

Madigan Army Medical Center Clinical Practice Guidelines

Hypercoagulable State

Madigan Army Medical Center
Maintained by Quality Services Division
Clinical Practice and Referral Guidelines Administrator

Last Review for this Guideline: **August 2010**
Clinical Guidelines require review every three years

Core Document

TITLE: Clinical Guideline For The Evaluation of Hypercoagulable State

INDICATIONS FOR THE CLINICAL GUIDELINE:

1. Thrombosis is a significant cause of morbidity and mortality in the United States.
2. There is a lack of consensus regarding the testing and optimal treatment of hereditary thrombophilia.
3. The main reason to test patients is to detect a strong thrombophilia (i.e., APLA syndrome, AT deficiency, homozygous FVL, double heterozygous FVL and prothrombin 20210 mutations, protein C deficiency, protein S deficiency). Identification of strong thrombophilia may decrease the threshold for recommending long-term anticoagulation; may trigger a discussion for enhanced anticoagulation prophylaxis perioperatively and during puerperal period; and may prompt a physician to advise against use of estrogen birth control methods.
4. Caution must be exercised when interpreting results of several tests for hereditary thrombophilia due to the increased risk of false positive results when these tests are utilized incorrectly.
5. The expense to the institution of performing a complete laboratory evaluation of a thrombophilic state can be costly.

METRICS:

1. Assays for antiphospholipid antibodies, protein C, protein S, and antithrombin are sent to Quest Diagnostics Laboratories.
2. Requests for protein C and S, and antithrombin testing will be reviewed by a pathologist.
3. Requests for protein C, protein S, and antithrombin testing will be denied and orders will be cancelled in CHCS if the patient is found to be:
 - a. Within less than two (2) weeks of thrombotic event
 - b. On anticoagulation therapy
 - c. Only off of anticoagulation therapy for less than three (3) weeks
4. Tests for lupus anticoagulant and activated protein C resistance are batched and performed on Thursdays of each week.

DATE:

Published: September 2010.

AUTHORS:

Contact the Clinical Guidelines Administrator at 968-3013 for information about the authors of this guideline.

AREAS OF DISAGREEMENT:

There are no major areas of disagreement between authors.

PUBLISHED GUIDELINES OF CARE AND OTHER REFERENCES UPON WHICH THE CLINICAL GUIDELINE IS BASED:

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1. Pat Foy, MD, Stephan Moll, MD: Thrombophilia: 2009 Update. Current Treatment Options in Cardiovascular Medicine 2009, 11:114128
2. CAP Consensus Conference XXXVI, Diagnosis Issues in Thrombophilia, Nov. 2001
3. C. S. Kitchens, MD, B.M. Alving, MD, C.M. Kessler, MD (2002). Consultative Hemostasis and Thrombosis, Elsevier Science (USA).
4. Washington State Clinical Laboratory Advisory Council, Hypercoagulable State Practice Guidelines, May 2008 (Revised).

CLINICAL PRACTICE GUIDELINE:

DO NOT collect specimens for a hypercoagulable work-up following an acute thrombotic event or while the patient is on anticoagulation therapy (see Key Points for explanation).

Routine screening for inherited thrombophilias is not indicated in patients with VTE provoked by immobility, surgery, and malignancy, or in those with arterial thrombosis with arteriosclerosis risk factors.

Primary hypercoagulable states can be suspected in patients who have:

1. “Spontaneous” thrombosis without obvious associated risk factors
2. Thrombosis at an early age (e.g. less than 45)
3. Recurrent thrombosis
4. Family history (first degree relative) of recurrent venous thrombosis at an early age
5. Thrombosis in unusual locations (e.g. visceral thrombosis, upper extremity thrombosis).

Applicable Laboratory tests:

1. Lupus anticoagulant/antiphospholipid antibody
2. Activated protein C (APC)/Factor V Leiden*
3. Prothrombin G20210A
4. Factor VIII level
5. Protein C**
6. Protein S**
7. Antithrombin**

*Activated protein C resistance (APC) is a screening test for Factor V Leiden. If APC is abnormal, a PCR test for Factor V Leiden will be performed reflexively.

**Functional assays are used initially for protein C, protein S, and antithrombin. If the functional assays show low levels of these proteins, immunologic assays are performed reflexively.

NOTE: Before concluding that a patient has an inherited thrombophilia when a deficiency of antithrombin, protein C, or protein S is observed, it is prudent to repeat the testing after an interval of several weeks for confirmation.

KEY POINTS:

1. **Following an acute thrombotic event:**
 - a. Protein C, protein S, and antithrombin may be falsely low due to ongoing consumption of these proteins. If normal, deficiency can be ruled out; however, if abnormal they should be repeated when the patient is asymptomatic and off antithrombotic medications for at least two (2) weeks.
 - b. Common acquired causes of protein C and S deficiency are **warfarin therapy**, liver disease, DIC, sepsis, **acute thrombosis**, estrogens, and inflammatory states.
 - c. Common acquired causes of antithrombin deficiency are DIC, sepsis, burns, severe trauma, **acute thrombosis**, liver disease, nephrotic syndrome, **OCP or estrogen, heparin**, and pregnancy.
 - d. Identified lupus anticoagulant/antiphospholipid antibodies may be reactive (not causative).
 - e. Factor VIII is an acute phase reactant. Elevated levels must be interpreted with caution and testing repeated when the patient is asymptomatic and off anticoagulation therapy for at least two (2) weeks.
2. **When on anticoagulation therapy:**
 - a. Antithrombin is decreased 20-30% during heparin therapy.
 - b. Protein C and protein S are decreased during warfarin therapy.
3. Activated protein C Resistance (APC)/Factor V Leiden, lupus anticoagulant/antiphospholipid antibody, and prothrombin 20210A testing can be performed at any time.
4. Although an association has been shown between elevated homocysteine levels and venous thrombosis, decreasing homocysteine levels does NOT reduce the risk of thromboembolic events. Therefore, testing for homocysteine levels is no longer recommended.

IMPACT STATEMENT TO INSTITUTION:

These clinical guidelines impact all providers who care for patients with venous thromboembolic events and/or patients who have a significant history of these events. The providers include the primary care/medicine services, surgical services, and emergency department. The guidelines will also impact the Department of Pathology.

LINKS WITHIN THE MAMC INTRANET:

The attachments could be placed on the MAMC Intranet.

METHODS OF PROVIDER EDUCATION:

1. Members of the clinical pathology service are available for consultation should questions arise regarding this guideline or while a patient is being considered for a hypercoagulable state workup. This consultative service will be an on-going effort as many of the tests require pathologist approval and necessitate direct communication between HCPs and the pathology staff.
2. For these guidelines to be universally implemented, staff physicians must not only be aware of them, but they must also emphasize the appropriate use of the tests to the residents. Initially this will require frequent reminding and emphasis on complying with the guidelines.

3. Practice recommendations should be listed on both the MAMC intranet and internet sites.

METHODS OF PATIENT EDUCATION:

Online education recourses:

1. National Alliance for Thrombosis and Thrombophilia (NATT): <http://www.stopthecлот.org/>
2. Thrombophilia Awareness Project: www.fvleiden.org

REVISION FREQUENCY:

This guideline will be reviewed and updated by the POC annually. If the changes are substantial the guideline will be subject to review and approval by the Clinical Guidelines Committee. Changes not deemed "substantial" will be approved by the Chair, Clinical Guidelines Committee.