Understanding Trochlear Nerve Palsy: Etiological Perspectives from the Literature

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Trochlear nerve palsy, congenital, traumatic, microvascular, idiopathic, diplopia, epidemiology

ABSTRACT:
Introduction: The trochlear nerve (cranial nerve IV) innervates the superior oblique muscle and is critical for eye movement control. As the thinnest and longest cranial nerve, it has unique anatomical and functional characteristics. Trochlear nerve palsy results in paralytic strabismus and diplopia, with treatment approaches varying based on etiology.
Aim: To synthesize and analyze existing literature on the prevalence and etiology of trochlear nerve palsy (TNP).
Methods: Literature review of major studies examining TNP, focusing on etiological distribution, clinical presentation, and demographic patterns across different patient populations.
Results: Congenital TNP prevalence varied between 8-77.45% across studies, with most common presentation in the fourth decade of life. Traumatic causes represented 20-35% of cases, predominantly affecting males (60%) in their third decade. Microvascular causes accounted for 13-24% of cases, mainly presenting in the seventh decade and associated with hypertension and diabetes. Idiopathic cases ranged from 4-23%. Rare causes included tumors (9%) and other miscellaneous conditions (15%). Diplopia was more frequently reported in acquired versus congenital cases.
Conclusions: TNP presents with diverse etiologies, varying significantly across studies. Standardized diagnostic criteria and longitudinal studies are needed for better categorization and understanding of disease progression. Early recognition of underlying causes is crucial for targeted treatment strategies, particularly in patients with trauma history or systemic vascular conditions.

2. Intro

2.1 The trochlear nerve

2.1.1 Anatomy and history of illustration

Thomas Willis, in 1664, accurately illustrated the trochlear nerve, which he referred to as the "pathetic nerve" (Haines, 2018) because, "… this nerve innervates the movement of the eyes hastily, based in the forces of passion and instinct of nature." For this reason, the trochlear nerve has been known as the "pathetic" nerve throughout the 19th century (Vilensky, Robertson, & Suarez-Quian, 2015).

The trochlear nerve is anatomically special in many ways:

- It has the lengthiest intracranial pathway, spanning about 6 cm in total.
- The muscle it innervates is also the longest of all extra-ocular muscles.
- It is the only cranial nerve that comes out of the posterior part of the brainstem.
- It is the only cranial nerve whose fibres decussate almost entirely inside the central nervous system.
- Out of all the cranial nerves, the trochlear nerve is the smallest in volume.

Because of its length, the trochlear nerve is predisposed to injuries such as trauma, tumors, and increased intracranial pressure. Still, injuries due to these causes are usually accompanied by secondary symptoms based on the anatomic location of nearby structures. Isolated injuries of the trochlear nerve due to these causes are infrequent (Dosunmu, Hatt, Leske, Hodge, & Holmes, 2018; Mollan, Edwards, Price, Abbott, & Burdon, 2008; von Noorden, Murray, & Wong, 1986).

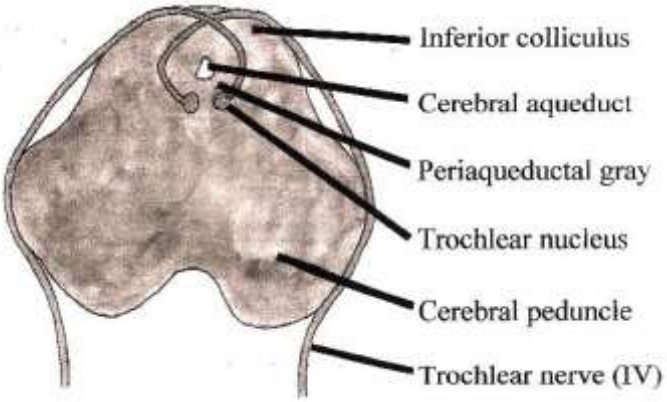
The trochlear nerve is a delicate bundle of nerve fibers. It consists of 1,700 to 3,400 nerve fibers and has a thin attachment to the brainstem (Vilensky, Robertson, & Suarez-Quian, 2015).

Generally, the trochlear nerve pathway can be categorized into three parts (Salmon, 2020) (Figure 2):

1. The trunk
2. The inter-cavernous section
3. The orbital section

The left and right trochlear nerves come out of their respective nuclei inside the brainstem (near the inferior colliculi), ending contralaterally from their respective departure points (Figure 1). In the decussation zone, because of their proximity, a single lesion may injure both nerves (Vilensky, Robertson, & Suarez-Quian, 2015).

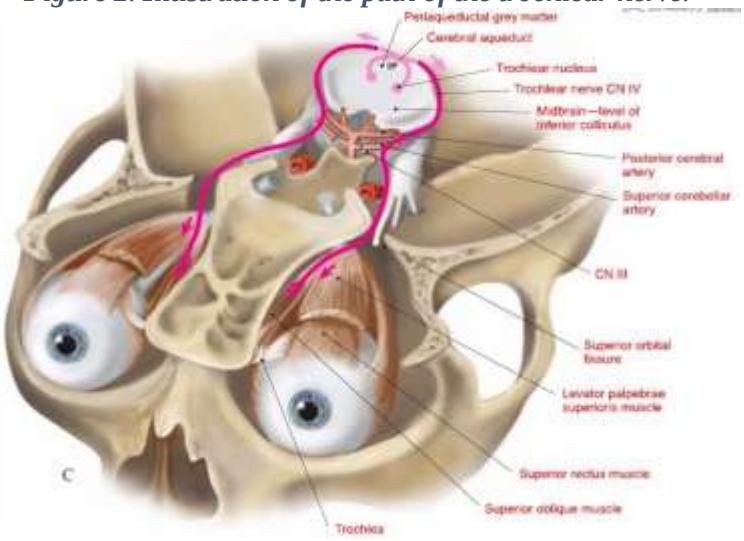
Figure 1. Trochlear nerve exits out of the brain stem and its relation with nearby structures.



Source: *Adapted from "Brain stem sagittal section" by Patrick J. Lynch, medical illustrator, 2006,* Creative Commons Attribution 2.5 License. *Retrieved from https://commons.wikimedia.org/wiki/File:Brain_stem_sagittal_section.*

After their respective exits from the brain stem, the trunk of the trochlear nerve is formed. The nerves first go laterally around the Pons and then straight until they perforate the Dura, to finally continue inside the cavernous sinus, forming the inter cavernous section of the nerves' pathway.

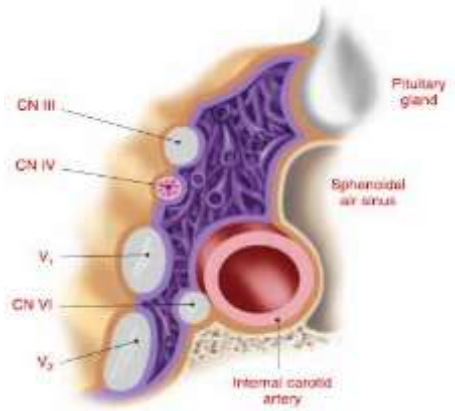
Figure 2. Illustration of the path of the trochlear nerve.



Source: Reproduced with permission from *Wilson-Pauwels, L., Steward, P., Akesson, E., & Spacey, S.* (2010). *Cranial nerves: Function and dysfunction* (2nd ed.). PMPH-USA.

Inside the cavernous sinus, the trochlear nerve goes ventrally above the abducens nerve and around the upper border of the trigeminal nerve ophthalmic branch, with which it is connected by fibrous tissue. In this zone, the trochlear nerve is in close relation with other important structures (Figure 3). The nerve's path then continues inside the orbit, which also constitutes its final sector. Spanning above the superior orbital fissure, above the levator palpebrae muscle's attachment, then going medially and ventrally, to finally synapse with the superior oblique muscle, which it innervates.

Figure 3. The relationship of the trochlear nerve to other significant structures during its passage through the cavernous sinus.



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2.1.2 Neuroanatomy

The trochlear nerve's nucleus is located at the level of the superior cerebellar peduncle's intersection fibers, part of which are in the central part of the tegmentum at the level of the inferior colliculus. The efferent somatic cells of the trochlear nucleus make up a group of oval- shaped cells inserted into the fibers of the Medial Longitudinal Fasciculus (Haines, 2018). The nucleus of the trochlear nerve supplies most of the contralateral neurons of the superior oblique muscle, while supplying only 10% of the neurons on the ipsilateral muscle (Conn, 2016).

The trochlear nerve has only somatic efferent nerve fibers. These fibers synapse with the superior oblique muscle, therefore a trochlear nerve palsy causes loss of the muscle's function in all its movements.

2.2 The superior oblique muscle

2.2.1 Anatomy

The superior oblique muscle is one of the two oblique extra-ocular muscles. These muscles attach to the eyeball in an angle, both attaching at the posterior part of the eyeball.

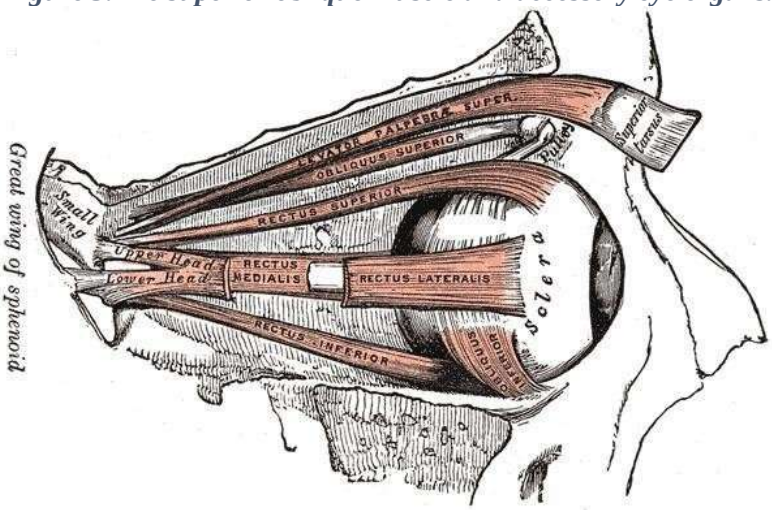
The superior oblique muscle attaches to the trochlea, a fibro-cartilagenous outing attached to the fovea of the frontal bone (Figure 4).

Figure 4.Illustration of the trochlea.

Source*: Patrick J. Lynch. Creative Commons Attribution 2.5 License, 2006. Retrieved from https://commons.wikimedia.org/wiki/File:Eye_movements_depressors.jpg.*

The superior oblique muscle originates from the periosteal layer of the sphenoid bone, then spans around the medial border of the orbit's roof, arriving at the trochlea. Here, it loops posterolaterally to finally attach in the outer and posterior quadrate of the eyeball (Figure 5).

Figure 5.The superior oblique muscle and accessory eye organs.



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The superior oblique muscle is the longest extra-ocular muscle, with its tendon's length being the main contributor. The muscle's tendon is approximately 11 mm in length.

The superior oblique muscle consists of type I (slow) fibers and type II (fast) fibers, like other extra-ocular muscles.

2.2.2 Function

The superior oblique muscle's actions are categorized as primary, secondary, and tertiary actions.

***Table 1.Extra-ocular muscles actions and innervation**. **Source**: Authors*

Nerve and muscle	Primary action	Secondary action	Tertiary action
Cranial Nerve III			
Superior rectus	Elevation (maximal in lateral gaze)	Intorsion	Adduction
Inferior rectus	Depression (maximal in lateral gaze)	Extorsion	Adduction
Medial rectus	Adduction	None	None
Inferior oblique	Extorsion	Elevation (maximal in medial gaze)	Abduction
Cranial nerve IV			
Superior oblique	**Intorsion (in straight and lateral gaze)**	**Depression (in straight and medial gaze)**	**Abduction (in straight gaze)**
Cranial nerve VI			
Lateral rectus	Abduction	None	None

The superior oblique muscle causes the eyeball to move in all three axes:

1. In straight gaze, when the muscle is activated, the eyeball moves in all three axes. In the X axis, the eye goes downwards (depression), in the Y axis abduction occurs while in

the Z axis there's intorsion of the eye (Figure 6, 7)

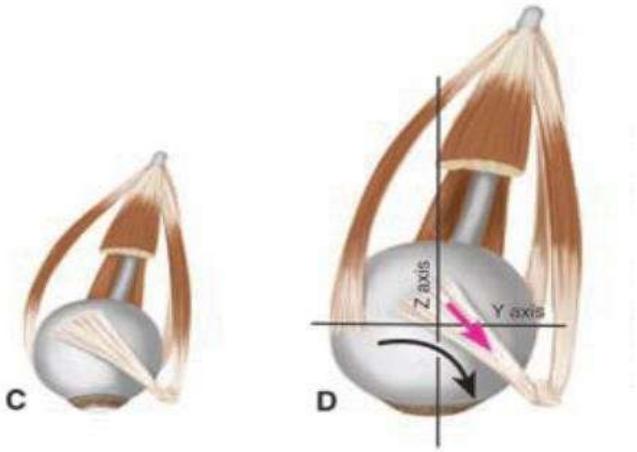
2. When the eye is in adduction, the superior oblique muscle causes eyeball depression by rotating the eye along its Y axis (Figure 8, 9). Being the sole depressor of the eye in this position, this isolated action of the superior oblique muscle is vital in the diagnostic process of trochlear nerve palsies.
   When the eye is in abduction, the superior oblique muscle causes eyeball intorsion by rotating the eye along its Z axis (Figure 10.)

Physiologically, normal eye alignment is dependent on proper coordination of all extra-ocular muscles in an agonist-antagonist manner. This has been studied since antiquity by Descartes in 1626, who on a study paper among other things concluded that:

1. *Agonist/antagonist muscles receive equal innervation. So, in straight-line gaze, the superior and inferior oblique muscles contract equally and the gaze line remains rectilinear. Or, in downward gaze, for example, the inferior rectus muscle contracts while the superior rectus muscle relaxes.*

Therefore, the superior oblique muscle, with its actions, contributes equally to normal eye alignment and movement, as other antagonist extra-ocular muscles.

Figure 6. Illustration of the superior oblique muscle in action. Source. Reproduced with



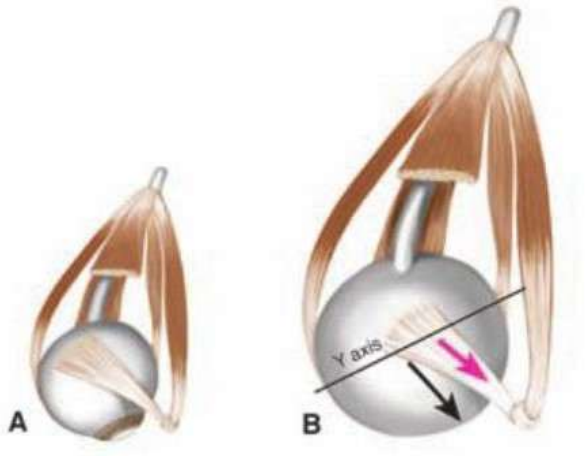
RIGHT EYE IN FORWARD GAZE

c) At rest: Superior oblique muscle in forward gaze

d) In action: In forward gaze, superior oblique muscle contraction rotates the eye in all axes, resulting in intorsion, depression and abduction

permission from *Wilson-Pauwels, L., Steward, P., Akesson, E., & Spacey, S.* (2010). *Cranial nerves: Function and dysfunction* (2nd ed.). PMPH-USA.

Figure 7. Illustration of the superior oblique muscle in action in forward gaze.
A)*Eye position after superior oblique muscle contraction. When looking downwards in forward gaze, the superior oblique muscle causes intortion and mild depression and abduction of the eye.****B)*** *The eye in neutral position.****C)****Eyeball in cases of trochlear nerve palsy. Because of amplification of the elevator action of the superior rectus muscle, there's eye hypertropia and mild extortion.****Source****: Created by the authors.*



RIGHT EYE IN ADDUCTION

a) At rest: The superior oblique while the eye is adducted

b) In action: In adduction, superior oblique contraction causes eyeball depression

Figure 8. Superior oblique muscle action in medial gaze. Source. Reproduced with permission from *Wilson-Pauwels, L., Steward, P., Akesson, E., & Spacey, S.* (2010). *Cranial nerves: Function and dysfunction* (2nd ed.). PMPH-USA.

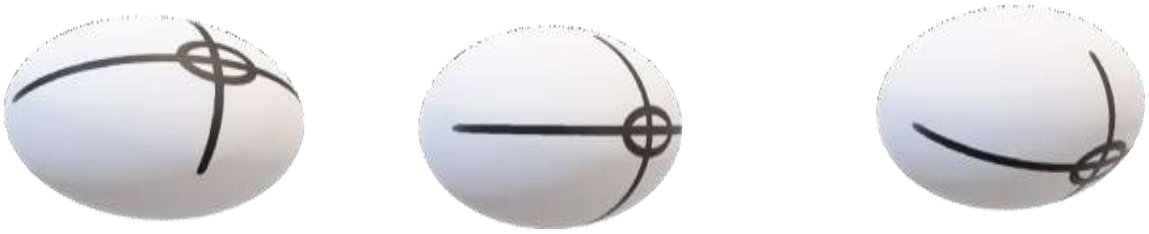


Figure 9. The superior oblique muscle in action in medial gaze.
A) The eye in elevation. When there's no underlying pathology, this is a normal action of the inferior oblique muscle. This position can also be pathological in trochlear nerve palsy, due to the eye remaining elevated in the adducted position because of lack of an antagonizing force by the superior oblique muscle to depress the eye. B) The eye in normal position in medial gaze. C) After contraction, the superior oblique muscle causes eyeball depression in medial gaze. ***Source****: Created by the authors.*

RIGHT EYE IN ABDUCTION

e) At rest: The superior oblique when the eye is abducted

f) In action – In adduction, superior oblique contraction causes intortion of the eye by rotating the eyeball along its Z axis.

Figure 10. Illustration of the superior oblique muscle's action in lateral gaze. Source. Reproduced with permission from*Wilson-Pauwels, L., Steward, P., Akesson, E., & Spacey, S.* (2010). *Cranial nerves: Function and dysfunction* (2nd ed.). PMPH-USA.

2.3 Trochlear nerve palsy

2.3.1 Intro

"Palsy" means weakening and partial loss of function of a nerve. In our case, trochlear nerve palsy leads to paralytic strabismus as a result of the inability of the muscles to keep both eyes aligned at the same level. This can result by any lesion along its path. As previously discussed, because of it being a very long and thin nerve, theoretically the possibility of lesions as a result of trauma is higher. Etiological evaluation of trochlear nerve palsies is the main issue that will be discussed in this research.

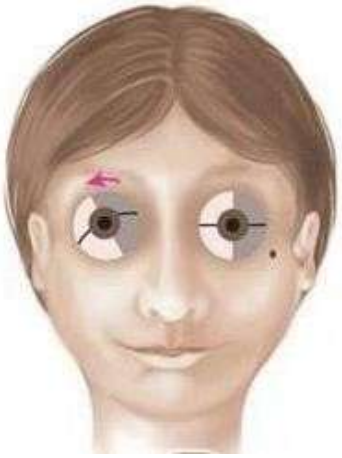
2.3.2 Clinical signs

Trochlear nerve palsy is the most frequent cause of vertical strabismus in children (Khanna et al., 2024), but patients can present at any age (Dosunmu, Hatt, Leske, Hodge, & Holmes, 2018; Khaier, Dawson, & Lee, 2012; Mollan, Edwards, Price, Abott, & Burdon, 2008).

Patients with trochlear nerve palsy usually complain of binocular double vision (that is, with both eyes open), and "tilting" of images (torsional diplopia). Because the superior oblique muscle depresses the eye in the adducted position, patients often complain of having double vision especially when going down the stairs or reading the newspaper.

On examination in forward gaze, ipsilateral hypertropia (deviation of the eye upwards) and extorsion (rotation from the outside) of the affected eye are observed. This happens because in forward gaze, the superior oblique muscle intorts and depresses the eyeball. (Figure 11)

Figure 11. Clinical picture illustration of a patient with trochlear nerve palsy. Hypertropia and extorsion of the eye can be noticed.



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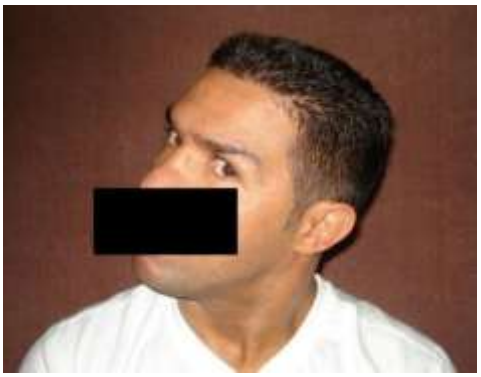
Another important clinical sign is when patients present with an abnormal head posture (ocular torticollis), which they may or may not be aware of (Figures 12, 13). This happens because torsional and vertical diplopia are usually improved by tilting the head to the opposite side of the lesion (thereby adjusting the longitudinal axis of the eye), causing patients to tilt their head instinctively. Looking at old photographs of the patient can also be helpful in the diagnostic process, in order to observe if there's been head tilting by the patient earlier. Some patients may even close one eye while reading, unconsciously.

The findings mentioned above speak of isolated paresis of the trochlear nerve. Cases of trochlear nerve palsy accompanied by secondary symptoms such as hemiparesis, headache, Horner's syndrome, etc., should be investigated more thoroughly. Inside the CNS, the trochlear nerve's axons can be injured by infarction, tumour, or demyelination. In the subarachnoid space, injuries by a tumour or meningitis may occur, while in the cavernous sinus, the nerve can be injured as a result of aneurysms of the internal carotid artery, thrombosis of the cavernous sinus, and tumours (Wilson-Pauwels, Steward, Akesson, & Spacey, 2010). It is rare for non-isolated lesions (such as subarachnoid haemorrhage) to present with trochlear nerve palsy as the sole symptom (Adachi, Hironaka, Suzuki, & Oharazawa, 2012; Raghavendra, Vasudha, & Shankar, 2010).

Figure 12.**A patient presenting with abnormal head posture. The head is tilted to the left**.



Source*: Reprinted from* Paradoxical head tilt in unilateral traumatic superior oblique palsy, *by M. R. Akbari, R. Bayat, A. Mirmohammadsadeghi, & R. Mirshahi, 2017,* Journal of Current Ophthalmology, *29(3), 221–223. Copyright 2017 by Iranian Society of Ophthalmology. Production and hosting by Elsevier B.V. Open access under the Creative Commons Attribution-NonCommercial-NoDerivatives (CC BY-NC-ND) License. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5587224/.*

Figure 13. When patients tilt their head to the affected side, the inferior oblique and inferior rectus muscles are activated to cause extorsion of the eye. The superior oblique muscle is not activated in this position. The eyes are aligned and diplopia improves.

Source: Reproduced with permission from*Wilson-Pauwels, L., Steward, P., Akesson, E., & Spacey, S.* (2010). *Cranial nerves: Function and dysfunction* (2nd ed.). PMPH-USA.

2.3.3 Clinical evaluation and diagnosis

Trochlear nerve palsy should be suspected in all patients presenting with vertical strabismus or those complaining of binocular vertical diplopia, and/or in all patients complaining of tilting of objects.

Diagnosis can be confirmed by a positive three-step test, first reported by Bielschowsky (1935). Therefore, this test is also known as the Parks-Bielschowsky test, based on its authors. Although it is a simple clinical test, if performed correctly, it has a high sensitivity rate in clinical diagnosis, about 75% (Lee, Yang, Kim, & Hwang, 2018).This test is performed in three steps:

1. First step – *Which eye is hypertropic (higher)?*

   Defining the hypertropic eye pinpoints the lesion to only 4 extraocular muscles. So, if strabismus is noticed and the right eye seems hypertropic, then we can conclude that there's either a problem with the right eye (it is higher than it should be), or the left eye is lower than it should be. Theoretically, the lesion may now be on:

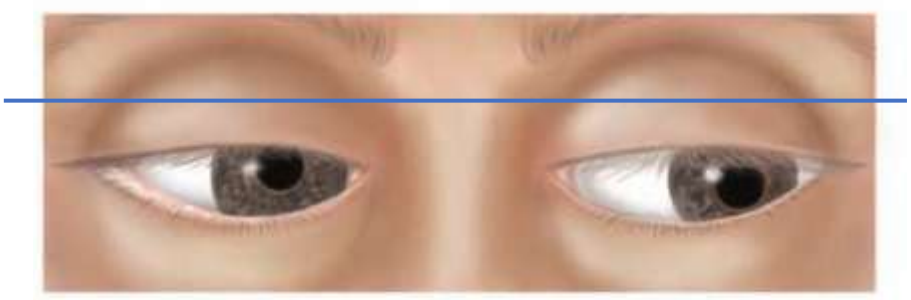
   1. Depressors of the right eye – Right superior oblique and Right Inferior Rectus (they are not contributing in lowering the right eye to the level of the left eye), or
   2. Elevators of the left eye – Leftinferior oblique and Left Superior Rectus (they are not contributing to raise the left eye to the level of the right eye).

2. Second step – *Does the hypertropia worsen in left or right gaze?*
   This step is done in order to isolate the depressor function of the superior oblique muscle, considering that, in adduction, the superior oblique muscle is the sole depressor of the eye.

   While gazing to the left, the right eye is in adduction. In this position, the sole elevator of the eye is the inferior obliquemuscle,with the superior oblique muscle being the sole depressor of the eye. In this case, the right superior and inferior oblique muscles contract in equal force but in opposite directions, and thus their forces are cancelled, and the eye remains in a neutral rectilinear position.

   Subsequently, when there's a palsy of the trochlear nerve, the superior oblique muscle is not able to respond to elevator force of the inferior oblique muscle and as such the inferior oblique muscle exerts itsaction un-antagonized and the eye goes upwards. This step can be continued further by telling the patient to look downwards when the right eye is in the adducted position. In this case, even though the inferior oblique muscle relaxes and "gives way" to the antagonizing muscle, the superior oblique muscle is unable to depress the eye and the eye remains in a "neutral" position while the other eye goes downwards. (Figure 14)

Figure 14.*Inability of the superior oblique muscle to depress the right eye. The left eye is pictured in normal abduction and depression*



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3. Third step – Does *the hypertropia worsen in right or left head tilting?*

   With this step, we test the intorsion ability of the affected eye (in our case, the right eye). In normal conditions, when we tilt our head to the right, the intortors of the right eye are the right superior oblique andrectus muscles, but the superior oblique muscle also exerts a depressing action on the eye, while the superior rectus elevates it. So, if one muscle is injured, the intorsion is to some extent corrected by the other muscle, but the secondary action of the auxiliary muscle is more pronounced. Thus, in our case, if the head is tilted to the same side of the lesion (right), the eye can be intorted to an extent by the superior rectus muscle, however, since its antagonistic muscle in terms of elevation – thesuperior oblique muscle, is lesioned, the superior rectus muscle exerts its elevator action unopposed, and the eye goes upwards. When tilting the head to the opposite side of the lesion, the muscles that participate inextorsion are the inferior oblique and inferior rectus muscles. In this case,the hypertropia does not worsen because the superior oblique muscle cannot perform its primary action.

Thus, hypertropia of the right eye that worsens by gazing to the left and tilting the head to the same side is diagnostic of trochlear nerve palsy. Inconsistencies in this evaluation suggest that there may not be an isolated lesion of the trochlear nerve, and other diagnoses should be considered.

2.3.5 Treatment

2.3.5.1 Non-surgical treatment

Observation and initiation of treatment should be started as early as possible. In trochlear nerve palsy with accompanying symptoms (headache, hemiparesis, etc.), aetiologic treatment is warranted, by which the diplopia will also be alleviated. The main goals are maximizing visual function and improving strabismus (Choi et al., 2024).

In microvascular lesions, only observation is usually performed because these lesions have a very good prognosis, with 90% of cases spontaneously healing within a year (Khaier, Dawson, & Lee, 2012).

In patients with traumatic trochlear nerve paresis, symptoms may improve over time depending on the degree of nerve damage and are typically observed for several months until treatment is considered. If the lesion does not heal on its own, prism treatment can be started, a treatment plan with typical excellent results (Choi et al., 2024; Tamhankar, Ying, & Volpe, 2011).

Additional treatment methods can relieve traumatic trochlear nerve palsy's symptoms until nerve function is restored (e.g., Botox injection into the inferior oblique muscle). Galantamine has also been proposed in traumatic palsies, although reports of its efficacy need further confirmation.

2.3.5.2 Surgical treatment

Surgical correction is needed in many cases, and the method of procedure depends on the degree of ocular deviation. The most used procedure is weakening of the inferior oblique muscle and additional intervention in the superior oblique muscle if required (Khanam &Sood, 2022). Treatment results are usually very favorable (Sanz, Escribano, de Liano, &Yela, 2017; Bradfield et al., 2012).

3. Aim of the paper

The aim of this paper is to systematically review the existing literature on the etiology of trochlear nerve palsy, examining its prevalence, classification, and presentation across different causes, including congenital, traumatic, microvascular, and idiopathic origins. The study seeks to highlight patterns in gender distribution, age at presentation, and diagnostic criteria, while identifying gaps in the current knowledge and suggesting directions for future research.

4. Methodology

The study was conducted through a comprehensive review of existing literature focused on the etiological evaluation of trochlear nerve palsy. Key databases such as PubMed, NCBI, and various authoritative medical textbooks were utilized to gather relevant research.

The data processing methodology involved a multi-step approach: an initial search in credible databases, categorization of the findings, analysis of abstracts, and filtering out non-relevant studies. Full-text readings were performed for selected articles, followed by a thorough screening of their references to ensure the inclusion of the most pertinent studies.

Relevant keywords used in the search included: "trochlear nerve," "trochlear nerve palsy," "diplopia," "strabismus," "cranial nerve injury," "cranial nerve inflammation," "superior oblique," and "superior oblique palsy."

The credibility of the included papers was assessed based on several factors: the inclusion of references and citations, the frequency of the paper being cited by other reputable authors, and the quality of the studies themselves. This rigorous process ensured the selection of high- quality, reliable sources for the review.

5. Results

5.1 Overview of Trochlear Nerve Palsy Etiologies

Trochlear nerve palsy can arise from various etiologies, with their relative frequencies varying across different studies in the literature. Major studies have consistently identified several primary categories: congenital, traumatic, microvascular, idiopathic, and other causes including tumors and infections. In reviewing the literature, the distribution of these etiologies has shown some variation, though certain patterns emerge consistently.

In one of the largest series studying trochlear nerve palsies, Keane (1990) analyzed 1,066 patients and found that trauma was the leading cause, accounting for 34% of cases. This was followed by idiopathic cases at 21%, other miscellaneous causes at 15%, microvascular causes at 13%, tumors at 9%, and congenital cases at 8%. Other studies have reported varying distributions, with congenital cases ranging from 8% to 50% across different series(Dosunmu, Hatt, Leske, Hodge, & Holmes, 2018; Mollan, Edwards, Price, Abbott, & Burdon, 2008; von Noorden, Murray, & Wong, 1986.)

These variations in reported frequencies might be attributed to differences in study populations, diagnostic criteria, and improvements in diagnostic capabilities over time. The relative distribution of these etiologies across three major studies is illustrated in Figure 15, demonstrating the range of findings across different research cohorts.

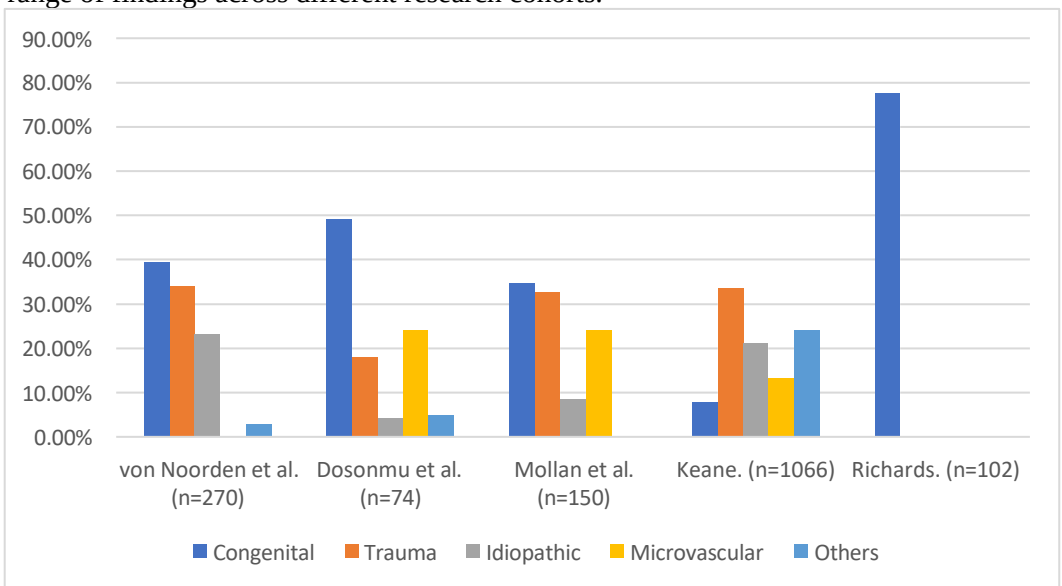

Figure 15. *Prevalence classification of trochlear nerve palsies based on etiology.* ***Source****: Created by the authors.*

Understanding the distribution of these etiologies is crucial for clinical practice, as it guides diagnostic approaches and influences the management of patients presenting with trochlear nerve palsy. Each of these etiologies presents with distinct characteristics and requires different management approaches, which will be discussed in detail in the following sections.

5.2 Congenital palsies

After conducting the literature review, the prevalence of congenital trochlear nerve palsies has been reported to range from 8% to 50% across various studies (Dosunmu, Hatt, Leske, Hodge, & Holmes, 2018; Mollan, Edwards, Price, Abbott, & Burdon, 2008; von Noorden, Murray, & Wong, 1986; Keane, 1990). One study reported a significantly higher prevalence of 77.45% (Richards, Jones, & Younge, 1992). In Keane's large series of 1,066 patients, congenital cases accounted for 8% of all trochlear nerve palsies.

Three of the studies with more detailed data are illustrated graphically (Figure 16).

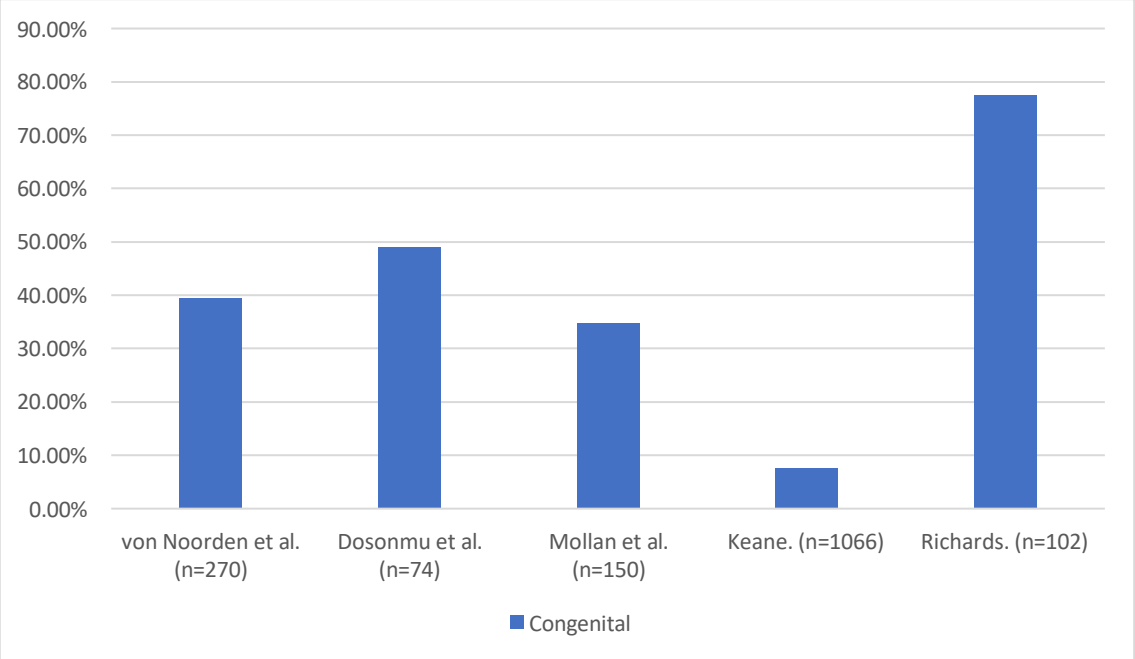

Figure 16. Percentage of congenital cases reported by different studies, including von Noorden et al. (n=270), Dosonmu et al. (n=74), Mollan et al. (n=150), and Keane et al. (n=1066).
***Source**: Created by the authors.*

Classification criteria for congenital palsies were similar in all studies and included criteria such as:

- Confirmation that strabismus or abnormal head posture have been noticed since birth (through photograph review or after reading older history reviews of the patient) and
- No history of trauma

One study included data about gender classification, in which a predominant male prevalence was found (Figure 17).

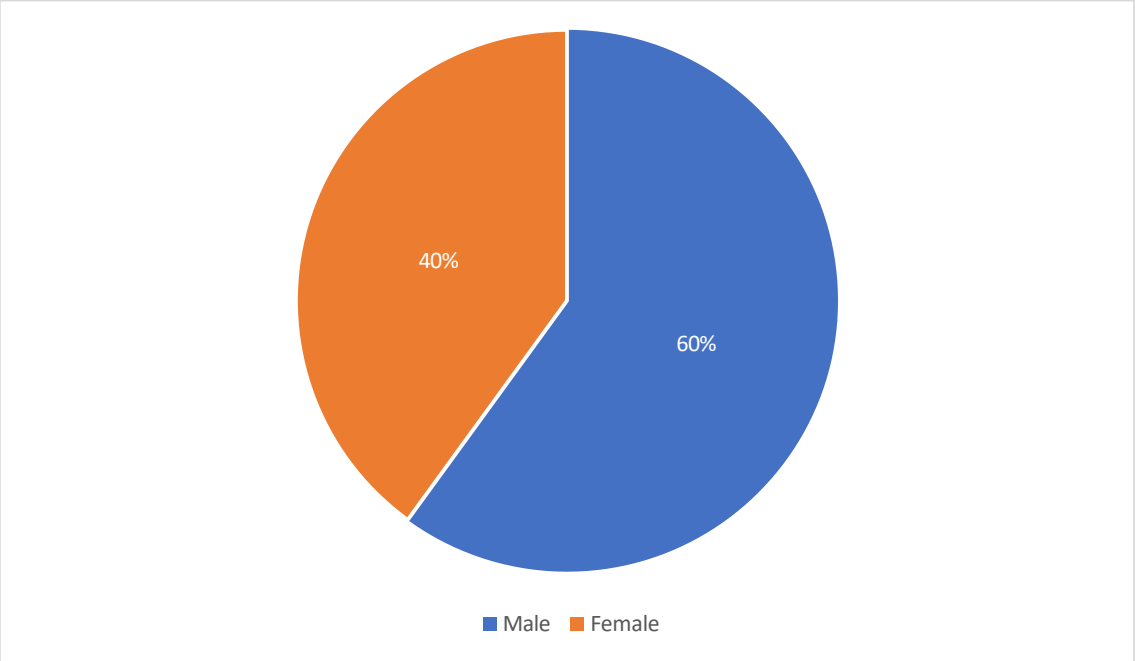

*Figure 17. Percentage of cases based on gender in the studies of von Noorden et al.**Source**: Created by the authors.*

The percentage of patients presenting with diplopia has been reported in the studies by von Noorden, Murray, and Wong (1986), where 21% of patients presented with diplopia, in contrast to patients with acquired palsies, where a higher percentage was observed.

Regarding the decade of life at presentation, the fourth decade of life has been found to be the most common age group for presentation (Dosunmu, Hatt, Leske, Hodge, & Holmes, 2018), followed by patients presenting in their second decade of life (Figure 19).

In contrast, Mollan, Edwards, Price, Abbott, and Burdon (2008) reported that the most common presenting decade of life was the second decade. Studies documenting the inheritance of congenital trochlear nerve palsies have noted cases with an autosomal-dominant inheritance pattern (Botelho & Giangiacomo, 1996; Bhola, Horne, Squirrell, Chan, & Kumar, 2001).

5.3 Traumatic palsies

The classification criteria for traumatic trochlear nerve palsies were quite consistent across all studies reviewed. The criteria typically included specific markers that were used to distinguish traumatic palsies from other forms. One of the primary criteria was the onset of symptoms following a closed traumatic head injury, which served as an important indicator that the palsy was likely the result of trauma. This symptom onset pattern helped researchers and clinicians to identify traumatic causes and differentiate them from other potential causes of trochlear nerve palsy.

The prevalence of traumatic trochlear nerve palsies has been reported to range from 20% to 35% in several studies (Figure 18) (von Noorden, Murray, & Wong, 1986; Dosunmu, Hatt, Leske, Hodge, & Holmes, 2018; Mollan, Edwards, Price, Abbott, & Burdon, 2008). These studies indicate that traumatic causes are a significant contributor to the overall incidence of trochlear nerve palsies, with a substantial number of cases attributable to trauma. In a particularly large study involving 1066 patients, Keane (1990) found that trauma was the leading cause of trochlear nerve palsy, accounting for 34% of all cases.

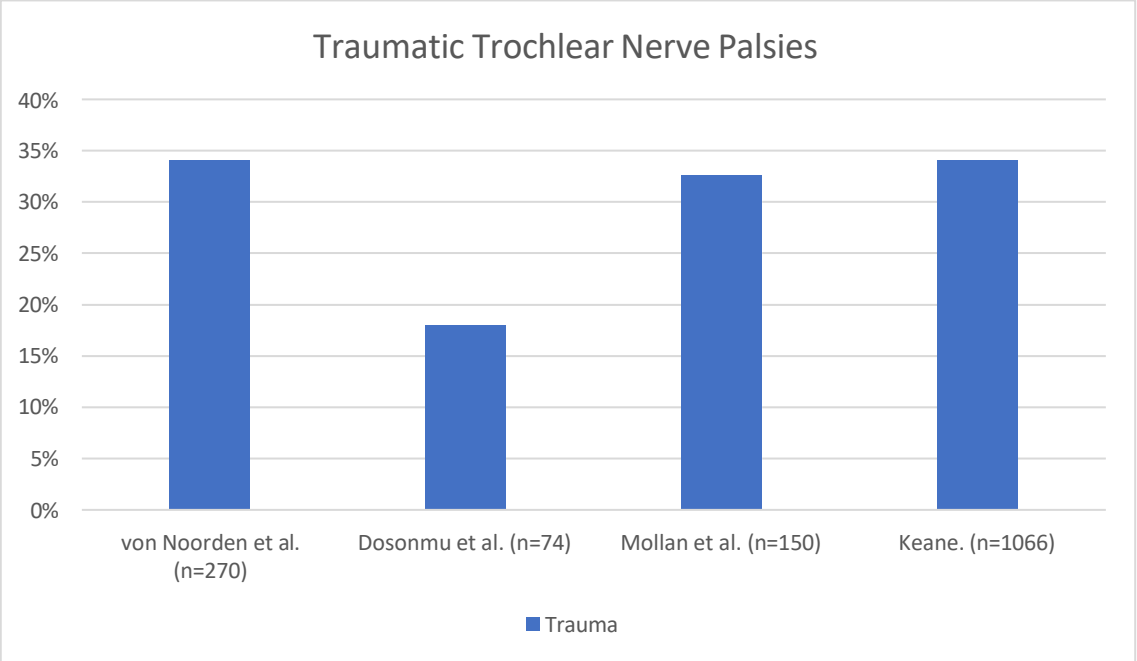

*Figure 18.Percentage of trauma cases reported by different studies, including von Noorden et al. (n=270), Dosonmu et al. (n=74), Mollan et al. (n=150), and Keane et al. (n=1066). The y-axis represents the percentage of trauma cases, while the x-axis lists the studies along with their sample sizes.**Source**: Created by the authors.*

When considering the gender distribution, von Noorden, Murray, and Wong (1986) observed that 60% of traumatic trochlear nerve palsies occurred in males, suggesting a higher incidence in men compared to women. However, no other studies were found that specifically categorized traumatic palsies by gender, leaving a gap in research on this potential trend. This finding raises interesting questions about the factors that might contribute to the higher incidence in males, such as lifestyle factors, engagement in high-risk activities, or occupational hazards that increase the likelihood of head trauma.

Regarding the age at presentation, patients presenting with traumatic trochlear nerve palsies were most commonly in their third decade of life (Figure 19) (Dosunmu, Hatt, Leske, Hodge, & Holmes, 2018). This finding was consistent with results from the study by Mollan, Edwards, Price, Abbott, and Burdon (2008), which also showed that the majority of patients with traumatic trochlear nerve palsies were young adults. This suggests that traumatic injuries, which are more common in younger populations due to active lifestyles and higher exposure to accidents, are a significant factor in the incidence of trochlear nerve palsies.

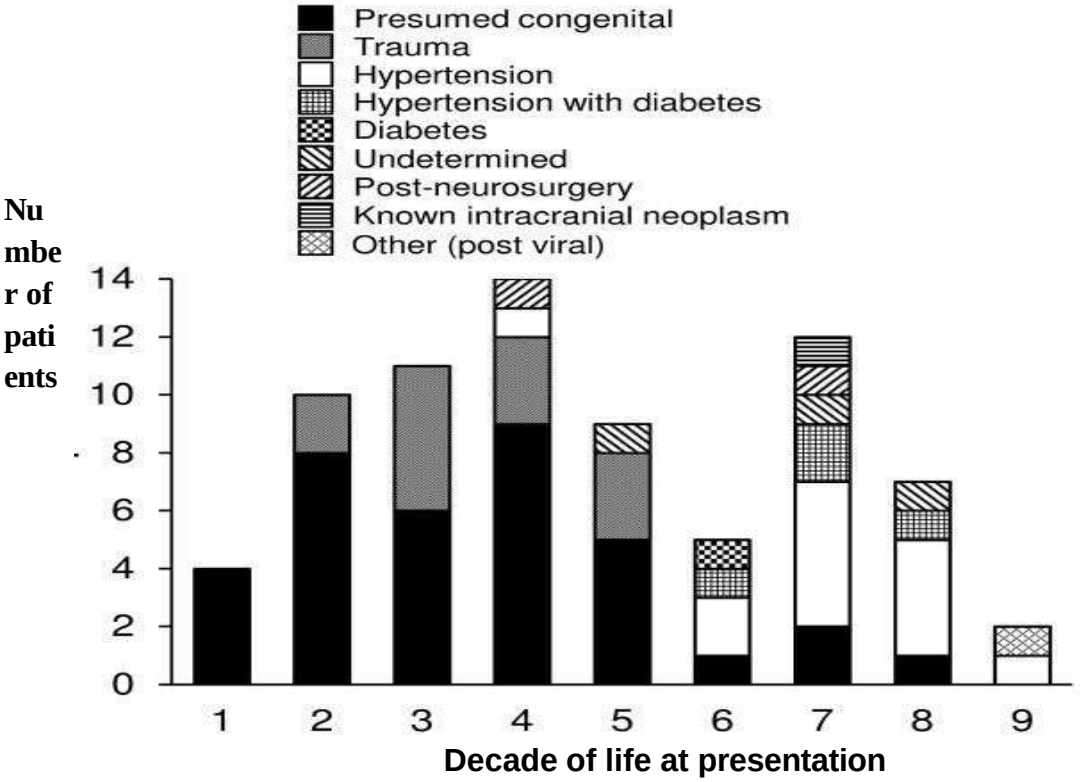

Figure 19. Decade of life at presentation. ***Source****: Reproduced from Dosunmu et al., 2018.*

Another important observation noted by von Noorden, Murray, and Wong (1986) was the higher incidence of diplopia (double vision) as a presenting symptom in acquired palsies, such as those caused by trauma, compared to congenital palsies. Diplopia was more commonly reported in patients with traumatic trochlear nerve palsies, and it was often one of the first symptoms to appear. In contrast, congenital palsies typically present with other symptoms, such as head tilt or vertical strabismus, and diplopia may not be as immediately noticeable. This distinction underscores the role of diplopia as a key symptom in diagnosing traumatic trochlear nerve palsies and highlights the differences in clinical presentation between acquired and congenital causes.

5.4 Microvascular palsies

The prevalence of trochlear nerve palsies with a microvascular origin has been reported to vary between 13% and 24% across different studies (Figure 20) (Dosunmu, Hatt, Leske, Hodge, & Holmes, 2018; Mollan, Edwards, Price, Abbott, & Burdon, 2008; Keane, 1990). This indicates that a significant proportion of trochlear nerve palsies are attributable to microvascular causes, with a notable emphasis on conditions that affect the vascular supply to the nerve. In Keane's large series, ischemic causes, often due to impaired blood flow or vascular insufficiency, accounted for 13% of all cases. This finding highlights the importance of vascular health in the development of trochlear nerve palsies, particularly in older populations or those with pre- existing vascular conditions.

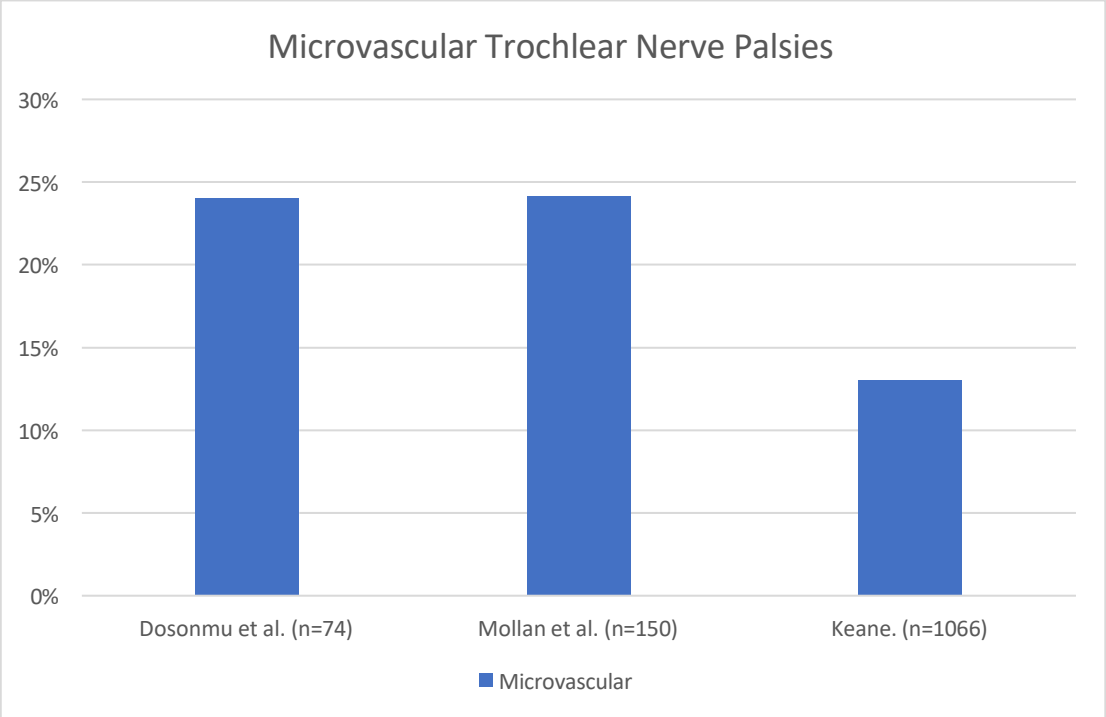

*Figure 20.***Percentage of microvascular cases across studies**. *The chart illustrates the proportion of microvascular cases reported by Dosonmu et al. (n = 74), Mollan et al. (n = 150), and Keane et al. (n = 1066).* ***Source****: Created by the authors.*

One of the key diagnostic criteria used to confirm microvascularpalsies includes the presence of hypertension and diabetes, as these conditions are known to negatively impact the microvascular system, leading to ischemia or other vascular abnormalities that can affect the trochlear nerve. Specifically, hypertension and elevated HbA1Clevels in patients with diabetes have been identified as significant factors that correlate with the development of microvascular trochlear nerve palsies (Dosunmu et al., 2018). These criteria help clinicians identify at-risk patients and provide a more accurate diagnosis by considering the underlying vascular conditions that may contribute to the palsy.

The mostcommondecadeoflife for the presentation of microvascular trochlear nerve palsies was found to be the seventhdecade (Figure 18). This is consistent with the fact that microvascular damage, often caused by conditions like hypertension and diabetes, tends to accumulate over time, making older adults more susceptible. The aging process, combined with the long-term effects of poorly managed vascular risk factors, likely contributes to the higher incidence of microvascular palsies in individuals in their 60s and 70s. The association with aging further emphasizes the need for early diagnosis and management of vascular health in older populations.

Interestingly, a classification based on gender was not found in these two studies. This absence of gender-specific data suggests that the prevalence of microvascular trochlear nerve palsies may be relatively equal between males and females, or that the studies did not find sufficient evidence to differentiate between the sexes in terms of risk factors or outcomes. This lack of gender-based classification leaves room for further research to determine whether there are gender-related differences in the incidence or presentation of microvascular palsies, particularly in relation to the vascular conditions that contribute to the condition.

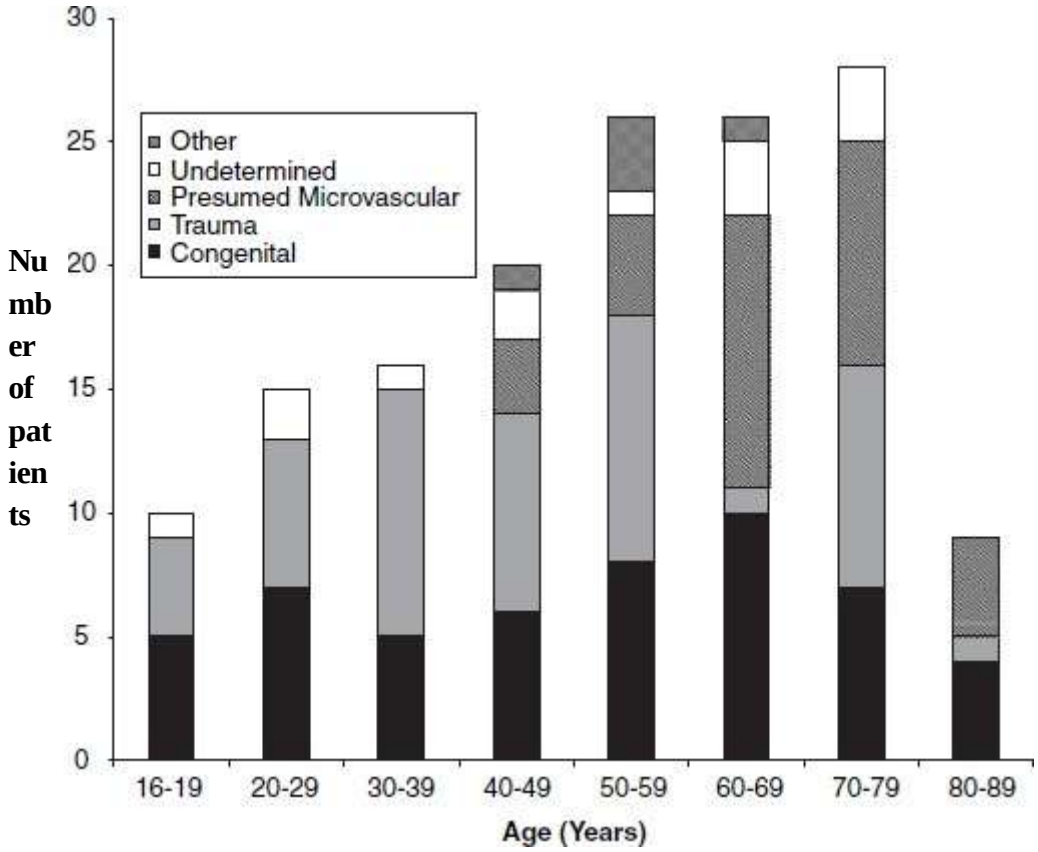

Figure 21. Number of patients and etiologies based on age-groups. ***Source****: Reproduced from Dosunmu et al., 2009.*

5.5 Idiopathic palsies

Classification criteria for idiopathic trochlear nerve palsies were outlined in the study by Dosunmu, Hatt, Leske, Hodge, and Holmes (2018)**,** which identified several key factors to determine an idiopathic diagnosis. These criteria included the following:

- A normal physical examinationandnormal patient history: This means that, despite the presence of symptoms such as double vision or ocular motility issues, there are no abnormal findings in the patient's general physical health or previous medical history. This rule-out process is essential to ensure that there are no underlying systemic conditions contributing to the palsy.

- Normal additional examinations: Additional diagnostic tests, such as imaging studies or neuro-ophthalmologic assessments, should not show any abnormalities. The absence of findings in these examinations suggests that the cause of the trochlear nerve palsy is not related to structural damage, neurological diseases, or other identifiable factors.

- Lack of systemic disease: In idiopathic cases, the patient does not have any known systemic conditions, such as hypertension, diabetes, or vascular diseases, that could potentially cause nerve damage. The absence of any underlying systemic disease further supports the idea that the palsy is of unknown origin.

The percentage of idiopathic palsies varied across studies. More recent studies, like the one by Dosunmu et al. (2018)**,** found the prevalence of idiopathic trochlear nerve palsies to be around 4%, which represents a lower proportion of cases compared to older studies. In contrast, earlier studies such as that by von Noorden, Murray, and Wong (1986**)** reported a significantly higher

rate, with idiopathic palsies accounting for 23% of cases (Figure 22). This discrepancy could be attributed to the advancements in diagnostic techniques, improved recognition of secondary causes, or changes in patient populations over time.

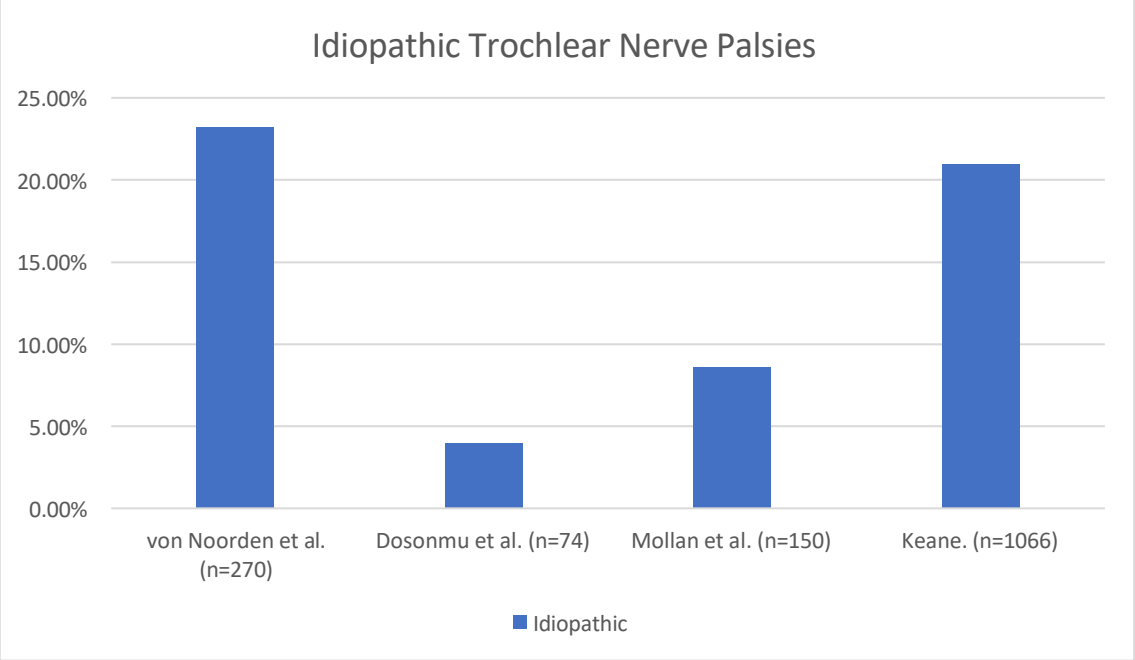

*Figure 22.***Percentage of idiopathic cases across studies.** *The chart illustrates the proportion of idiopathic cases reported by von Noorden et al. (n = 270), Dosonmu et al. (n = 74), Mollan et al. (n = 150), and Keane et al. (n = 1066).*

In Keane's (1990) large series of 1,066 patients, the percentage of cases with unknown causes was 21%, placing idiopathic palsies as a noteworthy but still uncommon cause of trochlear nerve dysfunction. Keane's findings were part of a comprehensive study that examined a wide range of patients, providing valuable insight into the prevalence of idiopathic cases in a large cohort. Despite this percentage, it is still clear that idiopathic cases make up a relatively small subset compared to traumatic or microvascular causes of trochlear nerve palsies.

5.6 Other

Rare causes of trochlear nerve palsy include brainstem tumors or tumors along the nerve's pathway, such as schwannomas (Jindal, 2015), metastatic lesions (Mielke, 2001), and meningeal infections (García-Zamora, Sánchez-Tocino, Villanueva-Gómez, Angles-Deza, & Pérez-Gutierrez, 2016). These causes are considered less common compared to microvascular or traumatic origins but are still significant. Brainstem tumors can directly affect the trochlear nerve or the nuclei from which it arises, leading to dysfunction. Schwannomas, which are benign tumors of the nerve sheath, can also involve the trochlear nerve and present with symptoms like diplopia and difficulty in eye movement. Metastatic lesions, where cancer from other parts of the body spreads to the nervous system, may also affect the trochlear nerve pathway, leading to similar symptoms. Meningeal infections, such as those caused by bacteria or viruses, can lead to inflammation and pressure on the trochlear nerve, resulting in palsy.

In Keane's (1990) comprehensive study of 1,066 patients, tumors were found to account for 9% of all cases of trochlear nerve palsy, a proportion that highlights the relatively low but notable contribution of tumors to this condition. Other miscellaneous causes, which included various rare or less well-defined factors, made up 15% of the total cases in Keane's cohort. These findings emphasize the diverse range of potential causes, although trauma and microvascular factors were more prevalent in the study.

6. Discussion

This review aimed to synthesize the existing literature on the prevalence and etiology of trochlear nerve palsy (TNP), drawing insights from several studies to provide a comprehensive overview of its clinical presentation, associated factors, and underlying causes.

Congenital trochlear nerve palsy (cTNP) showed considerable variability in prevalence across different studies, ranging from 8% to 77.45% (Dosunmu et al., 2018; Mollan et al., 2008; von Noorden et al., 1986; Keane, 1990). This broad range could reflect differences in study methodologies, population samples, and diagnostic criteria. Notably, Keane's large series (1990) reported a lower prevalence of 8%, suggesting that congenital cases may be underreported in some clinical settings. Conversely, Richards et al. (1992) found an unusually high prevalence of 77.45%, indicating the need for more consistent diagnostic approaches to understand the true incidence of congenital TNP. While genetic factors, particularly an autosomal-dominant inheritance pattern, have been identified as potential contributors to congenital TNP (Botelho & Giangiacomo, 1996; Bhola et al., 2001), further studies are necessary to elucidate the exact genetic mechanisms involved.

In terms of clinical presentation, diplopia was more commonly observed in acquired trochlear nerve palsies, especially those of traumatic and microvascular origin, than in congenital cases, as noted by von Noorden et al. (1986). This finding underscores the often more severe and symptomatic nature of acquired TNP, which typically leads to greater patient awareness and diagnosis. The age of onset for congenital TNP most frequently occurs in the fourth decade of life (Dosunmu et al., 2018), although some studies, like Mollan et al. (2008), have reported the second decade as the most common period of presentation, suggesting variability depending on the sample population and regional differences.

Traumatic trochlear nerve palsies, which accounted for 20% to 35% of cases in the studies reviewed (von Noorden et al., 1986; Dosunmu et al., 2018; Mollan et al., 2008), were found to be the leading cause in Keane's (1990) large cohort, representing 34% of cases. Additionally, males were disproportionately affected by traumatic TNP, with a prevalence of 60% in von Noorden et al. (1986). This aligns with the general understanding of trauma-related injuries being more common in males, possibly due to lifestyle and occupational factors. The most frequent age of onset for traumatic TNP was found to be the third decade of life (Dosunmu et al., 2018), a finding also corroborated by Mollan et al. (2008).

Microvascular TNP, often associated with systemic conditions like hypertension and diabetes, accounted for 13% to 24% of cases in the studies reviewed (Dosunmu et al., 2018; Mollan et al., 2008; Keane, 1990). The relatively consistent prevalence of microvascular causes across studies suggests a robust association between TNP and vascular risk factors. Diagnosis is often confirmed through the identification of hypertension or elevated HbA1c levels in patients with diabetes (Dosunmu et al., 2018), further supporting the role of systemic vascular health in the pathogenesis of microvascular TNP. The seventh decade of life was found to be the most common period for the presentation of microvascular TNP, indicating that age-related vascular changes may contribute significantly to the development of this form of palsy.

Idiopathic TNP, in which no underlying cause can be identified, was reported in 4% to 23% of cases across studies (Dosunmu et al., 2018; von Noorden et al., 1986). This variation likely reflects the challenge of diagnosing idiopathic cases, as other potential causes must first be excluded. Keane (1990) found that 21% of cases in his series were classified as idiopathic, highlighting the significant proportion of TNP cases that remain unexplained despite thorough diagnostic evaluation. The diagnostic criteria for idiopathic TNP typically include a normal physical examination, a lack of systemic disease, and normal results from additional tests (Dosunmu et al., 2018).

Lastly, rare causes of TNP, such as brainstem tumors, schwannomas, metastatic lesions, and meningeal infections, were documented in the literature. These rare etiologies accounted for a smaller proportion of cases, with Keane (1990) reporting that tumors were responsible for 9% of TNP cases and other miscellaneous causes contributing to 15% of cases. Although these causes

are less common, they underscore the importance of a thorough differential diagnosis when evaluating patients with TNP.

7. Conclusions

This review examined the prevalence and etiological factors contributing to trochlear nerve palsy (TNP) based on a review of multiple studies. The findings highlight considerable variation in the prevalence of TNP across studies, with congenital causes representing 8% to 50% of cases, traumatic origins accounting for 20% to 35%, and microvascular causes ranging from 13% to 24%. Diplopia was more commonly observed in acquired cases, especially traumatic and microvascular TNP, while congenital TNP typically presented with milder symptoms. Additionally, idiopathic TNP, where no underlying cause is identified, ranged from 4% to 23% across studies, suggesting a need for improved diagnostic criteria in cases where the etiology remains unclear.

However, the studies reviewed were diverse in terms of sample sizes, patient demographics, and diagnostic criteria, leading to variability in the results. The limitations of this analysis include the inability to control for regional and population-based differences and the reliance on studies with varying methodologies. Future research should focus on the development of standardized diagnostic tools and criteria to more accurately categorize TNP cases, particularly in idiopathic and congenital forms. Moreover, longitudinal studies tracking the progression and outcomes of TNP, especially in microvascular and idiopathic cases, would be valuable in providing further insight into the natural history of the condition.

The practical implications of these findings suggest that clinicians should be aware of the diverse etiologies of TNP, especially in patients with a history of trauma, systemic vascular conditions, or unexplained symptoms. Early recognition of the cause can lead to more targeted and effective treatment strategies. Additionally, a deeper understanding of the epidemiology and risk factors associated with TNP could assist in identifying at-risk populations, particularly in older adults and those with systemic diseases like hypertension and diabetes.

In conclusion, while this study provides important insights into the prevalence and causes of TNP, there remains a need for more refined diagnostic approaches and additional research to further elucidate the underlying mechanisms of the condition.

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