



Profilassi rischio TEV: underuse e overuse

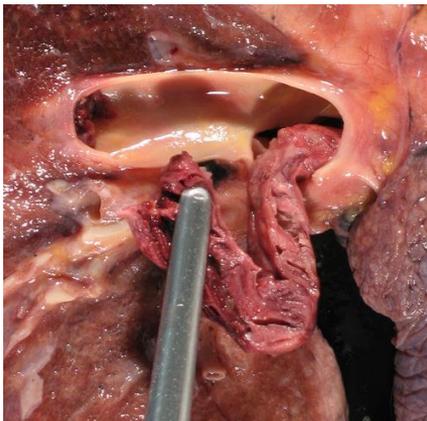
10 Novembre

***Ospedale San Giovanni "Calibita" – Sala Verde
Fatebenefratelli – Isola Tiberina Roma***

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There are an estimated 8 million and 12 million acutely-ill hospitalised medical patients annually in the US and EU, respectively

Venous thromboembolism (VTE) remains a significant cause of morbidity and mortality in this population, with hospitalisation for medical illness accounting for almost one quarter of the incident VTE events occurring in the community



Heit JA. The epidemiology of venous thromboembolism in the community.
Arterioscler Thromb Vasc Biol
2008; 28: 370–372.

Hospitalized Acutely Ill Medical Patients

For acutely ill hospitalized medical patients at increased risk of thrombosis, we recommend anticoagulant thromboprophylaxis with low-molecular-weight heparin [LMWH], low-dose unfractionated heparin (LDUH) bid, LDUH tid, or fondaparinux (Grade 1B) .

Remarks: In choosing the specific anticoagulant drug to be used for pharmacoprophylaxis, choices should be based on patient preference, compliance, and ease of administration (eg, daily vs bid vs tid dosing), as well as on local factors affecting acquisition costs (eg, prices of various pharmacologic agents in individual hospital formularies).

Meta-analysis of Thromboprophylaxis in Medical Patients

No Prophylaxis vs Anticoagulant Prophylaxis

Outcome	Trials	No Prophylaxis Patients	No Prophylaxis Risk	Rel Prophylaxis Risk	Risk Ratio	<i>p</i>
DVT	22	8,333	11.0%	> 4.9%	0.45	<0.001
PE	19	39,762	1.0%	> 0.6%	0.48	<0.001
Mortality	20	42,960	7.5%	7.3%	0.95	0.15
Bleeding	16	40,031	1.7%	< 3.8%	1.71	<0.001

ACP Meta-Analysis of VTE Prophylaxis in Medical Patients: *Summary*

Primary pharmacological prophylaxis—begun at the time of admission and continued for the duration of stay in hospital—does not reduce the burden of VTE in such patients, in that it lowers the rate of thrombotic events and VTE-related death, with no effect on total mortality



The TEVer Score: Thromboprophylaxis would be indicated from a score of 4 points or more

- Cancer YES | NO
- Previous VTE YES | NO
- Thrombophilia YES | NO
- Major Surgery (< 60 days) YES | NO
- Drug That Stimulate hematopoiesis, CVC YES | NO
- BMI > 30KG/M2 YES | NO
- Immobilization (<30 Minutes/Day Of Walking For 3 Or More Days) YES | NO
- Hormone replacement E/P therapy YES | NO
- Age > 70Aa YES | NO
- Recent Hospitalization (>=2 days in the preceding 90 days) YES | NO
- Varicose veins YES | NO
- Respiratory Failure YES | NO

Submit

Table 1: Risk factors for VTE in hospitalised medical patients – the Padua VTE RAM * [adapted from Ref (45)].

Risk factor	Points
Reduced mobility	3
Active cancer	3
Prior venous thromboembolism (excludes superficial thrombophlebitis)	3
Already known thrombophilic condition	3
Recent (<1 month) trauma and/or surgery	2
Elderly age (>70 years)	1
Heart and/or respiratory failure	1
Acute myocardial infarction or ischaemic stroke	1
Ongoing hormonal treatment	1
Obesity (BMI>30)	1
Acute infection and/or rheumatologic disorder	1
* A score of 4 or more constitutes at VTE risk.	

Huang W, Anderson FA, Spencer FA, et al. Risk-assessment models for predicting venous thromboembolism among hospitalised non-surgical patients: a systematic review. J ThrombThrombolysis 2013; 35: 67–80

The VTE RAMs consistently (with negative predictive values of ~99 %) point to the fact that only about 35–50 % of the medically-ill population are at sufficient VTE risk to warrant pharmacologic thromboprophylaxis, using a symptomatic VTE event rate of 1.0 % as the clinical threshold suggested by the ACCP guidelines by which benefits of a pharmacologic approach may outweigh bleed risks

IMPROVE Bleed Score

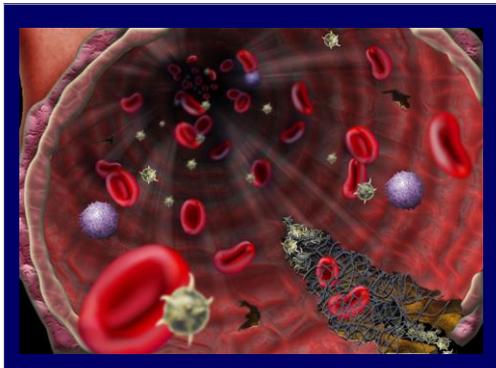
Accordingly, having identified significant risk factors for bleeding in a large population of hospitalized medical patients, the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) Investigators have derived a risk score—the IMPROVE Bleeding Risk Score (IBS), which has been validated for stratifying the bleeding risk in acutely ill medical patients

Bleeding risk factors	Points
Renal failure GFR 30–59 vs ≥ 60 ml/min/m ²	1
Male vs female	1
Age 40–80 vs <40 years	1.5
Current cancer	2
Rheumatic disease	2
CV catheter	2
ICU/CCU	2.5
Renal failure GFR <30 vs ≥ 60 ml/min/m ²	2.5
Hepatic failure (INR >1.5)	2.5
Age ≥ 85 vs <40 years	3.5
Platelets $<50 \times 10^9$ cells/l	4
Bleeding in 3 months before admission	4
Active gastroduodenal ulcer	4.5

ICU, intensive care unit; CCU, critical care unit; CV, central venous; GFR, glomerular filtration rate; INR, international normalized ratio. * A score of 7 or more constitutes high bleed risk.

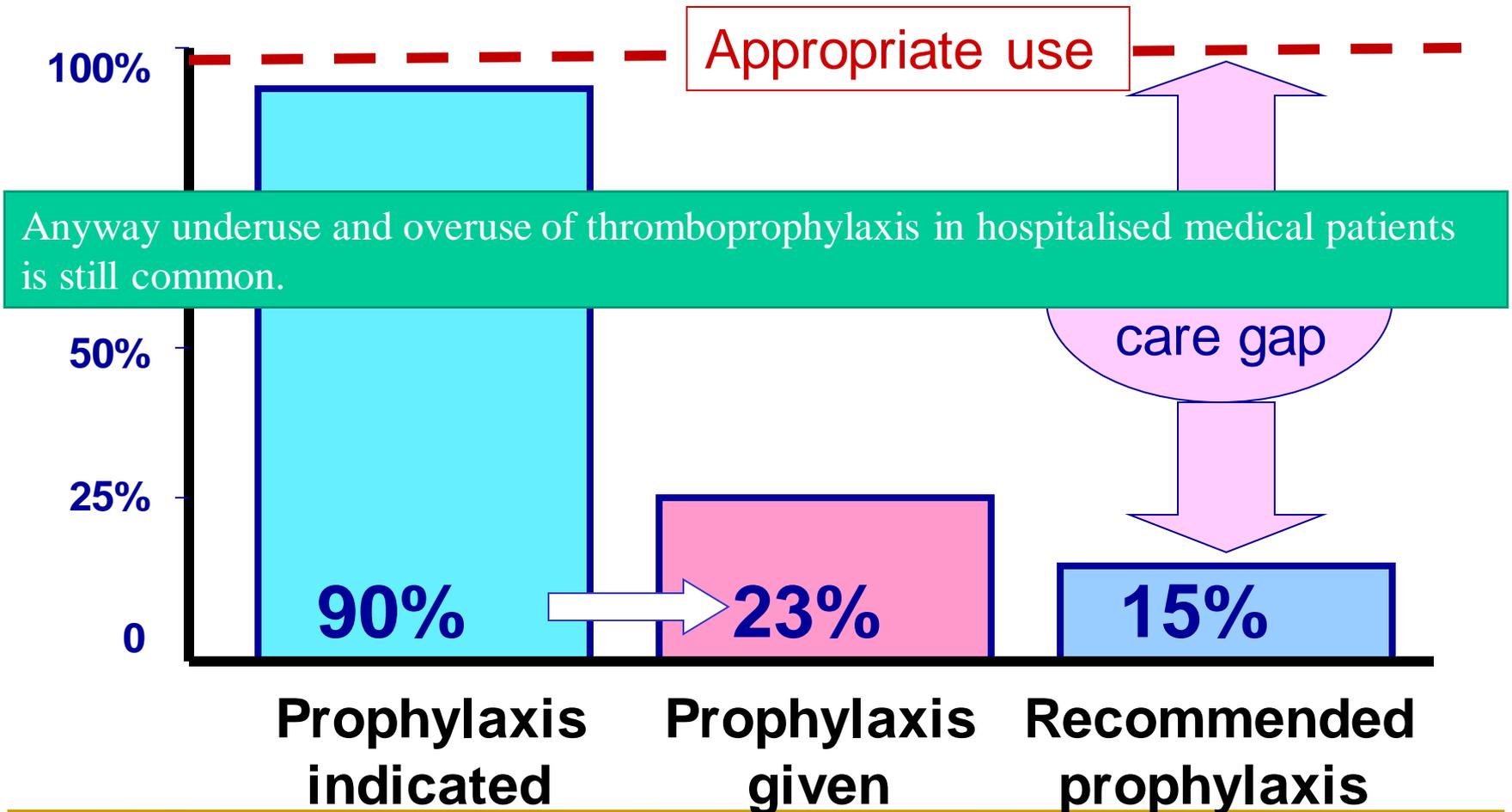
The extensive use of RAMs in hospitalized medical patients leads to a statistically relevant decrease in anticoagulant prescription, and a decrease in health expenditure due to pharmacological prophylaxis, without affecting VTE rate and the incidence of major bleeding.

Depietri L, Marietta M, Scarlini S et al (2018)
The STIME study Intern Emerg Med.



Prophylaxis Use in *Medical Patients*

1,894 medical patients in 29 hospitals in 6 provinces



Underuse

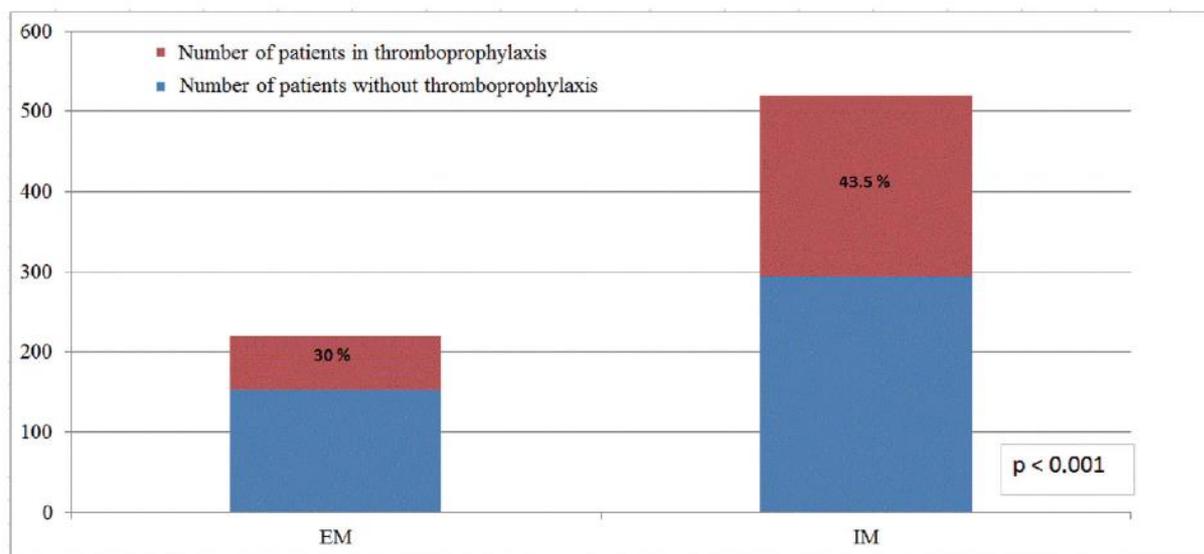


Table 2 Use of LMWH TPX in patients positive for each risk score in IM and EM departments

Risk score	IM			EM			p value
	tot	n	%	tot	n	%	
Immobilization	157	110	70.1	56	30	53.6	0.033
Kucher	66	36	54.5	18	9	50.0	0.794
Chopard	296	164	55.4	103	48	46.6	0.123
ACCP08	93	62	66.7	24	15	62.5	0.81
Padua	165	100	61%	75	34	45%	0.035

Bold indicates a statistically significant difference ($P < 0.05$).

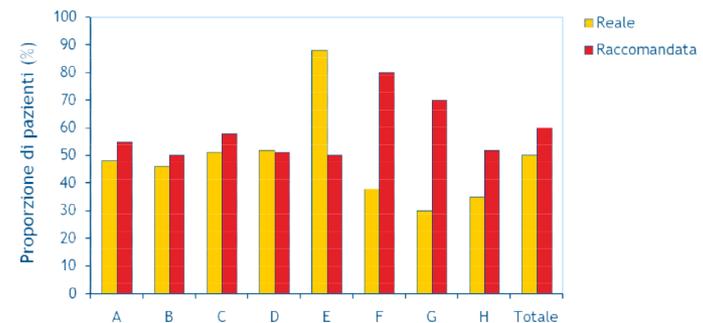
Venous thromboembolism: A Call for risk assessment in all hospitalised patients

ISTH Steering Committee for World Thrombosis Day*

In hospitalised medical patients, appropriate thromboprophylaxis was used in 70 % or more of patients in only one country and was used in less than 50 % of patients in 23 countries.!!!!

Quanti pazienti ricevono la profilassi ?

- Proporzione di pazienti internistici che ha ricevuto vs quelli che avrebbero dovuto ricevere profilassi secondo le raccomandazioni, in 8 ospedali svizzeri



Chopard P et al. J Intern Med 2005; 257:352-357

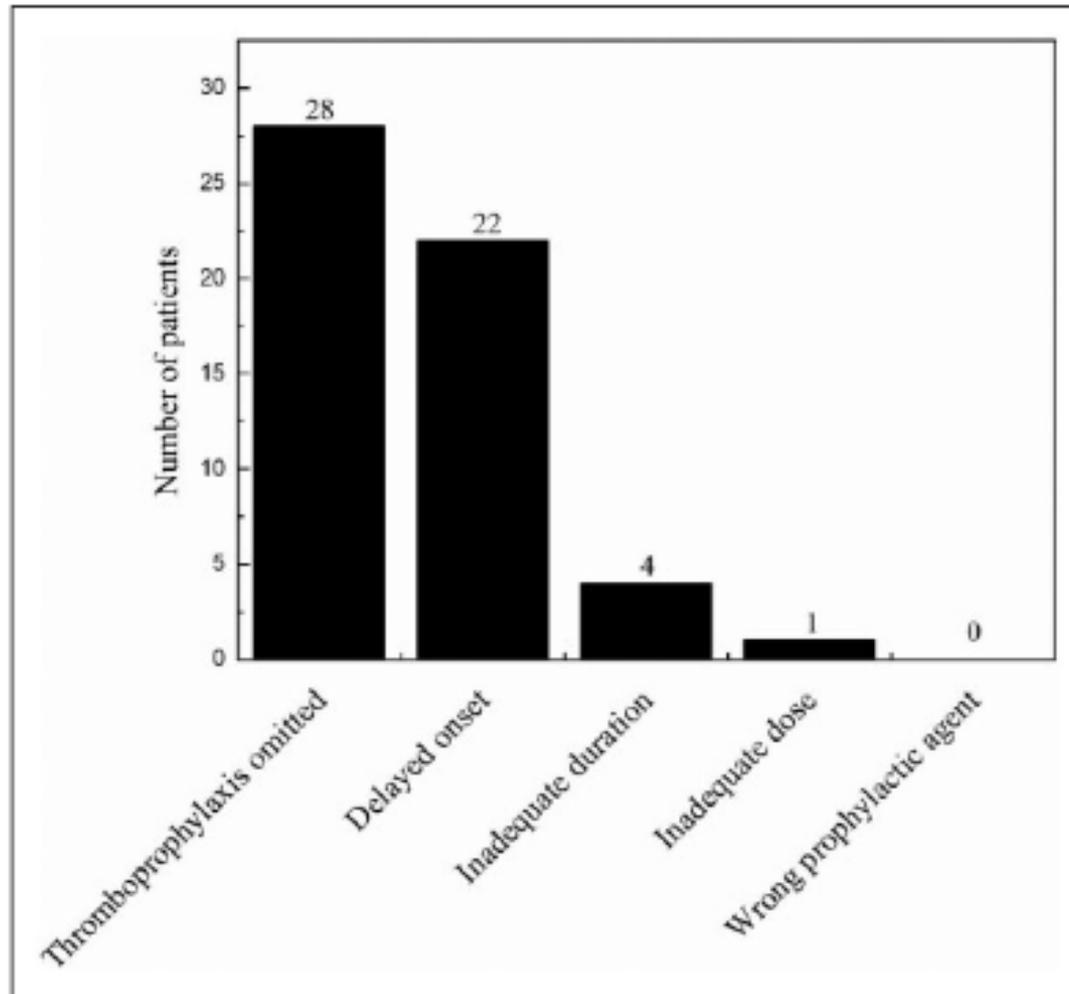
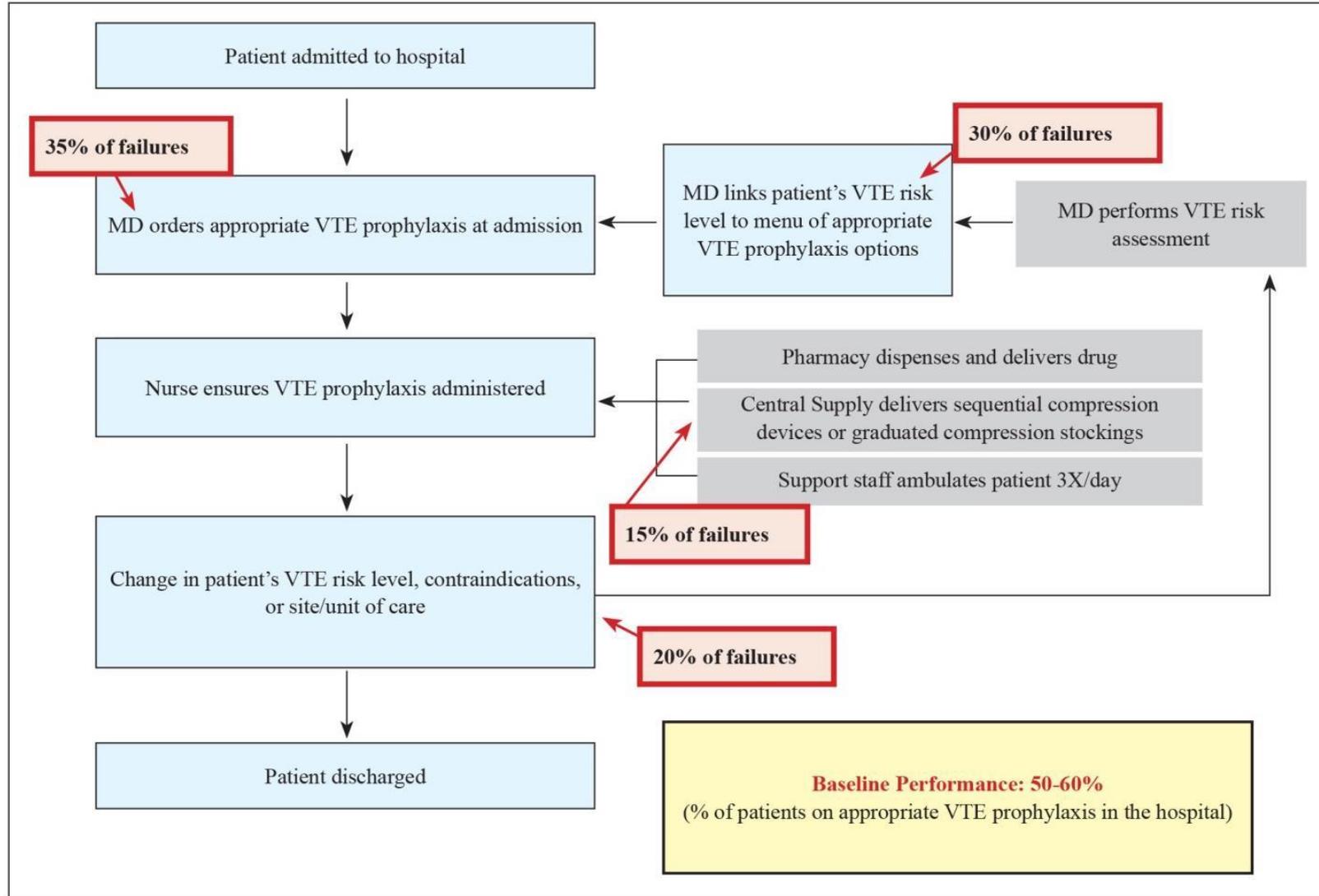


Figure 1. Reasons for inadequacy of prophylaxis in preventable VTE (n=55).

	High Risk* N = 962	No Prophylaxis N = 366	Prophylaxis N = 596	P
Geneva risk, mean score \pm SD	5.2 \pm 2.4	5.1 \pm 2.4	5.3 \pm 2.4	0.10
Cardiac failure, n (%)	172 (17.9)	62 (16.9)	110 (18.5)	0.55
Respiratory failure, n (%)	341 (35.5)	123 (33.6)	218 (36.6)	0.35
Recent stroke <3 months, n (%)	30 (3.1)	9 (2.5)	21 (3.5)	0.36
Recent myocardial infarction <4 wks, n (%)	26 (2.7)	6 (1.6)	20 (3.4)	0.11
Acute infection/sepsis, n (%)	403 (41.9)	117 (32.0)	286 (48.0)	<0.001
Acute inflammatory/rheumatic disease, n (%)	56 (5.8)	23 (6.3)	33 (5.5)	0.63
Active malignancy, n (%)	351 (36.5)	155 (42.4)	196 (32.9)	0.003
Myeloproliferative syndrome, n (%)	31 (3.2)	22 (6.0)	9 (1.5)	<0.001
Nephrotic syndrome, n (%)	21 (2.2)	8 (2.2)	13 (2.2)	1.00
Prior VTE, n (%)	120 (12.5)	46 (12.6)	74 (12.4)	0.95
Known thrombophilia, n (%)	8 (0.8)	4 (1.1)	4 (0.7)	0.48
Immobilization**, n (%)	403 (41.9)	145 (39.6)	258 (43.3)	0.26
Complete bed rest for >3 days, n (%)	108 (11.2)	26 (7.1)	82 (13.8)	0.002
Recent travel for >6 hrs, n (%)	38 (4.0)	18 (4.9)	20 (3.4)	0.23
Age >60, n (%)	735 (76.4)	273 (74.6)	462 (77.5)	0.30
Obesity (BMI >30), n (%)	180 (18.7)	64 (17.5)	116 (19.5)	0.45
Chronic venous insufficiency, n (%)	85 (8.8)	27 (7.4)	58 (9.7)	0.21
Pregnancy, n (%)	2 (0.2)	0 (0.0)	2 (0.3)	0.27
Hormonal therapy***, n (%)	56 (5.8)	25 (6.8)	31 (5.2)	0.30
Dehydration, n (%)	150 (15.6)	56 (15.3)	94 (15.8)	0.85
Bleeding requiring medical attention, n (%)	64 (6.7)	40 (10.9)	24 (4.0)	<0.001
Calculated creatinin-clearance <30 ml/min ¹ , n (%)	106 (11.0)	40 (10.9)	66 (11.1)	0.94
Thrombocytopenia <100,000/ml, n (%)	105 (10.9)	70 (19.1)	35 (5.9)	<0.001

* defined as: low risk = Geneva risk score <3 points, high risk = Geneva risk score \geq 3 points. ** defined as complete bed rest or inability to walk for >30 mins per day for >3 days. *** contraceptive or substitutive. ¹using the Cockcroft-Gault formula.

Process Map of VTE Prophylaxis With Common Areas of Failure



OVERUSE

Tabella 1. Tromboprofilassi e punteggio di rischio per tromboembolismo venoso.

Punteggio	Totale	No eparina	Eparina
0	279 (38.6%)	232 (53%)	47 (16.5%)
1	196 (27.1%)	114 (26%)	82 (28.9%)
2	158 (21.9%)	63 (14.4%)	95 (33.5%)
3	63 (8.7%)	20 (4.6%)	43 (15.1%)
4	26 (3.6%)	9 (2.1%)	17 (6.0%)
Totale	722	438	284

La tromboprofilassi veniva effettuata anche nel 16,5 % dei pazienti negativi per tutti gli scores considerati!!!

OVERUSE

Tabella 3. Positività per i singoli fattori nei pazienti negativi alle scale internazionali di rischio tromboembolico.

N fattori di rischio		SI tromboprofilassi	No tromboprofilassi
0	209	27	182
1	62	18	44
2	8	2	6
tot	279	47	232

Vincentelli GM, Monti M, et al
The overuse of thromboprophylaxis in medical patients: Main clinical aspects.
Giornale italiano di cardiologia (2015).

Quali sono i fattori che influenzano di più l'inizio della tromboprofilassi?

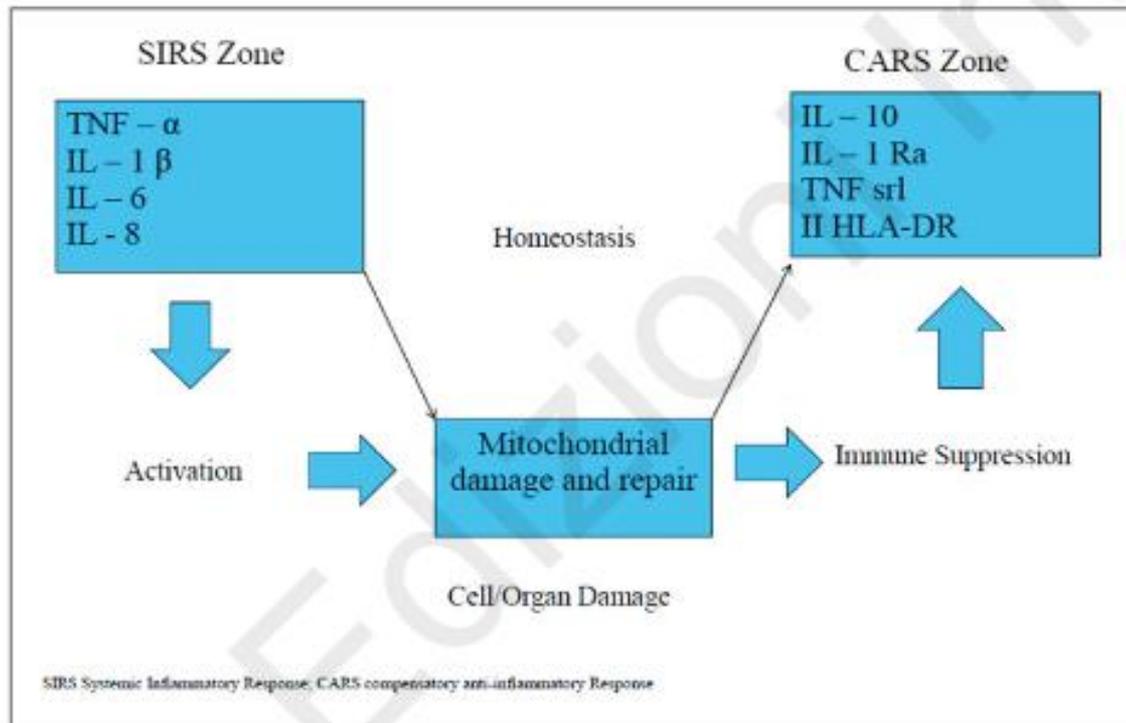
età (OR 1.04; IC 95% 1.002-1.09)

infezione severa (OR 2.31; IC 95% 1.25-4.35)

insufficienza venosa cronica (OR 3.02; IC 95% 1.96-4.67)

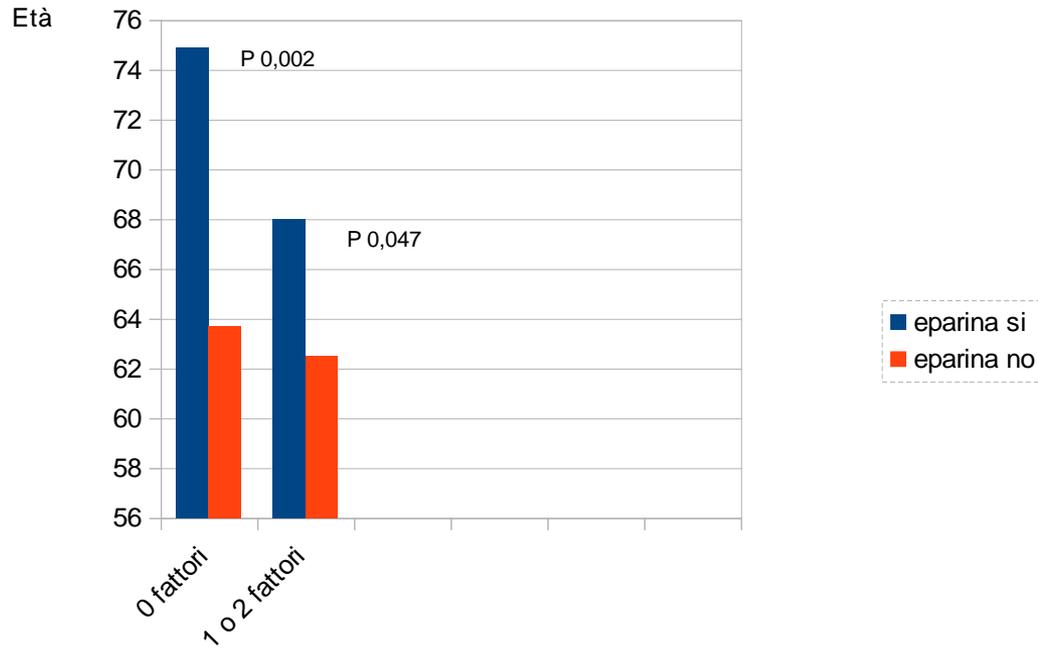
**L'età diviene il fattore principale nella decisione di somministrazione la
terapia
in assenza di altri fattori di rischio.**

Sepsi e TEV



An unusual case of septic shock
Monti M., Vincentelli G.M., Monti A., D'Arco M.F., Borgognoni F.
Prevention and Research 2015

Età e TEV



**Seppur il rischio TEV aumenta con l'avanzare dell'età ,
il rapporto tra età e TEV non ha una correlazione fisiopatologica**

[Blix K](#), [Brækkan SK](#), [Le Cessie S](#), [Skjeldstad FE](#), [Cannegieter SC](#), [Hansen JB](#).

[Eur J Epidemiol](#). 2014;29(4):277-84.

Conclusion

While waiting for the “ideal” RAM or strategy to best identify the individual VTE risk, the thrombotic/haemorrhagic risk profile of medical patients should be routinely assessed, and the use of prophylaxis be tailored to individual thrombotic/haemorrhagic risk.

The simultaneous assessment of the thrombotic and haemorrhagic risk is the key for an adequate safe prophylaxis, a higher appropriateness of antithrombotic prophylaxis.

It is also conceivable that the combined use of RAMs with biomarkers such as D-dimer will further help identify at risk patients and improve patient stratification

Grazie per l'attenzione...
