Review article: The role of hypotension in perioperative stroke

Article de synthèse: Le rôle de l'hypotension dans l'accident vasculaire cérébral périopératoire

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Abstract

Purpose A stroke is an uncommon but potentially devastating complication after surgery. Although hypoperfusion is often mentioned as a possible cause of a perioperative stroke, a thorough investigation is needed into the role of intraoperative and/or postoperative hypotension in the occurrence and development of perioperative cerebral ischemia. In this review article, we present an overview of the available literature on the possible role of hypotension in perioperative stroke, and we place these studies in a broader context.

Principal findings Perioperative strokes are most frequently thromboembolic in origin and commonly occur within the first 72 postoperative hours after a symptom-free interval. Case reports have shown a causal relationship between hypotension and perioperative stroke; nevertheless, many other factors contribute to its pathophysiology. Hypotension contributes as a primary factor or likely more frequently as a secondary factor in the development of a perioperative stroke. Among the main difficulties in studying this association is the lack of standardized definitions of perioperative hypotension, baseline blood pressure, and the length of the postoperative period. To guide future research, we propose a selection of problems to address in order to

gain more insight into the problem of perioperative cerebral ischemia.

Conclusions Unusually low blood pressure will eventually result in neurological damage; however, the threshold and duration at which an association might be found between a perioperative stroke and hypotension have not been well investigated. Thus, the exact role of hypotension in the etiology of perioperative stroke is still largely unknown.

Résumé

Objectif L'accident vasculaire cérébral est une complication peu fréquente mais potentiellement dévastatrice après une chirurgie. Bien que l'hypoperfusion soit souvent nommée comme cause possible d'un accident vasculaire cérébral périopératoire, des recherches approfondies sont nécessaires pour déterminer le rôle de l'hypotension peropératoire et/ou postopératoire dans la survenue et le développement de l'ischémie cérébrale périopératoire. Dans cet article de synthèse, nous présentons une vue d'ensemble de la littérature existante traitant du rôle possible de l'hypotension dans l'accident vasculaire cérébral périopératoire, et nous plaçons ces études dans un contexte plus large.

Constatations principales Les accidents vasculaires cérébraux périopératoires sont le plus souvent d'origine thromboembolique et surviennent fréquemment au cours des 72 heures suivant la chirurgie après un intervalle sans symptôme. Les présentations de cas ont montré une relation causale entre l'hypotension et l'accident vasculaire cérébral périopératoire; néanmoins, de nombreux autres facteurs contribuent à sa physiopathologie. L'hypotension contribue en tant que facteur primaire, ou probablement plus fréquemment en tant que facteur secondaire, au développement d'un accident vasculaire cérébral périopératoire. Parmi les principales difficultés dans l'étude de cette association, citons l'absence de définitions normalisées de l'hypotension périopératoire, de

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la tension artérielle de base et de la durée de la période postopératoire. Afin de guider les recherches futures, nous proposons une sélection de questions à étudier afin d'acquérir de plus amples connaissances concernant le problème de l'ischémie cérébrale périopératoire.

Conclusion *Une tension artérielle inhabituellement basse entraînera en fin de compte des lésions neurologiques; toutefois, le seuil et la durée nécessaires pour conclure à une association entre un accident vasculaire cérébral périopératoire et l'hypotension n'ont pas été suffisamment étudiés. Dès lors, le rôle précis de l'hypotension dans l'étiologie de l'accident vasculaire cérébral périopératoire est encore très peu connu.*

Permanent and temporary cognitive or neurologic impairment in the perioperative period is of great importance to patients, their families, and their caregivers. A range of well-defined and less well-defined entities are involved, and in interpreting the literature, it is important to have a clear understanding of what has been studied. In 1978, the World Health Organization defined a stroke as a focal or global neurologic deficit of cerebrovascular cause that persists beyond 24 hr or is interrupted by death within 24 hr.¹ A transient ischemic attack (TIA) has a similar definition except that it lasts less than 24 hr. Strokes are classified by etiology into ischemic strokes (85%) and hemorrhagic strokes (15%). Ischemic strokes result from a critical reduction in blood flow and are categorized as embolic, thrombotic, and hemodynamic or hypotensive. Hemorrhagic strokes are caused by subarachnoid hemorrhage, arteriovenous malformations, and other vascular causes of intracerebral hemorrhage. Delirium is a well-defined acute fluctuating disturbance of consciousness and cognition,² while postoperative cognitive dysfunction is a more general deterioration of cognitive ability associated with surgery.³ Adding to the difficulty in understanding is the fact that “postoperative” is not defined and can mean any time period from the postanesthesia care unit (PACU) up to one month or longer after surgery.⁴

Although a postoperative stroke is most often embolic in origin, an association between intraoperative hypotension and the occurrence of a postoperative stroke is often assumed, perhaps because of the endemic nature of hypotension.⁵ Therefore, in this review, we focus on the possible role of intraoperative hypotension in the occurrence and development of postoperative cerebral ischemia, and we present an overview of the current knowledge on

this controversial subject. Our primary focus is on patients undergoing non-neurosurgical noncardiac procedures; however, there is a much larger amount of literature regarding the association of neurological injury with cardiac surgery, and we have drawn on that literature where appropriate.

Epidemiology

Stroke is uncommon after surgery, and the exact frequency varies with different types of surgery and patient comorbidities.^{6,7} A postoperative stroke is reported to occur in 0.08–0.7% of patients after general surgery, in 0.8–3% after peripheral vascular surgery, in 4.8% after head and neck surgery, in 2–3% (6% if TIAs are included) after carotid endarterectomy, in 8.7% after aortic repair, and in 1.4 (isolated coronary artery bypass graft) –9.7% (double- or triple-valve surgery) after cardiac surgery.^{5,7–9} Furthermore, patients with advanced age, previous stroke or TIA, or postoperative atrial fibrillation are at increased risk for postoperative stroke.^{4,5,7,8}

Most postoperative strokes do not occur immediately after surgery; there is usually a symptom-free interval before ischemia becomes apparent. In a recent retrospective study, only 8% of strokes were apparent in the PACU.¹⁰ Two peaks in stroke timing have previously been described. Approximately 45% of occurrences are identified within the first day after surgery, and 55% occur after uneventful recovery from anesthesia from the second day onward,^{11,12} although a more linear distribution of strokes has recently been described occurring in a more constant rate in the postoperative period.¹³ This uneven distribution of postoperative strokes combined with the widely varying occurrence of intraoperative hypotension with differing definitions¹⁴ has greatly complicated the little research that has been done on an association between postoperative stroke and intraoperative hypotension.

Etiology and pathophysiology

Intraoperative or early postoperative strokes associated with procedures that manipulate the heart, aorta, or carotids, or those that release particles from the cardiopulmonary bypass pump are predominantly embolic.^{5,15–17} The etiology is not clear in other patients because reports from administrative databases do not usually detail the pathology. In those studies that do provide pathology, thrombosis accounts for approximately 60% of occurrences.⁴

Watershed infarcts

Areas of the brain that are between non-anastomosing arterial vessels, i.e., end arteries, are termed watershed or border-zone areas. They are critically dependent on adequate perfusion pressure in the border-zone vessels. A reduction in perfusion below a critical value will result in ischemia because of inadequate collateral circulation.¹⁶ Infarction of watershed areas has been regarded as the hallmark of hemodynamic strokes. There are two major watershed regions (Fig. 1). The cortical watershed areas are between the cortical branches of the anterior, middle, and posterior cerebral arteries. The internal or sub-cortical watershed is located in the white matter (centrum ovale) along and slightly above the lateral ventricles between the deep (lenticulostriate) and the cortical branches of the middle cerebral artery and the anterior cerebral arteries (Fig. 2).

There is much controversy about the relative contribution of low-flow states and multiple micro-emboli to the pathophysiology.¹⁷ For example, it is hard to determine whether a local low-flow state due to hypoperfusion results in platelet micro-emboli or whether platelet micro-emboli result in local hypoperfusion. Irrespective of the sequence, there is synergistic interaction.¹⁸ Systemic hypotension would further compound this interaction. Emboli are thought to be an important component of cortical watershed infarcts, especially when there is atheroma of the large conducting arteries. Hemodynamic factors are thought to be more important for deep white matter infarcts.¹⁷

Fig. 1 A magnetic resonance image showing the areas of the brain typically associated with watershed infarction. The areas are the cortical border zones supplied by the anterior cerebral artery (ACA) and middle cerebral artery (MCA), and the MCA and posterior cerebral artery (PCA). The internal border zone is supplied by the lenticulostriate (LSA) branches of the MCA and the cortical branches of the MCA (see text for details)

Fig. 2 The angiogram shows the cortical border zone between the middle cerebral artery (MCA) and the anterior cerebral artery (ACA). Both are branches of the internal carotid artery (ICA). The internal border zone is supplied by the lenticulostriate branches near the origin of the MCA and the cortical branches of the MCA

Congenital variation of the circle of Willis

The Circle of Willis is comprised of the anastomoses of cerebral arteries from the left and right carotid and vertebral arteries and ensures collateral flow should one of these major arteries become occluded. Anatomical variations with absent interconnections can be found in 47–79% of the population.^{19,20} The most frequent variation is an absent or hypoplastic posterior communicating artery. Supplementary collateral flow can occur between the external and internal carotid circulation, e.g., through the ophthalmic artery and also through leptomeningeal channels. The latter are small vessels, less than 1 mm, that grow between the cortical conducting arteries. A persistent complete fetal-type posterior circulation results in the complete separation of the posterior and anterior circulations and occurs in 1–4% of the population.²¹ Development of collaterals usually occurs slowly, although hypoplastic vessels may have the capacity to be more acutely dilated. The contribution of the abnormalities to perioperative stroke is unknown, especially in the context of hypotension, although, as shown in a recent case report, they may be an important factor for some patients.^{22,23}

Intraoperative hypotension

Intraoperative hypotension is a common event during surgery; however, it is a very poorly defined term, and depending on the definition used, it can occur in 5–99% of patients undergoing surgery.^{14,24,25} Bijker *et al.* reviewed

four major anesthesia journals for their definitions of hypotension.¹⁴ Almost 50 different definitions were found utilizing systolic pressure and/or mean pressure either as an absolute or as a percentage of the baseline value. Diastolic pressure was never used. The most frequent definitions were 1) a 20% decrease in systolic pressure from the baseline value (13% of the articles), 2) a combination of systolic pressures below 100 mmHg or a greater than 30% decrease from the baseline value (8% of the articles), and 3) a systolic pressure below 80 mmHg (7% of the articles). A definition of “baseline” was provided in only 50% of the manuscripts but was most frequently the blood pressure immediately before induction of anesthesia. The majority of articles stated how frequently blood pressure was measured, but only 10% of articles specified a minimum duration for which reduced blood pressure would constitute hypotension. Due to a combination of factors, namely, the relatively infrequent occurrence of perioperative stroke, the poorly defined duration of the postoperative period (wherein a stroke would be considered associated with intraoperative events), and the wide range of definitions for intraoperative hypotension, an association between intraoperative hypotension and postoperative stroke is very hard to study and therefore largely unknown.¹⁴

Although it seems intuitively obvious that hypotension should be strongly associated with perioperative stroke, it is difficult to find clear evidence. Hypotension was thought to be a cause in 9% of strokes associated with cardiac surgery and thought not to be a factor in a case-control study of general surgery patients suffering a stroke.^{12,26} Similarly, case series in patients with carotid stenosis did not find hypotension to be the major etiological factor.²⁷

Watershed infarctions, which are expected to be encountered after hypotension, are rarely seen, whereas intraoperative hypotension is an often occurring side effect of anesthesia. In a review article in 2007, Selim *et al.* concluded that “deliberate hypotension induced by anesthesia does not seem to adversely affect cerebral perfusion, nor does it considerably increase the risk of perioperative stroke due to hypoperfusion in patients with carotid stenosis”.⁵ Further study is needed to investigate the hypothesis that hypotension is a primary cause of intraoperative or postoperative stroke. In a retrospective case-control study, 42 patients (0.1%) suffered a stroke after general surgery.¹⁵ A wide range of definitions of intraoperative hypotension was used to investigate the association with postoperative stroke. Only a mean blood pressure that decreased more than 30% from the baseline blood pressure was significantly associated with the occurrence of a postoperative stroke. This provided some evidence that indeed intraoperative hypotension can cause or aggravate postoperative stroke by compromising (collateral) blood flow to potentially ischemic, but still viable, brain areas

(the so-called penumbra). Nevertheless, the size of this effect (odds ratio 1.013; 95% confidence interval [CI] 1.000 to 1.025) is not as large as suggested by the POISE trial (see below) (odds ratio 2.14; 95% CI 1.95 to 3.96). Thus, a true cause-effect relationship cannot be established with certainty. It should be remembered though that hypotension in the presence of an embolic or thrombotic stroke will worsen the outcome.^{28,29}

Beta-blockers

The POISE trial, a randomized trial investigating the effect of perioperative high-dose metoprolol vs placebo in patients undergoing noncardiac surgery, revived the discussion on the possible association between intraoperative hypotension and postoperative stroke.³⁰ A significant increase in the risk of stroke was found in the metoprolol group. The *post-hoc* analysis determined that the intraoperative and postoperative risk factors were new onset atrial fibrillation (odds ratio 3.5), significant bleeding (odds ratio 2.18), and clinically significant hypotension (odds ratio 2.14). Clinically significant hypotension was defined as a systolic blood pressure below 100 mmHg for an unspecified time at any time during hospital admission. A meta-analysis reported a relationship among beta-blockers, hypotension, and stroke,³¹ but the POISE trial contributed the largest number of patients to this analysis. There are substantial differences among studies, including the drugs, dosages, regimens, definitions of outcome, and patient populations reported. The literature is also unclear about the temporal relationship between hypotension and the onset of stroke, concurrent or sequential, i.e., potential cause or just modulator. In a recent study, it was suggested that the type of beta-blocker used is important and that atenolol, contrary to metoprolol, does not increase the risk of adverse outcome.³² A possible explanation for this different effect of atenolol might lie in its hydrophilic character, making it almost unable to enter the central nervous system. This is contrary to the more lipophilic metoprolol, which does penetrate brain tissue and can occur in high concentrations in the brain.³³ Epidemiological studies have found non-selective beta-blockers to be associated with a higher risk of stroke than highly beta-1 selective agents, and this may place metoprolol at a disadvantage compared with atenolol and bisoprolol.³⁴ Ragoonanan *et al.* have proposed an interaction among the stroke risk factors identified in the POISE trial (i.e., metoprolol, hypotension, and hemorrhage).³⁵ Their rodent study showed that metoprolol significantly impaired the cardiac response to anemia and reduced cerebral tissue oxygenation through either systemic effects or perhaps local vascular effects. Thus, the role of beta-blockers in stroke is substantially more complex than simply the

induction of hypotension and may reflect specific actions of drug sub-classes on cardiovascular and cerebral homeostatic mechanisms.

The POISE trial could not separate the relative contributions of intraoperative and postoperative hypotension. Indeed, the role of postoperative hypotension has not been extensively studied, but it could be of great significance because postoperative blood pressure monitoring and management is much less focused than intraoperative monitoring. Limburg *et al.* noted postoperative hypotension to have occurred more frequently in their stroke cases than in their controls, and Cao *et al.* found a statistically significant association between postoperative hypotension and recurrent stroke in cardiac surgery patients.^{26,36}

Patient position

The risk of cerebral ischemia in the head-up position, especially when combined with hypotension, has been a topic of debate in the anesthesia literature for over six decades.^{37,38} The recommendation derived from outcome parameters of the time suggested that a systolic blood pressure of 60 mmHg measured at the heart level would allow adequate cerebral perfusion.³⁹ The debate was reactivated recently by the publication of a report of four middle-aged patients who suffered diverse catastrophic cerebral injuries from having shoulder surgery in the beach chair (upright) position. The authors speculated that neck rotation, embolism, and hypotension may have been causative.⁴⁰ An important aspect of the controversy relates to where blood pressure should be measured, at the level of the heart or the head. If the cerebral circulation is viewed as a siphon, i.e., a continuous fluid column, then the reduction in arterial pressure is matched by a reduction in central venous pressure so that the pressure gradient for flow through the intracranial circulation is unchanged. If the cerebral circulation is viewed as a “waterfall”, then the actual perfusion pressure at head level determines flow.⁴¹ An approach to reconciling this debate, excluding the small possibility of a congenital absence of critical intracranial collaterals (see above), would be to view cerebral circulation in completely healthy patients as being closer to a siphon and to view cerebral circulation in patients at risk of intracranial vascular disease, with intracranial disease, or with reduced oxygen carrying capacity as being closer to the “waterfall”. In either circumstance, a minimum pressure is needed.

A number of studies have used cerebral oximetry to assess the safety of the beach chair position. Many studies do show a reduction in this surrogate outcome, but the risks remain speculative due to lack of a large study reporting on neurological outcome.^{42,43}

Postoperative atrial fibrillation

Further evidence of a predominantly embolic mechanism of postoperative strokes is found in the strong association between postoperative atrial fibrillation and stroke.^{7,44,45} In turn, intraoperative hypotension is a risk factor for the development of atrial fibrillation.^{46,47} Assuming hypotension increases the risk of postoperative atrial fibrillation, one could also speculate that it also increases the risk of a postoperative stroke, without being the direct cause.

Management

Treatment thresholds

A long-standing approach to a blood pressure threshold has been the use of the purported population autoregulation threshold. We do not recommend such an approach. Autoregulation is a homeostatic mechanism to maintain cerebral blood flow over the wide range of blood pressures that a person usually encounters. Studies in awake healthy subjects indicate that the lower limit of autoregulation is a mean pressure of approximately 70 mmHg, which is higher than the 50 mmHg still shown in current textbooks.^{48,49} The population lower limit is “mobile” because it can be changed to higher levels with chronic hypertension and can return to a normal level with treatment of hypertension; it is also acutely modulated by PaCO₂ and sympathetic tone.⁵⁰⁻⁵² In addition to these factors, there is a huge range of thresholds in healthy awake individuals (43-110 mmHg), making it impossible to know the lower limit of autoregulation in any patient at any given time.⁴⁸

At present, it is impossible to provide a solid evidence-based threshold value at which to treat low blood pressures. Sparse evidence can be found in two retrospective studies (conducted by one of the authors of this review) that tested a range of threshold values for associations with one-year mortality and postoperative stroke.^{15,53} An association with one-year mortality could not be found. A 30% decrease in mean arterial pressure from immediately preoperative baseline was found to be associated with ischemic stroke within ten days of general surgery (odds ratio 1.013; 95% CI 1.000 to 1.025). Other threshold values, including absolute mean blood pressure thresholds (in mmHg) or systolic blood pressure values, either as absolute or percentage, were not associated with a postoperative stroke. Nevertheless, this retrospective case-control study with a very slight increase in odds ratio should be considered hypothesis generating, and no definitive conclusion can be drawn based on these studies alone.

Using a percentage decrease from a patient’s usual blood pressure range seems to make more sense than a

population-based absolute blood pressure. Determining the appropriate baseline blood pressure is difficult as blood pressure normally fluctuates 20–30% between awake and sleep states, and immediately preoperative blood pressures commonly exceed the patient's usual range.^{54–56} Further, a reduced amount of drop in nocturnal blood pressure and/or nocturnal hypertension has been associated with adverse cardiovascular outcomes, i.e., these patients normally have less blood pressure fluctuation.⁵⁷ A currently reasonable approach in healthy patients would be to accept a mean blood pressure within 25–30% of the immediate preoperative values measured in the preoperative holding area and first blood pressure on entering the operating room.¹⁵ This would keep blood pressure within the range encountered nocturnally.⁵⁴ A mean blood pressure lower than 30% should be treated. Blood pressure should probably be kept closer to the baseline value in patients at increased risk of stroke, especially if combined with reduced cardiac output and/or oxygen carrying capacity.

Treatment methods

The question that remains unanswered is whether treatment of low blood pressure improves outcome and how best to accomplish the increase in blood pressure.^{28,58} Several studies investigating the effect of different inotropic or vasopressor agents on cerebral blood flow or cerebral oxygenation illustrate that treatment of low blood pressure does not automatically improve flow or oxygenation. Norepinephrine increases arterial pressure but does not increase the cerebral perfusion pressure, and in higher doses, it even has a negative effect on cerebral oxygenation.^{59,60} Phenylephrine also decreased cerebral oxygen saturation, probably through a reduction in cardiac output, whereas ephedrine left it unchanged.^{61,62} Maintaining normocapnea prevented this effect of phenylephrine.⁶³ Clinical studies in patients with neurological injuries, such as stroke, subarachnoid hemorrhage, and head trauma, do not uniformly support the benefits of raising blood pressure.^{28,58}

Management of perioperative stroke

When a postoperative stroke is suspected, non-contrast computed tomography of the brain, preferably within 30 min of the presenting symptoms, is the quickest diagnostic imaging test⁶⁴; however, it is relatively insensitive for detecting very acute and small infarctions, especially in the posterior fossa.⁶⁵ Multimodal computer tomography and magnetic resonance imaging may then provide additional information, although emergency treatment should not be delayed.

Initial treatment consists of general supportive care and prevention of complications, which is usually best achieved in an acute stroke unit or a similar intensive care unit. Hypoxia and hemodynamic instability are both associated with poor neurological outcome after a stroke and causes, such as partial airway obstruction, hypoventilation, intravascular volume depletion, myocardial ischemia, or arrhythmias should therefore be corrected urgently. Similarly, hyperglycemia should be treated and blood glucose should be kept in the normal range. Drug-induced hypertension has been suggested for treatment of selected patients with acute ischemic stroke, but this is not based on large clinical trials, and current consensus does not recommend this treatment.⁶⁴ The current American Heart Association guideline recommends cardiac monitoring for at least the first 24 hr and actively treating any serious arrhythmia.⁶⁴

Unfortunately, many of the advanced treatment options of acute stroke, such as thrombolysis and mechanical recanalization, may not be suitable for patients who just underwent surgery. Even so, given the benefit to be gained, patients may be eligible for intravenous or intra-arterial thrombolysis, and active discussion with the appropriate specialists should take place. Currently, acetylsalicylic acid is the only oral antiplatelet agent that has been found to be beneficial in the treatment of acute ischemic stroke; therefore, it should be used in the perioperative period whenever deemed safe.⁶⁴

Outcome

Compared with a mortality rate of 13% after a stroke in a nonsurgical setting, the outcome after a postoperative stroke is often devastating, with mortality ranging from 26% after general surgery to 87% in patients who experienced a previous stroke.⁴ However, it is very difficult to estimate the mortality or morbidity resulting from the postoperative stroke, since the patients have a “baseline” morbidity or mortality risk that is associated with the surgical procedure itself. Nevertheless, a six-fold increase in mortality (4–22%) has been described in patients with a postoperative stroke after cardiac surgery compared with patients without a stroke.¹¹ In a recent study, a mortality rate of 26% was reported amongst stroke patients after noncardiac surgery. Fifty-two percent of the stroke patients from this cohort were able to live independently, 7% had minor symptoms, 24% had some restrictions, and 21% needed assistance but remained independent.¹⁵

Future directions

It is apparent from the above discussion that it is difficult to define the exact contribution of hypotension. Is it the cause

of perioperative stroke or only a modulator of perioperative embolic or thrombotic strokes? Some may argue that it matters not whether hypotension is causative or only contributory and that blood pressure should be rigidly clamped at some predetermined value. However, prevention and treatment are best when the etiology and the consequences of the treatment are clearly understood; no effective drug is innocuous. Progress will require specific steps regarding hypotension and perioperative stroke in general (Table). A standardized definition is needed for intraoperative and postoperative hypotension so that reports can be more easily compared. As hypotension is frequently described as relative to a “baseline” value, a standardized definition would be helpful, and, at the very least, publications should ensure that the definitions are included in the manuscript. Similarly, “perioperative” would benefit from a standardized definition. Thirty postoperative days is the definition commonly used to define “perioperative” in the carotid endarterectomy literature and may be appropriate for perioperative stroke. The exact contribution of hypotension needs to be understood in relation to the multiplicity of known and unknown factors that contribute to perioperative stroke (Table). For example, the relationship between

acute anemia, hypotension, and perioperative stroke needs to be better understood as both anemia and hypotension are frequent accompaniments of surgery.⁶⁶

Conclusion

Stroke is a potentially catastrophic complication of surgery. It is regarded as a rare complication, but, in fact, it occurs more frequently than most anesthesiologists realize. Perioperative risk factors are easy to identify, i.e., age, previous stroke, atrial fibrillation, significant arterial vascular disease, and hypercoagulable states after surgery. Given these risk factors, it is not surprising that the majority of perioperative strokes are thrombotic or embolic in etiology. Defining the contribution of hypotension has been difficult, as intraoperative hypotension is endemic while intraoperative stroke is infrequent. It is known that an unusually low blood pressure for an unusually long period will result in neurologic injury. Hypotension can therefore injure neural tissue directly, but in the perioperative period, it likely contributes more frequently to injury by compounding the effects of a thrombus or embolus. Defining the blood pressure thresholds for treatment will require a large amount of prospectively collected data together with standardized definitions. Finally, hypotension will need to be understood in the context of several other potentially important determinants of perioperative stroke (Table).

Table Problems to be addressed

Determine standardized definitions for:
Baseline blood pressure
Intraoperative hypotension
Postoperative hypotension
Perioperative period
Acquire documentation of temporal association between hypotension and onset of stroke
Determine if prevention or treatment of hypotension improves neurological outcome
Determine if different inotropic or vasopressor drugs differ in modifying neurological outcome
Determine the contribution and mechanism by which perioperative drugs contribute to perioperative stroke, e.g., beta-blockers
Acquire detailed reporting of pathological findings in perioperative stroke, especially the etiology
Determine the genomic predisposition to perioperative stroke
Determine the key inflammatory mediators of perioperative stroke and how to modulate them
Determine the contribution of endocrine disease and metabolic syndrome to perioperative stroke
Determine the contribution of acute and chronic disease states, e.g., anemia, sepsis, obstructive sleep apnea
Determine the contribution of silent or covert brain infarction to perioperative stroke
Validate a simple clinical screening tool for early detection of postoperative stroke, e.g., Face-Arm-Speech Test (FAST)
Develop a Stroke Risk Index
Develop a standardized approach to evaluation and treatment of perioperative stroke

Key points

- Perioperative stroke is most commonly embolic in origin, but the exact etiology is often more complex and multifactorial.
- The exact role of perioperative hypotension in the occurrence and development of a stroke is still largely unknown.
- Intraoperative blood pressure is best managed in relation to a baseline blood pressure instead of an estimated autoregulation threshold.
- Standardized definitions are needed for perioperative hypotension and stroke and for the perioperative period.
- It is unknown whether prevention of intraoperative hypotension reduces the incidence of stroke.
- Future research needs to focus on hypotension in the context of other important determinants of perioperative stroke.

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Competing interests None declared.

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