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The Management of Traumatic Optic Neuropathy: A Systematic Review and Meta-Analysis

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Abstract: **Introduction:** Traumatic optic neuropathy (TON) is a serious condition resulting from optic nerve injury, often due to head trauma. This study systematically reviews the existing literature to evaluate the effectiveness of various treatments in improving visual outcomes in TON patients. **Methods:** A comprehensive literature search was conducted across databases including Medline (via PubMed), Web of Science, Cochrane Library, and EMBASE from January 1992 to October 2024. Studies were selected based on inclusion criteria that focused on TON patients treated with corticosteroids, conservative therapy, erythropoietin therapy, or surgical interventions. Quality assessment of the included studies was performed using the Joanna Briggs Institute (JBI) Risk of Bias Tool for each design. Data extraction and quality assessment were performed by two independent reviewers, with a meta-analysis conducted to evaluate the pooled visual acuity (VA) improvement rates. **Results:** A total of 23 studies were included, encompassing 1,851 patients with TON. The meta-analysis revealed a pooled VA improvement rate of 50.6% across all treatment modalities. Specifically, corticosteroid-only treatment resulted in a 56.2% improvement rate, while combined corticosteroid and surgical decompression showed a 42.9% improvement rate. Conservative therapy had a 47.8% improvement rate. The heterogeneity among studies was significant (I2= 89.9%), and no significant publication bias was detected. Subgroup analyses indicated varied outcomes, with some studies reporting better results with early intervention. **Conclusion:** The treatment of TON remains challenging, with no single modality showing clear superiority. The corticosteroids and surgical interventions provide potential benefits; however, conservative therapy might be appropriate for certain cases. Future research should focus on optimizing treatment protocols and exploring new therapeutic options, such as erythropoietin to improve visual outcomes in TON patients.

Keywords: Optic nerve injuries; Steroids; Adrenal cortex hormones; Treatment outcome

1. Introduction

Traumatic optic neuropathy (TON) is a severe and potentially vision-threatening condition resulting from trauma to the optic nerve. This condition can occur due to various types of head injuries, including blunt trauma, penetrating injuries, and fractures of the optic canal. The pathophysiology of TON involves both primary mechanical damage to the optic nerve and secondary ischemic and inflammatory processes that contribute to further neuronal injury (1, 2).

Management of TON is challenging, and there is no consensus on the optimal treatment approach. Therapeutic options for TON include conservative therapy, erythropoietin therapy, and surgery. Conservative therapy typically involves observation and supportive care for the possibility of spontaneous recovery (3). Erythropoietin therapy also has shown potential neuroprotective effects and is being explored as a treatment for TON (4, 5). Surgical interventions, such as optic canal decompression, aim to relieve pressure on the optic

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nerve and mitigate damage (6). These therapies offer alternative or adjunctive approaches, but their effectiveness varies, and there is no definitive guideline on the optimal treatment strategy. Among the various treatment modalities, corticosteroids have been widely studied and used due to their potent anti-inflammatory properties. The theoretical benefit of corticosteroids in TON lies in their ability to reduce edema and inflammation, which may help to preserve optic nerve function and improve visual outcomes. However, the use of corticosteroids in TON remains controversial due to the lack of robust evidence supporting their efficacy and concerns about potential side effects (1, 7).

Previous studies on these therapies have yielded mixed results, with some reporting beneficial effects on visual recovery and others showing no significant improvement or even detrimental outcomes (8). This variability in findings has led to uncertainty and debate within the medical community regarding the best management practices for TON.

Given the clinical importance and the ongoing controversy surrounding the treatment of TON, a comprehensive evaluation of the existing evidence is warranted. This systematic review aims to critically analyze and synthesize the available literature on the effects of corticosteroids, conservative therapy, erythropoietin therapy, and surgical interventions in traumatic optic neuropathy. By examining the outcomes of various studies, we seek to provide clarity on the efficacy and safety of these treatments, ultimately guiding clinical decision-making and informing future research directions.

2. Methods

2.1. Study design and setting

In this systematic review and meta analysis, a comprehensive literature search was conducted across multiple databases, including Medline (via PubMed), Web of Science, Cochrane Library (CENTRAL), and Embase, to identify studies evaluating the efficacy of corticosteroids, conservative therapy, and surgical interventions in the treatment of traumatic optic neuropathy (TON) until Oct 5, 2024. First, keywords that were used for retrieving studies were: "optic nerve injuries" or "traumatic optic neuropathy" or "TON" and "Steroids" and "corticosteroids" or "ST". The search strategy in each database is presented in Supplemntary table 1.

Second, the search was limited to articles published in English from January 1992 to December 2023. The search strategy utilized specific keywords and Medical Subject Heading (MeSH) terms relevant to TON and the treatment modalities under investigation. To augment the sensitivity of the search strategy, references of selected articles were double-checked. Also, a further search was conducted in Google Scholar, and the 10 first pages of the search results were inspected to ensure that the related articles were retrieved. Two reviewers (MF and FT) independently screened each full-text article for eligibility and resolved discrepancies through discussion. The main outcome measure was the improvement in visual acuity from baseline to the last follow-up.

2.2. Inclusion and exclusion criteria

Studies were included if they met the following criteria:
1. Study design: Randomized controlled trials (RCTs), cohort studies, and case series with at least 10 patients
2. Articles' language: Only publications in the English language
3. Timeline: Time interval between January 1992 and December 2023.
4. Participants: Patients diagnosed with traumatic optic neuropathy
5. Interventions: Studies evaluating corticosteroids, conservative therapy, erythropoietin therapy, or surgical interventions.
6. Outcomes: Visual acuity improvement, optic nerve function, and any reported side effects

Studies were excluded if they were:
1. Non-English publications
2. Reviews, editorials, or opinion pieces
3. Case reports with fewer than 10 patients
4. Animal studies or in vitro research

2.3. Data extraction

Data extraction was performed independently by two reviewers (MF and FT) using a standardized form. Discrepancies were resolved through discussion or consultation with a third reviewer. Extracted data included:
1. Study main characteristics: Name of first author, year of publication, country, study design, sample size, and follow-up duration
2. Patient characteristics: Age, sex, and baseline visual acuity
3. Intervention details: Type, dosage, and duration of corticosteroid therapy; specifics of conservative therapy; control; and surgical techniques
4. Outcomes: Changes in visual acuity, optic nerve function, and reported side effects or complications

2.4. Quality assessment

Quality assessment of the included studies was conducted independently according to the study design by two reviewers (MF and FT) using a predefined quality assessment tool. The quality of randomized controlled trials (RCTs), cohort studies, and case series studies was assessed using The Joanna Briggs Institute (JBI) Risk of Bias Tool (9, 10, 11). For non-randomized studies of interventions (NRSI), we used The Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) assessment tool (12), and for quasi-experimental studies, the revised JBI critical appraisal tool was used (13). Discrepancies in the assessments were resolved through discussion or, if necessary, by consulting a third reviewer.

2.5. Statistical analysis

For data analysis, "R" version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria) and its package "meta"

were utilized. The meta-analysis was performed on the percentage of patients showing visual acuity (VA) improvement as well as percentages of patients with no light perception (NLP), light perception (LP), counting fingers (CF), and hand motion (HM). The pooled percentages and 95% confidence intervals (CIs) were estimated. The heterogeneity in meta-analyses was evaluated using the I2 statistics. An I2>50% was considered a high level of heterogeneity in this study. For all meta-analyses, a random effect model (DerSimonian and Laird method) was used considering the high level of inherent heterogeneity. P values<0.05 were statistically significant in the present meta-analysis. Egger's regression test was also used in this study to evaluate the publication bias and funnel plot asymmetry. Considering the heterogeneity, both subgroup and meta-regression analyses were performed for RCT and non-RCT studies. The former was performed based on the treatment intervention received, including the control group (no intervention), corticosteroid only, or both corticosteroid and surgical decompression. Meta-regression was also conducted to assess the potential association between the treatment intervention and the percentage of patients showing VA improvement.

3. Results

3.1. Characteritics of included studies

The study selection process is depicted in Figure 1. Initially, 1261 records were identified through database searches (PubMed/Medline: 168, Embase: 848, Web of Science: 234, Cochrane Library: 11). After removing duplicates, 1005 records remained. The titles and abstracts of these records were screened, resulting in the exclusion of 960 irrelevant studies. Full-text articles of the remaining 45 records were evaluated for eligibility, leading to 23 studies being included in the review. Twenty-two studies were excluded for reasons such as inadequate sample size and not meeting the inclusion criteria.

The included studies varied in design, encompassing a mix of retrospective and prospective cohort studies, non-randomized controlled trials, and interventional case series. Specifically, there were 15 cohort studies (both retrospective and prospective), 2 non-randomized controlled trials, 4 randomized controlled trials, and 2 interventional case series. These studies were published between 1992 and 2023 and conducted in various countries, including the USA, Iran, Taiwan, Nepal, China, India, Turkey, Singapore, Italy, Poland, Japan, and 16 other nations. The sample sizes ranged from 9 to 658 participants, with a total of 1,851 patients reviewed across all studies.

Common inclusion criteria were patients with traumatic optic neuropathy and a vision assessment in indirect trauma patients. Exclusion criteria typically involved penetrating ocular injuries and optic nerve avulsion. The efficacy of corticosteroid therapy for traumatic optic neuropathy demonstrated variability across individual study results, as depicted

in Table 1.

3.2. Quality of Included Studies

The quality of the 23 included studies is presented in Tables S2-S5. Using the JBI Risk of Bias tool, all included cohort and RCT studies were judged to be at low risk of bias. According to the ROBINS-I tool, there was a moderate risk of bias in the two non-randomized controlled trials, regarding the Bias due to confounding and Bias in the selection of participants into the study. However, the two case-series studies included in the review had no bias.The quality of the 23 included studies is presented in Tables S2-S5. Using the JBI Risk of Bias tool, all included cohort and RCT studies were judged to be at low risk of bias. According to the ROBINS-I tool, there was a moderate risk of bias in the two non-randomized controlled trials, regarding the Bias due to confounding and Bias in the selection of participants into the study. However, the two case-series studies included in the review had no bias.

3.3. Qualitative synthesis

The included studies varied in methodology, sample size, and demographics, with participants' ages ranging from young children to older adults. Treatments primarily involved high-dose methylprednisolone, either alone or combined with surgery. Visual acuity (VA) improvement was the primary outcome measured, and significant variations were observed across different treatment groups . Generally, combined therapy (surgery + steroid) showed better VA outcomes compared to steroids alone, but the results were inconsistent (14). Some studies reported substantial improvement in VA with steroids alone, especially when treatment was initiated early. Follow-up periods and steroid dosages varied widely, indicating a lack of standardized treatment protocols. The findings suggest a potential benefit of steroids in managing traumatic optic neuropathy, but the optimal treatment approach remains uncertain due to varying study designs and outcomes. Further standardized trials are needed to establish clear guidelines (15).

3.4. Quantitative synthesis

This meta-analysis investigated the efficacy of corticosteroids in the treatment of traumatic optic neuropathy (TON) by comparing visual acuity (VA) improvement across different treatment interventions: corticosteroid only, corticosteroid with surgical decompression, and control (no intervention). The overall pooled VA improvement percentage in the total population was 50.6% (95%CI: 43.5% - 57.8%). The I2 value was 89.9% showing a significant level of heterogeneity. Based on subgroup analysis, the pooled VA improvement percentage among patients who received corticosteroids only was 56.2% (95%CI: 47.4% - 65.1%) with an I2 value of 83.5%. The pooled VA improvement percentage among patients who received corticosteroids and underwent decompressive surgery was 42.9% (95%CI: 27.2% - 58.6%) with an I2 value of 94.1%. The pooled VA improvement per-

centage among patients who received no intervention (control group) was 47.8% (95%CI: 34.2% - 61.4%) with an I2 value of 78.1%. Figure 2 includes the forest plot demonstrating the results of the subgroup analysis. The results of Egger's test of funnel plot asymmetry showed no significant publication bias among the studies for both corticosteroids only (p=0.1990) and corticosteroids with decompressive surgery (p=0.5297) subgroups (Figure 3).

3.5. Subgroup analysis based on visual acuity

The pooled percentage of different groups of visual acuity was also calculated before and after the intervention. In this regard, patients with NLP showed a baseline pooled percentage of 37.4% (95% CI: 28.1% - 46.8%) and a post-treatment percentage of 25.4% (95% CI: 18.3% - 32.5%) in the corticosteroid only subgroup. This group of patients showed a baseline pooled percentage of 64.6% (95% CI: 49.3% - 80.0%) and a post-treatment percentage of 36.2% (95% CI: 24.2% - 48.1%) in the decompressive surgery with corticosteroid subgroup. Moreover, patients with LP showed a baseline pooled percentage of 9.2% (95% CI: 4.6% - 13.8%) and a post-treatment percentage of 4.7% (95% CI: 2.2% - 7.3%) in the corticosteroid-only subgroup. This group of patients showed a baseline pooled percentage of 4.0% (95% CI: 1.1% - 7.0%) and a post-treatment percentage of 6.0% (95% CI: 3.5% - 8.5%) in the decompressive surgery with corticosteroid subgroup.

Further, patients with CF showed a baseline pooled percentage of 11.0% (95% CI: 7.2% - 14.7%) and a post-treatment percentage of 11.2% (95% CI: 6.9% - 15.5%) in the corticosteroid-only subgroup. This group of patients showed a baseline pooled percentage of 12.4% (95% CI: 3.9% - 20.8%) and a post-treatment percentage of 11.2% (95% CI: 6.7% - 15.7%) in the decompressive surgery with corticosteroid subgroup.

Additionally, patients with HM showed a baseline pooled percentage of 10.5% (95% CI: 5.9% - 15.1%) and a post-treatment percentage of 7.8% (95% CI: 4.0% - 11.6%) in the corticosteroid-only subgroup. This group of patients showed a baseline pooled percentage of 8.1% (95% CI: 6.0% - 10.2%) and a post-treatment percentage of 12.3% (95% CI: 7.1% - 17.4%) in the decompressive surgery with corticosteroid subgroup.

3.6. Meta-regression

In addition to subgroup analysis, meta-regression was performed to evaluate the potential association between interventions and VA improvement. Based on the results, no significant difference in the percentage of VA improvement was found between the control and the corticosteroid-only subgroups (Estimate: 0.08, 95% CI: [-0.08; 0.25], p = 0.3259). Likewise, no significant difference in the percentage of VA improvement was found between the corticosteroid and surgical decompression subgroup and the control subgroup (Estimate: -0.06, 95% CI: [-0.28; 0.16], p = 0.6091).

4. Discussion

This systematic review and meta-analysis aimed to evaluate the efficacy of various treatment modalities for traumatic optic neuropathy (TON), specifically focusing on corticosteroids, conservative therapy, erythropoietin therapy, and surgical interventions. The findings highlight significant variability in the effectiveness of these treatments, reflecting the ongoing controversy and lack of consensus in the management of TON.

The use of corticosteroids in TON has been a subject of debate, with our meta-analysis showing an overall visual acuity (VA) improvement rate of 56.2% in the corticosteroid-only group. This aligns with studies such as the one conducted by Levin et al., which reported a 50% improvement rate, suggesting a potential benefit in reducing inflammation and edema (14). However, other studies, including a meta-analysis by Li et al., have highlighted the lack of consistent evidence supporting corticosteroids' effectiveness, with some trials showing no significant improvement compared to controls (16). Our findings also indicate high heterogeneity (I2 = 83.5%), which may be due to differences in corticosteroid dosages, timing, and patient characteristics across studies. Surgical decompression combined with corticosteroid therapy demonstrated a VA improvement rate of 42.9%, lower than corticosteroids alone. This result is consistent with findings from studies like those by Steinsapir and Goldberg, which suggest that while surgical interventions can be beneficial, their success largely depends on the timing and extent of optic nerve damage (16). Conversely, a study by Cook et al. highlighted that early surgical intervention could lead to better outcomes, especially in cases with significant optic canal involvement (17). The variability in outcomes underscores the need for more standardized protocols and better patient selection criteria. Our review found that conservative therapy, often involving observation and supportive care, resulted in a 47.8% VA improvement rate. This rate is similar to the findings reported by Yu-Wai-Man et al., who suggested that some patients might experience spontaneous recovery without aggressive interventions (17). However, the lack of a standardized approach and the potential for significant visual loss in untreated cases make this a less favored option, especially when timely interventions could prevent irreversible damage.

Although not extensively covered in the studies included in our meta-analysis, erythropoietin has been explored as a neuroprotective agent in other literature. Studies like those by Sampaolesi et al. suggest erythropoietin could offer benefits similar to corticosteroids by reducing inflammation and promoting neuronal survival (7). However, the data is limited, and more robust clinical trials are necessary to establish its role in TON treatment conclusively.

5. Limitations and future recommendation

Some limitations can be highlighted in this study. First, the difference in baseline characteristics can cause errors in the interpretation of results.

Second, the high heterogeneity observed in the meta-analysis indicates variability in study design, patient populations, and treatment protocols in this study. Based on this, conclusions about outcomes should be interpreted with caution. Another limitation is that publication bias could not be assessed, and thus could not be excluded because of the low number of included studies.

Finally, caution should be taken in interpreting the outcomes pooled from a low number of studies and the present meta-analysis could not rigorously confirm or refute those outcomes. This inconsistency highlights the need for more rigorous and standardized clinical trials. Future research should focus on defining optimal treatment protocols, including the timing and dosage of interventions, and developing more precise diagnostic criteria to better stratify patients based on the severity of their condition.

6. Conclusions

While corticosteroids and surgical interventions show potential benefits in treating traumatic optic neuropathy, the variability in outcomes and the lack of standardized treatment protocols make it challenging to establish definitive guidelines. Conservative therapy may be appropriate in select cases, but the risk of significant visual impairment warrants caution. Erythropoietin presents a promising avenue for future research but requires further investigation. Clinicians should consider individual patient factors and the current evidence base when deciding on the best treatment approach for TON.

7. Declarations

7.1. Acknowledgments

The authors thank all those who contributed to this study.

7.2. Authors' Contributions

MF conceived the study and drafted the manuscript and key discussion points with support from SHA, SS, and AV. FT managed the planning of the tables (with feedback from all authors), and management of references. All authors provided important intellectual contributions and guidance throughout the event of the manuscript. ZK, MFR, and RT provided guidance on the presentation of the findings and guidance on final revisions. All authors read and approved the final version of the manuscript.

7.3. Conflict of interest

The authors declare that they have no conflict of interest.

7.4. Availability of data and materials

Not applicable.

7.5. Funding and support

The authors state that no funding is involved.

7.6. Ethical approval

This study was approved and registered by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.TEB.POLICE.REC.1402.045).

7.7. Using artificial intelligence chatbots

None.

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Table 1: Characteristics of included studies

Author	Title	Inclusion criteria	Exclusion criteria	Methodology	Steroid dosage & type	Number (F/M)	Age (year)	Follow-up	Study Groups & VA improvement (%)
Joseph A Mauriello et al. (1992) (18) USA	Management of traumatic optic neuropathy - a study of 23 patients	Patients with loss of vision after trauma, afferent pupillary defect treated within the first 48 hours of injury	Penetrating ocular injuries optic nerve avulsion	Retrospective cohort	Methylprednisolone 1 g loading dose then 250 mg intravenously every 6 hours for 72 hours	23 (1/22)	12 - 90 years (mean 51)	8m	Only steroid :57; Surgery + Steroid: 75; Only surgery: 33
Ping-I Chou et al. (1996) (19) Taiwan	Clinical experiences in the management of traumatic optic neuropathy	Sudden visual loss following blunt head injury, intact globe, normal fundus, obvious afferent pupillary defect	Avulsion of the optic nerve ,traumatic anterior ischemic optic neuropathy, eyeball rupture, or severe head injury with intracranial hemorrhage	Retrospective cohort	Oral prednisolone 60-80 mg/day; i.v. dexamethasone. 1-3 mgk/day	58 (5/53)	7-72 years (mean 26)	1 & 3 m	Only steroid: 57; Control; Surgery + Steroid: 60
Levin LA et al. (16) 16 countries	The Treatment of Traumatic Optic Neuropathy	Optic nerve injury cases who had a vision assessment within 3 days of injury	No ocular exam data ,Penetrating ocular injuries, 1st vision exam >3 day after injury	NRCT	Methylprednisolone (or equivalent of another corti- costeroid) as (1) megadose for 5400 mg (2) very high dose for 2000 –5399 mg (3) high dose for 500 –1999 mg (4) moderate dose for 100–499 mg and (5) low dose for 100 mg.	127 (19/108)	Mean 34 ±18	Mean 5.3±2.4 years	Only steroid: 52; Control: 57; Surgery + Steroid: 32
JZ. Mariak et al. (1999) (20) Poland	High-dose steroid therapy of traumatic optic neuropathy may fail to protect the optic nerve permanently	Presented with clinical signs of traumatic optic neuropathy	Injury to the eyeball	Retrospective cohort	Dexamethasone 20 mg every 6 h tapered after 48 h to 24 mg/day	15 (3/12)	Median 29.7 (14 -50)	>1 month	Significant deterioration over time for steroid group
S. Mine et al. (1999) (21) Japan	Outcome of Traumatic Optic Neuropathy. Comparison Between Surgical and Nonsurgical Treatment	Indirect traumatic optic neuropathy caused by closed head injury	Evidence of injury to the globe	Prospective cross sctional	Dexamethasone	36 (6/31)	A:(19-62) Mean 31.3±18.4 B: 9-60 Mean 32.1±14.2	N/A	Only steroid: was not significant; Surgery + Steroid: was not significant
Stilianos E. Kountakis et al. (2000) (22) USA	Endoscopic optic nerve decompression for traumatic blindness	Indirect traumatic optic neuropathy (TON)	N/A	Retrospective cohort	Methylprednisolone, treated with high-dose corticosteroid therapy for 48 hours	34 (5/29)	15-65 (mean 28)	N/A	Only steroid : 91.7; Control: 77.8

Table 1: Characteristics of included studies (continued)

Author	Title	Inclusion criteria	Exclusion criteria	Methodology	Steroid dosage & type	Number (F/M)	Age (year)	Follow-up	Study Groups & VA improvement (%)
Kitthaweesin et al. (2001) (23) Thailand	Dexamethasone and Methylprednisolone in Treatment of Indirect Traumatic Optic Neuropathy	Patients diagnosed with indirect traumatic optic neuropathy	Unconsciousness, optic canal fracture detected by CT scan of the orbit, other ocular pathology known to interfere with VA, or patients for whom corticosteroids are contraindicated	RCT	Methylprednisolone loading dose of 30 mg/kg followed by continuous infusion of 4 mg/kg per hour for 24 hours; in some cases, 15 mg/kg every 6 hours until 72 hours	21 (1/20)	26.3 ± 11.8	2w & 2m	Only steroid (Dexamethasone): 70; (methylprednisolone): 45.45
Yip C.-C. et al. (2002) (24) Singapore	Low-dose intravenous methylprednisolone or conservative treatment in the management of traumatic optic neuropathy	Traumatic visual loss with afferent pupillary defect without direct injury to the globe or optic nerve	Blunt or penetrating ocular injury and optic nerve avulsion, traumatic optic neuropathy due to optic nerve sheath hematoma and to optic nerve impingement by bony fragments from optic canal fractures	Retrospective cohort	The first group: 4 mg of dexamethasone intravenously and then 3 mg/kg four times a day. The second group: 30 mg/kg of methylprednisolone and then 15 mg/kg four times a day thereafter. After 72 hours the intravenous treatments were discontinued and replaced by 1 mg/kg/day of oral prednisolone, which was discontinued within two weeks.	21 (2/19)	12-65 (Mean 37.1)	Median: 1 year (range 10 days - 2 years)	Only steroid: 44.4; Control: 33.3
Rajiniganth et al. (2003) (15) India	Traumatic optic neuropathy: visual outcome following combined therapy protocol	Indirect optic nerve injury with visual loss	N/A	NRCT	Methylprednisolone 125-250 mg 6-hourly	44 (3/41)	Mean 28.6	Minimum 3m (mean: 3.8 m)	Improvement of VA in 5 of 21 patients in whom treatment was started after 7 years; VA improvement in 16 of 23 patients in whom treatment was started before 7 days after injury.
Ching-Hua Hsieh et al. (2003) (25) Taiwan	Indirect Traumatic Optic Neuropathy Complicated With Periorbital Facial Bone Fracture	Patients with indirect traumatic optic neuropathy complicated with facial bone fractures	Comatose patients were excluded due to the difficulties in performing accurate visual examinations on them	Retrospective cohort	30 mg/kg methylprednisolone + 1 mg/kg per day for 11 days prednisolone; Methylprednisolone Initial Dose: 1000 to 2000 mg of intravenous methylprednisolone (approximately 30 mg/kg of body weight) immediately after diagnosis of traumatic optic neuropathy. Follow-up Dose: 500 mg every 6 hours for 72 hours	45 (9/36)	14-96 (Mean 35.4)	N/A	Only steroid: 27.7±12.1; Surgery + Steroid: N/A

Table 1: Characteristics of included studies (continued)

Author	Title	Inclusion criteria	Exclusion criteria	Methodology	Steroid dosage & type	Number (F/M)	Age (year)	Follow-up	Study Groups & VA improvement (%)
Wan Hazabbah Wan Hitam et al. (2010) (26) Malaysia	Traumatic optic neuropathy: a review of 24 patients	Patients with traumatic optic neuropathy	N/A	Retrospective cohort	Intravenous methylprednisolone 250mg for 3 days followed by oral prednisolone 1 mg/kg for 11 days	24 (0/24)	5-77 (Mean: 33)	6m-3 years	Only steroid: 91.7; Control: 77.8
E. Emanuelli et al. (2014) (27) Italy	Post-traumatic optic neuropathy: our surgical and medical protocol	Patients with traumatic optic neuropathy who underwent surgical endoscopic decompression and steroid treatment	N/A	Retrospective cohort	Methylprednisolone loading dose of 30 mg/kg followed by continuous infusion of 4 mg/kg per hour for 24 hours; in some cases 15 mg/kg every 6 hours until 72 hours	26 (7/19)	15-76 Mean (35.5)	Up to 41 months	Surgery + Steroid: 65
M. Sosin et al. (2016) (28) USA	Treatment Outcomes following Traumatic Optic Neuropathy	Sudden or progressive vision loss following facial trauma	Patients who could not cooperate with visual examination such as comatose patients.	Retrospective cohort	Megadose steroid treatment; Various (mega, high, medium, and low dose)	109 (28/81)	8-82 Mean 38.0 ± 17.5	Mean follow-up of 12.9 weeks.	Only steroid: 55.6; Surgery + Steroid: 40; Control: 40
Pokharel et al. (2016) (29) Nepal	Visual Outcome after Treatment with High Dose Intravenous Methylprednisolone in Indirect Traumatic Optic Neuropathy	Cases with blunt trauma to eye, with decreased vision and presence of relative afferent pupillary defect; CT scan of cases revealing normal optic canal with no fractures and no bony fragments impinging optic nerve.	Patients who did not have a CT scan after injury or those with direct trauma to optic nerve, open globe injuries, or trauma to the posterior segment preventing evaluation of disc.	Case series	Methylprednisolone 1 gr IV for 3 days	10 (2/8)	Mean 27.1	3m	Only steroid: rapid and beneficial improvement in visual acuity after high dose of intravenous steroid treatment in cases with indirect traumatic optic neuropathy.
Nazife Sefi-Yurdakulet al. (2017) (30) Turkey	Risk factors affecting the visual outcome in patients with indirect traumatic optic neuropathy	Indirect TON due to facial and cranial trauma	Indirect TON patients administered megadose steroids, patients with direct TON or any other previous ocular or neurologic pathology, and those with a follow-up less than two months	Retrospective cohort	1000 mg intravenous methylprednisolone per day divided into 4 equal doses for three consecutive days. This was followed by 1 mg/kg/day oral steroids tapered every 5 days and finally discontinued according to the patient's clinical status.	46 (2/44)	Group 1 (Steroid): 34.7 ± 11.4 Group 2 (Control): 37.5 ± 17.7	Group steroids: 8.1 ± 13 months; Group control: 15.4 ± 24.4 months	Only steroid: 61.9; Control: 52

Table 1: Characteristics of included studies (continued)

Author	Title	Inclusion criteria	Exclusion criteria	Methodology	Steroid dosage & type	Number (F/M)	Age (year)	Follow-up	Study Groups & VA improve-ment (%)
Kashkouli et al. (2017) (31) Iran	Traumatic optic neuropathy treatment trial (TONTT): open label phase 3 multicenter semi-experimental trial	TON was defined as reduced best corrected visual acuity (BCVA), color vision, and positive relatively afferent pupillary defect (RAPD) with normal fundus and optic nerve examination and no evidence of direct trauma to optic nerve on spiral orbital and optic canal CT scan. Included were patients with TON of 5 years of age and within 3 weeks after the trauma.	Patients with direct optic nerve trauma, associated ocular, orbital or central nervous system (CNS) injury, decreased level of consciousness, concurrent CNS trauma requiring medical or surgical treatment, and any medical history which might be interfering with corticosteroid and erythropoietin (EPO) treatments.	RCT	Methylprednisolone 250 mg intravenously over 30 minutes, four times a day for three consecutive days	100 (12/88)	EPO Group: Mean 29.39; Steroid Group: Mean 23.86 Observation Group: Mean 28.81	3m	Only steroid: 81.63; Control: 76.27; Erythropoietin: 93.75
Hsin-Hung Chen et al. (2020) (32) Taiwan	Surgical Decompression or Corticosteroid Treatment of Indirect Traumatic Optic Neuropathy	Indirect TON and normal vision before the injury were enrolled	Cornea injury, Eyeball rupture, Direct optic nerve injury (e.g. optic nerve injured by bone fragment or disrupted optic nerve), Visual defect before trauma (e.g. glaucoma), Unclear consciousness, Traumatic injury more than 2 weeks previously, Ineligibility for surgical or corticosteroid treatment due to underlying diseases	RCT	Methylprednisolone Initial dose: 30 mg/kg; Subsequent dose: 15 mg/kg every 6 hours for 3 days	30 (4/26)	Surgery Group: mean 29 (range 16–45); Steroid Group: mean 24 (range 12–44)	Patients were followed up at 1 week, 1 month, 3 months, 6 months, and 9 months.	Only steroid: 55.6; Surgery + Steroid: 66.7
Bo Yu et al. (2020) (33) China	Newly onset indirect traumatic optic neuropathy-surgical treatment first versus steroid treatment first	Newly onset indirect traumatic optic neuropathy (ITON) within 3 days of trauma	Bilateral ITON, Previous treatment, History of consciousness impairment, Refusal of surgery	RCT	Methylprednisolone 20 mg/kg per day for 3 days before ETOCD (Group B) and for 6 days after surgery (Group A) and 3 days after surgery (Group B)	66	Group A: 33.74 ± 11.53; Group B: 32.72 ± 9.80	3m	Surgery + Steroid: 46.9

Table 1: Characteristics of included studies (continued)

Author	Title	Inclusion criteria	Exclusion criteria	Methodology	Steroid dosage & type	Number (F/M)	Age (year)	Follow-up	Study Groups & VA improve-ment (%)
John et al. (2020) (34) India	Traumatic optic neuropathy: Early detection and intervention in a tertiary care centre	All patients who present with head trauma or ocular trauma and diagnosed with TON (defective vision and relative afferent pupillary defect) after ocular examination were included.	Patients who were unconscious and presented with non reactive pupil of both eyes; Patients who were discontinued on IV steroids due to contraindication or intolerance. Patients who were not regular on follow-up. Patients who were not willing to sign the consent form to take part in research	Retrospective cohort	Methylprednisolone 1 g IV bolus dose followed by 500 mg twice daily for 3 days then shifted to oral steroids and dose tapered for 4-6 days	29 (0/29)	Mean 27.90 ± 5.14	1m	Only steroid: 82.7
Yang Gao et al. (2021) (35) China	Endoscopic trans-ethmosphenoid optic canal decompres-sion is an optimal choice to save vision for indirect traumatic optic neuropathy	Diagnosed with ITON, underwent ETOCD surgery and/or Smart Pulse Technology (SPT) , followed up for at least 3 months, no history of other ocular disorders or ocular surgery, steady vital indexes with good consciousness for assessing visual acuities and other ophthalmic examinations, no other severe non-ophthalmic complications found by systemic examination	Patients with contraindications for high dose steroid treatment	Case series	Methylprednisolone Intravenous high dose steroid (1 g methylpred-nisolone per day for adults or 15 mg/kg/d methylpred-nisolone for children) was given to patients daily for 3 days.	140 (15/125)	5-62 (Mean 26.9 ± 14.1)	At least 3 months	Only steroid :37.5; Surgery + Steroid: 68.2; Only surgery: 82
Wang Wei et al. (2022) (36) Taiwan	The outcome of surgical and non-surgical treatments for traumatic optic neuropathy: a comparative study of 685 cases	All cases with visual loss and pupillary afferent disorder in the involved eye due to craniofacial trauma evaluated by an ophthalmologist to eliminate injury to the eyeball and fundus fractures of orbit and optic canal evaluated by high-resolution computed tomography (HRCT).	N/A	Retrospective cohort	Methylprednisolone 1000 mg intravenously for 3 days	685 (64/621)	5-67 mean 32.3±14.9	Week 1, month 1, and 3 months after discharge with some patients followed up to 2 years (average follow-up 3.87±1.04 months)	Only steroid: 35.4; Surgery + Steroid: 42.8

Table 1: Characteristics of included studies (continued)

Author	Title	Inclusion criteria	Exclusion criteria	Methodology	Steroid dosage & type	Number (F/M)	Age (year)	Follow-up	Study Groups & VA improvement (%)
Wen-Guei Yang et al. (2004)(37)	Outcome for Traumatic Optic Neuropathy - Surgical Versus Nonsurgical Treatment	Patients with traumatic optic neuropathy (TON) after maxillofacial trauma and reduced vision with an afferent pupillary defect in the involved eye.	Patients with penetrating ocular injuries or optic nerve avulsion.	Retrospective cohort	Initial 30 mg/kg loading dose of SoluMedrol (methyl-prednisolone) followed by 15 mg/kg every 6 hours	42 (6/36)	Surgical: 7-75 mean 25.3 ± 14.1 Non-surgical: 6-61 mean 27.39 ± 14.30	At least 3 months	Only steroid: 72.7; Surgery + Steroid: 62.5
Naveen K. Challa et al. (1999) (38)	Clinical Spectrum of Indirect Traumatic Optic Neuropathy in South Indian Subjects	All the patients who were diagnosed with Indirect traumatic optic neuropathy were included and their records were verified. History of blunt trauma was only included in the study.	Patients diagnosed with direct traumatic optic neuropathy (optic nerve avulsion, optic nerve transection, optic nerve sheath hemorrhage) or penetrating injuries were excluded.	Retrospective cohort	Initial 30 mg/kg loading dose of SoluMedrol (methyl-prednisolone) followed by 15 mg/kg every 6 hours for 3 days & oral steroids	37 (2/35)	Median 28 (12-51)	N/A	Only steroid: 38; Control: 16

F/M: female to male ratio; VA: visual acuity; m: month; N/A: not applicable; NRCT: non-randomized controlled trial; RCT: randomized controlled trial; CT: computed tomography; TON: traumatic optic neuropathy; ETOCD: Endoscopic trans-ethmosphenoid optic canal decompression; IV: intravenous; ITON: indirect traumatic optic neuropathy.

Table S 1: Search strategy of databases

PubMed/Medline	
#1	(((optic nerve injuries[MeSH Terms]) OR (traumatic optic neuropathy[Title/Abstract])) OR (TON[Title/Abstract]))
#2	((Steroids[MeSH Terms]) OR (corticosteroids[Title/Abstract]))
#3	(((optic nerve injuries[MeSH Terms]) OR (traumatic optic neuropathy[Title/Abstract])) OR (TON[Title/Abstract])) AND ((Steroids[MeSH Terms]) OR (corticosteroids[Title/Abstract]))
Embase	
#1	'corticosteroid'/exp OR 'steroid'/exp OR corticosteroid:ti,ab,kw OR steroid:ti,ab,kw
#2	'traumatic optic neuropathy'/exp OR 'traumatic optic neuropathy':ti,ab,kw
#3	('corticosteroid'/exp OR 'steroid'/exp OR corticosteroid:ti,ab,kw OR steroid:ti,ab,kw) AND 'traumatic optic neuropa-thy'/exp OR 'traumatic optic neuropathy':ti,ab,kw
Web of Science	
#1	(TS=(corticosteroid)) OR TS=
#2	((TS=("traumatic optic neuropathy")) OR TS=("Optic Nerve Injuries")) OR TS=(TON)
#3	#1 AND #2
Cochrane Library	
#1	MeSH descriptor: [Steroids] explode all trees
#2	(corticosteroids):ti,ab,kw
#3	#1 OR #2
#4	(TON):ti,ab,kw OR (traumatic optic neuropathy):ti,ab,kw
#5	MeSH descriptor: [Optic Nerve Injuries] explode all trees
#	#4 OR #5
#7	#3 AND #6

canal decompression; IV: intravenous; ITON: indirect traumatic optic neuropathy.
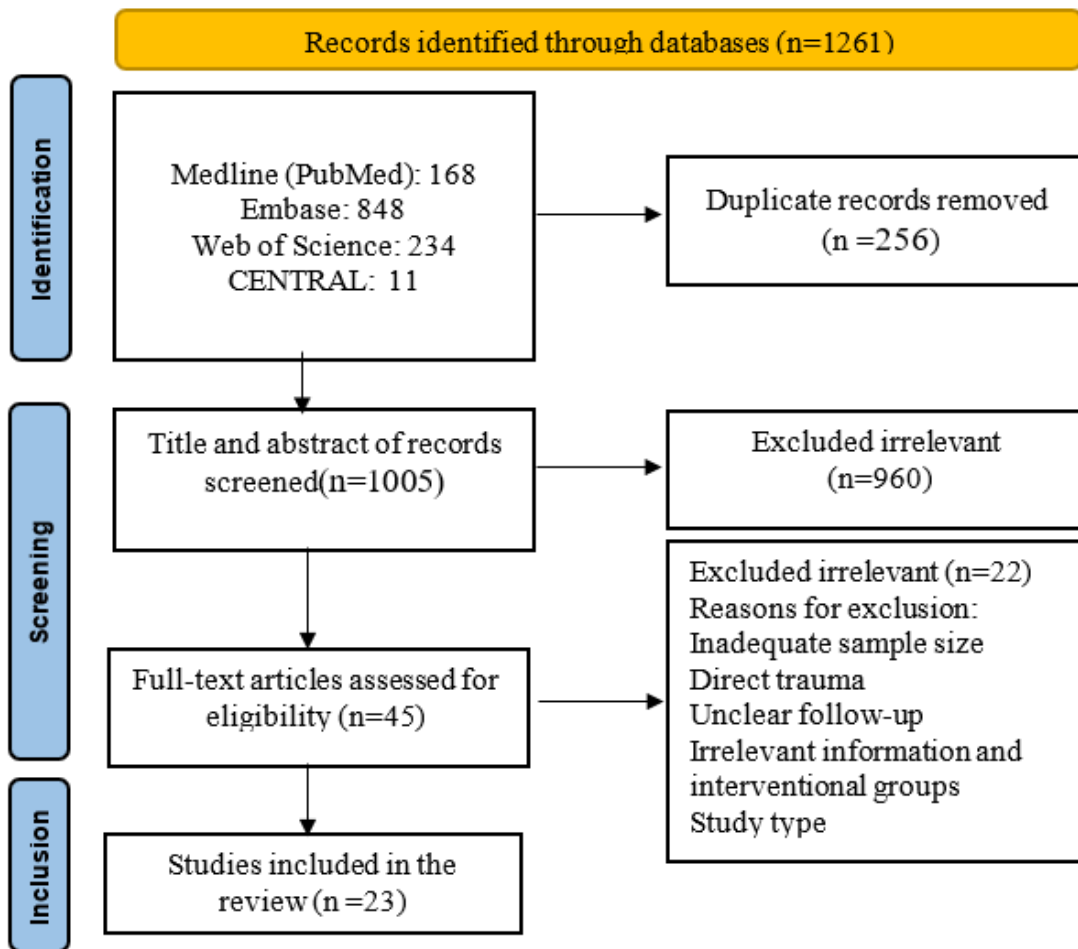
Figure 1: Flow chart of study selection for inclusion in the systematic review and meta-analysis.

Table S 2: Critical appraisal for randomized controlled trials included in the review using The Joanna Briggs Institute (JBI) risk of bias tool

First author	Questions													Total score
	1	2	3	4	5	6	7	8	9	10	11	12	13	
Kitthaweesin, 2001	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	13/13
Kashkouli, 2017	Yes	No	Yes	No	No	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	9/13
Hsin-Hung Chen, 2019	Yes	No	Yes	No	No	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	9/13
Bo Yu, 2020	Yes	No	Yes	No	No	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	8/13

1. Was true randomization used for assignment of participants to treatment groups?

2. Was allocation to groups concealed?

3. Were treatment groups similar at the baseline?

4. Were participants blind to treatment assignment?

5. Were those delivering the treatment blind to treatment assignment?

6. Were treatment groups treated identically other than the intervention of interest?

7. Were outcome assessors blind to treatment assignment?

8. Were outcomes measured in the same way for treatment groups?

9. Were outcomes measured in a reliable way?

10. Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?

11. Were participants analyzed in the groups to which they were randomized?

12. Was appropriate statistical analysis used?

13. Was the trial design appropriate and any deviations from the standard randomized controlled trial design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?
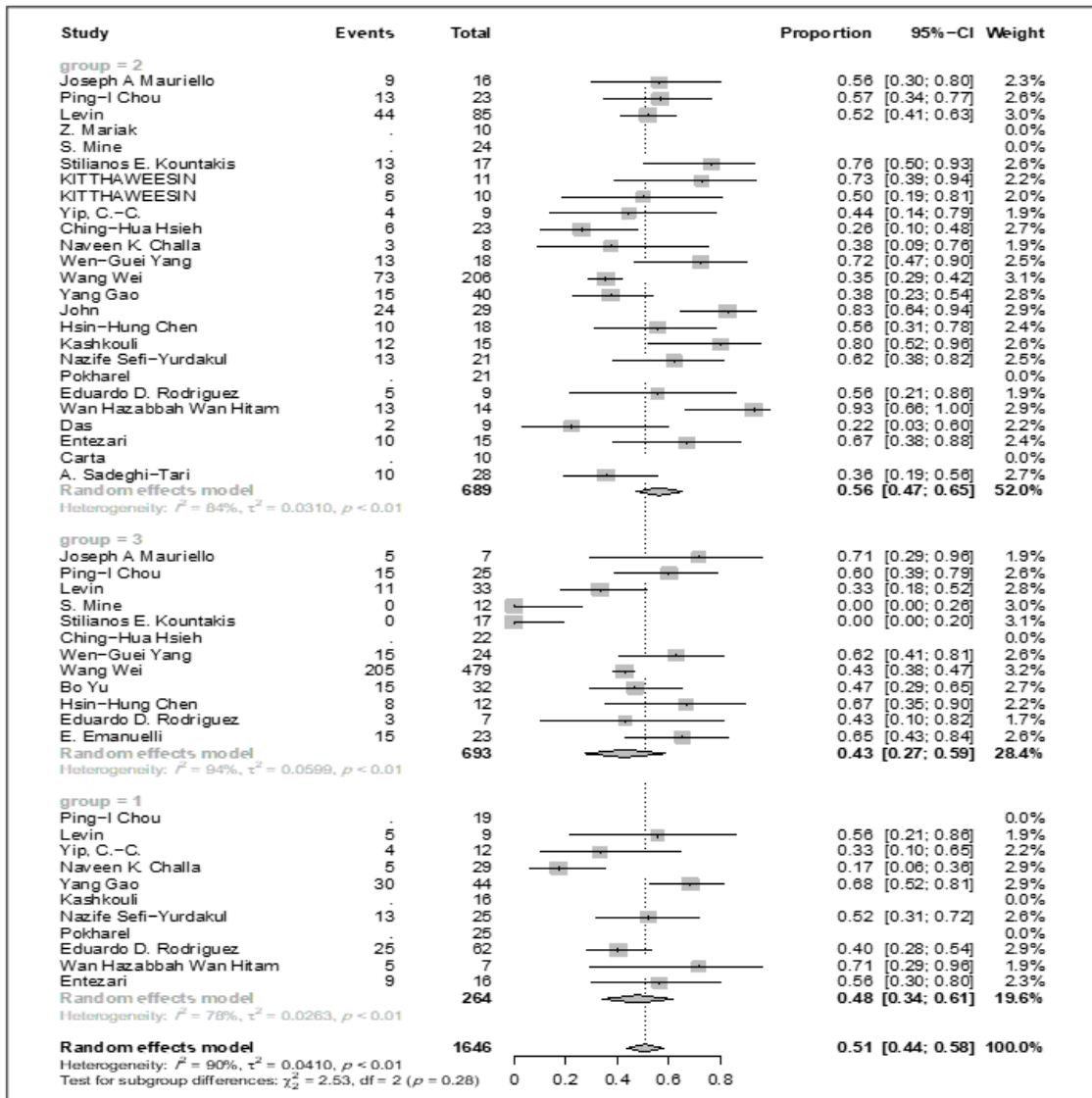
Figure 2: Forest plots and pooled proportions of visual improvement in patients who received no intervention (control), corticosteroid only, and corticosteroid with decompressive surgery. Group1= control, group2= steroid, group 3= surgery + steroid. CI: confidence interval.
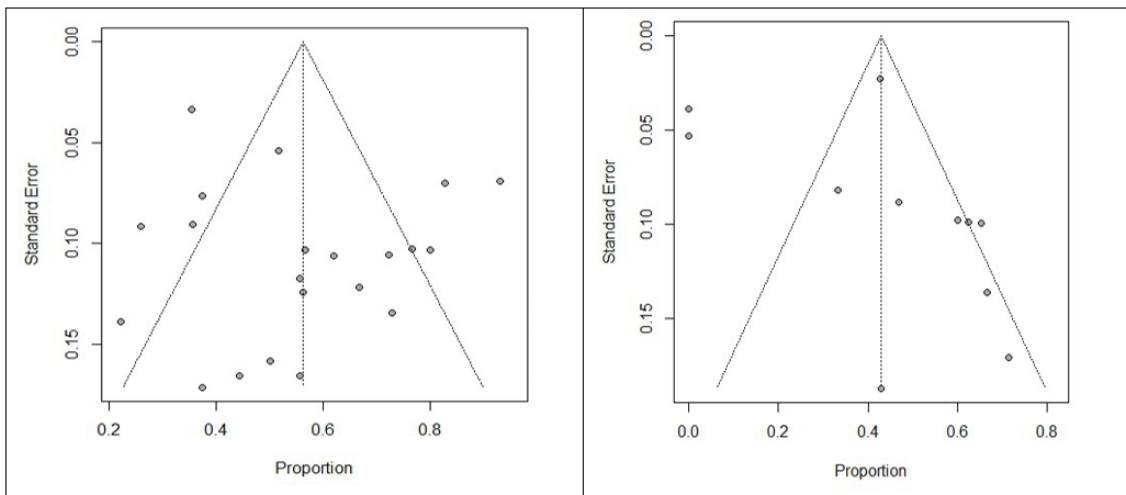

Figure 3: Funnel plot of meta-analysis of visual acuity (VA) improvement in patients who received only corticosteroid (left) and both corticosteroid and surgical decompression (right).

Table S 3: Critical appraisal for cohort studies included in the review using The Joanna Briggs Institute (JBI) Risk of Bias Tool

First author	Questions											Total score
	1	2	3	4	5	6	7	8	9	10	11	
Joseph A Mauriello, 1992	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	No	Yes	No	7/11
Ping-I Chou, 1996	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	7/11
JZ. Mariak, 1999	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Unclear	7/11
Naveen K. Challa,1999	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	N/A	Yes	7/11
S. Mine, 1999	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	9/11
StiliaNos E. Kountakis,2000	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	10/11
Yip, C.-C,2000	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	No	N/A	Yes	7/11
Ching-Hua Hsieh, 2003	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	10/11
Wan Hazabbah WH, 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	9/11
E. Emanuelli, 2014	N/A	Yes	Yes	Yes	Yes	N/A	Yes	Yes	Yes	Yes	Yes	
Eduardo D. Rodriguez, 2016	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	No	Yes	7/11
Nazife Sefi-Yurdakul,2017	Yes	Unclear	Yes	Yes	Yes	Yes	No	Yes	Yes	Unclear	Yes	8/11
John, 2020	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	No	Yes	No	Yes	7/11
Wang Wei,2022	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	7/11
Wen-Guei Yang, 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	9/11

1. Were the two groups similar and recruited from the same population?
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?
3. Was the exposure measured in a valid and reliable way?
4. Were confounding factors identified?
5. Were strategies to deal with confounding factors stated?
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?
7. Were the outcomes measured in a valid and reliable way?
8. Was the follow up time reported and is sufficient long enough for outcomes to occur?
9. Was follow up complete, and if not, were the reasons for loss to follow up described and explored?
10. Were strategies to address incomplete follow up utilized?
11. Was appropriate statistical analysis used?
N/A: not applicable.

Table S 4: Critical appraisal for case-series studies included in the review using The Joanna Briggs Institute (JBI) Risk of Bias Tool

First author	Questions										Total score
	1	2	3	4	5	6	7	8	9	10	
Pokharel, 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10/10
Yang Gao, 2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10/10

1. Were there clear criteria for inclusion in the case series?
2. Was the condition measured in a standard, reliable way for all participants included in the case series?
3. Were valid methods used for identification of the condition for all participants included in the case series?
4. Did the case series have consecutive inclusion of participants?
5. Did the case series have complete inclusion of participants?
6. Was there clear reporting of the demographics of the participants in the study?
7. Was there clear reporting of clinical information of the participants?
8. Were the outcomes or follow up results of cases clearly reported?
9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information?
10. Was statistical analysis appropriate?

Table S 5: Quality assessment of non-randomized studies of interventions using ROBINS-I tool (n=2)

Study	Type of bias							Overall risk of bias
	1	2	3	4	5	6	7	
Levin et al. 1999	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Rajiniganth et al. 2003	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate

1. Confounding
2. Selection of participants into the study
3. Classification of interventions
4. Deviations from intended interventions
5. Missing data
6. Measurement of outcomes
7. Selection of the reported result