Peterson

Blood
Volume 122(14):2310-2317
October 3, 2013

Comparison of randomized controlled trials of different preparations of LMWH vs VKA for the long-term management of cancer-associated thrombosis.



Lee A Y Y , and Peterson E A Blood 2013;122:2310-2317

American Society of Clinical Oncology

Making a world of difference in cancer care

Recommendations for Venous Thromboembolism Prophylaxis and Treatment in Patients with Cancer

ASCO Clinical Practice Guideline

ASCO Cl. Pr. G. U. Gary H. Lyman, et all 2013 V. 31 N..17.JUNE 10 2013

Clinical Questions

1. Should hospitalized patients with cancer receive anticoagulation for VTE prophylaxis?
2. Should ambulatory patients with cancer receive anticoagulation for VTE prophylaxis during systemic chemotherapy?
3. Should patients with cancer undergoing surgery receive perioperative VTE prophylaxis?
4. What is the best method for treatment of patients with cancer with established VTE to prevent recurrence?
5. Should patients with cancer receive anticoagulants in the absence of established VTE to improve survival?
6. What is known about risk prediction and awareness of VTE among patients with cancer?

VOLUME 31 · NUMBER 17 · JUNE 10 2013

JOURNAL OF CLINICAL ONCOLOGY ASCO SPECIAL ARTICLE

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

Table 1. VTE Prophylaxis and Treatment Recommendations

2013 Recommendation	Strength of Evidence Type and Strength of Recommendation	2007 Recommendation
Inpatients		
1.1 Hospitalized patients who have active malignancy with acute medical illness or reduced mobility should receive pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications.	Evidence: strong Recommendation type, strength: evidence based, strong	Hospitalized patients with cancer should be considered candidates for VTE prophylaxis with anticoagulants in the absence of bleeding or other contraindications to anticoagulation.
1.2 Hospitalized patients who have active malignancy without additional risk factors may be considered for pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications.	Evidence: moderate Recommendation type, strength: evidence based, strong	
1.3 Data are inadequate to support routine thromboprophylaxis in patients admitted for minor procedures or short chemotherapy infusion or in patients undergoing stem-cell/bone marrow transplantation.	Evidence: insufficient Recommendation type, strength: informal consensus, moderate	
Outpatients		
2.1 Routine pharmacologic thromboprophylaxis is not recommended in cancer outpatients.	Evidence: moderate Recommendation type, strength: evidence based, strong	Routine prophylaxis with an antithrombotic agent is not recommended.
2.2 Based on limited RCT data, clinicians may consider LMWH prophylaxis on a case-by-case basis in highly selected outpatients with solid tumors receiving chemotherapy. Consideration of such therapy should be accompanied by a discussion with the patient about the uncertainty concerning benefits and harms as well as dose and duration of prophylaxis in this setting.	Evidence: moderate Recommendation type, strength: evidence based, weak	
2.3 Patients with multiple myeloma receiving thalidomide- or lenalidomide-based regimens with chemotherapy and/or dexamethasone should receive pharmacologic thromboprophylaxis with either aspirin or LMWH for lower-risk patients and LMWH for higher-risk patients.	Evidence: moderate Recommendation type, strength: evidence based, strong	Patients receiving thalidomide or lenalidomide with chemotherapy or dexamethasone are at high risk for thrombosis and warrant prophylaxis. Until such time as data are available from RCTs, LMWH or adjusted-dose warfarin (INR approximately 1.5) is recommended in patients with myeloma receiving thalidomide plus chemotherapy or dexamethasone. This recommendation is based on extrapolation from studies of postoperative prophylaxis in orthopedic surgery and a trial of adjusted-dose warfarin in breast cancer. RCTs evaluating antithrombotic agents are needed in patients with multiple myeloma receiving thalidomide or lenalidomide plus chemotherapy and/or dexamethasone. Research identifying better markers of ambulatory patients with cancer most likely to develop VTE is urgently needed.

Risk of TEV in Cancer Patients: Guide Lines

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., Editor

Prophylaxis against Venous Thromboembolism in Ambulatory Patients with Cancer

Table 2. Comparison of Recommendations Regarding Prophylaxis against Venous Thromboembolism.*

Potential Indication	Recommended Use of Prophylaxis			
	Author	ACCP	ASCO	NCCN
Treatment of multiple myeloma with thalidomide or lenalidomide with high-dose dexamethasone, doxorubicin, combination chemotherapy, or other risk factors	Yes†	Suggest	Yes	Yes
Cancer associated with high risk of venous thromboembolism (pancreatic or gastric)				
With other risk factors	Yes†	Suggest	Consider	Consider
Without other risk factors	Consider‡	No	Consider	Consider
Cancer associated with intermediate risk of venous thromboembolism (lung, ovarian, primary central nervous system, bladder, lymphoma)				
With other risk factors	Consider‡	Suggest	Consider	No
Without other risk factors	No‡	No	Consider	No
Cancer associated with low risk of venous thromboembolism				
With other risk factors	Consider‡	Suggest	Consider	No
Without other risk factors	No	No	Consider	No

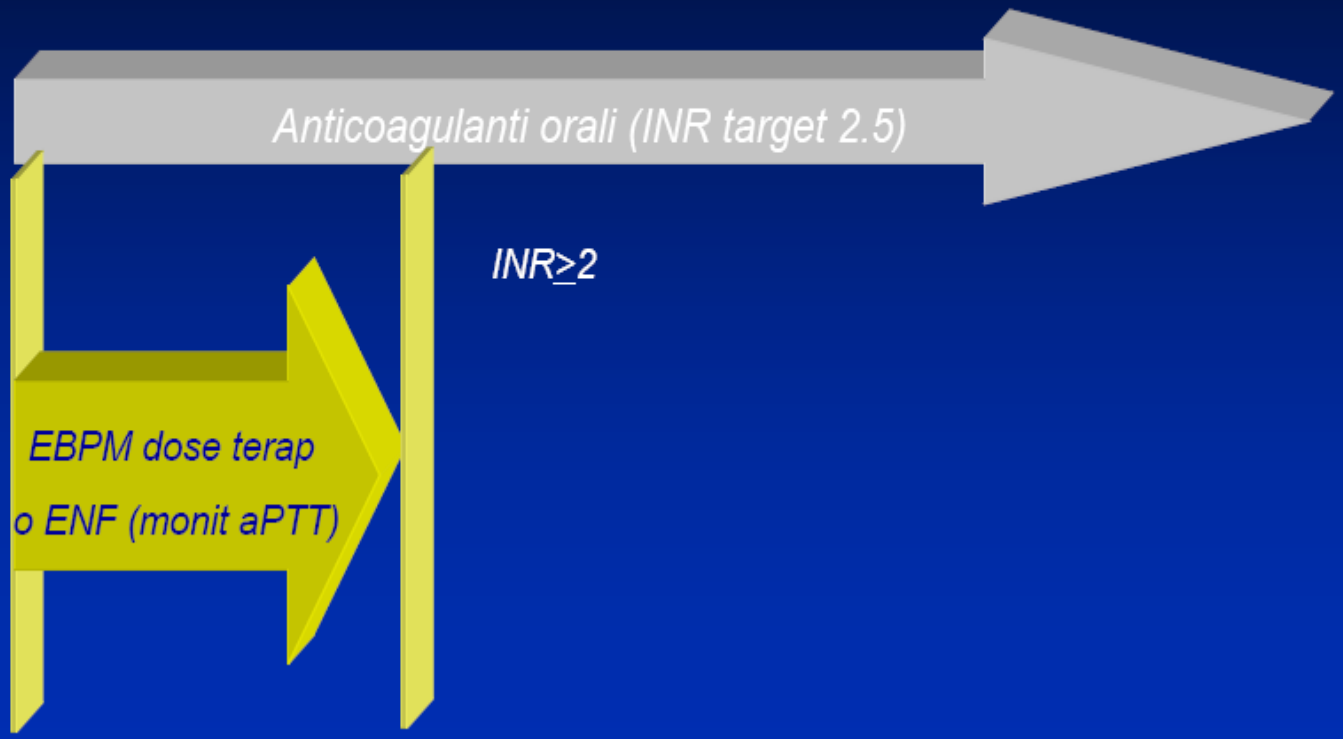
Prevention of tromboembolism in Cancer: Contraindications

Relative Contraindications to Prophylactic or Therapeutic Anticoagulation

- Recent CNS bleed, intracranial or spinal lesion at high risk for bleeding
- Active bleeding (major): more than 2 units transfused in 24 hours
- Chronic, clinically significant measurable bleeding > 48 hours
- Thrombocytopenia (platelets < 50,000/mcL)
- Severe platelet dysfunction (uremia, medications, dysplastic hematopoiesis)
- Recent major operation at high risk for bleeding
- Underlying coagulopathy
- Clotting factor abnormalities
  - Elevated PT or aPTT (excluding lupus inhibitors)
  - Spinal anesthesia/lumbar puncture
- High risk for falls

http://www.nccn.org/professionals/physician_gls/PDF/vte.pdf

Terapia del TEV con EBPM e ACO



Optimal dosing of LMWHfor initial treatment of cancer-associated VTE: international GLs

Guideline	Preference	Drug	Regimen
ASCO 2013-2014	LMWH		
		dalteparin	200 U/Kg daily
			100 U/kg every 12 h
		enoxaparin	1.5 mg/Kg daily[1]
			1 mg/Kg every 12 h
		tinzaparin	175 U/Kg daily
NCCN 2014	LMWH		
		dalteparin	200 U/Kg daily
		enoxaparin	1mg/Kg every 12 h
ACCP 2012	LMWH	**NA**	Weight adjusted therapeutic doses[2]
ESMO 2011	LMWH or iv UFH	dalteparin	200 U/Kg daily
		enoxaparin	100 U/Kg every 12 h
International Consensus 2013	LMWH	**NA**	NA

administration is suggested when the approved daily dose regimen uses the same daily dose as the twice-daily regimen (eg. dalteparin and nadroparin; enoxaparin 2 mg/Kg once daily is not used)

Chest 2012; Mandalà M, Ann Oncol 2011; Farge D, J Thromb **Hemost** 2013

LMWH dosing for long term treatment (≥ 3m) of cancer-associated VTE: international GLs

Guideline	Preference	Drug	Regimen	Duration
ASCO 2013-2014	LMWH	Dalteparin Enoxaparin Tinzaparin	200 U/kg OD for 1 m then 150 U/kg OD 1 mg/kg BID (1.5 mg/kg OD) 175 U/kg OD	At least 6 months. Beyond 6 months in patients with active cancer[1]
NCCN 2014	LMWH (advanced or MTS) or VKA	Dalteparin Enoxaparin	200 U/kg OD for 1 m then 150 U/kg OD 1mg/kg BID	At least 3 months. Indefinite in patients with active cancer[2]
ACCP 2012	LMWH	NA	Weight adjusted therapeutic doses[6]	Extended[3] (unless very high bleeding risk)
ESMO 2011	LMWH	NA	75-80% of initial dose	6 months[4]
International Consensus 2013	LMWH	NA	NA	At least 3 months Individual evaluation for indefinite anticoagulation[5]

beyond 3 months without a scheduled stop date. 4. Consider indefinite treatment in: patients with CR and very high risk of recurrence; patients receiving CHT in a palliative setting. 5. Benefit-risk ratio, tolerability, patients preference, cancer activity. 6. A once daily over twice daily administration is suggested when the approved daily dose regimen uses the same daily dose as the twice-daily regimen (eg. dalteparin, nadroparin.; enoxaparin 2 mg/Kg once daily is not used).

Optimal dosage of LMWH for long-term treatment of cancer-associated thrombosis

Systematic reviews comparing LMWH and VKAs in the long-term treatment of VTE did not consider the influence of the dose.

Full therapeutic (3 m) or intermediate doses (3-6 m) of LMWH for the whole treatment period in RCT and meta-analyses showing benefit of LMWH vs VKA .

Full doses of tinzaparin for long term (6 m) treatment of cancer-associated VTE beneficial vs VKA and safe (CATCH trial).

International GLs recommend full or intermediate doses; ASCO 2013 and ESMO 2011 GLs suggest a 25% reduction of initial dose (Clot trial).

Impossible to make definitive conclusions about the relative safety and efficacy of different doses of LMWH (lack of studies)

Table 1. Consensus guidelines on treatment of deep vein thrombosis or pulmonary embolism in patients with cancer

	ACCP 2012[21]	NCCN 2011[13]	ASCO 2013[14]
Initial/acute treatment	Not addressed in cancer patients.	LMWH Dalteparin 200 U/kg OD Enoxaparin 1 mg/kg BID Tinzaparin 175 U/kg OD Fondaparinux 5 mg (<50 kg), 7.5 mg (50-100 kg), or 10 mg (>100 kg) OD APTT-adjusted UFH infusion	LMWH is preferred for initial 5-10 d of treatment in patients with a CrCl >30 mL/min.
Long-term treatment	LMWH preferred to VKA [2B].* In patients not treated with LMWH, VKA therapy is preferred to dabigatran or rivaroxaban [2C].* Patients receiving extended therapy should continue with the same agent used for the first 3 mo of treatment [2C].*	LMWH is preferred for first 6 mo as monotherapy without warfarin in patients with proximal DVT or PE and metastatic or advanced cancer. Warfarin 2.5-5 mg every day initially with subsequent dosing based on INR value targeted at 2-3.	LMWH is preferred for long-term therapy. VKAs (target INR, 2-3) are acceptable for long-term therapy if LMWH is not available.
Duration of treatment	Extended anticoagulant therapy is preferred to 3 mo of treatment [2B].*	Minimum 3 mo. Indefinite anticoagulant if active cancer or persistent risk factors.	At least 6 mo duration. Extended anticoagulation with LMWH or VKA may be considered beyond 6 mo for patients with metastatic disease or patients who are receiving chemotherapy.

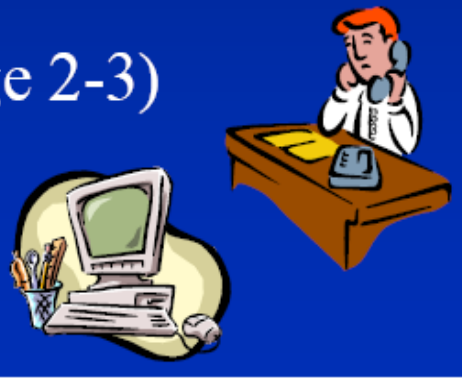
ACCP, American College of Chest Physicians; BID, twice-daily dosing; NCCN, National Comprehensive Cancer Network; OD, once-daily dosing.

*ACCP adaptation of the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) Working Group evidence-based recommendations: 2B, weak recommendation, moderate-quality evidence; 2C, weak recommendation, low- or very-low-quality evidence.[16]

Profilassi long-term del TEV

" Difetti " del Warfarin

- Una lunga emivita di 36-42 ore
- Profilo farmacocinetico non prevedibile
- Interazioni con cibi e farmaci
- Finestra terapeutica ristretta
- Monitoraggio frequente
- Aggiustamento della dose (INR range 2-3)



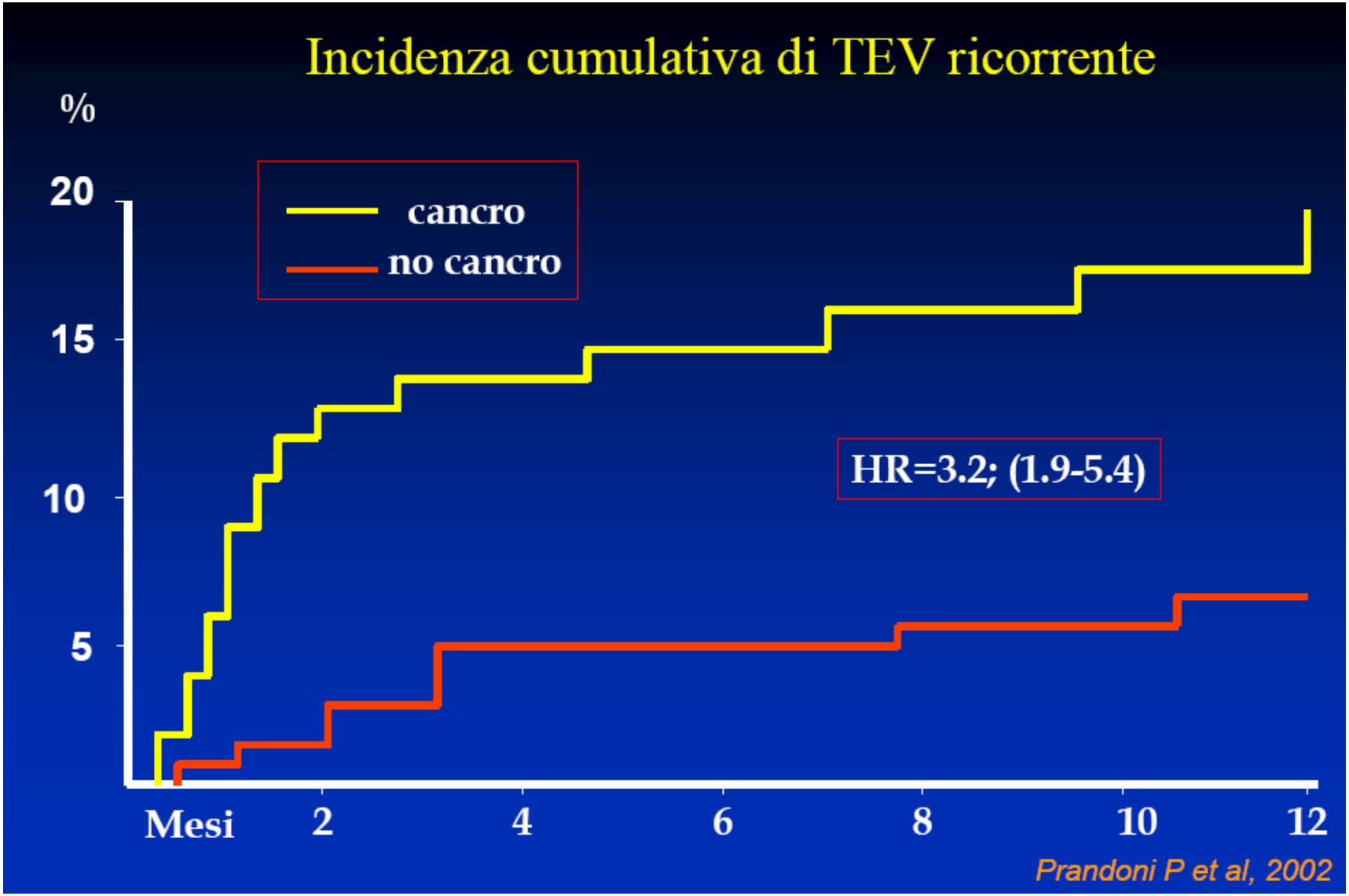
Profilassi long-term del TEV

Warfarin nei pazienti oncologici

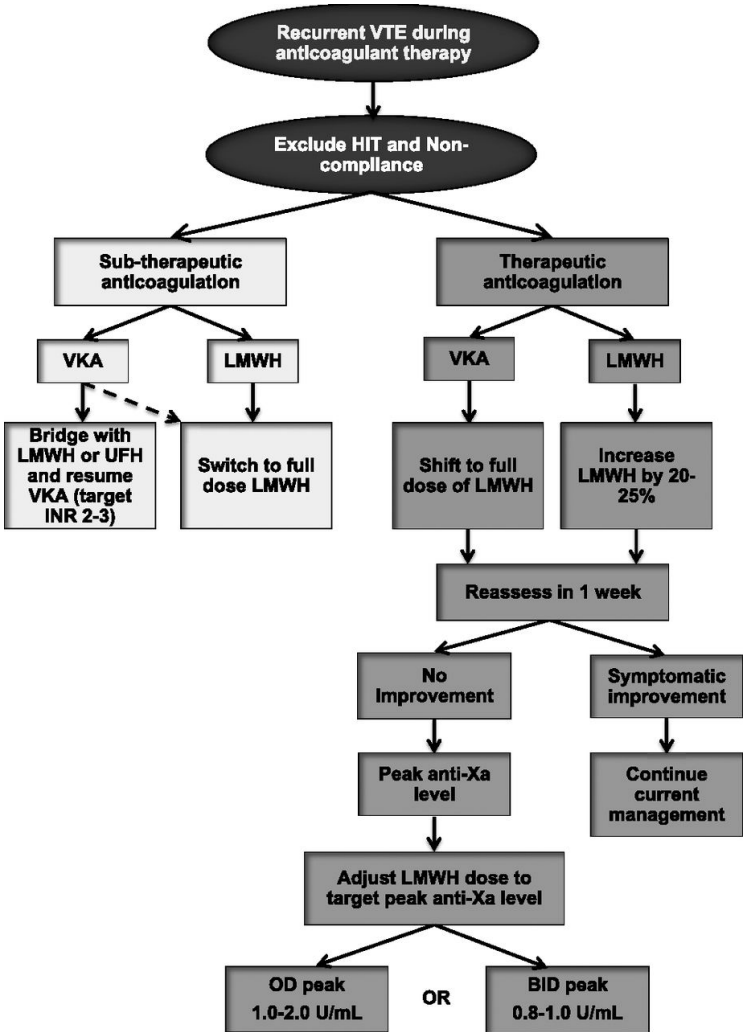
Spesso complicata

- Difficoltà di mantenere INR in range (anoressia, vomito, disfunzione epatica, interazioni farmacologiche)
- Frequenti interruzioni x piastrinopenia o x esecuzione di manovre invasive
- Accesso venoso sovente difficoltoso
- Aumentato rischio di recidive e di emorragie

Management of anticoagulation with LMWH in cancer-related VTE: challenging situations

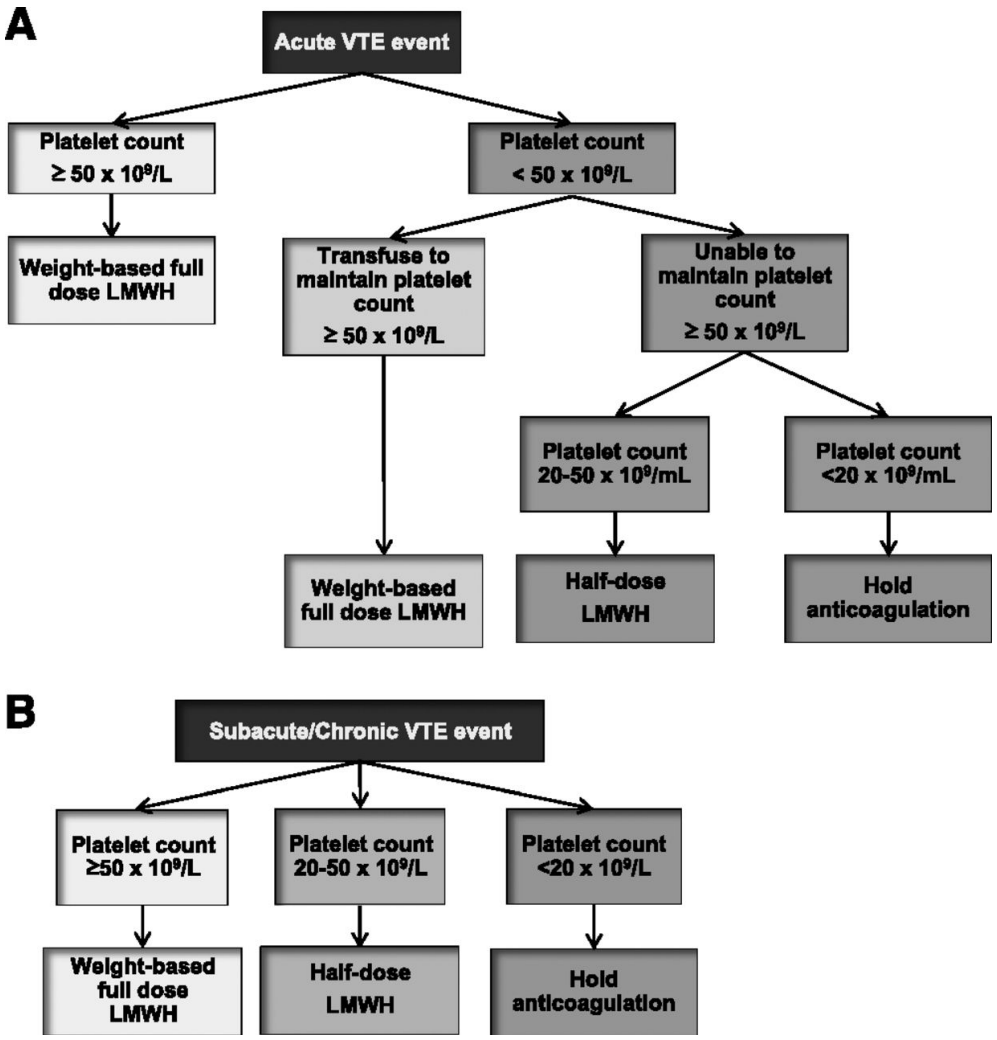

Incidenza cumulativa di TEV ricorrente
%
20
15
10
5
cancro
no cancro
HR=3.2; (1.9-5.4)
Mesi
2
4
6
8
10
12
Prandoni P et al, 2002

Management algorithm of recurrent VTE in patients with cancer.



Lee A Y Y , and Peterson E A Blood 2013;122:2310-2317

Management algorithm of VTE in patients with cancer and thrombocytopenia.



Lee A Y Y , and Peterson E A Blood 2013;122:2310-2317

Management of CVC-related thrombosis in cancer patients

No RCT evaluating different management strategies.

No CT assessing whether line removal is necessary, harmful or beneficial.

Remove CVC only if:

CVC is no longer required

CVC is nonfunctional or defective

CVC-related sepsis is documented or supsected

Anticoagulation (LMWH or LMWH/VKA) if deep veins involved (axillay, subclavian or more proximal veins) for al least 3 months and while CVC remains in place (unless contraindicated) (NCCN 2.2014)

EBPM nei pazienti con IRC

1) Non sono controindicate nei pazienti con IR.

2) Uso ottimale di EBPM nei pz con IR moderata non è ben definito.

3) La terapia con EBPM a dosi *terapeutiche* nei pz con IR moderata aumenta il rischio di complicanze emorragiche.

4) Nei pazienti con IR moderata sottoposti a dosi *profilattiche* quotidiane di EBPM non è stato osservato un aumento delle complicanze emorragiche nonostante aumento dell'attività anti-Xa.

5) La maggioranza degli esperti e LG raccomanda correzione delle dosi se CrCL < 30 mL/min (scarse evidenze sul valore di CrCl al di sotto del quale vanno corrette le dosi di EBPM).

EBPM in cancer patients with severe RI (CCl < 30 mL/min)

Choice of anticoagulant should be individualized.

Extensive practical experience suggests that UFH followed by VKA is a practical approach.

GLs recommendations:

NCCN 2.2014:

- **prefer UFH and VKA (for long term treatment);**
- **LMWH: dose adjustment according to manufacturer recommendations.**

ACCP 2012:

- **UFH if therapeutic doses needed;**
- **LMWH: consider Anti-Xa monitoring;**
- **enoxaparin: 50% dose reduction;**
- **check manufacturer recommendations (lacking in most cases).**

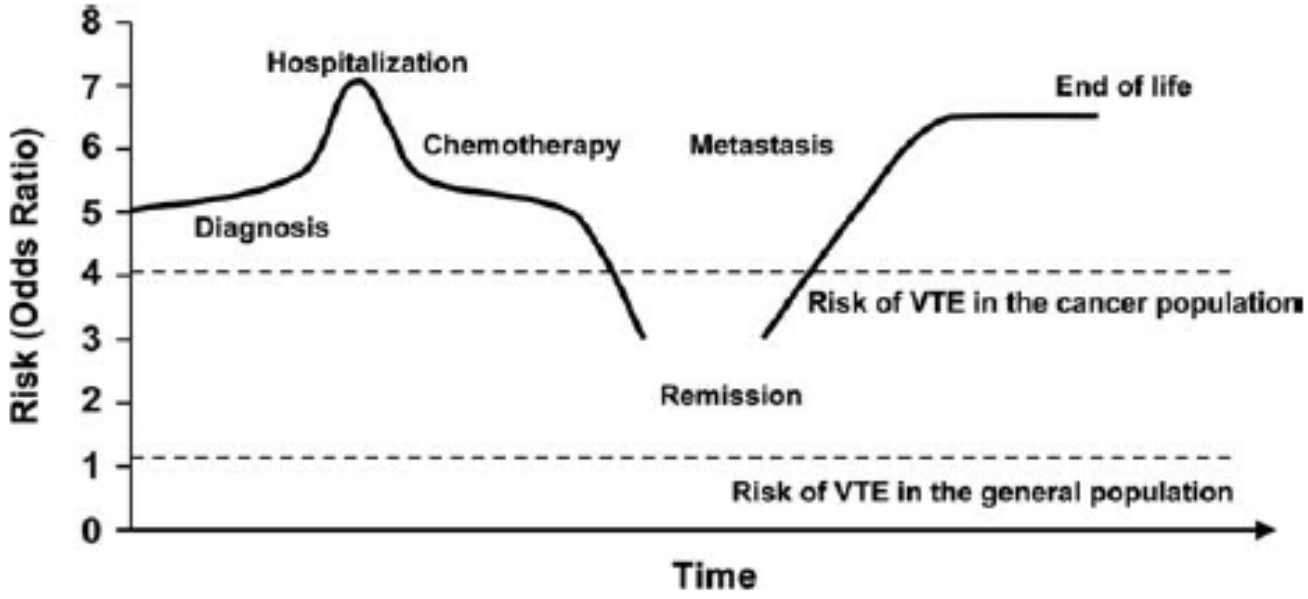
ASCO 2014:

- **prefer UFH and VKA;**
- **LMWH: dose adjustment based on Anti-Xa levels**

International Consensus:

- **prefer UFH followed by VKA**
- **LMWH: dose adjustment based on Anti-Xa levels**

ONCOLOGO → VALUTARE IL RISCHIO DI TE



La problematica tromboembolica deve essere, oggi, trattata dallo specialista oncologo/ematologo sia in termini di profilassi che trattamento del TE. La valutazione del rischio tromboembolico varia durante la storia della malattia del paziente.

Il medico deve conoscere, valutare e informare il paziente del suo rischio tromboembolico durante tutto il corso della sua malattia.

CONCLUSIONI

- TRATTAMENTO. I pazienti con TE devono preferire l'uso di EBPM rispetto alla warfarina, in quanto quest'ultima ha molte interazioni con i farmaci chemioterapici e di terapia di supporto. La durata minima del trattamento con EBPM in questi pazienti è di 3 mesi, ma è consigliabile arrivare a 6 mesi. In virtù del lungo trattamento a cui sono sottoposti i pazienti oncologici devono essere trattati preferibilmente con EBPM in monosomministrazione, rispetto alla bi-somministrazione (Lineeguida CHEST).
- PROFILASSI CHIRURGICA. I pazienti che si sottopongono a chirurgia addominale o pelvica maggiore devono essere profilassati per almeno 4 settimane. Le calze elastiche non possono mai sostituirsi alla profilassi farmacologica in questi pazienti, neanche nel caso di interventi di chirurgia minori che richiedono solo 1 settimana di profilassi.

CONCLUSIONI

- PROFILASSI PT OSPEDALIZZATO. Il paziente ospedalizzato, allettato e con cancro attivo deve essere profilassato con EBPM. Il paziente ospedalizzato, con cancro attivo, deve essere valutato per la profilassi. Il paziente sottoposto a piccoli interventi in giornata non deve essere profilassato.
- PROFILASSI PT AMBULATORIALE. Nei pazienti ambulatoriali il rischio tromboembolico deve essere costantemente monitorato e in caso di alto rischio, il medico deve informare il paziente e discutere con lui l'eventuale profilassi con EBMP. I pazienti con MM e trattati con lenalidomide o talidomide devono essere profilassati con EBPM se ad alto rischio, riservando l'aspirina solo nei casi di basso rischio di TE.