Review Article

Perioperative stroke – Prediction, Prevention, and Protection

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ABSTRACT

Stroke culminates into 6.2 million deaths annually and is thereby a leading cause of disability and death worldwide. In patients undergoing noncardiac, nonneurological surgery, perioperative stroke can eventuate into a catastropic aftermath with almost eight-fold rise in mortality. In cardiac, neurological, and carotid surgery, stroke rate accounts to be high (2.2%–5.2%) and is a significant instigator of morbidity and mortality as well. These facts kindle interest to review the predictive parameters, preventive measures, and all the possibilities in the management and protection against perioperative stroke.

Key words: Atrial fibrillation, coronary artery bypass surgery, ischaemic stroke, noncardiac surgery, nonneurological surgery, perioperative stroke, risk factors, stroke, stroke prevention

INTRODUCTION

The surgical population ascribes up to six times higher risk of stroke than normal.[1] Anaesthesia and surgery *per se* accentuate the risk of perioperative stroke (PS), more so with emergent surgeries. Surgery essentially precipitates systemic inflammation and hypercoagulability, thereby contributes to thrombogenesis and rupture of vessel plaque in the perioperative settings.[2]

History of cerebrovascular disease (stroke or transient ischaemic attack [TIA]) is one of the component of the integrated perioperative risk evaluation scores, such as the revised cardiac risk index by Lee *et al*.[3,4] Currently, the incidence of perioperative ischaemic stroke in noncardiac, nonneurological, and nonmajor vascular surgery ranges from approximately 0.1% to 1.9%.[2] Moreover, stroke after cardiac surgery is debilitating and has profound repercussions effecting increased hospital stay and in-hospital mortality.[5-7] Besides, in coronary artery bypass grafting (CABG) surgery, PS is an independent predictor of mortality and morbidity.[8]

METHODS

An online literature search was performed using the following keywords: stroke, perioperative stroke, coronary artery bypass surgery, ischaemic stroke, risk factors, noncardiac surgery, and nonneurological surgery. The various engines searched were PubMed, NIH.gov, ScienceDirect, Cochrane data base, and Google.com. The relevant articles were included for the purpose of review. A manual search of references from relevant articles was also carried out, and various textbooks of anesthesiology were reviewed for relevant literature.

DEFINITION

The world health organization has described stroke as rapidly developing signs of focal or global disturbance of cerebral function with symptoms lasting for a day or longer or leading to death with no apparent cause other than vascular origin, whereas the PS is defined as that arising in the perioperative period, which is intraoperative or within 3–30 days following surgery.[1,9]

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PREDICTION BY RISK FACTORS OF PERIOPERATIVE STROKE

It is increasingly recognized that one can identify a high-risk patient for PS.[10] Risk factors in the general population for stroke are age, male gender,[11] heredity, obesity, diabetes mellitus, hypertension, smoking, physical inactivity, acute stress[12,13] and h/o migrane, previous stroke, and renal failure or dysfunction. The cardiovascular causes are essentially valvular heart diseases like mitral stenosis, atrial fibrillation (AF), left atrial enlargement, ischemic heart disease, and congestive heart failure.[2] Furthermore, the risk factors are TIA, thrombotic risks with polycythaemia, increased fibrinogen, decreased antithrombin III, pregnancy, and oral contraception.[1]

These risk factors can be assorted into modifiable factors, namely, antithrombotic drugs, beta blockers, hypotension, and hypercoagulability, and nonmodifiable factors being age, previous stroke, and renal failure.[14]

Macellari *et al.* have done extensive literature search in their study and state that the procedure-related risk factors are primarily the timing of surgery (urgent or elective), type and duration of surgery, type of anaesthesia (general versus regional anaesthesia), intraoperative complications (such as arrhythmias and sustained hypotension), hyperglycaemia, dehydration, and blood loss.[7]

Additional risk factors in the case of CABG surgery are the chronic renal insufficiency, recent myocardial infarction, moderate to severe left ventricular dysfunction, and low cardiac output syndrome.[6] Also, arrhythmias and combined CABG with mitral or aortic or both valve surgeries carry risk.

Age

The incidence increases with age as much as six-fold rise in octagenerians and above. Advanced age is not a cause of stroke *per se* but rather a marker of increased atherosclerotic burden.[15] The PS risk is higher in an older patient with cardiovascular disease than a younger patient with no risk factors for vascular disease.[16] Besides, advanced age is associated with more undiagnosed cerebrovascular diseases[17] and there is a cumulative risk, over time, of coexistent hypertension, atherosclerosis, diabetes mellitus, and cardiac diseases.[10]

Previous stroke

A patient with history of previous stroke merits special attention as it is a strong predictor of PS.[18] Up to 85% patients survive first episode of stroke and remain at risk for future cerebrovascular complications.[9] In cardiac surgery, history of cerebrovascular disease is the strongest preoperative predictor of stroke.[15] Likewise, carotid artery occlusive disease and atherosclerosis of the ascending aorta have increased incidence of stroke after cardiac operations.[19]

Atrial fibrillation

It leads to thromboembolism and global hypoperfusion due to fast ventricular rate and subsequent hypotension. In patients for cardiac or noncardiac surgery, new onset perioperative AF has long-term risk of subsequent stroke and is a comorbid diagnosis.[7,14]

Acute renal failure forms an independent risk factor for PS in noncardiac nonneurosurgical patients.[14]

Recent myocardial infarction

Recent myocardial infarction within 24 hours before CABG was associated with three times higher risk of stroke. A higher incidence of stroke after recent myocardial infarction is probably related to the haemodynamic instability, increased blood thrombogenicity, and pronounced sympathetic activation in postmyocardial infarction patients.[6]

Diabetes and peripheral vascular disease are also independent predictors of stroke, wherein patients are at increased risk of atherosclerotic embolization and impaired autoregulation of cerebral blood flow.[15]

Previous cardiac surgery is also identified as a risk factor for stroke.[15]

PATHOPHYSIOLOGY

Surgery triggers acute systemic inflammatory response. It initiates and exacerbates ischaemic cerebral injury, thrombosis, embolism, small vessel obstructions, and watershed infarctions.[20] Majority of perioperative cerebral events occur within 7 postoperative days. The venous thrombosis, alterations in clotting factors and platelets, and fibrinolyisis all lead to hypercoagulability state in the postoperative period.[1]

PS are essentially ischaemic, the reason being cerebral atherosclerosis, hypercoagulability, and hypotension. Thrombotic stroke ensues from hypercoagulability albeit cardioembolic stroke results from disease states such

as AF.[2] According to the American Heart Association and American Stroke Association (AHA/ASA), haemorrhagic stroke is a focal collection of blood within the brain parenchyma, subarachnoid space, or ventricular system that is not caused by trauma. Perioperatively, this may plausibly occur due to factors, such as uncontrolled hypertension, cerebral vascular malformations, and anticoagulant or antiplatelet agents. Fortunately, haemorrhagic stroke represents only 1%–4% of all PS.[2,14]

As it may be, in acute stroke, the cerebral autoregulation is impaired and cerebral blood flow (CBF) depends on cerebral perfusion pressure (CPP). This impairment in cerebral autoregulation peaks at 5 days after stroke and recovers over 3 months period during which the cerebral perfusion depends on systemic blood pressure.[14] Hence, during this period, maintaining the systemic blood pressure is crucial to maintain the CPP.

PREVENTION OF PERIOPERATIVE STROKE

The intent of preventive strategy is to improve perioperative care inculcating modifications of the risk factors and the risk management, designed with the policy to prevent both primary and secondary strokes. Primary stroke is a stroke occurring in a patient with no history of stroke, whereas secondary stroke occurs in a patient who has already had a stroke or TIA. The fundamental prevention plans are primarily focused around the variables such as cessation of smoking, anticoagulation for AF, antihyperlipidaemic medications, and glycaemic control. In-hospital initiation of secondary prevention therapy yields high rates of adherence in the stroke due to thromboembolic events.[21] Hypercoagulability check and withholding of anticoagulants[7] are pivotal in the prevention policy.

The fundamentals to be considered in cases wherein preoperative carotid artery revascularization is needed are in case of >70% symptomatic carotid stenosis, the carotid stenting, or endarterectomy before elective surgery should be offered. For <50% stenosis, it is not indicated, albeit in asymptomatic patients with >60% stenosis, surgery favors the outcome as per European asymptomatic carotid surgery trial.[20,22]

Time of elective surgery

In a patient with existing preoperative stroke for elective noncardiac surgery, a prudent approach is to delay the surgery to reduce perioperative risk. The Society for Neuroscience in Anesthesiology and Critical Care (SNACC) recommends a delay of at least 1 month between stroke and elective surgery.The data analysis by Jorgensen *et al.* suggest that elective surgery should be deferred until 6 months after a stroke owing to the plausible association of increased risks of PS and mortality.[18]

Statins

Patients with previous stroke may be on statins for secondary stroke prevention. Statins withdrawal in patients with acute stroke has 8.7-fold rise in the risk for early neurological deterioration.[20] and is also associated with increased risk of death or dependency. Hence, it should be continued in the acute phase of ischaemic stroke or should be initiated 2 weeks prior to the surgery to decrease the risk of PS.[23,24] Though statins act through various pathways, the anti-inflammatory effects in particular confer stroke protection.[2]

Antiplatelet drugs

Aspirin is recommended to be continued, whereas clopidogrel is stopped 5–7 days prior to surgery.[14] Oral anticoagulants are stopped 5 days before major surgery and patients who are at high risk of thromboembolism should receive bridging anticoagulation with subcutaneous low-molecular-weight heparin (LMWH) or intravenous (IV) unfractionated heparin.[25]

Antithrombotic agents

The risk of thromboembolism needs to be counterbalanced with the risk of bleeding.[7] Vitamin K antagonists, namely, warfarin, should be stopped 5 days prior to surgery. Bridging anticoagulation is recommended in high-risk patients like AF with CHADS score (a scoring system for risk estimation of stroke in patients with nonrheumatic AF based on presence of congestive cardiac failure, hypertension, advanced age, diabetes, or stroke) >4, prosthetic heart valve, history of venous thromboembolism, previous stroke, or TIA within 6 months.[14] Landercasper J *et al.* in their study on PS risk studied 173 consecutive patients with a history of previous cerebrovascular accident who underwent general anaesthesia for surgery. Five patients (2.9%) had documented postoperative cerebrovascular accidents from 3 to 21 days after surgery and also state the finding that postoperative stroke was more common in patients on preoperative heparin sodium.[26]

PROTECTION AND MANAGEMENT STRATEGY OF PERIOPERATIVE STROKE

The management of PS is predominantly based on the general supportive care and prevention of

complications.[20] It also aims toward re-establishment of blood supply to the ischaemic areas of brain.[14] Partial airway obstruction, hypoventilation, aspiration, pneumonia, and atelectasis can lead to hypoxia that may worsen the brain injury, hence needs to be addressed instantaneously.[20] Early recognition leads to better neurological outcome after PS. Sedation can mask presenting clinical features, thereby minimizing sedation in suspected cases helps earlier detection of stroke.[14]

Investigations

Ischaemic stroke can be differentiated from intracranial haemorrhage and nonvascular causes of neurological symptoms like tumors by noncontrast computerised tomography (CT). Additional information can be sought by multimodal CT and magnetic resonance imaging as well.[20] The atherosclerotic disease of the ascending aorta can be identified using transesophageal echocardiography.[27] Neuromonitoring, such as electroencephalography and somatosensory evoked potential monitoring, helps to detect decrease in the CBF.[23] Monitoring cerebral ischaemia with transcranial Doppler or electroencephalogram and evoked potentials is quite reasonable.[20] Also, cerebral oximetry and jugular bulb venous oximetry are pivotal. Carotid duplex ultrasonography may identify significant carotid disease in high-risk patients.[6]

The treatment aims toward considering the following points in the protection against PS.

Intraoperative and postoperative hypotension

Judicious management of hypotension needs to be done in the intra- and postoperative period, more so in the suspect cases as Peri Operative Ischemic Evaluation Study (POISE) trial suggests that hypotension might contribute to the risk of stroke. As stated by Bijker *et al.*, 30% decrease in mean arterial pressure from immediately preoperative baseline is associated with ischaemic stroke within 10 days of general surgery (odds ratio: 1.013; 95% CI: 1.000–1.025).[28] Moreover, cautious management of blood pressure in severely hypertensive patients seems prudent considering the risk of precipitating ischaemic stroke during aggressive blood pressure reduction.[15] Additionally, the hypotension particularly in the recovery period has been noted as a predictive event.[9]

Normoglycaemia

Hyperglycaemia worsens brain injury.[9] Current expert consensus recommends treating hyperglycaemia >150 mg/dL with a target glucose range of 60–180 mg/dL.[14]

Beta-blockers and Angiotensin converting enzyme inhibitors

Perioperative beta-blockade has emerged as a risk factor for stroke across the general surgical population. Further, there exists increased risk with nonselective beta-blockers.[2] The POISE-1 trial demonstrated that perioperative metoprolol in noncardiac surgical patients with cardiovascular risk factors was associated with a significantly higher incidence of stroke and mortality. The observational studies in noncardiac surgical populations also suggest that routine administration of metoprolol is associated with a higher risk of stroke compared with other beta-blockers with more selectivity for the β1 adrenergic receptor, such as atenolol or bisoprolol.[18] Angiotensin converting enzyme inhibitors (ACEIs) can cause hypotension not responding even to vasopressors that forms the risk factor for PS. Therefore, the risk benefit ratio needs to be balanced and accordingly preoperative beta-blockers, statins, and ACEI therapy should be continued albeit monitored earnestly in the perioperative period.[25]

Type of surgery

The incidence of PS depends on the type of surgery as the following figures suggest. The type of surgery and the incidences are as follows: general surgery 0.08%–0.7%, orthopedic surgery 0.2%–0.9%, lung operations 0.6%–0.9%, and head and neck surgery 4.8%. CABG surgery has highest incidence of major ischaemic complications (3%–5%) and up to 80% suffer cognitive dysfunction.[1]

Other neuroprotective strategies

These include use of drugs like thiopentone, isoflurane, sevoflurane, magnesium, and hypothermia.[29] The advanced treatment of acute stroke includes thrombolysis, and mechanical recanalization of occluded arteries and administration of heparin are not suitable for patients after surgery.[20] Intravenous alteplase (recombinant tissue plasminogen activator) is the only approved thrombolytic agent at present indicated for acute ischaemic stroke.[30] IV alteplase is recommended for selected patients who may be treated within 3 hours of ischaemic stroke and can be extended up to 4.5 hours.[31] Such thrombolysis is relatively contraindicated within 14 days after a major surgery[14,20] Intracranial haemorrhage is the major complication associated with it.[30] Also, IV alteplase should not be administered to patients who have

received a treatment dose of low-molecular-weight heparin within the previous 24 hours.[31]

SUMMARY

PS is a potentially ruinous complication of surgery. It deserves attention because of the serious debility and associated mortality. The author reiterates the importance of scrupulous preoperative evaluation to identify the possible risk factors. Haemodynamic stability in the perioperative period certainly is a fundamental fix. With the rigorous management strategies, PS can be successfully halted to a minimum.

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Conflicts of interest

There are no conflicts of interest.

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