Utility of Routine Coagulation Studies in Emergency Department Patients with Suspected Acute Coronary Syndromes*

Dagan Schwartz MD

Department of Emergency Medicine, Mt. Sinai Medical Center, Cleveland, OH, USA
Department of Emergency Medicine, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

Key words: acute coronary syndromes, coagulation, prothrombin time, partial thromboplastin time, emergency department

Abstract

Background: Many emergency departments use coagulation studies in the evaluation of patients with suspected acute coronary syndromes.

Objectives: To determine the prevalence of abnormal coagulation studies in ED patients evaluated for suspected ACS, and to investigate whether abnormal international normalized ratio/partial thromboplastin time testing resulted in changes in patient management and whether abnormal results could be predicted by history and physical examination.

Methods: In this retrospective observational study, hospital and ED records were obtained for all patients with a diagnosis of ACS seen in the ED during a 3 month period. ED records were reviewed to identify patients in whom the cardiac laboratory panel was performed. Other data included demographics, diagnosis and disposition, historical risk factors for abnormalities of coagulation, ED and inpatient management, INR/PTT, platelet count and cardiac enzymes. Descriptive statistical analyses were performed.

Results: Complete data were available for 223 of the 227 patients (98.7%). Of these, 175 (78.5%) were admitted. The mean age was 64.2 years. Thirteen patients (5.8%) were diagnosed with acute myocardial infarction. Of the 223 patients, 29 (13%) and 23 (10%) had INR and PTT results respectively beyond the reference range. Seventy percent of patients with abnormal coagulation test results had risk factors for coagulation disorders. The abnormal results of the remaining patients included only a mild elevation and therefore no change in management was initiated.

Conclusions: Abnormal coagulation test results in patients presenting with suspected ACS are rare, they can usually be predicted by history, and they rarely affect management. Routine coagulation studies are not indicated in these patients.

IMAJ 2005;7:502–506

Many emergency departments use cardiac laboratory panels as part of their evaluation of patients with suspected acute ischemic coronary syndromes [1,2]. Most of these include coagulation tests, typically prothrombin time and partial thromboplastin time. The rationale for using such tests in a cardiac laboratory panel includes the potential need to treat patients with anticoagulants or thrombolysis and as screening tests for unrecognized bleeding disorders or hypercoagulable states. In such patients, the data obtained could modify the dosage of anticoagulants and serve as a baseline value for ongoing monitoring. Furthermore, screening for a previously undetected bleeding disorder can be justified in patients who will undergo invasive procedures such as cardiac catheterization and coronary bypass surgery.

Routine testing for PT-INR and PTT in patients with suspected coronary ischemia is common in emergency departments. An estimated 5 million adult patients present to emergency departments in the United States every year with non-traumatic chest pain [1]. Considering the number of patients evaluated, the savings achieved by eliminating a significant number of these tests could be substantial. Many studies have evaluated the efficacy of routine coagulation studies, most of them in the surgical and anesthesia literature as preoperative screening tests [3–11]. Additional studies evaluated their utility prior to angiographic tests [12], on admission to the general medicine ward [13], and one study evaluated their importance in patients with a probable diagnosis of deep vein thrombophlebitis [14]. None of these studies found any justification for routine administration of the tests in any of the above-mentioned conditions. Other studies have shown that obtaining a history of previous bleeding, liver disease or therapy with anticoagulants is a better predictor of significant bleeding disorders [15–17].

The purpose of this study was to determine the prevalence of abnormal coagulation tests in a cohort of ED patients evaluated for suspected ACS. The secondary aims were to determine whether abnormal PT-INR/PTT testing resulted in changes in patient management and whether abnormal laboratory results could be predicted by patient history and physical examination.

Patients and Methods

We identified all patients with a possible acute coronary syndrome seen in the emergency department of an urban tertiary care medical center during the 3 month period January to March 1998. We utilized the ED and hospital discharge summary's ICD-9 diagnoses. We evaluated all patients with the following ICD diagnoses and their corresponding codes: atypical chest pain, musculoskeletal chest pain, unstable angina, coronary arteriosclerotic disease, abnormal electrocardiogram, acute myocardial infarction, chest pain, intermediate coronary syndrome (acute

ED = emergency department
ACS = acute coronary syndromes
INR = international normalized ratio
PTT = partial thromboplastin time
PT = prothrombin time

coronary syndrome), or angina pectoris. Patients' hospital charts and ED documentation were then reviewed for all patients identified as having any of the above as either a primary or a secondary diagnosis. Since the study was purely retrospective, it was exempt from approval by the Institution Review Board.

All records were reviewed to identify patients in whom the complete cardiac laboratory panel was performed in the emergency department. These patients comprised the study group. Patients whose laboratory values were not available or whose medical records were not found were excluded. The cardiac laboratory panel at our institution included creatine phosphokinase, CPK-MB, troponin, complete blood count, prothrombin time, partial thromboplastin time, INR, Na+, K+, Cl-, glucose, blood urea nitrogen, creatinine, and bicarbonate.

The medical records included emergency department electronic records (for each patient seen in the ED two electronic records are generated – one by the resident and a second by the attending physician). Both records are stored in a computerized system and were obtained independently. Additionally, all records from the medical records department were obtained, including nursing triage and follow-up sheets, ED and intensive care unit order sheets, admission and follow-up physician notes, laboratory results, final diagnoses, billing sheets, and discharge summaries for all patients admitted. The investigator determined the variables to be abstracted from the medical record prior to data gathering.

The following information was collected from the charts: demographic data, chief complaint, hospital admission and discharge dates, discharge diagnosis, and risk factors for abnormalities of coagulation. The last included a history of bleeding disorder, liver disease, current or past daily alcohol consumption, and current use of anticoagulant medications. Lack of mention of a risk factor for a coagulation disorder in the ED charts was classified as "no risk factor present." For cases where the ED physician noted inability to collect the information due to the patient's condition, risk factors were classified as "unknown." These patients were documented as having a positive risk factor for a coagulation disorder. Documentation of physical examinations was reviewed for findings associated with liver disease or signs of a potential bleeding disorder. Charts were further reviewed regarding therapy with heparin, thrombolysis, percutaneous transluminal coronary angioplasty or coronary artery bypass graft, and whether patients underwent cardiac catheterization during admission. All laboratory results for the following tests sent from the ED were collected: PT-INR, PTT and platelet count, CPK including MB fraction and troponin. The standard dose of heparin for ACS was either 80 units/kg bolus followed by 18 units/kg/hour or a 5,000 unit bolus followed by a 1,000 unit/hr. Deviations from a standard heparin dosing protocol were identified. Changes in patient management due to abnormal coagulation test results were defined as follows: change in

CPK = creatine phosphokinase
AMI = acute myocardial infarction
CI = confidence interval

heparin dosing, repeated coagulation studies, administration of blood products, or postponement of any procedures. The classification was performed independently by two investigators who then discussed any discrepancies in order to reach a consensus.

Statistics were primarily descriptive. Data were entered on a spreadsheet and analyzed using commercially available software (SPSS for Windows, version 8.0). Means, standard deviations and 95% confidence intervals are given.

Results

A cardiac laboratory panel was ordered for 227 patients seen in the ED during the study period. The charts for 226 (99.6%) of these patients were available for review. The complete laboratory protocol results were available for 223 (98.7%) of these patients, who constituted the study group. Of these, 173 were admitted to an ICU (76%). Two patients were admitted to a non-monitored bed (0.9%) and 48 (22%) were discharged from the ED (including 3 patients who were transferred to other facilities and one patient who left against medical advice). Thirteen patients (5.8%) were diagnosed with AMI, 18 patients (8.1%) with indeterminate coronary syndrome, 4 (1.8%) with unstable angina, 16 (7.2%) with congestive heart failure, 64 (28.7%) with unspecified chest pain, and 21 (9.4%) with coronary artery disease. All remaining patients had a non-cardiac discharge diagnosis.

PT-INR and PTT test results

Of the 223 PT-INR tests, 29 (13%) were beyond the reference range of 1.25 (mean 2.38, 95% confidence interval 1.70–3.07). Twenty of these patients (8.6%) were assessed to be at increased risk for abnormal coagulation tests based on history obtained in the ED (history of bleeding disorder, daily alcohol consumption, history of liver disease, history of current treatment with anticoagulants, or inability to obtain a medical history). The remaining 8 patients (3.6%) with abnormal results all had a mild PT-INR elevation (highest PT-INR result in this group being 1.73, mean 1.44, 95% CI 1.28–1.59) [Table 1]. No change in therapy was initiated for any of the 29 patients in view of these test result abnormalities.

Of the 223 PTT tests, 23 (10%) were beyond the reference

Table 1. Patients with elevated PT and PTT test results, degree of elevation and presence of risk factors

No. of patients with elevated PT-INR		
Range (sec)	Patients at risk	Patients without known risks
13.6–16.5	10	9
16.6–19.5	3	0
19.6–36.0	7	0
No. of patients with elevated PTT		
Range (sec)	Patients at risk	Patients without known risks
34.4–44.3	11	7
44.4–54.3	2	0
54.4–120.0	2	0

range of 34.3 (mean 46.8, 95% CI 36.1–57.4). Fifteen (6.7%) of these patients were assessed to be at increased risk for abnormal coagulation tests based on history obtained in the ED (history of bleeding disorder, daily alcohol consumption, liver disease, history of current treatment with anticoagulants, or inability to obtain a medical history). The remaining 8 patients (3.6%) with abnormal results all had mild elevation of the PTT value (highest PTT result in this group being 44.2, mean 37.3, 95% CI 37.6–40.0) [Table 1]. No change in therapy was initiated in view of these test result abnormalities.

Treatment with heparin and tissue plasminogen activator

Heparin therapy was instituted in the ED in 34 patients (14.6%). They all received the institutional standard dose of heparin regardless of initial PT-INR and PTT results. Heparin therapy was instituted in an additional 33 patients in the ICUs within 24 hours of admission. All these patients received standard heparin dosing except for one patient known to be on coumadin and for whom the loading dose was omitted. Three patients received TPA (during their stay in the ED).

Risk factors

Forty-seven of the 223 patients in the study population (21%) had one or more risk factors for coagulation abnormalities. In two of the patients a reliable past medical history could not be obtained. Twenty patients received anticoagulants, 5 suffered from known liver disease, and 28 patients had a history of daily alcohol consumption [Table 2].

Invasive procedures

Of the 223 patients, 45 underwent cardiac catheterization and 8 subsequently underwent coronary artery bypass surgery. Seven underwent PTCA. We found no case of a procedure being cancelled or postponed, even when PT-INR or PTT values were elevated beyond the reference range. Additionally, no patient was pretreated with fresh frozen plasma or vitamin K prior to the procedures regardless of the result of their PT-INR and PTT tests.

Cost

During the 3 months surveyed 223 patients were evaluated in the ED. The charge for PT-INR/PTT tests was US$45. Of the sur-

---

TPA = tissue plasminogen activator
PTCA = percutaneous transluminal coronary angioplasty

Table 2. Identified risk factors in patients with elevated coagulation test results

Patients with elevated PTT results*	Patients with elevated PT results*	Risk factors
9	11	Anti-coagulant therapy
1	2	Known liver disease
8	11	Alcohol abuse
1	1	No available medical history
8	8	No identified risk factors

* Some patients had more than one risk factor

veyed patients, 81% had no risk factors for coagulation abnormalities. If the number of patients for whom PT-INR PTT testing was potentially not indicated is extrapolated over a year, it would result in 723 patients annually. The total savings in charged services in this hospital alone would be $32,535 a year.

Discussion

In our study, 29 (13%) of the PT-INR results and 23 (10%) of the PTT results were abnormal. Sixty-seven percent of all abnormal results were in patients identified with at least one risk factor. Forty-seven patients were found to have at least one risk factor. This subgroup accounted for only 67% of all abnormal results but for 100% of the results above the normal range by two or more standard deviations.

It is probably justifiable to administer PT-INR/PTT testing to patients with known or suspected bleeding disorder, or to those on anticoagulant therapy who present with an acute medical problem such as chest pain. Many studies have assessed the value of routine pre-procedural or pre-admission testing for coagulation abnormalities. No study to date has investigated the specific role of PT-INR and PTT testing as part of a cardiac evaluation in the ED.

The commonly cited benefits of routine PT-INR PTT testing in all patients with suspected acute coronary syndromes are: a) to identify patients with a previously unrecognized bleeding disorder and to appropriately modify the dosage in the subset of patients who will receive heparin, b) to treat patients with a previously unrecognized bleeding disorder who will undergo invasive procedures such as cardiac catheterization and CABG prior to the procedure, and c) as a screening test to identify previously unknown medical problems such as anticardiolipin antibodies and the presence of lupus anticoagulant [18,19].

Numerous studies have evaluated the utility of routine testing for bleeding diathesis in asymptomatic patients, but no study has evaluated the role of these tests in the emergency department. Some studies evaluated their utility as a preoperative/pre-procedural tool to predict bleeding complication and the need for pre-procedural treatment [7,20,21].

With regard to the possible utility of PT-INR and PTT as a screening test, many studies [13,22,23] have shown that due to the infrequency of these disorders and the questionable clinical applicability in asymptomatic patients, they are not indicated. One study [13] tested the appropriateness of PT-INR/PTT testing in patients admitted to the medical service. They used a set of PT-INR/PTT testing guidelines that included history or evidence on examination of a bleeding disorder. Additional criteria for patients undergoing invasive procedures were history or evidence on examination of the following: malnutrition, liver disease, lack of clinical information, or patients on anticoagulant therapy. The authors found that 81% of the tests performed were not indicated. Only 1% of the patients who underwent the tests without indication had an abnormality of PT-INR and 5% had a significant elevation of PTT. An appropriate change in therapy was instituted in one patient. Repeated physical examination of that patient found ecchymoses that was missed

on the initial examination. Another study evaluated the need for PT-INR and PTT testing prior to instituting anticoagulation in 199 patients admitted through the ED. The study questioned the need for baseline PT-INR/PTT values prior to instituting heparin and showed that not even once was the initial heparin dose altered in view of an abnormal result. The study also pointed out that rarely was there documentation of historical information on pre-existing coagulopathies in patients treated with heparin [14].

In our study PT-INR PTT testing would have been indicated based on history in only 43 (19%) of the 223 patients. We found values beyond the reference range for PT-INR and PTT in 13% and 10% accordingly. The percentage of abnormalities in patients without risk factors was 5% and 4% respectively. Only in one patient in the whole study group was therapy affected by these laboratory results. The patient was known to be on coumadin and therefore did not receive a bolus dose when heparin was initiated. PT-INR and PTT tests were not repeated for evaluation of abnormalities recorded on the initial test except for patients receiving heparin.

Previous studies have suggested that routine coagulation testing in the preoperative, pre-angiographic and pre-admission setting is not warranted. Furthermore, in the deep vein thrombosis study [14], heparin doses were not changed based on initial results of PT-INR and PTT and the authors concluded that baseline PT-INR PTT studies are not necessary prior to initiation of anti-coagulation therapy. Additionally, such testing may unnecessarily delay the initiation of anti-coagulation therapy. When the likelihood of acute coronary ischemia is high, anti-coagulation therapy should be started as soon as possible without waiting for PT-INR PTT results. In patients started on heparin therapy testing should be done 4–6 hours after initiation to help titrate the subsequent dosage. Regarding the other patients, the vast majority was not treated with anti-coagulation and did not undergo any invasive procedures. The only possible justification for performing the tests is as a screening tool. PT-INR and PTT testing as a screening tool in patients with no risk factors has been proven to lack diagnostic utility and to be less sensitive than a focused history and physical examination.

Elimination of unnecessary coagulation testing could offer substantial cost savings, especially in view of the large number of patients presenting to the emergency departments with complaints of possible ACS. The cost of PT and PTT testing is relatively low, $40–80 per patient. Assuming the lower cost of $40 per test panel, and according to the 81% unnecessary tests obtained in our study, the potential cost savings in the United States alone would be $162,000,000 a year [24].

Limitations

Given that this is a retrospective study it is subject to the typical biases associated with this type of data collection. Specifically, historical and physical examination findings of risk factors may have been underestimated, however this would tend to underemphasize their role. An additional concern may be that the study population does not represent the total population in our study cohort. The incidence of aggressive management in our study population, including heparin and TPA, was indeed relatively low, possibly the result of a low risk population. In view of the lower rate of ED intervention in our study population, the study might have underestimated the number of patients in whom heparin and TPA therapy might have been modified due to abnormal coagulation results. However, despite this, the percentage of acute MI, CABG surgery and cardiac catheterizations in our patient population was on par with U.S. averages for ED chest pain patients [25]. This study is descriptive and did not involve formal hypothesis testing, and as such can only formulate hypotheses on the utility of routine coagulation studies in patients with ACS. The sample size was also too small to detect rare events such as unsuspected coagulopathies.

Conclusion

The incidence of significant abnormalities of coagulation laboratory results was low, and most of them could have been predicted by history and physical examination. The unpredicted abnormalities were minor and had no clinical significance. The findings suggest no justification to include PT-INR and PTT testing as part of a protocol for assessment of ED patients suspected of having acute coronary syndromes.

References

1. Chest pain protocol passes tests for sensitivity, patient satisfaction. Hosp Technol Ser 1997;16(7):6.
2. Gomez MA, Anderson JL, Karagounis LA, Muhlestein JB, Mooers FB. An emergency department-based protocol for rapidly ruling out myocardial ischemia reduces hospital time and expense: results of a randomized study (ROMIO). J Am Coll Cardiol 1996;28(1):25–33.
3. Patel RI, DeWitt L, Hannallah RS. Preoperative laboratory testing in children undergoing elective surgery: analysis of current practice. J Clin Anesth 1997;9(7):569–75.
4. Barnard NA, Williams RW, Spencer EM. Preoperative patient assessment: a review of the literature and recommendations [see comments]. Ann R Coll Surg Engl 1994;76(5):293–7.
5. Kang J, Brodsky L, Danziger I, Volk M, Stanievich J. Coagulation profile as a predictor for post-tonsillectomy and adenoidectomy (T + A) hemorrhage [see comments]. Int J Pediatr Otorhinolaryngol 1994;28(2-3):157–65.
6. Macpherson CR, Jacobs P, Dent DM. Abnormal peri-operative haemorrhage in asymptomatic patients is not predicted by laboratory testing. S Afr Med J 1993;83(2):106–8.
7. Burk CD, Miller L, Handler SD, Cohen AR. Preoperative history and coagulation screening in children undergoing tonsillectomy [see comments]. Pediatrics 1992;89(4 Pt 2):691–5.
8. Aghajanian A, Grimes DA. Routine prothrombin time determination before elective gynecologic operations. Obstet Gynecol 1991;78(5 Pt 1):837–9.
9. Laposata M, Teruya J. Reappraisal of preoperative coagulation testing [Editorial]. Am J Clin Pathol 1990;94(6):795–6.
10. Rohrer MJ, Michelotti MD, Nahrwold DL. A prospective evaluation of the efficacy of preoperative coagulation testing. Ann Surg 1988;208(5):554–7.
11. Kaplan EB, Sheiner LB, Boeckmann LJ, et al. The usefulness of preoperative laboratory screening. JAMA 1985;253(24):3576–81.
12. Darcy MD, Kanterman RY, Kleinhoffer MA, et al. Evaluation of

coagulation tests as predictors of angiographic bleeding complications. *Radiology* 1996;198(3):741–4.

13. Hubbell FA, Frye EB, Akin BV, Rucker L. Routine admission laboratory testing for general medical patients. *Med Care* 1988;26(6):619–30.

14. McKinley L, Wrenn K. Are baseline prothrombin time/partial thromboplastin time values necessary before instituting anticoagulation? *Ann Emerg Med* 1993;22(4):697–702.

15. Peterson P, Hayes TE, Arkin CF, et al. The preoperative bleeding time test lacks clinical benefit: College of American Pathologists' and American Society of Clinical Pathologists' position article. *Arch Surg* 1998;133(2):134–9.

16. Kitchens CS. Preoperative PTs, PTTs, cost-effectiveness, and health care reform. Radical changes that make good sense [Editorial, see comments]. *Chest* 1994;106(3):661–2.

17. Sramek A, Eikenboom JC, Briet E, Vandenbroucke JP, Rosendaal FR. Usefulness of patient interview in bleeding disorders [see comments]. *Arch Intern Med* 1995;155(13):1409–15.

18. Pittman DL, Morgan WB. Making sense of coagulation tests, a practical approach. *Mo Med* 1993;90(9):595–9.

19. Turnbull JM, Buck C. The value of preoperative screening investigations in otherwise healthy individuals. *Arch Intern Med* 1987;147(6):1101–5.

20. Houry S, Georgeac C, Hay JM, Fingerhut A, Boudet MJ. A prospective multicenter evaluation of preoperative hemostatic screening tests. The French Associations for Surgical Research. *Am J Surg* 1995;170(1):19–23.

21. Kozak EA, Brath LK. Do "screening" coagulation tests predict bleeding in patients undergoing fiberoptic bronchoscopy with biopsy? [see comments]. *Chest* 1994;106(3):703–5.

22. Groopman DS, Powers RD. Effect of "standard order" deletion on emergency department coagulation profile use. *Ann Emerg Med* 1992;21(5):524–7.

23. Erban SB, Kinman JL, Schwartz JS. Routine use of the prothrombin and partial thromboplastin times [see comments]. JAMA 1989;262(17):2428–32.

24. Bell CM, Crystal M, Detsky AS, Redelmeier DA. Shopping around for hospital services: a comparison of the United States and Canada [see comments]. JAMA 1998;279(13):1015–17.

25. Burt CW. Summary statistics for acute cardiac ischemia and chest pain visits to United States EDs, 1995-1996. *Am J Emerg Med* 1999;17(6):552–9.

Correspondence: Dr. D. Schwartz Head, Dept. of Emergency Medicine, Faculty of Health Sciences, Ben-Gurion University of the Negev, P.O. Box 653, Beer Sheva 84105, Israel.
Phone: (972-8) 647-7681
Fax: (972-8) 647-7683
email: sdagan@bgu.ac.il

Capsule

Long live catalase

Cell and tissue damage caused by free radical oxygen molecules have been linked to aging pathologies, yet the idea that antioxidant defenses can prolong life is controversial. Schriner and team generated transgenic mice that over-express catalase in mitochondria, a major source within the cell of oxygen free radicals. Catalase removes damaging hydrogen peroxide that can generate reactive oxygen species. In the transgenic mice, cellular oxidative damage and age-related decline in heart function were reduced and cataract formation was delayed. In addition, life span increased by nearly 20%. Thus, antioxidant enzymes can promote mammalian longevity.

Science 2005;308:1909

Eitan Israeli

Capsule

I smell new neurons

Most neurogenesis in the brain occurs in the context of early development. However, even through adulthood, a steady stream of newly generated neurons supplies the olfactory bulb. Neuronal progenitors from the subventricular zone of the brain migrate together as a chain to the olfactory bulb. Ng et al. (*Science* 2005;308:1923) identified prokineticin 2 (PK2) as one of the signals that calls the neurons to their destination. Prokineticin proteins are secreted, and in other locations also regulate processes such as gastrointestinal motility and pain sensitization. The mammalian retina, like other regions of the brain, develops in a sequential manner. Cells of a given function are born earlier, whereas those born later are dedicated to other functions. Kim et al. (p. 1927) clarified how one signaling molecule, growth and differentiation factor 11 (GDF11), affects this trajectory of differentiation in the retina differently than in the olfactory epithelium. In the developing retina, GDF11 does not affect proliferation of progenitor cells as it does in the olfactory epithelium, but signals to the progenitor cells competence to produce certain types of differentiated cells.

Eitan Israeli