Review

The Role Of Coagulation Testing Prior To Surgery

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Abstract: Preoperative coagulation screening has been among the most debated of all laboratory tests, especially in children. Although an undiagnosed coagulopathy could result in serious surgical morbidity, commonly used screening tests such as bleeding time, prothrombin time, activated partial thromboplastin time, and platelet count, do not reliably predict abnormal perioperative bleeding. Laboratory testing should be considered in patients either the history or medical condition suggests a possible hemostatic defect, in patients undergoing surgical procedures that might induce hemostatic disturbances (eg, cardiopulmonary bypass), when the coagulation system is particularly needed for adequate hemostasis (eg, tonsillectomy), and in patients for whom even minimal postoperative bleeding could be critical (eg, neurosurgery). In the case of minor surgery and a negative history of clotting disorders, no tests are suggested.
***Keyword(s)*:** *preoperative coagulation tests, bleeding time, prothrombin time, activated partial thromboplastin time, platelet count*

Abstrak: Skrining koagulasi preoperatif adalah salah satu pemeriksaan laboratorium yang paling diperdebatkan terutama pada anak-anak. Walaupun koagulopati dapat menyebabkan morbiditas operasi, skrining tes yang biasa dilakukan seperti waktu perdarahan, *prothrombin time*, *activated partial thromboplastin time*, dan hitung leukosit, tidak reliabel untuk memprediksi perdarahan abnormal perioperatif. Tes laboratorium perlu dilakukan pada pasien yang dimungkinkan mengalami defek hemostasis berdasarkan riwayat ataupun kondisi medis, pada pasien yang akan menjlankan prosedur operasi yang menyebabkan gangguan hemostasis (misal: *cardiopulmonary bypass*), saat sistem koagulasi memerlukan hemostasis yang adekuat (misal: tonsilektomi), dan pada pasien yang walaupun terjadi perdarahan minimal postoperatif dapat menyebabkan kegawatan (misal: *neurosurgery*). Pada operasi minor dan tidak adanya riwayat gangguan pembekuan, tidak ada tes yang disarankan.
Kata kunci: *preoperative coagulation tests, bleeding time, prothrombin time, activated partial thromboplastin time, platelet count*

Preoperative evaluation in pediatric patients has been one of routine clinical practice for pediatricians, as well as other clinicians. In addition to history and physical examination, prothrombin time (PT) and activated partial prothrombin time (APTT) are employed widely prior to invasive procedure and surgery, despite many controversies about the need of such testing and its value in predicting risk of perioperative bleeding.[1] Optimisation of its usefulness is dependent on knowledge of the clinical context and the limitations of the tests, as well as an understanding of the relative prevalence of abnormalities of coagulation and haemostasis and their clinical significance.[2]

Understanding PT and APTT tests

The PT test assesses the extrinsic and common pathways of coagulation and should detect important deficiencies (or rarely inhibitors) of factors II, V, VII, X and very low fibrinogen concentration. Its main utility besides for anticoagulant monitoring is to detect acquired haemostatic disorders (in particular DIC, liver disease or vitamin K deficiency). APTT is a measure of the integrity of intrinsic and common pathway of coagulation. APTT should detect deficiencies or inhibitors of the intrinsic and common pathway factors (factor II, V, VIII, IX, X, XI, XII and fibrinogen). APTT originally developed to

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identify patient with clinical suspicion of haemophilia and von Willebrand disease (vWD).[2,3]

Nowadays probably <0.1%–1.0% of PTTs ordered in current medical practice fit that indication with the most common indication now being routine admission order or routine presurgical patients who have no bleeding symptoms nor suspected have bleeding disorder. The question asked of the PTT has evolved from "*why does this patient bleed*?" to "*will this patient bleed*?" As the PTT was never intended to answer that question, one must be careful regarding interpretation or results of that test. [4]

General limitation of PT/APTT tests includes normal biological variation; low disease prevalence of all inherited bleeding disorders and many acquired ones; and insensitivity to some clinically important bleeding disorders (factor XIII deficiency and alpha2 antiplasmin deficiency). Indiscriminate screening for low prevalence disorders in a low-risk population results in a low positive predictive value and a high number of false positives. On the other hand, APTT is normal in F XIII deficiency and alpha2 antiplasmin deficiency, and although both are of low prevalence, those conditions may cause life-threatening surgical bleeding.[2]

Many prelaboratory and laboratory phenomena may also influence the PT/APTT results. Sampling artefact is one of the most common cause of prolonged PT/APTT. Difficult venipuncture (which is common especially in pediatric patients), heparin contamination and insufficient sample volume resulting in excess citrate are among the causes of sampling error affecting PT/APTT results.[1,2,4] PT/APTT tests also have some technical variability associated with instrumentation and reagents with different sensitivity to coagulation factor deficiencies. Several physiological conditions has been known as a cause to rise F VIII markedly, such as pregnancy or as a response to physical stress and trauma, which can mask the detection of mild hemophilia or Von Willebrand Disease. On the contrary, some factor deficiencies which do not cause bleeding are associated with a prolonged APTT, such as deficiency of F XII, prekallikrein and high molecular weight kininogen.[1,2] Halbmeyer et al reported the prevalence of moderate and severe F XII deficiency was 2.3 % of otherwise healthy Austrian blood donors[5] and in 10.3% of patients undergoing cardiac surgery,[6] which is among the most common causes of unexpected prolongation of the APTT. As well as APTT, prolongation of PT may be an occasional manifestation of lupus anticoagulant, a condition which is not associated to bleeding tendency. Lupus anticoagulant can be found in 1.2–3.8% of healthy individuals, but the incidence increases with age and chronic disease. Kitchen showed the poor correlation of APTT results and hemorrhagic potential (Table 1).[4]

Controversies of routine coagulation screening test : the pros and cons evidence

Proponents of the routine coagulation screen argue that the approach may assist in the detection of unsuspected bleeding disorders prior to an operation or invasive procedure. This is considered to be especially important in paediatric practice where due to their age, there may not have been any prior haemostatic challenge to reveal an underlying bleeding disorder.[4] Jonnavithula et al reported a rare case of an 8-year-old girl who undergo surgery and the preoperative screening test showed prolonged PT and APTT values. Further studies revealed functional activity of F X was <8% of normal activity. She was then received transfusion of FFP to correct the deficient factor and the surgery was done successfully.[7] However, congenital F X deficiency is an extremely rare disorder with total number of patient is 967 in the world.[8]

Sandoval et al[9] reported a retrospective study of 3950 outpatients hematology records and found 131 patients referred due to preoperative prolonged APTT. Seventy boys and 61 girls with median age 6 years (range 1 week – 22 years) were identified as having prolonged APTT with median prolongation 5.3 seconds above upper limit of normal value (39 seconds). Further studies revealed 28 of this 131 patients (21.3%)

Table 1. Poor correlation of PTT results and hemorrhagic potential[4]

Hemorrhage	Normal PTT Result	Prolonged PTT Result
No	Normal Patients	Some with FXI deficiency
		FXII deficiency
		HMWK deficiency
		PK deficiency
		LA
		Some with thrombin and FV alloantibodies from bovine thrombin
		Rattlesnake envenomation
		Technical abnormalities Erythrocytosis Heparin contamination Premature *in vivo* clot Partially activated sample Interfering substances
Yes	FVII deficiency	FVIII deficiency
	FXIII deficiency	FIX deficiency
	Most with vWD	Some with FXI deficiency
	Some with FXI deficiency	Some with thrombin and FV alloantibodies from bovine thrombin
	Therapeutic LMWH administration	Fibrinogen FII, V, or X deficiency
	Hyperfibrinolisis	DIC
	Malignancies (APL, prostate)	Hepatic insufficiency
	Alpha-2PI deficiency	Vitamin K deficiency
		Therapeutic heparin or warfarin usage

LA, lupus anticoagulant; HMWK, high molecular weight kininogen,; PK, prekallikrein; DIC, disseminated intravascular coagulation; alpha-2PI, alpha-2-plasmin inhibitor; vWD, von Willebrand disease; APL, acute promyelocytic leukemia; LMWH, low molecular weight heparin

had bleeding disorders : von Willebrand disease (14 patients), F XI deficiency (8 patients), F VIII deficiency (2 patients), vitamin K deficiency (2 patients), liver disease (1 patient) and 12 patients had nonbleeding coagulopathy due to F XII deficiency (8 patients), F IX carrier (2 patients) and lupus anticoagulant (2 patients). The author concluded that preoperative screening with PT and APTT is useful in identifying occult bleeding disorders, since 75% of patients with confirmed bleeding disorders did not have a personal and 83% did not have a family history of bleeding.[9]

However, bleeding history is subjective and common symptoms are found in up to 25% of a healthy population without bleeding disorders including epistaxis, gum bleeding, and post-partum haemorrhage.[10] The use of a standardized bleeding questionnaire has been suggested as being better than indiscriminate coagulation testing as a screening tool for perioperative bleeding,[11] and there are suggestions that in patients with congenital bleeding disorders, a structured history is at least as informative as laboratory testing to predict bleeding.[12,13]

Rapaport[14] in his review in 1983 suggested there are four reasons for advocating coagulation screening tests in addition to the history : (1) to protect against the doctor who fails to take an adequate history;(2) in patients who give an unreliable history, e.g., the patient with a mild bleeding disorder who does not realize that the bleeding he or she has experienced after trauma or surgery is excessive;(3) in patient who may have an abnormality, such as factor XI deficiency, that causes bleeding only after surgery and may not yet have had surgery or dental extractions; (4) a patient who has withstood surgery without abnormal bleeding may later acquire a hemostatic defect, such as thrombocytopenia, that has remained asymptomatic. According to Rappaport, screening tests have a role in preoperative evaluation, which is determined by a general evaluation of the patient's clinical status, by the information obtained from a screening bleeding history, and by the type of surgery planned. Furthermore, it is important that doctors and their institutions develop a standardized procedure for taking a screening history on all preoperative patients.[14]

Burk et al[15] reported a prospective study of laboratory (complete blood count, PT, APTT and BT) and bleeding history in 1603 children undergoing tonsillectomy. There were 31 patients (2%) had initial laboratory results abnormality which are persisted in repeated test after 7-10 days later in 15 patients (0.9%). The etiology of prolonged APTT in those patients are lupus inhibitor (5 patients), non-lupus inhibitor (6 patients), mild deficiency F VIII (1 patient) and 2 patients with undefined cause in whom the prolongation of APTT resolves within 5 weeks. From surgical outcome, 37 patients (2.3%) had postoperative bleeding severe enough to prolong hospital stay or readmission. Only one patient who bled had an abnormal bleeding history or coagulation screening (patient with von Willebrand disease). From this study, history had a high specificity (0.86) and moderately useful negative predictive value (0.68) with low sensitivity (0.03) and low positive predictive value (0.07) in identifying patients who bled perioperatively. Laboratory abnormalities had a high specificity (0.99) and high negative predictive value (0.98) with a low sensitivity (0.03) and low positive predictive value (0.07) in predicting postoperative bleeding. The authors concluded that in predicting perioperative bleeding, history and laboratory screening had a high specificity but a very low positive predictive value due to poor sensitivity and a low prevalence of bleeding. Some children with bleeding disorders may be identified first during routine preoperative coagulation testing, and replacement therapy or delay or cancellation of surgery may reduce or prevent perioperative hemorrhage. However, the large number of false positive laboratory tests and bleeding histories, coupled with the relative rarity of inherited and acquired coagulopathies, raises doubts about the overall value of routine screening.[15]

Munro et al[16] in 1997 reported a systematic review of the evidence of routine prepoerative testing. The results from available studies was that in routine coagulation test,

abnormalities of PT results is up to 4.8% and APTT result are still reported in up to 15.6% of tests and did not predict increased bleeding. The authors concluded that hemostatic tests have no value in predicting perioperative bleeding in the absence of clinical features. The evidence reviewed in this study does not support a policy of routine preoperative testing for bleeding disorders in all patients, and conversely provides no evidence that such a policy would be harmful. Benefits would probably only occur in the small proportion (< 1%) of patients who have an abnormal test result and for whom management is altered.[16]

Chee and Greaves[2] in 2003 reported a study of systematically reviewed literature that addresses the value of routine coagulation tests in helping to predict bleeding risk. The study included five reviews and six studies that were not included in the reviews. A non-significant difference in bleeding rate between patients with normal and abnormal coagulation test results was demonstrated from the metanalysis pooled data from four prospective tonsillectomy trials, in which routine PT APTT screening were performed.[17] The study concluded that indiscriminate coagulation testing is not useful in a surgical or a medical setting, due to the limited sensitivity and specificity of the tests, coupled with the low prevalence of bleeding disorders resulting in a high number of false positives, poor positive predictive value for bleeding and numerous false negatives resulting in false reassurance. Since most abnormal results can be predicted and most cases of significant bleeding disorder identified from a complete clinical assessment, the employment of selective laboratory testing is more cost effective and represents evidence-based clinical practice.[2]

Guidelines

The British Committee for Standards in Haematology (BCSH)[18] in 2008 has published guidelines on the assessment of bleeding risk prior to surgery or invasive procedure. The aim of this guideline is to provide rational approach to the use of bleeding history and coagulation tests prior to surgery or invasive procedure. Nine observational studies which allow calculation of predictive values and likelihood ratio of coagulation test in perioperative bleeding were included. The positive predictive value (0.03 – 0.22) and likelihood ratio (0.94 – 5.1) for coagulation test indicate that they are poor predictors of bleeding. Based on the systematic review the guideline recommends that indiscriminate coagulation screening prior to surgery or other invasive procedures to predict postoperative bleeding in unselected patients is not recommended (*Grade B, level III*), and patients undergoing surgery should have a bleeding history taken, including detail previous surgery and trauma, family history and detail medication that may cause bleeding tendency (*Grade C, level IV*).[18] The systematic review did not include studies of intracranial, neurosurgical, or ophthalmic surgery due to a paucity of data, and although testing may be more justifie in procedures with a higher risk from bleeding, the arguments regarding poor sensitivity and specificity of the coagulation tests remain.[19]

Ministry of Health Republic Indonesia[20] in 2003 has released Health Technology Assessment (HTA) on "Routine examination prior to elective surgery" based on systematically reviewed literatures by an expert panel. The HTA recommended that hemostasis screening test should not routinely done in every patient before elective surgery (*Recommendation : Grade C*). Hemostasis screening should be done in pediatric patients with : (1) history or clinical suspicion of having coagulation disorders; (2) will undergo any surgery that would disturb coagulation (e.g. *cardiopulmonary bypass)*; (3) will undergo any surgery/procedures that needs adequate hemostasis (e.g. tonsillectomy); (4) high possibility of massive bleeding during and/or after surgery (e.g. neurosurgery). In adult patients, the HTA recommended that hemostasis screening should be done in patients with history of coagulation disorder, patients on anticoagulant medication and/or would need anticoagulant therapy post surgery, and patients with liver and/renal diseases.[20]

CONCLUSION

The issue of whether routine preoperative coagulation screening (PT & APTT) is necessary remains in debate for years. One may argue that the tests will detect bleeding disorder and predict bleeding risk prior to surgery, however the limitations of the tests are frequently underappreciated. Their limited sensitivity and specificity coupled with the low prevalence and variable clinical severity of inherited bleeding disorders in most populations results in a large number of false positives, a low positive predictive value and false negatives. Many of the abnormal results detected are transient and of no clinical significance but prompt further unnecessary, time-consuming and expensive tests. This generates anxiety, may delay planned procedures, or worse, can erroneously precipitate the administration of blood products.[2] We strongly suggest that clinicians should follow guidelines and perform the coagulation tests prior to surgery appropriately based on clinical indication. It is also important that every institution should develop standardized procedure of presurgery assessment including structured bleeding history, family history and laboratory examination.

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