# A Protocol of Dual Prophylaxis for Venous Thromboembolism Prevention in Gynecologic Cancer Patients

## Green Journal - November 2008

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Journal Club

# Background

- In GYN cancer patients, the incidence of PE with single-agent prophylaxis remains between 1.2% and 4%,and as high as 6.8% in patients with ovarian cancer.
- In a 2006 survey of Society of GYN Oncologists, 22-41% use SCDs alone for prophylaxis and at least 42% employed dual prophylaxis with SCDs and an anticoagulant
- Dual-agent prophylaxis has been shown to be superior to single-agent prophylaxis in neurosurgery, orthopedic surgery, and general surgery

# Objective

- To evaluate the feasibility of implementing a quality improvement protocol for VTE prevention in postoperative gyn-onc patients
- In January 2006, an evidence based protocol was adopted at University of Wisconsin Hospital, mandating that all gyn-onc patients have dual VTE prophylaxis with SCDs and an anticoagulant such as heparin or low molecular weight heparin
- Incidence of VTE in 2006 was compared to cases of VTE that occurred in 2005 prior to implementation of the protocol

# Methods

- SDCs were used as sole therapy in patients with contraindications to anticoagulation
- Those with a history of HIT received Arixtra
- The initiation of postoperative anticoagulants could be delayed at the surgeon’s discretion in patients felt to be at a high risk for bleeding
- Platelet counts and hematocrit were drawn regularly throughout hospitalization
- Patients were seen daily in the hospital and examined for signs/symptoms of DVT/PE

# Algorithm

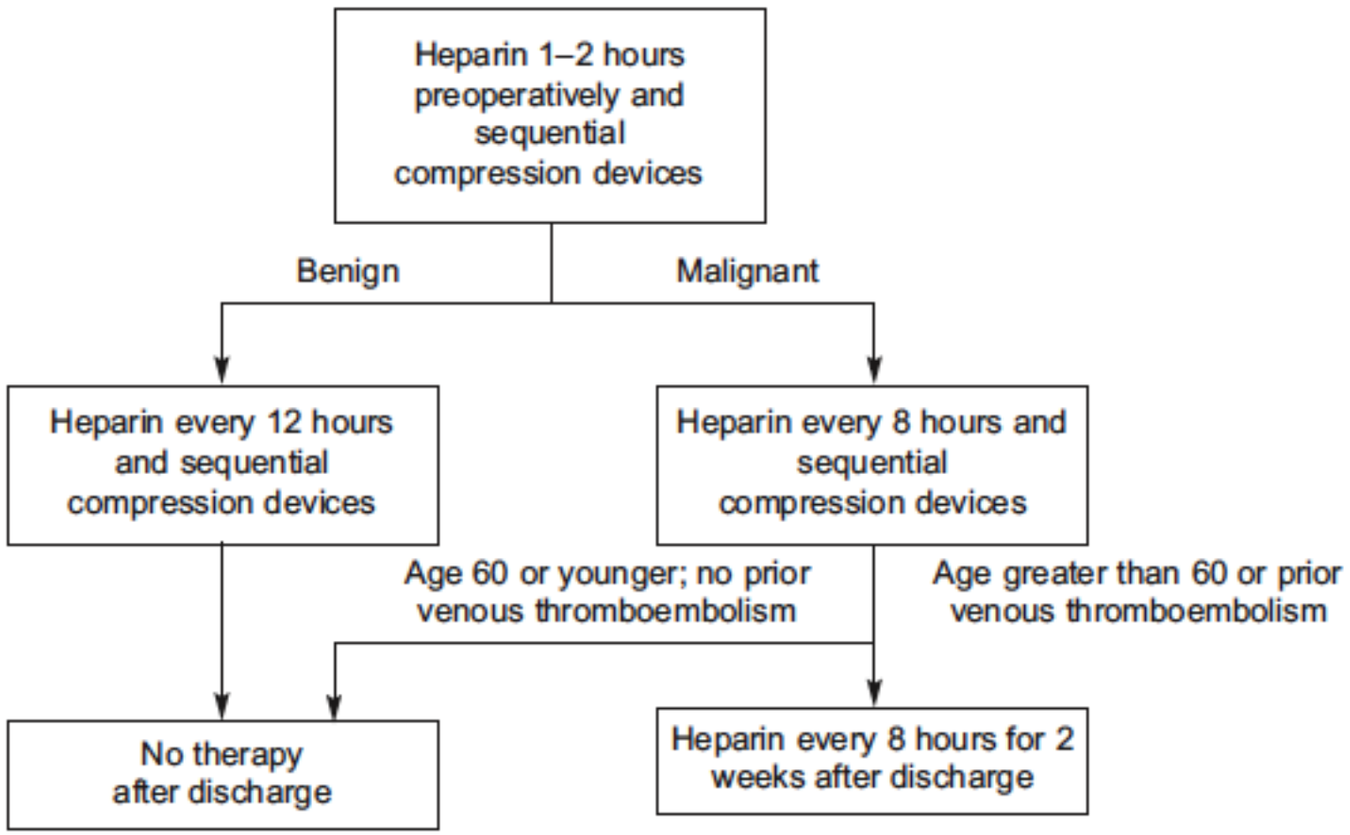


**Fig. 1.** Algorithm for venous thromboembolism prophylaxis for patients on the gynecologic oncology service. Heparin dose was 5,000 units subcutaneously. Daily low molecular weight heparin could be substituted for heparin postoperatively and/or after hospital discharge.

*Einstein. DVT and Pulmonary Embolus Prevention. Obstet Gynecol 2008.*

# Methods

- Any DVT or PE diagnosed within 6 weeks of surgery was identified through review of EMR
- Primary outcome: compliance with the protocol
- Secondary outcomes: VTE, PE, DVT incidence as well as the rate of bleeding complications and HIT
- Continuous outcomes were compared between groups using Wilcoxon two-sample rank test and categorical outcomes were compared using the $x^2$ for association
- Incidence of VTE, PE and DVT was compared between groups using logistic regression, both in univariable and multivaribles models, to minimize risk of confounders

# Exclusions

- Patients who were actively being treated for PE/DVT
- History of heparin-induced thrombocytopenia
- Already on anticoagulation for another purpose (valvular disease or IVC filter)
- Was not used in patients having minor procedures
- Patients who were admitted more than once during the study period - only data from initial admission and 6 week follow up period was included

# Demographics

**Table 1. Patient Demographics**

| Patient Characteristics | Preprotocol (n=294) | Protocol (n=311) | *P* |
|---|---|---|---|
| Age (y) | 55 (46–66) | 54 (47–62) | .34 |
| White race | 281 (95.6) | 297 (95.5) | .88 |
| Weight (kg) | 79 (65–97) | 76 (63–97) | .16 |
| Malignant | 235 (79.9) | 237 (76.2) | .31 |
| Cancer type | | | .83 |
| Uterine | 95/235 (40.4) | 101/237 (42.6) | |
| Ovarian/fallopian/ peritoneal | 93/235 (39.6) | 87/237 (36.7) | |
| Cervical | 20/235 (8.5) | 26/237 (11) | |
| Vulvar/vaginal | 20/235 (8.5) | 17/237 (7.2) | |
| "Other" | 7/235 (3) | 6/237 (2.5) | |

Data are median (interquartile range, 25th–75th percentile) or n/N (%).

# Surgical Characteristics

**Table 2. Surgical Characteristics**

| Surgical Characteristics | Preprotocol (n=294) | Protocol (n=311) | *P* |
|---|---|---|---|
| Type of surgery | | | .01 |
| Laparotomy | 253 (86.1) | 243 (78.1) | |
| Laparoscopy/robotic | 22 (7.5) | 46 (14.8) | |
| Vulvar/vaginal | 19 (6.5) | 22 (7.1) | |
| LND performed | 134 (45.6) | 141 (45.3) | .98 |
| Operative time (hr) | 3.5 (2.8–4.3) | 2.9 (2.2–3.9) | <.001 |
| Hospitalization time (d) | 4.0 (3–6) | 3.0 (2–4) | .007 |
| Follow-up interval (d) | 32 (22–45) | 30 (21–39) | .01 |
| History of previous PE and/or DVT | 5 (1.7) | 4 (1.3) | .93 |

LND, lymph node dissection; PE, pulmonary embolism; DVT, deep vein thrombosis.

Data are median (interquartile range, 25th–75th percentile) or n/N (%).

# Results

- In 2005 and 2006, 644 patients were admitted to gyn-onc service for major surgery -> 39 were excluded
- Patients were followed for 6 weeks postoperatively
- Adherence to protocol determined by the percentage of patients who received an anticoagulant while in the hospital and the percentage of women who went home on an anticoagulant if they met criteria for prolonged prophylaxis -> goal was 90%
- 305 out of 311 (98.1%) who met inclusion criteria in 2006 were on an anticoagulant and 91.1% of those who met criteria were discharged home on anticoagulation
- In 2005, only 53% received anticoagulants during hospitalization

# Results

**Table 3. Summary of Venous Thromboembolic Events**

| Event | Preprotocol (n=294) | Protocol (n=311) | Univariable Analysis | Multivariable Analysis* |
|---|---|---|---|---|
| VTE | 19 (6.5) | 6 (1.9) | 0.29 (0.11–0.72) | 0.33 (0.12–0.88) |
| PE | 14 (4.8) | 4 (1.3) | 0.26 (0.09–0.8) | 0.29 (0.09–0.93) |
| DVT | 7 (2.4) | 2 (0.6) | 0.27 (0.06–1.29) | † |

VTE, venous thromboembolism; PE, pulmonary embolism; DVT, deep vein thrombosis.
Data are n (%) or odds ratio (95% confidence interval).
Incidence of venous thromboembolism equals the number of patients with pulmonary embolism, deep vein thrombosis, or both.
* Controlled for hospital stay, operating time, and laparoscopy.
† A multivariable analysis for deep vein thrombosis was not performed due to the small numbers of events.

# Results

- Two patients (0.7%) were reoperated on for bleeding in 2005 and three patients (1%) in 2006 (P=.95)
- 3.6% had their anticoagulation stopped prior to discharge due to bleeding concerns
- No patients in either group were diagnosed with HIT during the follow up

# Discussion

- Results show a 70% reduction in the incidence of VTE which is both clinically and statistically significant -> number needed to treat of 22 and no increased risk of bleeding complications
- In 2005 a majority (53%) of patients got some form of anticoagulant but implementing a specific protocol for timing and dose of anticoagulants seems to have a greater effect than surgeon preference
- Study was performed at University of Wisconsin hospital in an academic institute and the protocol could likely easily be transferred to a similar setting
- Main weakness is retrospective design and possibly of confounders that could not be identified or measured