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Perioperative stroke after non-cardiac, non-neurological surgery

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Learning objectives

By reading this article, you should be able to:

- Identify patients with risk factors for perioperative stroke.
- Implement perioperative optimisation strategies for high risk patients.
- Discuss issues related to postoperative screening and management of stroke.
- Discuss recent evidence about the frequency and sequelae of covert perioperative stroke.

Key points

- The incidence of perioperative stroke after non-cardiac surgery is 0.1–1.9%.
- Patients should be screened for risk factors for perioperative stroke.
- Elective surgery should preferably be delayed for 9 months after a previous stroke; emergency surgery should not be delayed.
- Perioperative strokes are under-recognised and are associated with a high morbidity and mortality.
- Covert stroke occurs in 7% of patients undergoing non-cardiac surgeries and is associated with postoperative cognitive decline.

Clinical scenario

A 75-yr-old man presents for total knee replacement. Further questioning reveals that he suffered an ischaemic stroke 2 months ago, and has mild residual weakness of his left hand. He has a history of atrial fibrillation and takes warfarin. Should you delay his surgery? How should you manage his anticoagulation?

Perioperative stroke is a devastating complication of surgery that is relatively under-recognised and uncharacterised compared with other perioperative complications. Although the reported incidence varies by population studied, approximately 0.1–1.9% of patients having non-cardiac, non-neurological surgery will experience a stroke.[1,2] The consequences of perioperative stroke can be devastating and these patients do poorly, with a rate of disability and mortality higher than after stroke unrelated to surgery. Although perioperative stroke is relatively understudied compared with postoperative complications of similar incidence and severity, recent evidence has provided more insight into how we can prevent, identify and manage this complication. We provide a narrative review of the evidence summarising the definitions, epidemiology, prevention and management of perioperative

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stroke in non-cardiac non-neurological surgery (Fig. 1), and we refer readers to a published consensus statement from the Society for Neuroscience in Anesthesiology and Critical Care (SNACC) on the perioperative care of patients at high risk of perioperative stroke.[3]

Definition, aetiology and epidemiology of perioperative stroke

Definition and aetiology of perioperative stroke

The SNACC Consensus Statement defines 'perioperative stroke' as a brain infarction of ischaemic or haemorrhagic aetiology that occurs during surgery or within 30 days after surgery.[3] This can be further divided into two categories: 'overt stroke' is an acute brain infarct with clinical manifestation lasting longer than 24 h, and, although not the focus of this review, a 'covert stroke' represents a brain infarct that is not recognised at the time of onset because of unappreciated, subtle or misclassified clinical manifestations but is detected on brain imaging done at the time or subsequently.[4]

Perioperative strokes can result from multiple aetiologies. The majority of perioperative strokes are reported to be cardioembolic in origin.[3] Many anaesthetists believe intraoperative hypotension is a common cause.[5] However, perioperative strokes resulting solely from hypoperfusion are relatively uncommon.

Incidence and epidemiology of perioperative stroke

Although perioperative stroke is a significant source of perioperative morbidity and mortality, many patients and anaesthetists underestimate the incidence and impact on postoperative mortality.[5,6] A large retrospective analysis of the US National Inpatient Sample (NIS) found that non-fatal stroke occurred in 0.54% of patients undergoing non-cardiac surgery, similar to the rate of non-fatal acute myocardial infarction (0.76%).[7] Data from 523,059 non-cardiac, non-neurological surgical patients from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) database showed an overall incidence for perioperative stroke of 0.1%, increasing to 1.9% in a subset of high-risk patients.[2] Other studies have found an overall incidence of 0.4% in patients undergoing hemicolectomy, lobectomy or total hip replacement.[1] In this study using the NIS data, the risk of perioperative stroke was higher for hemicolectomy (0.7%) and lobectomy (0.6%), compared with total hip replacement (0.2%).[1]

Interestingly, the rate of perioperative ischaemic stroke appears to be increasing with time despite decreasing rates of overall perioperative mortality, major adverse cardiovascular events and declining incidence of stroke in the community.[7] Smilowitz and colleagues found an increase in perioperative ischaemic stroke from 0.54% to 0.78% of surgeries from 2004 to 2013, despite a reduction in the risk of non-fatal perioperative myocardial infarction over the same period.[7] Secondary analysis showed that this trend was present regardless of sex and emergency surgery status. The increasing rates of perioperative stroke in surgical patients may be attributable to an aging surgical population and increasing prevalence of risk factors for perioperative stroke such as pre-existing cerebrovascular disease and atrial arrhythmias, although this remains speculative.

Risk factors for perioperative stroke

The risk factors for perioperative stroke have been identified in numerous publications, and together provide a reasonable overview of the patient- and surgery-specific variables that lead to increased risk (Table 1). Many risk factors have been associated with perioperative stroke, and patients with multiple comorbidities have a higher incidence of perioperative stroke.[8] Older age is an important risk factor, particularly in those aged >85 yrs, and a history of prior stroke, atrial

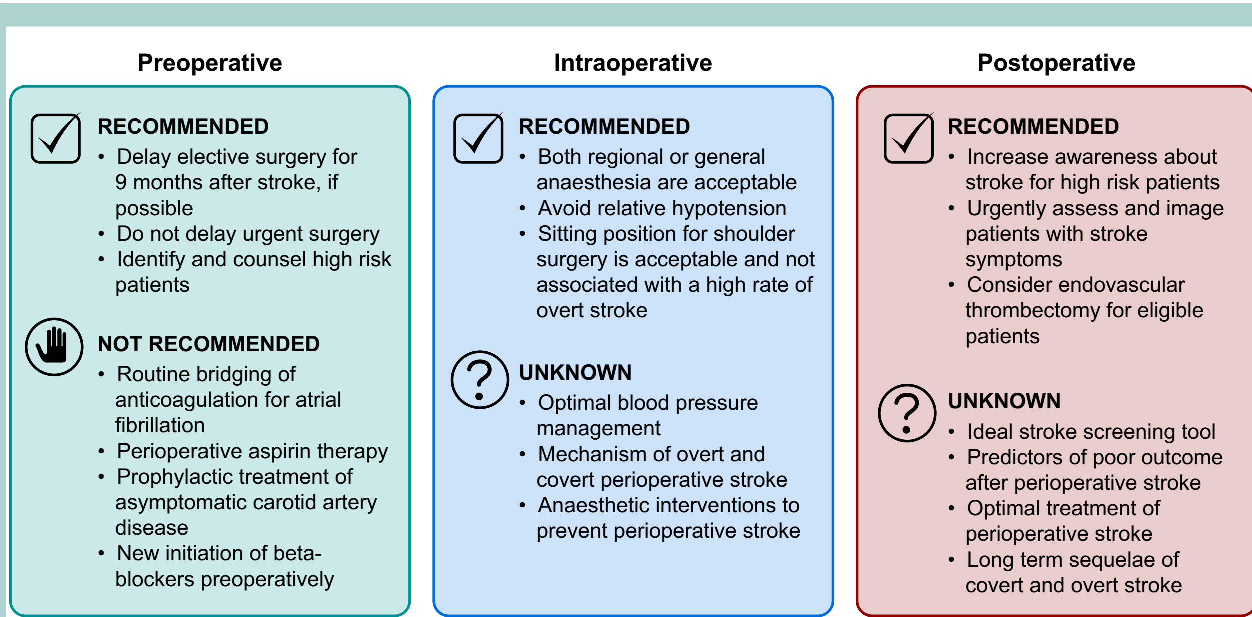

Fig 1 Summary of recommended management, including areas for further investigation.

Table 1 Previously identified patient and surgical risk factors for perioperative stroke in non-cardiac, non-neurological surgery. TIA, transient ischaemic attack; COPD, chronic obstructive pulmonary disease

Patient factors	Surgical factors
Older age[1,2,6,7]	Vascular surgery[6]
History of prior stroke or TIA[1,2,8,21]	Thoracic surgery[1,6]
Hypertension[2]	Transplant surgery[6]
History of atrial fibrillation[1]	Endocrine surgery[6]
Valvular disease[1]	Burn surgery[6]
Cardiovascular disease[1,2]	Otolaryngology surgery[6]
Renal disease[1,2]	Hemicolectomy[1]
Diabetes mellitus[1]	
Smoker or COPD[2]	
Patent foramen ovale[9]	
Migraine with or without aura[10]	

fibrillation, hypertension, valvular disease, renal disease and a history of congestive heart failure.[1,2,8,9] Patent foramen ovale has only recently been recognised as a risk factor for stroke after surgery, with a two-fold increase in the year after surgery, and this risk was reduced by the addition of post-operative antithrombotic therapy.[10] In another study, patients with a history of migraine, particularly those with aura, experienced a nearly two-fold increased risk of perioperative stroke after adjustment for confounders.[11] Finally, sex and race have been inconsistently associated with risk of perioperative stroke; the risk varies with the group of patients studied.[1,2,7,8]

Several procedures have been associated with a higher risk of perioperative stroke in analyses of large, non-cardiac surgery databases (Table 1). Vascular, thoracic and transplant surgeries are associated with the highest risk whereas obstetric and gynaecological surgeries have the lowest risk.[8]

Prevention of perioperative stroke

Carotid stenosis

Patients presenting for non-cardiac, non-neurological surgery should be evaluated for general risk factors for stroke including carotid stenosis, although its role in perioperative stroke is not well defined. The indications for further intervention should follow established guidelines for the management of carotid stenosis in general, and prophylactic carotid artery stenting or endarterectomy before surgery is not recommended.[12] Regardless of the surgical context, carotid endarterectomy is generally recommended for patients with symptomatic high grade (50–99%) stenosis, although carotid artery stenting can be considered in high-risk surgical candidates. The relative risks and benefits of intervention for asymptomatic patients with carotid stenosis are less well defined, and may be considered in highly selected patients.[12]

Perioperative management of anticoagulation

Several potential interventions to reduce the risk of perioperative stroke have been considered, and recent evidence has informed clinical decision-making before surgery. First, perioperative bridging of anticoagulation has long been considered to be a potential strategy to minimise the risk of perioperative stroke in patients with atrial fibrillation who are anticoagulated with warfarin. For most procedures, warfarin is withheld for 5–7 days before surgery, and not restarted for several days after surgery, leading to a prolonged period where the patient is not sufficiently anticoagulated and at risk for thromboembolic complications including stroke. The Bridging Anticoagulation in Patients who Require Temporary Interruption of Warfarin Therapy for an Elective Procedure or Surgery (BRIDGE) trial was designed to answer the question of whether bridging with low molecular weight heparin (LMWH) was non-inferior to not bridging to prevent arterial thromboembolism (stroke, transient ischaemic attack and systemic embolism).[13] This trial revealed two important findings for anaesthetic practice; first, not bridging was non-inferior to bridging for the prevention of arterial thromboembolism (0.4% *vs* 0.3% of patients experienced this complication, respectively; P=0.73 for non-inferiority) and second, bridging with LMWH resulted in a nearly three-fold greater incidence of major bleeding. Together, these results suggest that bridging of warfarin therapy should be avoided for most patients with atrial fibrillation. Although bridging does not appear to be necessary or advisable for most patients with atrial fibrillation who undergo surgical procedures, guidelines (from the European Society of Cardiology [ESC] and the American College of Cardiology/American Heart Association) recommend a more cautious approach in those at higher risk of periprocedural stroke (e.g. $CHADS_2$ score >3, recent transient ischaemic attack or stroke, rheumatic heart disease or mechanical heart valve).[14,15] In these cases, the relative risks of stroke and bleeding, and the duration of time the patient will not be anticoagulated must be considered in relation to bridging therapy. For patients taking direct oral anticoagulants (DOACs) for atrial fibrillation (i.e. apixaban, dabigatran or rivaroxaban), a temporary interruption of 1–2 days before and resumption 1–3 days after surgery resulted in a low rate of arterial thromboembolism or ischaemic stroke (0.3%).[16] This rate is similar to that seen in other groups undergoing non-cardiac, non-neurosurgical procedures. Current ESC guidelines do not recommend routine periprocedural bridging of anticoagulation for patients taking DOACs.[15]

The optimal perioperative management of antiplatelet therapy to prevent stroke has also been investigated, although the evidence available to guide our management is limited. The Perioperative Ischemic Evaluation (POISE-2) trial randomised 10,010 patients undergoing non-cardiac surgery to receive either aspirin or placebo, and further stratified patients according to those who initiated or continued aspirin.[17] No difference in the primary outcome (death or non-fatal myocardial infarction) was found, and aspirin did not result in a significant reduction in stroke (hazard ratio=0.84; 95% confidence interval [CI], 0.43–1.64). Similar to the bridging of anticoagulation trial discussed above, perioperative aspirin treatment resulted in an increased risk of major bleeding in this study. Therefore, the continuation or initiation of aspirin does not appear to confer protection against perioperative stroke in non-cardiac surgery, non-neurological surgery. Furthermore, in the absence of cardiac stenting, current guidelines recommend against initiating or continuing aspirin therapy for the prevention of cardiac events.[14]

Perioperative management of beta-blocker therapy

The use of perioperative beta blockers has been proposed as a potential way to reduce cardiovascular complications in patients having non-cardiac surgery. The POISE trial was a large, randomised trial that randomised patients to extended-release metoprolol or placebo, and found that although metoprolol reduced the incidence of myocardial infarction, it resulted in more deaths and a higher rate of stroke (1% *vs* 0.5%; odds ratio [OR]=2.17; 95% CI, 1.26–3.74; P=0.0053).[18] Several reasons for this observation have been proposed. Clinically significant hypotension was associated with perioperative stroke and more common in the metoprolol group in this study, possibly accounting for this finding although the timing of the hypotension was not noted, which makes it difficult to draw firm conclusions. In addition, non-cardiac selective beta-blockers such as metoprolol may impair cerebral vasodilation in the presence of anaemia, and have been associated with a higher rate of perioperative stroke than highly cardiac-specific beta-blockers such as bisoprolol.[19] A recent meta-analysis examining the effect of perioperative beta-blocker use in vascular surgical patients found that beta-blocker use did not reduce the risk of stroke (OR=2.45; 95% CI, 0.89–6.75; P=0.08), and did not improve perioperative outcomes overall.[20] Finally, the abrupt cessation of beta-blockers has been associated with an increase in 30 day perioperative mortality (OR=3.93; 95% CI, 0.47–0.98; P=0.04).[21] Taken together, the evidence shows that beta-blockers do not reduce the risk of perioperative stroke in low-risk patients and may increase the risk of stroke if initiated immediately before surgery.[22] In contrast, chronic beta-blocker therapy should be maintained in the perioperative period.[23]

Timing of elective and emergency surgery

A history of previous stroke is a well-established risk factor for perioperative stroke.[1,2] Two recent trials have offered insight as to the optimal interval between stroke and subsequent non-cardiac, non-neurological surgery. Until recently, the optimal timing of surgery after ischaemic stroke was unclear, but it has frequently been stated that it is acceptable to proceed after 30 days. More recently, an analysis of a large cohort of nearly 500,000 elective surgical patients in Denmark revealed that the risk of perioperative ischaemic stroke, major adverse cardiac events and mortality was lowest around 9 months after a stroke.[9] Concerningly, patients with a stroke less than 3 months before their surgery had a 68-fold higher risk of recurrent stroke, even after adjusting for confounding variables. Notably, the increased perioperative risk associated with prior stroke was similar between low- and high-risk surgeries. The decision to delay surgery must be carefully considered and the increased risk of stroke balanced with the risks of delaying surgery (e.g. for cancer).

The timing between stroke and emergency surgery has also been investigated in a similar cohort of surgical patients in Denmark, this time undergoing emergency surgery.[24] The risk of perioperative stroke, cardiovascular events and mortality was highest in those patients who had had a previous stroke within 3 months of surgery. However, patients undergoing urgent surgery (<72 h after stroke) had a lower risk of major adverse cardiovascular events compared with those who underwent early surgery (i.e. 4–14 days after stroke). The reasons for this observation are not immediately clear. The authors hypothesised that the higher risk period coincides with dysregulated cerebral autoregulation, but this requires further confirmation. These results suggest that urgent surgery should not be delayed in patients who have had a recent stroke and, given the concerns about autoregulation, tight haemodynamic control is recommended.[22]

Management of anaesthesia

Perioperative arterial blood pressure may play an important role in the risk of perioperative stroke although the current literature is conflicting. One retrospective case–control study did not find a relationship between arterial pressure and perioperative stroke.[25] Another case–control study found that hypotension, as defined by a 30% reduction in mean blood pressure from baseline, was significantly associated with stroke after non-cardiac, non-neurological surgery, although this relationship was weak.[26]

The POISE trial (see above) in 2008 also found that extended release metoprolol before surgery resulted in clinically significant hypotension and bradycardia, and patients given metoprolol were more likely to experience a stroke.[18] Finally, brain hypoperfusion from the sitting position has been postulated to increase the risk of perioperative stroke, although a review of 4169 patients who underwent shoulder surgery in the sitting position did not find any postoperative strokes, despite frequent hypotension.[27] These data suggest that although intraoperative hypotension may be an important contributor to perioperative stroke, most strokes occur postoperatively.[19] We require results from future randomised clinical trials to define this risk more precisely (e.g. arterial pressure thresholds) and to determine if interventions to correct hypotension lead to a reduction in the incidence and severity of postoperative stroke. For example the Perioperative Ischemic Evaluation-3 (POISE-3) trial is a multicentre, randomised controlled trial currently underway that will investigate the role of hypotension in patients undergoing non-cardiac surgery who are at risk of perioperative cardiovascular events including stroke.

Mode of anaesthesia (i.e. regional or general anaesthesia) has also been hypothesised to be a modifiable risk factor for perioperative stroke. However, the balance of current evidence does not support this hypothesis, although limited data are available. In a large Danish study looking at the time elapsed between stroke and emergency surgery, the mode of anaesthesia did not modify the risk of stroke in a further sensitivity analysis.[24] In addition, an analysis of the US National Surgical Quality Improvement (NSQIP) database did not show a relationship between type of anaesthesia and postoperative stroke, even with adjustment for multiple confounding variables (adjusted HR=0.96; 95% CI, 0.78–1.18; P=0.73).[28] Therefore, the choice of anaesthetic modality should be based on other clinical indications, rather than risk of perioperative stroke.

Intraoperative neurophysiological monitoring has been investigated as a tool to detect and prevent intraoperative cerebral ischaemia during non-cardiac surgery, that is EEG, cerebral oximetry and evoked potential monitoring. Although these techniques have been shown to detect neurological insults such as stroke during carotid endarterectomy, there is currently no robust evidence that using monitors such as cerebral oximetry prevents perioperative stroke or mortality after non-cardiac surgery.[29]

Postoperative screening and management of perioperative stroke

The higher morbidity and mortality associated with perioperative stroke compared with strokes in the community setting may result from delayed recognition and imaging, and surgical concerns about managing stroke in the perioperative period. The peak incidence of perioperative stroke occurs 1–2 days after surgery, with only about 10% presenting on the day of surgery.[19] In a small retrospective cohort study, 15% of patients with a stroke presented with mental status changes only with no appreciable deficit, and residual anaesthesia complicated the recognition of deficits.[30] Furthermore, detection and appropriate imaging for stroke were frequently delayed beyond the period of eligibility for thrombolysis therapy.

Anaesthetists play an important role in the recognition of perioperative stroke and screening tools may be appropriate in patients at high risk of perioperative stroke. Several screening tools for stroke have been considered for the postoperative period. The modified National Institutes of Health Stroke Scale (mNIHSS) (Table 2) was found to be a practical and reliable stroke screening tool, although it has not been validated to detect strokes in surgical patients to date.[31,32]

If clinical assessment suggests a perioperative stroke, then immediate imaging should be performed using non-contrast CT or MRI to determine whether an ischaemic or haemorrhagic stroke is the cause.[3] Clinical evaluation should also include measurements of arterial pressure, oxygen saturation, temperature, blood glucose and routine haematological laboratory studies to exclude alternative causes, and a thorough neurological assessment conducted. Further urgent consultation with a stroke neurology service will determine appropriate further management, which may include blood pressure management, thrombolysis or endovascular thrombectomy.

Table 2 The modified National Institutes of Health Stroke Scale (NIHSS), which can be used to assess patients with possible perioperative stroke[26]

Item	Score
Level of consciousness questions	0=answers both correctly 1=answers one correctly 2=answers neither correctly
Level of consciousness commands	0=performs both tasks correctly 1=performs one task correctly 2=performs neither task
Gaze	0=normal 1=partial gaze palsy 2=total gaze palsy
Visual fields	0=no visual loss 1=partial haemianopsia 2=bilateral haemanopsia
Left arm	0=no drift 1=drift before 10 s 2=falls before 10 s 3=no effort against gravity 4=no movement
Right arm	Same as scoring for left arm
Left leg	Same as scoring for left arm
Right leg	Same as scoring for left arm
Sensory	0=normal 1=abnormal
Language	0=normal 1=mild aphasia 2=severe aphasia 3=mute
Neglect	0=normal 1=mild 2=severe

Outcome after perioperative stroke

Perioperative stroke is an independent predictor of 30 day in-hospital morbidity and mortality after non-vascular, non-neurological surgery; and is a risk factor for developing cardiovascular and pulmonary complications.[33] In patients who have a non-fatal stroke, 58.5% will either require subsequent assistance with activities of daily living or be incapacitated.[18] Retrospective data analyses show that perioperative overt stroke increases the risk of death with an absolute in-hospital mortality of approximately 20%.[1,2,33] However, a previous report demonstrated considerable variation between hospitals in mortality after perioperative stroke (range, 22.5–46.4%).

Perioperative covert stroke

The incidence and impact of covert perioperative stroke have only recently been examined in the non-cardiac surgery population. Covert stroke is silent clinically, and remains undetected after surgery unless brain imaging is undertaken. The NeuroVISION trial was a prospective cohort study of 1114 patients older than 65 yrs, who underwent elective non-cardiac surgery and had a perfusion-weighted brain MRI within a week of surgery.[4] This study was the first to document an incidence of perioperative covert stroke of 7% (95% CI, 6–9%). Furthermore, patients who experienced a perioperative stroke were more likely to experience postoperative delirium (HR=2.24; 95% CI, 1.06–4.73) and postoperative cognitive decline (OR=1.98; 95% CI, 1.22–3.20). These results indicate a need to further define the significance of covert perioperative stroke, whether this observation causes cognitive complications, and how to prevent this complication.

Knowledge gaps in perioperative stroke

Historically, perioperative stroke has been relatively neglected, but in the past 10 yrs there has been a welcome and rapid increase in research and knowledge in this area. Nevertheless, many questions require further investigation. First, the pathophysiology of perioperative stroke needs to be better defined, including the mechanisms, timing and modifiers in the perioperative period, which are distinct from non-surgical stroke. The recent data demonstrating the potential role of covert perioperative stroke in postoperative delirium and cognitive function have opened up a whole range of research questions, including the underlying mechanism for this observation, and whether the ischaemic changes seen on imaging are directly responsible for the cognitive changes or whether this represents a marker of patients at risk for delirium, cognitive decline and stroke in general. Next, we need to find ways to increase awareness amongst patients and health care providers about risk factors, and develop tailored pathways for high-risk patients as they progress through surgery and recovery. Unlike cardiac complications, we still lack a practical and validated screening tool to identify strokes in surgical patients and ensure they receive timely care if they occur. Although the mNIHSS has been validated in the non-surgical patients, it has not been formally validated in the perioperative period and could represent a tool for patients undergoing surgery. Early identification of perioperative stroke *should* lead to more timely intervention, follow-up and improved outcomes. Lastly, we need to identify interventions to prevent both covert and overt perioperative strokes in high-risk patients, and to improve outcome in patients who have a stroke after surgery.

Conclusions

Although perioperative stroke after non-cardiac, non-neurological surgery is relatively uncommon, it has significant morbidity and mortality and the incidence may be increasing. Previous research has identified several patient and procedural risk factors, including older age and prior stroke. Delaying elective or routine surgery for 9 months after a previous stroke should be considered, although the decision should be individualised and take into account the risks of such a delay. Perioperative strokes are commonly under-recognised and undertreated, at least in part because of low awareness of this complication and lack of a validated screening tool. Covert stroke is an emerging area of research, and may contribute to postoperative cognitive decline. More research is warranted to identify the underlying mechanisms of perioperative stroke, and strategies to prevent it.

Declaration of interests

A.L. declares that they have no conflict of interest. A.F. is the Vice-President for Education and Scientific Affairs of the Society for Neuroscience in Anesthesiology and Critical Care.

MCQs

The associated MCQs (to support CME/CPD activity) are accessible at www.bjaed.org/cme/home by subscribers to *BJA Education*.

References

1. Bateman BT, Schumacher HC, Wang S, Shaefi S, Berman MF. Perioperative acute ischaemic stroke in noncardiac and nonvascular surgery: incidence, risk factors, and outcomes. *Anesthesiology* 2009; **110**: 231–8
2. Mashour GA, Shanks AM, Kheterpal S. Perioperative stroke and associated mortality after noncardiac, non-neurologic surgery. *Anesthesiology* 2011; **114**: 1289–96
3. Vlisides PE, Moore LE, Whalin MK *et al*. Perioperative care of patients at high risk for stroke during or after non-cardiac, non-neurological surgery: 2020 guidelines from the Society for Neuroscience in Anesthesiology and Critical Care. *J Neurosurg Anesthesiol* 2020; **32**: 210–26
4. Neuro VI. Perioperative covert stroke in patients undergoing non-cardiac surgery (NeuroVISION): a prospective cohort study. *Lancet* 2019; **394**: 1022–9
5. Sewell D, Gelb AW, Meng L, Chui J, Flexman AM. Anaesthetists' perception of perioperative stroke risk during non-neurologic and non-cardiac surgery. *Can J Anaesth* 2018; **65**: 225–6
6. Roughead T, Chui J, Gelb AW, Meng L, Sewell D, Flexman AM. Knowledge and perceptions about perioperative stroke: a cross-sectional survey of patients scheduled for non-neurologic and non-cardiac surgery. *Can J Anaesth* 2020; **67**: 13–21
7. Smilowitz NR, Gupta N, Ramakrishna H, Guo Y, Berger JS, Bangalore S. Perioperative major adverse cardiovascular and cerebrovascular events associated with noncardiac surgery. *JAMA Cardiol* 2017; **2**: 181–7
8. Al-Hader R, Al-Robaidi K, Jovin T, Jadhav A, Wechsler LR, Thirumala PD. The incidence of perioperative stroke: estimate using state and national databases and systematic review. *J Stroke* 2019; **21**: 290–301
9. Jorgensen ME, Torp-Pedersen C, Gislason GH *et al*. Time elapsed after ischaemic stroke and risk of adverse cardiovascular events and mortality following elective noncardiac surgery. *JAMA* 2014; **312**: 269–77
10. Friedrich S, Ng PY, Platzbecker K *et al*. Patent foramen ovale and long-term risk of ischaemic stroke after surgery. *Eur Heart J* 2019; **40**: 914–24
11. Timm FP, Houle TT, Grabitz SD *et al*. Migraine and risk of perioperative ischaemic stroke and hospital readmission: hospital based registry study. *BMJ* 2017; **356**: i6635
12. Naylor AR, Ricco JB, de Borst GJ *et al*. Editor's choice — management of atherosclerotic carotid and vertebral artery disease: 2017 clinical practice guidelines of the European Society For vascular surgery (ESVS). *Eur J Vasc Endovasc Surg* 2018; **55**: 3–81
13. Douketis JD, Spyropoulos AC, Kaatz S *et al*. Perioperative bridging anticoagulation in patients with atrial fibrillation. *N Engl J Med* 2015; **373**: 823–33
14. January CT, Wann LS, Calkins H *et al*. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American heart association task force on clinical practice guidelines and the heart rhythm society in collaboration with the society of thoracic Surgeons. *Circulation* 2019; **140**: e125–51
15. Steffel J, Verhamme P, Potpara TS *et al*. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Eur Heart J* 2018; **39**: 1330–93
16. Douketis JD, Spyropoulos AC, Duncan J *et al*. Perioperative management of patients with atrial fibrillation receiving a direct oral anticoagulant. *JAMA Intern Med* 2019; **179**: 1469–78
17. Devereaux PJ, Mrkobrada M, Sessler DI *et al*. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014; **370**: 1494–503
18. Group PS, Devereaux PJ, Yang H *et al*. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet* 2008; **371**: 1839–47
19. Ashes C, Judelman S, Wijeysundera DN *et al*. Selective beta1-antagonism with bisoprolol is associated with fewer postoperative strokes than atenolol or metoprolol:

a single-center cohort study of 44,092 consecutive patients. *Anesthesiology* 2013; **119**: 777–87

20. Hajibandeh S, Hajibandeh S, Antoniou SA, Torella F, Antoniou GA. Effect of beta-blockers on perioperative outcomes in vascular and endovascular surgery: a systematic review and meta-analysis. *Br J Anaesth* 2017; **118**: 11–21
21. Wallace AW, Au S, Cason BA. Association of the pattern of use of perioperative β-blockade and postoperative mortality. *Anesthesiology* 2010; **113**: 794–805
22. Minhas JS, Rook W, Panerai RB *et al*. Pathophysiological and clinical considerations in the perioperative care of patients with a previous ischaemic stroke: a multidisciplinary narrative review. *Br J Anaesth* 2020; **124**: 183–96
23. Jørgensen ME, Andersson C, Venkatesan S, Sanders RD. Beta-blockers in noncardiac surgery: did observational studies put us back on safe ground? *Br J Anaesth* 2018; **121**: 16–25
24. Christiansen MN, Andersson C, Gislason GH *et al*. Risks of cardiovascular adverse events and death in patients with previous stroke undergoing emergency noncardiac, nonintracranial surgery: the importance of operative timing. *Anesthesiology* 2017; **127**: 9–19
25. Hsieh JK, Dalton JE, Yang D, Farag ES, Sessler DI, Kurz AM. The association between mild intraoperative hypotension and stroke in general surgery patients. *Anesth Analg* 2016; **123**: 933–9
26. Bijker JB, Persoon S, Peelen LM *et al*. Intraoperative hypotension and perioperative ischaemic stroke after general surgery: a nested case-control study. *Anesthesiology* 2012; **116**: 658–64
27. Yadeau JT, Casciano M, Liu SS *et al*. Stroke, regional anesthesia in the sitting position, and hypotension: a review of 4169 ambulatory surgery patients. *Reg Anesth Pain Med* 2011; **36**: 430–5
28. Saied NN, Helwani MA, Weavind LM, Shi Y, Shotwell MS, Pandharipande PP. Effect of anaesthesia type on postoperative mortality and morbidities: a matched analysis of the NSQIP database. *Br J Anaesth* 2017; **118**: 105–11
29. Yu Y, Zhang K, Zhang L, Zong H, Meng L, Han R. Cerebral near-infrared spectroscopy (NIRS) for perioperative monitoring of brain oxygenation in children and adults. *Cochrane Database Syst Rev* 2018; **1**. Cd010947
30. Vlisides PE, Mashour GA, Didier TJ *et al*. Recognition and management of perioperative stroke in hospitalized patients. *A A Case Rep* 2016; **7**: 55–6
31. Meyer BC, Lyden PD. The modified national Institutes of health stroke Scale: its time has come. *Int J Stroke* 2009; **4**: 267–73
32. Sun Z, Yue Y, Leung CC, Chan MT, Gelb AW. Clinical diagnostic tools for screening of perioperative stroke in general surgery: a systematic review. *Br J Anaesth* 2016; **116**: 328–38
33. Lewis DJ, Al-Ghazawi SS, Al-Robaidi KA, Thirumala PD. Perioperative stroke associated in-hospital morbidity and in-hospital mortality in common non-vascular non-neurological surgery. *J Clin Neurosci* 2019; **67**: 32–9