Regular Article

Assessment of the risk of bleeding in patients undergoing surgery or invasive procedures: Guidelines of the Italian Society for Haemostasis and Thrombosis (SISET)

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A R T I C L E   I N F O

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A B S T R A C T

Synopsis of recommendations: The Italian Society for Thrombosis and Haemostasis (SISET: Società Italiana per lo Studio dell’Emostasi e della Trombosi) promoted the development of a series of guidelines which would adopt evidence-based medicine methodology on clinically relevant problems in the field of haemostasis and thrombosis. The objective of the present guidelines is to provide recommendations for the pre-operative and pre-procedural assessment of the bleeding risk with the aim of reducing the incidence of preventable bleeding complications and limiting laboratory tests to the those necessary.

The predictive value of haemostatic tests for bleeding complications after surgery or invasive procedures has been evaluated in prospective or retrospective cohort studies only. All retrieved studies were of low methodological quality with a high potential for bias because none conducted a blinded outcome assessment. In addition, different criteria for the severity of bleeding events and different reference values of the laboratory tests were adopted. The low methodological quality limits the validity of the results of these studies. Some of the clinical queries proposed by the working group were not addressed by the studies available in the literature. The areas with evidence, although of low quality, are the following: general surgery in adults (for history, PT, APTT, platelet count and bleeding time), neurosurgery in adults (for history, PT, APTT, platelet count), adenotonsillectomy in children (for history, PT, APTT, platelet count and bleeding time), invasive procedures in adults (for PT, APTT, platelet count), dental extractions (for the bleeding time only), cataract extraction (for platelet count). No studies are available in children for major surgery other than adenotonsillectomy, neurosurgery and invasive procedures.

1-All recommendations by the multidisciplinary working group (MWG) are of grade D, as they are derived from expert consensus obtained with the RAND corporation method. The following criteria were considered for each consensus: prudential attitude for the necessity of a baseline value in case of subsequent unexpected abnormal bleeding, possibility to detect bleeding disorders especially in children.

2-The MWG recommended that a detailed personal and family history for bleeding, preferably with locally designed structured questionnaires, and physical examination should be considered good practice procedures before any surgical or invasive intervention.

3-The MWG consistently recommended that PT, APTT and platelet count should be performed routinely before surgery or invasive procedures (except for diagnostic endoscopies) both in adults and children even

Abbreviations: PT, prothrombin time; APTT, activated partial thromboplastin time; TEG, thromboelastography; PFA-100, Platelet Function Analyzer -100; NICE, National Institute of Clinical Excellence.

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Introduction and objectives

Background

Surgery and invasive procedures can be associated with abnormal bleeding which is influenced by both patient-related factors and type of intervention. The prevalence of acquired and congenital disorders predisposing to bleeding is uncertain, due to non-uniform diagnostic criteria, especially for mild, clinically silent forms, and the variability among different ethnic groups. Interventions can be associated with severe bleeding complications both in relation to their type (e.g., after adeno-tonsillectomy) and their clinical consequences (e.g., after endo-ocular surgery or neurosurgery or spinal or peridural anaesthesia).

The risk of bleeding is usually assessed by eliciting the personal and family history for abnormal bleedings, and performing laboratory tests that explore haemostatic functions. These laboratory tests generally include the prothrombin time (PT), the activated partial thromboplastin time (APTT), the platelet count, the bleeding time and, more rarely, PFA-100 closure time, thromboelastography and platelet aggregation tests. However, the choice and interpretation of these tests and the clinical management of patients with abnormal results is highly variable. The appropriate choice of laboratory tests requires an accurate assessment of the clinical situation, the evaluation of the prevalence of bleeding disorders, the test characteristics, the cost and the consequences of false-positive and false-negative results.

The accuracy of the aforementioned approach may be unsatisfactory, as the frequency of self-reported bleeding episodes may vary between 5% and 30% in the general population [1], and because the frequency of false-positive results of laboratory tests may be rather high. For instance, the finding of prolonged APTT is not uncommon due to the presence of anti-phospholipid antibodies or to FXII deficiency, which interfere with the in vitro test but are not associated with an increased risk of bleeding in vivo. An additional problem is the variability of the haemostatic tests, due to the lack of standardization for some of them (e.g., APTT, bleeding time).

A systematic review of the literature evaluated the usefulness of pre-operative laboratory tests, including tests of haemostasis, before elective surgery in patients without a positive personal history for abnormal bleeding [2]. The reported frequency of altered haemostatic tests was variable and their clinical relevance appeared uncertain as the patient clinical management was changed in very few instances. The review concluded that the benefit of pre-operative tests in individuals without a positive history for abnormal bleeding is uncertain [2].

Evidence based guidelines on the use of pre-operative tests before elective surgery have been published by the National Institute for Clinical Excellence (NICE), a government organization in the United Kingdom, in 2003 [3]. The recommendations were based on expert consensus only, due to the scarcity of adequate evidence in the literature. Haemostatic tests, such as PT and APTT, were not recommended either in adults or children because of their low predictive value, except in the presence of personal or family history of abnormal bleeding. In adults, the use of haemostatic tests was suggested, but not recommended, only in patients with ASA (American Society of Anaesthesiology) grade 3 (i.e., with serious but not life-threatening systemic diseases) with kidney disease undergoing minor surgery, intermediate or major surgery and in ASA grade 3 patients with cardiovascular disease undergoing major surgery. In addition, the NICE guidelines concluded that the lack of evidence of the benefits of pre-operative tests limited the strength of recommendations, which were based on a consensus among the panel participants.

More recently, the British Committee for Standards in Haematology has published guidelines on the assessment of bleeding risk prior to surgery or invasive procedures [4]. On the basis of a literature review indicating a poor predictive value of pre-operative haemostatic tests, their recommendation is that patients with a negative bleeding history do not require routine coagulation screening prior to surgery. However, due to the lack of adequate studies, their recommendation is of grade C. Moreover, recommendations should take into account the cultural and social context in which they may be implemented. Accordingly, in the absence of any evidence against pre-operative haemostatic tests, any decision about their performance should take into account the necessity of baseline tests in case of unexpected peri- or post-operative bleeding complications, even in case of a negative personal and family history for bleeding.

The objective of the present guidelines is to provide recommendations to all those involved in the pre-operative or pre-procedural care (both hospital staff and general practitioners) with the aim of reducing the incidence of preventable bleeding complications and limiting laboratory tests to the bare necessary. The expected benefits of implementation of the guidelines is the reduction of complications, length of hospital stay, request of consultations or additional haemostatic tests, use of inappropriate testing, with the potential consequence of erroneously considering at risk of bleeding normal subjects, and postponing surgical or other invasive procedures.

Material and methods

The guidelines were issued following a predefined methodology defined by the SISSET Guidelines program steering group and approved by the SISSET Executive Committee. Details on the methodology are published elsewhere. A full description of the methods has been published [5].

Evidence and recommendations

Bleeding history and physical examination

Background

Patient history and physical examination are essential parts of the pre-operative or pre-procedural evaluation of the bleeding risk. Structured questionnaires have been recommended for eliciting the relevant elements of patient history with the aim of determining
bleeding risk [6,7]. Specifically developed questionnaires have also been recommended for children in whom the personal history may be less informative while the family history could be more significant [8]. However, rare bleeding disorders are often recessive and both personal and family history may be silent in children.

**Evidence**

Neither validated questionnaires for bleeding history nor randomized studies comparing the value of structured questionnaires with non-structured history taking for bleeding risk are available. Only a prospective cohort study in 17 French centres evaluated the prognostic value of a structured questionnaire for peri- and post-operative bleeding complications and need for blood transfusions or re-intervention in adult patients undergoing major surgery [9]. The study enrolled 2498 patients undergoing elective surgery and 744 patients undergoing emergency surgery. 1840 patients underwent abdominal surgery, while the remaining patients underwent parietal, soft-tissue, gynaecological, thoracic, urologic, vascular or endocrine surgery.

Among 2291 patients with a negative history and physical examination who underwent major surgery, 3 had fatal bleedings (0.1%), 109 had bruises (4.8%), 68 had haematomas (3.0%) and 11 had bleedings that required re-intervention (0.48%). Among 951 patients with at least one clinical risk factor for bleeding, 2 had fatal bleedings (0.21%), 83 had bruises (8.7%), 38 had haematomas (4.0%) and 11 had bleedings that required re-intervention (1.2%).

The results of this study indicate that a negative history of bleeding is associated with a low risk of peri- or post-operative fatal haemorrhage and necessity of re-intervention. However the study has some methodological flaws. In particular, the validity of the results is limited by the lack of a blinded outcome assessment, adjustment for ASA grade and the definition of the duration of follow-up.

In children, three prospective cohort studies evaluated the prognostic value of non-structured history taking or structured questionnaires for peri- or post-operative bleeding complications and necessity of transfusions before adenoidectomy and/or tonsillectomy [10–12]. The risk of abnormal bleeding in this type of intervention is reported between 2 and 6%. The results of these studies indicate that the predictive value of clinical history for bleeding complications is uncertain, and other factors such as surgical technique or older age seem more relevant. The methodological quality of these studies is low for the lack of blinded outcome assessment.

**Good practice point**

A detailed personal and family history of abnormal bleeding and physical examination are mandatory before any surgical or invasive procedures. In particular, the working group recommends the use of structured questionnaires for bleeding history [6–8]. The recommendation ascribes a high value to an adequate and thorough personal and family history of bleeding which can be facilitated by a standardized approach, in spite of the lack of evidence for the effectiveness of this approach. These questionnaires should be developed in each institution by consensus and routinely employed before any surgical or invasive procedure.

Finally, it should be borne in mind that, in children, the personal history of bleeding may be less informative than in adults and therefore family history may be more relevant.

**PT, APTT and platelet count before surgery in adults and children**

**Background**

Haemostasis tests such as PT and APTT and platelet count are routinely employed pre-operatively.

**Evidence**

No randomized clinical trials are available evaluating the prognostic value of PT and APTT for post-operative bleeding complications in adults or children. Only 4 prospective studies [9,13–15] and 12 retrospective studies [16–27] assessed the prognostic value of PT and APTT for abnormal bleeding after surgery in adults. Bleeding complications varied from 0% to 8.1% with a frequency of abnormal tests ranging between 0.4% and 45.9% and a change in the clinical management of the patients ranging between 0% and 7.3% of cases.

The methodological quality of the prospective studies is low because they lacked blinded outcome assessment and ASA grade adjustment. In addition, different criteria for the severity of bleeding events, different reference values for the laboratory tests and variable duration of the follow-up were adopted. The low methodological quality of the studies does not provide an adequate level of evidence. As a result, the working group recommendations are based on consensus (Table 1, panel A). These recommendations apply to major and minor surgery, ocular surgery (posterior segment) and neurosurgery.

In case of cataract surgery, a randomized clinical study showed that pre-operative evaluation of the platelet count did not change the incidence of post-operative complications [28].

In children, studies are available for adenotonsillectomy only. A systematic review [29] pooled the results of 4 prospective studies and 6 retrospective studies published until October 2000 assessing the predictive value of PT and APTT for abnormal bleeding after adenotonsillectomy in paediatric patients [8,10–12,30–35]. In the prospective studies, the frequency of bleeding complications ranged between 2.3% and 11.2%. The pooled results in 3384 patients reported 116 bleeding complications (3.4%): their incidence in patients with normal PT and APTT was slightly, but not significantly lower (3.3%, 95% confidence intervals: 2.5%–4.1%) than in patients with abnormal tests (8.7%, 95% CI: 1.5%–15.9%). The authors concluded that pre-operative PT and APTT have a low predictive value in identifying patients at risk of bleeding. However, the number of subjects evaluated in the systematic

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**Table 1**

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<thead>
<tr>
<th>Panel A: Consensus on the appropriateness of PT, APTT and platelet count before surgery in adults</th>
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**COMMENT:** the tests are considered appropriate almost unanimously

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<tr>
<th>Panel B: Consensus on the appropriateness of PT, APTT and platelet count before surgery in children</th>
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**COMMENT:** the tests are considered appropriate almost unanimously

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**COMMENT:** the tests are considered appropriate but the consensus is not unanimous

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<th>Panel D: Consensus on the appropriateness of PT, APTT and platelet count before invasive procedures in children</th>
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**COMMENT:** the tests are considered appropriate almost unanimously
review was inadequate to detect a significant difference because of the low frequency of bleeding complications and of abnormal PT and APTT in the general paediatric population which would require a larger sample size. The quality of the review is also limited by the incomplete breadth of the literature search (Medline only).

After the year 2000, two retrospective studies in children undergoing adenoidectomy and/or tonsillectomy were published [36,37] but they are at high risk of bias due to the type of experimental design.

No randomized clinical trials are available on the predictive value of platelet count for post-operative bleeding complications either in adults or in children.

There are 4 retrospective cohort studies [38–41] and one prospective cohort study [9] in adults, whose methodological problems have already been addressed above.

Retrospective studies indicate that the platelet number is inversely correlated with the risk of abnormal bleeding [39]. In children two prospective studies with low methodological quality [12,42] are available on the prognostic value of the platelet count for post-operative bleeding.

Due to the lack of studies of adequate quality, the working group recommendations are based on consensus (Table 1, panel A and B). These recommendations apply to major and minor surgery, ocular surgery (posterior segment) and neurosurgery.

PT, APTT and platelet count are considered appropriate before surgery both in adults and children (grade D), even in case of a negative bleeding history.

The recommendation is based on:

— possibility to detect haemorrhagic disorders, especially in children who can have a negative history for bleeding
— necessity of a baseline test in case of peri- or post-operative complications
— usefulness of the pre-operative platelet count to detect heparin induced thrombocytopenia in patients undergoing thromboprophylaxis with heparin or low molecular weight heparin.

PT, APTT and platelet count before invasive procedures in adults and children

Evidence

A systematic review of the literature [43] pooled the results of studies in invasive procedures in adults published until August 2004, which included a randomized clinical trial and 25 observational studies, 9 of which were prospective [44–68]. These studies evaluated invasive procedures such as percutaneous liver or kidney biopsy, nephrostomy tube placement, transhepatic biliary tube placement, epidual injection or lumbar puncture, central vein cannulation or implantation of a venous access device, angiography or venography or cardiac catheterization, thoracocentesis or paracentesis, or endoscopy. The conclusions of the systematic review indicate that PT and APTT are not predictive of peri- and post-operative complications. The review has some methodological flaws, and it was based on an incomplete literature search (Medline only).

No new studies were published after the publication of this systematic review in 2004 and no data are available in children.

There are no controlled studies on the predictive value of platelet count for bleeding complications after invasive procedures in adults or children. One prospective [69] and three retrospective studies [70–72] reported an inverse relationship between the platelet count and the risk of bleeding after invasive procedures. The prospective study [69] had a small sample size and lacked blinded outcome assessment.

Due to the lack of studies of adequate quality, the working group recommendations are based on consensus (Table 1, panel C and D).

PT, APTT and platelet count are considered appropriate before invasive procedures both in adults and children (except diagnostic endoscopies) (grade D), even in case of a negative bleeding history.

The recommendation is based on:

— possibility to detect haemorrhagic disorders, especially in children with congenital haemorrhagic disorders in whom the history of bleeding can be negative
— necessity of a baseline test in case of peri- or post-procedural complications.

Bleeding time before surgery or invasive procedures in adults and children

Four prospective [9,73–75] and two retrospective studies [76,77] showed that the bleeding time is not predictive of bleeding complications of surgery in adults. In addition, the study by Lehman et al [75] showed that withholding the bleeding time in the routine pre-operative care did not have negative consequences in terms of incidence of post-surgical bleeding complications.

Two prospective studies in children undergoing tonsillectomy [10,12] showed that the bleeding time is not predictive of the bleeding risk. Prospective and retrospective studies showed that the bleeding time is not useful to predict the bleeding risk in adult patients undergoing invasive procedures [73,74,78–82]. The methodological quality of the prospective studies is low due to the lack of blinded outcome assessment. No studies are available on the usefulness of measuring the bleeding time in children before undergoing invasive procedures.

Due to the lack of studies of adequate quality, the working group recommendations are based on consensus (Table 2, panel A and B).

The bleeding time is NOT considered appropriate before surgery or invasive procedures in adults or children (grade D).

| Panel A: Consensus on the appropriateness of bleeding time before surgery and invasive procedures in adults |
| RAND BALLOT: Results and comments |
| Inappropriate | Uncertain | Appropriate |
| Participants (n=10) | Inappropriate | Uncertain | Appropriate |
| Participants (n=10) | Inappropriate | Uncertain | Appropriate |
| Participants (n=10) | Inappropriate | Uncertain | Appropriate |
| Participants (n=10) | Inappropriate | Uncertain | Appropriate |
The recommendation is based on:
- variability and lack of standardization of the test
- invasiveness of the test
- lack of predictive value
- difficulties in the execution of the test in children.

Fibrinogen, PFA-100, thromboelastography and platelet aggregation test

No data are available on the predictive value of these tests for abnormal bleeding in surgery or invasive procedures either in adults or in children, except for a prospective study of thromboelastography before renal biopsy of low methodological quality, which suggested that thromboelastography is predictive for the risk of bleeding risk [66].

Due to the lack of studies of adequate quality, the working group recommendations are based on consensus (Table 2, panel C and D). Fibrinogen, PFA-100 closure time, thromboelastography and platelet aggregation test are NOT considered appropriate before surgery or invasive procedures in adults and children.

The recommendation is based on:
- variability and lack of standardization of the tests
- redundancy of fibrinogen in case of normal PT and APTT.

Use of the haemostatic tests before dental extractions

Evidence

Dental extractions may involve significant bleeding, which can be limited by local haemostatic measures. There is only a prospective study in 30 subjects in whom the bleeding time was not correlated with post-extraction bleeding [83].

In the absence of studies, the working group suggests by consensus that:
- multiple or complex extractions, or those that are complicated by infections should be considered equivalent to interventions of minimal surgery. In case of simple extractions, laboratory tests are not appropriate, while the bleeding history should be elicited (Table 3, panel A and B).

Economical and legal implications

These recommendations differ from those provided by previously published guidelines. These recommendations ascribe a relatively high value to preventing bleeding events and a relatively low value to cost. However, costs may be different in different health systems and abnormal tests, also where these are false positive, will elicit costs of repeated and additional coagulation tests with additional time spent by haemostasis consultants in the evaluation of the tests. However a formal economic evaluation is beyond the scope of these guidelines and previously published economic analysis were not retrieved from the literature on this issue. The lack of a haemostatic baseline test in those with a negative history might not be an acceptable routine approach to the surgeon or those in charge of invasive procedures in case of unexpected bleeding complications. Moreover, it should be borne in mind that a baseline platelet count is deemed necessary in all cases for monitoring heparin induced thrombocytopenia in case of thromboprophylaxis with heparin after surgery.

Medical-legal aspects are not usually taken into account in guidelines. Bleeding events may not be predicted by pre-operative haemostatic tests and in case of a negative history the risk of bleeding is low and the prevalence of bleeding defects is low. However, the bleeding history especially in children may be silent not only in case of mild but also in moderate-severe bleeding defects. The MWG did not recommend many tests such as bleeding time, which are still routinely performed pre-operatively, but reached a consensus on performing PT, APTT and platelet counts until better evidence becomes available. Prudential considerations were taken into account for the possibility to detect silent bleeding disorders which may cause surgical bleeding complications. In these cases, abnormal peri- or postoperative bleeding events may spark litigation for the lack of a pre-operative test which can potentially detect the presence of haemorrhagic disorders.

Implications for research

The strength of the recommendations is limited by the low quality of available studies and this may imply either, a) lack of evidence of predictivity of the tests or, b) lack of evidence that tests are not predictive.

Further studies with adequate sample size are required to establish the predictive value of haemostatic tests for bleeding complications after surgery or invasive procedures. In particular, validation studies of structured questionnaires for bleeding history both in adults and children would be clinically relevant. A registry of major bleeding complications in subjects with normal tests as well as multicentre, prospective, observational studies of adequate statistical power, at least for those procedures with a high incidence of bleeding, could be useful. Moreover, a formal economic analysis of determining PT, APTT and platelet count before surgery or invasive intervention even in subjects with a negative personal history of bleeding is deemed necessary.

Notes for implementing the guidelines

The implementation of these guidelines involves a preliminary phase of monitoring the requested pre-operative and pre-procedural laboratory tests and bleeding complications in a representative sample of patients undergoing surgery and invasive procedures. Meetings are encouraged for the presentation and sharing of the contents of the guidelines with the health professionals involved in the care of patients. Subsequently, the tests requested in pre-operative or pre-procedural phase and the bleeding complications can be monitored in a representative sample of patients to compare the data obtained before and after sharing the guideline.

Table 3

<table>
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<tr>
<th>Panel A: Consensus on the appropriateness of PT, APTT and platelet count and bleeding time before dental extractions in adults</th>
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References


