Peri-operative strokes in non-cardiac, non-vascular, non-neurological surgery

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INTRODUCTION

Compared to the cardiorespiratory system, there is no regular peri-operative monitor of function available for the neurological system, yet it is the one organ system for which there is no temporary (such as dialysis) or permanent (such as transplant) replacement. In fact, if a person is brain dead, that person is considered to be legally dead. This review attempts to broadly summarise the facts regarding peri-operative strokes in the non-cardiac, non-neurologic, non-vascular surgical population, pertinent to a generalist anaesthetist.

BASIC DEFINITIONS

Cerebrovascular accident (CVA): The WHO defines a CVA as “a focal or global neurological deficit of cerebrovascular cause that persists beyond 24hrs or is interrupted by death within 24hrs.”

Transient ischaemic attack (TIA): A TIA is not a CVA, as the symptoms of acute loss of ocular or cerebral function does not extend beyond 24hrs.

Perioperative stroke occurs during or up to 30 days post-operatively.

EPIDEMIOLOGY

Bateman et al (3) did a retrospective study, reviewing the data of 371 641 patients from the National Inpatient Sample, which uses ICD-10 coding for the diagnosis of conditions. The study specifically looked at patients who had undergone hemi-colectomy, total hip replacement (THR) and lung lobectomy (Table 1). It is hypothesized that the very low incidence of stroke in the THR group may be due to regular postoperative thrombo-prophylaxis. On the other hand, the higher CVA incidence in the hemi-colectomy and lung lobectomy groups may be explained by the indication for surgery often being malignancy, with a higher risk for venous thrombo-embolism in the first place. The study demonstrated a consistently higher incidence of stroke with increase of age.

Mashour et al (4) used data collected prospectively from 523 059 patients undergoing non-cardiac, non-vascular, non-neurological surgery, in the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database (Table 2). This study confirms that different operations carry different risks for a CVA as a complication. As in the study by Bateman et al, the incidence consistently increases with age. The overall incidence of perioperative stroke in the study population however, was only 0.1%, owing to most surgeries, such as appendicectomy or arthroscopy demonstrating a 0% CVA incidence. (4) Mashour et al did further analysis of the data and developed a system for risk index classification, demonstrating that the more independent risk factors a patient carries for stroke, the higher the incidence of a perioperative stroke. (4) (Table 3).

Peri-operative stroke significantly influences mortality. There was an 8-fold increase in 30 day perioperative mortality for patients following a perioperative stroke compared to non-stroke patients. (4) There is also a difference in mortality rates for patients suffering stroke in the perioperative period compared to medical patients. In non-surgical stroke patients the documented mortality rate is 12.6%, compared to a much higher 26% in general surgery patients.
Table 1: (3)

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>18-64 y/o</th>
<th>≥ 65 y/o</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemicolecotomy</td>
<td>0.7%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Total hip replacement</td>
<td>0.2%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Lung lobectomy</td>
<td>0.8%</td>
<td>0.8%</td>
</tr>
</tbody>
</table>

Table 2: (4)

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>All age</th>
<th>≥ 65 y/o</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemicolecotomy</td>
<td>0.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Hip arthroplasty</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Lung resection</td>
<td>0.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Amputation</td>
<td>0.8%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Abdominal exploration</td>
<td>0.5%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Hepatobiliary</td>
<td>0.3%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Overall incidence</td>
<td></td>
<td>0.1%</td>
</tr>
</tbody>
</table>

Table 3: (4)

<table>
<thead>
<tr>
<th>Perioperative risk class</th>
<th>Nr of risk factors</th>
<th>Stroke %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>≤ 2</td>
<td>0.1</td>
</tr>
<tr>
<td>Medium risk</td>
<td>3-4</td>
<td>0.7</td>
</tr>
<tr>
<td>High risk</td>
<td>≥ 5</td>
<td>1.9</td>
</tr>
</tbody>
</table>

PATHOPHYSIOLOGY

Perioperative strokes are mostly ischaemic in nature. More than 60% of peri-operative strokes related to cardiothoracic surgery are embolic in origin. Compare this to perioperative strokes in the non-cardiac, non-neurological population where 68% are due to cerebrovascular thrombosis, 16% due to emboli and only 5% being haemorrhagic in nature. (2)
What is different about the nature of perioperative strokes, causing it to carry such a high burden of mortality?

After the ischaemic or haemorrhagic event, be it in a non-operative or peri-operative stroke, an inflammatory response is mounted. The surgical stress response and stroke inflammatory response release exactly the same inflammatory markers into the circulation (IL-1, IL-6, TNF-α, CRP). These lead to synergistic amplification of the pro-atherogenic state (leading to plaque rupture) and the pro-thrombotic state (leading to activation of the coagulation cascade and platelets, decreased fibrinolysis and endothelial dysfunction). Blood-brain barrier disruption is amplified as well. Endothelial dysfunction further predisposes to reactive vasospasm, plaque rupture and thrombosis. (2) (Figure 1) The endothelial dysfunction is further worsened when the anaesthetic includes Nitrous Oxide, due to an acute elevation in levels of homocysteine. (5) This synergistic amplification between stroke pathology, surgery and anaesthesia, ultimately contributes to the increase of mortality rate in perioperative stroke patients. (2)

Figure 1: Ng et al, Anaesthesiology 2011; 115:879-890 (2)

Postoperative events:
A delay in diagnosis of perioperative strokes possibly further contribute to increased morbidity and mortality. The delay in diagnosis may be due to distracting factors, such as immobility due to post-operative pain, or residual effects from anaesthetic agents, including muscle relaxants, analgesics, sedatory premedications, regional or neuraxial anaesthesia (6). Post-operatively, the patient may become even more hypercoagulable, due to bed rest and immobility, dehydration and withholding of antiplatelet drugs and anticoagulants. Forty five percent of perioperative strokes are identified within the first 24hrs post surgery, the other 55% occur between 2-30 days postoperatively. (7)

RISK FACTORS FOR PERIOPERATIVE STROKE

Patient related risk factors

- Renal disease: Renal disease is associated with accelerated atherosclerosis and hypotension due to fluid shifts associated with dialysis. (3)
- History of previous stroke or TIA.(3)
• Age ≥ 62yr: This is a problem as our general population (and thus perioperative population) is steadily aging. (4)

• Valvular heart disease: The damaged valve may be a nidus for the formation of an embolism and fixed cardiac output lesions may impair perfusion peri-operatively. (3)

• Other cardiac risk factors:
  o Congestive cardiac failure (3)
  o Myocardial infarction in the last 6 months (4)
  o Hypertension needing pharmacological treatment (4)

• Current smoker (4)

• Chronic obstructive pulmonary disease (4)

• Gender: Female gender slightly higher incidence (OR 1.21; CI 1.07-1.36) (3)

**Atrial Fibrillation**

Atrial fibrillation is a major independent risk factor for peri-operative strokes (OR1.95, CI1.69-2.26). It causes ischaemic stroke via cardio-embolism formation or hypoperfusion due to hypotension in rapid, unstable atrial fibrillation. (3)

It is imperative that patients with atrial fibrillation have risk stratification done pre-operatively in the non-cardiac, non-vascular, non-neurosurgical population as well.

There are many risk stratification tools available, including the clinical prediction models CHADS2, CHA2DS2-vasc, R2CHADS2, RCRI. (Figure 2)

A VISION sub-study by McAlister et al (8), compared these risk stratification tools to identify which one has the most prognostic value in an inpatient, non-cardiac postoperative setting. (8) CHADS2 had superior post-operative stroke and mortality risk prediction compared to RCRI, which ultimately helps to identify patients that will need more intensive monitoring peri-operatively (8). Based on the CHADS2 score, the atrial fibrillation patient is subdivided into high, moderate and low risk groups for thrombosis, to aid in subsequent decision making. (9) (10) (Figure 3).

Possible biomarkers (eg BNP for CCF), need further investigation, as it may improve atrial fibrillation risk stratification even further. (8)

**Type of surgery**

The different incidences of perioperative strokes with varying types of surgery implies differing risk associated with different types of surgery. For example, hip arthroplasty carries higher risk than knee arthroplasty and vascular surgery has a higher risk than general surgery. (2) Head and neck surgery carries a higher risk for CVA, as the reason for surgery is often malignancy, patients often have multiple comorbidities (including independent risk factors for stroke) and extreme movements of the neck including extreme rotation and hyper-extension may disrupt plaques and obstruct carotid vessels, leading to ischaemic strokes peri-operatively. Furthermore, neo-adjuvant radiotherapy may accelerate atherosclerosis as well. (2)

Shoulder surgery carries its own risk for strokes. Beach chair positioning of the patient intra-operatively causes postural hypotension and subsequent (possibly missed) cerebral hypoperfusion. There is a 0.8mmHg reduction in the mean arterial pressure for each 10mm upwards gradient between the BP cuff position (usually the contralateral brachial artery) and the brainstem. Thus the further away the BP cuff from the level of the brainstem, the bigger the difference (eg BP cuff on the lower limb.) (11)
PREMEDICATION AND PRE-OPERATIVE CONSIDERATIONS

Beta-blockers

This is based on the results of the original POISE trial (2008) (12), a double blind, prospective RCT, comparing the effects of pre-operative (2-4hrs pre-operative) commencement of extended release Metoprolol, to a placebo. Even though there was a statistically significant decrease in non-fatal MI and myocardial infarction in the Metoprolol group, there was a statistically significant increase in stroke, non-fatal stroke and total mortality, as well as clinically significant bradycardia and hypotension. (12) A retrospective observational study done by Mashour et al (2013) (13), comparing the effects of peri-operative Metoprolol to other cardio-selective β-blockers, in non-cardiac surgery, showed a significantly higher incidence of peri-operative stroke in the Metoprolol group, compared to those taking Labetalol, Bisoprolol or Esmolol. The hypothesis is that Metoprolol is the least selective of all the cardio-selective β-blockers, thus inhibiting β₂ mediated cerebral vasodilation, reducing oxygenation of cerebral tissue. (13)
The *Perioperative Stroke Consensus Statement* by Mashour et al (2014) (11), advocates the continuation of β-blockers peri-operatively in those patients already taking β-blockers. Severe caution must however be exercised with the initiation of β-blockers in the perioperative period, in β-blocker naïve patients, until further studies have been done on the safety of individual β-blockers.

**Aspirin**

The *POISE 2* trial (2014) (14), a double blind, prospective 2x2 factorial RCT, researched the effects of Aspirin on patients undergoing non-cardiac surgery vs a placebo. The group to receive aspirin, was further split into those already taking aspirin chronically (continuation stratum) and those not yet taking aspirin (initiation stratum). The study concluded that there was no significant difference between the aspirin vs placebo groups regarding death, stroke and non-fatal myocardial infarction. It did however demonstrate a significantly increased risk for major bleeding in the aspirin group (4.6% vs 3.8% p=0.04). (14) Exploring this further, significant bleeding my cause a supply-demand mismatch regarding myocardial (and cerebral) oxygenation, contributing to the development of an MI. There is thus no additional benefit to continue aspirin peri-operatively. (14) The *POISE 2* study group, promotes stopping aspirin at least 3 days prior to surgery to decrease bleeding risk, as 20% of platelets need normal COX-1 function to obtain haemostasis and every 24hrs, 12% of circulating platelets are replaced. (12% x 3 = 36%). The suggested time frame to restart aspirin is 8-10 days post operatively, or when bleeding risk is decreased. (14)

**Clonidine**

The *POISE 2* trial (2014) (15) also investigated the effects of pre-operative (2-4hrs) Clonidine vs placebo, in 10 010 patients undergoing non-cardiac surgery, provided that the subject was not bradycardic or hypotensive. Clonidine was associated with a statistically significant increase in non-fatal cardiac arrest, and clinically significant hypotension and bradycardia. There was no increase in stroke incidence. Clonidine use is thus not recommended in the high risk patient. (15)

**Anticoagulation bridging**

**Vitamin K antagonists Warfarin**

Historically, it was believed that all patients receiving Warfarin therapy, needed the Warfarin stopped 5 days prior to surgery and bridged with heparin, be it low molecular weight heparin (LMWH) or unfractionated heparin. The *BRIDGE* trial (2015) (16) has shed new light on this topic of bridging. This was a double blind, placebo controlled RCT, comparing bridging anticoagulation with LMWH vs bridging with a placebo, when Warfarin therapy is interrupted for non-cardiac, non-neurological surgery in patients with atrial fibrillation and atrial flutter specifically. The results of the study showed that there was no substantial difference in the incidence of peri-operative arterial thromboembolism (stroke, TIA and systemic embolism) between the bridging (0.3%) and non-bridging (0.4%) groups. There was neither a noteworthy difference in the incidence of MI, DVT, pulmonary embolism or death. There was however, a statistically significant lower incidence of both major and minor bleeding in the non-bridging group (1.3%) compared to the bridging group (3.2%). (16) The participants excluded were those with stroke, TIA or systemic embolism in the last 3 months, mechanical heart valves and CHADS2 scores of ≥ 5. The thrombotic risk in these
patient groups are proven to be high, and should receive bridging anti-coagulation when their Warfarin therapy is interrupted peri-operatively. (16)

The American College of Chest Physicians’ *Perioperative Management of Antithrombotic Therapy* guidelines (10) endorse a risk-benefit analysis comparing the risk for thrombosis to the risk of haemorrhage. (9)

**Thrombotic risk assessment:** Patients with mechanical heart valves, atrial fibrillation and venous thromboembolism are subdivided into high, moderate and low risk (Figure 3). High risk patients should be bridged and low risk patients should not be bridged. In moderate risk patients, one needs to individualise and balance the thrombotic and bleeding risks to determine if a patient needs bridging or not. (9, 10)

**Bleeding risk assessment:** There is a distinction between bleeding risk due to the type of surgery (10) (Table 4) as well as patient risk factors for bleeding, using the HAS-BLED score (Table 5). A score of ≥ 3 is indicative of a high bleeding risk. (17)

**Table 4:** (10)

<table>
<thead>
<tr>
<th>↑Bleeding risk surgeries:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urological surgery</td>
</tr>
<tr>
<td>Pacemaker or ICD implantation</td>
</tr>
<tr>
<td>Colonic polyp resection</td>
</tr>
<tr>
<td>Kidney/Liver/spleen surgery</td>
</tr>
<tr>
<td>Bowel resection</td>
</tr>
<tr>
<td>Extensive tissue injury</td>
</tr>
<tr>
<td>Cardiac/neuro/spine surgery</td>
</tr>
</tbody>
</table>

**Table 5:** (17)

<table>
<thead>
<tr>
<th>HAS-BLED score: Patient bleeding risk:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (SBP &gt;160mmHg)</td>
</tr>
<tr>
<td>Abnormal renal and or liver function (1 point each)</td>
</tr>
<tr>
<td>Stroke (Previous)</td>
</tr>
<tr>
<td>Bleeding tendency</td>
</tr>
<tr>
<td>Labile INR's on Warfarin</td>
</tr>
<tr>
<td>Elderly (age&gt;65y/o)</td>
</tr>
<tr>
<td>Drugs (anti-PLT or NSAIDS) or alcohol excess (1 point each)</td>
</tr>
</tbody>
</table>

**Non-Vitamin K oral anticoagulants:**

*The Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation (2015), (18)* gives guidelines on the management of these drugs peri-operatively. The last dose of the anticoagulant is based on the bleeding risk of the surgery, as well as the renal function of the patient. Importantly, with the non-vitamin K oral anticoagulants, there is no need to bridge with unfractionated heparin or LMWH (18) (Figure 4).
Statins

There is no specific research available regarding the incidence of stroke and the use of Statins peri-operatively in the non-cardiac, non-vascular, non-neurological surgical population. Blanco et al (19) investigated the effects of statin withdrawal vs continuation of statins, in patients on chronic statin therapy who have suffered an acute ischaemic stroke. Statin withdrawal was coupled with higher mortality rates, early neurological deterioration and infarct size, compared to the group on statin continuation. (19) Furthermore, Heyer et al. demonstrated a lower incidence of peri-operative strokes and a decreased incidence of cognitive dysfunction, in carotid endarterectomies for asymptomatic stenosis. (20)

Based on these findings, current guidelines promote the uninterrupted use of statins peri-operatively in the non-cardiac, non-vascular, non-neurosurgical population in those patients already on statin-therapy, until further studies are done. (2)

Carotid endarterectomy before elective surgery

If a pre-operative patient, that needs non-urgent elective surgery, has symptomatic carotid artery stenosis of a high grade (stenosis > 70%), the patient should be offered carotid revascularization. (2) Revascularization is most advantageous if performed within 2 weeks of symptom onset. If performed after 12 weeks of symptom onset, the risk outweighs the benefit of revascularization. (9) Thus, if a patient presents for elective surgery within 12 weeks of TIA, stroke or neurological symptom onset, the patient should be investigated by means of carotid artery imaging, such as carotid Doppler. (9) Prophylactic revascularization of patients with asymptomatic carotid artery stenosis (<50%) awaiting elective general surgery, is not supported in the literature, as there has been no statistically significant link proven between asymptomatic carotid artery stenosis and perioperative stroke. (21)

Figure 4: Heidbuchel et al, Europace (2015) 17, 1467-1507 (18)

Table 10 Last intake of drug before elective surgical intervention

<table>
<thead>
<tr>
<th>Drug</th>
<th>Low risk</th>
<th>High risk</th>
<th>Low risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>≥24 h</td>
<td>≥48 h</td>
<td>≥24 h</td>
<td>≥48 h</td>
</tr>
<tr>
<td>Apixaban--edoxaban--rivaroxaban</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl ≥ 80 ml/min</td>
<td>≥24 h</td>
<td>≥48 h</td>
<td>≥24 h</td>
<td>≥48 h</td>
</tr>
<tr>
<td>CrCl 50–80 ml/min</td>
<td>≥36 h</td>
<td>≥72 h</td>
<td>≥24 h</td>
<td>≥48 h</td>
</tr>
<tr>
<td>CrCl 30–50 ml/min*</td>
<td>≥48 h</td>
<td>≥96 h</td>
<td>≥24 h</td>
<td>≥48 h</td>
</tr>
<tr>
<td>CrCl 15–30 ml/min*</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>≥24 h</td>
<td>≥48 h</td>
</tr>
<tr>
<td>CrCl &lt; 15 ml/min*</td>
<td>Not indicated</td>
<td>Not indicated</td>
<td>≥36 h</td>
<td>≥48 h</td>
</tr>
</tbody>
</table>

There is no need for bridging with LMWH/LFH

INTRA-OPERATIVE CONSIDERATIONS

Intra-operative Blood pressure control

A case control study of 48 421 patients undergoing non-cardiac, non-neurological surgery, done by Bijker et al (22), investigated the impact of intra-operative hypotension on the incidence of peri-operative strokes. The results indicated that a fall in intra-operative MAP in excess of 30% beneath baseline, is linked to peri-operative strokes. Furthermore, the risk of peri-operative strokes increased 1.013 times for each minute that the MAP was ≥30% beneath baseline. (22)
The study authors also hypothesize that intra-operative hypotension may be a predictor of post-op haemodynamic instability, where patients are exposed to prolonged episodes of hypotension due to less vigilant monitoring. (22)

Most guidelines, as a safety mechanism, suggest not allowing the MAP to drift below 20% of baseline (just before entering theatre, when the BP is even higher than normal), especially in those at risk for peri-operative strokes. (2)

**Ventilation**

Ventilation strategies should be employed to maintain normocarbia, as hypocarbia from hyperventilation may cause deleterious cerebral vasoconstriction. (11)

**Intra-operative blood loss and anaemia**

Kamel et al (2012) (23) investigated the link between major peri-operative haemorrhage (>4 units PRC transfused) and stroke or Q-wave MI, by examining a cohort of 651 775 patients from the NSQIP database who had undergone non-cardiac, non-neurological elective surgery. The results showed a statistically significant increase in peri-operative strokes and MI's in those who had major haemorrhage compared to those who did not suffer a major haemorrhage. (23) Moreover, patients on Beta-blockers peri-operatively, cannot adequately compensate haemodynamically for acute blood loss. The suggested target haemoglobin for such patients is 9g/dl. (11)

**Glucose control**

Avoid hyper- or hypoglycaemia, as both are linked to increased morbidity. It is suggested to target blood glucose of 7.8 - 10 g/dl for critically ill patients. (2)

**DIAGNOSIS**

One of the key factors of effectively managing a peri-operative stroke is early detection and recognition. The Face (drooping), Arm (unilateral weakness), Speech (slurred), Time (to call for help), aka (FAST) pre-hospital stroke recognition instrument was designed for non-medical staff to identify symptoms of stroke in order to seek help in a timely manner. (6) Something more robust and definitive is necessary in the in-hospital setting, especially in the peri-operative population. The ideal stroke assessment scale is summarised in figure 5. (6)

**Table 5:** (6)

<table>
<thead>
<tr>
<th>Ideal stroke assessment scale:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quick and easy to perform</td>
</tr>
<tr>
<td>Simple</td>
</tr>
<tr>
<td>Good inter-rater reliability</td>
</tr>
<tr>
<td>Ability to distinguish distracting factors</td>
</tr>
<tr>
<td>Detect neurological deficits</td>
</tr>
</tbody>
</table>

There are a multitude of stroke assessment scales available, none of which fulfil the criteria of the ideal stroke assessment scale for the population in question. These include, but are not limited to:
- Fugl-Meyer assessment scale: 155 items, takes 35 min by a trained observer (6)
- Oxbury initial severity scale: Must be performed by a neurologist (6)
- Mathew stroke scale: Associated with poor inter-rater reliability (6)
- Western perioperative neurologic scale: Performed after cardiac surgery (6)

NIHSS: The National Institutes of Health Stroke Scale, according to Sun et al (6), seems to most closely resemble the ideal stroke assessment scale in the non-cardiac, non-neurological, non-vascular surgical patient. It is quickly completed in 5 minutes. The PedNIHSS has been developed for children between 2-19 years old. Peri-operatively it has been used for cardiac, carotid and aneurysm surgery. However, no assessment scale has been tested in the non-cardiac, non-vascular, non-neurologic surgery population. POSIC: The Peri-operative Strokes in Chinese study, testing the modified NIHSS (m-NIHSS) in the non-cardiac, non-neurological perioperative population is currently underway. However, the results of the study are still pending. (6) (Figure 5)

There are however many hurdles in implementing the routine use of a stroke assessment scale, including understaffed nursing teams in overfilled wards, with no time to complete the m-NIHSS at each interview. A possible solution is a ‘two tiered assessment system’, where the FAAST tool, (FAST plus an extra “A” for residual anaesthesia) is used as a quick and easy assessment tool by nursing staff during each overview of the patient. If any abnormalities are noted, the nursing staff should alert the attending doctor, who then does an m-NIHSS. (6)
MANAGEMENT

Once a peri-operative stroke has occurred and has been correctly identified, the patient needs prompt and effective treatment to minimise cerebral ischaemic injury. Many larger international centres deploy an “Acute Stroke Team”, led by the neurology team, who acts swiftly once a peri-operative stroke is suspected or identified. (2) This highlights the need for a multidisciplinary approach when this potentially devastating complication occurs.

The aim of the Acute Stroke Team is to get a non-contrast CT brain within 25 minutes of the differential diagnosis. This will distinguish an ischaemic stroke from a haemorrhagic stroke, which will guide further management. (2)

The management includes prevention of secondary brain injury, as well as specific treatment targeted at revascularisation.
Prevention of secondary brain injury

A degree of neuro-protection is necessary in the acute phase post CVA, in order to prevent the ischaemic penumbra from becoming permanently damaged, ultimately enlarging the infarct size. Again, in larger centres, these patients are best managed in specialized ‘Acute Stroke Units” (2) or in neurocritical care units (11).

Supportive management, as per the AHA/ASA Guidelines for the Early Management of Patients with Acute Ischaemic Stroke (24) includes:

- **Airway**: Maintain and/or protect the airway. If the GCS is ≤8 or severe bulbar dysfunction is present causing airway obstruction with an associated aspiration risk, the patient may need to be intubated. (24)

- **Breathing**: Avoid hypoxaemia (saturation monitor: maintain oxygen saturation ≥94%, with supplemental oxygen if necessary). Ventilation has the added benefit of controlling the PaCO₂, which becomes very important in malignant cerebral oedema. (24)

- **Circulation**: Avoid hypotension. As the cerebral autoregulation is disrupted, the cerebral perfusion pressure becomes directly dependent on the systemic blood pressure. Rapid correcting of possible sources of hypotension is therefor of utmost importance. Possible causes to consider include blood loss, dehydration, dysrhythmias and myocardial ischaemia (cardiac monitoring is necessary for at least 24hrs post CVA, as arrhythmias and myocardial ischaemia are common complications of acute CVA). Drug induced hypertension and intentional haemodilution is not endorsed by the American Heart Association. Blood pressure treatment is indicated with a systolic blood pressures of >220mmHg and diastolic pressures of >120mmHg if no thrombolysis is planned, and with a systolic blood pressure of >185mmHg or diastolic pressures of >105mmHg, if it is planned. (24)

- **Disability/Dextrose**: Prolonged untreated hypoglycaemia may cause irreversible brain damage. (24) Hyperglycaemia associated with acute ischaemic stroke, likely related to a stress response, is associated with worse outcomes. Measure blood glucose and maintain normoglycaemia. (24)

- **Exposure**: Diagnose cause of and treat fever (Temperature ≥38°C) promptly, as pyrexia is associated with poor neurological outcome in the presence of an acute ischaemic stroke, due to greater metabolic demands and free radical production. (24) It is known that moderate hypothermia is linked to neuroprotection post cardiac arrest. However, further investigation is needed to delineate the usefulness and safety of induced hypothermia in the setting of an acute ischaemic stroke. Thus, Aim for normothermia. (24)

Revascularization

The drug of choice for an ischaemic stroke is intravenous recombinant tPA (rtPA), administered within 3 hours post symptom onset, as “time is brain.” There are, however, multiple definite and relative contra-indications to IV rtPA. Intraspinal and intracerebral surgery and active internal bleeding are absolute contra-indications. It is imperative to note that serious trauma or major surgery in the preceding 14 days, is only a relative contra-indication, and a risk-benefit analysis should be made by the multidisciplinary team regarding the administration of rtPA (24) (Figure 6).

Alternative management include endovascular mechanical thrombolysis or clot retrieval, intra-arterial fibrinolysis or mechanical clot disruption/extraction. These may all be promising alternatives for those patients who do not meet the inclusion criteria, or for those who meet the exclusion criteria for intravenous rtPA. (24) There is paucity in research regarding revascularization in peri-operative patients.
TIMING OF SURGERY AFTER A STROKE

Timing of surgery after a stroke is of the utmost importance. After a stroke, cerebral autoregulation is impaired for about 3-6 months, thus cerebral blood flow becomes dependant on cerebral perfusion pressure. This stabilises at about 9 months post infarct. (2) A Danish cohort study including 481,183 surgeries, by Jorgensen et al (25), assessed time passed between stroke and surgery, and the incidence of major adverse cardiac events (MACE). The results showed remarkable significance between time lapsed after stroke before surgery and MACE. The odds ratios (OR) for MACE were as follows: stroke <3months prior: OR 14.23, stroke 3-6months prior: OR 4.85, stroke 6-12months prior: OR 3.04 and stroke >12 months prior: OR 2.47. These results suggest that the risk steadily declines as time passes, but levels out at around 9months post stroke. (25) Practically, the urgency of the surgery will determine the decision making process:

- Emergency surgery: Continue with surgery immediately (but cautiously)
- Time sensitive surgery (eg cancer): Use clinical judgement and consider the risk/benefit balance
Elective surgery: Currently most guidelines state 3 months post stroke is safe to continue with elective surgery, (2, 9, 11) but the aforementioned study conducted by Jorgensen et al, concluded that a 6-9 months delay might be safer. (25)

COVERT STROKE

All the above referenced research pertains to overt strokes (an overt stroke is a symptomatic CVA). There is another, less well known entity, known as a covert stroke. This is an asymptomatic cerebrovascular event, only detectable by a diffusion weighted MRI. Diagnosis of a covert stroke is seldom made at occurrence of the neurovascular incident as it is by definition asymptomatic. It is however, associated with accelerated development of dementia with significant negative effects on cognitive and motor function and quality of life. Furthermore, covert stroke is a risk factor for further overt stroke and death. (26)

An international prospective cohort study by Mrkobrada et al. (2016), was done on 100 patients 65yr and older, undergoing non-cardiac, non-neurological surgery. These patients had MRI diffusion weighted imaging done between day 3 and day 10 post-operatively, to determine the incidence of peri-operative covert strokes. (26)

MRI is very sensitive to cytotoxic brain oedema, which is the pathognomonic feature of acute cerebral ischaemia, so old infarcts were not mistaken for peri-operative strokes. With this in mind, the results showed a one in ten, thus 10% incidence of peri-operative strokes in the population sampled. This might even be an underestimation, as the MRIs were only done between post-operative days 3 and 10, excluding days 11 to 30. A bigger study is however needed to investigate these results further. (26)
CONCLUSION

The brain is an important organ, yet often plays second fiddle to the heart, lungs and kidney. Peri-operative stroke is not an uncommon peri-operative complication, with the reported incidence varying from 1 in 1000 (overt strokes) to 1 in 10 (covert strokes). This can have devastating implications for the patient and significantly increases morbidity and mortality. Appropriate risk stratification is imperative in managing and counseling surgical patients. The complicated patient with multiple co-morbidities pose a special challenge with regard to managing their chronic medications and with the current gaps in research it often boils down to individual risk/benefit analysis.

Once a peri-operative stroke is suspected, prompt diagnosis and effective management, including both supportive and specific treatment is paramount to ensure the best possible outcome for the patient.
REFERENCES


