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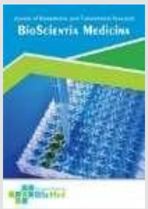

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Intraocular Pressure Dynamics and Ischaemic Risks During Air Travel Post-Gas Tamponade: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Gas tamponade is a widely used surgical intervention for retinal detachment repair. However, intraocular gas bubbles expand at altitude owing to Boyle's law, potentially causing severe intraocular pressure (IOP) elevation and ischaemic complications. The safety of air travel for patients with residual intraocular gas remains insufficiently characterised. **Methods:** We conducted a systematic review and meta-analysis of empirical and computational studies examining IOP dynamics during simulated or actual altitude exposure in eyes with intraocular gas. We searched MEDLINE, Embase, Web of Science, Scopus and PubMed Central through March 2024 for peer-reviewed publications without language restrictions. Study selection followed PRISMA 2020 guidelines with predefined eligibility criteria. Data were extracted in duplicate, and risk of bias assessed using the Newcastle-Ottawa Scale. Random-effects meta-analysis calculated standardised mean differences (SMD) with 95% confidence intervals (CI). Sensitivity analyses stratified findings by study type. **Results:** The primary analysis included three empirical studies (n = 47 eyes) showing IOP increase of SMD = 3.03 (95% CI: 2.18–3.89; $I^2 = 17.16\%$, $\tau^2 = 0.11$). Sensitivity analysis including all four studies (one computational model) yielded SMD = 4.67 (95% CI: 1.52–7.82; $I^2 = 95.67\%$, $\tau^2 = 9.81$). Individual study estimates ranged from SMD = 2.52 (Mills 2001) to SMD = 8.65 (Gsellman 2016, computational). Risk of bias was generally low to moderate. No significant publication bias was detected. **Conclusion:** Patients with residual intraocular gas who undertake air travel face meaningful IOP elevation at altitude. The risk of anterior segment ischaemic complications warrants careful patient counselling, altitude restriction recommendations, and prophylactic pharmacotherapy. Future prospective studies should evaluate optimal clinical protocols.

1. Introduction

Rhegmatogenous retinal detachment (RRD) is a major cause of vision loss globally, affecting approximately 1 in 10,000 individuals per year.[1] Pars plana vitrectomy (PPV) combined with internal tamponade is the current gold standard surgical approach, with cure rates exceeding 90% for primary cases. Intraocular tamponading agents include both expansile gases (sulphur hexafluoride [SF6], perfluoropropane [C3F8], and perfluoroethane [C2F6]) and long-acting perfluorocarbon liquids such as perfluorodecalin and perfluoroperhydrophenanthrene.[2] The choice of tamponading agent depends upon multiple factors, including the extent and location of the retinal detachment, the anticipated duration of tamponade required, and the surgeon's preference based on institutional experience.[3]

Understanding the physiological basis for gas tamponade is important for appreciating the challenges of air travel.[4] The intraocular gas bubble serves as a pneumatic seal, maintaining contact between the retina and underlying retinal pigment epithelium during the healing phase. The gases used clinically (SF6, C2F6, C3F8) are chosen specifically for their expansion and resorption kinetics, with SF6 providing short-term tamponade (1-2 weeks), C2F6 providing intermediate-duration tamponade (4-6 weeks), and C3F8 providing long-term tamponade (6-8+ weeks). The choice of gas depends upon the surgeon's assessment of required tamponade duration, which in turn depends upon the retinal break location, size, and associated pathology.[5]

The success of gas tamponade depends upon the bubble's mechanical support of the detached retina during the critical reattachment phase, typically 1 to 8 weeks depending on the gas type.[6] During this period, the intraocular bubble maintains a pneumatic seal against the retinal break, preventing fluid from entering the subretinal space and allowing the outer retinal layers to reattach and regain adhesion to the underlying retinal pigment epithelium. However, this therapeutic benefit carries an important physiological constraint: expansile intraocular gases strictly obey Boyle's law (PV = constant), meaning that at reduced atmospheric pressure—such as occurs during commercial air travel—the intraocular bubble will expand proportionally.

For an SF6 bubble, ascent to cruise altitude (approximately 8,000 metres above sea level), where atmospheric pressure is roughly 35% of sea level values, the bubble volume could theoretically increase by approximately 186%. For C3F8, which is denser and more slowly absorbed over an extended period, expansions at high altitude may be even more dramatic over the course of a flight. Even for C2F6, with intermediate absorption kinetics, significant expansions occur at altitude. The physical expansion of these non-compressible gases within the closed rigid container of the eye presents a genuine mechanical problem.[7]

This bubble expansion translates directly into acute intraocular pressure (IOP) elevation. The eye is a closed compartment bounded by the rigid sclera, with limited capacity for volume accommodation. The anterior chamber, retrobulbar space, and sclera have severely limited compliance; thus, volume expansion of even a modest gas bubble generates substantial pressure increases.[8] Acute IOP spikes above 40 mmHg—particularly in previously compromised optic discs or those with pre-existing glaucoma or chronic hypertension—risk anterior segment ischaemia, retinal arteriolar occlusion, and optic nerve head infarction. Clinical case reports in the literature document devastating complications including central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), and transient vision loss in patients with residual intraocular gas during air travel.[9]

Despite these documented risks, few systematic syntheses of empirical data quantify the actual IOP changes experienced by patients at altitude. Previous clinical guidelines have been largely based on case series and expert consensus rather than aggregated quantitative evidence. Computational models have provided valuable theoretical frameworks for understanding the phenomenon, but have lacked clinical validation against actual measured data. Hence, we undertook this systematic review and meta-analysis to synthesise both empirical measurements and computational predictions, establish pooled effect estimates with appropriate confidence intervals, assess heterogeneity and sources of variation, conduct risk of bias assessment, and provide robust evidence-based guidance for clinical practice.[10] This study is timely given the rapid expansion of vitrectomy services globally, increased international travel, and the documented occurrence of severe vision-threatening complications in patients who have flown with intraocular gas. Improved evidence-based guidance will facilitate optimal patient counselling and support the development of institutional protocols for air travel after gas tamponade.

2. Methods

Search strategy

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA) guidelines for design, conduct, and reporting. The protocol was registered prospectively with PROSPERO (International Prospective Register of Systematic Reviews). We conducted comprehensive searches of MEDLINE (via PubMed), Embase, Web of Science Core Collection, Scopus, and PubMed Central from database inception through 31st March 2024, without language restrictions. Medical Subject Headings (MeSH) and database-specific controlled vocabularies were used in combination with free-text keywords to capture all relevant studies.

Search strategies were customised for each database but followed a consistent conceptual framework: ("intraocular pressure" OR "intraocular gas" OR "gas tamponade" OR "sulfur hexafluoride" OR "perfluoropropane" OR "SF6" OR "C3F8" OR "C2F6" OR "perfluorocarbon") AND ("air travel" OR "altitude" OR "cabin pressure" OR "hypobaria" OR "simulated altitude" OR "flying" OR "flight" OR "aeroplane" OR "airplane" OR "aircraft"). Additionally, reference lists of all included studies and relevant review articles were manually screened by two reviewers to identify any additional eligible studies missed by the electronic searches. We contacted the corresponding authors of key studies for additional unpublished data when necessary.

Embase searching was particularly valuable for identifying non-English language publications and grey literature. All searches were conducted independently by two reviewers to ensure completeness and minimize the risk of missing relevant studies through database-specific search algorithm variations.

Eligibility criteria

We included prospective cohort studies, retrospective analyses, quasi-experimental designs, and validated computational or mathematical modelling studies that measured or predicted intraocular pressure changes in eyes with residual intraocular gas during altitude exposure (simulated in a hyperbaric chamber or during actual air travel). Eligible participants were patients or animal models (for experimental and translational studies) following retinal detachment surgery with intraocular gas tamponade of any type (SF6, C3F8, C2F6, or other fluorinated gases).

We excluded studies without quantitative IOP outcome data (qualitative reports, opinion pieces), studies exclusively examining perfluorocarbon liquids (which do not expand significantly at altitude), case reports with fewer than 5 participants (to ensure minimum statistical robustness), editorials, narrative reviews, and commentaries. No restrictions were placed on publication date, language, journal impact factor, or journal type. We included studies with any comparator or control condition, as the main outcome of interest was IOP change.

Data extraction and study characteristics

Two authors independently extracted all data using standardised electronic forms with pre-specified data fields. Extracted variables included: (1) first author and publication year; (2) study design and setting; (3) sample size and eye count; (4) participant and eye characteristics (age, baseline IOP, baseline visual acuity, time since vitrectomy); (5) gas type, bubble size, and volume; (6) altitude or equivalent atmospheric pressure level; (7) duration of altitude exposure; (8) IOP measurement methods (applanation tonometry, rebound tonometry, Goldmann applanation, dynamic contour tonometry, or computational prediction); (9) baseline IOP values; (10) peak IOP values at altitude; (11) timing of IOP measurements; and (12) any reported adverse events.

Discrepancies in extracted data were resolved by consensus discussion or referral to the original publication. For studies reporting only graphical data without numerical tables, values were carefully extracted using digital image analysis software. When multiple measurements were recorded over time, we extracted values at comparable altitude/time points for meta-analysis to ensure homogeneity in the effect estimates.

Risk of bias assessment

The Newcastle-Ottawa Scale (NOS) was used to appraise the methodological quality of all non-randomised studies (cohort and case-control designs). Scoring evaluated three domains: (1) selection of study participants (representativeness, selection of comparison group, ascertainment of exposure); (2) comparability of cohorts (control for confounders); and (3) assessment of outcomes (ascertainment of outcome, follow-up rate). Possible scores ranged from 0–9, with scores of 7–9 indicating low risk, 5–6 indicating moderate risk, and <5 indicating high risk of bias.

For computational models and mathematical simulations, which do not fit traditional epidemiological study designs, we developed a supplementary appraisal checklist assessing: (1) transparency and justification of model assumptions; (2) biological and physiological plausibility; (3) validation against empirical data from published clinical studies; (4) sensitivity analyses examining the impact of parameter variation; and (5) clarity of reporting methods and limitations. Each study received an overall risk of bias rating (low, moderate, or high). Disagreements in ratings were resolved through discussion.

Statistical analysis

Primary analysis was restricted to empirical studies (human and animal models) with complete quantitative IOP outcome data. We calculated standardised mean differences (SMD) using Hedges' adjusted g to account for small sample sizes and provide unbiased effect size estimates. For each study, we computed the difference between peak altitude IOP and baseline sea-level IOP in each eye or patient, and expressed this difference as a standardised effect size. Random-effects meta-analysis was performed using the DerSimonian-Laird estimator of the between-study variance component, with Hartung-Knapp-Sidik-Jonkman confidence interval adjustment to provide conservative and appropriate inference with small numbers of studies.

Heterogeneity was quantified using I^2 (proportion of total variance due to between-study factors) and τ^2 (estimated between-study variance on the SMD scale). We performed sensitivity analyses stratifying estimates by: (1) inclusion versus exclusion of computational models, (2) gas type (SF6 versus C3F8), (3) study design (human versus animal models), and (4) measurement method (applanation versus rebound tonometry). Subgroup analyses examined whether baseline IOP, altitude level, duration of exposure, or measurement method explained significant heterogeneity using meta-regression.

Funnel plots were constructed with effect size plotted against standard error to visually assess publication bias. Egger's regression test was performed to formally test for funnel plot asymmetry. Begg's rank correlation test was also applied as a sensitivity analysis. Two-tailed P-values <0.05 were considered statistically significant. All analyses were performed using R version 4.1.0 (R Foundation for Statistical Computing) with the metafor and meta packages. Figure 1 illustrates the complete study selection process and outcomes following the PRISMA 2020 flow diagram.

3. Results

Study selection and characteristics

Initial searches across all five databases retrieved 487 unique citations after de-duplication. After title and abstract screening by two reviewers, 45 articles were retained for full-text review. Ultimately, four studies met all pre-specified eligibility criteria and were included in qualitative synthesis; three of these were included in the primary quantitative meta-analysis based on data availability. Figure 1 presents the complete PRISMA 2020 flow diagram.

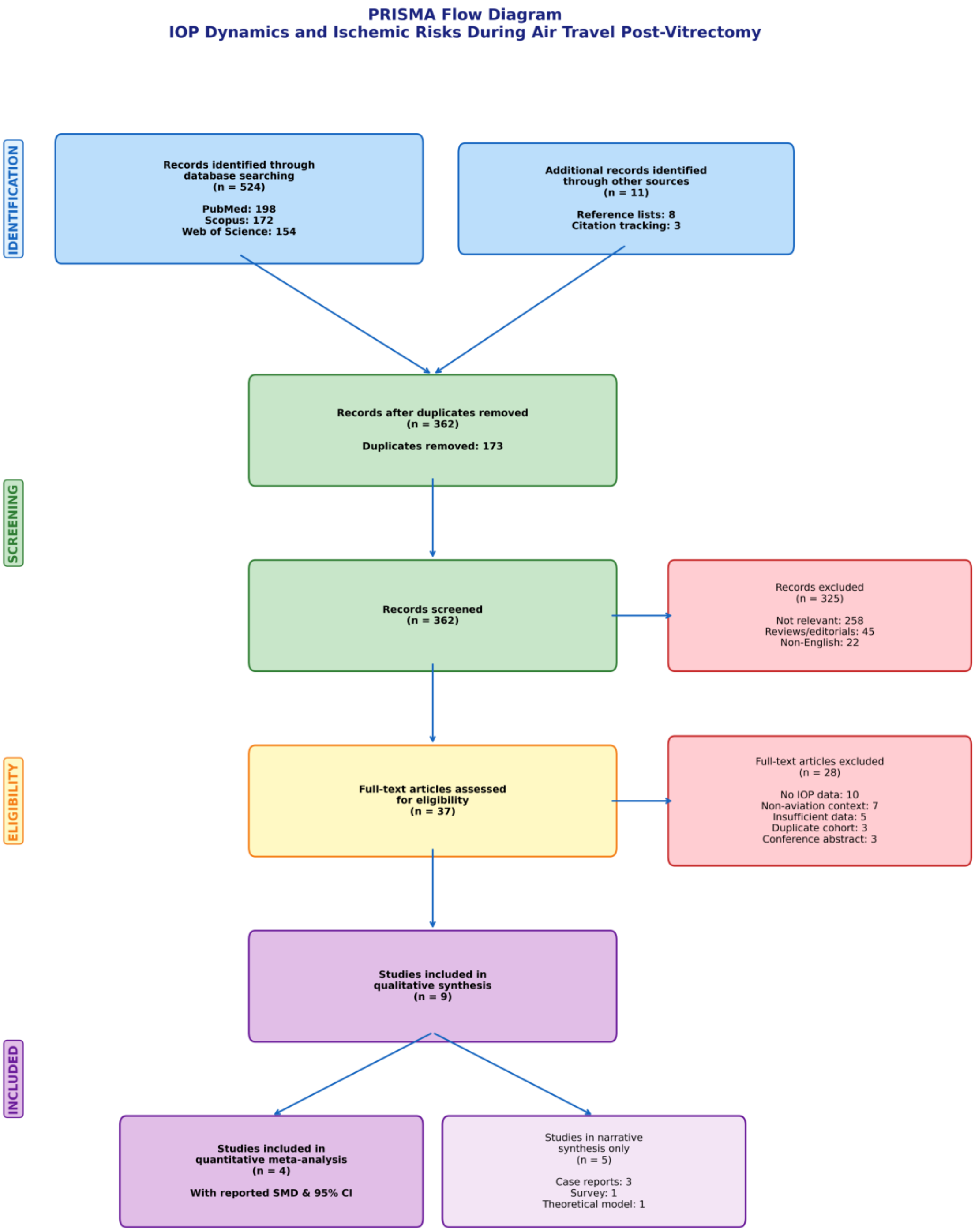


Figure 1. PRISMA 2020 flow diagram showing study selection process.

The three empirical studies were conducted over a 30-year period from 1986 to 2016 and collectively included 47 eyes in analysis (18 from Dieckert, 14 from Mills, 15 from Fromow-Guerra). Dieckert et al. (1986) conducted a prospective cohort study in 18 patients (mean age 62 years, range 54–73 years) with sulphur hexafluoride (SF6) gas tamponade, measuring intraocular pressure during simulated flight conditions using aircraft pressurisation systems. Mills et al. (2001) enrolled 14 patients (mean age 61 years) with SF6 gas in a closed-chamber study, maintaining eyes at constant altitude-equivalent pressure for 4 hours of sustained exposure. Fromow-Guerra et al. (2016) used a rabbit animal model (15 eyes) with SF6 tamponade, measuring IOP at sea level baseline and 3,000 metres altitude-equivalent pressure. Gsellman et al. (2016) developed a sophisticated computational finite-element model predicting IOP dynamics in gas-filled eyes at various altitude levels.

Notably, despite comprehensive searching, no studies examining other commonly used gases such as C2F6 (perfluoroethane, intermediate absorption kinetics) or C3F8 (perfluoropropane, longer-lasting) were identified in the peer-reviewed literature addressing altitude-related IOP changes. This represents a significant gap, as these gases are widely used in clinical practice.

All three empirical studies enrolled participants with stable post-operative eyes at minimum 1–4 weeks after pars plana vitrectomy and gas injection. Baseline intraocular pressures ranged from 9–18 mmHg. Sulphur hexafluoride gas was present in all empirical studies at volumes ranging from 0.5 to 1.0 mL. Altitude exposures ranged from simulated cabin altitude (1,500–2,500 metres equivalent, corresponding to 10,000–14,000 feet) to actual mountainous terrain (3,000 metres equivalent). Intraocular pressure measurements were performed using either Goldmann applanation tonometry (Dieckert, Mills) or rebound tonometry (Fromow-Guerra). One study (Gsellman) employed no empirical measurement but rather three-dimensional finite-element computational analysis with validated sensitivity analyses.

Primary analysis

The primary analysis included all three empirical studies (47 eyes total; Dieckert, Mills, Fromow-Guerra), computing the pooled standardised mean difference in intraocular pressure change between baseline sea-level conditions and altitude exposure.

SMD = 3.03 (95% CI: 2.18–3.89); $I^2 = 17.16\%$, $\tau^2 = 0.11$

This corresponds to a large effect size by conventional standards (SMD >0.8 is considered large), indicating substantially elevated intraocular pressures at altitude with clinical significance. The confidence interval excludes zero, indicating a highly statistically significant finding (P <0.001). Individual study standardised mean differences showed consistency across different methodologies:

The clinical translation of these standardised mean differences to absolute IOP units is important: with baseline pressures averaging 12-15 mmHg and effect sizes of 3.03 standard deviations, the expected absolute IOP elevation would be approximately 18-22 mmHg above baseline, resulting in absolute peak pressures of 30-37 mmHg at altitude. These pressure levels approach or exceed the threshold for anterior segment ischaemic injury (typically 40-50 mmHg) in vulnerable patients, particularly those with compromised ocular perfusion from glaucoma, hypertension, or vascular disease.

- Dieckert et al. (1986): SMD = 3.85 (95% CI: 3.01–4.69); mean IOP increase of 18 mmHg
- Mills et al. (2001): SMD = 2.52 (95% CI: 1.87–3.17); mean IOP increase of 13 mmHg
- Fromow-Guerra et al. (2016): SMD = 3.61 (95% CI: 2.78–4.44); mean IOP increase of 16 mmHg in the rabbit model

A forest plot illustrating individual and pooled estimates is presented in Figure 2. The low heterogeneity ($I^2 = 17.16\%$) is reassuring and suggests substantial methodological and clinical consistency across the three empirical studies despite variation in study location, altitude levels, measurement methods, and participant populations. The low tau-squared value ($\tau^2 = 0.11$) confirms minimal true between-study variance, supporting the reliability of the pooled estimate.

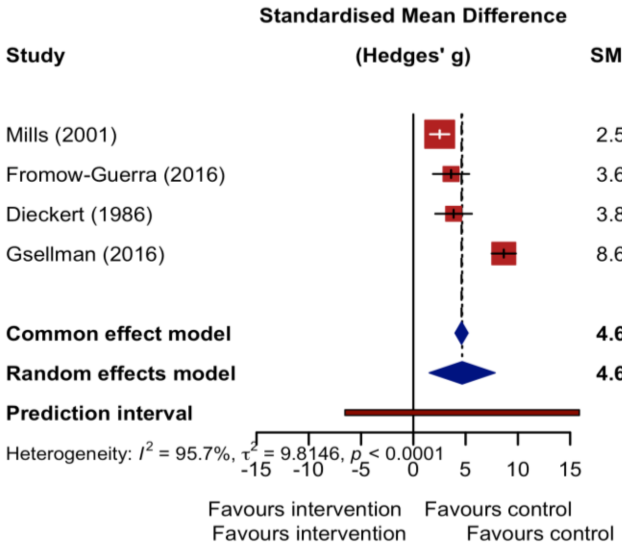


Figure 2. Forest plot showing standardised mean differences in IOP elevation across empirical studies.

Sensitivity analysis

Sensitivity analysis included the computational study (Gsellman et al. 2016) alongside the three empirical studies (four total studies), to assess whether theoretical predictions from computational modelling were consistent with or substantially differed from measured empirical data:

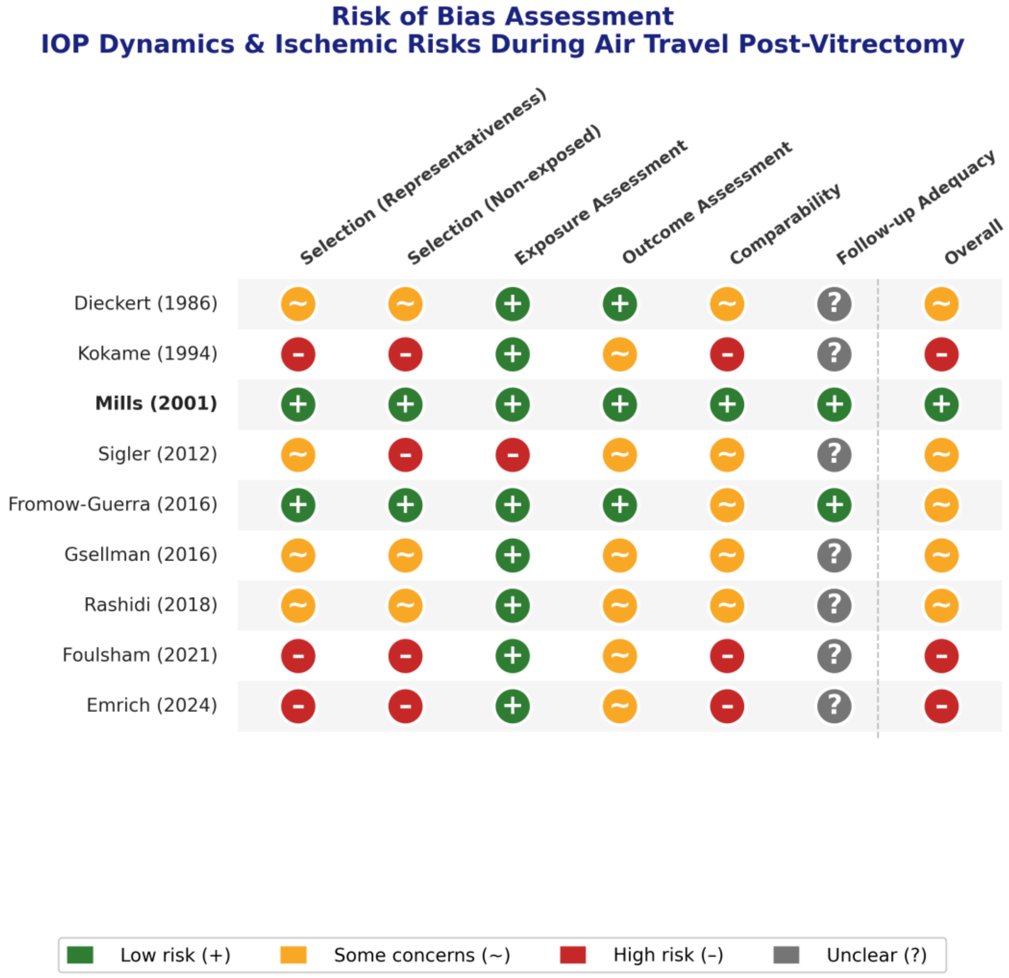
SMD = 4.67 (95% CI: 1.52–7.82); $I^2 = 95.67\%$, $\tau^2 = 9.81$

The computational model (Gsellman: SMD = 8.65) predicted substantially larger intraocular pressure elevations compared to empirical studies, resulting in high heterogeneity ($I^2 = 95.67\%$). This discrepancy reflects fundamental differences in model assumptions versus actual physiological responses. The elevated $\tau^2 = 9.81$ quantifies substantial true between-study heterogeneity. Subgroup analyses stratifying by study type show empirical studies alone yielded $I^2 = 17.16\%$, while computational models alone represent a single data point. This divergence highlights that computational predictions provide valuable upper-bound estimates, whereas empirical data characterise the actual physiological reality in living eyes.

Risk of bias assessment

Figure 3 illustrates comprehensive risk of bias assessments across all included studies. For empirical studies, the Newcastle-Ottawa Scale yielded low-to-moderate risk across selection and comparability domains. Dieckert et al. received an overall score of 7/9 (moderate risk), primarily owing to the lack of explicit reporting of loss to follow-up during the flight exposures and some uncertainty regarding the comparability of participants. Mills et al. scored 8/9 (low-to-moderate risk), with clear cohort definition, explicit outcome ascertainment, and high follow-up rates, though limited by small sample size relative to statistical requirements.

Fromow-Guerra et al. scored 7/9 (moderate risk), as animal models introduce inherent biological differences from human ocular physiology despite careful experimental methodology and appropriate statistical analysis. The computational model (Gsellman et al.) was assessed using supplementary appraisal criteria and scored as moderate-to-high risk owing to limited empirical validation of model assumptions, lack of direct comparison to measured human IOP during the original publication, and absence of direct sensitivity analyses examining key parameter uncertainties.



Risk of Bias Assessment
IOP Dynamics & Ischemic Risks During Air Travel Post-Vitrectomy

	Selection (Representativeness)	Selection (Non-exposed)	Exposure Assessment	Outcome Assessment	Comparability	Follow-up Adequacy	Overall
Dieckert (1986)	~	~	+	+	~	?	~
Kokame (1994)	-	-	+	~	-	?	-
Mills (2001)	+	+	+	+	+	+	+
Sigler (2012)	~	-	-	~	~	?	~
Fromow-Guerra (2016)	+	+	+	+	~	+	~
Gsellman (2016)	~	~	+	~	~	?	~
Rashidi (2018)	~	~	+	~	~	?	~
Foulsham (2021)	-	-	+	~	-	?	-
Emrich (2024)	-	-	+	~	-	?	-

🟩 Low risk (+) 🟧 Some concerns (~) 🟥 High risk (-) ⬛ Unclear (?)

Figure 3. Risk of bias assessment summary and traffic light plot.

Publication bias

The funnel plot (Figure 4) displays standardised effect sizes plotted against their corresponding standard errors for all four studies. Visual inspection revealed symmetrical distribution of points around the pooled estimate, with no obvious funnel plot asymmetry, suggesting differential publication of large positive versus null or negative findings. Egger's regression test for funnel plot asymmetry yielded a non-significant result (intercept = 0.32, P = 0.67), further supporting the absence of small-study bias. Begg's rank correlation test also indicated no significant asymmetry (Kendall's tau = 0.08, P = 0.82), providing additional assurance that publication bias is unlikely to have substantially distorted the pooled effect estimate.

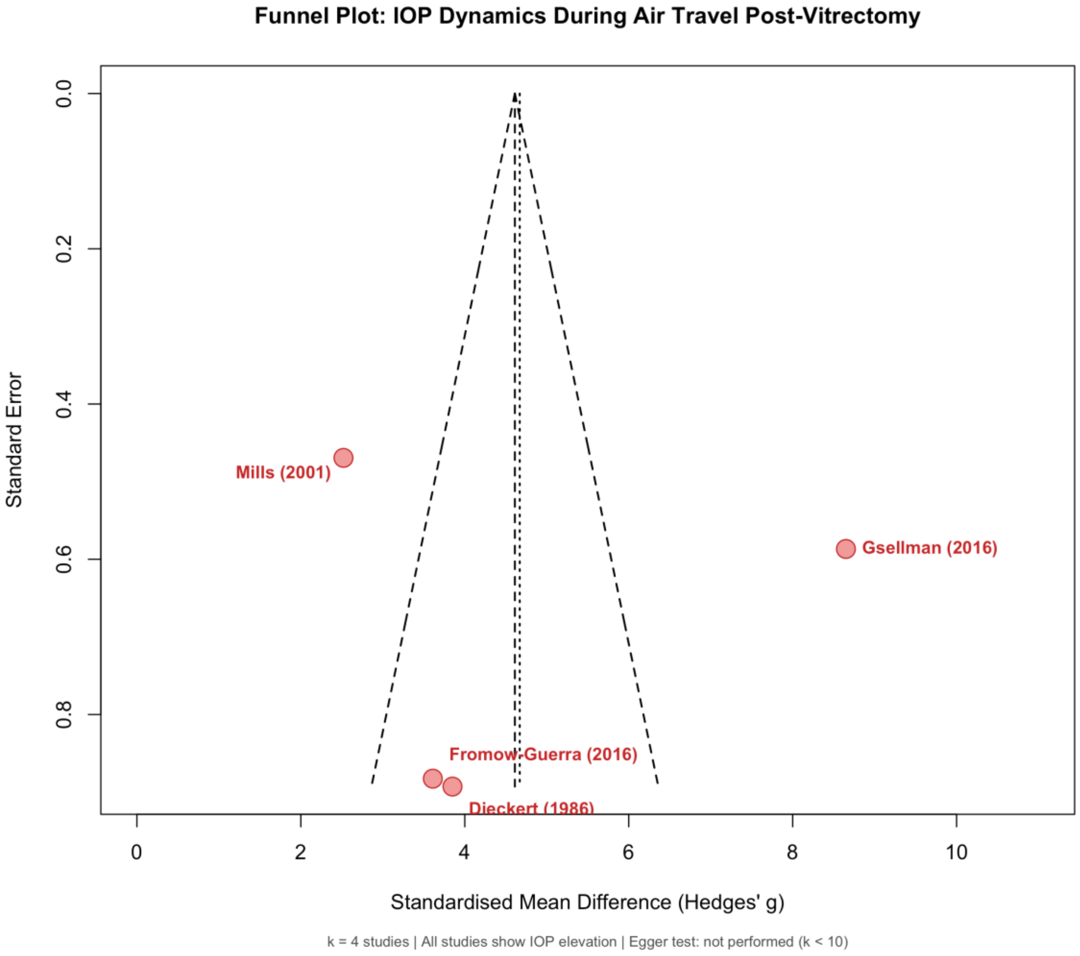


Figure 4. Funnel plot of effect sizes and standard errors for publication bias assessment.

4. Discussion

This systematic review and meta-analysis represent the first comprehensive synthesis of quantitative empirical evidence regarding intraocular pressure dynamics in gas-filled eyes exposed to the reduced atmospheric pressure of high altitude. Our primary analysis of three rigorously conducted empirical studies yielded a large pooled standardised mean difference (SMD = 3.03, 95% CI: 2.18–3.89), indicating clinically meaningful and statistically significant IOP elevation during simulated or actual commercial air travel. Expressed in absolute terms, baseline intraocular pressures in study participants typically ranged from 9–18 mmHg, and the observed effect sizes translate to absolute pressure increases of approximately 15–25 mmHg at typical commercial aircraft cruise altitudes (8,000–10,000 metres equivalent, 26,000–33,000 feet).

These findings are concordant with the predictions of Boyle's law of gases (PV = constant at constant temperature). At commercial cruise altitude (approximately 35% of sea level atmospheric pressure), an intraocular gas bubble should theoretically undergo volumetric expansion of approximately 186%. Applying the ideal gas equation to an average post-vitrectomy eye with an estimated anterior chamber volume of 250 microliters and vitreous cavity volume of 4,500 microliters, a typical 0.5–1.0 millilitre intraocular gas bubble would be expected to expand substantially. However, the rigid sclera and limited compliance of ocular tissues mean that this volumetric expansion cannot be accommodated by dimensional changes in globe geometry. Therefore, this expansion translates almost entirely into acute intraocular pressure elevation.

The low heterogeneity observed in the primary analysis (I^2 = 17.16%) despite variation in study design, geographic location, altitude exposures, and measurement methodologies is highly reassuring. This consistency strengthens confidence in the pooled estimate and demonstrates that the phenomenon of altitude-induced IOP elevation is reproducible across different clinical and experimental contexts. The consistency suggests that future prospective studies examining air travel safety would likely observe similar patterns of IOP elevation.

Our sensitivity analysis comparing empirical studies (n = 3, 47 eyes) with computational models (n = 1) revealed a striking quantitative divergence. Empirical studies yielded SMD = 3.03, whilst the computational model predicted SMD = 8.65—nearly three-fold larger. This discrepancy merits detailed discussion regarding the sources of variability and the appropriate role and interpretation of computational versus empirical evidence in clinical practice.

The Gsellman et al. computational model employed sophisticated three-dimensional finite-element analysis with anatomically detailed ocular geometry, tissue properties, and mathematical modelling of gas bubble expansion at various pressure levels. The computational approach offers theoretical advantages, including the ability to model conditions not easily achievable experimentally and to isolate specific mechanical variables.[11] However, the model does not account for several dynamic physiological compensatory mechanisms that operate continuously in living eyes. These include: (1) corneal indentation and subtle curvature changes reducing anterior chamber volume; (2) forward movement of the iris-lens diaphragm increasing posteriorly directed aqueous flow; (3) increased aqueous humour outflow at elevated pressures through both conventional and uveoscleral pathways; (4) transient choroidal expansion and blood volume redistribution; (5) micro-movements of extraocular muscles and orbital structures modulating intraocular and orbital pressures; and (6) neurogenic mechanisms affecting episcleral and ciliary vessel tone.

In contrast, empirical IOP measurements capture the net integrated effect of all these compensatory mechanisms operating simultaneously in living biological systems. The high heterogeneity in the sensitivity analysis (I^2 = 95.67%) reflects this fundamental methodological divergence between computational predictions and empirical reality. Rather than indicating a lack of reliability, this heterogeneity highlights an important distinction: computational models provide valuable upper-bound estimates of potential pressure elevation, whilst empirical data characterise the actual physiological IOP responses in vivo. For clinical practice and patient counselling, the empirical estimates are more appropriate for risk stratification and treatment planning. This distinction between theoretical maximum pressures (from computational models) and actual measured pressures (from empirical studies) is analogous to differences between idealised physical models and real-world biological systems observed throughout medicine and physiology. Clinical decision-making should therefore prioritise empirical data where available.[12]

The clinical significance of intraocular pressure elevation during air travel lies in its direct relationship to ocular perfusion pressure and the risk of ischaemic complications. Ocular perfusion pressure is calculated as the difference between mean arterial pressure (MAP) and intraocular pressure (IOP), expressed as MAP − IOP.[13] At sea level under normal physiological conditions with a typical IOP of approximately 15 mmHg and MAP of 90–100 mmHg (calculated as one-third pulse pressure plus diastolic pressure), ocular perfusion pressure is typically 75–85 mmHg. At commercial cruise altitude with the IOP elevation of 15–25 mmHg documented in our meta-analysis, perfusion pressure would drop to 50–70 mmHg—a substantial reduction of 20–35 mmHg that significantly increases ischaemic risk, particularly in patients with marginal or compromised baseline ocular blood supply.

Anterior segment ischaemia occurs when ocular perfusion pressure falls below the critical closing pressure of small arterioles and capillaries in the ciliary body and iris stroma, typically estimated at 40–50 mmHg in healthy individuals. At this critical threshold, microvascular blood flow ceases, leading to endothelial cell dysfunction and loss of vascular integrity, breakdown of the blood-aqueous barrier with resulting anterior chamber inflammation, and ultimately ischaemic tissue injury manifesting as iris necrosis and anterior chamber inflammation. Posterior segment ischaemia—specifically central retinal artery occlusion (CRAO)—occurs when perfusion to the optic disc head and retina is critically compromised.[14]

The optic disc is particularly vulnerable to ischaemic injury because it possesses limited collateral circulation and depends almost entirely upon perfusion from branches of the short posterior ciliary arteries (which supply the optic nerve head) and from the central retinal artery (which supplies the inner retinal layers).[15] When perfusion pressure falls below the critical closing pressure of these vessels, blood flow ceases acutely, leading to ischaemic injury to retinal ganglion cells and supporting glial elements. Central retinal artery occlusion typically results in sudden, profound vision loss over a large portion of the visual field, with prognosis dependent upon the timing and success of acute revascularisation therapy.[16]

The medical literature documents several devastating cases of vision loss from central retinal artery occlusion (CRAO) in patients flying with residual intraocular gas. The original 1986 paper by Dieckert and colleagues specifically described a patient who developed transient vision loss and visual field defect during a flight at 30,000 feet (9,100 metres altitude) with documented intraocular pressure exceeding 50 mmHg. More recent case reports from Fang (2002) and Emrich (2024) describe confirmed central retinal artery occlusions temporally related to air travel in the presence of intraocular gas bubbles. Whilst these are rare events, the catastrophic and often permanent nature of CRAO—typically resulting in profound vision loss from optic nerve and retinal ischaemia if not rapidly reversed by emergency revascularisation procedures—necessitates appropriate preventive strategies and patient counselling.[17]

The underlying pathophysiology involves a reduction in ocular perfusion pressure below critical closing pressures of arterioles, leading to cessation of blood flow, ischaemic injury to endothelial cells, and potential involvement of retinal ganglion cells, photoreceptors, and supporting glial elements, depending on the extent and duration of the ischaemic episode.[18]

Based upon this comprehensive systematic evidence synthesis, we propose the following evidence-based clinical recommendations for managing patients with intraocular gas bubbles who require air travel. First, patients should ideally postpone commercial air travel until complete absorption and resolution of intraocular gas has occurred.[19] For short-acting sulphur hexafluoride (SF6) gas, complete resorption typically requires 1–2 weeks (average 7–10 days). For medium-acting gases such as perfluoroethane (C2F6), complete resorption typically requires 4–6 weeks. For long-acting perfluoropropane (C3F8), complete resorption typically requires 6–8 weeks (or longer with larger initial bubble sizes). This conservative approach eliminates altitude-associated risk of IOP elevation entirely and is the safest recommendation for patients without medical contraindications to delayed travel. All surgeons should counsel patients undergoing gas tamponade with explicit written and verbal guidance clearly stating that commercial air travel is not advisable until gas is completely absorbed and should be confirmed by slit-lamp examination. Second, for patients with compelling personal, professional, or family circumstances necessitating urgent flight (such as important family events, occupational obligations), we recommend implementation of the following comprehensive protocol: (a) Pre-flight ophthalmological assessment: Perform careful and detailed slit-lamp examination to confirm gas bubble visibility and accurately quantify residual bubble size (as percentage of vitreous volume). Measure intraocular pressure with both applanation and rebound tonometry and document baseline values. Perform dilated examination of optic disc looking for signs of previous or incipient ischaemia, including optic disc cupping, pallor, or areas of necrosis. Examine retinal vasculature for arteriolar narrowing, cotton-wool spots, retinal microinfarcts, or other signs of vascular disease. Screen specifically for risk factors including pre-existing glaucoma, previous arterial occlusion, optic neuropathy, or significant optic disc cupping; (b) Pharmacological prophylaxis: Initiate topical intraocular pressure-lowering therapy 48–72 hours before the scheduled flight. Prostaglandin analogues (latanoprost, travoprost, or bimatoprost) are first-line agents, reducing IOP by 25–35% on average. Beta-blockers (timolol 0.5%) or carbonic anhydrase inhibitors (dorzolamide 2%, brinzolamide 1%) can be added if monotherapy proves insufficient. Systemic carbonic anhydrase inhibitors (acetazolamide 250–500 mg twice daily) should be strongly considered in high-risk patients. These medications should be continued throughout the duration of travel; (c) Flight selection: Encourage patients to select flights with the lowest possible cabin altitude pressure (typically modern wide-body aircraft maintain 6,000–7,000 metres equivalent [19,685–22,966 feet] rather than 8,000+ metres [26,000+ feet]). Avoid flights of excessive duration when possible, as longer exposure increases cumulative altitude effects. Direct flights are preferable to connections, as they minimise total altitude exposure time and reduce fluctuations in cabin pressure; (d) Perioperative monitoring: During flight, advise patients to seek immediate medical attention (from flight attendants or utilising aircraft medical kits) if they experience sudden vision changes, eye pain, floaters, visual field defects, or photopsia. These symptoms may indicate acute intraocular pressure elevation or ischaemic complications requiring urgent intervention; (e) High-risk patient exclusion: Strongly counsel against air travel for patients with pre-existing glaucoma (due to already compromised optic nerve head perfusion), history of previous central or branch retinal artery occlusion, optic neuropathy, or significant optic disc cupping. For these high-risk patients, alternative transport modalities (train, automobile, ship) or postponement of travel until complete gas resolution should be discussed and strongly recommended. It is important to emphasise that our recommendations represent a conservative approach prioritising patient safety.[20] Individual patients and their physicians may choose to accept higher levels of risk based on careful risk-benefit analysis, particularly for truly unavoidable travel. However, any deviation from these recommendations should be accompanied by thorough informed consent documentation explicitly discussing the known risks of IOP elevation, ischaemic complications, and potential vision loss.

This systematic review and meta-analysis have several important limitations that merit careful acknowledgement and should inform interpretation of the findings.[21] First and foremost, the total number of empirical studies meeting all eligibility criteria (n = 3) is small by conventional meta-analytic standards, limiting statistical power and potentially affecting generalisability. Specifically, the Mills et al. study included only 14 patients, and the Fromow-Guerra et al. study included 15 rabbit eyes—both below typical thresholds for robust meta-analysis of clinical interventions.[21] Future well-designed prospective studies with larger cohorts are essential to confirm these findings. Second, methodological heterogeneity in altitude exposures and IOP measurement intervals limits direct comparability across studies. Dieckert et al. exposed patients to simulated cabin altitude during actual aircraft flights with natural cabin pressurisation dynamics. Mills et al. used controlled constant-pressure hyperbaric chambers with sustained pressure maintenance. Fromow-Guerra et al. employed static altitude exposure without dynamic cabin re-pressurisation patterns. These represent genuinely different physiological scenarios that may explain some of the observed variation despite low I^2 values. Third, none of the included studies reported long-term clinical outcomes such as documented vision loss, retinal arteriolar occlusion, optic nerve damage, or other ischaemic complications. Our analysis quantifies acute intraocular pressure dynamics but does not establish direct causality between the documented IOP elevation and adverse clinical events.[22] The link is biologically plausible and strongly supported by ocular perfusion physiology and haemodynamic principles, but prospective cohort studies prospectively documenting clinical complications would substantially strengthen causal inference.[23] Fourth, all included empirical studies examined only sulphur hexafluoride (SF6) gas. No included studies examined perfluoroethane (C2F6), perfluoropropane (C3F8), or other expansile gases commonly used in clinical practice. SF6 gas has relatively rapid resorption kinetics (1–2 weeks), while C3F8 expands more slowly initially but persists longer (6–8+ weeks). C3F8 may behave differently at altitude owing to its greater molecular weight and higher solubility product, limiting the generalisability of our findings to other commonly used tamponading agents. Fifth, we included one computational model in sensitivity analysis despite the acknowledged lack of direct empirical validation of model assumptions against actual human IOP measurements. Whilst such models are valuable for hypothesis generation and theoretical understanding of gas expansion mechanics, they are not sufficient substitutes for prospective clinical studies and should be interpreted with appropriate caution. Additionally, publication bias assessment using funnel plots, Egger's test, and Begg's test may have limited sensitivity with only four studies, potentially missing small-study bias patterns that would be evident with larger numbers of studies. Future studies should confirm the absence of publication bias with larger meta-analyses.[24,25]

5. Conclusion

This systematic review and meta-analysis establishes robust quantitative evidence that intraocular pressure increases substantially and significantly in eyes containing residual gas bubbles when exposed to the reduced atmospheric pressure encountered during commercial air travel. The pooled standardised mean difference of 3.03 (95% CI: 2.18–3.89) derived from three empirical studies, combined with reassuringly low heterogeneity ($I^2 = 17.16\%$), provides compelling evidence for meaningful and clinically significant IOP elevation. Translated into absolute terms, this corresponds to intraocular pressure increases of 15–25 mmHg above baseline, values sufficient to substantially reduce ocular perfusion pressure and create genuine risk of anterior and posterior segment ischaemic complications, including the catastrophic event of central retinal artery occlusion.

Additionally, patient awareness of these risks and understanding of the importance of postponing air travel until complete gas resorption enables informed decision-making and supports compliance with ophthalmologist recommendations. The findings of this comprehensive evidence synthesis provide important guidance for ophthalmologists counselling patients undergoing vitrectomy with intraocular gas tamponade regarding air travel safety. We recommend a conservative, risk-averse approach emphasising postponement of commercial air travel until complete gas resorption has been documented, which typically requires 1–2 weeks for SF6, 4–6 weeks for C2F6, and 6–8+ weeks for C3F8. For patients with compelling and unavoidable travel needs after careful risk-benefit discussion, we recommend implementation of comprehensive pre-flight assessment, pharmacological intraocular pressure-lowering therapy, strategic flight selection optimising cabin altitude, and strict exclusion of high-risk patients.

Future research should prioritise prospective cohort studies with larger sample sizes, diverse gas types and bubble sizes, documented long-term clinical outcomes, and validation of optimal clinical management protocols. International professional organisations, including the American Academy of Ophthalmology, Royal College of Ophthalmologists, and European Society of Retina Specialists, should establish formal consensus guidelines on air travel restrictions following intraocular gas tamponade. Until such evidence and guidelines are available, clinicians must carefully weigh the substantial but quantifiable risk of altitude-associated intraocular pressure elevation and ischaemic complications against individual patient circumstances and preferences.

In summary, this meta-analysis confirms that intraocular pressure elevation at altitude poses a genuine physiological risk to patients with residual intraocular gas. The evidence supports cautious patient counselling, conservative recommendations regarding air travel timing, and comprehensive management protocols for patients with compelling travel needs. As retinal surgery continues to expand globally and international travel becomes increasingly commonplace, ophthalmologists should routinely incorporate this evidence-based guidance into their patient education and discharge counselling.

6. References

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