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Early Surgery and High Dose Steroids in Treating Patients with Indirect Traumatic Optic Neuropathy: A Meta-Analysis and Systematic Review

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ABSTRACT

Introduction: Optic nerve injury is a devastating cause of permanent visual loss after blunt or penetrating injury occurring in up to 7% of head trauma cases. No single treatment strategy and timing of intervention has proved optimal. Timely and appropriate management is key to improving visual outcomes. We compared whether immediate surgical decompression or steroids would lead to improvement of visual outcomes in individuals with indirect traumatic optic neuropathy.

Methods: We searched from several online databases and included studies of patients with direct Optic nerve injury, those who received combined treatment with surgery and steroids, and those with delayed initiation of treatment were excluded.

Results: The final search yielded eleven eligible studies. Both interventions showed similar results in improvement of visual function (RR 2.35, 95% CI 0.87 to 6.34, p=0.09, I2 0%). Both early and late intervention also showed similar results in improvement of visual function (RR 1.72, 95% CI 0.89 to 3.35, p=0.11, I2 61%). Among patients who underwent early surgical decompression, the rate of visual acuity improvement was 73% with those who underwent transcranial surgery and 69% with those who underwent endoscopic surgery.

Conclusion: This study shows that immediate surgical decompression and early high dose steroid administration are equally effective in improving visual function. Patients with no light perception (NLP) and light perception (LP) pre treatment resulted to better visual improvement with steroids while those with counting fingers (CF) and more than CF pre treatment, resulted to better visual improvement with surgical decompression.

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Introduction

Optic nerve injury is a devastating cause of permanent visual loss after blunt or penetrating injury occurring in up to 7% of head trauma cases [1]. Majority of affected individuals are young males, commonly due to motor vehicle accidents, bicycle accidents, falls, and assaults. It may occur a result of a direct contusive force on the optic canal and nerve or due to forces that are transmitted indirectly causing nerve compression and disruption of vascular supply. Up to 70% of patients present with severe visual loss if left untreated [2,3].

Management of traumatic optic neuropathy has been centered on decompressing the optic nerve to re-establish its function. While numerous therapeutic protocols exist, from simple observation to steroid therapy, to surgical decompression, or a combination of both, no single treatment strategy and timing of intervention has proved optimal. Timely and appropriate management is key to improving visual outcomes.

Objectives

The general objective of this study is to establish whether early surgical decompression of Optic nerve or high dose steroids is more effective in improving visual function among patients who sustained indirect traumatic optic neuropathy. Specifically, we wanted to determine whether those who received early intervention (<7 days) had significant improvement in visual outcomes as well as the rates of visual improvement among the different surgical approaches utilized.

Methods

The reporting of this study complies with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines.

Study Eligibility

We searched for prospective randomized studies as well as prospective and retrospective cohort studies that enrolled adult patients who sustained indirect traumatic optic neuropathy and received immediate treatment with early surgical decompression alone or high dose steroids alone. Comparative studies were included for the meta-analysis.

Participants
People of either sex, aged 18 years or over who sustained indirect optic nerve injury who received treatment within three days with either surgical decompression alone or high dose steroids alone were allowed.

We excluded studies that included patients who sustained direct optic nerve injury, who received combined treatment with surgery and steroids, and who received initiation of treatment three days after injury.

Interventions
Surgical approaches included transcranial optic nerve decompression, endoscopic trans-conjunctival optic canal decompression and endoscopic trans-ethmoidal optic canal decompression. High dose steroids at 30mg/kg within the first hour of injury and 5-15mg/kg/day given for seven days was utilized. Variations in timing of treatment initiation and dosage were not allowed.

Outcomes
Primary outcome of interest was improvement in visual function after treatment initiation with minimum follow-up of 1 week. Improvement of Visual function was determined through pre-treatment and post-treatment comparison of changes in light perception and color change, Snellen visual acuity chart (converted to logarithm of minimum angle of resolution equivalents), fundus findings, and intraocular pressure at time of last follow-up.

Literature Search
The following databases were searched: the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE/PubMed, the US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov), Embase database, Health Research and Development Information Network (HERDIN), and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP; apps.who.int/trialsearch). The following search terms were agreed upon and used: "Traumatic optic neuropathy," "Surgery", "Steroids". Bibliographies of relevant articles to identify other published or unpublished studies that may be relevant to our study were also checked.

Data Extraction
Two reviewers (Custodio and Malilay) independently performed the literature search and identified relevant studies. The abstracts of search results for eligible studies were screened and the full published articles for those likely to be relevant were collected. The two reviewers independently collected data from each of the included studies. Disagreements were resolved through discussion with the third reviewer (Navarro). Data obtained from each relevant study was tabulated and include characteristics of participants, imaging, interventions, results, and outcomes during follow-up (Figure 1).

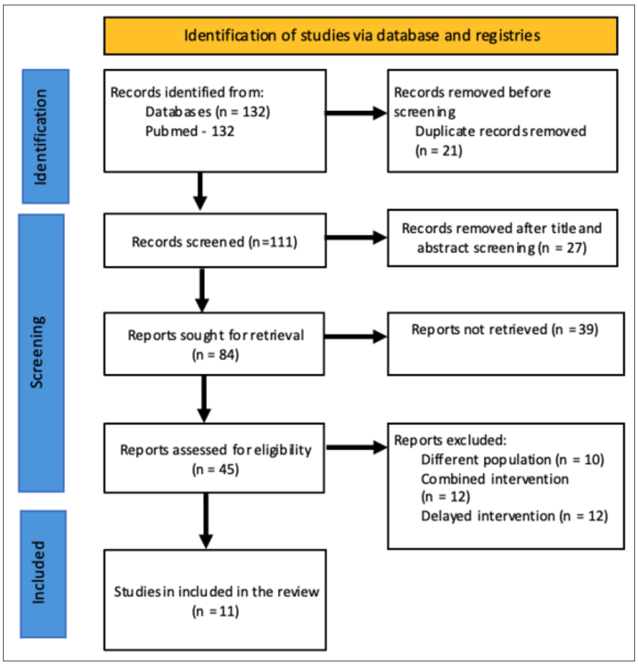

Figure 1: Identification of Studies via Database and Registries

Risk of Bias
The risk of bias was assessed using the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool for nonrandomized studies (Table 1).

Table 1: Risk of Bias

Study	Chen et al [4].	Urolagin et al [5].	Levin et al [6].	Mine et al [7].	Lesell et al [8].
Confounding Bias	High	High	Low	High	High
Selection Bias	Low	High	High	Low	Low
Classification of intervention bias	Low	Low	Low	Low	Low
Deviation from intended intervention bias	Low	Low	Low	Low	Low
Missing data bias	Low	Low	Low	Low	Low
Measure of outcome bias	Low	Low	Low	Low	Low
Selection of results bias	Low	Low	Low	Low	Low

Statistical Analysis
Analysis was performed using the RevMan program (Version 5.4. The Cochrane Collaboration, 2020). Risk ratios (RRs) and their corresponding confidence intervals (CI) were calculated for the different outcomes, and forest plots were created. We calculated a weighted estimate of the RR across reports using the Mantel-Haenszel method using a random effects model for comparable studies. Overall heterogeneity was measured using the I^2 statistic, where >50% suggests high heterogeneity. Relevant data was tabulated for systematic review.

Results
The initial search resulted in 132 publications of which 11 were included in the meta-analysis: 5 studies were included to compare specific interventions used and 6 studies were included in comparing timing of intervention in improvement of visual outcomes.

Meta-Analysis on Surgery Versus Steroids

The included studies had a total of 114 patients from 1989-2019 across 1 randomized controlled trial and 4 retrospective cohort studies. The patients age varied between studies from 18-62 years old. The male/female ratio was 3:1 and the follow-up ranged between 1 week to 11 months.

Chen et al. performed a randomized controlled trial study which included a total of 30 patients who sustained indirect traumatic optic neuropathy from 2011-2013 in Chang Gung Memorial Hospital, Taoyuan, Taiwan. Majority of patients were males, 16-45 years old. Patients were diagnosed clinically through decrease or loss of vision with history of head trauma. Twelve patients underwent immediate endoscopic transconjunctival optic canal decompression alone, while 18 patients received high dose steroids alone for three days. Patients were followed-up for 1 week to 9 months for improvement of visual function [4].

Urolagin et al. performed a single-institution, retrospective cohort study which included a total of 8 patients who sustained indirect traumatic optic neuropathy from 2008-2011 in Nehru Nagar, Belgaum, Karnataka, India. Majority of patients were males, 21-60 years old. Patients were diagnosed clinically through decrease or loss of vision with history of head trauma. Two patients underwent immediate transcranial optic nerve decompression alone, while 6 patients received high dose steroids alone for eleven days [5].

Levin performed a multi-institution, retrospective cohort study which included a total of 133 patients who sustained indirect traumatic optic neuropathy from 1994-1997 in University of Wisconsin Medical School, Madison, Wisconsin, U.S.A. Majority of patients were males, 18-52 years old. Patients were diagnosed clinically through decrease or loss of vision with history of head trauma. One patient underwent immediate endoscopic transconjunctival optic canal decompression alone, while 34 patients received high dose steroids alone for seven days. Patients were followed-up for 1 to 6 months for improvement of visual function [6].

Mine et al. performed a single-institution, retrospective cohort study which included a total of 36 patients who sustained indirect traumatic optic neuropathy from Chiba University School of Medicine, Inohana, Chuo-ku, Chiba-shi, Japan. Majority of patients were males, 19-62 years old. Patients were diagnosed clinically through decrease or loss of vision with history of head trauma. Twelve patients underwent transcranial optic nerve decompression alone, while 24 patients received high dose steroids alone [7].

Lesell et al. performed a multi-institution, retrospective cohort study which included a total of 33 patients who sustained indirect traumatic optic neuropathy from 1976-1987 in Boston, Massachusetts, U.S.A. Majority of patients were males, 18-49 years old. Patients were diagnosed clinically through decrease or loss of vision with history of head trauma. One patient underwent immediate transcranial optic nerve decompression alone, while 4 patients received high dose steroids alone. Patients were followed-up for 1 to 11 months for improvement of visual function [8].

The ROBINS-I tool was used to assess the risk of bias for each of the individual studies, and the results are presented in Table 1. All of the studies were judged to have high risk for confounding bias, as they did not control for factors that might have determined the intervention used such as dose, type and timing of radiation treatment. The risk of bias in the other domains were low.

All outcomes were available for all studies. Visual improvement occurred with early surgical decompression alone in 71% of patients (n = 20/28) and with steroids alone in 51% of patients (n = 41/80). Among patients who underwent early surgical decompression, the rate of visual acuity improvement was 73% with those who underwent transcranial surgery and 69% with those who underwent endoscopic surgery. Overall, both early surgical decompression and high dose steroids did not show any statistically significant difference in improvement of visual function with homogenous results among the included studies. (RR 2.35, 95% CI 0.87 to 6.34, p=0.09, I^2 0%) (Figure 2).

Study or Sub...	Early Surgery		Steroids		Weight	Odds Ratio
	Events	Total	Events	Total		M–H, Random, 95% CI
Lesell 1989	0	1	1	4	7.1%	0.78 [0.02, 32.37]
Levin 1999	1	1	15	34	9.2%	3.77 [0.14, 99.24]
Mine 1999	10	12	14	24	33.1%	3.57 [0.64, 19.97]
Urolagin 2012	1	2	1	6	8.0%	5.00 [0.15, 166.59]
Chen 2019	8	12	10	18	42.6%	1.60 [0.35, 7.30]
Total (95% CI)		28		86	100.0%	2.35 [0.87, 6.34]
Total events	20		41			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.07$, df = 4 (P = 0.90); $I^2 = 0\%$

Test for overall effect: Z = 1.69 (P = 0.09)

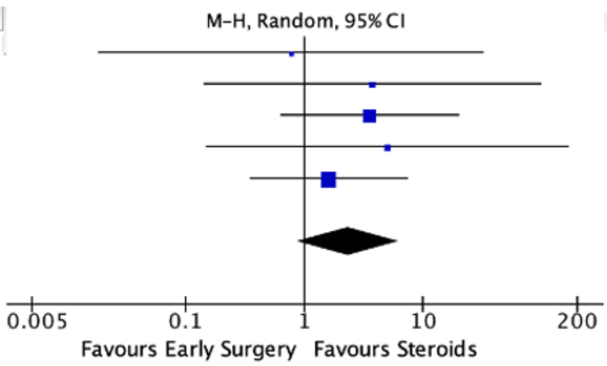

Figure 2: Forrest Plot on Surgery vs Steroids on Visual Outcome

Meta-Analysis on Timing of Intervention

The included studies had a total of 514 patients from 2004-2020 across 6 retrospective cohort studies. All patients reported received either surgical decompression or steroids. Outcomes were available for all studies included [2,3,9-12].

Visual improvement occurred in 57% of patients who received early intervention within 7 days from injury, and in 42% of patients who received late intervention 7 days after injury. Overall, both early and late intervention did not show any statistically significant difference in improvement of visual function with homogenous results among the included studies. (RR 1.72, 95% CI 0.89 to 3.35, p=0.11, I2 61%) (Figure 3).

Study or Subgroup	early		late		Weight	Odds Ratio
	Events	Total	Events	Total		M-H, Random, 95% CI
Yang 2004	10	22	8	20	14.4%	1.25 [0.37, 4.26]
Chen 2007	4	10	8	20	11.1%	1.00 [0.21, 4.71]
Quin-tai 2007	30	56	27	40	19.4%	0.56 [0.24, 1.29]
Li 2008	85	141	11	35	20.2%	3.31 [1.50, 7.29]
Yu 2016	20	33	14	42	18.0%	3.08 [1.19, 7.94]
Yan 2020	46	75	7	20	16.8%	2.95 [1.05, 8.25]
Total (95% CI)		337		177	100.0%	1.72 [0.89, 3.35]
Total events	195		75			

Heterogeneity: $Tau^2 = 0.41$; $Chi^2 = 12.73$, df = 5 (P = 0.03); $I^2 = 61\%$
Test for overall effect: Z = 1.61 (P = 0.11)

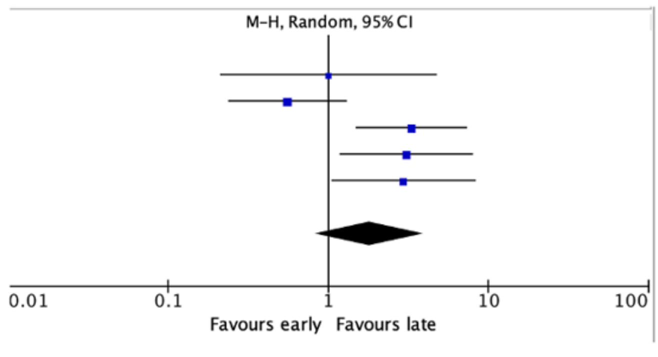

Figure 3: Forrest Plot on Early vs Late Management

Systematic Review on Visual Improvement

A total of 151 patients received high dose steroids (Table 2). Majority of these patients had pre-treatment visual acuity of more than counting fingers. Among patients with NLP, 26 of them improved after treatment (59%), 8 patients with LP improved after treatment (61%), 8 patients able to CF improved after treatment (50%) and 37 patients with more than CF improved after treatment (55%).

On the other hand, a total of 71 patients underwent surgical decompression. Majority of these patients had pre-treatment visual acuity of NLP. Among patients with NLP, 15 of them improved after treatment (57%), 7 patients with LP improved after treatment (36%), 9 patients able to CF improved after treatment (55%) and 3 patients with more than CF improved after treatment (61%).

Table 2: Post Treatment Improvement after Surgery and Steroids

	Steroids	Surgery
NLP	26/44	15/26
LP	8/13	7/19
CF	8/16	12/26
>CF	37/78	3/5

Discussion

Traumatic optic neuropathy is an uncommon but often devastating cause of permanent visual loss after blunt or penetrating injury. Visual impairment occurs in 0.7-7% of closed head injuries [1]. Approximately 80% of individuals affected are young males, and is commonly due to motor vehicle and bicycle accidents (45%), falls (27%) and assault (13%).

There are two mechanisms of injury to the optic nerve: through direct contusive force on the nerve and indirect transmission of forces causing nerve compression and disruption of vascular supply. The shearing force is transmitted to the neurovascular supply of the nerve leading to ischemic injury, vasospasm and edema. This increases intracanalicular pressure causing impaired visual function. Surgical decompression directly restores blood supply to surviving retinal ganglion cells and prevent apoptosis. High dose steroids on the other hand limit free radical damage, reduce traumatic edema and necrosis of the optic nerve [13-16].

Management of indirect traumatic optic neuropathy has been centered on decompressing the optic nerve to re-establish its function. There are three major therapeutic options for TON being used; these include medical decompression with high dose steroids, surgical decompression, and combination of these two methods. In a study by Perez , patients who underwent early intervention had significantly better outcomes (62.8% vs 46.3%) [17]. Wei et al noted that surgical decompression combined with high dose steroids resulted to better visual outcomes than steroids alone [18]. Spontaneous improvement in visual outcomes to pre-operative baseline status have been reported in 20% of cases [5]. To date, no standardized protocol have been accepted and controversy exists concerning the optimal treatment as well as the timing of intervention. No analytical study has employed utilizing surgical decompression alone compared to steroids.

This review shows that visual improvement occurred in 71% of patients who underwent immediate surgical decompression compared to 51% who were immediately given high dose steroids. However, the difference is not statistically significant and both interventions are equally effective in improving visual outcomes. Specifically, patients with NLP and LP pre-treatment resulted to better visual improvement with steroids (59% and 61% vs 57% and 36%). On the other hand, those with CF and more than CF pre-treatment, resulted to better visual improvement with surgical decompression (55% and 61% vs 50% and 55%). Furthermore, we also found out that both early and late intervention resulted in similar improvement in visual outcomes, seen in 57% and 42% of patients, respectively.

With advances in the surgical equipment and technique, optic nerve decompression has become more widespread and less risky. among patients who underwent early surgical decompression, there was higher rate of visual function improvement with transcranial surgery than endoscopic surgery (73% and 69% respectively). Transcranial surgery offers a greater degree of circumferential decompression with lower risk of CSF leak and vascular injury than Endoscopic surgery [2]. However, endoscopic technique offers advantages of decreased morbidity, rapid recovery time, more acceptable cosmetic results and less operative stress. In a study by Wang et al, complications of surgical decompression include CSF leak and Diabetes insipidus. High dose steroids may be associated with gastrointestinal bleeding and impaired wound healing [19].

Our review is limited by the scarcity of available studies resulting in a small sample size. Additionally, majority of studies included were retrospective in nature. Also, pre-operative visual outcomes reported varied (NLP, LP, HM). Despite including individuals who were treated early, there were differences in the exact time of initiation of intervention from time of injury.

Future studies comparing surgical decompression and medical optic nerve decompression may be done using large prospective cohort or randomized controlled trials to allow for standardized treatments within groups. This may help identify the specific subsets of patients with which the specific intervention is ideal. Studies involved may include the same specific surgical intervention and dosage of steroids [20-22].

Possible sources of heterogeneity include the following: timing of intervention from injury, specific surgical procedure done, variation in dosage of steroids, differences in measuring visual outcomes and diversity among patient characteristics between studies [23].

Conclusion

This meta-analysis and review shows that immediate surgical decompression and early high dose steroid administration are equally effective in improving visual function. Patients with NLP and LP pretreatment resulted to better visual improvement with steroids while those with CF and more than CF pretreatment, resulted to better visual improvement with surgical decompression. Furthermore, those who received both early and late intervention resulted in similar improvement in visual outcomes Higher rate of visual improvement was noted with transcranial surgery than endoscopic surgery [24].

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