RATIONAL TESTING

Preoperative risk assessment for bleeding and thromboembolism

Donald M Arnold,[1 3] Julia Anderson,[1 2] Clive Kearon[1]

Personal and family histories are the most important assessments of a patient's individual risk for bleeding and thrombosis with surgery, and will often rule out the need for routine coagulation testing

[1]Michael De Groote School of Medicine, McMaster University, Hamilton, ON, Canada
[2]Department of Haematology, Royal Infirmary of Edinburgh, Edinburgh
[3]Canadian Blood Services, Hamilton, ON, Canada
Correspondence to: C Kearon, Hamilton Health Sciences, Henderson Division, 711 Concession Street, Hamilton, ON, Canada L8V 1C3
kearonc@mcmaster.ca

Cite this as: *BMJ* 2009;339:b2299
doi: 10.1136/bmj.b2299

The patient

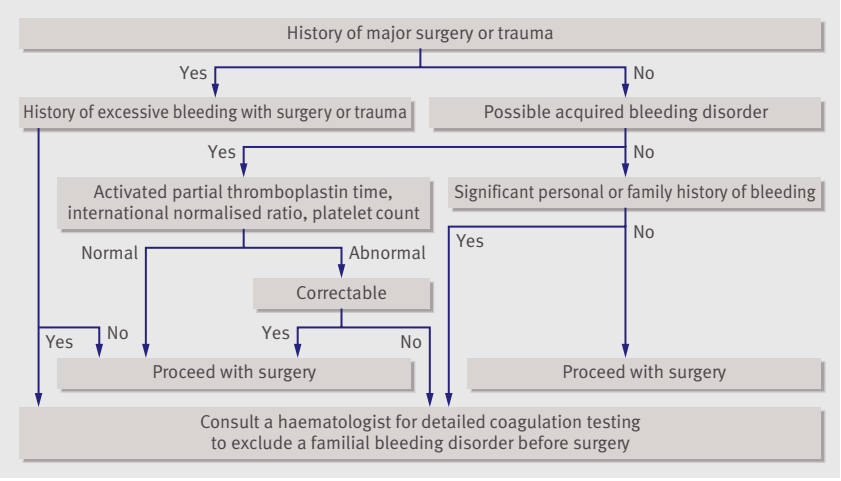
A 64 year old woman who is scheduled to have a total hip replacement is concerned that she may have a heightened risk of bleeding or thrombosis because she was told her father had died of a "clotting complication" after a car crash when he was 40 years old. It is not known if bleeding or pulmonary embolism was suspected of contributing to her father's death. The patient would like to know if she should have testing before her surgery to find out if she is at risk for bleeding or venous thromboembolism.

What is the next investigation?

The next investigation depends on the patient's personal and family history.

Personal medical history

The first and the most important step in the assessment of a patient's personal risk of bleeding (figure) and thrombosis with surgery is to review the medical history and current drugs (use of anticoagulant or antiplatelet therapy, for example).



Assessing a patient's risk of bleeding and thrombosis with surgery

Risk of bleeding

This patient has had three children, a tonsillectomy as a child, and a cholecystectomy, none of which was complicated by excessive bleeding. Based on clinical experience and a systematic review that evaluated the ability of a history of bleeding to predict postoperative bleeding,[1] the lack of excessive bleeding after these major haemostatic challenges strongly suggests that she does not have a longstanding major bleeding disorder. She describes having heavy menstrual periods, but she did not require intervention such as dilatation and curettage, iron therapy for anaemia, or hysterectomy. Menorrhagia may point to a bleeding disorder such as mild von Willebrand disease, but in general, only symptoms severe enough to require intervention are of concern.[2 3] Regardless of the severity of her menorrhagia, since she did not bleed excessively with previous major haemostatic challenges, an underlying bleeding disorder is unlikely.

Risk of thrombosis

She has never had venous thromboembolism, does not have cancer or another chronic medical condition that is associated with venous thrombosis, and is not receiving oestrogen; however, she is overweight, which is a risk factor for venous thromboembolism, including after surgery.[4] Her personal history thus does not suggest a major predisposition to either bleeding or thrombosis.

Family history

Hereditary predisposition to bleeding (haemophilia, von Willebrand disease, and platelet function defects) or to thromboembolism (factor V Leiden, G20210A prothrombin gene mutation, or deficiency of protein C, protein S, and antithrombin) may be indicated by the patient's family history.[2 5-8] None of her nine first degree relatives (including three brothers and a son), with the possible exception of her deceased father, has ever had abnormal bleeding or venous thromboembolism. Among many other relatives on her father's side, an aunt had a pulmonary embolism after a colectomy

Learning points

- Personal and family histories are the most important assessments of a patient's individual risk for bleeding and thrombosis with surgery
- Routine screening for a bleeding tendency before surgery (prothrombin time (international normalised ratio), activated partial thromboplastin time, and platelet count) is not recommended
- Patients who have had one or more major haemostatic challenges (surgery or trauma) without excessive bleeding are unlikely to have a clinically important hereditary bleeding disorder
- If a personal or family history suggests a bleeding disorder, normal routine screening results do not exclude this possibility; such patients should be referred to a haematologist
- The extent and nature of surgery are the factors that most strongly influence the risk of developing postoperative venous thromboembolism
- The presence or absence of a familial predisposition to thrombosis rarely influence decisions about the use of venous thromboembolism prophylaxis with surgery, and preoperative testing for such abnormalities is not necessary

for cancer when she was 64 years old, with no known history of excessive bleeding. The patient's family history thus does not suggest a hereditary bleeding disorder but is compatible with a predisposition to venous thromboembolism.

Routine coagulation testing

Universal routine coagulation testing (the prothrombin time—often expressed and reported by medical laboratories as an international normalised ratio, INR; activated partial thromboplastin time; and platelet count) is not recommended before surgery because, as has been shown in two systematic reviews, abnormal results obtained by screening asymptomatic people do not predict bleeding.[1 9] In patients with a suspected bleeding disorder, abnormal results of routine coagulation testing point to a clinically important abnormality such as liver disease or haemophilia; however, normal results on routine testing would not exclude important abnormalities such as a platelet function defect, von Willebrand disease, factor XIII deficiency, or mild haemophilia. Consequently, if the personal or family history suggests a hereditary bleeding disorder, the patient should be referred to a haematologist, as normal routine coagulation testing is not sufficiently reassuring to allow surgery without detailed coagulation testing.

If there is concern about the possibility of an acquired, rather than a hereditary, bleeding disorder, routine coagulation testing is helpful as normal results will exclude most of these conditions (liver disease, acquired thrombocytopenia, severe disseminated intravascular coagulation), and abnormal results may point to an easily correctable cause, such as vitamin K deficiency. If a condition is suspected that predisposes to bleeding without affecting routine coagulation tests (renal failure, for example), disease specific testing is required.

Laboratory tests to further assess risk of thrombosis

All patients who have had hip replacement are at high risk for venous thromboembolism because the surgery is major and is associated with trauma to the femoral vein.[4] Consequently, all patients who have a total hip replacement require aggressive prophylaxis for venous thromboembolism, usually with an anticoagulant drug that is given for at least 10 days and preferably for longer (benefit has been established by many randomised trials).[4] Although a hereditary predisposition to thrombosis would be expected to increase the risk of postoperative thromboembolism, this increase in risk is minor compared with the risk of thrombosis that is associated with the surgical procedure.[4 8] Therefore, determining whether the patient has a hereditary predisposition to thrombosis will not influence her perioperative management and is not necessary before surgery. Testing for hereditary predispositions to thrombosis is costly and, as with other forms of genetic testing, should not be done without discussing the implications of testing with the patient.

Outcome

This patient has had several major haemostatic challenges without excessive bleeding, so she was reassured that she was unlikely to have a bleeding disorder and that she did not need to have coagulation testing before surgery. It was explained that she might have a familial predisposition to thrombosis but, as her planned surgery was associated with a high risk of developing thrombosis, she would receive aggressive prevention for venous thrombosis regardless of the results of testing.

Her hip was replaced without abnormal bleeding, and she received venous thromboembolism prophylaxis with a low molecular weight heparin for 30 days postoperatively. She had neither bleeding nor thrombotic complications.

Contributors: The three authors contributed equally to the contents of this article, and all approve the final version. CK is guarantor.

Funding: DMA is supported by a Canadian Institutes of Health Research New Investigator Award in partnership with Hoffman-LaRoche. CK is supported by the Heart and Stroke Foundation of Canada and a Canadian Institutes of Health Research Team Grant in Venous Thromboembolism (FRN 79846). Funding agencies have had no influence on this article's contents.

Provenance and peer review: Not commissioned; externally peer reviewed.

Patient consent not required (patient anonymised, dead, or hypothetical).

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This series of occasional articles provides an update on the best use of key diagnostic tests in the initial investigation of common or important clinical presentations. The series advisers are Steve Atkin, professor, head of department of academic endocrinology, diabetes, and metabolism, Hull York Medical School; and Eric Kilpatrick, honorary professor, department of clinical biochemistry, Hull Royal Infirmary, Hull York Medical School.

LESSON OF THE WEEK

Digoxin specific antibody fragments (Digibind) in digoxin toxicity

Dorothy Ip, Hafiz Syed, Maurice Cohen

Digoxin levels may be falsely raised after administration of digoxin specific antibody

North Middlesex Hospital, London N18 1QX
Correspondence to: D Ip
dorothyip@doctors.org.uk

Cite this as: *BMJ* 2009;339:b2884
doi: 10.1136/bmj.b2884

Digoxin levels are requested in patients who present with symptoms of digoxin toxicity. Digoxin specific antibody fragments (Digibind) are indicated but can falsely raise digoxin levels. The administration of a further dose of Digibind should be guided by the patient's symptoms rather than the digoxin level.

Case report

A 78 year old woman was admitted with acute renal impairment and syncope after a lower respiratory tract infection and poor hydration. Her complex medical history included chronic atrial fibrillation, hypertension, congestive cardiac failure, and curative right hemicolectomy for caecal carcinoma. Regular medications included amlodipine, lisinopril, furosemide, spironolactone, digoxin, warfarin, lansoprazole, and quinine sulphate.

On admission, she was hypotensive and bradycardic. Apart from a painful left ankle, other systems were normal on examination. Initial blood tests showed a normocytic anaemia, hyponatraemia, hyperkalaemia, acute on chronic renal failure, raised inflammatory markers, international normalised ratio of 5.3, and digoxin concentration of 4.8 nmol/l. Her chest x ray film was normal, but her ankle radiograph showed fracture of the left tibula and fibula.

Our diagnoses were chest infection, acute on chronic renal failure, complicated by digoxin toxicity causing bradycardia induced syncope and by traumatic fracture of the left ankle.

Her diuretics, angiotensin converting enzyme inhibitor, antihypertensive drug, warfarin, and digoxin were all stopped. Her care plan included careful fluid management, treatment of hyperkalaemia, cardiovascular monitoring, and orthopaedic review.

Four hours after her admission, she became unresponsive with a pulse of 30 beats/min in atrial fibrillation and blood pressure of 108/41 mm Hg. There was no documentation of heart block. Her haemodynamic status did not improve with atropine, and digoxin-specific antibody fragments (Digibind) were given. She regained consciousness after receiving digoxin specific antibody with a pulse of 47, but her blood pressure remained unchanged.

On day 2 of her admission, the biochemist informed the on-call medical team that the digoxin concentration in the morning was 7.4 nmol/l. A further dose of digoxin specific antibody fragments were given, despite her clinical improvement. After this second dose, she developed atrial fibrillation with a rapid ventricular response requiring rate controlling treatment.

Discussion

In digoxin toxicity, initial management should be cessation of digoxin and correction of electrolytes, acid-base disturbances, and arrhythmias. Several drugs, such as amiodarone, calcium channel blockers, and quinine sulphate, can increase the plasma concentration of digoxin and should be reviewed.

Digoxin specific antigen binding fragment has a half life of 15-20 hours with normal renal function. As digoxin specific antibody fragments have a large volume of distribution, improvement of symptoms and signs of digoxin toxicity occurs within a few hours.

Digibind is indicated in life threatening digoxin toxicity, the clinical manifestations of which include ventricular tachycardia or fibrillation, progressive and bradyarrhythmia not responsive to atropine, a serum potassium concentration of >5 mmol/l in the context of possible life threatening digoxin toxicity.

Digoxin specific antibody fragments interfere with digoxin immunoassay measurements.[1] Clinicians should be cautious when interpreting digoxin concentration after their administration. Patients should be assessed for symptoms and signs of toxicity before further doses are given. In this case, the second dose was not indicated, as the digoxin concentration was falsely raised after the initial administration of digoxin specific antibody fragments.

In patients with signs of digoxin toxicity, digoxin measurements should be taken 6-12 hours after the dose has been given. If toxicity is a concern in patients taking digoxin as a new medication, measurement should be done only after the plasma concentration has reached a steady state, usually within 7-10 days but longer in patients with renal impairment.

The drugs for managing rate control in permanent atrial fibrillation as recommended by National Institute for Health and Clinical Excellence guidelines are digoxin, β blockers, and calcium channel blockers.[2] After digoxin specific antibody fragments have been given, restarting digoxin should be postponed until their effects have been eliminated.[1] This may require several days, and longer in patients with renal impairment.

Contributors: MH is guarantor.

Competing interests: None declared.

Patient consent obtained.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Accepted: 3 November 2008