LUMEN ET VIRTUS
ISSN: 2177-2789

OCULOCARDIAC REFLEX IN OPHTHALMIC AND NON-OPHTHALMIC SURGERY: EPIDEMIOLOGY, MECHANISMS, PREVENTION AND MANAGEMENT

REFLEXO OCULOCARDÍACO EM CIRURGIAS OFTÁLMICAS E NÃO OFTÁLMICAS: EPIDEMIOLOGIA, MECANISMOS, PREVENÇÃO E MANEJO

REFLEJO OCULOCARDÍACO EN CIRUGÍA OFTÁLMICA Y NO OFTÁLMICA: EPIDEMIOLOGÍA, MECANISMOS, PREVENCIÓN Y MANEJO

https://doi.org/10.56238/levv16n55-018

Submitted on: 11/04/2025 **Publication date:** 12/04/2025

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ABSTRACT

Introduction: The oculocardiac reflex is a trigeminovagal response that may occur during ophthalmic and non-ophthalmic procedures involving manipulation of orbital structures, leading to bradycardia, arrhythmias, or hemodynamic instability. Its clinical relevance spans pediatric and adult surgery, requiring coordinated preventive and therapeutic strategies.

Objective: The objective of this systematic review was to assess the epidemiology, mechanisms, preventive strategies, and management approaches for the oculocardiac reflex in ophthalmic and non-ophthalmic surgeries. Secondary objectives included evaluating risk factors, comparing anesthetic techniques, analyzing clinical outcomes, identifying gaps in the literature, and proposing implications for clinical practice.

Methods: A systematic search was conducted across PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and ICTRP. Eligible studies included human or animal research published in the last five years, with extension to ten years only if fewer than ten eligible studies were found. Inclusion criteria encompassed observational studies, randomized trials, and experimental investigations addressing the reflex in surgical settings. Data extraction and study selection followed PRISMA guidelines, with independent reviewers assessing risk of bias using RoB 2, ROBINS-I, and QUADAS-2. Certainty of evidence was graded using GRADE.

Results and Discussion: A total of 18 studies met the eligibility criteria and were included in the final analysis. These studies collectively demonstrated that the incidence of the reflex

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varies widely by procedure type, age group, anesthetic depth, and surgical technique. Evidence supported multifactorial prevention involving adequate anesthesia, optimized ventilation, and selective use of anticholinergics. Management algorithms consistently emphasized immediate cessation of the triggering stimulus and pharmacologic intervention when necessary. Despite heterogeneity across studies, the overall certainty of evidence ranged from low to moderate.

Conclusion: Current evidence reinforces that the oculocardiac reflex remains a clinically significant phenomenon requiring proactive prevention and rapid intraoperative recognition. Standardized perioperative protocols and improved methodological quality in future studies may enhance safety and guide individualized risk-based management strategies.

Keywords: Oculocardiac Reflex. Anesthesia. Ophthalmologic Surgical Procedures. Cardiac Arrhythmias.

RESUMO

Introdução: O reflexo oculocardiaco é uma resposta trigeminovagal que pode ocorrer durante procedimentos oftálmicos e não oftálmicos que envolvam manipulação de estruturas orbitárias, levando à bradicardia, arritmias ou instabilidade hemodinâmica. Sua relevância clínica abrange cirurgias pediátricas e adultas, exigindo estratégias preventivas e terapêuticas coordenadas.

Objetivo: O objetivo desta revisão sistemática foi avaliar a epidemiologia, os mecanismos, as estratégias de prevenção e as abordagens de manejo do reflexo oculocardiaco em cirurgias oftálmicas e não oftálmicas. Os objetivos secundários incluíram avaliar fatores de risco, comparar técnicas anestésicas, analisar desfechos clínicos, identificar lacunas na literatura e propor implicações para a prática clínica.

Métodos: Foi realizada uma busca sistemática nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e ICTRP. Estudos elegíveis incluíram pesquisas em humanos ou animais publicadas nos últimos cinco anos, com extensão para dez anos apenas se menos de dez estudos elegíveis fossem encontrados. Os critérios de inclusão abrangeram estudos observacionais, ensaios randomizados e investigações experimentais que abordassem o reflexo em contextos cirúrgicos. A extração de dados e a seleção dos estudos seguiram as diretrizes PRISMA, com avaliadores independentes examinando o risco de viés por meio dos instrumentos RoB 2, ROBINS-I e QUADAS-2. A certeza da evidência foi classificada utilizando o GRADE.

Resultados e Discussão: Um total de 18 estudos atendeu aos critérios de elegibilidade e foi incluído na análise final. Esses estudos demonstraram coletivamente que a incidência do reflexo varia amplamente de acordo com o tipo de procedimento, faixa etária, profundidade anestésica e técnica cirúrgica. A evidência apoiou a prevenção multifatorial envolvendo anestesia adequada, ventilação otimizada e uso seletivo de anticolinérgicos. Os algoritmos de manejo enfatizaram de forma consistente a interrupção imediata do estímulo desencadeante e a intervenção farmacológica quando necessária. Apesar da heterogeneidade entre os estudos, a certeza geral da evidência variou de baixa a moderada.

Conclusão: As evidências atuais reforçam que o reflexo oculocardiaco permanece um fenômeno clinicamente significativo, exigindo prevenção proativa e reconhecimento intraoperatório rápido. Protocolos perioperatórios padronizados e melhor qualidade metodológica em estudos futuros podem aprimorar a segurança e orientar estratégias individualizadas de manejo baseadas no risco.

Palavras-chave: Reflexo Oculocardiaco. Anestesia. Procedimentos Cirúrgicos Oftalmológicos. Arritmias Cardíacas.

RESUMEN

Introducción: El reflejo oculocardíaco es una respuesta trigeminovagal que puede ocurrir durante procedimientos oftálmicos y no oftálmicos que implican manipulación de estructuras orbitarias, lo que puede provocar bradicardia, arritmias o inestabilidad hemodinámica. Su relevancia clínica abarca cirugías pediátricas y de adultos, lo que requiere estrategias preventivas y terapéuticas coordinadas.

Objetivo: El objetivo de esta revisión sistemática fue evaluar la epidemiología, los mecanismos, las estrategias de prevención y los enfoques de manejo del reflejo oculocardíaco en cirugías oftálmicas y no oftálmicas. Los objetivos secundarios incluyeron evaluar factores de riesgo, comparar técnicas anestésicas, analizar desenlaces clínicos, identificar vacíos en la literatura y proponer implicaciones para la práctica clínica.

Métodos: Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y ICTRP. Los estudios elegibles incluyeron investigaciones en humanos o animales publicadas en los últimos cinco años, ampliándose a diez años solo si se encontraban menos de diez estudios elegibles. Los criterios de inclusión comprendieron estudios observacionales, ensayos aleatorizados e investigaciones experimentales que abordaran el reflejo en contextos quirúrgicos. La extracción de datos y la selección de estudios siguieron las directrices PRISMA, con revisores independientes evaluando el riesgo de sesgo mediante RoB 2, ROBINS-I y QUADAS-2. La certeza de la evidencia se calificó utilizando GRADE.

Resultados y Discusión: Un total de 18 estudios cumplió los criterios de elegibilidad y se incluyó en el análisis final. Estos estudios demostraron colectivamente que la incidencia del reflejo varía ampliamente según el tipo de procedimiento, el grupo etario, la profundidad anestésica y la técnica quirúrgica. La evidencia respaldó una prevención multifactorial que incluye anestesia adecuada, ventilación optimizada y uso selectivo de anticolinérgicos. Los algoritmos de manejo destacaron de manera consistente la interrupción inmediata del estímulo desencadenante y la intervención farmacológica cuando fuese necesaria. A pesar de la heterogeneidad entre los estudios, la certeza general de la evidencia osciló entre baja y moderada.

Conclusión: La evidencia actual refuerza que el reflejo oculocardiaco sigue siendo un fenómeno clínicamente significativo que requiere prevención proactiva y reconocimiento intraoperatorio rápido. Protocolos perioperatorios estandarizados y una mejor calidad metodológica en estudios futuros pueden mejorar la seguridad y orientar estrategias individualizadas de manejo basadas en riesgos.

Palabras clave: Reflejo Oculocardiaco. Anestesia. Procedimientos Quirúrgicos Oftálmicos. Arritmias Cardíacas.

1 INTRODUCTION

The oculocardiac reflex is a trigeminovagal response triggered by traction or pressure on ocular or periocular structures, presenting a significant risk during a variety of ophthalmic and non-ophthalmic procedures[1]. This reflex may manifest as bradycardia, arrhythmias, or even transient asystole, making its recognition essential for anesthesiologists and surgeons[1]. Its occurrence is classically associated with pediatric strabismus surgery, but its presence in adult procedures has gained increasing attention in recent years[1]. The variability in its presentation reflects the influence of surgical technique, anesthetic depth, and patient-specific autonomic characteristics[2]. Understanding these diverse contributors is essential to improving perioperative safety in populations at risk[2].

The epidemiology of the oculocardiac reflex demonstrates substantial heterogeneity across surgical categories, with incidences reported as high in pediatric muscle surgery and lower yet clinically relevant in adult orbital or eyelid procedures[2]. This variability is further influenced by physiological factors such as baseline vagal tone, respiratory status, and the use of medications that alter cardiac conduction[2]. Studies consistently highlight that the reflex is more prevalent in children, due to enhanced autonomic responsiveness, but adults are by no means exempt[3]. Reports of reflex activation during orbital decompression, glaucoma surgery, vitreoretinal manipulation, and maxillofacial procedures underscore its wide relevance[3]. Such diversity highlights the need for a unified framework for risk stratification across surgical disciplines[3].

The underlying mechanism involves afferent impulses from the ophthalmic branch of the trigeminal nerve and efferent output through the vagus nerve[3]. This neural arc results in immediate parasympathetic activation that suppresses sinoatrial node activity, potentially leading to abrupt hemodynamic compromise[4]. The magnitude of the reflex is shaped by anesthetic agents, autonomic modulation, and the intensity or duration of muscular traction[4]. Variations in surgical handling, including the pace and direction of extraocular muscle manipulation, have been shown to modulate reflex intensity[4]. These features make interdisciplinary knowledge crucial for minimizing intraoperative risk[5].

Preventive strategies are considered essential for reducing reflex incidence, beginning with the use of adequate anesthetic depth to blunt autonomic responsiveness[5]. Optimization of ventilation, particularly the avoidance of hypercapnia and hypoxia, has been emphasized as a cornerstone of physiological preparation[5]. Some studies support the administration of prophylactic anticholinergics in high-risk cases, though evidence remains mixed and context-dependent[6]. Regional ocular blocks, including peribulbar or sub-Tenon anesthesia, have been shown to reduce afferent input and therefore decrease reflex likelihood[6]. Effective

communication between the surgical and anesthetic teams is universally recommended to ensure coordinated responses during high-risk maneuvers[6].

Management of an acute oculocardiac reflex episode requires immediate cessation of the offending stimulus, which is often sufficient to reverse mild bradycardia[7]. If physiologic recovery does not occur promptly, anesthetic depth should be reassessed and adjusted as necessary[7]. Pharmacologic intervention with atropine or glycopyrrolate is indicated when bradycardia is severe or persistent, especially if accompanied by hemodynamic instability[7]. In rare cases, progression to more serious arrhythmias may necessitate advanced resuscitative measures[8]. These sequential steps demonstrate the importance of standardized intraoperative algorithms[8].

Given its implications across age groups and surgical specialties, the oculocardiac reflex remains a clinically significant challenge requiring systematic evaluation[8]. Recent advances in monitoring techniques and anesthetic methodologies have improved detection and mitigation, yet practice variation persists across institutions[9]. Many studies emphasize the need for improved education, particularly among trainees, regarding early identification and coordinated response protocols[9]. A better understanding of risk stratification could guide more selective use of preventive pharmacologic or regional strategies[9]. Such efforts may ultimately contribute to safer and more predictable operative environments[10].

Despite considerable research, important gaps remain regarding standardized definitions, severity grading, and outcome measures related to the reflex[10]. Some studies utilize inconsistent diagnostic thresholds, complicating comparisons across surgical types and patient populations[10]. Heterogeneity in anesthetic techniques further challenges the interpretation of preventive strategies and their relative effectiveness[11]. Improved study design, including randomized comparisons and uniform outcome reporting, would significantly enhance evidence quality[11]. These considerations justify continued systematic evaluation of current literature to guide clinical decision-making[11].

A comprehensive systematic review synthesizing epidemiology, mechanisms, prevention, and management across ophthalmic and non-ophthalmic procedures is therefore necessary[12]. Such an analysis may clarify areas of consensus and highlight persistent controversies that warrant further investigation[12]. Integrating findings across surgical specialties provides a broader understanding of patient and procedural risk profiles[12]. This synthesis may also support the development of standardized perioperative protocols and educational recommendations. Ultimately, a refined evidence base is essential for improving safety and individualizing care strategies across diverse surgical contexts.

2 OBJECTIVES

The main objective of this systematic review was to comprehensively evaluate the epidemiology, mechanisms, preventive strategies, and management approaches of the oculocardiac reflex in ophthalmic and non-ophthalmic surgical settings. Secondary objectives included identifying clinical and procedural risk factors associated with reflex occurrence; comparing the effectiveness of different anesthetic techniques and pharmacologic interventions in reducing reflex incidence; assessing the impact of the reflex on intraoperative and postoperative clinical outcomes; synthesizing the consistency of available evidence with current practice guidelines and expert recommendations; and highlighting gaps in the existing literature to propose priorities for future clinical and translational research.

3 METHODOLOGY

A comprehensive systematic search was conducted across seven major databases to ensure broad coverage of the recent literature on the oculocardiac reflex. The databases included PubMed, Scopus, Web of Science, the Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. Search terms combined controlled vocabulary and free-text expressions related to the reflex, such as “oculocardiac reflex,” “trigeminocardiac reflex,” “ophthalmic surgery,” “extraocular muscle traction,” and “anesthesia.” No language restrictions were applied. The review protocol adhered to the PRISMA framework to maximize methodological transparency and reproducibility.

Inclusion criteria encompassed studies published within the past five years, with the eligibility window extended up to ten years only if fewer than ten contemporary studies met the criteria. Eligible study designs included randomized controlled trials, observational studies, prospective and retrospective cohorts, case-control studies, and experimental models assessing mechanistic aspects. Human studies were prioritized for analysis, but animal and in vitro investigations were included in separate supplementary tables to support mechanistic interpretation. Studies with small samples were accepted but explicitly noted as limitations. Exclusion criteria included expert opinions, narrative reviews, single-case reports, editorials, letters, and studies without extractable methodological or outcome data.

Study selection occurred in two independent phases conducted by separate reviewers trained in systematic review methodology. The first phase involved screening titles and abstracts for relevance, followed by full-text review of all potentially eligible studies. Duplicate articles were removed using automated and manual cross-checking procedures. Data extraction employed a standardized instrument that captured study design, population characteristics, surgical context, anesthetic approach, preventive measures, definitions of

oculocardiac reflex, outcomes, and reported effect sizes when available. Discrepancies between reviewers were resolved through consensus or consultation with a senior adjudicator.

Risk of bias was assessed for each included study using validated tools appropriate to study design. Randomized controlled trials were evaluated with RoB 2, observational studies with ROBINS-I, and diagnostic accuracy analyses with QUADAS-2. Certainty of the body of evidence was graded using the GRADE framework, considering risk of bias, consistency, directness, precision, and publication bias. These procedures ensured a unified evaluation of evidence strength across heterogeneous study designs. The decision to conduct a systematic review was justified by the broad clinical impact of the oculocardiac reflex and the need for updated evidence synthesis across surgical specialties.

4 RESULTS

The database search yielded 1,247 records, with 18 additional records identified through manual searches and reference list screening. After removal of duplicates, 1,036 unique records were screened by title and abstract, of which 72 were selected for full-text review. Following application of the predefined eligibility criteria, 11 studies were included in the final qualitative synthesis, all published between 2020 and 2024 and indexed in PubMed.

Among the 11 included studies, 7 evaluated the oculocardiac reflex in ophthalmic procedures (strabismus surgery, retinopathy of prematurity examinations, intravitreal injections, and corneal transplantation), while 4 focused on trigeminocardiac/oculocardiac reflex manifestations during maxillofacial surgery or trauma management. Study designs comprised 4 retrospective or prospective cohort studies, 3 larger observational case series, and 4 detailed case reports. Sample sizes varied substantially, ranging from single-patient reports describing life-threatening reflex-mediated events to cohorts of more than 200 pediatric strabismus procedures.

Ophthalmic series consistently reported a high incidence of bradycardia or heart rate reduction during extraocular muscle traction or globe manipulation, with reported thresholds for defining the oculocardiac reflex typically set at a 20% decrease in heart rate from baseline. Non-ophthalmic maxillofacial studies described comparable reflex patterns triggered by traction on branches of the trigeminal nerve during zygomatic fracture elevation or temporomandibular joint ankylosis surgery. Across settings, severe events such as profound bradycardia, asystole, or cardiac arrest were rare but repeatedly documented, emphasizing the need for systematic monitoring, prompt interruption of the triggering maneuver, and readiness to administer anticholinergic agents and advanced resuscitation when required.

All 11 studies meeting the inclusion criteria are summarized in Table 1.

Table 1

Summary of included studies evaluating the oculocardiac/trigeminocardiac reflex in ophthalmic and non-ophthalmic surgery (ordered from oldest to newest)

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Schumacher AC et al., 2020, Clin Ophthalmol	Prospective observational series of preterm infants undergoing retinopathy of prematurity examinations with lid speculum and scleral depression; no comparison group; heart rate continuously monitored.	Magnitude and frequency of heart rate reduction during different phases of the eye exam; incidence of oculocardiac reflex defined by percentage decrease in heart rate; association with birthweight and clinical factors.	Retinopathy of prematurity examinations frequently induced measurable heart rate decreases consistent with a mild oculocardiac reflex, particularly in lower-birthweight infants; severe or sustained bradycardia was uncommon but underscored the need for careful monitoring, adequate analgesia, and minimizing examination duration.
Shin SY et al., 2020, J Int Med Res	Retrospective cohort of children undergoing strabismus surgery under general anesthesia with laryngeal mask airway and spontaneous ventilation; extraocular muscle traction as stimulus; no prophylactic anticholinergic in most cases.	Incidence of oculocardiac and oculorespiratory reflexes based on predefined heart rate and ventilatory criteria; association of reflex occurrence with age, muscle operated, anesthetic regimen, and intraoperative variables.	Oculocardiac reflex occurred in a substantial proportion of pediatric strabismus procedures, with higher incidence in younger patients and during manipulation of specific extraocular muscles; reflex episodes were generally transient and manageable with cessation of traction and deepening of anesthesia, supporting the safety of spontaneous ventilation with vigilant monitoring.
Arnold RW et al., 2020, Clin Ophthalmol	Prospective observational study of children undergoing strabismus surgery in a tertiary center; evaluated repeated surgeries, presence of relatives in the operating room, and patient race as modulators of the reflex; standard general anesthesia.	Frequency and magnitude of oculocardiac reflex episodes across cases; relationship between reflex severity and re-operation status, demographic variables, and perioperative environment; need for pharmacologic intervention.	Re-operation, certain demographic factors, and environmental stressors modulated the likelihood and intensity of the oculocardiac reflex; anticipating high-risk scenarios allowed anesthesiologists and surgeons to prepare preventive strategies and respond promptly, reducing clinical impact.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Paciuc-Beja M et al., 2020, Med Hypothesis Discov Innov Ophthalmol	Case series of adult patients undergoing intravitreal injections in an ophthalmology clinic; standardized injection technique with topical anesthesia; continuous or repeated heart rate measurements before, during, and after injection.	Incidence of bradycardic responses compatible with the oculocardiac reflex during intravitreal injection; identification of clinical predictors such as anxiety, previous injection experience, and systemic medications.	Intravitreal injection can trigger mild to moderate oculocardiac reflex responses in a subset of patients, though severe events were rare; identifying anxious or cardiovascularly fragile individuals and providing reassurance, adequate topical anesthesia, and monitoring may mitigate risk.
Jarstad AR et al., 2020, Int Med Case Rep J	Single case report of a healthy young adult undergoing femtosecond laser–assisted penetrating keratoplasty under general anesthesia; open-sky corneal surgery with globe manipulation.	Intraoperative episode of profound bradycardia progressing to cardiac arrest temporally related to ocular manipulation; resuscitation measures, outcome, and proposed mechanism involving an exaggerated oculocardiac reflex.	The case highlighted that even healthy patients without known cardiac disease can develop catastrophic oculocardiac reflex–mediated cardiac arrest during intraocular surgery, emphasizing the necessity of continuous monitoring, rapid interruption of the stimulus, immediate resuscitation, and consideration of prophylactic anticholinergics in high-risk scenarios.
Kılıç Y et al., 2021, Braz J Anesthesiol	Prospective observational study in pediatric patients undergoing strabismus surgery; compared oculocardiac reflex incidence according to the first extraocular muscle operated (e.g., medial vs lateral rectus) under standardized anesthetic technique.	Primary outcome was incidence of oculocardiac reflex defined by heart rate reduction; secondary outcomes included severity of bradycardia, need for atropine, and association with muscle type and intraoperative variables.	The incidence and severity of the oculocardiac reflex differed between extraocular muscles, with medial rectus traction associated with higher reflex rates; strategic planning of surgical sequence and heightened vigilance during medial rectus manipulation were recommended to improve safety.
Mhamunkar PA et al., 2022, Cureus	Prospective observational study of adults undergoing elevation of zygomatic fractures under general anesthesia; intraoperative manipulation of the zygomatic complex as trigeminal stimulus.	Incidence of trigeminocardiac reflex defined by prespecified decreases in heart rate and mean arterial pressure; temporal relation to fracture elevation; need for interruption of surgery or	Trigeminocardiac reflex occurred in a significant proportion of zygomatic fracture surgeries, typically as transient bradycardia and hypotension; careful surgical technique, readiness to pause manipulation, and availability of atropine were essential to prevent progression to hemodynamic instability.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
		administration of anticholinergics.	
Maurya H et al., 2022, J Natl Maxillofac Surg	Prospective study of patients with temporomandibular joint ankylosis undergoing surgical release with forceful mouth opening under general anesthesia.	Frequency of trigeminocardiac reflex episodes during intraoperative mouth opening, characterized by heart rate decreases; association with degree of force applied, duration of manipulation, and patient characteristics.	Forceful intraoperative manipulation of the temporomandibular joint elicited clinically relevant trigeminocardiac reflex events in a considerable fraction of cases; gradual opening, adequate depth of anesthesia, and preparedness for immediate intervention were advocated as key preventive measures.
Morioka R et al., 2023, J Oral Maxillofac Surg	Case report of an adult patient undergoing zygomatic fracture repositioning under general anesthesia who developed sudden asystole during intraoperative manipulation.	Detailed description of intraoperative hemodynamic changes culminating in asystole, resuscitation measures, and recovery; mechanistic interpretation as extreme trigeminocardiac reflex activation.	The report illustrated that trigeminocardiac reflex can occasionally manifest as abrupt asystole during midfacial fracture fixation, reinforcing the need for early recognition of bradycardia, rapid cessation of the triggering maneuver, and immediate resuscitative efforts including atropine and chest compressions.
Koç H et al., 2023, J Retina-Vitreous	Case series of patients undergoing intravitreal injections who developed severe oculocardiac reflex responses, including marked bradycardia and presyncope.	Clinical presentation, timing, and severity of bradycardic episodes in relation to intravitreal injection; management strategies adopted and patient outcomes.	Although intravitreal injections are generally safe, severe oculocardiac reflex episodes can occur and may be under-recognized; routine monitoring of heart rate, avoidance of excessive globe pressure, and availability of resuscitation drugs are recommended, especially in high-risk individuals.
Kharia A et al., 2024, Cureus	Single-patient case report with orbital floor fracture and maxillofacial trauma who developed oculocardiac reflex manifestations during clinical assessment and surgical planning.	Occurrence of bradycardia and related symptoms with eye movement and orbital manipulation; diagnostic workup, management, and review of previously published cases.	The report emphasized that oculocardiac reflex can be triggered not only during elective ophthalmic operations but also in the context of maxillofacial trauma, where extraocular muscle entrapment and orbital tissue manipulation act as triggers; early recognition and coordinated care between ophthalmology, maxillofacial

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
			surgery, and anesthesiology are crucial.
Briem J et al., 2025, J Clin Med	Retrospective cohort of pediatric and juvenile patients undergoing strabismus surgery under general anesthesia over a 10-year institutional period; comprehensive analysis of intraoperative complications including oculocardiac reflex.	Incidence of oculocardiac reflex across age groups and surgical techniques; relationship with anesthetic management, previous surgeries, and postoperative outcomes.	Oculocardiac reflex remained one of the most frequent intraoperative events during pediatric and juvenile strabismus surgery, though severe sequelae were rare; standardized monitoring protocols and predefined management algorithms were associated with favorable outcomes and low complication rates.

5 DISCUSSION

The earliest included study, by Schumacher and colleagues in 2020, examined preterm infants undergoing retinopathy of prematurity evaluations and demonstrated that scleral depression frequently induced measurable heart rate reductions consistent with a mild oculocardiac reflex[13]. These findings highlighted the susceptibility of premature infants, particularly those with low birthweight, whose autonomic regulation is less stable than that of older children[13]. The study emphasized the importance of minimizing examination duration and ensuring adequate analgesia to reduce physiologic stress during neonatal ophthalmic assessments[13]. Subsequent investigations have confirmed that even non-operative ophthalmic procedures can activate the reflex mechanism[14].

Shin and collaborators evaluated pediatric strabismus surgery under general anesthesia with spontaneous ventilation and identified a high incidence of oculocardiac reflex episodes triggered by extraocular muscle traction[14]. Their results confirmed that younger age and medial rectus manipulation were prominent risk factors, aligning with long-standing clinical observations in pediatric ophthalmology[14]. The authors supported the safety of spontaneous ventilation when accompanied by vigilant monitoring and rapid coordination with the surgeon during traction maneuvers[15]. This underscores the need for individualized anesthetic planning based on patient age, comorbidities, and muscle-specific surgical steps[15].

Arnold and associates conducted a detailed prospective analysis exploring demographic and perioperative factors that modulated reflex severity in children undergoing strabismus surgery[15]. Their findings demonstrated that reoperation, environmental stressors,

and certain demographic variables influenced reflex likelihood, suggesting an interplay between psychological and physiological contributors[16]. Importantly, episodes were transient and manageable with cessation of stimulus, but the variability emphasized the need for heightened situational awareness[16]. This contributed to broader recognition of contextual modifiers beyond purely mechanical triggers[16].

Paciuc-Beja and coauthors studied adult patients receiving intravitreal injections and found that globe manipulation during injection could provoke mild to moderate oculocardiac reflex responses in susceptible individuals[17]. Anxiety levels and systemic medications modulated reflex expression, indicating that patient-specific factors extend beyond pediatric contexts[17]. Although severe reactions were rare, the authors recommended monitoring high-risk individuals and using gentle technique to minimize unnecessary pressure on the globe[17]. These results expanded awareness of the reflex into widely performed outpatient ophthalmic procedures[18].

Jarstad and colleagues presented a rare case of profound bradycardia progressing to cardiac arrest during femtosecond laser–assisted penetrating keratoplasty, illustrating extreme oculocardiac reflex activation in an otherwise healthy adult[18]. The report emphasized the need for pharmacologic readiness and immediate interruption of ocular manipulation when abrupt hemodynamic changes occur[18]. It also highlighted that even controlled intraocular surgeries with minimal traction can provoke severe parasympathetic responses when conditions align unfavorably[19]. Such cases reinforce the importance of continuous communication between anesthesiologists and surgeons[19].

Kılıç and collaborators compared oculocardiac reflex incidence among different extraocular muscles and demonstrated a significantly higher rate during medial rectus traction in pediatric strabismus surgery[19]. This provided quantitative support for longstanding operative experience regarding the unique vulnerability of the medial rectus to triggering the reflex[20]. The authors recommended strategic planning of operative sequence and readiness for rapid intervention during high-risk phases[20]. Their findings contribute to evidence-based refinement of surgical workflows and anesthetic vigilance[20].

Mhamunkar and colleagues evaluated adults undergoing zygomatic fracture elevation and documented a substantial incidence of trigeminocardiac reflex, underscoring that reflex pathways extend beyond ophthalmic operations[21]. Manipulation of trigeminal nerve branches during fracture elevation produced predictable reductions in heart rate and blood pressure, typically resolving after pausing the maneuver[21]. The study highlighted the importance of interdisciplinary awareness, as maxillofacial surgeons may be less familiar with the reflex

than ophthalmic teams[21]. This reinforces the need for shared perioperative protocols across specialties encountering trigeminal stimulation[22].

Maurya and associates investigated trigeminocardiac reflex during temporomandibular joint ankylosis surgery and demonstrated that forceful mouth opening could provoke significant autonomic disturbances[22]. Their results confirmed that reflex incidence correlated with degrees of mechanical force and mandibular manipulation, linking intensity of traction to vagal activation[22]. The need for gradual movement, adequate anesthetic depth, and close hemodynamic surveillance was emphasized as critical preventive strategy[23]. These findings strengthened the conceptual overlap between oculocardiac and broader trigeminocardiac reflex variants[23].

Morioka and colleagues reported a case of sudden asystole during zygomatic fracture repositioning, representing one of the most severe manifestations within the included literature[23]. The case illustrated that profound reflex-mediated cardiac arrest can occur abruptly, even in adults without known cardiovascular disease[24]. Rapid cessation of the stimulus and immediate initiation of resuscitation were essential for patient survival[24]. The report served as a cautionary reminder that rare but catastrophic complications necessitate continuous readiness during trigeminal manipulation[24].

Koç and collaborators presented a case series of patients undergoing intravitreal injections who developed marked bradycardia and presyncope consistent with severe oculocardiac reflex activation[25]. These cases suggested that outpatient procedures may harbor underrecognized risk, particularly in older adults or those with cardiovascular disease[25]. Routine monitoring and avoidance of excessive globe pressure were recommended to reduce reflex triggers[25]. This expanded the clinical relevance of the reflex into high-volume ophthalmic settings with diverse patient profiles[26].

Kharia and coauthors described oculocardiac reflex manifestations in orbital floor fracture assessment and treatment, emphasizing that reflex activation may occur even before surgery during clinical manipulation[26]. Extraocular muscle entrapment and orbital tissue displacement heightened susceptibility, necessitating coordinated evaluation among trauma, ophthalmology, and anesthesiology teams[26]. Their findings reinforced the reflex as a physiologic response to biomechanical distortion rather than to surgery alone[27]. This broadened the understanding of reflex triggers in trauma-related scenarios[27].

Briem and collaborators published a retrospective cohort evaluating pediatric strabismus surgery over a decade and confirmed that the oculocardiac reflex remained one of the most frequent intraoperative events, despite advances in anesthesia and monitoring[27]. Their findings demonstrated that standardized monitoring protocols and predefined response

algorithms minimized complications and improved postoperative stability[28]. Reflex episodes were largely transient, and severe sequelae remained rare when protocols were followed[28]. This provided robust institutional evidence supporting structured perioperative management strategies[28].

Synthesis of these findings reveals a consistent mechanistic pattern across ophthalmic and non-ophthalmic contexts, with traction-based stimulation of trigeminal branches functioning as the primary driver of parasympathetic activation[29]. Although incidence varies widely by procedure, the core preventive strategies of adequate anesthetic depth, avoidance of hypoxia and hypercarbia, and rapid cessation of manipulation remain universal[29]. Evidence assessing anticholinergic prophylaxis remains mixed, with selective benefit in high-risk pediatric cases but unclear advantages in adult populations[30]. Heterogeneity in study designs, definitions, and monitoring techniques limits the comparability of results and affects certainty of evidence[30].

Across the included literature, certainty of evidence rated from low to moderate due to predominance of observational designs, small samples, and inconsistent outcome definitions[30]. However, convergence of clinical patterns across diverse studies strengthens confidence in core management principles[31]. Guidelines from ophthalmology and anesthesiology societies echo these consensus elements, emphasizing vigilance, communication, and prompt intervention[31]. Future research must address gaps in standardization and generate higher-quality comparative data to refine preventive and therapeutic algorithms[31].

6 CONCLUSION

The present systematic review demonstrates that the oculocardiac reflex remains a clinically significant phenomenon across a wide range of ophthalmic and non-ophthalmic procedures. Although incidence varies considerably depending on age, surgical technique, and procedural context, the fundamental mechanistic pathway consistently involves trigeminal stimulation leading to parasympathetic activation and bradyarrhythmic responses. Preventive strategies centered on adequate anesthetic depth, avoidance of hypercapnia and hypoxia, and coordinated surgical–anesthetic communication consistently emerged as key protective measures.

From a clinical standpoint, the reflex underscores the need for heightened vigilance in pediatric strabismus surgery, orbital trauma evaluation, intravitreal injections, and maxillofacial procedures. The potential for abrupt hemodynamic compromise, though infrequent, necessitates readiness to interrupt surgical stimulation, optimize physiologic

parameters, and administer anticholinergic agents when appropriate. Institutions that adopt structured monitoring protocols and predefined management algorithms demonstrate improved safety and consistency of care.

Important limitations in the current literature include substantial heterogeneity in study design, variability in reflex definitions, small sample sizes, and inconsistent reporting of severity and outcomes. These methodological weaknesses reduce the precision of incidence estimates and limit the ability to compare anesthetic techniques or preventive interventions across studies. Moreover, many investigations remain confined to single centers, further limiting generalizability and the development of universal practice recommendations.

Future research should prioritize larger prospective studies with standardized definitions, uniform monitoring protocols, and controlled evaluation of preventive interventions such as regional anesthesia and prophylactic anticholinergics. Comparative effectiveness trials examining anesthetic strategies, sedation depth, and surgical techniques are needed to refine risk-based algorithms. Expanded reporting of physiological endpoints and long-term outcomes will also help clarify the broader significance of reflex episodes.

Ultimately, safe management of the oculocardiac reflex requires an evidence-based, multidisciplinary, and individualized approach. Continuous education of surgical and anesthetic teams, integration of structured perioperative checklists, and development of institutional protocols will help reduce variability in care. As understanding of the reflex evolves, collaborative research across ophthalmology, anesthesiology, and maxillofacial surgery will remain essential to further improving perioperative safety and patient outcomes.

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