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Meta-analysis

Differences in the involved sites among different types of demyelinating optic neuritis in traditional MRI examination: A systematic review and meta-analysis

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ABSTRACT

Background: Magnetic resonance imaging (MRI) plays a significant role in assessing optic neuropathy and providing more detailed information about the lesion of the visual pathway to help differentiate optic neuritis from other visual disorders. This study aims to systematically review the literature and verify if there is a real difference in lesion location among different demyelinating optic neuritis (DON) subtypes.

Methods: A systematic search was conducted including 8 electronic databases and related resources from the establishment of the database to August 25th, 2020. We classified DON into 5 subtypes and divided the visual pathways into five segments mainly comparing the differences in the involved visual pathway sites of different subtypes.

Results: Fifty-five studies were included in the analysis, and the abnormal rate was as high as 92% during the acute phase (within 4 weeks of symptom onset). With respect to lesion location, the orbital segment of the optic nerve was the most frequently involved (87%), whereas optic tract involvement was very rare. Involvement of the orbital segment was more common in myelin oligodendrocyte glycoprotein antibody-related optic neuritis (MOG-ON) (78%) and chronic relapsing inflammatory optic neuropathy (CRION) (81%), while the lesion was found to be located more posteriorly in neuromyelitis optica spectrum disorder-related optic neuritis (NMOSD-ON). With respect to lesion length, approximately 77% of MOG-ON patients had lesions involving more than half of the optic nerve length.

Conclusions: MRI examination is recommended for DON patients in the acute phase. In MOG-ON, anterior involvement is more common and the involved length is mostly more than 1/2 of the optic nerve length, whereas posterior involvement, intracranial segment, optic chiasm, or optic tract, is more common in NMOSD-ON.

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1. Introduction

Optic neuritis (ON), an inflammatory demyelinating disorder of the optic nerve, mainly refers to demyelinating optic neuritis (DON), which is a common cause of vision loss in neuro-ophthalmology. Exciting developments have occurred over the past decades in the diagnosis and treatment of ON. A series of related guidelines and expert consensus have been put forward throughout the world.[1–4] The diagnosis is mainly dependent on clinical manifestations; however, it is difficult to confirm the location and extent of optic nerve lesion only via clinical symptoms and signs. Atypical ON is potentially much more vision-threatening and merits a different treatment approach. Therefore, imaging examination, especially magnetic resonance imaging (MRI), plays an important role in assessing optic neuropathy and provides more detailed information about the lesion of the visual pathway, contributing greatly to the early clinical diagnosis and management of ON. Generally, the main findings of optic nerve abnormalities in orbital MRI are characterized by optic nerve enlargement with high signal intensity on T2-weighted images and

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contrast effect in the optic nerve on post-contrast fat-suppressed T1-weighted images.[5] During an episode of ON, the optic nerve may appear normal or swollen; in chronic cases, the optic nerve becomes atrophic.[6] Specific location and extension of optic nerve lesions in the acute phase of the ON episode may facilitate a subtype diagnosis.[7] In this study, we aimed at systematically reviewing the literature and verifying if there is a real difference in lesion location among different subtypes of DON.

DON was diagnosed according to the evidence-based guidelines for diagnosis and treatment of DON in China (2021).[8] According to the clinical features and the specific antibody in serum, DON can be classified into the following 6 subtypes: neuromyelitis optica spectrum disorder-related optic neuritis or aquaporin 4 antibody-positive optic neuritis (NMOSD-ON/AQP4-ON), myelin oligodendrocyte glycoprotein antibody-related optic neuritis (MOG-ON), multiple sclerosis-related optic neuritis (MS-ON), chronic relapsing inflammatory optic neuropathy (CRION), and idiopathic demyelinating optic neuritis (IDON). If the article did not show the specific subtype of DON, it will be termed 'undefined'.

2. Methods

2.1. Search strategy

This study was a systematic review and meta-analysis of the conventional MRI manifestation of different types of DON. A systematic search was performed in English or Chinese language from database building to August 25th, 2020. Combining synonym retrieval and lower word retrieval, two reviewers independently searched databases, including Chinese database, CNKI, CBM, WANGFANG, and VIP, and four English databases, Pubmed, Embase, Cochrane Library, and Web of Science. Furthermore, related guideline websites, Chinese Clinical Guide library website, National Institute for clinical excellence (NICE), National Guideline Clearinghouse (NGC), Scottish Interschool Guide Network (SIGN), World Health Organization (WHO), Guideline International Network (GIN), and other resources, grey literature, and trace relative literature were also retrieved. For the "Patient", ON, we used "optic neuritis" as subject terms, while neuromyelitis optica, MOG-Ab related disorders, and chronic relapsing inflammatory optic neuropathy were used as subordinate words. For intervention, "magnetic resonance imaging" and "magnetic resonance spectroscopy" were used as the medical subject heading terms (MeSH terms). Subject and free word retrieval were combined for each word and the detailed search terms and strategies are shown in supplement 1.

2.2. Study selection

Potentially eligible studies were selected by abstracting the title or abstract according to the pre-determined standards. If the title and abstract were inadequate to arrive at a final decision, we obtained the full paper to reach a consensus. The inclusion and exclusion criteria were as follows: 1) For patients, we included 6 subtypes of DON patients, NMOSD-ON/AQP4-ON, MOG-ON, MS-ON, CRION, IDON, and undefined DON, and infection and immune-related ON were excluded. 2) For the intervention, both contrast-gadolinium-enhanced T1-weighted fat-suppressed imaging and fat-suppressed T2-weighted imaging were performed in all enrolled patients during the acute phase (within 4 weeks of symptom onset). The scanning range ranged from the back of the eyeball to the intracranial optic tract. The thickness of the scanning layer was 2–3 mm and the interval between the layers was 0–0.5 mm. Both axial and coronal acquisitions were obtained. 3) The visual pathways were divided into the following five segments: the orbital, canalicular, intracranial, optic chiasm, and the tract. The main outcomes were the number of abnormal enhancements or long T2 signal of optic nerve MRI results. 4) The article types included case reports and reviews. Studies with findings at the cellular level or in animals were excluded. 5) The articles that did not contain the related data were also excluded. Two investigators independently screened the literature, and disagreements between the two authors were resolved by discussion. If they did not reach a consensus, a third author was invited to resolve the conflict.

2.3. Data extraction and quality assessment

The following data were independently extracted by two researchers: basic information (the title, journal, first author, publication year, and subtype of DON), the number of patients or eyes examined, and the orbital MRI results (the abnormal number of the specific involved part or lesion length). The quality of each included study was evaluated by two authors depending on the differential study type. For the case series, the Joanna Briggs Institute's (JBI) quality assessment tool including 10 items was used. For the case-control study, the Newcastle-Ottawa Scale (NOS) was used to evaluate from the following three perspectives: selection, comparability, and exposure.

2.4. Statistical analysis

A meta-analysis was conducted using Review Manager 5.4. All outcomes were noncomparative binary data. According to the total number and the abnormal number, we converted the primary data to *P*-value and standard error (SE) value, which was analytical data input into Review Manager 5.4. The calculated odds ratio (OR) value was needed to obtain the rate and its 95% CI by using the conversion calculation. The specific operation steps were in accordance with the literature.[9] I^2 was used to evaluate the heterogeneity among studies. A fixed-effects model or random-effects model was used according to the I^2. Potential publication bias was assessed by funnel plots. We performed subgroup analysis according to the DON subtypes. Sensitivity analyses were performed by removing individual studies sequentially to identify the potential influence of a single study on the overall risk estimate. The results were considered robust if they did not show a significant change.

3. Results

3.1. Study characteristics and quality assessment

We retrieved 6416 records from 8 electronic databases and related resources. Finally, 55 studies were included in the systematic review and meta-analysis[7,10–20,21–31,32–42,43–53,54-63] and the detailed screening flow chart is shown in Fig. 1. Most of the original researches originated from China, and only 17 studies were from the USA, Japan, Korea, UK, France, Italy, Australia, Denmark, and Turkey. The articles published spanned from 1996 to 2020. The basic information of the included studies is listed in Table 1. All included studies were considered to be of relatively high quality, and the details of quality assessment are provided in Table S1 and Table S2.

3.2. The abnormal rate of MRI examination in different DON subtypes

MRI abnormalities were found in 972 of 1252 patients; moreover, this number reached up to 645 in 723 affected eyes. The abnormal rate was 81% when analyzed by the number of patients (n = 9, OR 0.07, 95%CI: 0.05~0.12, $p < 0.001$); furthermore, the abnormal rate could reach up to nearly 92% when analyzed by the number of eyes (n = 11, OR 0.92, 95% CI: 0.81~0.97, $p < 0.001$). Forest maps are presented in Fig. 2 and Fig. S1 according to the number of eyes or patients, respectively. Subgroup analysis showed that the ability to detect anomalies of MOG-ON (92%) and CRION (93%) was the highest although limited to a small sample (n = 5, OR 0.92, 95%CI: 0.76~0.98, $p < 0.001$; n = 1, OR 0.93, 95%CI: 0.75~0.98, $p < 0.001$). However, the abnormal rate was 62% in NMOSD-ON (n = 9, OR 0.62, 95%CI: 0.49~0.74, $p = 0.07$), and the corresponding rate was 69% (n = 3, OR 0.69, 95%CI: 0.30~0.92, $p = 0.34$) and 77% (n = 5, OR 0.77, 95%CI: 0.42~0.94, $p = 0.13$) in IDON and MS-ON,

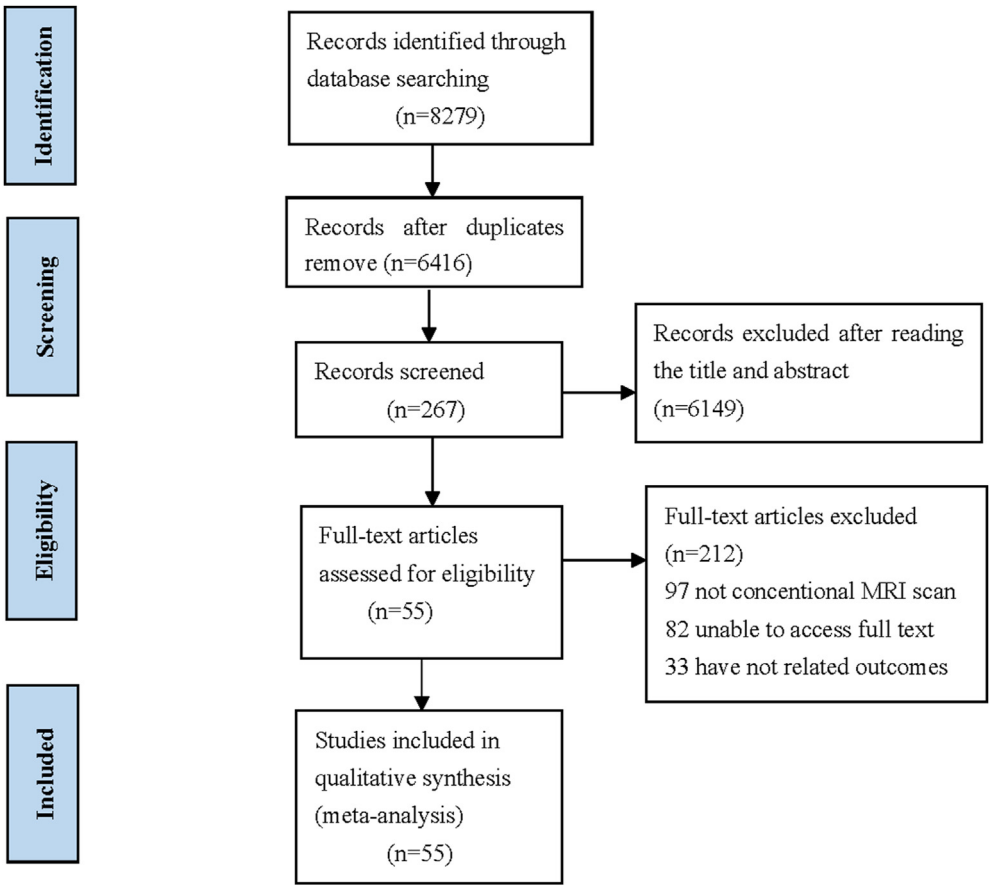

Fig. 1. The flow diagram of the screening of the literature.

respectively. Table 2 shows the differences in involved segments of different subtypes according to the number of patients or eyes.

Following were the differences in involved parts among different subtypes according to the number of patients.

3.3. Differences in involvement of the orbital segment among different DON subtypes

When analyzed by the different parts of the optic pathway, the abnormal rate for the intraorbital segment was 59% in total; for MOG-ON and CRION, the abnormal rate remained relatively high (78% and 81%, respectively). However, it was merely 30% for NMOSD-ON, 58% for IDON, and 41% for MS-ON. It could be concluded that MOG-ON and CRION had a higher probability of involvement of the intraorbital segment of the optic nerve. Fig. S2 shows the forest map of each subtype for involvement of the intraorbital segment.

3.4. Differences in involvement of the canalicular segment among different DON subtypes

Fig. S3 exhibits the differences in involvement of the canalicular segment among different subtypes. The abnormal rate was 37% for the whole, and 21%, 24%, 26%, 39%, and 30% for NMOSD-ON, MOG-ON, IDON, MS-ON, and CRION, respectively. Both the whole and subgroups showed a relatively lower rate of involvement of the canalicular segment.

3.5. Differences in involvement of the intracranial segment among different DON subtypes

For the cranial segment, the overall anomaly rate was 26% for DON patients. It seemed that the abnormal rate was the highest for NMOSD-ON (34%), while, for MOG-ON, IDON, MS-ON, the rates were 25%, 11%, and 22%, respectively. These results indicated that NMOSD-ON was more likely to show involvement of the intracranial segment than the other subtypes. The detailed forest map results are shown in Fig. S4.

3.6. Differences in involvement of the optic chiasm segment among different DON subtypes

When analyzing the optic tract segment, it remained highest for NMOSD-ON than other subtypes although overall involvement of the optic tract was comparatively rare. For MOG-ON, the abnormal rate for involvement of the optic chiasm was 12%, and for IDON and MS-ON, the rate was less than 10%. Forest map results are shown in Fig. S5.

3.7. Differences in involvement of the optic tract segment among different DON subtypes

Optic tract involvement was very rare. The outcome for NMOSD-ON was 12%, 7% for the overall, and less than 10% for the other subtypes. Fig. S6 displays the specific results.

3.8. The incidence of lesion length > 1/2 full-length optic nerve in MOG-ON

We also analyzed the occurrence of the lesion length > 1/2 full-length optic nerve. Due to the limited data of other subsets, we merely analyzed MOG-ON. Only 3 studies were included in the analysis, and the results displayed that approximately 77% of MOG-ON patients had lesions involving more than half of the optic nerve length. Concrete results are presented in Fig. 3.

The above publication bias results are shown in the funnel plot

Table 1
Basic information of included studies.

Basic information			Total number		Abnormal number		Involvement of the visual pathway					
country	study	type	patients	eyes	patients	eyes	orbital segment	canalicular segment	intracranial segment	optic chiasm segment	optic tract segment	lesion length > 1/2
China	Zheng 2020	MOG-ON	12	18		18						
China	Zhang 2020	NMOSD-ON/ AQP4-ON	30		11	17				3 case		
China	Cui 2020	MOG-ON	8		5							4 case
China	Wu 2019	undefined	67	85	67	85	69 eye	12 eye		4 eye		
China	Sun 2019	undefined	33	52		20						
China	Song 2019	MOG-ON	62	106	59					8 case	2 case	52 case
China	Liu 2019	NMOSD-ON/ AQP4-ON	70	70						25 case/ eye		
	Liu 2019	MS-ON	40	40						5 case/eye		
China	Zhang 2018	NMOSD-ON/ AQP4-ON	11		8							
China	Yang 2018	NMOSD-ON/ AQP4-ON	12	19	12	19	8 case 12 eye	1 case 2 eye	2 case 4 eye	2 case 4 eye	2 case 4 eye	
China	Sun 2018	IDON	58	116	58	116				8 case 16 eye		35 case 70 eye
China	Meng 2018	CRION	27		25		22 case	8 case				
China	Li 2018	NMOSD-ON/ AQP4-ON	56		40							
China	Qin 2017	MS-ON	29	54	29	54						
China	Jia 2016	NMOSD-ON/ AQP4-ON	16	25	9	16						
China	Qin 2015	MS-ON	20	38	20	38	34 eye	9 eye	8 eye			
	Qin 2015	NMOSD-ON/ AQP4-ON	11	21	11	21	19 eye	12 eye	15 eye			
China	Liu 2015	IDON	77	98	28							
China	Jiang 2015	undefined	28		16							
China	Chen 2015	MS-ON	62		20							
	Chen 2015	NMOSD-ON/ AQP4-ON	70		30							
China	Zhong 2009	undefined	19	25	19		10 case	7 case	2 case			
China	Tang 2009	undefined	41									
China	Yan 2008	undefined	98	154		132	135 eye	109 eye	97 eye	56 eye	23 eye	
China	Yan 2007	undefined		88		74	63 eye	58 eye	51 eye	29 eye	15 eye	
China	Lu 2007	NMOSD-ON/ AQP4-ON	15		11							
China	Zhou 2005	undefined	49		47							
China	Zhou 1999	undefined	40	75			65 eye	22 eye	12 eye	4 eye	3 eye	
China	Tian 1999	undefined	8		8							
China	Hou 2020	MOG-ON	16		13		12 case	12 case	4 case	1 case		
China	Song1 2019	MOG-ON	63		62							
China	Song2 2019	MOG-ON	106	179			171 eye	123 eye	66 eye	12 eye	2 eye	157 eye
China	Song3 2019	NMOSD-ON/ AQP4-ON		54			51 eye	41 eye	32 eye	15 eye	3 eye	
China	Song4 2019	NMOSD-ON/ AQP4-ON		9			9 eye	4 eye	3 eye	1 eye	0 eye	
	Song5 2019	IDON		23			19 eye	13 eye	4 eye	0 eye	0 eye	
China	Liu1 2019	NMOSD-ON/ AQP4-ON	58	64				31 eye	23 eye	26 eye	4 eye	
	Liu1 2019	MOG-ON	27	41				35 eye	23 eye	8 eye	2 eye	
China	Liu2 2009	MOG-ON		21			21 eye	18 eye	6 eye	1 eye	0 eye	
	Liu2 2009	CRION		12			12 eye	7 eye	2 eye	0 eye	0 eye	
China	Liu3 2009	MOG-ON		21			20 eye	18 eye	8 eye	2 eye	0 eye	
	Liu3 2009	NMOSD-ON/ AQP4-ON		42			39 eye	21 eye	12 eye	8 eye	3 eye	
	Liu3 2009	IDON		41			37 eye	15 eye	6 eye	3 eye	1 eye	
USA	Bursztyn 2019	undefined	92		77							
China	Zhao 2018	MOG-ON	20				16 case	6 case	3 case	3 case	1 case	
	Zhao 2018	NMOSD-ON/ AQP4-ON	45				9 case	26 case	16 case	10 case	3 case	
Denmark	Soelberg 2018	undefined	31	33	25		23 case	13 case				
China	Lu 2018	NMOSD-ON/ AQP4-ON	26	36			29 eye	25 eye	23 eye	15 eye		
	Lu 2018	MS-ON	28	32			25 eye	16 eye	10 eye	1 eye		
USA	Chen 2018	MOG-ON	50		50		46 case		36 case	6 case	1 case	40 case
USA	Vanikieti 2017	NMOSD-ON/ AQP4-ON, Thai cohort	16	19			17 eye	13 eye	6 eye	4 eye	0 eye	

(*continued on next page*)

Table 1 (*continued*)

Basic information			Total number		Abnormal number		Involvement of the visual pathway					
country	study	type	patients	eyes	patients	eyes	orbital segment	canalicular segment	intracranial segment	optic chiasm segment	optic tract segment	lesion length > 1/2
	Vanikieti 2017	NMOSD-ON/ AQP4-ON, American-Caucasian cohort	14	10			10 eye	3 eye	5 eye	3 eye	2 eye	
	Vanikieti 2017	NMOSD-ON/ AQP4-ON	30	29			27 eye	16 eye	11 eye	7 eye	2 eye	
Korea	Son 2017	IDON	19		11		11 case	5 case	2 case	1 case	0 case	
	Son 2017	NMOSD-ON/ AQP4-ON	9		5		5 case	2 case	1 case	1 case	0 case	
	Son 2017	MS-ON	8		5		3 case	1 case	0 case	0 case	1 case	
China	Kang 2017	NMOSD-ON/ AQP4-ON	47		28							
France	Buch 2017	NMOSD-ON/ AQP4-ON		16			11 eye	6 eye	10 eye	7 eye	3 eye	
	Buch 2017	IDON		32			30 eye	9 eye	5 eye	1 eye	0 eye	
China	Zhou 2016	undefined	42		35							
Australia and USA	Ramanathan 2016	MOG-ON	19				10 case	3 case	6 case	1 case		
	Ramanathan 2016	NMOSD-ON/ AQP4-ON	11				3 case	1 case	7 case	7 case		
	Ramanathan 2016	MS-ON	13				3 case	5 case	2 case	2 case		
Japan	Akaishi1 2016	MOG-ON		19			14 eye	19 eye	19 eye	0 eye	0 eye	
	Akaishi1 2016	NMOSD-ON/ AQP4-ON		9			8 eye	4 eye	4 eye	4 eye	1 eye	
	Akaishi1 2016	IDON		9			8 eye	6 eye	1 eye	1 eye	0 eye	
Japan	Akaishi2 2016	NMOSD-ON/ AQP4-ON	23	26				14 eye	13 eye	7 eye	3 eye	
	Akaishi2 2016	MOG-ON	12	17				17 eye	17 eye	2 eye	0 eye	
USA	van der Walt 2015	undefined	23		20		13 case	8 case				
USA	Mealy 2015	NMOSD-ON/ AQP4-ON	26				8 case	6 case	6 case	7 case	5 case	
	Mealy 2015	MS-ON	26				14 case	13 case	7 case	1 case	0 case	
USA	Pula 2014	NMOSD-ON/ AQP4-ON	6							2 case		
	Pula 2014	MS-ON	25							2 case		
UK	Hickman 2014	undefined	33					31 case				
Turkey	Göksemin 2004	MS-ON	10		7							
USA	Rizzo 2002	undefined		32		32						
USA	Kupersmith 2002	undefined	107		101		78 case	48 case	23 case			
Italy	Onofrj 1996	undefined		21		20						

(Figs. S7–S13). There was still some publication bias in these studies, mainly for MS-ON, IDON, and undefined. One possible explanation for this occurrence was the differences in disease between different races or different countries differ in the classification and understanding of disease.

4. Discussion

In general, conventional orbital MRI protocols for ON include axial and coronal T1-weighted imaging, T2-weighted imaging, and contrast-enhanced T1-weighted imaging. It has been suggested that both water and fat signals should be suppressed.[5,64] For MRI magnetic field strength, 1.5T or 3T is recommended.[5] In the acute phase, the optic nerve is enlarged with a high-intensity signal on T2-weighted imaging and has a contrast effect on post-contrast-enhanced T1-weighted imaging.[5] This study is the first systematic review and meta-analysis on the differences in lesion sites among different DON subtypes during a conventional MRI scan. We could determine that the anomaly rate was as high as 92% when DON patients underwent an MRI examination in the acute phase, which is consistent with Kupersmith et al. finding that 94% of abnormal optic nerve enhancement occurred in 107 acute ON patients.[21] Interestingly, the abnormal rate differed among the different subtypes; it was only 62% in NMOSD-ON, 69% in IDON, and 77% in MS-ON; while, for MOG-ON and CRION, the rates were 92% and 93%, respectively. The International Panel for NMO Diagnosis (IPND) revised and reached the International Consensus Diagnostic Criteria for NMOSD in 2015. Additional MRI requirements were recommended for NMOSD without AQP4-IgG and NMOSD with unknown AQP4-IgG status. However, for AQP4 positive patients, MRI was not strictly required, which may lead to a low abnormal rate in NMOSD-ON. MOG-ON is a disease that has only been recognized recently, and the international recommendations on its diagnosis and antibody testing were proposed in 2018. It usually manifests as serious bilateral disc edema and it may have a crossover with CRION in clinical classification[23]; therefore, it has a relatively higher abnormal rate.

In general, the orbital segment of the optic nerve is the most

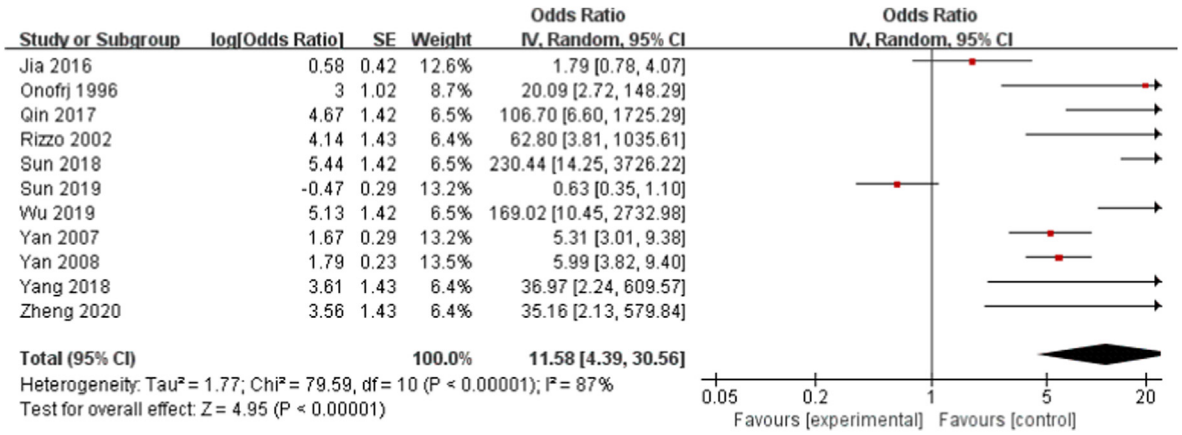

Fig. 2. The abnormal rate according to the number of eyes.
The terms in the x-axis "Favours [experimental] or [control]" represent "OR > 1 or OR < 1", respectively, which means the abnormal ratio > 50% or < 50% of patients with optic neuritis when undergoing an MRI examination to [experimental]. Specifically, "Favours [experimental]" signifies an abnormal ratio < 50%. "Favours [control]" signifies an abnormal ratio > 50%. The weighted plot shows that the majority of studies have an odds ratio favouring control, which means that when a patient with optic neuritis underwent an MRI examination, the MRI abnormal rate was > 50%.

Table 2
Differences in the 5 segments of DON subtypes (according to the number of patients/eyes).

Subtypes/segments	orbital	canalicular	intracranial	optic chiasm	optic tract	total
Total (eyes)	0.87	0.53	0.39	0.17	0.10	0.92
Total(patients)	0.59	0.37	0.26	0.15	0.07	0.81
NMOSD-ON(patients)	0.30	0.21	0.34	0.21	0.12	0.62
MOG-ON(patients)	0.78	0.24	0.25	0.12	0.03	0.92
IDON(patients)	0.58	0.27	0.11	0.06	none	0.69
MS-ON(patients)	0.41	0.39	0.22	0.08	0.07	0.77
CRION(patients)	0.81	0.30	none	none	none	0.93

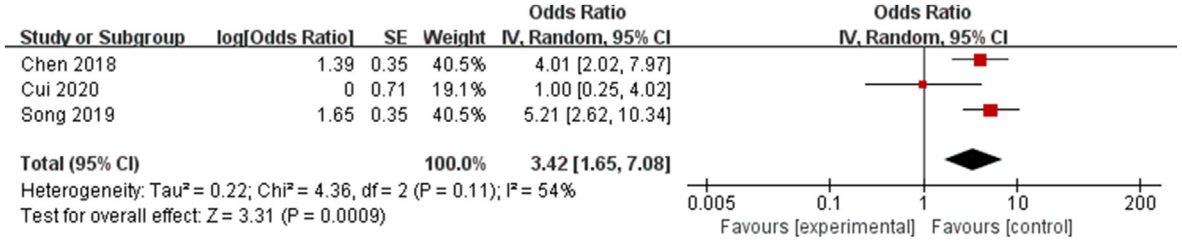

Fig. 3. The incidence of lesion length > 1/2 full-length of optic nerve in MOG-ON.
The weighted plot shows that the majority of studies have an odds ratio favouring control, which means that the incidence of lesion length > 1/2 full-length of optic nerve in MOG-ON was > 50%.

frequently involved (87%), whereas optic tract involvement is very rare. This can be explained by the fact that oligodendrocytes form a myelin sheath around the axons posterior to the lamina cribrosa, and the orbital segment of the optic nerve is relatively longer (25 mm) than the canalicular segment and the intracranial segment (10 mm); therefore, it is not difficult to understand that the orbital segment is more prone to injury.

In terms of the predominant location of optic nerve involvement, MOG-ON and CRION tended to affect the more anterior portion, the orbital segment; whereas, in NMOSD-ON, the lesion was found to be located relatively posterior, including intracranial, optic chiasm, and chiasmal involvement. Our study is consistent with the finding by Caron-Cantin et al.,[65] considering that AQP4-ON is a primary astrocytopathy in which specific AQP4 antibody attack astrocytic process leading to astrocyte destruction, secondarily demyelination, neurons disintegration via complement or antibody-dependent pathways; whereas, for MOG-ON, MOG immunoglobulin-G target MOG protein expressed on oligodendrocytes membranes, leading to primary demyelination. The differences in lesion may be due to uneven distribution of antibody distribution along the optic nerve. Further histopathologic studies on MOG and AQP4 are needed to provide evidence to support. In MS-ON, on reviewing the available evidence, orbital and canalicular segments were involved more than the posterior three sections. Due to the limited data for CRION, no further conclusions can be drawn. IDON, which means that the accurate etiology is unknown, could progress to any subtype with the development of follow-up time and the emergence of new clinical manifestations, consistent with the whole, and it is more common in terms of involvement of the anterior portion.

Optic nerve lesion length may be one of the most useful parameters for distinguishing among different types of ON. Consistent with most studies, MOG-ON patients had significantly extensive optic nerve lesions, our review showed that more than half of the patients (77%) had a 'longitudinally extensive' optic nerve lesion (over 1/2 of the optic nerve length).[65] Unfortunately, additional subgroup analyses were not performed due to limited data.

This is the first systematic review and meta-analysis of MRI features among different DON subtypes, which may be helpful for differentiating

and diagnosing DON subtypes combined with other ophthalmic examination results during an initial presentation of ON when confirmation with antibody testing may not be available. In brief, we recommend conventional MRI for DON patients in the acute phase, and the anomaly rate was 92%, and generally, the orbital segment is the most frequently involved. In MOG-ON, anterior involvement is more common and has a 'longitudinally extensive' lesion; whereas posterior involvement, intracranial segment, optic chiasm, or optic tract, is more common in NMOSD-ON.

Our study has several limitations. First, most of the studies originated from China; therefore, presence of ethnic heterogeneity is inevitable among patients from different regions. Also, due to the difference in detection methods for serum demyelinating antibodies, there may be some heterogeneity among the same subtypes. Second, due to the limited sample size and retrospective studies, publication bias and information bias could not be avoided. Third, underlying confounders, such as the MRI examination time after symptom onset and the treatment received before the examination, may have inevitably underestimated the MRI manifestation.

Study Approval

The authors confirm that any aspect of the work covered in this manuscript that involved human patients or animals was conducted with the ethical approval of all relevant bodies and the study was performed in accordance with the Declaration of Helsinki.

Author Contributions

The authors confirm contribution to the paper as follows: Conception and design of the study: JXF and SHW; Data collection: JXF and YPW; Analysis and interpretation of results: JXF, HLS, HFZ, QGX; Drafting the manuscript: JXF and YPW; Critical revision of the manuscript for intellectual content: JXF, YPW, and HFZ. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

ON	optic neuritis
DON	demyelinating optic neuritis
MRI	magnetic resonance imaging
AQP4-ON	aquaporin 4 antibody-positive optic neuritis
MS-ON	multiple sclerosis-related optic neuritis
NICE	national institute for clinical excellence
NGC	national guideline clearinghouse
SIGN	scottish interschool guide network
WHO	world health organization
CRION	chronic relapsing inflammatory optic neuropathy
NMOSD-ON	neuromyelitis optica spectrum disorder-related optic neuritis
MOG-ON	myelin oligodendrocyte glycoprotein antibody-related optic neuritis
IDON	idiopathic demyelinating optic neuritis
GIN	guideline international network
JBI	joanna briggs institute's
NOS	newcastle-ottawa scale
SE	standard error
OR	odds ratio
MeSH terms	medical subject heading terms
IPND	international panel for NMO diagnosis

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aopr.2021.100019.

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