

Venous Thromboembolism Prophylaxis in Hospitalised Patients -Radical or Right On

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MY TALK TODAY

1. Introduction
2. Magnitude of the problem
3. VTE Prophylaxis Guidelines at TTSH

Introduction

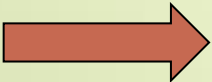
- ▶ Venous thromboembolism (PE and DVT) is a common clinical problem in hospitalised patients and has substantial morbidity and mortality
- ▶ Unrecognised VTE :
 - Acute : recurrent PE (fatal)
 - Chronic : post-thrombotic syndrome (PTS)
chronic thromboembolic pulmonary
hypertension (CTPH)

VTE - A Silent Killer

- ▶ Often a Silent Disease
- ▶ Proven DVT but no clinical suspicion of PE
 - Half of these "asymptomatic" patients have undiagnosed PE.
- ▶ 2/3 of patients with proven PE have no DVT symptoms.
1/3 of the cases: it is impossible to find the original site of DVT without an autopsy
- ▶ Studies show that between 5% and 10% of all in-hospital deaths are a direct result of PE

Introduction

- ▶ Proximal Lower Limb DVT – Clinically Important

50% untreated cases  PE

- ▶ 30% untreated PE  DEATH

(Death usually results from Recurrent PE)

ENDORSE : WORLDWIDE

(Lancet 2008)



68,183 patients; 32 countries; 358 sites

First patient enrolled August 2, 2006; Last patient enrolled January 4, 2007

VTE in North America

- ▶ Annually
 - DVT 160 / 100,000
 - PE : non fatal 20 / 100,000
 - : fatal (autopsy) 5 / 100,000
- ▶ Venous ulceration : 300/100 000 (25% DVT)
- ▶ Annual costs of CVI – \$1 to 3 billion
(1–2% of the total health care budget)

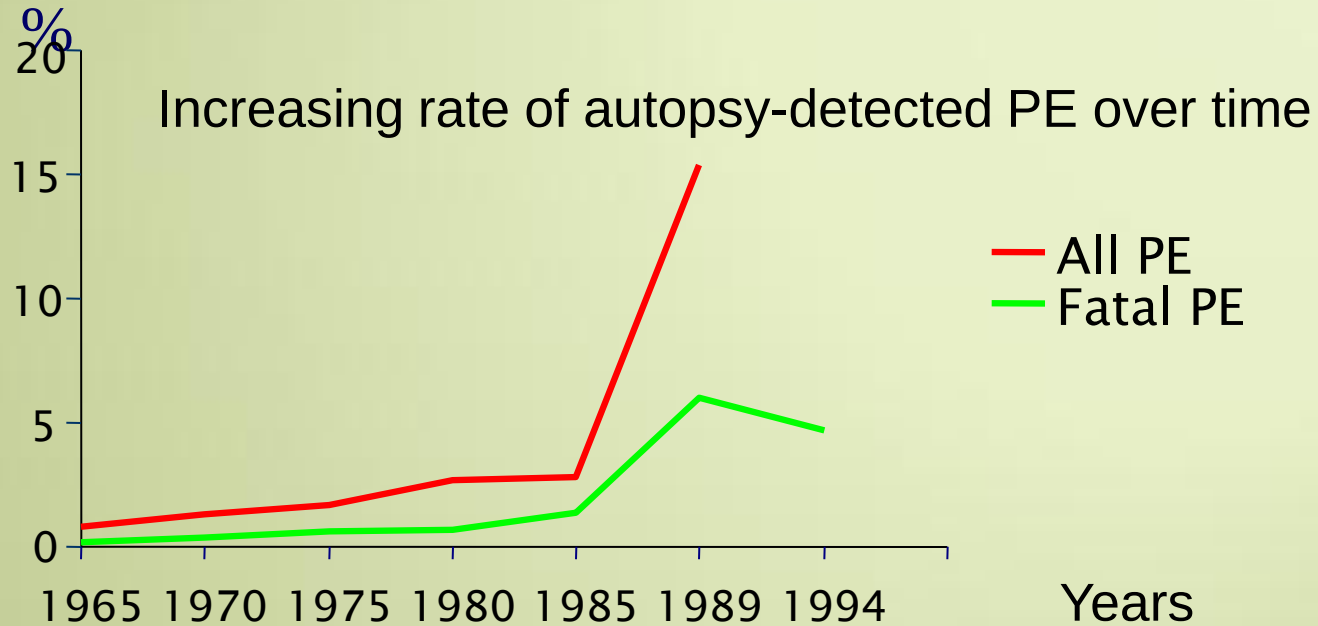
Causes of Death in Europe

Deaths due to VTE (543,454)¹ exceed combined deaths due to:^{2,3}

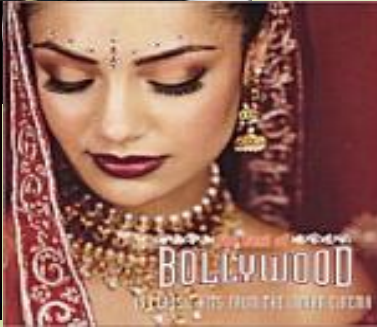
AIDS	(5,860)
Breast cancer	(86,831)
Prostate cancer	(63,636)
Road traffic accidents	(53,599)

¹Cohen AT *et al.* *Thromb and Haem* 2007; 98:756–764; ²Eurostat statistics on health and safety 2001 (<http://epp.eurostat.cec.eu.int>), ³Hirsh J, Hoak J. *Circulation* 1996;93:2212—45

Autopsy Studies In Asia : VTE Incidence



Who is An ASIAN ?



VTE IN ASIA

- SMART (Surgical Multinational Asian Registry in Thrombosis) 2005
- SMART venography (2007)
- AIDA (Assessment of the Incidence of DVT in Asia) 2005
- ENDORSE (Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care Setting) 2008

	Number of Patients	Asymptomatic DVT, %		Symptomatic VTE, %	
		Total	Proximal	DVT	PE
<u>ASIAN</u> Studies					
<u>SMART study (1)*</u>					
Major orthopaedic surgery	2,420	–	–	0.9	0.3
Total hip replacement	408	–	–	1.0	0
Total knee replacement	944	–	–	1.4	0.3
Hip fracture surgery	1,068	–	–	0.5	0.3
<u>SMART venography study (2)</u>					
Major orthopaedic surgery	326	36.5	9.2	0.9	0
Total hip replacement	134	16.4	2.2	0.7	0
Total knee replacement	192	49.0	14.0	1.0	0
(1) Leizorovicz A, Turpie AGG, Cohen AT, et al. Epidemiology of venous thromboembolism in Asian patients undergoing major orthopedic surgery without thromboprophylaxis. The SMART study. J Thromb Haemost. 2005; 3: 28-34					
(2) Leizorovica A, on behalf of the SMART Venography Study Steering Committee. Epidemiology of post-operative venous thromboembolism in Asian patients. Results of the SMART venography study. Haematologica 2007; 92: 1197-1201					

	Number of Patients	Asymptomatic DVT, %		Symptomatic VTE, %	
		Total	Proximal	DVT	PE
<u>AIDA Study (3)</u>					
Major orthopaedic surgery	407	41.0	10.2	–	0.5
Total hip replacement	175	25.6	5.8	–	–
Total knee replacement	136	58.1	17.1	–	–
Hip fracture surgery	96	42.0	7.2	–	–
<u>SAKON et al (4)</u>					
Major abdominal surgery	173	23.7	2.9	–	0.6

(3) Piovella F, Wang C, Lu H, et al. Deep-vein thrombosis rates after major orthopedic surgery in Asia. An epidemiological study based on postoperative screening with centrally adjudicated bilateral venography. J Thromb Haemost 2005; 3: 2664–2670.

(4) Sakon M, Maehara Y, Yoshikawa H, et al. Prevalence of venous thromboembolism following major abdominal surgery: a multi-center, prospective epidemiological study in Japan. J Thromb Haemost 2006; 4: 581–586.

	Number of Patients	Asymptomatic DVT, %		Symptomatic VTE, %	
		Total	Proximal	DVT	PE
<u>WESTERN Studies</u> **					
<u>Samama et al (5)</u>					
Total hip replacement	85	37.3	16.0	1.3	0
<u>Leclerc et al (6)</u>					
Total knee replacement	65	57.8	18.6	–	1.5
<u>Agnelli et al (7)</u>					
Hip fracture surgery	82	57.5	35.6	0	1.2
<u>Ockelford surgery (8)</u>					
Major abdominal surgery	88	15.9	–	–	2.3

(5) Samama CM, Clergue F, Barre J, et al. Low molecular weight heparin associated with spinal anaesthesia and gradual compression stockings in total hip replacement surgery. Br J Anaesth 1997; 78: 660–665.

(6) Leclerc JR, Geerts WH, Desjardins J, et al. Prevention of deep vein thrombosis after major knee surgery – a randomized, double-blind trial comparing a low mo-lecular weight heparin (enoxaparin) to placebo. Thromb Haemost 1992; 67: 417–423.

VTE: West vs. East

	WEST	EAST
Hip Replacement	40%	20%
Knee Replacement	80%	60%
General Surgery	28%	3%
Colorectal Surgery	44%	28%

Liew NC,et al. Asian J Surg 2003; Kakkar VV ,et al. Lancet 1972

VTE in Singapore

- Prevalence
 - LH Lee et al, 2002
 - » January 1996 to December 1997
 - » Duplex US → Symptomatic DVT
 - » Acute DVT: 15.8 per 10, 000 hospital admissions
 - » *Versus* 7.9 per 10, 000 hospital admissions (1989 – 1990)
 - HJ Ng et al, 2009
 - » 2002 – 2003
 - » Primary and secondary DVT prevalence: 45.3 per 10, 000 hospital admissions

VTE : Tan Tock Seng Hospital



–Sule AA et al. 2011

- 721 patients admitted to Level 5 wards
Department of General Medicine.
- November through December 2009
 - Follow-up period: 3 months
- Mortality (n = 42)
 - Infection (Pneumonia, UTI): 3.61% (n = 27)
 - Sudden death: 2.23% (n = 15)

VTE : Tan Tock Seng Hospital



Sudden or acute death: 2.23% (n = 15)

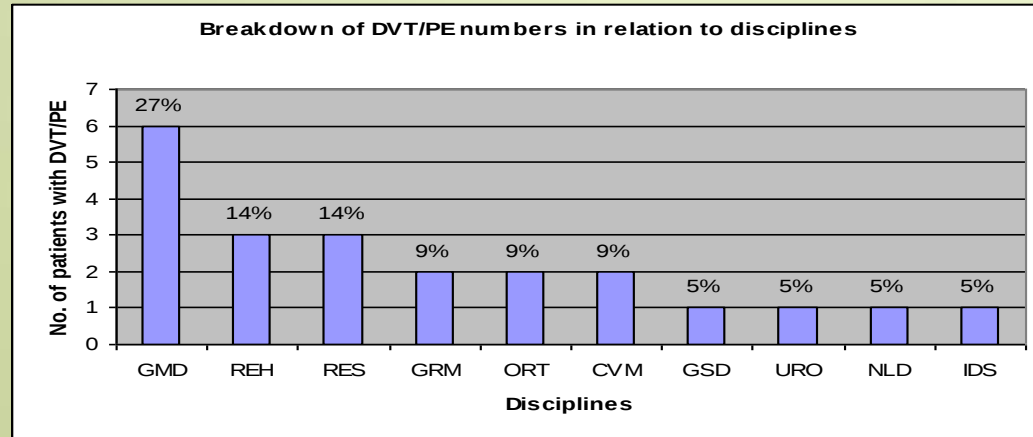
- Acute Myocardial Infarction (n = 2)
- Death secondary to PE (n = 13, 1.80%)

Diagnosis	No of cases	Criteria
Definite PE	2 (0.27%)	CT scan or autopsy diagnosis of PE
Probable PE	3(0.42 %)	Wells score > 6, with evidence of <u>malignancy</u> and no other obvious cause of death like infection (normal CRP or CV event)
Suspected PE	8(1.1%)	Wells score > 6, with <u>no other obvious cause</u> of death

VTE : Tan Tock Seng Hospital



- Patients with confirmed diagnosis of DVT / PE
- March – Sep 2010 (6 months)
- No of VTE : 30 days of prior or current admission* = 86
 - Medical (22)



*No documentation of DVT / PE on admission

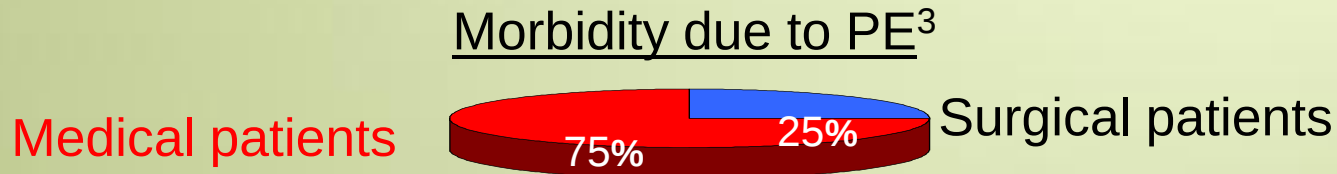
VTE at TTSH

New VTE including DVT/ PE /Both – 2 years (Oct. 2010 – Dec. 2012)

Number of VTE Patients	Total	LL- DVT	PE	Both
	314	177(67% Prox.)	91(28.9%)	46(14.6%)
Demographics	Mean Age		Male	Female
	64.2 (SD +/- 0.9)		132(42%)	182(52%)
Ethnicity	Chinese	Malay	Indian	Others
	212 (67.5%)	39 (12.4%)	34 (10.8%)	29(9.3%)
Hospitalization (Within 1 month)	Total	Medical	Surgical	
	127(40.4%)	76(59.8%)	51(40.2%)	

Acutely Ill Medical Patients are the most vulnerable

- Acutely ill medical patients
 - ~60% of all hospital admissions¹
 - $\frac{3}{4}$ of the fatal PE occurring in the hospital²



1. Cohen AT. Semin Thromb Hemost 2002;28 S3:13-7.

2. Sandler DA, et al. J R Soc Med 1989;82(4):203-5.

VTE prophylaxis remains substantially underutilized in medical patients

- VTE prophylaxis remains substantially underutilized in medical patients
 - Non surgical patients are less likely to receive prophylaxis than surgical patients
 - Recent studies show that up to 2/3 of medical patients do not receive appropriate thromboprophylaxis

Why is VTE Prophylaxis Underutilised in Medical Patients

- **Heterogeneity of the conditions** in medical patients, makes it difficult to assess risk level of patients.
- **Lack of evidence for a mortality reduction** associated with pharmacologic prophylaxis in acutely ill medical patients
- Other Concerns
 - bleeding
 - unfamiliarity with anticoagulants,
 - cost of prophylaxis, particularly in the developing countries

TTSH VTE Prophylaxis Guidelines

- ▶ 2014– TTSH VTE Prophylaxis Guidelines Workgroup
Pankaj Handa et al.
- ▶ Hospital patients are a heterogeneous population. Therefore, all patients must be routinely assessed for risk of thromboembolism and bleeding prior to initiation of VTE prophylaxis.
- ▶ Following patient groups are excluded from VTE risk assessment
 - Patients attending emergency department
 - Patients attending day care surgery/endoscopy
 - Patients under the age of 18 years
 - Patients already on anticoagulation (VKA, NOAC, Heparin)

TTSH VTE Prophylaxis Guidelines

1. Risk Stratification

Consider patient at increased risk of VTE if they have :

Risk Factors	Points
Active cancer	3
Previous VTE (personal/ first degree relative)	3
Reduced mobility	3
Known thrombophilic condition	3
Recent Surgery(<1 month)	1
Elderly(>70yrs)	1
Heart and \ or Respiratory failure	1
Acute myocardial infarction/ ischaemic stroke	1
Acute infection and/ or rheumatologic disorder	1
Ongoing Hormonal Treatment	1
Obesity (BMI more than 30 kg/m ²)	1

TTSH VTE Prophylaxis Guidelines

2. Bleeding Risk Assessment

- ▶ Consider high bleeding risk if the patient has :

Active bleeding

Platelet count $< 75 \times 10^9/L$

Recently diagnosed peptic ulcer

Liver Disease (INR > 1.5) / Severe Renal Disease (Cr Cl < 30 ml/mt)

Acute Stroke

Lumbar puncture/ epidural /spinal anaesthesia in previous 4 hours / in next 12 hours

Uncontrolled hypertension ($> 230/120$ mmHg)

Age > 85 years

Inherited Bleeding Disorders(e.g. Haemophilia)

Acutely Ill Hospitalised Medical Patients

Classify patients into - High Risk VTE: 4 or >
- Low Risk VTE: < 4

Asses the risk of thrombosis and bleeding (based on tables 1 and 2) All hospitalized medical patients who have had or are expected to have reduced mobility for more than 72 hours	Recommendations - High risk VTE : LMWH/ UFH - Low risk of VTE: No VTE prophylaxis - High VTE risk and High Bleeding risk : Mechanical prophylaxis. Once bleeding risk decreases consider switching over to pharmacologic prophylaxis - <u>Duration</u> - until resolution of medical illness /discharge. Do not extend after hospital discharge
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Orthopaedic Surgery

Type of Surgery	VTE Prophylaxis	Duration
THR and TKR	-On Admission: Offer mechanical prophylaxis to all - Post Operatively: Add pharmacological prophylaxis, if No contraindications. Choose any ONE of following: - LMWH / UFH : 12 hours after surgery - Rivaroxaban : 12 hours after surgery - Apixaban : 12 hours after surgery	Mechanical Prophylaxis: Till there is no significant immobility Pharmacological Prophylaxis: Minimum: 10-14 days Preferably : 35 days from the date of surgery
Hip Fracture surgery	On Admission: Offer mechanical prophylaxis to all - Add pharmacological prophylaxis, if NO contradictions (Table 2) - Choose either of LMWH /UFH Start on admission Stop 12 hours before surgery Resume 12 hours after surgery	Mechanical Prophylaxis: Till there is no significant immobility Pharmacological Prophylaxis: Minimum: 10-14 days Preferably : 35 days from the date of surgery
Knee Arthroscopy AND Below Knee Injuries	Consider VTE prophylaxis if the VTE risk is assessed to be High. - Offer mechanical prophylaxis on admission - Add pharmacological prophylaxis post operatively if Bleeding risk is considered Low. Continue VTE prophylaxis till patients no longer has significantly reduced mobility	

Non Orthopaedic Surgery

Risk	Type of surgery	Recommended prophylaxis
High	• Multiple trauma • Major surgery at age > 60 years • Major surgery at age 40-60 years with risk factors (Table 1) • Major surgery at any age + history of VTE	• LMWH / UFH (12 hours post operatively once the bleeding risk is considered Low) and IPCD • IPCD only if anticoagulants contraindicated
Intermediate	• Major surgery, age 40-60 years without risk factors • Minor surgery, age < 40 with risk factors (Table 1) • Minor surgery, age > 60 years • Minor surgery, < 60 years with risk factors	• LMWH/UFH with / without TED/IPCD
Low	• Major surgery, age < 40, without risk factors • Minor surgery, age < 60, without risk factors	• Consider TED/ IPCD

Major surgery – intra-abdominal surgery or any general surgery operation >45 minutes . #Minor surgery – surgeries <45 minutes (other than intra-abdominal surgery) using general or regional anaesthesia

Pharmacological Prophylaxis

LMWH : the drug of choice in most of the patients (Cr Cl >30)

UFH : the drug of choice in patients with renal failure (Cr Cl < 30 ml /mt)

NOACs : Avoid use in patients with renal failure

Weight	<50kg	50–100 kg	100–150 kg
Cr Cl < 30 ml/m	UFH 5000 units BD SC	UFH 5000 units BD SC	UFH 7500–10000 units BD SC
Cr Cl > 30 ml/m	* Enoxaparin 20mg OD SC	Enoxaparin 40mg OD SC	Enoxaparin 40mg BD SC
NOACs	Rivaroxaban 10 mg po OD / Apixaban 2.5 mg BD		
	Dabigatran : Initial dose of 110mg, taken within 1–4h post-op continue with 220mg OD thereafter		

Take Home Message

- ▶ VTE is a Global disease. There is Good Evidence in literature that is a significant problem is Asia as well.
- ▶ Despite significant advances in the prevention and treatment, PE remains the most common preventable cause of hospital death.
- ▶ High incidence of VTE and the availability of effective methods of prevention mandate that VTE prophylaxis should be considered in suitable hospitalised patients