THERAPEUTICS

New oral anticoagulants for thromboprophylaxis in patients having hip or knee arthroplasty

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EDITORIAL by Ferner

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This is the first of a series of occasional articles on therapeutics for common or serious conditions, covering new drugs and old drugs with important new indications or concerns. The series advisers are Robin Ferner, honorary professor of clinical pharmacology, University of Birmingham and Birmingham City Hospital, and Philip Routledge, professor of clinical pharmacology, Cardiff University. To suggest a topic for this series, please email us at practice@bmj.com.

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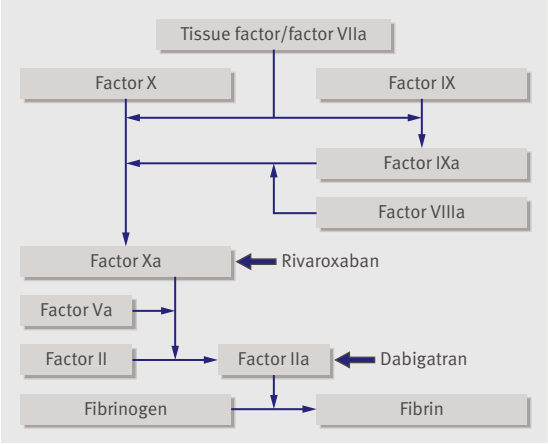
Listen to a podcast interview with Jeff Weitz, who discusses the use of new oral anticoagulants for thromboprophylaxis in patients having hip or knee arthroplasty, at bmj.com/podcast

The newest oral anticoagulants, dabigatran etexilate (hereafter referred to as dabigatran) and rivaroxaban, have been approved in more than 70 countries for prevention of venous thromboembolism after elective hip or knee arthroplasty. Dabigatran targets thrombin (factor IIa) and rivaroxaban targets factor Xa[1] (figure).

Evidence based guidelines recommend anticoagulant thromboprophylaxis with subcutaneous agents such as low molecular weight heparin or fondaparinux or oral agents such as warfarin, dabigatran, or rivaroxaban for at least 10 days after knee arthroplasty and for up to 35 days after hip arthroplasty.[2 3] Unlike low molecular weight heparin and fondaparinux, dabigatran and rivaroxaban can be taken orally, and, unlike warfarin, these agents do not require coagulation monitoring and dose adjustments.

Table 1 summarises the advantages and disadvantages of the new oral anticoagulants compared with low molecular weight heparin, fondaparinux, and warfarin. Large randomised controlled trials are currently evaluating the new oral anticoagulants as alternatives to warfarin for stroke prevention in patients with atrial fibrillation, treatment of venous thromboembolism, and management of patients with acute coronary syndrome. Emerging data comparing dabigatran and rivaroxaban with warfarin for these indications are promising, and dabigatran was recently approved by the US Food and Drug Administration and Health Canada for stroke prevention in atrial fibrillation.[4 5] However, our review will focus on their use for prevention of venous thromboembolism in major orthopaedic surgery, which is the only indication approved in the United Kingdom. We will not consider other new oral anticoagulants such as apixaban, which are under regulatory review but not yet licensed for clinical use.



Sites of action of the new oral anticoagulants. By targeting thrombin, thrombin inhibitors (such as dabigatran) block thrombin mediated conversion of fibrinogen to fibrin, which leads to clot formation, as well as thrombin mediated feedback activation of coagulation factors V and VIII. Factor Xa inhibitors (such as rivaroxaban and apixaban) block the conversion of prothrombin to thrombin by the prothrombinase complex (the complex of factor Xa and factor Va bound to the surface of the activated platelet). Heparin targets thrombin and factor Xa equally well, whereas low molecular weight heparin targets factor Xa to a greater extent than thrombin, and fondaparinux targets only factor Xa. Vitamin K antagonists, such as warfarin, reduce the levels of factors II, VII, IX, and X as well as protein C and S

CASE SCENARIO

A 78 year old woman has had an elective left hip arthroplasty and on discharge her orthopaedic surgeon prescribes a further, 28 day postoperative course of anticoagulant prophylaxis. She sees her general practitioner a week later, concerned that these "blood thinners" are tablets, whereas she had daily injections after her knee replacement three years ago. Her general practitioner explains that the tablets have recently become available and that guidelines recommend them as an alternative to injections as they are as effective, more convenient, and safe.

How well do the new oral anticoagulants work?

Dabigatran has been evaluated for prevention of venous thromboembolism in four phase III randomised controlled trials involving 8185 patients having hip or knee arthroplasty (table 2).[6-9] In the two hip arthroplasty trials, dabigatran or enoxaparin was continued for 28 to 35 days,[6 7] and in the two knee arthroplasty trials the same drugs were given for 10 to 14 days.[8 9] In patients having hip arthroplasty, dabigatran 150 mg or 220 mg once daily was not worse than enoxaparin 40 mg once daily for the prevention of total venous thromboembolism and for all cause mortality.[6 7] In patients having knee arthroplasty, dabigatran 150 mg or 220 mg once daily was not worse than enoxaparin 40 mg once daily[8] and was worse than enoxaparin 30 mg twice daily for prevention of total venous thromboembolism and for all cause mortality.[9] Table 2 gives details of these trials and data on numbers needed to treat.

Table 1 | Advantages and disadvantages of the new oral anticoagulants compared with low molecular weight heparin, fondaparinux, and warfarin

Comparisons	Feature	Clinical implications
Compared with low molecular weight heparin or fondaparinux		
Advantages	Oral administration	More convenient for patients
Disadvantages	Higher potential for drug interactions	More drug restrictions
	New agent	Less mature safety database
Compared with warfarin		
Advantages	Rapid onset of action	No need for "bridging" anticoagulation in patients who need immediate anticoagulant effect
	Predictable anticoagulant effect	No need for routine coagulation monitoring
	Low potential for food interactions	No need for dietary precautions
	Lower potential for drug interactions	Fewer drug restrictions
Disadvantages	No antidote	Inability to reverse anticoagulant effect in patients with bleeding or needing urgent intervention
	New agent	Less mature safety database

Table 2 | Efficacy and safety of dabigatran compared (on the basis of four phase III randomised controlled trials) with enoxaparin for prevention of venous thromboembolism in patients having hip or knee arthroplasty

Surgery	Hip arthroplasty (RE-NOVATE trial[6]) (n=3494)	Hip arthroplasty (RE-NOVATE II trial[7]) (n=2055)	Knee arthroplasty (RE-MODEL trial[8]) (n=2076)	Knee arthroplasty (RE-MOBLIZE trial[9]) (n=2615)
Total venous thromboembolism or death				
Enoxaparin (% of patients)	6.7	8.8	37.7	25.3
Dabigatran 220 mg (% of patients):	6.0	7.7	36.4	31.1
Absolute risk reduction (95% CI)	NS	NS	NS	−5.8 (−0.8 to −10.8)
Number needed to treat	NA	NA	NA	−17*
Dabigatran 150 mg (% of patients):	8.6	NA	40.5	33.7
Absolute risk reduction (95% CI)	NS	NA	NS	−8.4 (−3.4 to −13.3)
Number needed to treat	NA	NA	NA	−12*
Major bleeding (% of patients)†				
Enoxaparin	1.6	0.9	1.3	1.4
Dabigatran 220 mg	2.0	1.4	1.5	0.6
Dabigatran 150 mg	1.3	NA	1.5	0.6

CI=confidence intervals.

NS=not significant (P>0.05).

NA=not applicable.

*Number needed to treat is negative because enoxaparin was superior to dabigatran; this number therefore refers to how many patients would need to be treated with enoxaparin to prevent one event.

†Absolute risk reduction between dabigatran and enoxaparin was not statistically significant.

Table 3 | Efficacy and safety of rivaroxaban compared (on the basis of four phase III randomised controlled trials) with enoxaparin for prevention of venous thromboembolism in patients having hip or knee arthroplasty*

Surgery	Hip arthroplasty (RECORD1[10]) (n=4541)	Hip arthroplasty (RECORD2[11]) (n=2509)	Knee arthroplasty (RECORD3[12]) (n=2531)	Knee arthroplasty (RECORD4[13]) (n=3148)
Total venous thromboembolism or death				
Enoxaparin (% of patients)	3.7	9.3	18.9	10.1
Rivaroxaban (% of patients)	1.1	2.0	9.6	6.9
Absolute risk reduction (95% CI)	2.6 (1.5 to 3.7)	7.3 (5.2 to 9.4)	9.3 (5.9 to 12.4)	3.2 (0.7 to 5.7)
Number needed to treat	38	14	11	31
Major bleeding (%)†				
Enoxaparin	0.1	0.1	0.5	0.3
Rivaroxaban	0.3	0.1	0.6	0.7

CI=confidence interval.

*Absolute risk reduction and number needed to treat data are provided if statistically significant differences exist.

†No statistically significant differences in major bleeding were found between rivaroxaban and enoxaparin in the individual trials, but in a meta-analysis of the results of the four RECORD trials, which included major bleeding at the surgery site, the rate of major plus clinically relevant non-major bleeding was higher with rivaroxaban than with enoxaparin at the end of the treatment period.[14]

Rivaroxaban has been evaluated for prevention of venous thromboembolism in four phase III randomised controlled trials (the RECORD trials) involving 12 729 patients having hip or knee arthroplasty (table 3).[10-13] In the two hip arthroplasty trials rivaroxaban was continued for 31 to 39 days in both trials,[10 11] and enoxaparin was continued for 31 to 39 days in one trial[10] and 10-14 days in the other.[11] In the two knee arthroplasty trials, both treatments were given for 10 to 14 days.[12 13] In patients having hip arthroplasty, rivaroxaban 10 mg once daily was superior to enoxaparin 40 mg once daily for prevention of total venous thromboembolism and for all cause mortality.[10 11] In patients having knee arthroplasty, rivaroxaban 10 mg once daily was superior to enoxaparin 40 mg once daily for prevention of total venous thromboembolism and for all cause mortality.[12 13]

How safe are the new oral anticoagulants?

Postoperative bleeding is the major safety concern in patients having hip or knee arthroplasty. The definitions of major bleeding varied in the trials with the different agents, which complicates cross study comparisons. On the basis of a definition that included bleeding from the surgery site, major bleeding rates were similar for dabigatran and enoxaparin.[6-9] When bleeding from the surgery site was included in a meta-analysis of the results of the four RECORD trials, the rate of major plus clinically relevant non-major bleeding was higher for rivaroxaban than for enoxaparin.[14]

What are the precautions?

Box 1 summarises the precautions that prescribers should consider when treating patients with dabigatran or rivaroxaban.

Age and renal impairment

As both dabigatran and rivaroxaban are partly cleared renally, consider their use with caution in patients with renal impairment. Dabigatran is contraindicated in patients with a creatinine clearance <30 mL/min and should be prescribed at a dose of 150 mg once daily for patients who are aged over 75 years or have a creatinine clearance of 30 to 50 mL/min.[16] All other patients should receive dabigatran 220 mg once daily. Rivaroxaban is contraindicated in patients with a creatinine clearance <15 mL/min.[17]

Drug interactions

Dabigatran is contraindicated in patients taking quinidine or ketoconazole, potent inhibitors of the P-glycoprotein membrane transporter, as they increase dabigatran concentrations.[18] Dabigatran should also be avoided in patients taking rifampicin, a potent inducer of the P-glycoprotein efflux membrane transporter that reduces dabigatran concentrations.[18] Dabigatran should be prescribed at a dose of 150 mg once daily in patients taking amiodarone or verapamil (moderately potent inhibitors of P-glycoprotein[16]), although when dabigatran was compared with warfarin for stroke prevention in patients with atrial fibrillation, concomitant use of amiodarone with a maximum 300 mg daily dose of dabigatran did not lead to adverse outcomes.[18] Clopidogrel is a substrate for P-glycoprotein, but no evidence exists of a clinically relevant interaction between

Box 1 | Practical points for use of dabigatran and rivaroxaban for preventing venous thromboembolism in patients having hip or knee arthroplasty

Dose

Dabigatran

- Use 150 mg once daily in patients aged over 75 years, those with a creatinine clearance of 30-50 mL/min, and those taking amiodarone or verapamil; use 220 mg once daily in all other patients

Rivaroxaban

- Use 10 mg once daily

Coagulation monitoring

- Routine coagulation monitoring is not needed

Contraindications

- Dabigatran is contraindicated in patients taking quinidine, ketoconazole, or rifampicin
- Rivaroxaban is contraindicated in patients taking ketoconazole, itraconazole, ritonavir, or rifampicin

Renal function

- Calculate creatinine clearance in all patients before treating with a new oral anticoagulant.* Dabigatran is contraindicated if the estimated creatinine clearance is <30 mL/min, and rivaroxaban is contraindicated if the estimated creatinine clearance is <15 mL/min.

Invasive procedures

- Stop prophylactic doses of dabigatran and rivaroxaban 24-48 hours before invasive procedures
- If the risk of bleeding is high, measure the activated partial thromboplastin time or prothrombin time. A normal activated partial thromboplastin time with dabigatran and a normal prothrombin time with rivaroxaban indicate a lack of a residual anticoagulant effect

Management of bleeding

- Stop the drug
- No specific antidotes for dabigatran or rivaroxaban exist. Platelets and fresh frozen plasma may be helpful for treating bleeding but will probably not reverse the anticoagulant effect of the new drugs. Agents such as recombinant activated factor seven (rVIIa) or activated prothrombin complex concentrates may be useful for treatment of severe or life threatening bleeding, but their efficacy is unproved
- Dialysis or haemofiltration using a charcoal filter may remove dabigatran from the circulation[15]

*Creatinine clearance can be estimated using the Cockcroft-Gault equation: estimated glomerular filtration rate = (140 – age) × (weight (kg)) × (constant)/serum creatinine (μmol/L), where constant is 1.23 for men and 1.04 for women.

clopidogrel and dabigatran. Dabigatran does not interact with the cytochrome P450 system.

Rivaroxaban should be avoided in patients taking potent inhibitors of both cytochrome P450 3A4 and P-glycoprotein, such as azole antifungals (for example, ketoconazole and itraconazole) and protease inhibitors (for example, ritonavir) as these increase the plasma concentrations of the drug.[15] Rivaroxaban should also be avoided in patients taking rifampicin, which is a potent inducer of cytochrome P450 3A4 and P-glycoprotein that reduces rivaroxaban exposure by about 50%.

Invasive procedures

Prophylactic doses of dabigatran and rivaroxaban should be stopped for 24-48 hours before invasive procedures, with the time depending on the type of procedure and the associated risk of bleeding. A normal activated partial thromboplastin time or thrombin time with dabigatran and a normal prothrombin time with rivaroxaban indicate a lack of a residual anticoagulant effect.

Management of bleeding

Although no specific antidotes exist for dabigatran or rivaroxaban, minor bleeding may respond to mechanical pressure. For more serious bleeding, infusion of platelets and fresh frozen plasma may be helpful, but such treatment has not been formally evaluated and will probably not reverse the anticoagulant effect of the new drugs. Agents such as recombinant factor VIIa or activated prothrombin complex concentrates may be useful for treatment of severe or life threatening bleeding, but their efficacy is unproved. Dialysis or haemofiltration using a charcoal filter may remove dabigatran from the circulation[15]; these measures are not useful to remove rivaroxaban because of its high protein binding.

How are the new oral anticoagulants taken and monitored?

Box 1 summarises the practical considerations in the treatment of patients with dabigatran or rivaroxaban. Box 2 provides some tips for patients.

Either dabigatran or rivaroxaban would be a reasonable choice for extended prophylaxis in the original case scenario. Dabigatran is taken orally at a daily dose of 150 mg or 220 mg, and for the case above a daily dose of 150 mg may be the safer option; treatment starts with a half dose (75 mg or 110 mg) orally one to four hours after surgery. Rivaroxaban is given orally at a daily dose of 10 mg, with the first dose given six to eight hours after surgery. Treatment should be continued for 28 to 35 days in patients having hip arthroplasty and for 10 to 14 days in those having knee arthroplasty.[2] Neither food nor concomitant administration of proton pump inhibitors materially affects the absorption of dabigatran or rivaroxaban.

Routine coagulation monitoring is not needed for dabigatran or rivaroxaban. Dabigatran prolongs the activated partial thromboplastin time and the thrombin time, whereas rivaroxaban prolongs the prothrombin time. However, the effect of these drugs on these tests is not dose linear, and, given the relatively short half lives of the new oral anticoagulants, the extent of their effect on tests of coagulation depends on when the blood was collected relative to the timing of the last dose of administered drug.

How cost effective are the new oral anticoagulants?

Dabigatran and rivaroxaban are likely to be at least as cost effective as enoxaparin for the prevention of venous thromboembolism in patients having hip or knee arthroplasty because they exhibit similar efficacy and safety, and the acquisition costs of the drugs are similar. In the UK the daily drug acquisition costs are £3.84 for low molecular weight heparin, £4.20 for dabigatran 220 mg once daily, and £4.50 for rivaroxaban,[2] whereas the cost of a one month supply of warfarin is about £1. For inpatients or those needing a nurse for home injection, the cost of administration of subcutaneous enoxaparin is higher than that of the new oral anticoagulants, offsetting its slightly lower

Box 2 | Tips for patients

- Dabigatran and rivaroxaban are anticoagulant drugs that are used to prevent the development of blood clots in the legs and lungs in patients who have hip or knee replacement surgery
- The treatment is taken as one or two capsules or pills, once daily
- Before starting treatment you must tell your doctor about all of the other medicines that you are taking
- Some patients taking dabigatran develop gastric irritation, which generally resolves by itself without having to stop the treatment. Symptoms might be avoided by taking the drug with food. If symptoms persist, consult your doctor
- Dabigatran and rivaroxaban can be associated with minor bruising. If you develop bleeding you should consult your doctor immediately
- Treatment once a day should be continued for 28 to 35 days after hip surgery and for 10 to 14 days after knee surgery
- You will have to stop taking dabigatran or rivaroxaban treatment for one to two days before any planned surgery

acquisition cost.[19] A cost effectiveness analysis from the Irish healthcare perspective found that both rivaroxaban and dabigatran were more cost effective than enoxaparin, with rivaroxaban being the most cost effective.[20]

How do the new oral anticoagulants compare with other drugs?

Dabigatran and rivaroxaban are convenient alternatives to low molecular weight heparin and warfarin in prophylaxis for major orthopaedic surgery. However, data on longer term safety are pending. Table 1 compares the new oral anticoagulants with low molecular weight heparin, fondaparinux, and warfarin.

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Endpiece

Banker, speculator, or gambler?

> When as a young and unknown man I started to be successful I was referred to as a gambler. My operations increased in scope and volume. Then I was known as a speculator. The spheres of my activities continued to expand and presently I am known as a banker. Actually I have been doing the same thing all the time.

Sir Ernest Cassel (1852–1921) quoted in *Money Talks*, edited by Robert W Kent, 1985

Sir Ernest Cassel was a merchant banker and the private banker to Edward VII. He founded the Cassel Hospital in London, currently a personality disorder service run by the West London Mental Health NHS Trust.

Submitted by Sanju George, specialist registrar, Queen Elizabeth Psychiatric Hospital, Birmingham UK

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SAFETY ALERTS

Early detection of complications after laparoscopic surgery: summary of a safety report from the National Patient Safety Agency

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Following a Department of Health review in July 2010, the National Patient Safety Agency will be abolished and some of its functions transferred to a Patient Safety subcommittee of the new NHS Commissioning Board. Reports of incidents are, however, still encouraged at www.npsa.nhs.uk.

Why read this summary?

Laparoscopic surgery is increasingly common—in 2005-6, 84% of the 49 077 cholecystectomies in England were undertaken laparoscopically.[1] The technique is safe for most patients, and advantages include faster recovery and shorter hospital stay. A small number of people develop complications, however, some of which are specific to laparoscopy. These include gas emboli, arrhythmias, and shock when establishing the pneumoperitoneum (first step in any laparoscopic procedure). Injury to the bile duct and other organs is also more likely, given limited vision and control of the operative field compared with open surgery.

Although most injuries are identified and dealt with during surgery, some are difficult to detect. One study of cases from US litigation claims showed that two thirds of laparoscopic injuries were initially missed.[2] Some complications—such as diathermy damage to bowel, which results in late perforation or injury to the bile duct—may not present until several days after surgery.[3] Late presentation of complications can cause problems because many laparoscopic procedures are done as day cases (sometimes in stand alone units). Signs can be subtle so may be missed by staff caring for patients after discharge in the community or on general wards. Delayed recognition of complications was the second most common reason for English litigation claims relating to laparoscopic cholecystectomy during the past 15 years.[4]

Between April 2005 and April 2010, healthcare staff in England and Wales reported to the National Patient Safety Agency (NSPA) 11 deaths and 37 serious incidents in patients who had deteriorated after laparoscopic surgery. These incidents are probably greatly under-reported, given what audit data show about complication rates.[5]

A typical incident reads: "The patient underwent laparoscopic cholecystectomy, deteriorated a day later. He was diagnosed with pancreatitis and transferred to HDU [high dependency unit], then ITU [intensive therapy unit]. On day two a laparotomy showed a bowel perforation. [Patient name] died later that day."

This article is based on a safety report from the NPSA issued in September 2010 (NPSA/2010/RRR016; www.nrls.npsa.nhs.uk/resources/?entryid45=82748) on the need for timely detection of patients who deteriorate after laparoscopic surgery. The guidance does not cover actions to minimise entry related injuries or compare the safety of laparoscopic versus open surgery, because voluntary incident reports cannot reliably provide relative rates of complications.

Problems identified by the National Patient Safety Agency

Incident data suggested that complications can present days after surgery and that action was often delayed. The NPSA's review of incidents, litigation data, and local investigation reports also identified some common system failings. These included inconsistencies in policies for discharging patients, with no criteria for senior medical review in the recovery period; knowledge gaps among staff (general practitioners or nursing staff on general wards) about signs of serious postoperative deterioration and the need for rapid action; and lack of clarity on where patients should go for advice and assessment if problems do occur. A recent survey of laparoscopic surgeons in Great Britain and Ireland indicated that fewer than one in seven had a protocol in place for monitoring patients.[6]

What can we do?

The NPSA guidance asks organisations to review discharge policies, specifying observations required in the immediate postoperative period and defining strict criteria for medical review; provide information on discharge to patients, carers, and general practitioners on signs of deterioration; and give patients a single telephone contact number for urgent medical advice if problems occur.

For individual clinicians

Before procedure

Inform the patient about complications, including rare ones (such as delayed presentation of perforation or visceral vessel injury) and the general signs to look for, including persistent abdominal tenderness or pain. Provide the patient with written information at time of consent, ideally 24 hours before the procedure.

Give patients a single number on discharge (same for weekdays and weekends) for contact with surgical team if they feel very unwell within 24 hours of the procedure

Schedule lists to allow for recovery time (more complex procedures or patients in the morning).[7]

After discharge

Have a high index of suspicion for patients who are generally unwell after the procedure. Be aware that complications after laparoscopic procedures can present in more subtle ways than for open surgery—for example, without florid signs of circulatory instability and peritonitis, abnormal temperature, or abnormal white cell count. Look out for general signs of poor recovery, given that most patients are generally well (mobile, with recovered appetite) hours after laparoscopic procedures.

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- Safer treatment doses for low molecular weight heparins (*BMJ* 2010;341:c5884)
- Safer administration of insulin (*BMJ* 2010;341:c5269)
- Reducing the risk of retained swabs after vaginal birth (*BMJ* 2010;341:c3679)
- Checking for pregnancy before surgery (*BMJ* 2010;341:c3402)

Monitor vital signs using Modified Early Warning Score or Paediatric Early Warning Score (further information on how to recognise patients who are deteriorating is available at: www.patientsafetyfirst.nhs.uk).

Any of the following should alert the clinician to the possibility of a complication related to laparoscopic surgery:

- Increasing or persistent abdominal pain
- Abdominal distension or tenderness
- Continued or increasing opioid requirements
- Nausea, poor appetite
- Reluctance or inability to mobilise
- Rigors, fevers, or persistent pyrexia
- Tachycardia or any arrythmia
- Poor urine output
- Bile stained fluid or excessive blood in a drain
- Raised inflammatory markers.

Although bile or excessive blood in a drain is an ominous sign, its absence does not preclude an abdominal complication. It can also not be relied on as a sign, because only a minority of surgeons now insert drains routinely.

Contact a senior member of the surgical team if one or more of these features persists in a patient in the first 24 hours.

Be aware that some complications will be apparent only a few days after discharge. Examples include diathermy damage to bowel and bile leakage after cholecystectomy, where there may be minimal signs and symptoms for the first few days after surgery.

If complications are suspected, even if initial investigations (imaging or repeat laparoscopy) are negative, they cannot definitively be ruled out. Patients should be treated on the basis of their clinical condition.

Further information on recognising and managing complications is available from professional bodies.[8]

What more do we need to know?

While developing this guidance, the NPSA considered specifying a standard (such as six hours) for postoperative monitoring. Most stakeholders thought that evidence to support a minimum observation period was lacking and that an arbitrary time limit was not justified. Some complications may occur some time after an uneventful laparoscopic procedure. A fixed monitoring period would also affect productivity of day case units, making afternoon lists difficult. However, scheduling lists should allow for appropriate monitoring of more complex cases.

Some questions remain about appropriate management once complications have been identified, such as indications for computed tomography versus repeat laparoscopy. Currently, this is determined by local priorities, availability of facilities, and clinical preference. More evidence is also needed on ways to minimise entry related complications, such as the Hasson technique (introducing the first port under direct vision with a blunt trochar), because practice seems to vary considerably.[9]

We do not know enough about current practice and frequency of complications. A recent survey of 648 members of the Association of Surgeons of Great Britain and Ireland, prompted by early discussion with the NPSA, suggested that more than two thirds had witnessed visceral or major vessel injury during laparoscopic surgery in the previous 12 months.[6] More reliable data on harm are needed—the last national audit of laparoscopic cholecystectomy in England was carried out in 1994.

How will we know when practice has become safer?

Organisations were given until March 2011 to implement actions from the NPSA guidance and will have to report compliance at that point. Safer processes for local audit could include: making sure that a 24 hour a day contact telephone number and descriptions of warning signs are available to staff and patients at discharge; monitoring possible markers of surgical complications, such as number of patients still in hospital two days after a laparoscopic procedure, number of postoperative endoscopic retrograde cholangiopancreatographies (ERCPs), and number of readmissions for the same condition. Further national clinical audits are needed to monitor activity, harm, and trends over time.

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Endpiece

Elocution lesson

> You must learn to talk clearly. The jargon of scientific terminology which rolls off your tongues is mental garbage.

Martin Henry Fischer (1879–1962), US physician and author

In *Fischerisms* (1944), edited by Howard Fabing and Ray Marr

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