



Review Article

# Orbital varices: Epidemiology, clinical presentation, and treatment outcomes – A scoping review

Ahmed Shakir Ali Al-Wassiti<sup>1</sup>, Danisha Kumar<sup>2</sup>, Toka Elboraay<sup>3</sup> , Mustafa Ismail<sup>4</sup>

<sup>1</sup>Department of Surgery, University of Baghdad, College of Medicine, Al Risafa, Baghdad, Iraq, <sup>2</sup>Department of Neurosurgery, Dow University of Health Sciences, Karachi, Pakistan, <sup>3</sup>Department of Neurosurgery, Faculty of Medicine, Zagazig University, Al-Sharqia Governorate, Zagazig, Egypt, <sup>4</sup>Department of Neurosurgery, Neurosurgery Teaching Hospital, Al Risafa, Baghdad, Iraq.

E-mail: Ahmed Shakir Ali Al-Wassiti - ahmed.alwassiti@comed.uobaghdad.edu.iq; Danisha Kumar - danisha.kumar21@dmc.duhs.edu.pk; Toka Elboraay - tokaelboraay20@gmail.com; \*Mustafa Ismail - mustafalorance2233@gmail.com



**\*Corresponding author:**

Mustafa Ismail,  
Department of Neurosurgery,  
Neurosurgery Teaching  
Hospital, Al Risafa, Baghdad,  
Iraq.

mustafalorance2233@gmail.com

Received: 14 May 2024

Accepted: 29 June 2024

Published: 26 July 2024

**DOI**

10.25259/SNI\_368\_2024

**Quick Response Code:**



## ABSTRACT

**Background:** Orbital varices are vein dilations in the orbit presenting various symptoms. This scoping review synthesizes existing evidence on their epidemiology, clinical features, and treatment efficacy.

**Methods:** Literature was reviewed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. PubMed and Scopus were searched until April 31, 2024, for articles on clinically diagnosed ocular varices detailing diagnostic methods, treatments, and outcomes. Exclusions were reviews, animal studies, and incomplete case reports. Data on study characteristics, diagnosis, management, and outcomes were extracted and assessed for quality and bias.

**Results:** Eight studies met the inclusion criteria, with sample sizes ranging from 4 to 30 and ages from 1 to 87 years. Diagnostic tools included magnetic resonance imaging and computed tomography, while treatments ranged from conservative methods to invasive procedures and radiosurgery. Notably, higher symptom resolution rates were associated with observational strategies and minimally invasive surgeries. However, Gamma Knife radiosurgery, although promising, posed risks of vision impairment in some cases.

**Conclusion:** The management of orbital varices has evolved significantly with newer, less invasive techniques improving outcomes and reducing recovery times. Despite advancements, challenges such as disease recurrence and the need for personalized treatment regimens persist, underscoring the ongoing need for research to refine and standardize treatment approaches.

**Keywords:** Minimally invasive surgery, Orbit, Orbital varices, Radiosurgery, Venous varix

## INTRODUCTION

Orbital varices are a specific type of aberrant blood vessels in the orbit. They are characterized by venous enlargements that are unusually uncommonly large, showing different symptoms due to their size, situation, and the presence of phlebectasia.<sup>[11,16]</sup> Although rare, their epidemiology, clinical course, and therapeutic outcomes need to be comprehended. This scoping review seeks to consolidate the available literature on orbital varices through recent studies. The review presents an overview of the epidemiological patterns, clinical presentation, and the effectiveness of various methods in treating orbital varices.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2024 Published by Scientific Scholar on behalf of Surgical Neurology International

Recent studies point to the varying presentations and the managements available in dealing with orbital varices. For example, Mokhtarzadeh *et al.*<sup>[11]</sup> note that even after interventions such as surgical excision and embolization, orbital varices could recur, especially when patients had an active lifestyle involving lifting activities, pointing to a mechanical basis for their exacerbation. In another, the role of Gamma Knife radiosurgery was explored and described as a promising and minimally-invasive modality of treatment, which provided relief in symptoms in the majority of the study patients, even as they alluded to the risk of severe complications such as vision loss.<sup>[14]</sup> In the surgical areas, Goldberg *et al.*<sup>[5]</sup> have been able to demonstrate that orbital tumors, varices included, can be resected endoscopically without bony marginotomy, thus significantly reducing patient morbidity as well as time for recovery. In contrast, Bullock and Bartley<sup>[2]</sup> were able to present a case series on dynamic proptosis related to orbital varices, which represented early descriptive data and thus constituted an integral part of knowledge useful in the differential of such conditions from orbital pathologies.

Understanding and correlating the clinical presentation of a patient with the response to treatment is important to alter the management strategy for orbital varices optimally. This review aims to provide clinicians with a consolidated source of information on the epidemiology, clinical features, diagnostic approaches, and treatment outcomes of orbital varices, thereby aiding in the recognition and effective management of this complex entity.

## MATERIALS AND METHODS

### Literature search

A comprehensive literature search was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.<sup>[12]</sup> The electronic databases PubMed and Scopus were searched from their inception to April 31, 2024. The search strategy employed a combination of Boolean operators “OR” and “AND” with search terms: “orbital varices,” “orbital veins,” “variceal management,” and “orbital surgery.” All identified references were uploaded to Mendeley to facilitate management and removal of duplicates.

### Study selection

Inclusion and exclusion criteria were carefully defined in an effort to ensure that the data retrieved for the study were relevant and accurate. The studies were included if they involved patients with clinically diagnosed orbital varices and had described in detail the methods of diagnosis, the different types of approaches to treatment adopted, and the outcomes post-treatment, with the consideration that all the studies must be published in English. Exclusion criteria were

as follows: Reviews of the literature, chapters in books, and studies that had included animal models or cadaveric data. Further, exclusion included studies not directly related to orbital varices, studies in which precise clinical data regarding diagnosis and treatment outcomes were not described, and case reports involving a small number of cases with an inadequate sample or not having enough detailed clinical follow-up. This stringent selection process was devised to obtain the most accurate and applicable information on the subject of orbital varices.

Two reviewers (M.I. and D.K.) independently screened the titles and abstracts of the articles retrieved. Discrepancies were resolved through discussion or, if needed, by consulting a third reviewer (A.A.). Full texts of potentially relevant studies were then assessed for eligibility based on the predefined criteria. References of selected articles were hand searched to identify additional studies that met the inclusion criteria.

### Data extraction

Data extraction was performed by one reviewer (D.K.) and verified independently by two other reviewers (M.I. and A.A.) Extracted information included authors, year of publication, sample size, patient demographics (age and gender), clinical presentation, methods of diagnosis, treatment modalities employed, clinical outcomes, and any reported complications. Details regarding the type and frequency of follow-up assessments, as well as any long-term care plans, were also collected.

### Data synthesis and quality assessment

The primary outcomes of interest were the clinical efficacy of treatment modalities and patient outcomes following interventions for orbital varices. Each study’s level of evidence was assessed according to the Oxford Center for Evidence-Based Medicine 2011 guidelines. The risk of bias for each included study was evaluated independently by two authors (M.I. and D.K.) using the Joanna Briggs Institute’s checklists for observational studies and it showed an overall low bias [Supplementary File 1].<sup>[7,9]</sup> Given the nature of the studies, which predominantly fell into Level IIIb of evidence, a meta-analysis was not conducted; instead, a qualitative synthesis of the results was performed to draw comprehensive conclusions from the data.

## RESULTS

### Study selection and characteristics

A comprehensive search and review process resulted in the inclusion of eight pivotal studies out of 440, spanning from 1984 to 2019, each contributing unique insights into the management of orbital varices. These studies encompass

a variety of methodologies ranging from case series to observational cohorts, with sample sizes varying from as few as 4 to as many as 30 subjects [Figure 1]. The studies extensively covered demographic data, showing a median age range from 1 to 87 years, with a slight predominance of male subjects in certain studies. Clinical presentations were diverse and often related to the direct effects of orbital varices, such as dynamic proptosis, pain, and changes in ocular motility [Table 1].<sup>[1-3,5,8,11,13,16]</sup>

### Diagnostic and management approaches

The diagnostic tools used in all studies included only advanced imaging modalities, such as magnetic resonance imaging (MRI) and computed tomography scans, with clinical evaluations and some tests, such as high-frequency ultrasonography and fluorescein angiography. Treatment approaches showed a high level of variation and, in doing so, showed an increasingly conservative and technological advancement in approach over time, with significant differences between each study. Particularly, Jain *et al.*<sup>[8]</sup> purely followed up on the patients who did not receive any interventional treatments, while Xu *et al.*<sup>[16]</sup> used Gamma Knife radiosurgery to obliterate it, which demonstrates how the approach to orbital varices is changing from intervention to observation.

### Treatment outcomes

In most of the studies mentioned, the results of treatment applied in the case of orbital varices were favorable, and improvement of symptoms was noticed in the majority of cases. For example, Jain *et al.*<sup>[8]</sup> observed eight in 28 eyes of the patients, and in cases treated conservatively without implementing some special procedures, stable conditions or regression of the symptoms were noted, which indicates that conservative approaches could be very feasible in some cases. On the other hand, the studies of Goldberg *et al.*<sup>[5]</sup> and those of Beyer *et al.*<sup>[11]</sup> explored the surgical approach, including both traditional and minimally invasive procedures. Symptoms improved significantly or disappeared completely in most of the patients after the surgical procedures and related complications were minimal, which indicates the effectiveness of the surgical approach to the treatment of orbital varices. In the instance of a special treatment approach, the study undertaken by Xu *et al.*<sup>[16]</sup> researched Gamma Knife radiosurgery and found that it reduced varix in 71.4% of patients, as observed by MRI technique, where no varix was noted 6–18 months after the radiosurgery. However, this approach also had some risks because, in a single case, the loss of sight was observed, which indicates that a special selection of patients should be undertaken in correlation with the risks of such treatment modalities.

### Complications

In all studies, complications were rare and mostly minor, with exceptions like the reported vision loss in Xu *et al.*<sup>[16]</sup> On the whole, the risk of serious complications remains low, so with a cautious selection of the mode of treatment, orbital varices can be treated effectively with the least long-term detriment to the patient.

## DISCUSSION

The management of orbital varices poses significant challenges due to the complex anatomical and physiological characteristics of the orbit. Recent literature and case studies reflect a diversity of management strategies and outcomes, highlighting the importance of tailored approaches based on individual patient presentations.

### Surgical, non-surgical, and observational management

In earlier interventions, surgical excision was often considered a primary treatment for symptomatic orbital varices. Beyer *et al.*<sup>[11]</sup> describe a surgical approach involving vascular clips, which resulted in substantial improvements in most patients without recurrence, although one case failed due to hemorrhaging. The evolution of surgical techniques toward less invasive procedures is illustrated by Goldberg *et al.*<sup>[5]</sup>, who successfully utilized minimally invasive soft-tissue approaches under local or general anesthesia, avoiding the morbidity associated with bony marginotomy. In contrast, recent studies have explored observational and conservative management approaches. Jain *et al.*<sup>[8]</sup> observed stable conditions or regression of symptoms in patients managed conservatively without any intervention. This suggests that in select cases, observation can be a feasible option, particularly in patients with mild symptoms or when the risks associated with interventional treatments are deemed to outweigh potential benefits. The observation of patients with orbital varices can be a viable management strategy, particularly in cases where symptoms are mild or stable. However, it is essential to consider individual patient factors, the potential for recurrence, and the need for long-term data to assess the efficacy and safety of this approach fully. Combining observational strategies with minimally invasive interventions, as appropriate, may offer a balanced approach to managing this complex condition.

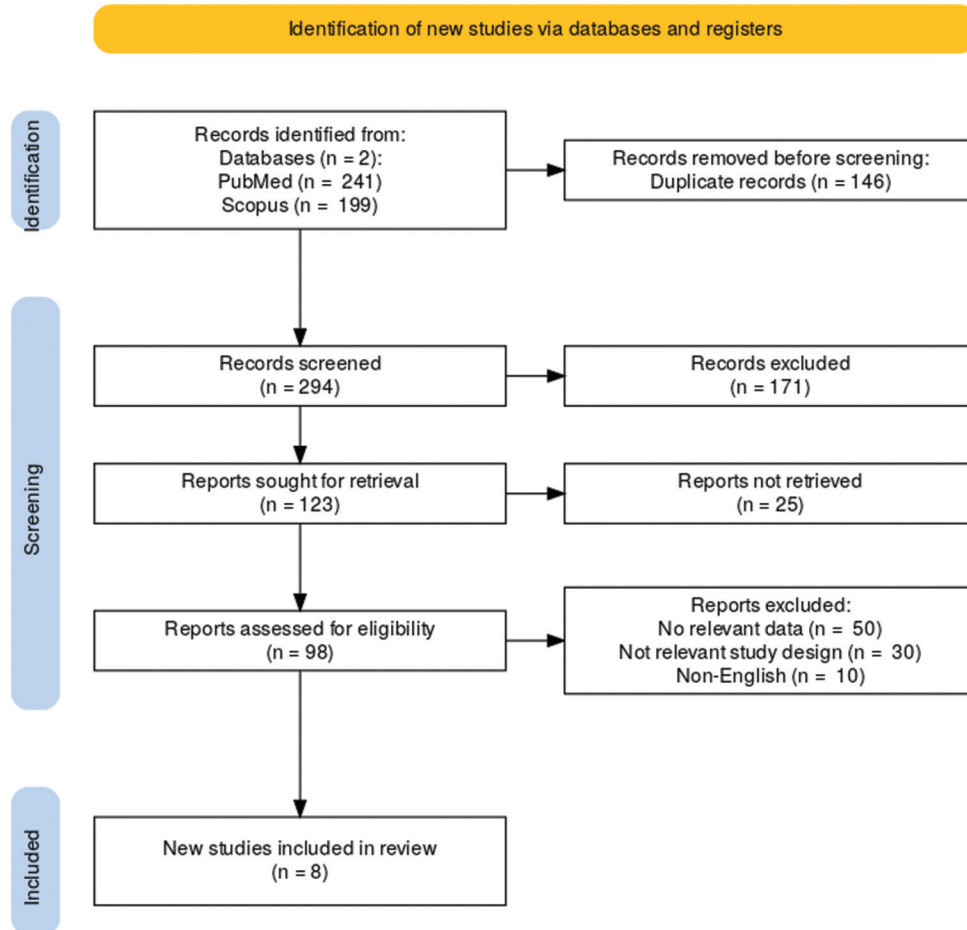
### Role of embolization

Embolization techniques have also evolved, offering a less invasive alternative or adjunct to surgery. Xiao *et al.*<sup>[15]</sup> report on the use of Glubran 2 acrylic glue for embolization, noting improvements in symptoms with minimal complications. This aligns with findings from Couch *et al.*<sup>[4]</sup>, who

**Table 1:** An overview of the included studies.

Author (s)	Year	Sample Size	Level of Evidence	Gender (% Male)	Age Range (Mean/Median $\pm$ SD)	Clinical Presentation	Diagnosis Methods	Treatment Approach	Outcomes	Complications
Jain et al. <sup>[8]</sup>	2019	26	IIIb	57.7	37–81 years (Mean age: 58.3 Median age: 57.5)	Varied symptoms related to iris varices	Clinical examination, slit-lamp biomicroscopy with photography, tonometry, gonioscopy with photography, dilated indirect ophthalmoscopy, high-frequency ultrasonography (20–50 MHz), and iris fluorescein angiography.	Observation	27 eyes had stable varix, and 1 eye showed regression.	No complications reported
Mokhtarzadeh et al. <sup>[11]</sup>	2014	4	IIIb	75	18–43 years (Median not specified)	Positional or Valsalva-induced pain or proptosis, objective increase in exophthalmos in a dependent position, diplopia	Clinical examination, MRI, CT	Embolization with n-butyl cyanoacrylate, craniotomy	All patients had a recurrence of symptoms, though milder than initial, post-operative diplopia with extreme gaze, but demonstrated resolution of all other symptoms and resolution of the Valsalva-induced proptosis.	Recurrences related to physical activities after first intervention, After second procedure revealed resolution of symptoms without further complications.
Goldberg et al. <sup>[5]</sup>	2014	30 (only one case of orbital varix)	IIIb	43.3	31–87 years (Median 48.5)	Middle to deep orbital tumors	MRI or CT scan	Minimally invasive soft-tissue approaches under local/general anesthesia	Improvement or no significant change in visual acuity and ocular motility. No recurrences	no severe intra- or postoperative surgical complications.
Xu et al. <sup>[16]</sup>	2010	14	IIIb	42.9	7–56 years (Median 24.5)	Intermittent proptosis, secondary to Valsalva-induced increased venous pressure.	Clinical examination, MRI/CT	Gamma knife radiosurgery	71.4% MRI showed no varix 6–18 months	One case of sight loss, no intraorbital hemorrhages. Reversible conjunctival edema in two cases.
Polito et al. <sup>[13]</sup>	1993	17	IIIb	41.1	9–72 years (Mean not specified)	Perimetric damage directly resulting from optic nerve compression; orbital affection with visual field defects.	Clinical examination, Doppler ultrasound, MRI/CT	Surgical excision or medical treatment	Steroid therapy showed an improvement in visual field alterations. Prednisone was administered, and the scotoma resolved.	A diffuse loss was primarily observed in two cases of large hemangiopericytomas.
Bullock and Bartley <sup>[2]</sup>	1986	26	IIIb	50	1–82 years	Dynamic proptosis, spontaneously induced by variable forces on the orbit	Clinical examination, CT scans	Varied, including surgery and non-surgical management	Varied outcomes, visual acuity was 20/20. No loss of visual and ocular motility.	One case had marked edema in the right temporal fossa, resulting in proptosis of the right eye with mastication.
Beyer et al. <sup>[1]</sup>	1985	5	IIIb	40	10–58 years	Varied symptoms related to orbital varices	Clinical examination	Surgical excision using vascular clips	Three cases were cured, and one was markedly improved. No recurrence was reported.	One case failed due to hemorrhaging.
Cline and Rootman <sup>[3]</sup>	1984	26 (only two cases of orbital varix)	IIIb	46.1	4–77 years	Pain, proptosis, discomfort, trauma, enophthalmos, diplopia, ptosis, sclerotic lids, coloboma, neurofibromatosis, Valsalva exophthalmos, Retinoblastoma	Clinical examination, X-ray, ultrasound, CT scan	Surgical repair, radiotherapy	Not mentioned	No major complications listed

MRI: Magnetic resonance imaging, CT: Computed tomography



**Figure 1:** Preferred reporting items for systematic reviews and meta-analyses flow diagram of the studies.

demonstrated that pre-surgical embolization with n-butyl cyanoacrylate can facilitate surgical excision by reducing the size of the varices and controlling bleeding, although recurrent varices were noted in cases of significant physical activity.

### Advances in radiosurgery

The development of radiosurgical techniques has opened a more optimistic view. Xu *et al.*<sup>[16]</sup> investigated the effect of Gamma Knife radiosurgery in orbital varices and proved the potential to alleviate symptoms in an important percentage of patients but also showed the associated risks, such as loss of sight – although this is an extremely rare risk.

### Case report insights

Individual case reports provide deeper insights into unique presentations and management challenges. For example, Tsai *et al.*<sup>[14]</sup> discuss the management of bilateral orbital varices, emphasizing the variability in treatment responses and

the need for individualized management plans. Similarly, Mokhtarzadeh *et al.*<sup>[11]</sup> highlight the potential for recurrence after surgical and embolization interventions, particularly in patients with active lifestyles that involve heavy lifting, underscoring the need for careful post-operative counseling and lifestyle modification. Lizana *et al.*<sup>[10]</sup> detail a 41-year-old woman with obesity and diabetes who developed bilateral central retinal artery occlusion (CRAO) following cranial surgery, a rare and severe complication. This underscores the importance of early ophthalmological evaluation and treatment in patients undergoing such procedures to prevent irreversible visual impairment. Despite early treatment with hyperbaric oxygen therapy, the patient showed only marginal improvement in her peripheral visual field. This case underscores the rarity and severity of bilateral CRAO as a complication following cranial surgery, emphasizing the need for vigilance and prompt ophthalmological evaluation in such patients to mitigate potentially devastating visual outcomes.

Furthermore, other complications can include thrombosis, leading to embolic events such as retinal artery occlusion,



spontaneous hemorrhage causing acute proptosis and vision loss, and infection leading to orbital cellulitis.<sup>[6,16]</sup> Vision loss can also result from compressive optic neuropathy or macular involvement. Although rare, neovascular glaucoma can occur, primarily due to chronic hypoxia rather than acute arterial occlusion. Surgical interventions carry risks of damage to adjacent structures, incomplete excision, and recurrence. Advances in embolization and radiosurgical techniques offer promising treatment avenues but require careful consideration of risks such as ischemia- and radiation-induced damage.<sup>[8]</sup> Understanding these complications is crucial for optimizing diagnostic and therapeutic strategies.

### Limitations

Inherent, however, are some limitations given the variation in research designs and the variation in methods of treatment: It uses retrospective data and is based on data that are already accessible. Much stronger prospective study designs are needed for further enlightenment on this and in techniques for the management of orbital varices, more so in their long-term efficacy and recurrence post-treatment.

In conclusion, ocular varices have evolved from conventional surgical techniques to less invasive ones, including radiosurgery options; all this contributes to better outcomes with less complication. While surgical intervention remains a cornerstone in the management of orbital varices, observational and less invasive approaches are gaining recognition. However, the problem is likely to be a recurring one and, thus, calls for a tailor-made, patient-centered approach to optimize the quality of care administered to these individuals.

### CONCLUSION

The management of orbital varices has evolved significantly from classical and invasive surgical techniques toward minimally invasive approaches, aided by adjunctive embolization and radiosurgery. Our review and analysis of the literature illustrate this evolution, with studies highlighting that by the effectiveness of Gamma Knife radiosurgery in reducing varices with minimal complications, compared to traditional surgical approaches. This shift reflects a broader trend toward less invasive interventions, reducing the risk of morbidity and improving recovery times. However, despite these advancements, the risk of recurrence remains, underscoring the need for a patient-centered approach based on individual factors. Future research should focus on long-term outcomes and the development of standardized protocols to further optimize the management of this complex condition.

### Ethical approval

The Institutional Review Board approval is not required.

### Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

### REFERENCES

1. Beyer R, Levine MR, Sternberg I. Orbital varices: A surgical approach. *Ophthalmic Plast Reconstr Surg* 1985;1:205-10.
2. Bullock JD, Bartley GB. Dynamic proptosis: A sign of orbital varices. *Arch Ophthalmol* 1986;104:1512-6.
3. Cline RA, Rootman J. Enophthalmos: A clinical review. *Ophthalmology* 1984;91:229-37.
4. Couch SM, Garrity JA, Cameron JD, Cloft HJ. Embolization of orbital varices with N-butyl cyanoacrylate as an aid in surgical excision: Results of 4 cases with histopathologic examination. *Am J Ophthalmol* 2009;148:614-8.e1.
5. Goldberg RA, Rootman DB, Nassiri N. Orbital tumors excision without bony marginotomy under local and general anesthesia. *J Ophthalmol* 2014;2014:424852.
6. Hayreh SS, Podhajsky PA, Zimmerman MB. Retinal artery occlusion: Associated systemic and ophthalmic abnormalities. *Ophthalmology* 2009;116:1928-36.
7. Howick J, Chalmers I, Glasziou P, Greenhalgh T, Heneghan C, Liberati A, *et al.* Explanation of the 2011 Oxford Centre for evidence-based medicine (OCEBM) levels of evidence (background document). Oxford Centre for Evidence-Based Medicine; 2011. Available from: <https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebml-levels-of-evidence> [Last accessed on 2024 May 07].
8. Jain S, Desai RU, Charalel RA, Quencer K, Doshi AH, Feuer W, *et al.* The efficacy and safety of propranolol as first-line treatment for infantile hemangiomas. *Pediatrics* 2019;143:e20183224.
9. Joanna Briggs Institute. Checklist for case series; 2020. Available from: <https://jbi.global/critical-appraisal-tools> [Last accessed on 2024 May 07].
10. Lizana J, Reinoso CM, Aliaga N, Marani W, Montemurro N. Bilateral central retinal artery occlusion: An exceptional complication after frontal parasagittal meningioma resection. *Surg Neurol Int* 2021;12:397.

11. Mokhtarzadeh A, Garrity JA, Cloft HJ. Recurrent orbital varices after surgical excision with and without prior embolization with n-butyl cyanoacrylate. *Am J Ophthalmol* 2014;157:447-50.
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
13. Polito E, Burrioni L, Pichierra P, Loffredo A, Vattovani O. Choroidal nevi: A comparison of the clinical and histopathological features with age. *Arch Ophthalmol* 1993;111:645-50.
14. Tsai A, Fong K, Lim W, Al Jajeh I, Chuah CT, Rootman J. Bilateral orbital varices: An approach to management. *Ophthalmic Plast Reconstr Surg* 2008;24:486-8.
15. Xiao LH, Lu XZ, Wang Y, Yang XJ, Wei HF, Zhu H. Preliminary observations of embolization treatment of orbital varices with Glubran 2 acrylic glue. [*Zhonghua Yan Ke Za Zhi*] *Chin J Ophthalmol* 2009;45:436-40.
16. Xu D, Liu D, Zhang Z, Zhang Y, Song G. Gamma knife radiosurgery for primary orbital varices: A preliminary report. *Br J Ophthalmol* 2010;95:1264-7.

**How to cite this article:** Al-Wassiti AS, Kumar D, Elboraay T, Ismail M. Orbital varices: Epidemiology, clinical presentation, and treatment outcomes – A scoping review. *Surg Neurol Int.* 2024;15:258. doi: 10.25259/SNL\_368\_2024

### Disclaimer

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Journal or its management. The information contained in this article should not be considered to be medical advice; patients should consult their own physicians for advice as to their specific medical needs.

## SUPPLEMENTARY FILE

**Supplementary File 1:** Risk of bias assessments for included studies.

Joanna Briggs Institute's checklist for case series – criteria

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 the 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 a 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?

Responses Options: Yes, No, Unclear, NA

Quality Rating: Poor 0–3; Fair 4–7; Good 8–10

NA: Not applicable

Study	1	2	3	4	5	6	7	8	9	10	Rating
Cline and Rootman–1984	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	9–Good
Beyer <i>et al.</i> –1985	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	9–Good
Bullock and Bartley–1986	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	9–Good
Polito <i>et al.</i> – 1993	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	9–Good
Xu <i>et al.</i> –2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	10 – Good
Goldberg <i>et al.</i> –2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	9–Good
Mokhtarzadeh <i>et al.</i> - 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	9–Good
Jain <i>et al.</i> –2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	9–Good
NA: Not applicable											