

IMPROVING DVT PREVENTION, DETECTION AND TREATMENT IN HIGH-RISK SPECIALTIES: PART II

Strategies to improve DVT prophylaxis, early identification, treatment and post discharge follow-up in the **Obstetrics/Gynecology**, and **Neurology** patients

Wednesday, September 10, 2008

Eastern: 12:30 – 2 p.m.

Central: 11:30 a.m. – 1 p.m.

Mountain: 10:30 a.m. – 12 p.m.

Pacific: 9:30 – 11 a.m.

This program will offer a live webcast during the first air date and will continuously stream thereafter. A link to the programs webcast will be available on the DVT program information page located at www.crmhealthcare.net

This program is being provided by:



The Research and Education Institute

for Texas Health Resources

This program is supported by an educational grant from
GlaxoSmithKline and sanofi-aventis U.S.

ABOUT THE PROGRAM

Each year, approximately two million people in the United States develop deep vein thrombosis (DVT), the most common form of venous thromboembolism. Diagnostic testing, however, has identified five groups of patients at particularly high risk of developing venous thromboembolic (VTE) disease: cardiac, gynecologic, neurologic, orthopedic, and oncology patients. The risk differs across various subgroups of these patient types, over the natural history of the diseases or conditions, and based upon treatment selected. Despite overwhelming data that prophylaxis is very effective at reducing these events; prophylaxis for venous thromboembolism in these critical patient subpopulations remains largely underutilized. Various factors account for underutilization, including poor knowledge on the part of both providers and patients. Because VTE prophylaxis recommendations differ for the various surgical settings or medical conditions, the immediate challenge in the management of DVT and pulmonary embolism (PE) is to improve the rates of prevention and detection of this potentially fatal yet preventable disease.

National experts will discuss barriers and provocative issues in DVT management, and will share mission-critical strategies to address this major cause of morbidity and mortality for these patient groups accounting for approximately half of hospital admissions. **Part I** will focus on the cardiac and orthopedic patients and the incidence and impact of factors related to DVT for these patients. **Part II** will focus on the gynecology and neurology patients. **Part III** will focus on the hospitalized and ambulatory cancer patient. Each program will highlight the VTE guidelines with emphasis on the specialty, and discuss VTE risk assessment, utilization of appropriate prophylaxis, prevention, treatment, and long-term management. Performance improvement recommendations will be made for the care of patients with DVT/PE.

TARGET AUDIENCE

This program is designed for neurologists, neurovascular surgeons, intensivists, cardiologists, cardiovascular surgeons, obstetricians and gynecologists, orthopedic surgeons, oncologists, hospitalists, advanced practice nurses, primary care physicians, and any other healthcare professionals involved in the prevention, diagnosis, or treatment of venous thromboembolism (VTE).

LEARNING OBJECTIVES

Upon completion of this activity, those participating in this activity should be able to:

1. Describe the impact of DVT/PE in the five specialties for patients in the US and to appreciate the world wide impact of VTE
2. Identify relevant DVT/PE recommendations and guidelines, including those of the ACCP, CMS and relevant professional societies
3. Define high risk groups for venous thromboembolism in hospitalized patients
4. Identify clinical factors that contribute to thromboembolic risk in the orthopedic, oncology, cardiology, neurology, and OB/GYN patient
5. Describe recommended strategies for prevention of venous thromboembolism for various risk groups

6. Discuss therapeutic approaches for thromboprophylaxis, including the risks and benefits associated with anticoagulants, low-molecular-weight heparins, and mechanical methods
7. Identify patients who qualify for extended-duration prophylaxis
8. Appropriately document DVT/PE patient care (including risk assessment, prophylaxis, and patient discharge instructions)

FACULTY

MEDICAL MODERATOR

William A. Brock, MD, FCCM, FCCP, FACP
Vice President, Chief Quality Officer
Presbyterian Hospital of Plano
Plano, Texas

FACULTY

Neurology

Joseph A. Caprini, MD, MS, FACS
Professor, Department of Surgery
Feinberg School of Medicine
Northwestern University
Chicago, Illinois

Gynecology

Thomas C. Krivak, MD
Assistant Professor
Department of Obstetrics, Gynecology and Reproductive Sciences
Division of Gynecologic Oncology
University of Pittsburgh Medical Center
UPMC Cancer Center at Magee-Womens Hospital
Pittsburgh, Pennsylvania

Moderator

Sonja Van Sickle

CME/CE CREDITS AWARDED

ACCREDITATION

PHYSICIAN

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NURSING

Presbyterian Hospital of Plano, Education Department, has approved this program for 3 this program for 3 contact hours (1.5 contact hours for each activity). This program has been approved by the American Association of Critical-Care Nurses (AACN).

RECEIVING A CERTIFICATE OF ATTENDANCE OR CME/CE CREDIT

Successful completion of this CE activity includes the following:

1. Attend the live broadcast or rebroadcast program.
2. At the program, sign in on the Sign-in Sheet.
3. Attend the entire session.
4. Complete an Evaluation Form and a Credit Request Form. Submission information will be on the forms.

A continuing education certificate will be mailed to participants who successfully complete program requirements following the activity.

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Joseph A. Caprini, MD, MS, FACS, is a consultant for Sanofi-Aventis, Coudien, GlaxoSmithKline, Convatec, and Eisai; has received Honoraria from Sanofi-Aventis, Coudien, GlaxoSmithKline, Convatec, and Eisai.

Thomas C. Krivak, MD, has no relevant financial relationships to report.

Venous Thrombosis A Leading Cause of Death in the US

- VTE kills 4 to 5 times more people annually than breast cancer or AIDS^{1,2}
- Pulmonary embolism is the cause of death in ~300,000 patients per year in the US¹
- In-hospital case fatality rate of VTED¹ = 12%
- PE: 1-year mortality rate of 39% in the elderly³
- DVT: 1-year mortality rate of 21% in the elderly³

PE may be the #1 preventable cause of death in hospitalized patients⁴

1. ACS. Breast cancer facts and figures, 2001.
 2. Anderson, et al. Arch Intern Med 1991.
 3. Kniffin WD Jr, et al. Arch Intern Med 1994;154(8):861-6.
 4. Claggett, et al. Chest 1995;108:312S-334S.

Estimated Annual Number of Incident and Recurrent Non-Fatal and Fatal VTE in U.S.

An incidence-based model was developed based upon the event-specific incidence rates in Olmstead County, MN and Yr. 2000 US census data.

Site of VTE

Non-fatal	Community	Hospital	Total
DVT	108,240	268,125	376,365
PE	85,358	151,700	237,058
TOTAL	193,598	419,825	613,423
Fatal			
DVT	649	1,609	2,258
PE	105,902	188,210	294,112
TOTAL	106,550	189,819	296,370

Abstract 910: Heit JA, Cohen AT, Anderson Jr FA, for the VTE Impact Assessment Group

Economic Impact of the Postphlebotic Syndrome

- Represents a permanent disability
- 2,000,000 work days lost annually
- 15 million Americans afflicted
- 4% of the US population has or will develop a venous leg ulcer
- 2 billion pounds spent in the United Kingdom/year on venous disease
- Preventable if thrombosis prophylaxis routinely employed

Nicolaides et al. Int. Angiol. 1997;16(1):3-38

Post Thrombotic Syndrome



The Evidence

Clot in a PFO as seen at surgery

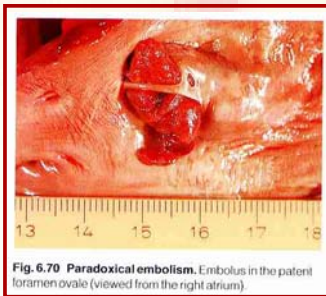


Fig. 6.70 Paradoxical embolism. Embolus in the patent foramen ovale (viewed from the right atrium).

Picture taken from [Colour Atlas of the CV System](#), Thomas et al.

Problem/Question

- Is PFO really implicated in cryptogenic stroke ?
- Prevalence of PFO in "Normal" Population
 - >10% - Lechat, et al - NEJM 5/88 (echo)
 - >15% - Webster, et al - Lancet 1988 (echo)
 - >25% - Mayo Autopsy Study

Problem/Question

- Is PFO really implicated in cryptogenic stroke ?
 - Prevalence PFO in Stroke Population <60 y.o.
 - 47% - Ranous, Mas, et al - STROKE 1/93
 - 50% - Webster, et al - Lancet 1988
 - 41% - Lausanne Study - Neurology 5/96
 - 40% - Lechat, et al - NEJM 5/88

The Many Faces of Venous Thromboembolism

- Prevent Fatal pulmonary emboli
 - 1-5% incidence in patients with >4 risk factors
 - 16.7% mortality at 3 months
 - 25% of those with Pulmonary emboli present as sudden death
- Prevent clinical venous thromboembolism
 - Morbidity, drugs, tests, hose, changes in lifestyle
- Prevent silent venous thromboembolism
 - Risk of subsequent event double that of control population
- Prevent embolic stroke (20-30% PFO rate)
 - 50% disabled; 20% die; 30% recover
- Prevent the post thrombotic syndrome
 - 25% incidence following DVT and 7% severe
 - May not be evident for 2-5 Years

Absolute Risk of DVT in Hospitalized Patients

Patient Group	DVT Prevalence, %
• Medical patients	10-20
• General surgery	15-40
• Major gynecologic surgery	15-40
• Major urologic surgery	15-40
• Neurosurgery	15-40
• Stroke	20-50
• Hip or knee arthroplasty, hip fracture surgery	40-60
• Major trauma	40-80
• Spinal cord injury	60-80
• Critical care patients	10-80

Chest. 2004;126:338S-400S. PMID: 15383478.

DVT in Gyn Oncology Surgery

• Walsh	1974	16/45	35%
• Bernstein	1980	14/39	36%
• Crandon	1983	30/79	40%
• Clarke-Pearson	1983	<u>63/382</u>	<u>17%</u>
		123/545	23%

Venous Thromboembolism

- Scope of Problem
 - Total VTE exceed total myocardial infarctions/year
 - Total VTE related deaths exceed myocardial infarction related deaths
 - 2.5 million cases DVT/yr
 - Approximately 40% of postoperative deaths in gynecologic surgery due to VTE

AHA 2006 Statistics

Virchow's Triad

The diagram consists of three overlapping orange circles arranged in a triangle. The top-left circle is labeled 'Venous Stasis', the top-right circle is labeled 'Vascular Injury', and the bottom-center circle is labeled 'Hypercoagulability'.

Chronic Venous Stasis



Risk Factors for VTE in Gynecologic Surgery

- Obesity
- Pelvic surgery
- Venous stasis
- Prior VTE
- Hormone therapy
- Thrombophilias

Clarke-Pearson, Obstet Gynecol 1987;69:146

Risk Factors for VTE in Gynecologic Surgery

- Age >40 >60
- Prior radiation therapy
- Prolonged Surgery > 4 hours
- Varicose veins

Clarke-Pearson, Obstet Gynecol 1987;69:146

Levels of Thromboembolism Risk in Surgical Patients without Prophylaxis

Level of risk	Calf DVT, %	Proximal DVT, %	Clinical PE, %	Fatal PE, %
Low - 1	2	0.4	0.2	<0.01
Moderate 2	10-22	2-4	1-2	0.1-0.4
High 3-4	20-40	4-8	2-4	0.4-1.0
Very High >4	40-80	10-20	4-10	0.2-5

Geerts WH, et al. Chest 2004; 125: 338S-406S

ACOG VTE Assessment

Level of Risk	Definition
Low	Age <40, surgery <30 minutes
Moderate	Age >40, any duration, no additional risk factor
High	Age >60 with surgery <30 min., Major surgery >40 additional risk factor
Highest	Age >60 with major surgery, plus prior VTE, cancer, or hypercoagulable state

ACOG Practice bulletin No 84, November 2007

Performance Measures Likely to Become JCAHO Mandates*

1. Proportion of inpatients with documented VTE risk assessment, receipt of VTE prophylaxis, or documented contraindication within 24 hours of hospital arrival
2. Proportion of patients with documented VTE risk assessment, receipt of VTE prophylaxis, or documented contraindication within 24 hours of transfer to the ICU

*Partial list of candidate measures

The nurses already have risk assessment fatigue since they are required to screen for fall risk, bedsore risk, etc.

Why wouldn't we have an assessment for the number one cause of in-hospital patient deaths---DVT???

Risk Factor Weighting*

- Major risk factors (3 points each)
 - Cancer
 - Prior VTE
 - Hypercoagulable states
- Intermediate risk factor (2 points)
 - Major surgery
- Minor risk factors (1 point each)
 - Advanced age (>70 years)
 - Obesity (BMI> 29)
 - Hormone replacement therapy or oral contraceptives
 - Bed rest (active order not related to surgery)

***Score of 4 or more require prophylaxis**

Kucher et al. NEJM; V352:969-977, 2005

Physician Assessment

Patient Intake Form

1. Personal History of DVT or PE
2. Family History of DVT or PE
3. Malignancy: Current or Previous
4. Personal History of Recent MI or stroke (≤ 1 month)
5. Recent Major Surgery (≤ 1 month)
6. Currently on BCP, HRT, or hormonal therapy for Breast or Prostate Cancer
7. Current or recent acute inflammatory or infectious process (≤ 1 month)
8. Currently immobile (unable to ambulate in the in-patient setting)
9. History of unexplained stillborn infant, recurrent spontaneous abortion, Premature birth with preeclampsia or growth-restricted infant.
10. Swollen legs
11. Varicose Veins
12. Obesity (BMI ≥ 30)
13. Age

Venous Thromboembolism Risk Factor Assessment

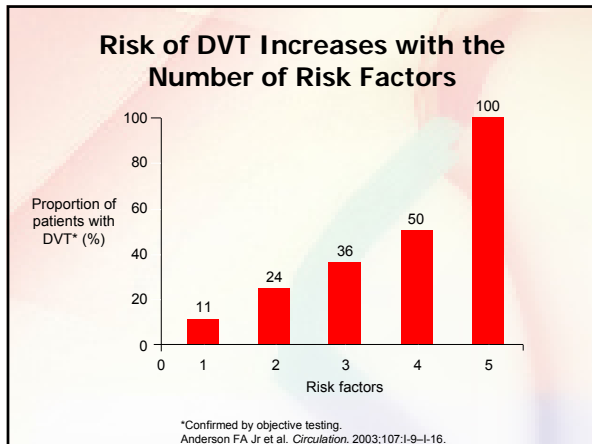
Patient's Name: _____ Age: ____ Sex: ____ Wgt: ____ RR: _____

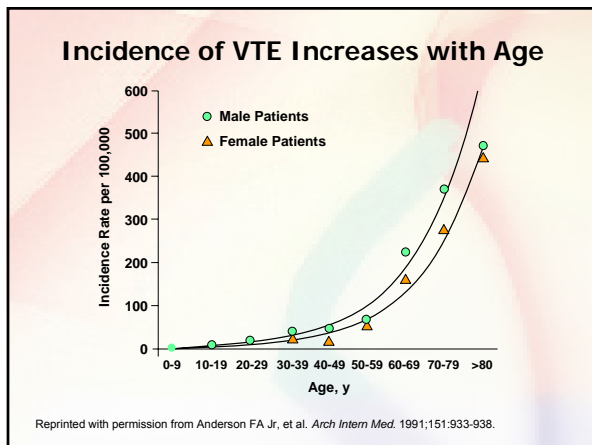
Choose All That Apply

Each Risk Factor Represents 1 Point <ul style="list-style-type: none"> <input type="checkbox"/> Age 41-69 years <input type="checkbox"/> Prior surgery performed <input type="checkbox"/> History of prior major surgery <input type="checkbox"/> Venous stasis <input type="checkbox"/> History of inflammatory bowel disease <input type="checkbox"/> Swollen legs (current) <input type="checkbox"/> Obesity (BMI >30) <input type="checkbox"/> Acute myocardial infarction (< 1 month) <input type="checkbox"/> Congestive heart failure (< 1 month) <input type="checkbox"/> Stroke (< 1 month) <input type="checkbox"/> Smoking lung disease (no pneumonia (< 1 month) <input type="checkbox"/> Abnormal pulmonary function (COPD) <input type="checkbox"/> Medical patient currently at bed rest <input type="checkbox"/> Leg greater than or beside <input type="checkbox"/> Other risk factors 	Each Risk Factor Represents 2 Points <ul style="list-style-type: none"> <input type="checkbox"/> Age 65-74 years <input type="checkbox"/> Major surgery (>60 minutes) <input type="checkbox"/> Anticoagulant surgery (>60 minutes) <input type="checkbox"/> Laparoscopic surgery (>60 minutes) <input type="checkbox"/> Previous malignancy <input type="checkbox"/> Central venous access <input type="checkbox"/> Morbid obesity (BMI >40)
Each Risk Factor Represents 3 Points <ul style="list-style-type: none"> <input type="checkbox"/> Age over 75 years <input type="checkbox"/> Major surgery lasting >3 hours <input type="checkbox"/> BMI > 50 (severe obese syndrome) <input type="checkbox"/> History of DVT, DVT/PE <input type="checkbox"/> Family history of DVT/PE <input type="checkbox"/> Chronic use of chemotherapy <input type="checkbox"/> Positive Factor V Leiden <input type="checkbox"/> Positive Prothrombin 20210A <input type="checkbox"/> Elevated serum homocysteine <input type="checkbox"/> Positive Lupus anticoagulant <input type="checkbox"/> Elevated antithrombin antibodies <input type="checkbox"/> Fibrinogen-induced thrombocytopenia (FIT) <input type="checkbox"/> Other thrombophilia 	For Women Only (Each Represents 1 Point) <ul style="list-style-type: none"> <input type="checkbox"/> Oral contraceptives or hormone replacement therapy <input type="checkbox"/> Pregnancy or postpartum (<1 month) <input type="checkbox"/> History of unexplained stillborn infant, recurrent spontaneous abortion (≥ 3), perinatal loss with toxemia or growth-restricted infant

Total Risk Factor Score

Please see Following Page for Physicians Safety Considerations. Revised November 4, 2005





Venous Thromboembolism after Acute Ischemic Stroke

- Up to 75% of stroke patients with hemiplegia who are not treated with thromboprophylaxis develop DVT
- Up to 20% develop a pulmonary embolism (PE)
- PE is fatal in 1% to 2% of acute ischemic stroke patients
- PE accounts for 25% of early mortality after stroke

Sherman et al. *Lancet*. 2007;369:1347-1355.

DVT FREE Registry

Key Findings

- 71% (3894/5451) Of all patients, including 2295 nonsurgical patients, received no prophylaxis in the 30 days before the diagnosis of DVT

Prophylaxis is underutilized!

Goldhaber SZ et al. *Am J Cardiol.* 2004;93:259-262.

Despite Evidence – Medical Patients at Risk Remain Unprotected

ENDORSE¹

	Medical	Surgical
No. of patients	37,356	30,827
At risk for VTE	42%	64%
Receiving ACCP Tx	40%	59%

IMPROVE²

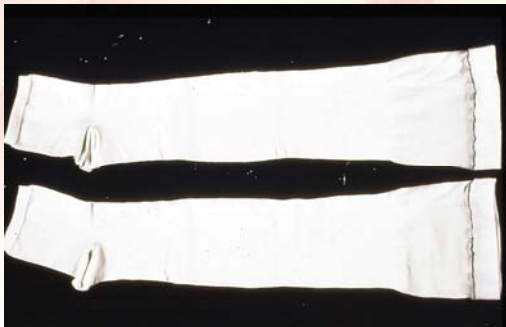
	United States	Other Countries
No. of patients	3,410	11,746
VTE prophylaxis	1852 (54%)	5788 (49%)
LMWH	476 (14%)	4657 (40%)
UFH	717 (21%)	1014 (9%)

1. Cohen AT, et al. Presented at: ISTH, July 8-11, 2007; Geneva, Switzerland.
2. Tapson VF, et al. *Chest.* 2007;132:936-945.

Prophylaxis-Methods

- Mechanical
 - Graduated compression stockings
 - Pneumatic compression devices
- Pharmacologic
 - Unfractionated Heparin
 - Low Molecular Weight Heparin
- Dual “Combination” Prophylaxis
- IVC Filters

Graduated Compression Stockings

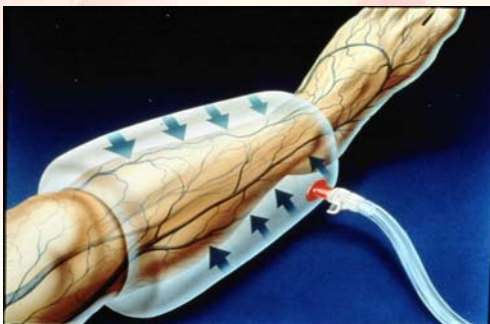


Graduated Compression Stockings

- Increases blood return by 20% over baseline
- Risk reduction 24-60%
- Body habitus prevents safe use in 15-20% of cases

Clarke-Pearson et al: Obstet Gynecol 1983;61:87-94

External Pneumatic Compression



Prevention of Venous Thromboembolism

- Pneumatic compression
- Few complications
- Placed prior to induction anesthesia
- Few contraindications

External Pneumatic Compression

- Augments blood return 180-240% over baseline
- Activates prostaglandin mediated fibrinolysis,¹ urokinase, TPA, and endothelial relaxing factor
- Should be applied prior to induction of anesthesia
- Compliance may be suboptimal in some centers

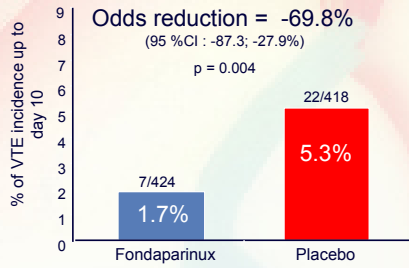
¹Knight et al: Lancet 1976;Dec 11:1265-8.

External Pneumatic Compression

Duration	% DVT		P
	Controls	EPC	
Perioperative ¹	12.4%	18.6%	NS
5 days ²	34.6%	12.7%	<0.005

¹Clarke-Pearson: Gyn Oncol 1984;18:226
²Clarke-Pearson: Obstet Gynecol 1984;63:92

VTE Prophylaxis in General Surgery



- Lowest venographic DVT rate ever seen in general surgery

Turpie, AG et al JTH 5 pgs 1854-1861, 2007

IPC in the Prevention of DVT

Effect of intermittent pneumatic compression (IPC) in the prevention of DVT diagnosed by surveillance with objective methods in non-orthopedic surgical randomized controlled studies (fibrinogen uptake test or phlebography)

Author	Control Groups		Intermittent Pneumatic Compression	
	Number of patients	DVT (%)	Number of patients	DVT (%)
Borow et al.	89	32 (36)	79	9 (11)
Butson	57	4 (7)	62	6 (10)
Clark et al.	36	7 (19)	37	1 (3)
Clarke-Pearson et al.	52	18 (35)	55	7 (13)
Coe et al.	24	6 (25)	29	2 (7)
Hillis et al.	50	15 (30)	50	6 (12)
Roberts et al.	104	27 (26)	94	6 (6)
Sabri et al.	39	12 (31)	39	2 (5)
Skillman et al.	48	12 (25)	47	4 (9)
Turpie et al.	96	20 (21)	103	8 (8)
Turpie et al.	63	12 (19)	65	1 (2)
Overall	658	165 (26)	660	52 (8)

Relative risk: 0.31 (95% CI 0.33 to 0.42)

VTE- Pharmacologic Prophylaxis

- Unfractionated Heparin (bid & tid doses)
- Low Molecular Weight Heparin
- Warfarin
- New agents

Low Dose Heparin-Gynecology

	No Therapy	Heparin
Ballard et al 110	29%	3.6%
Taberner et al 145	23%	6%

Low Dose Heparin-Oncology

	DVT
No therapy (n=97)	12 (12.4%)
Unfractionated Heparin (N=88) (q 12 hour dosing)	13 (14.8%)

Clarke-Pearson et al, AM J Obstet Gynecol 1983;145:606

Low Dose Heparin-Oncology

	DVT
Controls (n=103)	18%
Unfractionated Heparin (n=104) (q 8hr dosing)	9.6%
Unfractionated Heparin (n=97) (load with q8hr dosing)	6%

Clarke-Pearson et al, Obstet Gynecol 1990;75:684

Unfractionated Heparin

<u>Regimen</u>	<u># Trials</u>	<u># DVT (%)</u>
5000 Units Q 12 hr	34	289/2446 (11.8%)
5000 Units Q 8 hr	15	153/2039 (7.5%)

Clagett et al: Ann Surgery 1988;208:227-40

LMWH Compared to Unfractionated Heparin

	UFH (N=286)	LMWH (N=280)
DVT	1 (0.3%)	0 (0%)
PE	1 (0.3%)	5 (1.8%)
Blood Transfusion	57 (19.9%)	39 (13.9%)

>80% of patients with gynecologic malignancy

Ward et al Aust NZJ Obstet Gynecol 1998;38:91-95

- ### VTE Prophylaxis after Abdominal Surgery
- Data from 16 clinical trials conducted 1980-2003
 - Trials selected based on initial computerized literature search including PubMed, EMBASE
 - Compared LMWH vs UFH, placebo, or other LMWH
 - Risk stratification varied among studies
 - No formal statistical meta-analysis performed due to above listed differences
- Bergqvist D. Br J Surg. 2004;91:965-974.

VTE Prophylaxis after Abdominal Surgery

Conclusions:

- Patients undergoing abdominal surgery should be stratified by risk for thromboembolism and managed accordingly
- LMWH is a recommended alternative to UFH in moderate- or high-risk patients
- In patients with cancer:
 - High-dose LMWH may offer increased benefits without increased bleeding
 - Extended 4-week period of prophylaxis appears beneficial

Bergqvist D. *Br J Surg*. 2004;91:965-974.

Advantages of LMWH

- More predictable anticoagulant response
- Better bioavailability at lower doses
- Longer half-life; constant despite dosage
- Renally-excreted
- Less immunogenic
- Less risk of osteoporosis
- Laboratory monitoring unnecessary

Bonew: *Thromb Res* 2000;100:V113-20

Obstetrics Prophylaxis Case

- Patient is 26 weeks pregnant with PPRM and was placed on bed-rest
 - What prophylaxis
- Develops DVT
 - How would you treat
 - Peri-partum management of anticoagulation

Obstetrics and VTE Prophylaxis

- Women who are pregnant or postpartum are 4 x increased risk for VTE complications
 - 80% DVT
 - 20% PE
- Overall risk for VTE is 2 per 1,000 births
- Anticoagulation is safe during pregnancy
- UFH and LMWH do not cross placenta

Obstetrics and VTE Prophylaxis

- Options include UFH or LMWH
- LMWH q 12 hour dosing
- Monitoring Factor Xa levels monthly
- Dosing requirements may need to be increased during pregnancy (GFR)
- Change to UFH at 36 to 37 weeks
- Postpartum change to LMWH and warfarin for 3-6 months

Obstetrics and VTE Prophylaxis

- Would you recommend Thrombophilia workup?
- Would you use prophylaxis next pregnancy?
- How would you manage if patient had prior DVT and positive Thrombophilia evaluation?
- How long would you use prophylaxis postpartum?

Obstetrics and VTE Prophylaxis

Risk Factor	OR	CI
Thrombophilia	51.8	38.7-69.2
Prior VTE	24.8	17.2-36
APS	15.8	10.9-22.8
Lupus	8.7	5.8-13.0
Heart disease	7.1	6.2-8.3
Obesity	4.4	3.4-5.7
Cesarean Section	2.1	1.8-2.4

James AH, Am J Med 2007;120:S26-S34.

Obstetrics and VTE Prophylaxis

Risk	Example	Prophylaxis
Low	Transient risk factors, FH of VTE	SCD intra-partum
Moderate	H/o APO, H/o VTE, Thrombophilia with Family h/o VTE	LMWH ante-partum and postpartum (QD dosing)
High	Idiopathic VTE, VTE with thrombophilia, APS	LMWH ante and postpartum BID dosing
Highest Risk	H/O APS, antithrombin deficiency	Therapeutic full anticoagulation, full anticoagulation 6 weeks postpartum

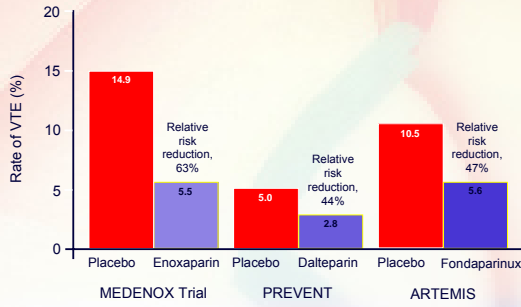
Duhl et al Am J Obstet Gynecol 2007;197:457

ACOG Prophylactic Regimens

Unfractionated Heparin	
Low Dose	5,000-7,500 U q12 7,500-10,000 U q12 10,000 U q12
Adjusted Dose	> 10,000 U tid APTT 1.5-2.5
LMWH	
Low Dose	Enoxaparin 40mg qd/bid Dalteparin 5,000U qd/bid
Adjusted Dose	Enoxaparin 30-80mg q12 Dalteparin 5,000-10,000U q12

ACOG Practice Bulletin Number 18, August 2000

Results of Trials of Prophylaxis for VTE in High-Risk Hospitalized Patients



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Medications and Doses for VTE Prophylaxis in Hospitalized Medical Patients

Medications and Doses for Prophylaxis of VTE in Hospitalized Medical Patients*

Drug [†]	Dose	Comment
Unfractionated heparin	5000 U subcutaneously, every 8 hr [‡]	
Low-molecular-weight heparins		
Enoxaparin	40 mg subcutaneously, once daily	More expensive than heparin; 20 mg daily not effective
Dalteparin	5000 U subcutaneously, once daily	More expensive than heparin
Fondaparinux [§]	2.5 mg subcutaneously, once daily	More expensive than heparin

* Anticoagulant prophylaxis should not be used if there is a risk of excessive bleeding, such as in patients with active or recent gastrointestinal bleeding, hemorrhagic stroke, or hemostatic defects such as severe thrombocytopenia.

[†] Unfractionated heparin and low-molecular-weight heparins should not be used in patients with current or previous heparin-induced thrombocytopenia.

[‡] A dose of 5000 U given subcutaneously every 12 hours has also been used. Expert opinion favors 8-hour dosing, although the 8- and 12-hour regimens have not been directly compared.

[§] Fondaparinux is approved by the Food and Drug Administration for prophylaxis in surgical patients, but the same regimen has been used in medical patients.

Reprinted with permission (requested) from Francis. *N Engl J Med.* 2007;356:1438-1444.

EXCLAIM: Extended-Duration Enoxaparin Prophylaxis in High-Risk Medical Patients

End points	Extended prophylaxis n=2013 (%)	Placebo n=2027 (%)	RR reduction (%)	P value
VTE events	2.8	4.9	44	.001
Symptomatic	0.3	1.1	73	.004
No Symptoms	2.5	3.7	34	.032

NNT = 46 patients to avoid one VTE event.

NNT = 224 to result in one major bleeding event.

Major bleeding occurred in 12 patients receiving enoxaparin and 3 patients receiving placebo (0.6% vs 0.1%; *P* = .0192).

Hull RD, et al. Abstract presented at: ISTH, July 8-11, 2007, Geneva, Switzerland.

**Venous Thromboembolism-
Prophylaxis**

- Dual prophylaxis
 - Highest risk patients
 - Combination pneumatic compression devices with Heparin
 - Not well studied
 - Practice is performed in highest-risk gynecologic oncology patients

Martino MA Gynecol Oncol 2007;106:439-445

**Practice Patterns Regarding
Dual Prophylaxis**

- 343/1073 SGO members completed surveys
- 41% preferred single modality prophylaxis with EPC
- 42% preferred dual prophylaxis
 - 73% recommended addition of LMWH to EPC after major surgery
 - 10% recommended addition of LMWH to EPC after minor surgery
- 17% preferred pharmacologic agent

Martino MA Gynecol Oncol 2007;106:439-445

Combination Prophylaxis

- Prospective study of gynecologic oncology patients
 - Protocol of SCD with Heparin or LMWH
 - 324 patients – 6 (2%) diagnosed with VTE
 - 298 patients 2005- 21 (7%)
 - OR=0.31 (95% CI 0.12-0.81)
 - Similar patient characteristics
 - No difference in postoperative complications

Einstein M, et al Gynecol Oncol 2008;108:S20 (presented SGO 2008 abstract 42)

DVT Prophylaxis in Stroke Patients Using a Combination of Physical and Pharmacological Methods

Patient Event	Heparin/Hose	Heparin/Hose/ Compression	P
All DVT	21/233 (9.0%)	1/432 (0.23%)	<0.001
All PE	6/233 (2.6%)	0/432 (0%)	0.002
Nonambulatory DVT	20/79 (25.3%)	1/148 (0.68%)	<0.001
Nonambulatory PE	6/79 (7.6%)	0/148 (0%)	0.002

Adapted with permission (requested) from Kamran et al. *Neurology*. 1998;50:1683-1688.

PREVAIL Study Design

- 1762 patients with acute ischemic stroke
- Patients unable to walk unassisted
- Enoxaparin 40 mg SC once daily versus UFH 5000 U SC twice daily for 10 days
- Efficacy end point: 14-day occurrence of VTE
- Safety end points: symptomatic intracranial hemorrhage, major extracranial hemorrhage, all-cause mortality up to 48 h
- 90-day follow-up

PREVAIL = Prevention of VTE After Acute Ischemic Stroke With LMWH Enoxaparin.

Sherman et al. *Lancet*. 2007;369:1347-1355.

PREVAIL: Incidence of VTE Up to Day 14

	Enoxaparin (n=666)	UFH (n=669)	RR (95% CI)	P
VTE	68 (10%)	121 (18%)	0.57 (0.44–0.76)	0.0001
PE	1 (<1%)	6 (1%)	0.17 (0.02–1.39)	0.059
Symptomatic VTE	2 (<1%)	7 (1%)	0.29 (0.06–1.38)	0.096
All DVT	67 (10%)	118 (18%)	0.57 (0.43–0.75)	<0.0001
Proximal	30 (5%)	64 (10%)	0.47 (0.31–0.72)	0.0003
Distal	44 (7%)	85 (13%)	0.52 (0.37–0.74)	0.0002
Proximal and distal	7 (1%)	31 (5%)	0.23 (0.10–0.51)	<0.0001

Adapted with permission (requested) from Sherman et al. *Lancet*. 2007;369:1347-1355.

Complications of Heparin Therapy



Cost Analysis of DVT Prophylaxis

Strategy	Cost/DVT prevented	Cost/PE prevented	Cost/Life year saved
35yo w/ CVX CA			
No prophylaxis			
EPC	\$810	\$3050	\$207
LDH	Dominated	Dominated	Dominated
LMWH	Dominated	Dominated	Dominated
65yo w/ OV CA			
No prophylaxis			
EPC	\$9396	\$35,378	\$5,132
LDH	Dominated	Dominated	Dominated
LMWH	Dominated	Dominated	Dominated

Maxwell et al: Obstet Gynecol 2000;95:206-14.

ACCP Guidelines-2008

Risk Category	Prophylactic Technique
<30 min, benign, Low risk	Early ambulation
Laparoscopy (No risk factors)	Early ambulation
Laparoscopy (Risk factors)	GCS, EPC, LDH or LMWH

ACCP Guidelines-2008

- On major gynecologic procedures, prophylaxis should be continued until patients leave the hospital
- For patients >60 yo, Hx DVT, Dx of cancer, consider continuation of prophylaxis with LMWH for 2-4 weeks

ACOG Guidelines

- November 2007 Practice Bulletin
- Similar recommendations as to the ACCP Guidelines

Prevention of Venous Thromboembolism

- Inferior Vena Caval Filters
 - No strict guidelines for utilization
 - Patients with DVT and contraindications for anticoagulation therapy
 - Significant risk for bleeding
 - Renal failure (LMWH)
 - Heparin-induced thrombocytopenia
 - Clot propagation while on pharmacologic therapy
 - Preoperative placement for prevention of PE

IVC Filters

	Filter (n=200)	No Filter (n=200)
Pulmonary Embolism		
Symptomatic	2	5
Asymptomatic	0	4
All	2 (1.1%)	9 (4.8%)
Major Bleeding	9 (4.5%)	6 (3.0%)
Death	5 (2.5%)	5 (2.5%)

Long term follow up increased recurrent DVT in filter group (patients also received LMWH or UFH)

Decousus et al NEJM 1998;338:409-415

Top 10

6. An informed patient can be your ally - it's best to educate them
7. For many patients, LMW Heparin offers ideal choice: efficacy, safety and compliance
8. Pneumatic compression is a valuable prophylaxis and needs more research related to its efficacy and compliance
9. Vena Cava filters are not a treatment for VTE - more research is needed to define their role in prophylaxis
10. Low risk procedures in high risk patients require prophylaxis similar to high risk procedures in average risk patients

Top 10

1. VTE is the number one preventable cause of death in hospitalized patients
2. Every hospital should have a program that reliably assesses patients for their individual risk for VTE
3. If you don't look for it, you won't find it - assess, assess, assess (90-day follow-up)
4. Appropriate prophylaxis for the highest risk patients should employ combined modalities
5. Patients at the highest risk need prophylaxis following hospitalization
