PREVENTION OF VENOUS THROMBOEMBOLISM IN GYNECOLOGIC SURGERY

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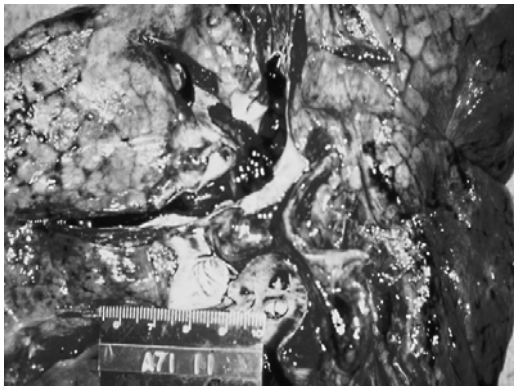
- I have no conflict of interest in the materials being presented.

Learning Objectives

Preventing VTE in Gynecologic Surgery

- **After this lecture the gynecologist will**
- **Explain the importance of venous thromboembolism in gynecologic surgery**
- **Identify the level of risk in preoperative patients**
- **Explain the pros and cons of various prophylactic methods**
- **Based on best evidence, use the appropriate method(s) of VTE prophylaxis in their practice**



Scope of the Problem

- **2.5 million cases DVT/yr**
- **600,000 episodes of pulmonary embolism (PE)**
- **PE causes 50,000 deaths/yr**
- **Over 11,000 postsurgical PE deaths/yr**
- **Approximately 40% of deaths following Gyn Surgery are due to PE**

Fatal Pulmonary Emboli

Two thirds of deaths from pulmonary embolism occur within 30 minutes of the first symptoms

Prevention of Postoperative VTE Issues

- Degree of risk for individual patient
- Outcomes Research: What are our best options?
- Intensity of prophylaxis
- Management Recommendations/Consensus Statements
- Future directions

Pathogenesis of Deep-Vein Thrombosis
Virchow's Triad

- Venous stasis
- Hypercoagulability
- Endothelial damage

Variables Associated with DVT in Gynecologic Surgery

- Past history of DVT
- Cancer
- Age >40 >60
- Prior radiation therapy
- Ankle edema
- Varicose veins
- Radical vulvectomy or exenteration
- Prolonged OR time (> 4 hrs)

Clarke-Pearson, Obstet Gynecol, 69:146, 1987

Additional DVT Risk Factors

- Pregnancy
- Thrombophilias
- Oral Contraceptives
- Obesity
- Air Travel

Thromboembolism Prophylaxis

- Low-dose heparin
- Low molecular weight heparin
- "Anti-embolism" stockings
- Pneumatic leg compression

- Warfarin
- IVC interruption

LOW-DOSE HEPARIN

Multicenter Trial - Lancet 1975

5,000 Units Subcutaneously On Call to OR and Every 8 Hours

	Controls (2076)	Heparin (2045)	
Fatal PE	16	2	(p<.005)
Death with Associated PE	6	3	(p<.005)

LOW-DOSE HEPARIN
In Benign Gynecologic Surgery

Controlled Studies in Gynecology

- **Low Dose Heparin 5000 u q 12 hours**

	Control	Heparin
Ballard (benign) 1973	29%	3.6%
Adolf (benign) 1978	29%	7%
Taberner (benign) 1978	23%	6%

Does Low Dose Heparin Work for Every Patient?

How about gynecologic cancer patients?

LOW-DOSE HEPARIN
In Gynecologic Oncology Surgery

- **5000 U every 12 hours for 7 day**

	DVT (FUT)	(%)
Controls (n=97)	12	(12.4)
Low-Dose Heparin (n=88)	13	(14.8)

Clarke-Pearson. Am J Obstet Gynecol 145:606, 1983

What about a more "intense" Low Dose Heparin Regimen for Cancer Patients?

LOW-DOSE HEPARIN (Intense Regimens)
Gynecologic Oncology Surgery

PROSPECTIVE STUDY GYNECOLOGY ONCOLOGY

	% DVT	
Control (103)	18	
8 hour regimen (104)	9.6	
"Load" regimen (97)	6	
		(p = .02)

Clarke-Pearson. Obstet Gynecol 75:684, 1990

LOW MOLECULAR WEIGHT HEPARINS (LMWH)

- **Enoxaparin (Lovenox), Dalteparin (Fragmin), Fondaparinux**
- **Effective in DVT prophylaxis**
  - **Equivalent to low dose heparin**
  - **Similar frequency of complications**
- **Convenience of once a day dosing**
  - **Dose varies between different LMWH's**
- **? Cost vs. Convenience**

LMWH versus LDUH in Gynecologic Surgery (83% of patients had gynecologic cancer)

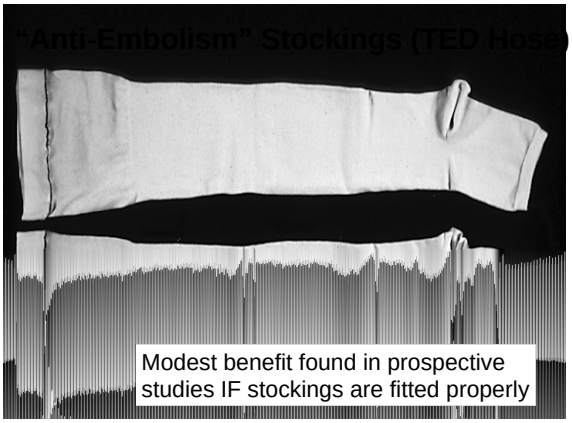
	LMWH (Dalteparin) 5000 u daily n=280	Low Dose Heparin 5000 u q 8 hours n=282	
DVT in 6 wks	0	1	
Pulmonary Emboli	5	1	(p=NS)
Transfusions	39	57	(p=NS)

Ward, Aust NZJ Obstet Gynecol 38: 91, 1998

Mechanical Methods for DVT Prevention

- Graded Compression Stockings
  - TED Hose
- Pneumatic Leg Compression
  - Sequential Compression
  - Single Chamber
  - Foot Compression

"Anti-Embolism" Stockings (TED Hose)



Modest benefit found in prospective studies IF stockings are fitted properly

Intermittent Pneumatic Compression

Intermittent Pneumatic Compression in Gynecologic Surgery

- Perioperative Leg Compression is effective in moderate risk patients
- Perioperative Leg Compression is **not effective** in high risk patients
- Prolonged Leg Compression is effective in high risk patients

Pneumatic Compression (5 days)	Controls	
12.7%	34.6%	(p<.005)

Clarke-Pearson, Gynecol Oncol, 18:226, 1984

WHICH IS BETTER?

Low-dose heparin

or

Intermittent Pneumatic Compression?

Low Dose Heparin vs IPC in Prevention of Postop VTE

Compression	Low-dose Heparin (N=107)	Intermittent Pneumatic (N=101)
Total DVT	7 (6.5%)	4 (4%)
Pulmonary Emboli	0	0
		(p = .54)

Clarke-Pearson, Am J Obstet Gynecol 168:1146, 1993

COMPLICATIONS

Low-dose Heparin

- **Increased postop transfusions**
- **Increased retroperitoneal drainage**
- **23% with PTT> 1.5 control**

Intermittent Pneumatic Calf Compression

- **None**

Clarke-Pearson, Am J Obstet Gynecol 168:1146, 1993

LMWH (dalteparin) vs. External Pneumatic Compression

- Prospective, Randomized Trial

	DVT	Pulmonary Emboli
External Pneumatic Compression	1/106	0
Low Molecular Weight Heparin	2/105	0

Maxwell, Obstet Gynecol 98: 989, 2001

External Pneumatic Compression vs. LMWH Complications

	External Pneumatic Compression	Low Molecular Weight Heparin
Estimated Blood Loss		
Median	350 ml	350 ml
Maximum	3100 ml	3700 ml
> 2000 ml	3	4
Transfusions (# pts)		
Intra op	22	20
Post op	12	13
Thrombocytopenia	4	2

Which is best?? Meta-analysis

Regimen	# Trials	# Patients	# DVT	Incidence (%)	Reduction of Relative Risk
Controls	54	4710	1074	25	-
Low Dose Heparin	50	7716	648	8	**68**
LMWH	13	4320	226	5	**80**
EPC	14	780	61	8	**67**
GC stockings	9	472	51	11	**56**

If Low Molecular Weight Heparins, Low Dose Heparin and External Pneumatic Compression have similar clinical benefit, how do we select the appropriate prophylactic method?

•Cost

•Maxwell, Obstet Gyecol 2000; 95: 206

•Compliance

•Patient preference

•Maxwell, Obstet Gynecol 2002; 100: 451

The Future: What's on the Horizon?

Combination Prophylaxis in the Extremely High-Risk

Who is at highest risk to fail External Pneumatic Compression?

1862 patients treated with EPC
Overall incidence of VTE = 1.3%
Patients with 2 or 3 of the following risk factors had a 16 fold increased risk of developing VTE

- ❑ **Age > 60 years**
- ❑ **Cancer**
- ❑ **Prior VTE**

Clarke-Pearson Obstet Gynecol 2003; 101: 157

The Future: What's on the Horizon?

Longer Duration of Prophylaxis

Randomized trial of patients undergoing "curative surgery" for abdominal and pelvic cancer

Treatment	%DVT (Venogram) @ 1 month	@ 3 months
Enoxaparin 40mg/d x 7 d	12%	13.8%
Enoxaparin 40mg/d x 28 d	4.8%	5.5%

Bergqvist NEJM 346: 975, 2002

VTE Prophylaxis in Laparoscopic Surgery

- What is the risk?
- What prophylaxis is appropriate?

Does Laparoscopic Surgery Increase Risk of VTE ?

In Theory: Maybe (Maybe not)

- **Venous Stasis**
  - **Intraperitoneal pressure 12-15 mm Hg**
    - **Increased femoral vein diameter**
    - **Increased femoral venous pressure**
    - **Decreased femoral venous peak outflow**
  - **More rapid return to normal levels of activity**
  - **Steep Trendelenberg position**
- **Endothelial injury**
  - **Venous distention (femoral vein) increases enodthelial tears**

Does Laparoscopic Surgery Increase Risk of VTE ?

In Theory: Maybe (Maybe not)

- **Increased release of clotting factors**
  - **Decrease in plasminogen activator**
  - **Increase plasminogen activator inhibitor,**

  D-dimer, Fibrinogen degredation products, soluable fibrin, prothrombin fragments 1, 2.
- **Prolonged operating time vs. more rapid recovery**

Laparoscopy Increases Operating Time

(Except in the hands of a gifted surgeon)

(GOG Lap-2) **TAH vs LAVH, BSO, Pelvic, Paraaortic lymphadenectomy**

	Median OR Time	(Range)
● Laparoscopy	3.3 hr	(0.7-10.1 hr)
● Laparotomy	2.2 hr	(0.7-6.3 hr)

What is the Incidence of VTE Following Laparoscopic Surgery?

- Only randomized prospective trial is GOG Lap-2.
- Endpoint: ***Clinical*** diagnosis of VTE
- Potential for bias
  - not blinded
  - no objective/prospective endpoint
- No record of which prophylactic method used (if any); not randomized

GOG Lap-2 Trial

Laparoscopic vs. Laparotomy Hysterectomy, BSO, pelvic and paraaortic lymphadenectomy (endometrial cancer)

Complication	Laparoscopy (n=1682)	Laparotomy (n=900)
DVT	0.8%	1.3%
Pulmonary Embolism	1.2%	1.3%
Death in 6 weeks	0.5%	0.7%
9 Deaths from PE		

Should We Provide VTE Prophylaxis for Laparoscopic Surgery?

Summary:

What should we do to prevent VTE following gynecologic surgery?

VTE Prophylaxis Guidelines ACCP Consensus 2004

- **Low Risk: early mobilization**
  - **Brief procedure < 30 min. Benign Disease (1C)**
- **Laparoscopy with additional risk factors**
  - **LDUH, LMWH, IPC, GCS (1C)**
- **Prophylaxis for ALL major gyn surgery**
  - **Benign disease without additional risk factors**
    - **LDUH 5000u q 12 h**
    - **LMWH < 3400 u q day**
    - **IPC (1B)**

Geerts W, et al. Chest 2004; 126: 338S

VTE Prophylaxis Guidelines ACCP Consensus 2004

- **Major Gyn Surgery Patients <u>with</u> additional risk factors**
  - **LDUH 5000 u tid**
  - **LMWH > 3400 u daily**
  - **IPC (1A)**
  - **Combination (1C)**
  - **Prophylaxis should continue until hospital discharge**
- **Continued prophylaxis: Cancer and > 60 years or prior VTE**
  - **Continue for 2-4 weeks (2C)**

Geerts W, et al. Chest 2004; 126: 338S

Prevention of Postoperative VTE Issues

- Degree of risk for individual patient
- Outcomes Research: What are our best options?
- Intensity of prophylaxis:
- Management Recommendations/Consensus Statements
- Future directions
  - Combination prophylaxis
  - Prolonged prophylaxis
  - laparoscopic surgery

Thank You