Physiology and Role of Intraocular Pressure in Contemporary Anesthesia

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More than 26 million Americans suffer with cataracts, and with 3.6 million cataract extractions performed annually in the United States, it is the most common surgical procedure. The integrity of the delicate structures of the eye that mediate vision is dependent on the intraocular pressure (IOP). Yet, IOP acts to compress the vessels within the globe—akin to a Starling resistor—and is a key component that determines the ocular perfusion pressure, defined as the difference between arterial pressure and IOP. The retina is one of the most metabolically active tissues in the body, and its functional integrity is dependent on an adequate blood supply, with retinal function linearly related to the ocular perfusion pressure. Retinal cell death has been demonstrated at low perfusion pressures (below 50 mm Hg). Modern ophthalmic surgery involves globe irrigation, manipulation, and instrumentation, resulting in dynamic pressure fluxes within the eye. Marked elevations of IOP (up to 4–5 times the normal value) with consequent borderline retinal and optic disk perfusion pressures occur for prolonged periods during many ophthalmic procedures. General surgeries, including laparoscopic, spinal, and cardiac procedures, especially, with their demand for steep Trendelenburg or prolonged prone positioning and/or hypotensive anesthesia, can induce IOP changes and ocular perfusion imbalance. These rapid fluctuations in IOP, and so in perfusion, play a role in the pathogenesis of the visual field defects and associated ocular morbidity that frequently complicate otherwise uneventful surgeries. The exact etiology of such outcomes is multifactorial, but ocular hypoperfusion plays a significant and frequently avoidable role. Those with preexisting compromised ocular blood flow are especially vulnerable to intraoperative ischemia, including those with hypertension, diabetes, atherosclerosis, or glaucoma. However, overly aggressive management of arterial pressure and IOP may not be possible given a patient's comorbidity status, and it potentially exposes the patient to risk of catastrophic choroidal hemorrhage. Anesthetic management significantly influences the pressure changes in the eye throughout the perioperative period. Strategies to safeguard retinal perfusion, reduce the ischemic risk, and minimize the potential for expulsive bleeding must be central to the anesthetic techniques selected. This review outlines: important physiological principles; ophthalmic and general procedures most likely to develop damaging IOP levels and their causative factors; the effect of anesthetic agents and techniques on IOP; recent scientific evidence highlighting the significance of perfusion changes during surgery; and key aspects of postoperative visual loss and management approaches for high-risk patients presenting for surgery. (Anesth Analg 2017;XXX:00–00)

Ophthalmic surgery accounts for the highest surgical caseload throughout the globe; this year, an estimated 3.6 million cataract procedures will have been performed in the United States, and more than 20 million worldwide.[1] Contemporaneously, all ophthalmic subspecialties continue to advance, aided by a seemingly endless evolution of supportive technology and surgical equipment. New surgical modalities now exist to treat a range of previously unmanageable conditions. Hand in hand with these developments, patient expectations have increased. Perioperative intraocular pressure (IOP) changes can dramatically affect clinical outcomes[2] and are influenced significantly by anesthetic management.[3]

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IOP is essential to maintain the refractive properties of the eye, and is defined as the pressure exerted by the contents of the eye against its containing wall. An increase in IOP reduces the perfusion of the ocular structures in a linear manner, and at elevated levels, it is more important than blood pressure (BP) in determining retinal function.[4] At pressures exceeding the ocular perfusion pressure (OPP), raised IOP causes compression of the vasculature, resulting in retinal ischemia and blindness in animal models. Acute IOP elevation, of the order of 20 mm Hg for 5 minutes, reduces blood flow to the retina, choroid, and optic nerve in healthy volunteers,[5] and may interfere with the delivery of essential neurotrophins from the brain to the retina.[6] Acute decreases in IOP (<6.5 mm Hg) can induce hypotonic maculopathy, which reduces visual acuity and can cause retinal detachment.[7] Acute increases in IOP in an "open" globe (eg, retinal surgery) potentially result in expulsive hemorrhage or extrusion of orbital contents.[8]

Substantial fluctuations in IOP occur during intraocular surgery, with variations between 0 and 120 mm Hg demonstrated during routine vitrectomy surgery,[9] and between 13 and 96 mm Hg in cataract procedures.[10] A 0.5-mL intravitreal injection increases IOP by more than 150% from its preinjection baseline level, to 43.81 ± 9.69 mm Hg.[11]

These intraoperative IOP fluctuations result in compromised blood flow to the optic nerve and retina as the OPP is markedly decreased,[5] which may partially account for the variable visual outcome after surgery. The anesthetic challenge is to optimize surgical conditions, minimize the risk of visual and other adverse outcomes by safeguarding retinal perfusion, and to manage the comorbidity challenges that present.

OCULAR PHYSIOLOGY

Normal IOP is 16 ± 5 mm Hg, with cyclic fluctuations of 2–3 mm Hg throughout the day,[12] peaking in the early morning, and lowest being at night due to circadian regulation of aqueous humor secretion.[13] Levels above 24 mm Hg are considered pathologic.

Factors Affecting IOP

Factors affecting IOP include neural influences, rate of aqueous humor flow, and episcleral venous pressure (via its effect on aqueous outflow and choroidal blood volume).

Neural Influences. The central nervous system influences IOP directly through neurogenic regulation of extraocular muscle tone from central diencephalic centers.[14] Increased tone or contraction of extraocular muscles can markedly increase IOP.

Aqueous Humor. The balance between the aqueous humor production and outflow rates is the chief physiological regulator of IOP.

The aqueous humor circulates from the posterior chamber into the anterior chamber, where temperature-dependent convection currents disseminate flow, allowing nutrient and metabolic exchange between the lens and cornea.[15]

At the iridocorneal angle, 75% of the aqueous humor drains into Schlemm's canal, and 25% drains directly through ciliary muscle fibers.[16] From here, the aqueous humor flows into the orbital venous system. Resistance to outflow can cause an acute rise in IOP, with an increase of 1 mm Hg for every 0.8 mm Hg increase in episcleral venous pressure (the major determinant for which is the central venous pressure [CVP]).[17]

Choroidal Blood Volume and Flow. The retina is one of the most metabolically active tissues in the body, and its functional integrity is dependent on adequate vascular perfusion. Blood flow is 1400 mL/min per 100 g of tissue[13]—20 times that of the brain grey matter—with a high oxygen extraction rate of 40%–50%.[18] This is achieved by flow through 2 morphologically and functionally distinct arterial systems: the retinal circulation and the choroidal circulation, which feed the inner and outer layers of the retina, respectively.[19]

The retinal circulation is an end-arterial system.[20] It receives no autonomic innervation, but is tightly autoregulated and influenced by the metabolic activity of the inner retina and optic nerve head.[21,22] The choroidal circulation supplies 85% of the retina, including the photoreceptors and retinal pigment epithelium.[13,19] Richly innervated by the autonomic nervous system,[23] the choroid forms a specialized dense vascular layer between the sclera and outer retina.

While the relationship between OPP, mean arterial pressure (MAP), and IOP is complex and shows considerable interindividual variation, both the choroidal and retinal circulations autoregulate in response to changes in OPP.[21,23,24]

Impairment of venous outflow will cause engorgement of the choroid, increased intraocular blood volume, and a transient rise in IOP.[25] Aqueous humor outflow will increase (over 15–30 minutes) to partially compensate for this IOP rise.

Vitreous Humor. The vitreous cavity comprises two-thirds of the volume of the globe.[26] It contains the vitreous humor, an almost acellular extracellular gelatinous matrix composed of 98%–99% water that has a relatively fixed volume and is not typically involved in IOP regulation.[27]

Although relatively stable under normal conditions, even a small change in vitreous volume may alter IOP. The vitreous is influenced by the osmotic pressure changes in the adjacent choroidal and retinal circulations.[28]

Ocular Perfusion Pressure

In most tissues, the perfusion pressure is dependent on the pressure differential between the arterial input and venous output. In the eye, the intraocular veins are subject to compression by the IOP and behave like Starling resistors (ie, the venous transmural pressure must exceed the IOP or they will collapse) (Figure 1).[29] Therefore, the mean OPP (MOPP) is the MAP in the ophthalmic artery minus the IOP or ocular venous pressure, whichever is highest.[30] Because IOP normally approximates the intraocular venous pressure, MOPP can be calculated by: MOPP = MAP – IOP.

In the sitting or standing position, the ophthalmic artery pressure is approximately 2/3 of the brachial artery pressure due to hydrostatic effects: MOPP = 2/3 MAP – IOP.[31] This calculation assumes that the MAP as measured at the brachial or radial artery is truly representative of the ophthalmic artery pressure.

Retinal vascular well-being is dependent on IOP; when the latter exceeds MAP, MOPP is 0, and ocular blood flow ceases entirely.[31] Increasing IOP while maintaining a constant MAP produces a set of pressure–flow curves (Figure 2).[32] Low OPP may be caused by an increase in IOP and/or a decrease in MAP.[24,32]

Autoregulation operates within a critical range of perfusion pressures and breaks down above or below this range. Studies suggest that the lower autoregulatory limit is reached at an IOP of 30–35 mm Hg, and that at an OPP of 30-35 mm Hg, the optic nerve flow becomes dysfunctional.[33]

Metabolic Control of Ocular Blood Flow

The retina exhibits neurovascular coupling whereby blood flow is increased during neural stimulation to meet tissue demands[34] through the release of tone-relaxing or tone-contracting mediators.[35,36]

Within the physiological range, IOP is minimally affected by arterial pressure changes.[37] Hyperoxia results in a marked vasoconstriction of retinal arterioles[36] that is 3–4 times greater than witnessed in the cerebral circulation.[30] Conversely, hypoxia induces arteriolar vasodilation and increases in retinal blood flow. Choroidal blood flow

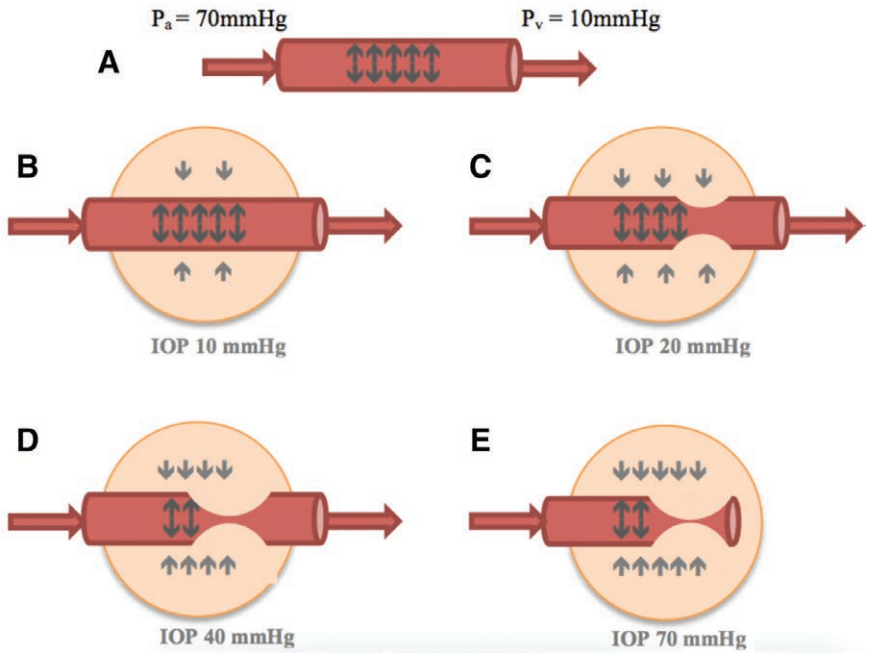

Figure 1. Ocular starling resistor. The role of intraocular pressure (IOP) in determining ocular blood flow. A, Blood flow is determined by the arterial pressure (P_a) – venous pressure (P_v) divided by resistance. B, When IOP is low, the pressure in the vessel exceeds the IOP (ie, transmural pressure gradient), and so the vessel remains distended. C and D, When IOP exceeds venous pressure, the vessel begins to collapse, which increases resistance to flow. E, If the IOP exceeds arterial pressure, the vessel collapses completely and blood flow ceases. This occlusion point is dependent on the relative value of the arterial pressure within the vessel and the surrounding IOP.[29]

increases by 3.6% for every 1 mm Hg increase in $Paco_2$, so a low-normal $Paco_2$ level (25–30 mm Hg) with consequent vasoconstriction reduces IOP.[38]

CLASSIFICATION OF OPHTHALMIC SURGERY

Perhaps unique to ophthalmic surgery, the surgical procedure itself induces large pressure fluxes that directly influence organ perfusion and affect ocular well-being.

Ophthalmic surgery may be classified as extraocular, intraocular, or mixed.[39] In extraocular procedures, where the globe is not incised, IOP has virtually no impact on the surgical procedure or outcome. Intraocular surgical procedures may be subdivided into open or closed, depending on whether intraoperative communication exists between the globe and the atmosphere.

During open-eye procedures, the concept of IOP does not exist because the eye is open to the atmosphere. However "positive vitreous pressure" may be caused by pressure on the scleral wall (extraocular muscle tension) or an intraocular mass (choroidal effusion or hematoma), causing a reduction in the volume of the scleral cavity.[40] This may be manifested by iris prolapse and lead to vitreous loss, choroidal effusion, or hemorrhage.

In the evolution toward closed-eye surgery, the first step was self-sealing beveled incisions in the cornea and sclera (eg, in phacoemulsification surgery) followed by surgical microincision vitrectomy (eg, 23-, 25-, and 27-gauge). These advances limit the ocular hypotony that results from fluid egress through open wounds. The modern trend is toward completely closed vitrectomy procedures using a valved trocar system that continuously seals the eye while a separate infusion line pressurizes it (Figure 3).

Closed intraocular surgery induces a varying degree of pressure development in the globe because no communication exists with the atmosphere to mitigate any pressure rise. The extent of IOP increase is directly related to the infusion pressure applied (dependent on the preset line pressure or the height of the infusion bottle). As multiple factors tend to increase IOP intraoperatively, the actual IOP is frequently considerably in excess of the delivered infusion line pressure.[9]

OPHTHALMIC SURGERY AND PERIOPERATIVE IOP CHANGES

The OPP substantially influences retinal function, and retinal susceptibility to an IOP challenge is linearly related to BP.[41] MAP elevation appears unable to fully compensate for the retinal dysfunction induced by the same degree of IOP elevation. For a given OPP level, the higher the IOP elevation, the greater the retinal dysfunction, possibly because raised IOP affects vascular supply and produces a mechanical stress on neurons independent of OPP.[24]

OPP and Surgical Outcome

Acute IOP elevations block retrograde transport of neurotrophic factors from the brain to the retina,[6] induce retinal ganglion cell structural[42] and functional[43] abnormalities, and reduce ocular blood flow by 7%–8% per 10-mm Hg increase.[44] After uneventful vitrectomy, 14% of patients experience visual field defects varying from unnoticed peripheral defects to total loss of vision.[45] Nearly 20% of these field defects show changes suggestive of an ischemic component.[2] Proposed mechanisms range from preexisting comorbidity problems to perioperative surgical or anesthesia insults. While a multifactorial etiology underlies these visual defects,[45] most postulated mechanisms share an ocular hypoperfusion theory in which the MOPP decreases to a potentially critical level perioperatively.[2,46]

The normal MOPP range is 45–55 mm Hg, with nocturnal reductions of 10%–20%.[47] But we cannot, as yet, define the critical MOPP value at which retinal or optic nerve function is damaged. Furthermore, this value is likely to show considerable interindividual variation. Nor do we know with certainty how long ischemia can be tolerated by the

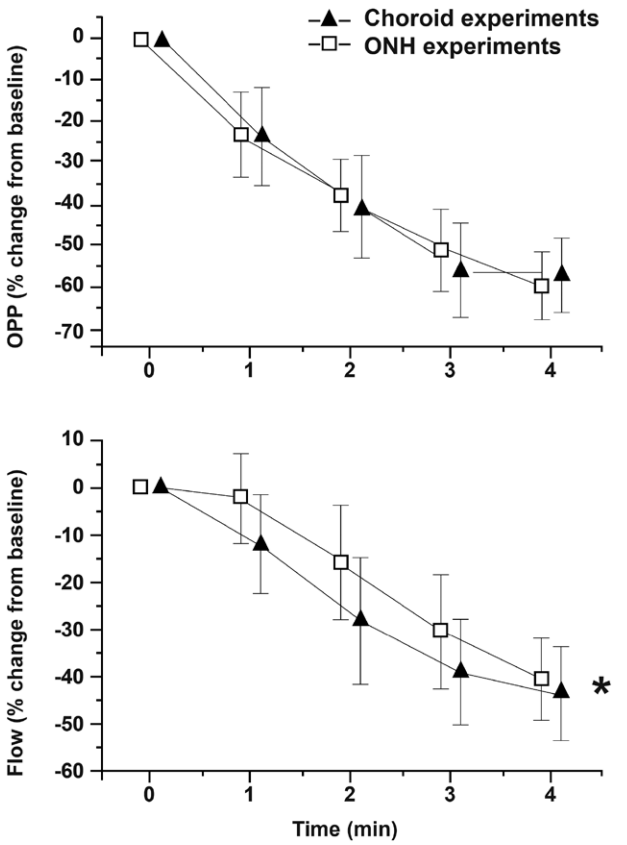

Figure 2. Reduction in OPP and choroidal and optic nerve head flow with artificial increases in intraocular pressure (IOP) in human volunteers.[32] Time 1–4 (min) on the x-axis corresponds to incremental increases in IOP to 50, 75, 100, and 125 mm Hg, respectively. As IOP is increased incrementally, both OPP and blood flow are reduced at each successive IOP level. Data are presented as percentage change from baseline, with time 0 min representing the baseline OPP and flow. Data are shown separately for the artificial IOP increase for choroidal (black triangles) and optic nerve head experiments (open squares). ONH indicates optic nerve head; OPP, ocular perfusion pressure.

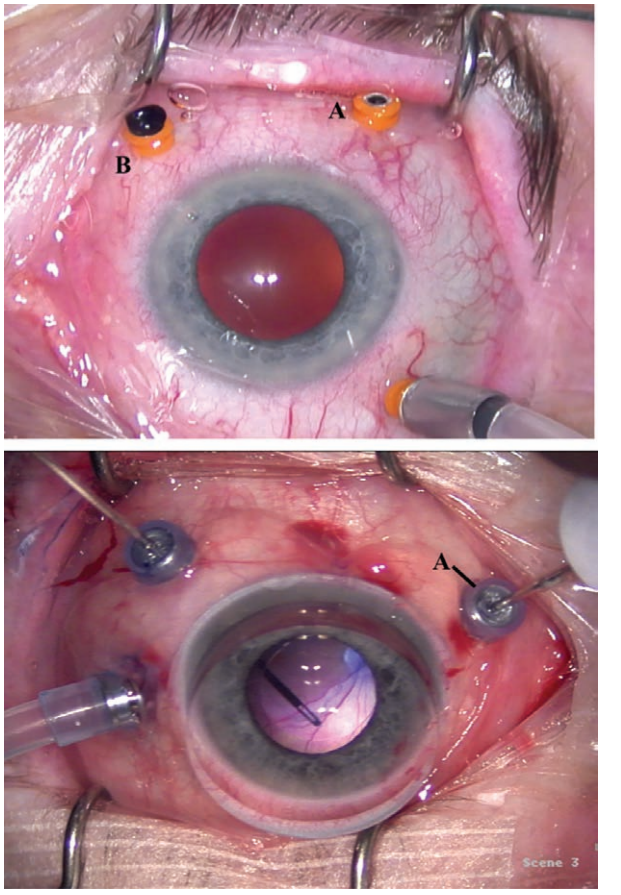

Figure 3. Vitrectomy systems. Open and closed. Top, Open vitrectomy (right eye) with infusion line and free communication with atmosphere through the trocar system (A) with egress of fluid—cap to seal off the open trocar to stop fluid escape (B). Bottom, Closed vitrectomy (left eye) with infusion line and insertion of surgical instruments through self-sealing trocar system with no communication with atmosphere (A).

intraocular structures. Ganglion cell damage occurs after 45 minutes of ischemia, with total optic atrophy at 240 minutes.[48]

The IOP during surgery depends on constantly changing parameters, including the cutting and suction speed, infusion rate, mechanical indentation of the globe, and fluid injection during the procedure. Nearly all these factors have a more marked effect on IOP during closed intraocular surgery.

Rossi et al[49] demonstrated a BP decrease and IOP increase throughout vitrectomy under peribulbar or retrobulbar blockade with deep intravenous sedation. Sustained IOP increases (of the order of 40–50 mm Hg and lasting several minutes) with further sporadic spikes in IOP (exceeding 70 mm Hg for a few seconds) were demonstrated. The sustained IOP increase was frequently due to increased infusion bottle height to facilitate hemostasis or a particular surgical step (eg, removal of silicon oil). The spikes in IOP typically resulted from globe manipulation or injections into the eye. The net result was an average 37.1% reduction in MOPP from baseline values and a MOPP below the physiological range of 50–60 mm Hg throughout surgery in 27.7% of cases. Furthermore, MOPP remained below the critical limit of 30 mm Hg for as much as 50% of the entire surgical time (Figure 4).[49]

Bansal et al[2] compared 7 patients who developed optic neuropathy after retinal detachment surgery with 42 matched controls. A total of 5 of these 7 patients (71%) demonstrated reduced OPP with associated systemic hypotension intraoperatively compared with 7 of the 42 patients (17%) in the control cohort (P = .01), implying that reduced OPP is associated with postvitrectomy optic neuropathy.[2]

Phacoemulsification also induces substantial IOP fluctuations, especially because maximum vacuum settings are frequently used to shorten the surgical time with a consequent need for higher infusion pressures.[10] Zhao et al[10] demonstrated an IOP greater than 60 mm Hg (the retinal perfusion pressure) during 3 simulated steps of phacoemulsification, with peak IOP reaching 96 mm Hg. Despite its short duration, cataract extraction increases the incidence of optic neuropathy due to supply/demand blood flow imbalance.[50,51]

Safeguarding the Retinal Circulation

Intraoperatively, the "safety check" of directly observing the effect on optic disk circulation of MAP and IOP

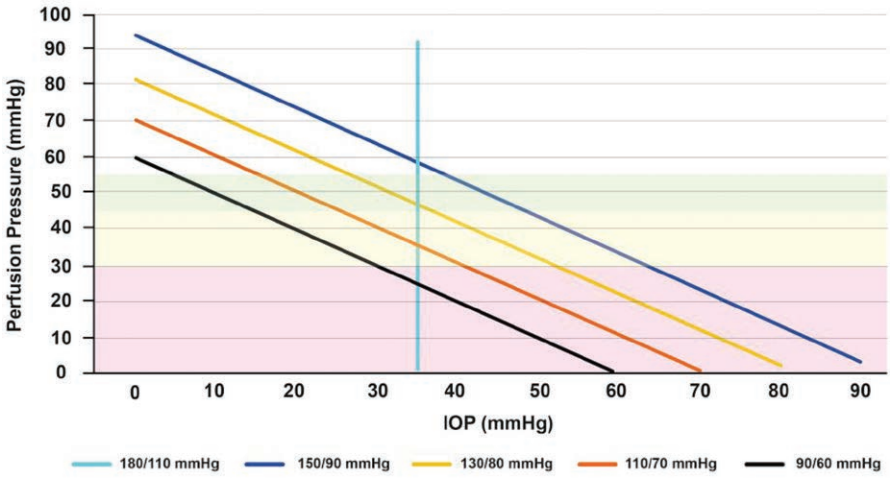

Figure 4. Mean ocular perfusion pressure (MOPP) versus intraocular pressure (IOP) during vitrectomy surgery. This normogram depicts mean ocular perfusion pressure (MOPP) (on y-axis) against IOP (on x-axis) as a function of systolic blood pressure (SBP) and diastolic blood pressure (DBP). The pink shaded area represents MOPP <30 mm Hg—the critical MOPP level associated with ischemic retinal damage. The yellow shaded area is below the normal physiological MOPP range of 45–55 mm Hg. Note that at an IOP = 35 mm Hg (deemed "safe" for most vitrectomy procedures), those with lower BP measurements experience critical MOPP values with ischemic risk. As IOP increases, insufficient MOPP values result even with dangerously high BP values. At IOP >50 mm Hg, increasing the BP is not a viable option to protect retinal perfusion; the only feasible approach is to maintain IOP within a strict range.[49]

alterations may be performed infrequently (Figure 5).[52] Ophthalmodynamometry, digitally indenting the globe while visualizing optic disk perfusion, estimates the perfusion closure risk.[53]

Any damage from reduced ocular perfusion would potentially be exaggerated in those patients with: (1) preexisting conditions that predispose to impaired retinal perfusion (eg, atherosclerosis, diabetes, hyperlipidemia, aging, high myopia, and retinal detachment)[54]; (2) hypotension (eg, from general anesthesia or deep sedation)[46,49]; and (3) increased intraoperative retinal oxygen demand (eg, with surgical trauma, low infusion fluid temperature, or extensive laser treatment). Defective autoregulation may exacerbate the situation. Face-down or prone positioning is associated with increases in IOP and potentially prolongs perfusion imbalance, especially if accompanied by postoperative hypotension (due to dehydration, antihypertensive medication, sedation etc).[55]

Short-term reduced ocular blood flow produces a gradient of retinal functional deficits, with the precise relationship between the 2 unclear.[56] The ischemic threshold appears to differ between patients with both the degree and duration of reduced perfusion important. The "watershed" zones between arterial distribution territories vary greatly in the ocular circulation, and these areas are most vulnerable to reduced perfusion.[57]

Intraoperatively, the extent of IOP rise should be controlled by keeping the infusion line pressure as low as is consistent with the surgical goals, and not routinely setting it at 30 mm Hg. If further infusion pressure elevation is temporarily required, its duration should be minimized (Figure 5). The anesthetist should communicate these goals clearly to the surgical team.

Newer vitrectomy machines, such as the R-Evolution 2.0 (Optikon, Rome, Italy), measure the globe infusion line pressure and allow a controlled-pressure irrigation system that offers real-time compensation for MOPP fluctuations.[58]

Choroidal Hemorrhage Risk

Any increase in OPP, by increasing MAP and/or reducing IOP, can precipitate choroidal hemorrhage, a devastating complication. The predisposing factors for which include advanced age, atherosclerosis, hypertension, and sudden ocular decompression.[8] The pathogenesis involves an increase in transmural pressure. Surgical incision with resultant ocular decompression decreases IOP and increases the pressure across the wall of all choroidal plexus vessels.[59] In this setting, the transmural pressure is highly sensitive to arterial and/or venous pressure elevations such as are produced by the Valsalva maneuver, coughing, sneezing, or bucking on the endotracheal tube (ETT).[60] An increase in vascular permeability (secondary to ocular inflammation) may also play a role. Surgical vigilance to prevent ocular hypotony and adequate anesthesia depth are important, as evidenced by the development of massive suprachoroidal hemorrhage in 6 patients who developed coughing while intubated after vitrectomy.[61]

Therefore, the patient's ocular ischemic risk factor profile should be reviewed preoperatively. The aim is to minimize retinal ischemic damage risk while limiting the transmural pressure gradient. Accurate BP readings are necessary, and an arterial line should be considered. While no exact "safe" transmural pressure or MOPP can be defined, it seems intuitively sensible to keep both MAP and IOP in their baseline ranges and to synchronously control their levels. Hypotension should be minimized, and BP should be targeted to maintain MOPP in the physiological range of 45–55 mm Hg.[47]

Careful control of IOP after surgery should be used to bring the IOP to ≤15 mm Hg in high-risk cases. Regular (at least hourly) BP should be checked, and the patient should not be discharged until the BP and IOP are stable and appropriately balanced. Fundoscopy to assess the optic disk and retinal circulation should be performed regularly in high-risk patients until the IOP settles, especially when posturing requirements are known to increase IOP.

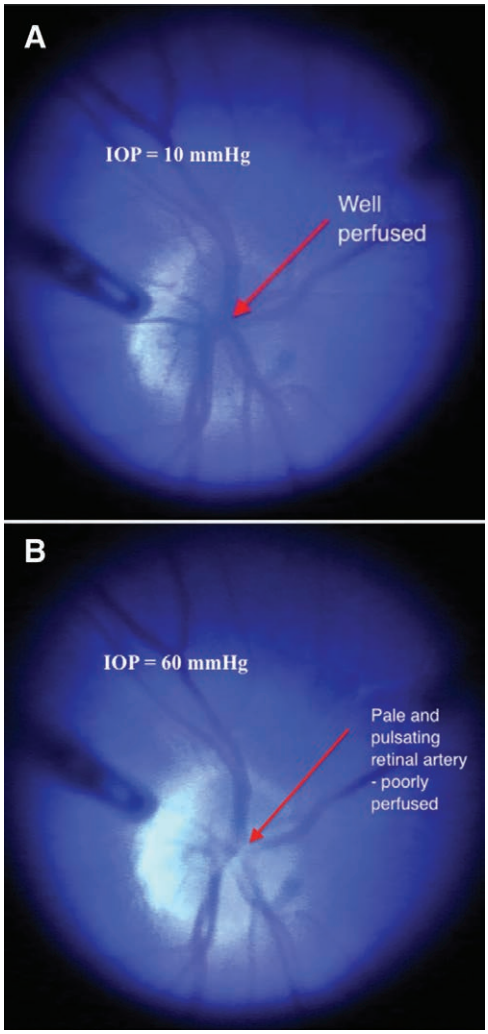

Figure 5. Direct visualization of the effect of intraoperative intraocular pressure (IOP) changes on optic disk vessels. Blood pressure = 95/60 mm Hg in both photographs from this patient. The optic disk vessels are well distended and perfused at an IOP of 10 mm Hg, with vessels traceable out to the periphery of the retina (A). At an IOP = 60 mm Hg, the disk has a paler appearance, is more pulsatile, and demonstrates blurring of its edges. The vessels are thinner and thread-like as the ocular perfusion is compromised secondary to the high IOP (B). (Note that the IOP is taken as corresponding to the preset infusion line pressure, which is frequently not accurate.)

ANESTHESIA AND THE IOP

Modern ophthalmic practice demands optimal conditions to achieve best surgical outcomes, including a stationary globe, low-normal IOP, MOPP control, management of transmural pressure, attenuation of the oculo-cardiac reflex, minimal bleeding, good oxygenation and normocarbia, and a smooth emergence from anesthesia. The available data have not indicated a marked difference in outcome between general and regional anesthesia for major complications such as vitreous loss.[62]

General Anesthesia

Induction and Maintenance of Anesthesia. All of the commonly used anesthetic induction agents are known to decrease IOP. Propofol, thiopental, and etomidate reduce IOP by up to 40%, 27%, and 30% respectively.[63,64] Propofol has the most profound effect, even at sedative doses of ≤1 mg/kg, for which an IOP reduction of 17%–27% is reported.[65] The mechanism of IOP reduction after induction of anesthesia is incompletely understood, but it includes depression of ocular centers in the brain resulting in extraocular muscle relaxation.[14]

Convincing evidence has now refuted the belief that ketamine increases IOP. In children, there is no clinically significant IOP increase at doses <4 mg/kg.[66] However, the effects of ketamine in adults and those with penetrating eye injuries need further evaluation.

All volatile anesthetic agents cause a reduction in IOP.[67,68] Sevoflurane and propofol decrease IOP equally during maintenance of anesthesia.[69] However, when combined with remifentanil, the IOP reduction is more significant with propofol than with sevoflurane.[70] Indeed, total intravenous anesthesia fulfils many of the requirements for ophthalmic anesthesia by lowering BP and IOP and reducing postoperative nausea. Nitrous oxide has no effect on IOP when combined with sevoflurane and remifentanil,[71] but it is contraindicated in vitreoretinal surgery involving gas tamponade.[72]

The overall effect of general anesthesia is a reduction in IOP despite laryngoscopy and intubation producing profound increases in sympathetic outflow.[73] Obtunding this sympathetic response is important with an "open" globe and in those vulnerable to ocular perfusion changes.

Opioids and Other Agents. Short-acting opioids fentanyl, alfentanil, and sufentanil significantly reduce IOP on induction of anesthesia and produce a sustained reduction in IOP below control values after both succinylcholine administration and laryngoscopy.[74,75] Remifentanil is at least as effective as fentanyl and alfentanil in this regard.[76] Premedication with the α-2 agonists clonidine and dexmedetomidine attenuates the IOP increase produced by laryngoscopy,[77] but it also decreases MAP, which may reduce the OPP. Gabapentin, as a premedication, has similar effects.[78] Midazolam appears to have little effect on IOP, making it a useful agent when evaluating IOP in children or anxious or uncooperative patients.[79]

Careful avoidance of postoperative nausea and vomiting is required because emesis is a strong predictor of delayed suprachoroidal hemorrhage. Most ophthalmic procedures have minimal systemic impact and are not unduly painful. A sub-Tenon's block limits the analgesia needs and reduces opioid requirements.

Airway Management. During general anesthesia, the most significant increases in IOP occur at laryngoscopy and emergence. Two groups require meticulous management: those with an open globe,[80] and those with glaucoma.[81] The latter may already have critical disk perfusion, and the increase in IOP during intubation is exaggerated in glaucomatous eyes.[82]

Limited intraoperative airway access probably favors endotracheal intubation (ETT) despite the lesser sympathetic response and IOP increase provoked with laryngeal mask (LM) insertion.[83] Direct laryngoscopy using a Macintosh blade doubles IOP (mean 6.7–13 mm Hg) on the first attempt, and a second attempt increases IOP by

an additional 30% (mean 17.2 mm Hg).[84] The McCoy blade induces a smaller increase in IOP and less hemodynamic change.[85]

Video laryngoscopes appear advantageous with regard to their effect on IOP. In studies comparing the Macintosh blade with the McGrath series 5 VL (Aircraft Medical, Edinburgh, United Kingdom),[86] the Glidescope VL (Verathon, Bothell, WA),[87] and the Airtraq VL (Prodol Meditec S.A., Vizcaya, Spain),[88] the Macintosh groups produced a more significant increase in IOP than any of the video laryngoscopes.

LM insertion produces no change[89] or a smaller increase in IOP[90] than that induced by direct laryngoscopy and intubation. In patients undergoing intraocular surgery, the IOP was significantly higher in the ETT group at all points reaching peak values around tracheal extubation, probably reflecting the greater sympathetic response to the ETT on emergence from anesthesia.[83]

Neuromuscular Blocking Agents. Succinylcholine is known to increase IOP by up to 10 mm Hg.[91] Extraocular muscle contraction during depolarization and fasciculation is thought to be an important contributing factor. However, succinylcholine administration elevates IOP despite complete extraocular muscle detachment from the eye.[92] Postulated reasons include reduced aqueous humor outflow, increased choroidal blood volume, and possibly increased CVP.[93] Pretreatment with nondepolarizing muscle relaxants is inconsistent in preventing this IOP increase.[94,95]

When compared with atracurium and succinylcholine, rocuronium demonstrated a greater reduction in IOP and equally favorable intubating conditions as succinylcholine.[96] Chiu et al[97] demonstrated that IOP after succinylcholine was significantly higher than after rocuronium (mean 21.6 [SEM 1.4] mm Hg versus 13.3 [1.4] mm Hg), respectively. Rocuronium is therefore a viable alternative to succinylcholine in an open-globe setting.

The incidence of coughing or bucking on the ETT during emergence from anesthesia is estimated at 38%–76%,[98,99] with an associated IOP elevation of 40 mm Hg.[60] An American Society of Anesthesiologists analysis of eye injuries associated with anesthesia found that 30% related to unplanned patient movement during surgery.[100] Techniques to minimize intraoperative coughing or bucking include "deep" extubation, a "no-touch" extubation technique, and the use of sympatholytics (such as remifentanil, fentanyl, intravenous lidocaine, and dexmedetomidine).[101–103]

Reversal of Neuromuscular Blockade. Yagan et al[104] found that IOP increased from 13.5 to 21 mm Hg after neostigmine/glycopyrrolate administration, with no change in IOP observed after sugammadex. The IOP was elevated after tracheal extubation in both groups, but was significantly lower in the sugammadex group at 1, 3, and 5 minutes, possibly reflecting the anticholinergic effect of glycopyrrolate that may reduce aqueous outflow.[105]
Smooth emergence is the goal, and while deep extubation can be performed, awake extubation is very safe, especially after a remifentanil-based technique.

Patient Positioning and Ventilation. An increase in CVP reduces venous drainage with resultant choroidal engorgement and decreased aqueous drainage. Supine, prone, and steep Trendelenburg positioning consequently increase the IOP,[106,107] which may be further exaggerated if accompanied by pneumoperitoneum.[108] The increased IOP during laparoscopic surgery in the Trendelenburg position is attenuated by dexmedetomidine without further OPP reduction.[109] A 30° "head-up tilt" or reverse-Trendelenburg reduces supine IOP values by 3 mm Hg, but also affects OPP[110] (Table 1).[55,60,106,107,111,112]

Although positive pressure ventilation increases the CVP, short-term mechanical ventilation with positive end expiratory pressure (PEEP) <15 cm H_2O does not cause a clinically significant IOP increase, and allows better manipulation of the $Paco_2$ than spontaneous ventilation.[113] PEEP at levels of 15 and 20 cm H_2O increased the IOP by 3 and 6 mm Hg, respectively.[114,115]

The "Open" Globe. In most open-globe injury cases, surgery can be delayed up to 6 hours to observe standard fasting guidelines. However, even after that interval, an empty stomach cannot be guaranteed. In addition, in cases of polytrauma, a rapid sequence induction might be unavoidable.

The anesthetist must prioritize securing the airway and hemodynamic stability, yet remain cognizant of the risk of ocular content extrusion and/or choroidal hemorrhage. Controlled airway management is therefore important.

Tradition cautions against succinylcholine due to the theoretical risk of expulsion of globe contents. This is perhaps unfair, because the only report of this complication occurring had confounding factors that make directly attributing it to succinylcholine difficult.[116] Rocuronium 0.9 mg/kg provides equivalent intubating conditions within 60 seconds, and is a sensible choice in this setting.[97,117] However, coughing increases IOP to multiples of the potential succinylcholine-induced rise,[60] so adequate neuromuscular blockade must be confirmed before laryngoscopy. Use of sympatholytics should be considered on a risk–benefit basis.

Regional Anesthesia

The orbital cavity has a capacity of 30 mL, and injection of any fluid would be expected to cause an increase in IOP.[118] Studies comparing retrobulbar, peribulbar, and sub-Tenon's block demonstrate an initial rise of 5–10 mm Hg in the IOP but a fall to below baseline values within 5 minutes.[119,120] The initial increase in IOP appears most marked in the peribulbar group, perhaps reflecting the higher volume typically injected (8–10 mL) compared with the retrobulbar and sub-Tenon's techniques (3–5 mL).[120]

Retrobulbar anesthesia reduces retrobulbar blood flow velocity, and it is theorized that tissue pressure from the local anesthetic volume could compress the posterior ciliary arteries or disturb autoregulation by causing vasoconstriction, thereby potentially contributing to ocular ischemia.[121]

Mechanical compression reduces the IOP by decreasing vitreous volume, increasing systemic absorption of orbital extracellular fluid, and increasing aqueous humor outflow.[122] Ocular compression device use is cautioned in hypertensive eyes (baseline IOP >35 mm Hg) because induced pressures

Table 1. Physiological Factors Increasing IOP[55,60,106,107,111,112]

Action	Magnitude of IOP Increase (mm Hg)
Supine position	3–5
Prone position	8–20
Blinking	10
Trendelenburg position (25°)	13
Cough	40
Eyelid squeeze	50–90

Abbreviation: IOP, intraocular pressure.

can exceed the central retinal artery perfusion pressure.[123] Digital pressure also reduces IOP after peribulbar and sub-Tenon's blocks, but similar caveats apply.

NONOPHTHALMIC SURGERY AND POSTOPERATIVE VISUAL LOSS

Postoperative visual loss (POVL) complicates 1/60,000–125,000 anesthetics.[124,125] It is a rare but devastating occurrence for which the pathophysiology is not fully understood (Table 2). Different clinical entities have been implicated, including ischemic optic neuropathy (ION), retinal vascular occlusion, and cortical blindness.

ION refers to any damage to the optic nerve from ischemia and may be due to hypoperfusion or hypoxia.[126] It is subdivided into anterior ION and posterior ION based on the segment of the optic nerve affected with the lamina cribrosa demarcating the junction between the 2.[127] The latter is a sieve-like perforation in the posterior aspect of the sclera that allows passage of the retinal ganglion cell axons and central retinal vessels. It also preserves the pressure gradient between the intraocular and extraocular spaces. Anterior to the lamina cribrosa, the photoreceptors, retinal ganglion cells, and their axonal projections that form the optic nerve are supplied by the posterior ciliary arteries (via the choroidal circulation). These vessels are vulnerable to compression by increased IOP in a manner akin to that seen in acute-angle glaucoma.[127] Posteriorly, the optic nerve is supplied by delicate pial vessels that are not directly affected by IOP but are vulnerable to compression in the setting of optic nerve edema.[128] Swelling of the optic nerve head leads to mechanical compression of the optic nerve fibers against the lamina cribrosa. This is followed by impairment of axonal flow and of capillary perfusion, with a compartment syndrome potentially developing within the adventitial sheath enveloping the optic nerve and central retinal artery and vein.[127]

Anterior ION is associated with reduced ocular perfusion (especially in the cardiac surgery setting) from hypotension, cardiopulmonary bypass, anemia, or hyperviscosity during induced hypothermia.[126]

Posterior ION is most commonly described after prone spinal surgery or laparoscopic surgery in the Trendelenburg position, in which reduced venous drainage results in optic nerve edema.[129] Increased optic nerve diameter is observed after 5 hours in the prone position[130] and after just 30 minutes in steep Trendelenburg position during robotic laparoscopic surgery.[131] In spinal surgery, positioning the head and orbit below the heart (eg, in a Wilson's frame), prolonged surgery (>6.5 hours), excessive blood loss (>44.7% circulating blood volume), and overhydration with crystalloid are independent risk factors for POVL.[132] Accordingly, the American Society of Anesthesiologists Task Force on Perioperative Visual Loss in spinal surgery recommends positioning the head at or above the level of the heart, continuous BP monitoring, blood loss replacement with colloids as well as crystalloids and periodical hemoglobin or hematocrit assessment. Staging of lengthy procedures should be considered in high-risk patients.[132] The implementation of these recommendations into clinical practice may account, in part, for the significant reduction in reported perioperative ION after spinal fusion surgery from 1998 to 2012.[133]

Table 2. Etiology of Perioperative Visual Pathway Hypoxia

Decreased perfusion pressure
Systemic hypotension: hemorrhage, induced hypotension, cardiopulmonary bypass
Decreased ophthalmic artery pressure: carotid artery stenosis, atherosclerosis
External pressure increases: Raised intraocular pressure, pressure on the eye, venous engorgement, small optic disk
Increased vascular resistance
Atherosclerosis
Embolism
Increased blood viscosity: polycythemia, sickle cell disease, dehydration, hypothermia
Reduced oxygen carrying capacity
Severe anemia: hemorrhage, preexisting anemia

During laparoscopic surgery, the venous congestion in the Trendelenburg position increases both CVP and IOP. The latter increases in a time-dependent manner: mean IOP doubling within 60 minutes, and in 25% of cases, tripling within 120 minutes. This IOP increase may be exacerbated by the pneumoperitoneum-induced increase in $Paco_2$.[131] Blecha et al[134] found an increase in IOP and optic nerve sheath diameter after 30 minutes in steep Trendelenburg position, rising from a mean baseline IOP of 19.9 to 30.7 mm Hg ($P = .008$). Patients <63 years of age are better able to tolerate changes in ocular dynamics. CVP was not measured in the study, but elevation of venous pressure is inevitable in this position. Taketani et al[131] reported significant visual field defects in 28% of robotic-assisted laparoscopic radical prostatectomy cases in the steep Trendelenburg position. Although these defects were transient, and all had recovered within 3 months, permanent visual loss has been reported.[135] Leveling the patient at hourly intervals for 5–7 minutes significantly reduced the IOP throughout surgery, and at the end of the procedure, 75% of patients (as opposed to 11% in the control group) returned to baseline IOP.[136] Again, venous pressures were not measured directly in the study.[131,136]

Retinal vascular occlusion (ie, central or branch retinal artery occlusion) may be unilateral or bilateral. It is most often associated with external compression of the eye due to poor intraoperative positioning, but can also be caused by increased IOP occluding the vasculature or a branch occlusion by embolus or vasospasm.[135] Meticulous care during patient positioning and regular assessment of the eyes to ensure the patient has not inadvertently moved should prevent retinal vascular occlusion due to ocular compression.

Table 3. Summary of Physiological and Perioperative Factors Affecting the Intraocular Pressure (IOP)

Effect		Factors to Consider
Preexisting condition		
Does the patient have existing: ↑IOP? Compromised retinal flow?		Assess ocular ischemic risk factor profile
Physiological factors		
↑CVP = ↑↑↑IOP		Positive pressure ventilation preferable: enhanced Pao_2, $Paco_2$, and depth of anesthesia control
↓CVP = ↓↓↓IOP		
↑$Paco_2$ = ↑↑IOP		
↓$Paco_2$ = ↓↓IOP		
↑MAP = ↑IOP		
↓MAP = ↓IOP		
Anesthetic technique		
Usually (except succinylcholine)	↓IOP	Limited airway access
Laryngoscopy	↑IOP	Videolaryngoscopy
Emergence	↑IOP	Sympatholytics ± dexmedetomidate
Coughing/bucking	↑↑↑IOP	Muscle relaxant status Smooth emergence: consider sugammadex
Surgery: open/closed		
Globe aspiration	↓↓IOP	Low/normal IOP preincision in high-risk cases
Infusion pressure (determined by the bottle height or line pressure)	↑↑IOP	Keep infusion line pressure as low as compatible with surgery
Globe indentation/fluid injection	↑↑↑IOP	Consider arterial line, maintain BP and MOPP in baseline range Assess optic disk perfusion
Postoperatively		
Vomiting	↑↑IOP	Antiemetics, Sub-Tenon's block
Posturing (prone, face down)	↑IOP	Consider IOP manipulation
Hypotension	↓MOPP	Avoid hypotension Regular fundoscopy

Abbreviations: ↑, increase; ↓, decrease; CVP, central venous pressure; IOP, intraocular pressure; MAP, mean arterial pressure; MOPP, mean ocular perfusion pressure; $Paco_2$, partial pressure of carbon dioxide; Pao_2, partial pressure of oxygen.

Cortical blindness can result from occipital lobe infarction. Intraoperatively, this is typically due to profound hypotension resulting in ischemia in the watershed zones of the occipital cortex.[129] However, it can also result from cerebral hemorrhage or from air or particulate embolism. Loss of vision may be temporary or permanent, with younger patients carrying a better visual prognosis.[137]

SUMMARY

The ever-expanding complexity of ophthalmic surgery produces rapidly changing intraoperative ocular pressure dynamics even in short, seemingly straightforward procedures. These IOP changes directly affect retinal and optic disk perfusion, thereby influencing visual outcome (Table 3).

While the etiological mechanisms underlying poor visual outcome after surgery need further evaluation, those patients with preexisting retinal perfusion impairment are especially vulnerable. Even modest increases in IOP can have adverse effects, and mitigation of any such increases is possible by optimal perioperative management. The exact ischemic retinal threshold, in terms of both time and pressure, is, as yet, undetermined. POVL is a rare complication for which contributing factors are only partially understood. The rapid unpredictable pressure fluctuations in the eye and the lack of an accurate intraoperative IOP or retinal function monitor pose further challenges. Nonetheless, vigilance in controlling IOP and MOPP, thereby safeguarding OPP and optic nerve well-being, must be a central component of ophthalmic anesthesia management during and after surgery.

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