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Review

Strategies to prevent ischemic optic neuropathy following major spine surgery: A narrative review☆

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ABSTRACT

Postoperative vision loss following a major spine operation is a rare but life-changing event. Most of reports have been linked to ischemic optic neuropathy, and patients undergoing surgery for scoliosis correction or posterior lumbar fusion seem to be at the highest risk. Despite that some key risk factors have been identified, much of the pathophysiology still remain unknown. In fact, whereas only a minority of patients at high risk will present this complication, others with similar risk factors undergoing different procedures may not develop it at all. On the other hand, even when all preventive measures have been taken, ischemic optic neuropathy may still occur. Therefore, it is appropriate for clinicians involved in these cases to inform their patients about the existence of a small but unpredictable risk of vision loss. Since ischemic optic neuropathy is deemed to be the leading cause of vision loss in the context of major spine surgery in prone position, this review will be focused on its main aspects related to the frequency, diagnosis, predisposing factors, and prevention. Regrettably, no treatment has been proved to be effective for this condition.

Contents

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Table 2
Main retrospective studies reporting significant risk factors associated with ischemic optic neuropathy (ION). The effect size is reported as Odds Ratio (OR) and Incidence Risk Ratio (IRR). However, they may not be comparable due to the different methodologies used. All studies used multivariate logistic regression, unless otherwise specified. Figures in brackets are range of age. * As percentage of fluid replacement. CI: confidence interval. NR: not reported. RC: retrospective cohort. PR: Poisson regression. PVD: peripheral vascular disease.

Risk factor	Author, year	Study design/analysis	Effect size	95% CI	p value
Age	Patil, 2008 [26]	RC, administrative data	(18–44) Reference	–	–
			(45–64) OR 3.7	1.26–10.92	NR
	Shen, 2009 [14]	Administrative data	(<50) Reference	–	–
			(50–64) OR 1.75	1.13–2.71	0.04
			(≥ 65) OR 1,65	1.05–2.60	0.04
	Rubin, 2016 [34]	Administrative data, PR	(per 10 y) IRR 1.24	1.05–1.45	0.009
Gender	Shen, 2009 [14]	Administrative data	(Male) OR 2.04	1.47–2.82	<0.001
	Lee, 2012 [10]	Multicenter case-control	(Male) OR 2.53	1.35–4.91	0.005
	Rubin, 2016 [35]	Administrative data, PR	(Female) IRR 0.30	0.16–0.56	0.0002
Obesity	Lee, 2012 [10]	Multicenter case-control	OR 2.83	1.52–5.39	0.001
	Rubin, 2016 [35]	Administrative data, PR	IRR 2.49	1.09–5.66	0.03
PVD	Patil, 2008 [26]	RC, administrative data	OR 6.4	2.18–18.55	NR
Diabetes	Patil, 2008 [26]	RC, administrative data	OR 2.3	1.06–4.79	NR
Anemia	Patil, 2008 [26]	RC, administrative data	OR 5.9	3.15–11.07	NR
Hypotension	Patil, 2008 [26]	RC, administrative data	OR 10.1	2.85–35.84	NR
Estimated blood loss	Lee, 2012 [10]	Multicenter case-control	(per liter) OR 1.34	1.13–1.61	0.001
Blood transfusion	Patil, 2008 [26]	RC, administrative data	OR 4.3	1.69–10.80	NR
	Rubin, 2016 [35]	Administrative data, PR	IRR 2.72	1.38–5.37	0.004
Anesthesia duration	Lee, 2012 [10]	Multicenter case-control	(per hour) OR 1.39	1.22–1.58	<0.001
Wilson frame	Lee, 2012 [10]	Multicenter case-control	OR 4.3	2.13–8.75	<0.001
Colloid infusion	Lee, 2012 [10]	Multicenter case-control	(per 5%) OR 0.67*	0.52–0.82	<0.001

venules (the main source of the intraocular blood volume), thus leading to raised IOP and AION [37]. This phenomenon has been clinically demonstrated by Molloy et al. [23]. They examined the IOP in anesthetized patients undergoing laparoscopic and robotic surgery. When positioned in ST for at least 2 h, IOP did not return to the baseline levels in most of them. Although these findings come from patients in supine position, the prospective nature of data and the quality of the trial suggest that results may also be applied to patients undergoing major spinal operations.

5.2.2. Factors associated with the surgery

Surgical-related risk factors include length of operation (>6 h), fluid overload, hemorrhagic shock [7,10], estimated blood loss >1 L [10,35], use of vasopressors, need for transfusion [35,36], anemia, and hypotension [17,18,33,36,42,48,56]. In a retrospective database analysis, spine fusions involving ≥8 levels (nearly 50% of POVL cases) and spine surgeries for deformity were reported to be risk factors [29]. These findings are in agreement with the increased risk in lengthy operations.

There is ongoing debate regarding the role of anemia and hypotension in the pathogenesis of ION [57]. It is important to note that blood pressure progressively decreases from the internal carotid artery to the small vessels supplying the optic nerve [37], and the ocular blood pressure is approximately two-thirds of that registered in the brachial artery [39]. Nevertheless, many cases have been reported with MAP within normal range [16,26,31], and intraoperative hypotension is relatively common in many other procedures [22]. In the analysis conducted by the POVL Study Group, neither intraoperative anemia nor hypotension were reported as significant risk factors in the context of spine surgery [10,57]. However, a practice advisory reported from the ASA Task Force on POVL has recommended to use deliberate hypotension only after determining risks and benefits on a case-by-case basis [51,57].

Other authors believe that maintaining deliberate hypotension throughout the procedure, particularly in prolonged cases and high risk patients (e.g., chronic hypertension), should be avoided [4,19,48]. Buono and Foroozan reported anemia and hypotension as putative

Table 3
Main risk factors related to postoperative vision loss (POVL) and preventive measures proposed to diminish the risk. Most recommendations are based on case reports and retrospective case series, thus compromising the quality of evidence [44,51]. N/A: non-applicable. MAP: mean arterial pressure. CVP: central venous pressure. $PaCO_2$: arterial carbon dioxide tension (see text). Visual symptoms: ocular pain, blurred vision, scotoma, blindness.

Stage	Risk factor	Prevention
Preoperative	Male sex	
	Age > 50 years old	N/A
	Abnormal anatomy/autoregulation [37]	
	Vascular disease	
	Renal failure	Careful optimization prior to surgery
	Coagulopathy disorders	
	History of glaucoma	Referral to ophtalmologist for screening
Intraoperative positioning	Prone	Consider all major spine surgeries at higher risk
	Wilson frame	Consider 3-pin head holder
		Consider using other frames
	Neck malposition [54]	Ensure proper positioning and check periodically
		Consider 3-pin head holder
	>30° steep Trendelenburg	≤10° reverse Trendelenburg
Surgery	Estimated blood loss	Continuous MAP and CVP monitoring
	Need of transfusion	Check periodically hemoglobin, lactate and $PaCO_2$
		Consider to start transfusion on an individual basis
	Hypotension	Avoid deliberate hypotension in high risk patients
	Length of operation	Consider staged procedure
	Vasoactive drugs	Available evidence insufficient to make any recommendations [51,56]
	Fluid overload	Use colloids along with crystalloids [51]
Postoperative	Visual symptoms	Get early ophthalmology consultation

findings at early stages [3,42,44,50]. The nature of the latter phenomenon is beyond the scope of this review, but the paradoxical pupillary dilation after illuminating the affected eye is a relevant finding. When the diagnosis is not obvious, a cerebral MRI with gadolinium infusion should be obtained to rule out other pathologies, including stroke and pituitary apoplexy [28].

At early stages, AION reveals optic disc edema with or without splinter hemorrhages, whereas PION has normal fundoscopy [17–19,42]. However, when examined within the 4 to 8 weeks after the surgery, optic disc pallor may be the only finding in both entities, and after approximately 2 months, the disc becomes atrophic (Fig. 3) [4,28].

5. Risk factors

In response to the growing incidence of ION, the poor understanding of its pathophysiology, and the fact that its exact etiology remains unknown [8,36], the American Society of Anesthesiologists (ASA) established a POVL registry in 1999 [5], and 6 years later created the ASA Task Force on POVL, to examine the main factors associated with this condition in the context of spinal procedures in prone position, and develop strategies for its prevention [51]. The main retrospective studies evaluating risk factors for POVL are summarized in Table 2.

In a retrospective analysis from the POVL registry [2], Lee et al. identified 83 patients with ION after spine surgery. Most cases involved fusion and/or instrumentation at >1 level, bled approximately >1 L, had systolic blood pressure ≤ 100 mmHg for >15 min, and lasted >6 h [5,6, 44]. In a further study, these authors also identified male sex, obesity, and Wilson frame use as risk factors, whereas intravenous colloid use was a protective factor (Table 2) [10].

Many of the risk factors identified for POVL can also be applicable to ION [20]. Table 3 summarizes the main factors associated with POVL and potential interventions to prevent it [20,51]. However, it is important to note that, from those patients undergoing spine surgery, only 2–3% of high risk patients will develop ION. Conversely, patients deemed at low risk can also present this complication, which occasionally may still be reversible [8,18,31]. Thus, further investigation is needed to understand the underlying mechanisms predisposing to develop ION.

5.1. Preoperative factors

Most authors have cited among patient-related risk factors age, male sex, obesity, smoking [10,20,24,25,35,36], renal failure, anemia, coagulopathy disorders, history of glaucoma, and vascular disease (e.g., hypertension, diabetes mellitus, atherosclerosis, coronary artery disease) [19,20,24,25,41]. Interestingly, other target organs of vascular disease, including the brain, are unaffected in patients developing ION, suggesting that individual anatomical and physiological disturbances of the optic nerve vasculature may play an important role [22].

In 2012, the POVL Study Group published a multicenter case-control analysis to identify risk factors associated with ION following spinal fusion surgery. They reported male sex and obesity as significant preoperative risk factors (Table 2) [10]. In another retrospective study, Rubin et al. also identified age as a preoperative variable influencing the development of IOP. Remarkably, vascular disease was not found to be a significant risk (Table 2) [35]. Estrogen neuroprotection may be implicated in the gender differences found in these and other studies [6,10,28,35], whereas age as a risk factor was in agreement with a previous report, which suggested that patients older than 50 years were at the greatest risk of developing ION [14]. This finding may be related to the trend to have more complex spine procedures or the higher risk to develop ischemia in elderly patients. In another retrospective database analysis, the mean age of patients with POVL was 37.6 years, suggesting that age may not play a protective factor [29].

5.2. Intraoperative factors

5.2.1. Factors associated with positioning: intraocular pressure

Despite the fact that IOP is significantly lower in patients undergoing general anesthesia [40], prone position itself is associated with elevated IOP [52]. In a clinical trial evaluating healthy and awake volunteers positioned prone, the median IOP was 46% higher compared to that obtained in the sitting position [13]. These findings are in line with the IOP changes reported in anesthetized patients undergoing spine surgery [40,43].

There is no evidence that the use of horseshoe-type headrest increases the risk of ION when compared with 3-pin head holder (however it does increase the risk of undetected eye compression and subsequent CRAO) [41,51,53]. In contrast, the use of a Wilson frame has been strongly associated with PION [10,19,24,25,33]. In the study conducted by the POVL Study Group, the use of this frame had the greatest odds ratio for ION [10]. It may be explained by the position of the head, which is usually placed lower than the heart [11], and the fact that these patients tend to have impaired venous return resulting from augmented intraabdominal pressure [33,36]. Certainly, any increase in intraabdominal pressure due to the design of the operating table or malpositioning of the patient -particularly in obese subjects-, will be transmitted to the orbital venous pressure due to the absence of venous valves within the central retinal and episcleral veins, thus increasing the choroidal blood volume and IOP, augmenting the resistance to the blood flow and eventually diminishing the ocular perfusion [13, 19,28,37].

Head position with respect to the body longitudinal axis is also crucial to allow free circulation towards and from the brain [54]. While neck flexion may decrease the venous return from the brain, head elevation can compromise the optic nerve blood flow, and lateral neck deviation or head rotation may obstruct the venous outflow [18,19,55]. In addition, head rotation can increase the IOP in the lower positioned eye [55]. Therefore, a neutral or slightly elevated head position is ideal to prevent AION [56].

The steep Trendelenburg (ST) position, defined as a table tilt >30° in relation with the horizontal axis with the head positioned lower, has been related to a significant increment of the blood volume of choroid

Fig. 3. Fundoscopic appearance of acute anterior ischemic optic neuropathy (A), acute posterior ischemic optic neuropathy (B) and chronic ischemic optic neuropathy (C), showing optic disc edema (note the blurred margins of the disc), normal fundoscopy and optic disc pallor (note the well-defined margins of the disc), respectively. Courtesy of Dr. Mona Khurana, Sankara Nethralaya Medical Research Foundation, Chennai, India.

1. Introduction

Among all possible neurological complications related to general anesthesia (e.g. delirium, postoperative cognitive decline, stroke, spinal cord ischemia) [1], waking up from an elective spine surgery with significant visual impairment is one of the most dreadful experiences one patient can ever have. Postoperative vision loss (POVL) has been described as an uncommon, devastating, and usually irreversible complication associated with major procedures involving heart, blood vessels, and spine, among others [2]. Immediately after or within the first days of a spine operation, there have been reported cases of POVL after cervical laminectomies, thoracic or lumbar fusions, and other complex spinal procedures [2–6]. The main causes for prone procedures include ischemic optic neuropathy (ION), central retinal artery occlusion (CRAO), cortical blindness, and external ocular injury [1,7] (Fig. 1).

External ocular injury and CRAO tend to be mainly related to improper positioning of the patient (the latter may be also explained by embolic phenomena), whereas cortical blindness has been linked to ischemia of the visual cortex [1,7,8]. However, the mechanisms involving ION seem to be more complex. Despite having identified and optimized some risk factors, ION is still the leading cause of POVL, and patients undergoing prone spine surgery are at the greatest risk along with cardiac surgery [9–11]. In this scenario, the role of the anesthesiologist on its prevention is unclear. Therefore, in this narrative review, the epidemiology, pathophysiology, diagnosis, risk factors, prevention and potential legal implications of ION following spine surgery in prone position are discussed.

2. Epidemiology

Visual impairment associated with neurosurgical operations is a well-known complication that has been reported as early as 1954 [12]. Of note, most of POVL cases are unrelated to direct pressure to the eye [13,14]. Over the last few years, case-reports regarding POVL involving ION after major spine surgery have considerably increased [15–19]. It may be due to an increasing awareness of the problem, discrepancies in the inclusion criteria of studies or a true growth in the incidence resulting from the advances in spinal instrumentation, that make it possible to treat more complex cases [1,20]. In the United States, it has been estimated that from all claims related to the injuries to the visual pathways, those associated with optical nerve injury had increased from 5% (1980–1994) to 38% (1995–2011) [21].

Most of POVL reports (77%) have been linked to spine surgery in the prone position [2,22,23]. For these procedures, Epstein recently reported that incidence of POVL ranged from 0.013 to 0.2% [24]. This estimation has been confirmed by other authors [7,17,19,26–30], and the highest risk appears to be in patients undergoing surgery for scoliosis correction, or posterior lumbar fusion [22,26]. For spinal fusion procedures, the POVL incidence was 0.03% in a 10-year dataset analysis [14]. However, in a case-control analysis the incidence has been reported as high as 0.36% [31].

It has been estimated that four in every five cases of POVL are caused by ION [2,8,16], from which more than a half develop bilateral disease [8]. In addition, most patients with perioperative ION are men on average 50 years old, many of which are relatively healthy [22]. ION can be further subdivided in anterior (AION) and posterior (PION) - see below-, depending on the vascular supply (Table 1). Although AION is more common in the general population [32], PION is the cause of the majority of cases related to prone spine surgery (Fig. 1) [30,33,34].

On the other hand, Rubin et al. [35] recently reported that in the United States, the incidence of postoperative ION had diminished by 2.7 times from 1998 to 2012, despite the increase in the number of spine procedures. After examining >2.500.000 posterior thoracic and lower back fusions performed during that period, they found an incidence of 1.02 per 100.000 spinal fusions (95% CI 0.72–1.32). However, they could not differentiate among severity or type of ION. Remarkably, the incidence had consistently decreased along three-year periods, in contrast with retinal artery occlusion, which remained essentially unchanged [35]. It has been speculated that this change in trend may be due to several factors: the use of Wilson frame has dramatically dropped in that country over the last decade, surgeons have optimized the technique (thus diminishing the blood loss and shortening the length of the procedure), minimally invasive spine operations have increased, and anesthesiologists are more concerned about the intraoperative hypotension. Yet, it is possible that many cases have not been coded as ION, thus biasing the sample [35,36]. Additionally, a significant number of POVL cases may remain underreported, thus representing a publication bias [23].

3. Pathophysiology

The optic nerve blood flow relies on optimal ocular perfusion pressure (OPP) [17,18,37] and low resistance to the blood flow [38]. The OPP is defined as the difference between mean arterial blood pressure

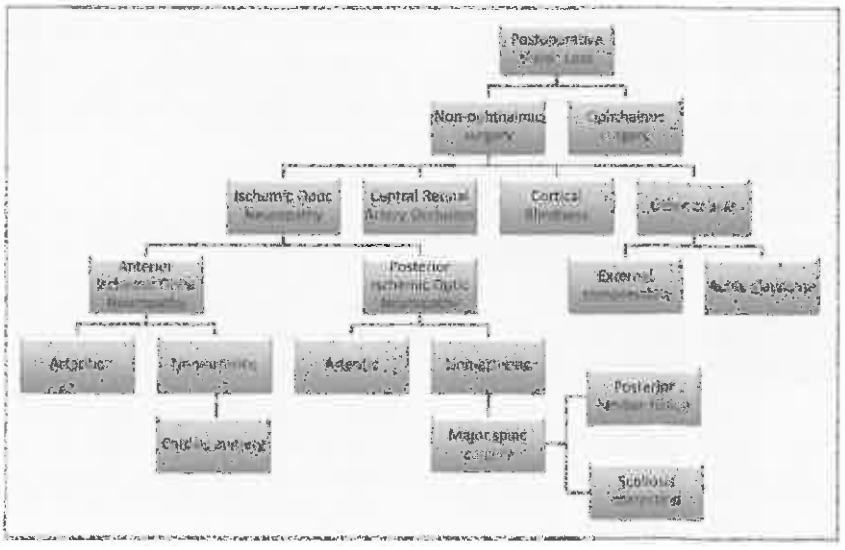

Fig. 1. Main causes of postoperative vision loss in the context of non-ophthalmic surgery [49].

Table 1
Main differences between non-arteritic anterior (AION) and posterior acute ischemic neuropathy (PION). *Optic cup diameter/optic disc diameter (in bilateral disease it is difficult to measure when there is optic disc edema) [31]. CABG: coronary artery bypass graft.

Description	AION	PION
Main cause	Multifactorial [49]	Hypoperfusion [48,57]
Surgery associated	Mainly CABG [22]	Mainly spine procedures [48]
Vascular disease [49]	Commonly associated	Rarely associated
Symptoms appearance [57]	Usually within first days	Usually during anesthesia recovery
Early fundoscopic exam [44]	Optic disc edema ± peripheral hemorrhages	Normal
Late fundoscopic exam [44]	Optic disc atrophy (pallor)	
Relative afferent pupillary defect	Usually present	
Cup-to-disc-ratio [31]*	Usually <0.2	Usually >0.2
Anemia and hypotension [33,57,58]	Rarely associated	Commonly associated
Long-term improvement [42]	Occasionally	Seldom
Treatment	Not available	

(MAP) and either central venous pressure (CVP) or intraocular pressure (IOP), whichever is higher. The resistance to the blood flow, in turn, is influenced by the central venous drainage, the hydrostatic pressure in the interstitium (following the Starling forces), and local autoregulation [39]. IOP intrinsically increases in the prone or lateral position -in this latter case, in the lower positioned eye- [40–43]. It appears that, when IOP reaches 40–50 mm Hg, local autoregulation is lost and the optic nerve head blood flow dramatically drops. In addition, some healthy subjects may not have autoregulation at all [39]. On the other hand, when OPP drops below that of IOP (normal range, 10–20 mm Hg), hypoperfusion and AION are impending [26,37,39].

It is worth noting that, however, raised IOP has nothing to do with PION. The point of demarcation between AION and PION is the lamina cribrosa, as depicted in Fig. 2 [44]. Whereas IOP is the measured pressure in the anterior chamber of the eye, PION occurs posterior to the lamina cribrosa. In patients with PION, interstitial fluid accumulation, which is usually a consequence of the prone position along with elevated IOP, is thought to elicit a compartment syndrome within the optic nerve, thus favouring the development of PION [29]. Accordingly, factors influencing the optic nerve blood flow seem to be more complex than the mere fact of measuring the ocular perfusion pressure, and probably also involve the pressure surrounding the optic nerve head and sheath.

The vascular supply of the optic nerve is provided by short posterior ciliary arteries (arising from the ophthalmic artery) and penetrating pial vessels (arising from collateral branches, coming mainly from the ophthalmic artery), in their anterior and posterior portions, respectively

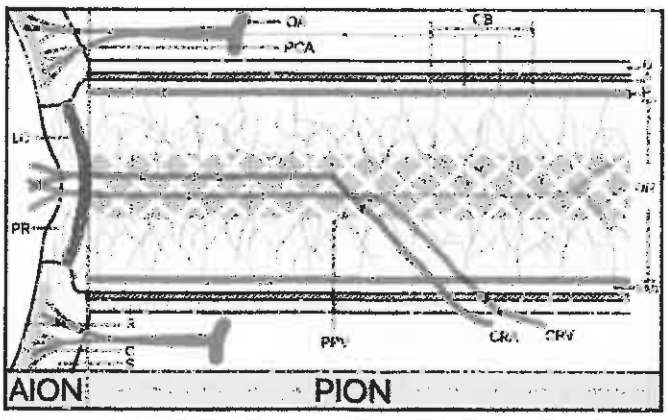

Fig. 2. Diagram of the vascular supply to the optic nerve. The diamond-shaped area represents the inner part of the optic nerve, a watershed zone susceptible to ischemia. OA: ophthalmic artery. PCA: posterior ciliary arteries. CB: collateral branches, arising from the OA.48 D: dura. A: arachnoid. P: pia. ON: optic nerve. SAS: subarachnoid space. CRV: central retinal vein. CRA: central retinal artery with penetrating branches PPV: penetrating pial vessels, arising from CB. R: retina. C: choroid. S: sclera. PR: prelaminar region. LC: lamina cribrosa. AION: anterior ischemic optic neuropathy. PION: posterior ischemic optic neuropathy [46].

[37,45,46]. Posterior ciliary arteries are subject to anatomical variation -which is present in as many as 20% of normal subjects- and impaired autoregulation, rendering the patient to develop AION. In contrast, penetrating pial vessels represent the main supply of the retrobulbar portion of the optic nerve, and do not have autoregulatory mechanisms at all (Fig. 2) [46]. As a result, they are sensitive to sustained arterial hypotension, thereby precipitating PION [19,28,45,47].

Furthermore, in some healthy subjects, there is a watershed area within the posterior portion of the optical nerve, which is believed to be crucial in the pathogenesis of PION (Fig. 2). It is created by the absence of anastomoses between penetrating pial vessels (also known as peripheral centripetal system), and penetrating branches arising from the central retinal artery (also known as axial centrifugal system). Thus, the lack of collateral circulation in the posterior portion of the optical nerve can render patients more vulnerable to develop PION (Fig. 2) [37,47,48].

Both AION and PION can be further classified in arteritic and non-arteritic disease (Fig. 1) [17]. Arteritic ION is a severe systemic condition that typically affects women >60 years old, and it is caused by systemic vasculitis (mainly giant-cell arteritis). They often have elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) [17,28,31, 49]. On the other hand, whereas the non-arteritic variant of AION may occur spontaneously in patients with pre-existing vascular disease, and in the context of POVL it is mostly associated with coronary artery bypass graft (CABG) surgery, non-arteritic PION has been mainly attributed to anemia and hypotension following spine surgery (Fig. 1) [28,31, 48].

Irrespective of the cause of ION (i.e., low ocular perfusion pressure, anemia, vascular disease or increased resistance to blood flow) [49], the subsequent impairment of the oxygen delivery depletes adenosine triphosphate (ATP) reserves, thereby inducing membrane depolarization. By means of intracellular Ca^{2+} overload resulting from reversal activation of Na^{+}- Ca^{2+} exchange pump, the ischemic insult leads to apoptotic cell death and irreversible neuronal injury [7].

4. Diagnosis

Intraoperatively, unexplained bradyarrhythmias caused by vagal stimulation may be the only manifestation of raised IOP. Following the procedure, patients complain of visual field deficits, including visual scotomas, altitudinal field defects (loss of function in the lower hemifield), and complete blindness [49]. Table 1 provides the main distinctive features of AION and PION. Although the visual impairment related to spine surgery is mainly caused by PION, this is a diagnosis of exclusion [3,15,48]. Usually, the symptoms from PION are more severe, but they do not get any worse [44]. Patients with ION may report bilateral, sudden, and painless visual loss [17,41]. Yet, some of them can be monocular, in which case the left eye is predominantly affected [3,15,33].

On clinical examination, poor pupillary light reflex and relative afferent pupillary defect (Marcus-Gunn phenomenon) may be the only

risk factors, after reviewing 83 cases of perioperative PION [48]. Hence, it would be reasonable to maintain the MAP as close as possible to the preoperative values.

In the largest retrospective study performed to date, Rubin et al. [35] identified need for transfusion (which may be a surrogate of blood loss) as a significant risk factor (Incidence Rate Ratio, 2.72; 95% CI, 1.38 to 5.37; $p = 0.004$). However, other intraoperative information was not available in this study (Table 2) [35]. In a case-series report of six patients in which POVL was diagnosed, it was found that all of them had significant anemia (hemoglobin <8.0 g dL^{-1}) and hypotension (MAP 24% to 46% lower than preoperative values) at one point of the operation [58]. These findings were further confirmed in a similar study [34]. Nonetheless, these risk factors, although very important, are insufficient to precipitate ION by themselves [49,55].

Brucculeri and colleagues have reported that IOP increases soon after drinking water in healthy individuals [59]. Hence, it has been speculated that fluid overload may also play a role as a trigger of ION, either increasing IOP (thus precipitating AION) or accumulating fluid into the optic nerve and around the lamina cribrosa (thus precipitating PION) [7, 56,60]. However, the available evidence is insufficient to make any recommendations with this regard [51].

The type of intravenous fluid administered intraoperatively does not seem to modify the tissue pressure surrounding the lamina cribrosa. In a randomized clinical trial evaluating patients undergoing prone spine surgery, the time-weighted average IOP was not significantly different in those receiving lactated Ringer's solution or 5% albumin [43].

Lastly, although it has been suggested that the use of vasoactive amines can precipitate the development of ION [24,25], it should be borne in mind that, contrary to the choroid, the optic nerve is not provided by alpha-adrenergic receptors and the blood-brain barrier prevents the free circulation of these agents, except in the prelaminar region of the nerve [7,49,56].

6. Prevention

6.1. Preoperative assessment

During the preoperative assessment, careful identification of risk factors should be undertaken and optimized [19]. Furthermore, patients with history of glaucoma need to be evaluated by an ophthalmologist and screened for raised IOP in the prone position [24,25,55]. Hemoglobin, blood pressure and glycemia (in patients with pre-existing diabetes) may also be optimized, when appropriate [24,25].

The possibility of a staged procedure should be discussed with the surgeon when a lengthy operation in the prone position is planned in high risk patients [7]. In fact, the length of the operation along with the head position strongly influence the IOP values in anesthetized patients [34,40,54].

6.2. Positioning

Once the patient has been adequately positioned and a foam headrest has been placed to protect eyes and face pressure points, it becomes challenging to check intermittently the neck position and look for inadvertent displacement of the foam headrest. Mirrors provided with some frames, including Proneview™ and Allen^{R} Advance Table may be helpful [37], but they are not entirely reliable to watch the neck position. Therefore, it is critical to ensure a proper positioning of the patient before starting the procedure, be attentive to positional changes of the table during the operation, and check periodically eyes clearance [50]. It has been suggested that the application of a 3-pin head holder may prevent abnormal positioning of the neck, thus eliminating the problems related with the neck posture [24,25]. However, it does not eliminate the risk of AION resulting from raised IOP [41].

Unintended intraoperative modification of the head position can displace the foam headrest (causing extrinsic compression to the eyes), modify the neck inclination or head rotation with respect to the body (thus impairing the venous return from the brain), or increase the abdominal pressure (thereby decreasing the venous return) [18]. Occlusion to the carotid and vertebral arteries has been also reported [52]. Hence, all precautions need to be taken to keep the head at the same level or higher than the heart, maintaining the neck in a neutral position or slightly elevated with respect to the body [18,51,52].

The operating table inclination by approximately 10° in reverse Trendelenburg has been proposed for all major spine procedures in prone position [19,24,25], in order to ameliorate the IOP increase intrinsically caused by the positioning. In a recent clinical trial performed in elective patients undergoing lumbar spinal fusion, when the neck was extended 10° in relation to the operating table, the IOP was significantly decreased compared to the neutral position [54]. Carey et al. also reported significantly lower IOP at 60 min in elective patients undergoing prone spine surgery, when positioned on 10° of reverse Trendelenburg, compared to a neutral prone position. However, the IOP increased in all cases irrespective of the table inclination, and remained high until the end of the operation [34].

6.3. Optimizing ocular perfusion

Optimization of ocular perfusion is crucial to prevent ION. Apart from MAP and hemoglobin monitoring [18,24,25,51], the improvement of the IOP can be accomplished with a careful positioning, as discussed above. This is of paramount importance in the maintenance of adequate ocular perfusion, particularly when the MAP is concurrently decreased or the bleeding is uncontrollable [13]. On the other hand, increasing the blood pressure may also cause significant intraoperative bleeding, thus extending the duration of the procedure [22,57].

Since the hemoglobin threshold to prevent ION is unknown, the decision to start blood transfusion should be made on a case-by-case basis [19,51]. Accordingly, blood samples need to be obtained regularly, not only for monitoring hemoglobin concentration, but also to measure lactate levels (as a surrogate of hypoperfusion) and arterial carbon dioxide tension ($PaCO_2$). In fact, high levels of $PaCO_2$ have been associated with raised IOP, and although $PaCO_2$ remains unchanged in prone position, the end-tidal carbon dioxide ($ETCO_2$) tends to decrease (probably as a result of increased dead space ventilation), rendering this latter an inaccurate estimator of the $PaCO_2$ in long procedures [61].

Whereas some authors have recommended the avoidance of fluid overload [18], the evidence to support the use of colloids over crystalloids in these patients is somehow conflicting. Epstein [24,25] and Larson [60] have recommended administering crystalloids rather than colloids, and some others have described the increased ratio of crystalloid to colloid as a risk factor [10,30]. In a multicenter case-control study, Lee et al. reported an Odds Ratio of 0.67 (CI: 0.52–0.82, $p < 0.001$) per each 5% of non-blood fluid replacement with colloids instead of crystalloids (Table 2) [10].

6.4. Postoperative screening

Most patients developing ION will complain of blurred vision during the immediate recovery period. Thus, they should be assessed for visual acuity and potential external injuries at the earliest opportunity. When suspected, an ophthalmologist needs to be urgently involved to exclude other causes (e.g., cortical blindness or retinal artery occlusion) and discuss alternative treatments [3,7,22]. Hemoglobin, blood pressure and oxygenation can be also optimized at this stage [51].

7. Treatment and prognosis

There is no definitive treatment for ION. Initial management may include blood pressure optimization, correction of volume depletion and blood transfusion, when appropriate. Some authors have reported benefit from intravenous or retrobulbar corticosteroids, antiplatelet

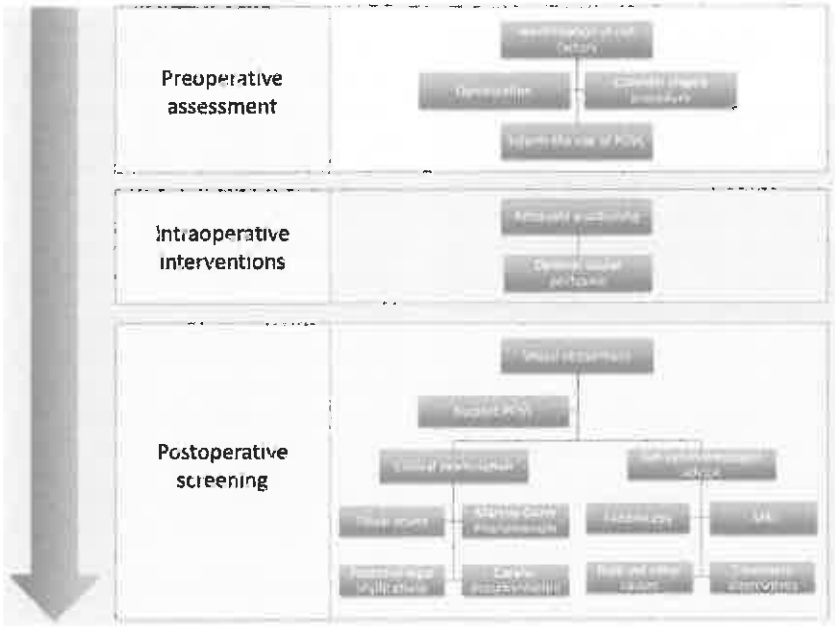

Fig. 4. A proposed clinical algorithm for sequential workup in patients with suspected POVL (postoperative vision loss).

therapy, acetazolamide, mannitol, furosemide and hyperbaric oxygen, but results are not conclusive and none of these treatments have proven to be effective in ION [3,7,17,20,51]. Optic nerve decompression for non-arteritic AION has been shown to be ineffective, and even harmful [62]. Alternatively, transvitreal optic neurotomy was effective in a small non-randomized clinical trial, but these results have not been supported by further research [63]. On the other hand, although partial and spontaneous remission have been reported, the chance of improvement is low, particularly in PION [18,42]. A proposed algorithm for sequential work-up in cases of suspected POVL is described in Fig. 4.

8. Legal implications

Clinicians are expected to inform the patient of not only the most frequent risks related to a surgical procedure, but also the uncommon catastrophic complications. The informed consent requires an optimal communication between doctor and patient, and must include, besides the professional practice standard -i.e., the typical risks of a given procedure-, a reasonable person standard: a more individualized level of information that a patient with competence and capacity requires, ideally with enough time in advance, before deciding whether or not they want to undergo the operation [64]. In a recent survey, it has been reported that four in every five patients who underwent prolonged spine surgery in the prone position would have preferred the physician to overtly disclose the risk of POVL [65].

Hence, the small but unpredictable risk of POVL should be explicitly mentioned during routine pre-operative assessment to any patient undergoing major spine surgery, and documented in the consent form [9, 10,18,66], particularly because most patients do not expect any visual complications when they are undergoing this operation. This responsibility is shared by both the anesthesiologist and the surgeon, but owing to the unclear etiology of this entity, there is still some reluctance to discuss this matter with patients [66]. Which of them should inform about this particular risk during the preoperative assessment remains debatable [65], but given the potentially devastating consequences, it should be mentioned by both team leaders [66].

Ischemic optic neuropathy is a serious complication with relevant medico-legal implications [7], and there is no specific treatment for this condition. Therefore, the avoidance of ION should be focused on its prevention [24,25]. Nonetheless, even when all preventive measures have been taken, ION may still occur [4,16,18,50,53]. Hence, apart from the standard recording of continuous blood pressure, estimated blood loss, fluid balance, and urine output, careful documentation needs to be done of visual disorders before surgery, head and neck position, eye protection, and frequent eye assessments [20,51]. In addition, MAP and hemoglobin should be also documented [51]. It has also been suggested the use of a live streaming video to allow continuous monitoring of the eye position and keep the recording as a case documentation [27].

Lastly, whenever a patient complains of visual disturbances after a major spine operation, an ophthalmologic consultation needs to be obtained at the earliest convenience [28]. Despite the fact that no treatment has been proved to be effective for ION, any delay in the assessment may have significant legal implications, since other potential causes need to be ruled out, and the best available therapeutic options should be offered to the patient to mitigate the ocular damage, when possible.

9. Future directions

Despite the efforts to have a better understanding of POVL, some questions still remain unanswered. For instance, the exact mechanism that triggers the ischemic injury is currently unknown [21], as there have been reported cases of ION without having any risk factors. More importantly, there is no reasonable explanation why patients with similar risk factors undergoing other procedures have lower risk to develop ION when compared to spine surgery, why only a small fraction of high-risk patients develop ION [36], and why some ischemic insults can still be reversible [8,18].

Unfortunately, clinical research in this topic has been particularly challenging [45]. While prospective studies may not be feasible because of the relative low incidence of ION and some ethical concerns, retrospective studies (e.g., case-control designs with matched controls) may be subject of biases and potential confounders. Over the last few years, several studies have been focused on surrogate endpoints including IOP [13,23,40,54], anemia and hypotension [58]. Regrettably, results have demonstrated relationship but not causality, and IOP does not seem to be an accurate surrogate of ocular perfusion pressure [67], the mean blood pressure probably being a more important factor [28].

Anesthesiologists may not be responsible for ION in many cases [43, 68]. However, in order to achieve a better understanding of this condition, it is vital to continue reporting new cases. With this aim, the American Society of Anesthesiologists' Committee on Professional Liability has created the Closed Claims Project, an international anonymous registry designed to collect, among others, cases associated with perioperative ION [2,5,6].

10. Conclusion

Over the last few years, ION has been a complication of great concern among anesthesiologists. Despite that the incidence in the context of major spine surgery seems to have decreased, clinicians involved in these procedures need to understand that ION should not be considered a single entity. Rather, it is the result of multiple predisposing factors causing significant impact in the ocular perfusion, venous drainage, and local autoregulation phenomena. Although some of these factors may still remain unknown, a better understanding of the pathophysiology of this condition hopefully will allow the anesthesiologist to more effectively prevent this devastating complication. Due to the gravity of this condition and the lack of effective treatment, patients undergoing major spinal operations should be informed of this risk.

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