

Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures

British Committee for Standards in Haematology

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Summary

Unselected coagulation testing is widely practiced in the process of assessing bleeding risk prior to surgery. This may delay surgery inappropriately and cause unnecessary concern in patients who are found to have 'abnormal' tests. In addition it is associated with a significant cost. This systematic review was performed to determine whether patient bleeding history and unselected coagulation testing predict abnormal perioperative bleeding. A literature search of Medline between 1966 and 2005 was performed to identify appropriate studies. Studies that contained enough data to allow the calculation of the predictive value and likelihood ratios of tests for perioperative bleeding were included. Nine observational studies (three prospective) were identified. The positive predictive value (0.03–0.22) and likelihood ratio (0.94–5.1) for coagulation tests indicate that they are poor predictors of bleeding. Patients undergoing surgery should have a bleeding history taken. This should include detail of previous surgery and trauma, a family history, and detail of anti-thrombotic medication. Patients with a negative bleeding history do not require routine coagulation screening prior to surgery.

Keywords: surgery, coagulation screen, bleeding, clinical history.

Objective

The aim of this guideline is to provide a rational approach to the use of bleeding history and coagulation tests prior to

surgery or invasive procedures to predict bleeding risk. The aim is to evaluate the use of indiscriminate testing. Appropriate testing of patients with relevant clinical features on history or examination is not the topic of this guideline. The target population includes clinicians responsible for assessment of patients prior to surgery and other invasive procedures.

Methods

The writing group was made up of UK haematologists with a special interest in bleeding disorders and an anaesthetist. First, the commonly employed coagulation screening tests were identified and their general and specific limitations considered. Second, Medline was systematically searched for English language publications from 1966 to September 2005. Relevant references generated from initial papers and published guidelines/reviews were also examined. Meeting abstracts were not included. *Key terms:* routine, screening, preoperative, surgery, coagulation testing, APTT, PT, bleeding, invasive procedures. *Inclusion criteria:* studies had to contain enough data to enable the calculation of (i) the predictive value (PV) and likelihood ratio (LR) of the coagulation test for postoperative bleeding and/or (ii) the PV and LR of the bleeding history for postoperative bleeding. The rationale and methods for the calculations are described in Appendix 1. Nine observational case series with usable data (Table I) and one systematic review were identified (Table II).

Data elements extracted from these articles were study type, surgical setting, number and age of patients and coagulation tests performed. *Outcome data* extracted included abnormal tests, positive bleeding history, postoperative bleeding and change in management as a result of coagulation screening. *Statistical analysis:* standard methods were used to calculate the PV and LR. 95% confidence intervals for proportions were calculated by the efficient-score method, corrected for continuity (Appendix 1) (Newcombe, 1998).

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Table I. Characteristics of the trials.

Reference	Surgical setting	Number of patients	Exclusion criteria	Definition of an abnormal coagulation test	Patients with abnormal coagulation test results (%)	Preoperative change in management (%)
Gabriel <i>et al</i> (2000)	Prospective Paediatric ENT	1479	No	Not stated	4	0.3
Houry <i>et al</i> (1995)	Prospective General surgery	3242	Yes†	PT <70% control APTT ratio >1.2 control	17	1
Burk <i>et al</i> (1992)	Prospective Paediatric ENT	1603	No	≥3SD above mean	2	1
Asaf <i>et al</i> (2001)	Paediatric ENT	PT = 373 APTT = 346	Yes*	PT >13 APTT >39.9 s (no normal range given)	PT = 32 APTT = 18	n/a
Howells <i>et al</i> (1997)	Paediatric ENT	261	Yes†	≥2SD above mean	15	0
Myssiorek and Alvi (1996)	ENT‡	1138	No	Not stated	1	0
Kang <i>et al</i> (1994)	Paediatric ENT	1061	No	Not stated	3	0.1
Manning <i>et al</i> (1987)	Paediatric ENT	994	Yes*	≥2SD above mean	6	0.1
Suchman and Mushlin (1986)	General surgery	APTT = 2134	Yes*	APTT >26.5 s (no normal range given)	16	n/a

Unless otherwise stated, all patients had PT and APTT performed.

ENT, ear, nose and throat; PT, prothrombin time; APTT, partial prothrombin time; s, seconds; SD, standard deviation; n/a, not applicable.

*Patients with known history of coagulopathy.

†Patients on anti-thrombotic drugs.

‡92% of patients were less than 20 years old.

A draft guideline was produced by the writing group, revised and agreed by consensus. Further comment was made by the members of the Haemostasis and Thrombosis Task Force of the British Committee for Standards in Haematology (BCSH). The guideline was reviewed by a sounding board of approximately 40 UK haematologists, the BCSH and the Committee of the British Society for Haematology and comments were incorporated where appropriate. Criteria used to quote levels and grades of evidence are as outlined in Appendix 7 of the Procedure for Guidelines commissioned by the BCSH (<http://www.bcsghguidelines.com/process1.asp>) (Appendix 2).

Summary of key recommendations

- 1 Indiscriminate coagulation screening prior to surgery or other invasive procedures to predict postoperative bleeding in unselected patients is not recommended. (Grade B, Level III).
- 2 A bleeding history including detail of family history, previous excessive post-traumatic or postsurgical bleeding and use of anti-thrombotic drugs should be taken in all patients preoperatively and prior to invasive procedures. (Grade C, Level IV).
- 3 If the bleeding history is negative, no further coagulation testing is indicated. (Grade C, Level IV).
- 4 If the bleeding history is positive or there is a clear clinical indication (e.g. liver disease), a comprehensive assessment, guided by the clinical features is required. (Grade C, Level IV).

The principles of the coagulation screening tests used most widely in an attempt to predict bleeding and their limitations

When a blood vessel is injured the vascular, platelet, coagulation and fibrinolytic systems react in a co-ordinated fashion to prevent blood loss whilst localising thrombus to the site of injury. Bleeding can arise from abnormalities in any one, or a combination, of the four components in the haemostatic system. The physiology is complex and current widely used laboratory tests cannot accurately reproduce the *in vivo* haemostatic processes.

Coagulation tests

The first-line clotting tests commonly used are the activated partial thromboplastin time (APTT) and the prothrombin time (PT). These are both measured using automated analysers. The standardized skin bleeding time (BT) is occasionally performed. Thrombin clotting time and fibrinogen are not generally considered to be first-line clotting tests and are not discussed further.

APTT. The APTT is a test of the integrity of the intrinsic and common pathways of coagulation. The *in vitro* clotting time is measured after addition to plasma of calcium and the APTT reagent, which contains phospholipid (a platelet substitute, also called 'partial thromboplastin' as it lacks tissue factor), and an intrinsic pathway activator e.g. kaolin. The APTT should be designed to detect bleeding disorders due to

Table II. Studies of patients with abnormal PT undergoing preinvasive procedures extracted from Segal and Dzik (2005) (see original paper for references).

Procedure	Reference	Patients with abnormal test results with major bleeding	Patients with normal test results with major bleeding*
Bronchoscopy	Kozak and Brath (1994)	3/28 = 0.11	28/218 = 0.13
	Zahreddine <i>et al</i> (2003)	1/14 = 0.07	43/412 = 0.10
Central line	Foster <i>et al</i> (1992)	0/122	0/57
	Doerfler <i>et al</i> (1996)	0/33	NR
	Fisher and Mutimer (1999)	1/580 = 0.002	NR
Femoral arteriogram	Wilson <i>et al</i> (1990)	0/9	0/300
	Darcy <i>et al</i> (1996)	1/85 = 0.012	15/915 = 0.016
Liver biopsy	MacDonald <i>et al</i> (2003)	1/10 = 0.1	NR
	Ewe (1981)	4/93 = 0.043	4/85 = 0.047
	Denzer <i>et al</i> , 2001	0/29	1/50 = 0.02
	Riley <i>et al</i> (1984)	1/20 = 0.05	NR
	Tobin and Gilmore (1989)	1/100 = 0.01	NR
	McVay and Toy (1990)	4/76 = 0.05	4/100 = 0.04
	Caturelli <i>et al</i> (1993)	0/49	NR
	Sawyer <i>et al</i> (1993)	2/100 = 0.02	NR
	Kamphuisen <i>et al</i> (2002)	0/27	0/9
	Steadman <i>et al</i> (1988)	0/67	NR
	Papatheodoridis <i>et al</i> (1999)	0/112	0/45
	Choo <i>et al</i> (2000)	0/18	NR
	Bruzzi <i>et al</i> (2002)	0/31	0/19
	Smith <i>et al</i> (2003)	3/203 = 0.015	0/168
Paracentesis	McVay and Toy (1991)	1/37 = 0.03	10/352 = 0.03
Renal biopsy	Davis and Chandler (1995)	1/9 = 0.11	33/110 = 0.30
	Thompson <i>et al</i> (2004)	2/10 = 0.2	0/15
Mixed	Friedman and Sussman (1989)	0/51	NR

NR, not reported.

*Patients may have thrombocytopenia with normal PT/INR.

deficiencies of factors VIII, IX, and XI and inhibitors of the intrinsic and common pathway factors (including lupus anticoagulant and therapeutic anticoagulants). Inevitably, it also detects deficiency of factor XII.

PT. The PT assesses the integrity of the extrinsic and common pathways. The *in vitro* clotting time is measured after addition of the PT reagent, which contains thromboplastin (phospholipids with tissue factor) and calcium to citrated plasma. PT prolongation should detect important deficiencies (or rarely inhibitors) of factors II, V, VII and X. Its main use is for anticoagulant monitoring and detection of acquired bleeding disorders (especially disseminated intravascular coagulation, liver disease and vitamin K deficiency).

Skin bleeding time. This is the only *in vivo* haemostasis test available. It is used to test for defects of platelet-vessel wall interaction and should detect inherited or acquired disorders of platelet function, von Willebrand disease (VWD) and abnormalities of vessel wall integrity.

Other tests. A number of tests designed to better reflect primary haemostasis and global haemostatic mechanisms have been developed. These include the platelet function analyser-100

(PFA-100), the thrombelastogram and measures of endogenous thrombin potential. Presently, these methods are not used routinely and have not been validated for use in a preoperative setting. For these reasons, they are not reviewed further here.

Limitations

Coagulation screening tests can be meaningfully interpreted only with knowledge of their limitations and the relevant clinical situation.

General limitations

***In vitro* assays:** Both the PT and APTT are *in vitro* laboratory assays that measure the time to clot formation in a test tube and require the addition of exogenous reagents. Interpretation requires caution, as they do not accurately reflect the *in vivo* haemostatic response.

Normal biological variation: In laboratory practice the 'normal' range is usually derived from disease-free subjects and defined as results falling within two standard deviations above and below the mean for the normal population. Therefore, by definition, 2.5% of healthy subjects have a prolonged clotting

time. In the absence of relevant clinical information, unnecessary further investigations may be prompted, generating delay, anxiety, cost and potential harm.

The PT and APTT tests were designed as diagnostic tests to confirm the clinical suspicion of a bleeding disorder. This is different from their use as screening tests in healthy populations where the prevalence of unsuspected bleeding disorders is low.

Insensitivity to some clinically important bleeding disorders: For reasons explained below, mild, but clinically significant haemophilia A or VWD may be missed, resulting in false reassurance. Although of much lower prevalence, factor XIII deficiency and alpha₂-antiplasmin deficiency may cause life-threatening surgical bleeding with normal APTT, PT and skin bleeding time. However, most patients will have a positive bleeding history.

Artefact due to sample collection or pathological conditions: Erroneous coagulation results can be caused by prolonged tourniquet placement, difficult or traumatic phlebotomy, inadequate sample volumes, heparin contamination, prolonged storage, sampling from a line and failure to adjust the amount of citrate anticoagulant when the haematocrit is significantly raised. Repeat testing with attention to technique, and ideally by direct venepuncture should exclude most of these artefacts. Burk *et al* (1992) found 35 abnormal test results (either PT, APTT, BT or a combination) in 1603 prospectively screened preoperative patients. Only 15 (43%) of these abnormal results persisted on retesting 7–10 d later.

Specific limitations. APTT

Technical variability: The two main factors are the use of different APTT reagents and different end-point detection methods. APTT reagents vary enormously in their phospholipid content and activator, resulting in significant differences in the sensitivity of reagents to coagulation factor deficiencies and inhibitors, especially lupus anticoagulants, but also heparin. Ideally, for screening purposes, the assay should be set up to detect any clinically significant deficiency of factor VIII (i.e. the lower limit of the normal range for the local population, usually around 45–50 iu/dl). However, some reagent/instrument combinations result in prolongation of the APTT only when the factor VIII concentration is less than 30 iu/dl. Mild, but clinically significant haemophilia A or VWD may be missed, resulting in false reassurance. Further, sensitivity of the APTT to common pathway factor deficiencies, especially fibrinogen and prothrombin, is low.

Disease and/or physiological variability: Clinically important diseases may be modified or masked by physiological response. For example, factor VIII rises markedly in pregnancy and in response to physical stress and trauma. This results in a shortening of the APTT, which may mask the detection of mild haemophilia A and VWD.

Detection of disorders that are not associated with a bleeding tendency: Two common causes of prolonged APTT in the general population are factor XII deficiency and the lupus anticoagulant inhibitor. Neither is associated with bleeding. Test sensitivity to lupus anticoagulant and factor XII deficiency varies depending on choice of reagents.

PT

Technical variability: Differences in the composition of the PT reagent can result in variable sensitivity. The same constraints relating to the ability to detect factor deficiencies apply as in the APTT. Similarly, some reagent/instrument combinations result in prolongation of the coagulation time only when a relevant factor level drops to less than 30 iu/dl.

Detection of disorders that are not associated with a bleeding tendency: Prolongation of PT is an occasional manifestation of lupus anticoagulant.

Skin bleeding time

Technical variability: Despite attempts at standardization, the test remains poorly reproducible and subject to a large number of variables. Technique-related factors include location and direction of the incision.

Poor sensitivity and specificity: The skin bleeding time does not necessarily reflect bleeding from any other site. A range of commonly encountered patient-related factors can prolong skin bleeding time without any clear relationship to bleeding risk. These include medications (aspirin and other non-steroidal anti-inflammatory drugs), severe renal failure, thrombocytopenia, paraproteinaemia and severe anaemia. Similarly, the bleeding time may be within the normal range in VWD, platelet storage pool disorder and in aspirin users, but increased perioperative bleeding may still occur (Lind, 1991).

From the above, it is clear that coagulation tests have considerable limitations due to technical factors, insensitivity to some significant bleeding disorders and sensitivity to some common abnormalities that carry no bleeding risk.

Predictive value of coagulation screening tests

Predictive value of coagulation tests for postoperative bleeding

We calculated the positive predictive value (PPV) and negative predictive value (NPV) of a prolonged clotting time for postoperative bleeding and the postoperative bleeding rates of patients with and without a prolonged clotting time (nine studies, Tables I and III) (Suchman & Mushlin, 1986; Manning *et al*, 1987; Burk *et al*, 1992; Kang *et al*, 1994; Houry *et al*, 1995; Myssiorek & Alvi, 1996; Howells *et al*, 1997; Gabriel

Table III. Predictive value and likelihood ratios for the value of clotting tests or bleeding history in predicting postoperative bleeding and bleeding rate for patients with abnormal and normal coagulation tests.

Reference	PPV and LR+ of coagulation test for postoperative bleeding (95% CI)		PPV and LR+ of bleeding history for postoperative bleeding (95% CI)		Bleeding rate for patients with abnormal coagulation test	Bleeding rate for patients with normal coagulation test	Absolute risk difference for bleeding rate between patients with and without abnormal coagulation test	95% CI of absolute risk difference for bleeding rate* (upper limit, lower limit)
	PPV	LR+	PPV	LR+				
Gabriel <i>et al</i> (2000)	0.16 (0.08–0.28)	1.65 (0.82–3.30)	0.23 (0.06–0.54)	2.64 (0.73–9.48)	0.174	0.100	0.074	-0.014, 0.210
Houry <i>et al</i> (1995)	0.04 (0.03–0.07)	1.33 (0.91–1.93)	0.04 (0.03–0.06)	1.27 (0.99–1.64)	0.045	0.032	0.013	-0.005, 0.036
Burk <i>et al</i> (1992)	0.06 (0.01–0.23)	2.84 (0.70–11.47)	n/a	n/a	0.065	0.023	0.042	-0.012, 0.206
Asaf <i>et al</i> (2001)								
PT	0.09 (0.05–0.16)	0.94 (0.56–1.57)	n/a	n/a	0.091	0.099	-0.008	-0.070, 0.069
APTT	0.11 (0.05–0.23)	1.18 (0.59–2.40)	n/a	n/a	0.115	0.095	0.020	-0.056, 0.138
Howells <i>et al</i> (1997)	0.03 (0.00–0.15)	0.95 (0.15–6.00)	0.13 (0.01–0.53)	4.7 (0.64–34.68)	0.026	0.027	-0.001	-0.043, 0.125
Myssiorek and Alvi (1996)	0.14 (0.03–0.44)	5.10 (1.18–21.96)	n/a	n/a	0.143	0.030	0.113	-0.006, 0.408
Kang <i>et al</i> (1994)	0.22 (0.09–0.43)	4.45 (1.86–10.63)	n/a	n/a	0.222	0.056	0.166	0.037, 0.372
Manning <i>et al</i> (1987)	0.03 (0.01–0.13)	0.95 (0.24–3.74)	n/a	n/a	0.035	0.036	-0.001	-0.034, 0.094
Suchman and Mushlin (1986)	0.03 (0.01–0.05)	2.08 (1.21–3.57)	0.02 (0.01–0.03)	5.04 (3.48–7.31)	0.026	0.010	0.016†	0.001, 0.041

PPV, positive predictive value; LR+, likelihood ratio for a positive test; n/a, not available; CI, confidence interval.

*Newcombe (1998) after EB Wilson, 1927 (with continuity correction).

†Significant difference at alpha ≤0.05

et al, 2000; Asaf *et al*, 2001). In these studies, coagulation testing was performed routinely in all patients. Two studies excluded patients on antithrombotics (Houry *et al*, 1995; Howells *et al*, 1997) and three studies excluded patients with a known history of coagulopathy (Suchman & Mushlin, 1986; Manning *et al*, 1987; Asaf *et al*, 2001). The PPV of a prolonged clotting time for postoperative bleeding ranged from 0.03 to 0.22. The likelihood ratio for a positive test (LR+) ranged from 0.94 to 5.10 and when limited to the three prospective studies, the LR+ was low (range 1.33–2.84) with 95% confidence intervals crossing 1.0 in all three studies. Moreover, the postoperative bleeding rates in patients with and without a prolonged clotting time were inconsistent but similar (Table III).

Paediatric tonsillectomy. Coagulation testing has been considered especially important in paediatric surgical practice where patients may not have been exposed to any prior haemostatic challenge. Six of nine studies identified consisted only of paediatric tonsillectomy patients and, in all six, coagulation tests were performed routinely in all patients independent of bleeding history (Manning *et al*, 1987; Burk *et al*, 1992; Kang *et al*, 1994; Howells *et al*, 1997; Gabriel *et al*, 2000; Asaf *et al*, 2001). The PPV of a prolonged clotting time for postoperative bleeding ranged from 0.03 to 0.22 (Table III). The LR+ ranged from 0.94 to 4.45 and when limited to the two prospective studies, the LR+ was low (1.65 and 2.8) with confidence intervals that crossed 1.0 in both studies. In addition, the postoperative bleeding rates in paediatric patients with and without a prolonged clotting time were similar (Table III).

Testing before invasive procedures. Recently Segal and Dzik (2005) performed an evidence-based review of the ability of a prolonged PT/raised International Normalized Ratio (INR) to predict excessive bleeding resulting from an invasive procedure. They identified 25 studies (one clinical trial and 24 observational studies) in a variety of settings (Table II). The results show that the bleeding rates for patients with and without abnormal coagulation test results were similar in groups of patients undergoing bronchoscopy, central vein cannulation, angiography, liver and kidney biopsy and paracentesis. Risk difference was calculated for 14 studies and showed little absolute difference (although the confidence intervals were wide).

Limitations

All the studies included are case-series; most were retrospective and may suffer from selection bias, imperfect recall and incomplete case record documentation. The studies are also heterogeneous in terms of inclusion criteria, confounding factors, definition of abnormal clotting test, methods used to extract the bleeding history and definition of postoperative bleeding. Also, no study has sample size or

post hoc power calculation. Finally, publication bias is not excluded by the review methodology employed, although this is unlikely to have been a significant factor as all the published studies are negative from the point of view of the clinical utility of coagulation tests. In addition, the patients included are probably representative of the general population and overall conclusions are in keeping with our current understanding of the limitations of coagulation testing.

Based on the evidence, the practice of indiscriminate coagulation testing is not justifiable, at least for the population of preoperative patients included in this systematic review. Although some defend it as a means of avoiding litigation, it has been demonstrated that 30–95% of unexpected laboratory results from screening tests are either not documented or not pursued further (Muskett & McGreevy, 1986; Johnson & Mortimer, 2002). Therefore, random screening could potentially increase rather than reduce the risk of litigation. There is also a perception that coagulation tests are inexpensive. While this may be true for individual tests, the cumulative cost is considerable, especially when the financial cost of consequential additional unnecessary tests and delays to treatment are considered. We did not include patients undergoing surgery conventionally associated with a higher risk of morbidity or mortality from bleeding complications e.g. intracranial, neurosurgical or ophthalmological surgery, as the few studies that have been published did not fulfil the inclusion criteria. Although some will argue that these patients justify screening regardless of their clinical history, the same disadvantage of routine screening will apply i.e. poor sensitivity and specificity. In the absence of good quality evidence to guide practice, the authors propose that if routine screening is practiced, robust mechanisms to follow-up on the results of the tests with appropriate management intervention should be in place.

Recommendation

Routine coagulation testing to predict postoperative bleeding risk in unselected patients prior to surgery or other invasive procedures is not recommended (Grade B, Level III).

Predictive value of the bleeding history for postoperative bleeding

We calculated the value of a positive bleeding history for the prediction of bleeding (four studies, Table III) (Suchman & Mushlin, 1986; Houry *et al*, 1995; Howells *et al*, 1997; Gabriel *et al*, 2000). The PPV of the bleeding history for postoperative bleeding ranged from 0.02 to 0.23. The LR+ ranged from 1.27 to 5.04 and, when limited to the two prospective studies (Houry *et al*, 1995; Gabriel *et al*, 2000), the LR+ was low (1.27 and 2.64) with 95% confidence intervals that crossed one in both studies.

Limitations

Only four informative studies were identified. Of these only two were prospective and different methods were used in each study to elicit the bleeding history. Currently, there is no standardised approach that has been validated for use as a screening tool. Bleeding symptoms are subjective and up to 25% of healthy subjects describe common symptoms such as excessive epistaxis, gum bleeding and postpartum haemorrhage but have normal laboratory test results (Sadler, 2003).

Although the evidence indicates that a poorly structured bleeding history does not predict postoperative bleeding, it has been demonstrated that the predictive power of the history for presence of a bleeding disorder is dependent on the precise questions asked (Sramek *et al*, 1995). In a case-control study comparing patients with a proven bleeding disorder with healthy volunteers and using a standardised questionnaire, it was shown that the presence of a positive family history and bleeding after traumatic events (except parturition) identified subjects with a bleeding disorder. In contrast, some reported symptoms were non-discriminatory including gum bleeds, epistaxis and blood in the urine or stool. It was concluded that a structured interview is useful as a screening tool. However, this questionnaire has not been evaluated in a preoperative setting and further studies should address this. Further, Tosetto *et al* (2006) looked retrospectively at the utility of a mucocutaneous bleeding score in predicting bleeding after surgery or tooth extraction in patients with VWD. The results showed that clinical assessment was at least as effective as laboratory testing in predicting bleeding after tooth extraction and superior in postsurgical bleeding. The authors are not aware of any structured bleeding history that has been validated prospectively in a large number of routine preoperative surgical patients. We recommend that the bleeding history should comprise of two sections. The first section should include brief questions about bleeding symptoms, prior haemostatic challenges, family history and drug history. If the first section is positive for bleeding symptoms, a quantitative description of the symptoms should be obtained.

By targeting a subgroup of patients with a positive bleeding history for further assessment and coagulation testing, it is plausible that the PV of the combination of an abnormal bleeding history and abnormal coagulation test may be higher for postintervention bleeding than either alone. Importantly, this strategy would enable testing to be focused on the minority of subjects in whom there is reasonable suspicion of the presence of a bleeding disorder.

Recommendation

Although the published data considered in this guideline indicate that an unstructured bleeding history is not a good predictor of postoperative bleeding (Grade B, level III) there

are indications that a structured approach may be predictive. Therefore there is insufficient evidence to conclude that the bleeding history has no PV for postoperative bleeding. A bleeding history, including family history, evidence of excessive post-traumatic or postsurgical bleeding and use of antithrombotic drugs should be taken in all patients prior to surgery or invasive procedures. (Grade C, Level IV).

Disclaimer

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Appendix 1

Rationale and methods for calculation of the predictive value, likelihood ratio and absolute risk difference

Predictive value. When a test is used for screening, it is not known who has and who does not have disease. It is therefore necessary to consider the probability of the presence or absence of disease given a positive or negative test result. To do this, the positive predictive value (PPV) and the negative predictive value (NPV) of the test are calculated (see figure below). The PPV and NPV are dependent on disease prevalence. When a disease has low prevalence, PPV will be low. In other words, if the population is at low risk of having the disease, a positive result is likely to be a false positive, even when the specificity and sensitivity of the test is close to 100%.

		Disease		
		Present	Absent	
Test result	Abnormal	a (true positive)	b (false positive)	Positive predictive value (PPV) $a/(a+b)$
	Normal	c (false negative)	d (true negative)	Negative predictive value (NPV) $d/(c+d)$
		Sensitivity $a/(a+c)$	Specificity $d/(b+d)$	

Likelihood ratio. Another important indicator of the diagnostic strength of a test is the likelihood ratio (LR). The likelihood ratio of a positive test (LR+) tells you how many times more likely a positive test result will occur in a patient with the disease, as compared to a patient without the disease. A LR of 1.0 means the test provides no additional information while ratios above or below this increase or decrease the probability of disease. The product of the LR and pre-test odds determines the post-test odds of disease. In general, LRs of greater than 10 generate large shifts in pre to post-test probability, while LRs of 1.0 to 3.0 are very weak. Conversely, LRs of less than 0.1 generate large shifts in pre to post-test probability, while LRs of between 0.3 and 1.0 are very weak.

$$LR+ = \frac{\text{Sensitivity}}{1 - \text{Specificity}}$$

Absolute risk difference. The absolute risk difference is the arithmetic difference of the bleeding rate between those with abnormal coagulation and those with normal coagulation tests i.e. it is the event rate between the two comparison groups. An absolute risk difference of zero indicates no difference between the two groups. A risk difference that is greater than zero indicates that the coagulation testing was effective in reducing the risk of that outcome.

Appendix 2

Classification of evidence levels

Ia	Evidence obtained from meta-analysis of randomized controlled trials.
Ib	Evidence obtained from at least one randomized controlled trial.
IIa	Evidence obtained from at least one well-designed controlled study without randomization.
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study*.
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Classification of grades of recommendations

- A Requires at least one randomized controlled trial as part of a body of literature of overall good quality and consistency addressing specific recommendation. (Evidence levels Ia, Ib).
- B Requires the availability of well conducted clinical studies but no randomized clinical trials on the topic of recommendation. (Evidence levels IIa, IIb, III).
- C Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV).

Evidence obtained from the literature searches should be assessed by the drafting group and recommendations formulated from this evidence. As in the summary, the recommendations need to be graded according to the strength of supporting evidence using levels and grades of evidence outlined in Appendix 7 of the Procedure for Guidelines commissioned by the BCSH (<http://www.bcshguidelines.com/process1.asp>). If there are several possible options for management, these should be enumerated and also linked to supporting evidence.

*refers to a situation in which implementation of an intervention is outwith the control of the investigators, but an opportunity exists to evaluate its effect.