Complete Summary

GUIDELINE TITLE

Prevention of deep vein thrombosis and pulmonary embolism.

BIBLIOGRAPHIC SOURCE(S)

American College of Obstetricians and Gynecologists (ACOG). Prevention of deep vein thrombosis and pulmonary embolism. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2007 Aug. 12 p. (ACOG practice bulletin; no. 84). [75 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American College of Obstetricians and Gynecologists (ACOG). Prevention of deep vein thrombosis and pulmonary embolism. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2000 Oct. 10 p. (ACOG practice bulletin; no. 21).

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin products sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE)

GUIDELINE CATEGORY

Prevention
Risk Assessment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Pulmonary Medicine
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To aid practitioners in making decisions about appropriate obstetric and gynecologic care
- To review the current literature on the use of thromboprophylaxis in gynecology patients and to provide evidence-based recommendations to guide clinical decision making

TARGET POPULATION

Women undergoing gynecologic surgery

INTERVENTIONS AND PRACTICES CONSIDERED

1. Surgical prophylaxis according to venous thromboembolism risk factors:
    - Graduated compression stockings
    - Intermittent pneumatic compression devices
    - Low-dose unfractionated heparin

- Low-molecular-weight heparin (LMWH) (dalteparin, enoxaparin)
- Combination prophylaxis (e.g., combination of pneumatic compression and heparin)
- Continuation of anticoagulant prophylaxis for up to 28 days postoperatively

Note: Discontinuation of oral contraceptives and hormone replacement therapy before surgery was considered, but not recommended.

2. Testing for clotting abnormalities (factor V Leiden mutation, prothrombin gene mutation G20210A, protein C, protein S, and AT-III deficiencies, antiphospholipid antibodies, fasting plasma homocystine levels, methylenetetrahydrofolate reductase 677T carriers)
3. Testing for heparin-induced thrombocytopenia (platelet counts)

MAJOR OUTCOMES CONSIDERED

- Effectiveness of thromboprophylaxis for preventing venous thromboembolism
- Prophylactic-related morbidity and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' (ACOG's) own internal resources were used to conduct a literature search to locate relevant articles published between January 1985 and November 2006. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document.

Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force.

I Evidence obtained from at least one properly designed randomized controlled trial.

II-1 Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Analysis of available evidence was given priority in formulating recommendations. When reliable research was not available, expert opinions from obstetrician-gynecologists were used. See also the "Rating Scheme for the Strength of Recommendations" field regarding Grade C recommendations.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A - Recommendations are based on good and consistent scientific evidence.

Level B - Recommendations are based on limited or inconsistent scientific evidence.

Level C - Recommendations are based primarily on consensus and expert opinion.

COST ANALYSIS

Two cost-effectiveness analyses have been performed in patients who have undergone gynecologic surgery. All methods were cost-effective, with pneumatic compression being the most cost-effective. Another study revealed the potential cost-effectiveness of combined prophylaxis in high-risk gynecologic cancer patients. The authors concluded that the use of intermittent pneumatic compression devices combined with low molecular weight heparin was cost-effective in a high-risk group.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practice Bulletins are validated by two internal clinical review panels composed of practicing obstetrician-gynecologists generalists and sub-specialists. The final guidelines are also reviewed and approved by the American College of Obstetricians and Gynecologists (ACOG) Executive Board.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of evidence (I-III) and levels of recommendations (A-C) are defined at the end of "Major Recommendations."

The following recommendations are based on good and consistent scientific evidence (Level A):

- Alternatives for thromboprophylaxis for moderate-risk* patients undergoing gynecologic surgery include the following:
    - Graduated compression stockings placed before initiation of surgery and continued until the patient is fully ambulatory
    - Pneumatic compression devices placed before initiation of surgery and continued until the patient is fully ambulatory
    - Unfractionated heparin (5,000 units) administered subcutaneously 2 hours before surgery and every 12 hours after surgery until discharge
    - Low-molecular-weight heparin (dalteparin, 2,500 antifactor-Xa units, or enoxaparin, 40 mg) administered subcutaneously, 12 hours before surgery and once a day postoperatively until discharge
- Alternatives for prophylaxis for high-risk* patients undergoing gynecologic surgery, especially for malignancy, include the following:

- Pneumatic compression devices placed before surgery and continued until hospital discharge
- Unfractionated heparin (5,000 units) administered subcutaneously 2 hours before surgery and every 8 hours postoperatively and continued until discharge
- Low molecular weight heparin (dalteparin 5,000 antifactor-Xa units or enoxaparin 40 mg) administered subcutaneously, 12 hours before surgery and once daily postoperatively until discharge

The following recommendations are based on limited scientific evidence (Level C):

- Alternatives for prophylaxis for highest-risk patients include the following:
    - Combination prophylaxis (such as the combination of pneumatic compression and either low dose unfractionated heparin or low molecular weight heparin)
    - Consideration of continuing low molecular weight heparin prophylaxis as an outpatient for up to 28 days postoperatively
- If administration of low molecular weight heparin 12 hours before surgery is impractical, initial dosing should commence 6 to 12 hours postoperatively.
- Low-risk patients who are undergoing gynecologic surgery do not require specific prophylaxis other than early ambulation.
- Until more evidence is accumulated, patients undergoing laparoscopic surgery should be stratified by risk category (and provided prophylaxis) similar to patients undergoing laparotomy.

*For classification of risk levels for thromboembolism among gynecologic surgery patients, see box and table below:

Venous Thromboembolism Risk Factors

- Surgery
- Trauma (major or lower extremity)
- Immobility, paresis
- Malignancy
- Cancer therapy (hormonal, chemotherapy, or radiotherapy)
- Previous venous thromboembolism
- Increasing age
- Pregnancy and the postpartum period
- Estrogen-containing oral contraception or hormone therapy
- Selective estrogen receptor modulators
- Acute medical illness
- Heart or respiratory failure
- Inflammatory bowel disease
- Myeloproliferative disorders
- Paroxysmal nocturnal hemoglobinuria
- Nephrotic syndrome
- Obesity
- Smoking
- Varicose veins
- Central venous catheterization

- Inherited or acquired thrombophilia

Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004;126(suppl):338S–400S.

Table: Risk Classification for Venous Thromboembolism in Patients Undergoing Surgery Without Prophylaxis

Level of Risk	Definition
Low	Surgery lasting less than 30 minutes in patients younger than 40 years with no additional risk factors
Moderate	Surgery lasting less than 30 minutes in patients with additional risk factors; surgery lasting less than 30 minutes in patients aged 40 to 60 years with no additional risk factors; major surgery in patients younger than 40 years with no additional risk factors
High	Surgery lasting less than 30 minutes in patients older than 60 years or with additional risk factors; major surgery in patients older than 40 years or with additional risk factors
Highest	Major surgery in patients older than 60 years plus prior venous thromboembolism, cancer, or hypercoagulable state

Modified from Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004;126(suppl):338S–400S.

Definitions:

Grades of Evidence

I Evidence obtained from at least one properly designed randomized controlled trial.

II-1 Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Levels of Recommendations

Level A - Recommendations are based on good and consistent scientific evidence.

Level B - Recommendations are based on limited or inconsistent scientific evidence.

Level C - Recommendations are based primarily on consensus and expert opinion.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall Benefits

Appropriate use of prophylaxis to prevent venous thromboembolism in gynecologic patients

Benefits of Specific Interventions

- *Graduated compression stockings* prevent pooling of blood in the calves. A Cochrane review of randomized, controlled trials reported a 50% reduction in deep vein thrombosis (DVT) formation with graduated compression stockings, and they were more effective when combined with a second prophylactic method. Low cost and simplicity are the main advantages of using graduated compression stockings. Knee-length stockings are as effective as thigh-length stockings and should be preferentially used.
- *Pneumatic compression*: Intermittent pneumatic compression devices reduce stasis by regularly compressing the calf with an inflatable pneumatic sleeve. When used during and after major gynecologic surgery, the devices are as effective as low-dose heparin and low molecular weight heparin in reducing DVT incidence.
- *Low-dose unfractionated heparin*: Two large meta-analyses of randomized clinical trials of patients who had undergone general surgery showed a two-thirds reduction in fatal pulmonary embolism with the use of low-dose unfractionated heparin every 8 hours compared with placebo or no prophylaxis. Advantages of low-dose unfractionated heparin include well-studied efficacy and low cost.
- *Low-molecular-weight heparin*: Advantages of low molecular weight heparin include greater bioavailability and a once-daily dosage. These benefits result

from a longer half-life, more predictable pharmacokinetics, and equivalent efficacy when compared with prophylactic use of low-dose unfractionated heparin. Low molecular weight heparin has more antifactor-Xa and less antithrombin activity than low-dose unfractionated heparin, which may decrease medical bleeding and wound hematoma formation. However, low molecular weight heparin is more expensive than low-dose unfractionated heparin. Heparin-induced thrombocytopenia is rarely observed with low molecular weight heparin, and screening for this is not recommended.

- *Dual prophylaxis: surgery*. Although data from randomized trials in gynecology patients are lacking, a combined approach seems appropriate in the highest-risk patients and this practice is recommended by the Seventh American College of Chest Physicians Consensus Conference.

POTENTIAL HARMS

- Improperly fitted stockings may act as a tourniquet at the knee or mid-thigh, causing an increase in venous stasis.
- Although blood loss during surgery does not seem to be increased by the preoperative use of low-dose unfractionated heparin administration, an increase in postoperative bleeding has been noted, specifically in wound hematoma formation. Additionally, use for more than 4 days warrants monitoring of platelet counts because 6% of patients will experience heparin induced thrombocytopenia.

QUALIFYING STATEMENTS

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These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Oct (revised 2007 Aug)

GUIDELINE DEVELOPER(S)

American College of Obstetricians and Gynecologists - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Obstetricians and Gynecologists (ACOG)

GUIDELINE COMMITTEE

American College of Obstetricians and Gynecologists (ACOG) Committee on Practice Bulletins - Gynecology

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Print copies: Available for purchase from the American College of Obstetricians and Gynecologists (ACOG) Distribution Center, PO Box 4500, Kearneysville, WV 25430-4500; telephone, 800-762-2264, ext. 192; e-mail: sales@acog.org. The ACOG Bookstore is available online at the ACOG Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on September 14, 2004. The information was verified by the guideline developer on December 8, 2004. This summary was updated by ECRI Institute on June 22, 2007 following the U.S. Food and Drug Administration (FDA) advisory on heparin sodium injection. This summary was updated by ECRI Institute on July 21, 2008. The updated information was verified by the guideline developer on August 11, 2008.

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