Physician Knowledge and Practices in the Evaluation of Coagulopathies in Stroke Patients

Cheryl D. Bushnell, MD, MHS; Larry B. Goldstein, MD

Background and Purpose—Coagulopathies are a rare cause of ischemic stroke. Prior studies demonstrate that current physician test-ordering practices for the evaluation of these conditions in patients with ischemic stroke is not optimal. We sought to determine neurologists’ views regarding their use of specialized coagulation testing to better understand the possible reasons for these practices.

Methods—A survey with multiple-choice and open-ended questions regarding knowledge of and approaches to the evaluation of coagulopathies was sent to a convenience sample of 79 neurologists (26 academic neurology faculty, 24 residents/fellows, and 29 community-based practitioners).

Results—Fifty-nine (75%) surveys were completed (response rates: faculty 73%, residents/fellows 88%, and community-based practice 66%). Specialized coagulation tests were reported to infrequently influence stroke patient management (<25% of the time or never for 95% of respondents). Factors reported to increase test-ordering included young patient age (76%), history of thrombosis (46%), history of miscarriages (36%), and having few traditional stroke risk factors (35%). Most (88%) indicated they would order specialized coagulation tests for a hypothetical young patient with no known stroke risk factors. In contrast, only 14% would obtain the tests for a patient having traditional stroke risk factors, and none would order the tests for a stroke patient with atrial fibrillation.

Conclusions—Physician-reported practices for obtaining specialized coagulation tests differ from those found in observational studies in which more indiscriminate test ordering was observed. Closing knowledge gaps and improving application of physician’s current knowledge to their test-ordering practices could help to optimize diagnostic testing for coagulopathies in patients with ischemic stroke. (Stroke. 2002;33:948-953.)

Key Words: cerebral infarction ■ coagulation ■ diagnosis ■ questionnaires

Coagulation disorders (thrombophilias) are a rare but recognized cause of ischemic stroke. The detection of inherited or acquired coagulation disorders is important for several reasons. The diagnosis may provide insight into subsequent risk for recurrent events and guide the choice of stroke prevention therapies, ie, anticoagulation. In addition, potential affected family members could be screened for inherited disorders. Also, education could be provided regarding predisposing factors for thromboembolism, such as pregnancy, surgery, or extended travel. Finally, given the variable expression of coagulation disorders, facilitating effects and interactions of concomitant traditional stroke risk factors can be assessed.

Coagulopathy evaluations are challenging because of the relative low prevalence of these disorders in stroke patients, their uncertain significance and potential interaction with traditional stroke risk factors, the high cost of testing, the lack of diagnostic gold standards, and the difficulty with interpretation of some tests in the setting of acute thrombosis.1-3 Although similar schemes for selecting patients for specialized coagulopathy evaluations have been developed (Table 1), none have been validated, and specific guidelines are not available to aid physicians in the evaluation of coagulopathies.1,2

We previously found that specialized coagulation tests were obtained in one third of stroke patients admitted to an academic medical center, but test-ordering practices were not optimal. For example, one third of tests were obtained in patients in whom results would be unlikely to affect therapy (eg, those with contraindications to or other reasons for anticoagulation).3 In addition, the majority of diagnostic evaluations were incomplete or equivocal, therefore the diagnosis could not be confirmed or excluded.5 We hypothesized that, because of the complexity of coagulopathy evaluations and the lack of consensus guidelines, the reason for suboptimal use of coagulation tests could be a result of a paucity of knowledge of the current coagulopathy literature. Alternatively, there could be discrepancies between knowledge and observed practice. To test these hypotheses, we surveyed a convenience sample of neurologists to determine their knowledge and perceived use of specialized coagulation tests for their patients with ischemic stroke.

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Methods

One-page surveys were mailed to a convenience sample of neurologists at an academic institution (faculty, residents, and fellows) and to nonacademic neurologists in 2 different urban communities in North Carolina. The community neurologists were included to reduce the potential bias and assess the generalizability of the results. Those who did not respond were sent a reminder letter and another copy of the survey 3 months after the initial survey was mailed and then were reminded by fax and/or contacted by telephone 3 weeks later. All participants consented before participation. This study was approved by the Duke Institutional Review Board.

The survey contained open-ended and multiple-choice questions (Appendix). The questions requested information from participants regarding their practice demographics (date or anticipated date of residency completion, estimated number of stroke patients cared for in a typical week, and practice type), their use of specialized tests when screening for a coagulopathy (protein C; protein S; antithrombin III [ATIII]; activated protein C resistance screening test [APCR]; factor V Leiden mutation [FVL]; prothrombin gene mutation [PG]; antiphospholipid antibodies [ACL]; and lupus anticoagulant [LA]), factors that influence their decision to order these tests, their view of the most prevalent coagulopathy in patients with ischemic stroke, and the frequency with which they felt these tests altered their patient management. The participants were also asked whether they would order specialized coagulation tests for any of the 3 hypothetical patients (Appendix), and if so, to indicate which tests they would order. Patient 1 had a high likelihood of coagulopathy based on a recent history of deep vein thrombosis, atrial fibrillation, and chronic obstructive pulmonary disease. Patient 2 was of the age typical for stroke and had atrial fibrillation, diabetes, and a history of hypertension. Patient 3 was of younger age, lack of stroke risk factors, and uncertain stroke etiology; the patient was initially ordered for coagulopathy screening and the frequency with which they felt these tests altered their patient management.

Statistical Analysis

The number of respondents who completed each question provided the denominator for proportions of responses. The prespecified subgroups for analysis were practice type, number of stroke patients cared for during an average week, and year of residency completion. χ² tests were used to compare proportions. Spearman rank correlations were used to compare nonparametric continuous variables (number of stroke patients per week and year of training completion).

Table 1. Testing for Coagulopathies²,⁴

<table>
<thead>
<tr>
<th>Type of Assay</th>
<th>Requires Confirmation</th>
<th>Pattern of Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary coagulopathies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antithrombin III</td>
<td>Functional</td>
<td>Yes, repeat in 2-3 mo</td>
</tr>
<tr>
<td>Protein C</td>
<td>Functional</td>
<td>Yes, repeat in 2-3 mo</td>
</tr>
<tr>
<td>Protein S</td>
<td>Functional and/or free antigen</td>
<td>Yes, repeat in 2-3 mo</td>
</tr>
<tr>
<td>Activated protein C resistance</td>
<td>APCR screen (APTT-based, FV-deficient plasma)</td>
<td>Yes, PT-based APCR screen or FVL genotyping</td>
</tr>
<tr>
<td>Prothrombin gene mutation</td>
<td>G20210A genotyping</td>
<td>No</td>
</tr>
<tr>
<td>Acquired coagulopathies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticardiolipin antibodies</td>
<td>ELISA</td>
<td>Yes</td>
</tr>
<tr>
<td>Lupus anticoagulant</td>
<td>APTT, DRVVT, KCT, TTI</td>
<td>Yes, mixing tests, confirm.</td>
</tr>
</tbody>
</table>

APPT indicates activated partial thromboplastin time; PT, protime; FV, factor V; FVL, factor V Leiden; NA, not applicable; DRVVT, dilute Russell viper venom test; KCT, Kaolin clotting time; TTI, tissue thromboplastin inhibition test; HPP, hexagonal phase phospholipid; PNT, platelet neutralization test.

Results

Of 79 surveys mailed, 59 (75%) were completed; 13 (16%) did not respond and 7 (9%) declined to participate. Of the 59 completed surveys, 19 (73% response rate) were returned by academic neurologists, 21 (88% response rate) by resident or fellow physicians in training, and 19 (66% response rate) by community-based neurologists (3 solo and 16 group practice physicians). Four (7%) of the 59 survey respondents (all academic neurologists) indicated they had never ordered specialized coagulation tests for a stroke patient. The physicians treated a median of 4 stroke patients per week (range 0 to 20). The median year of residency completion was 1996 (range 1970 to 2003).

The most common specialized coagulation tests reported as being initially ordered for coagulopathy screening were protein C and protein S levels, followed by ACL, and LA determinations (Figure 1). The respondents would most commonly repeat protein C, protein S, ATIII, and ACL, followed by LA and APCR levels when the initial result was abnormal (Figure 2).

Figure 1. Specialized coagulation tests reportedly obtained to screen for a coagulopathy in a patient with ischemic stroke. PC indicates protein C; PS, protein S; ATIII, antithrombin III; ACL, anticardiolipin antibodies; LA, lupus anticoagulant; APCR, activated protein C resistance; FVL, factor V Leiden mutation; PG, prothrombin gene mutation.
the hypothetical patient with a high likelihood of coagulopathy. These included protein C (90%), protein S (88%), ACL (90%), LA (90%), ATIII (80%), FVL (52%), APCR (49%), and PG (30%). None of the respondents indicated they would obtain any specialized coagulation tests for patient 2, who already had a defined reason for anticoagulation. An intermediate, but small, proportion (13.6%) of the 59 respondents reported they would order specialized coagulation tests for patient 3, who had an intermediate risk of a coagulopathy. Of those who would order specialized coagulation tests for this patient, all indicated they would obtain ACL, 75% protein C and protein S, 50% ATIII and LA, 50% FVL, 38% APCR, and 38% PG.

When asked to identify the coagulopathy most prevalent in patients with ischemic stroke, 46% answered “Don’t Know”, 28% “ACL and/or LA,” 18% “FVL/APCR,” 5% “Protein C,” or “Protein S” deficiency, and 2% “PG.” Of 58 respondents, 55 (93%) reported that patient factors influenced whether they would perform a specialized evaluation for coagulopathy. The most common factors are listed in Table 2. Of the 55 surveyed physicians providing a response, 11% (6 of 55) indicated coagulation tests “Never” influenced their patient management, 84% (46 of 55) indicated “Less than 25% of the time,” 4% (2 of 55) indicated “25 to 50% of the time,” and 2% (1 of 55) indicated “Greater than 50% of the time.”

There were no differences in reported physician ordering patterns for patients 1 or 3 based on the numbers of stroke patients seen in a typical week, the year of training completion, or practice type. There was a positive correlation between the reported number of stroke patients seen and how often coagulation tests were felt to alter management (Spearman rank 0.31, 95% CI = 0.02 to 0.59).

Because community-based neurologists’ practice patterns were not included in the previously completed observational study of coagulation test ordering, academic (faculty, residents, and fellows) and community-based (group and solo practice) responses to the survey were compared. There were no differences in the reported frequencies of test ordering, the frequency of use of tests, or the frequency of repetition of initially abnormal tests. Reported coagulopathy prevalence in stroke patients or factors influencing the decision to perform a coagulopathy screen were similar.

**Discussion**

The diagnostic yield of coagulation tests in patients with ischemic stroke is low, whether the assessment is based on pretest probability (prevalence in the target population) or the influence of the test on further patient management and outcomes. Our survey results are consistent with this low yield, because the majority of neurologists indicated that specialized coagulation test results influenced their stroke management for less than 25% of their patients. However, the data indicate limited knowledge of some features of coagulopathy in stroke patients and they suggest important discrepancies between knowledge and observed practice.

It has been recommended that certain coagulopathy tests, such as functional protein S, protein C, ATIII, ACL, and LA be repeated 2 to 3 months after a thrombotic event to establish a diagnosis because the tests may be falsely abnormal in the setting of acute thrombosis. One knowledge gap highlighted by the survey was that less than half of neurologists indicated they would repeat these tests if initially abnormal. This finding is consistent with the high number of equivocal results based on the observed use of these tests. Unconfirmed coagulation test abnormalities could lead to false-positive coagulopathy diagnoses in patients with ischemic stroke. Although there are no guidelines for selecting patients with specific coagulopathies for long-term anticoagulation, warfarin is often recommended for patients with coagulopathies and venous or arterial thrombotic events. Therefore, false-positive coagulopathy diagnoses in patients with ischemic stroke could potentially lead to the unnecessary use of warfarin.

**Figure 2.** Specialized coagulation tests neurologists would reportedly repeat when initial result was abnormal, stratified by practice type. PC indicates protein C; PS, protein S; ATIII, anti-thrombin III; ACL, anticardiolipin antibodies; LA, lupus anticoagulant; APCR, activated protein C resistance; Community, community neurologists, Training, residents/fellows.

**Table 2. Factors That Influence Physicians’ Ordering of Specialized Coagulation Tests**

<table>
<thead>
<tr>
<th>Factor</th>
<th>n (Total=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of patient</td>
<td>42</td>
</tr>
<tr>
<td>Hx of thrombosis</td>
<td>25</td>
</tr>
<tr>
<td>Hx of miscarriages</td>
<td>20</td>
</tr>
<tr>
<td>Lack of traditional risk factors</td>
<td>19</td>
</tr>
<tr>
<td>Family hx of thrombosis/stroke</td>
<td>14</td>
</tr>
<tr>
<td>No factors listed</td>
<td>9</td>
</tr>
<tr>
<td>Autoimmune disease</td>
<td>4</td>
</tr>
<tr>
<td>SLE</td>
<td>3</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td>3</td>
</tr>
<tr>
<td>Livedo reticularis</td>
<td>2</td>
</tr>
<tr>
<td>Oral contraception/pregnancy</td>
<td>2</td>
</tr>
<tr>
<td>Gender</td>
<td>2</td>
</tr>
<tr>
<td>Multiple strokes</td>
<td>2</td>
</tr>
<tr>
<td>Migraine history</td>
<td>1</td>
</tr>
<tr>
<td>Medications</td>
<td>1</td>
</tr>
<tr>
<td>Prolonged PTT</td>
<td>1</td>
</tr>
<tr>
<td>DIC</td>
<td>1</td>
</tr>
<tr>
<td>Cancer</td>
<td>1</td>
</tr>
<tr>
<td>AC eligibility</td>
<td>1</td>
</tr>
<tr>
<td>Renal/hepatic failure</td>
<td>1</td>
</tr>
</tbody>
</table>
The results also highlight several discrepancies between apparent physician knowledge and observed practices. For example, patient factors that could potentially increase the yield of specialized coagulation tests such as a history of thrombosis or miscarriage were considered important by nearly half of respondents. However, these same factors are poorly documented in the patients’ medical records (Table 2). Although these observational data were derived from an academic center, there is no reason to expect documentation would be better in a busy community-based practice.

Younger patient age and absence of small-vessel stroke have also been associated with an increase in the frequency of specialized coagulation testing. Although younger patient age was also listed by the majority of survey participants as a factor influencing test ordering, only 3 (5.5%) reported that stroke subtype influenced their test-ordering decisions.

Although a well-designed study demonstrating a low prevalence of hereditary coagulation disorders in patients with ischemic stroke has only recently become available, these disorders were considered a rare cause of even venous thrombosis at the time of our survey. Consistent with these data, only 5% of respondents listed protein C or S deficiencies as the most prevalent coagulopathy in patients with ischemic stroke. However, despite physicians’ apparent awareness of the low prevalence of hereditary coagulopathies in our survey, protein C and protein S are two of the most commonly ordered specialized coagulopathy tests.

Assuming the diagnosis of a coagulopathy could potentially lead to treatment with anticoagulant therapy, specialized testing for a coagulopathy would have limited value in a patient with another reason to be treated with these drugs. None of the participants responding to the survey indicated that they would order specialized coagulation tests for the hypothetical patient with atrial fibrillation. However, nearly one third of patients tested for coagulopathy have other defined reasons for anticoagulation. Therefore, this knowledge is not being applied in practice.

Discrepancies between self-reported and actual practices are not surprising and have been shown in other physician practice settings. For example, a study of cancer screening by community family practitioners found a significantly higher rate of self-reported physician use of screening tests or procedures as compared with patient survey and chart audit. A study of the treatment of bronchitis and sinusitis in children showed that although physicians generally believed that antibiotic resistance was a problem linked to overuse of antibiotics, the actual rates of antibiotic prescription were inappropriately high. The reasons for these discrepancies are uncertain.

Addressing knowledge gaps and discrepancies between knowledge and practice would likely require different types of approaches. Various methods to decrease inappropriate test-ordering have been studied, with mixed results. The rate of inappropriate test-ordering by house staff in a university hospital decreased by up to 46% with attending physician participation, feedback on test ordering, and use of explicit criteria for ordering selected diagnostic tests. In contrast, there was no decrease in the use of unnecessary tests in a controlled trial of an intervention consisting of general education about laboratory tests, feedback regarding use of these tests, and resident-physician participation in the design and conduct of the program. Many studies of physician test-ordering behavior have generally shown disappointingly little change in practices, in part, because of variability in physician specialties, education, practice settings, perceived cost of tests, patient expectations, and patient-dependent factors.

These difficulties in altering physician test-ordering behavior, coupled with our survey results demonstrating both gaps in knowledge and knowledge-practice discrepancies, suggest that multifaceted and complimentary strategies will need to be developed to address the problem. First, although schemes for selecting specialized coagulation testing have been published, clinical practice guidelines are needed to establish a consensus on a rational strategy for evaluating coagulopathies in patients with ischemic stroke. Succinct guidelines could also improve the estimation of pretest probabilities using relevant clinical factors before ordering, as shown in evaluations of coronary artery disease patients. However, guidelines alone may not improve practice or lead to better patient outcomes, even if widely disseminated or incorporated into Continuing Medical Education courses. Improving testing strategies will most likely require multiple interventions, including targeted audit and feedback that is specific to providers, input by peers or opinion leaders, reminder systems, and educational outreach. The physicians’ responses to the questions in this survey must be interpreted in the context of a general paucity of knowledge regarding diagnosis and treatment of coagulopathies. This study is also limited by the lack of consensus on the best approach for selecting patients with ischemic stroke for evaluation, and the optimal treatment strategy for treating these disorders is unknown once the diagnosis is established. There are currently no prospective, randomized controlled trials comparing warfarin to aspirin or placebo to determine the best strategy for stroke prevention in patients with coagulopathies. As a result, physician responses to our survey could reflect differences in factual knowledge or simply differences in attitude toward the diagnostic approach or stroke prevention management. For example, some physicians may order the specialized coagulation tests in the acute stroke period with no intention of changing their management, but want the results for future reference.

The diagnostic evaluation of coagulopathies is complex, and there remains no gold standard for diagnosis. Despite the unclear definition of best practices, the knowledge gaps and the discrepancies between reported knowledge and observed practice provide a benchmark for future efforts to improve diagnostic strategies and ultimately improve the care of stroke patients. In the interim, closing knowledge gaps, improving the application of physician’s current knowledge, and further education regarding strategies for test ordering could optimize diagnostic testing for coagulopathies in patients with ischemic stroke.
Appendix
Survey of Specialized Coagulation Tests in Ischemic Stroke Patients

Part I. General questions

1. What year did you (or will you) complete your Neurology residency training?

2. Approximately how many ischemic stroke patients do you treat in a typical week?

3. Type of practice (circle one)
   a. Group practice
   b. Duke faculty
   c. Resident
   d. Fellow

4. Which specialized coagulation tests would you initially order to screen for a coagulopathy? (Circle all that apply)
   - PT/PTT
   - Functional Protein C
   - Functional Protein S
   - Antithrombin III
   - Anticardiolipin antibody titers
   - Factor V Leiden mutation
   - Lupus anticoagulant
   - Prothrombin gene mutation
   - Activated protein C resistance (APCR) screen

5. Which specialized coagulation tests would you repeat if the initial result were abnormal? (Circle all that apply)
   - Functional Protein C
   - Functional Protein S
   - Antithrombin III
   - Anticardiolipin antibody titers
   - Factor V Leiden mutation
   - Lupus anticoagulant
   - Prothrombin gene mutation
   - Activated protein C resistance (APCR) screen

6. Are there specific historical or clinical factors that would influence your decision to order specialized coagulation tests for an ischemic stroke patient? (Circle one)
   a. Yes
   b. No
   c. If Yes, please list below:

7. Which coagulopathy do you think has the highest prevalence in ischemic stroke patients?
   a. Do not know

8. Have you ever ordered specialized coagulation tests in patients with acute ischemic stroke? (Circle one)
   a. Yes
   b. No
   c. If No, skip to Part II; if Yes, complete question 9.

9. How frequently have results of specialized coagulation tests altered your management of ischemic stroke patients?
   a. Never
   b. Less than 25% of the time
   c. 25-50% of the time
   d. More than 50% of the time

Part II. Hypothetical Patient Scenarios

10. A 57 yo black male was admitted with right hemiplegia and expressive aphasia. A thorough evaluation revealed only a mildly elevated total and LDL cholesterol, and intracranial irregularities/stenoses of the left ICA, M1, and A1 segments on cerebral angiogram.
   a. Would you order specialized coagulation tests on this patient? (Circle one)
      - Yes
      - No
   b. If Yes, which test(s) would you order (circle all that apply).
      - Functional Protein C
      - Functional Protein S
      - Antithrombin III
      - Anticardiolipin antibody titers
      - Factor V Leiden mutation
      - Activated protein C resistance (APCR) screen

11. A 65 yo black female presented with dysarthria and right facial weakness. Cardiac telemetry performed during admission revealed episodic atrial fibrillation with symptomatic rapid ventricular response. There was no evidence of extracranial carotid disease on screening ultrasound.
   a. Would you order specialized coagulation tests on this patient? (Circle one)
      - Yes
      - No
   b. If Yes, which test(s) would you order (circle all that apply).
      - Functional Protein C
      - Functional Protein S
      - Antithrombin III
      - Anticardiolipin antibody titers
      - Factor V Leiden mutation
      - Activated protein C resistance (APCR) screen

12. A 57 yo white male presented with right face, arm, and leg weakness, and dysarthria. Relevant risk factors include a 60 pack-year smoking habit, remote alcohol abuse, and mildly elevated cholesterol. Cardiac evaluation and extracranial carotid screen with ultrasound were negative.
   a. Would you order specialized coagulation tests on this patient? (Circle one)
      - Yes
      - No
   b. If Yes, which test(s) would you order (circle all that apply).
      - Functional Protein C
      - Functional Protein S
      - Antithrombin III
      - Anticardiolipin antibody titers
      - Factor V Leiden mutation
      - Activated protein C resistance (APCR) screen

Acknowledgment

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References


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