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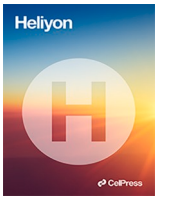

Research article

Timing of immunotherapeutic strategies for first-episode Isolated Anti-Myelin Oligodendrocyte Glycoprotein-IgG Associated Optic Neuritis: A single-centre retrospective study

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ABSTRACT

Background: There is no consensus on the timing of immunotherapeutic strategies for the first-episode anti-myelin oligodendrocyte glycoprotein-IgG (MOG-IgG) associated disorders (MOGAD) presenting with isolated optic neuritis (ON).

Objective: To investigate the optimal timing of intravenous methylprednisolone therapy (IVMP) and necessity of immunosuppressive therapy for the first-episode isolated MOG-IgG associated ON (iMOG-ON).

Methods: Adult patients with the first-episode iMOG-ON were enrolled. Primary outcomes were best-corrected visual acuity (BCVA) at last follow-up (i.e. final BCVA) and relapse, and their predictors were assessed by multivariate analysis.

Results: 62 patients were included. Logistic regression analysis revealed BCVA at the time of IVMP (odds ratio: 0.463 (95 % confidence interval (CI) 0.310-0.714) was a factor predictive of regaining a final BCVA of 0.0 logMAR vision, and its Youden optimal criterion was <0.175 logMAR by plotting the receiver operating characteristic curve. The time-dependent cox proportional hazards model exhibited MMF therapy was not associated with a high likelihood of relapse-free survival (HR = 1.099, 95 % CI 0.892–1.354, P = 0.376) after adjusting for age of onset, gender, and baseline MOG serum titers. Similar analysis exhibited evidently negative association between high MOG-IgG serum titers at baseline and relapse-free survival after adjusting for age of onset, gender, and MMF therapy (HR = 0.339, 95 % CI 0.155–0.741, P = 0.007).

Conclusions: During the first episode of iMOG-ON, the optimal timing of IVMP may be a short timeframe before visual acuity decreasing to 0.175 logMAR, and MMF therapy may not be recommended for patients with low MOG-IgG serum titers. Further long-term follow-up studies are required to validate these findings.

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1. Introduction

Anti-myelin oligodendrocyte glycoprotein-IgG (MOG-IgG) associated disorders (MOGAD) has developed into a new type of immune-mediated central nervous system inflammatory demyelinating diseases in the last few decades. It can manifest as monophasic or recurrent episodes of various phenotypes, including optic neuritis (ON), acute disseminated encephalomyelitis (ADEM), transverse myelitis, and sometimes brainstem or cerebellar features, cerebral cortical encephalitis, and tumefactive demyelinating lesions [1].

ON is one of the most common clinical phenotypes in adults with MOGAD, occurring in isolation or in conjunction with other neurological manifestations. Albeit visual acuity loss is often worse than 6/60 at nadir, rapid improvement usually occurs, with recovery to full or near normal acuity following acute corticosteroid therapy [1,2]. Some previous studies have found that initiating intravenous methylprednisolone therapy (IVMP) within 2 days may lead to better recovery of visual acuity and preservation of the macular ganglion cell layer after recurrent ON episodes [3]. However, diagnosing the first-episode MOGAD at such an early stage is difficult, and appropriate corticosteroid therapy is often delayed as a result. Hence, there is a pressing need to investigate the influence of timing of high-dose IVMP on visual outcomes even after 2 days since the occurrence of visual impairment.

30–80 % of patients with MOGAD experience relapses, so the growing interest is inclined towards exploring maintenance therapies for recurrent MOGAD [4–7]. However, consensus is lacking regarding the necessity of maintenance therapies following the first clinical attack of MOG-IgG associated ON (MOG-ON) [8,9].

Previous studies have generally not differentiated between isolated MOG-ON (iMOG-ON) and ON occurring alongside other clinical phenotypes of MOGAD [9,10]. The purpose of this study was to document our experience and explore the influence of timing of immunotherapeutic strategies on visual outcomes in the first-episode iMOG-ON.

2. Materials and methods

2.1. Study population

This single-center retrospective study enrolled adult patients with iMOG-ON at the Department of Neurology, Beijing Tongren Hospital, Capital Medical University, between June 2018 and May 2023.

Inclusion criteria were: (1) First episode of ON diagnosed according to the International consensus on ON [11]; (2) Absence of other neurological phenotypes (myelitis, ADEM, etc.); (3) Serum MOG-IgG positivity detected by the fixed cell-based assay (CBA) method and negative AQP4 antibodies. Fixed assays were considered clear positive by titers greater than or equal to 1:100. If titers were at least 1:10 and less than 1:100, low positives were determined, and under this circumstance, at least one of the supporting clinical or MRI features were required to diagnose MOG-ON: bilateral simultaneous clinical involvement, longitudinal optic nerve involvement (>50 % length of the optic nerve), perineural optic sheath enhancement, and optic disc oedema [1].

Exclusion criteria were: (1) Recurrent iMOG-ON; (2) Presence of retinal, glaucomatous, anterior segment, and other ocular diseases, (3) Alternative causes for ON.

Medical records were reviewed to obtain all patients' demographic details and clinical data, including gender, age of onset, afflicted eyes, best-corrected visual acuity (BCVA) at nadir, BCVA at the time of IVMP therapy, time intervals between the onset of visual impairment and IVMP (TIOVM), fundus images, MRI findings, and immunotherapeutic strategies. IVMP was intravenous pulse of methylprednisolone sodium succinate at 1000 mg/day for 3–5 days, which was determined by the treating clinician.

2.2. Study outcomes

All patients were followed up for at least 6 months. The primary outcome was BCVA at last follow-up (i.e. final BCVA) and relapse which was defined as a neurologic disturbance for at least 24 h in the absence of other identifiable causes, occurring more than 1 month after index onset and confirmed by a neurologist. A comprehensive eye examination was done blindly and independently by a trained optometrist. Decimal visual acuity was converted to the logarithm of the minimum angle of resolution (logMAR). Among these values, counting fingers was transformed as 2.0 logMAR, hand movement as 3.0 logMAR, light perception as 4.0 logMAR, and no light perception as 5.0 logMAR. Full visual recovery was defined as 0.0 logMAR during follow-ups. A final BCVA of 0.3 logMAR was equal to Snellen 20/40.

2.3. Statistical analysis

Statistical analyses were performed using IBM SPSS version 26.0 software (IBM, New York, NY). Number and percentage were presented for categorical variables, whereas descriptive statistics were expressed as median (25th percentile, 75th percentile) or M (p25, p75) for non-normally distributed continuous data. The Mann–Whitney *U* test was used to analyze differences in the continuous data, and the chi-square test was employed to test the distribution of categorical variables. Binary logistic regression was performed to identify predictors of visual prognosis. The validity conditions for the logistic regression were checked in order to have at least 10 events for each independent variable in the multivariable model. Non-redundant and clinically pertinent variables with a P value < 0.2 in univariate analyses were introduced in a multivariable logistic regression model. Subgroup analysis based on MOG-IgG serum titers and sensitivity analysis were performed to assess the robustness of our results utilizing a multivariate logistic regression model. The cutoff levels of BCVA at the time of IVMP were determined using a receiver operating characteristic (ROC) analysis to predict the occurrence of a final BCVA of 0.0 logMAR and 0.3 logMAR, respectively. Survival time was collected and analyzed using the Kaplan-

Meier method. Cox regression models were performed to predict the probability of relapse. A 2-tailed P value of less than 0.05 was considered significant for all.

3. Results

3.1. Clinical data

Of the 83 patients with iMOG-ON, 78 (93.98 %) received IVMP therapy. No patients received plasma exchange and intravenous immunoglobulins therapy. Final BCVA was not measured in 8 (10.96 %) of the 78 patients. 8 patients were lost to follow-up (Fig. 1).

A total of 62 patients with 85 affected eyes were included in the study, with a median age of onset of 44 (30.25, 56) years and a median symptom duration of 11 (7, 17) days (range, 2–40 days) prior to referral to our hospital. There were 38 (61.29 %) males. The median TIOVM was 15 (9, 21) days, with 96.47 % of eyes having a TIOVM of at least 5 days (Fig. 2).

3.2. Visual acuity assessment before IVMP therapy

Before the administration of IVMP, the median BCVA at nadir was 2.7 (1.0–3.0) logMAR, with 78.82 % of eyes having a nadir BCVA equal to, or worse than 1.0 logMAR, and 89.41 % of eyes having a nadir BCVA worse than 0.3 logMAR (Fig. 3).

At the time of IVMP, the median BCVA was 1.6 (0.15–2.5) logMAR, with 61.18 % of eyes having a BCVA equal to, or worse than 1.0 logMAR, and 89.41 % of eyes having a BCVA worse than 0.3 logMAR (Fig. 3).

3.3. Impact of timing of IVMP on final BCVA

The median follow-up period was 28 months. A total of 69 (81.18 %) afflicted eyes experiencing a TIOVM of more than 7 days. No statistical differences were found in final BCVA (P = 0.661), age of onset (P = 0.054), gender distribution (P = 0.738), BCVA at nadir

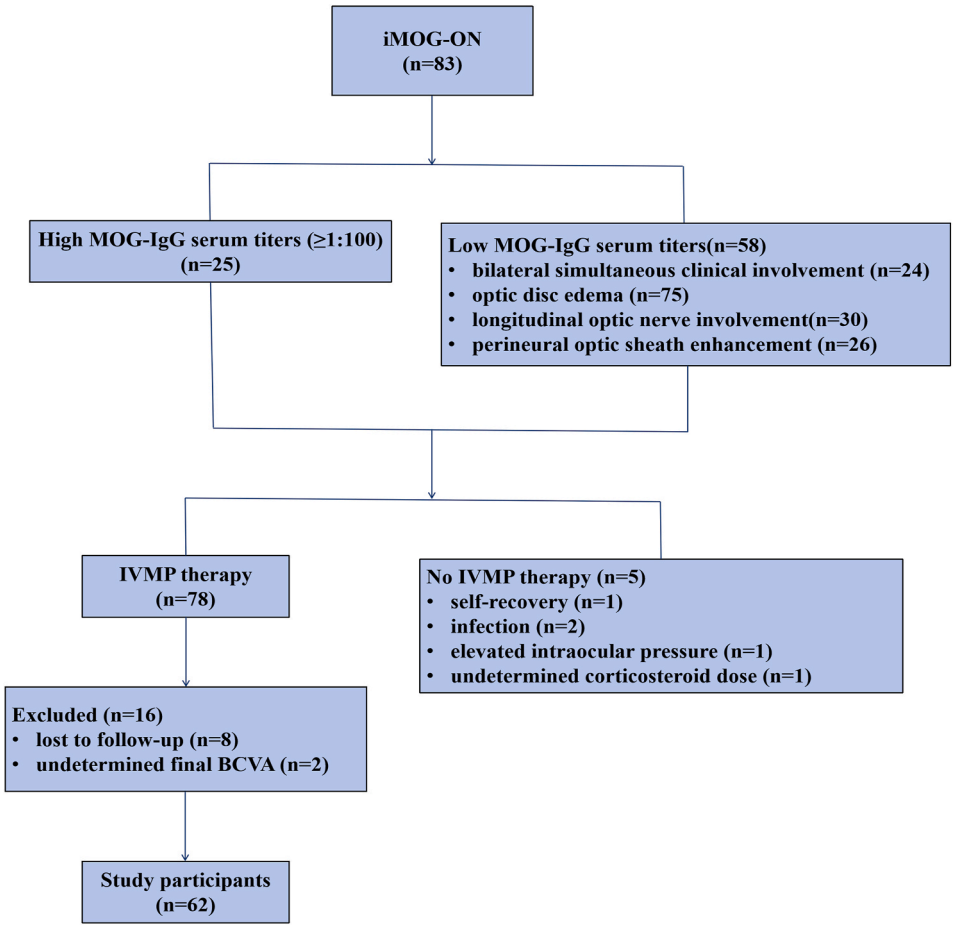


Fig. 1. Flow chart summary of the enrollment of patients with isolated anti-myelin oligodendrocyte glycoprotein-IgG (MOG-IgG) antibody-mediated ON (iMOG-ON). IVMP, intravenous methylprednisolone therapy.

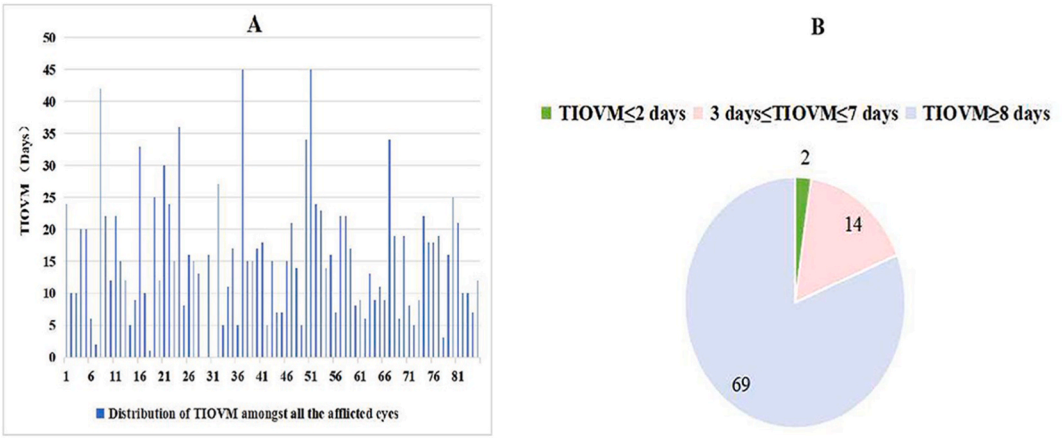


Fig. 2. A summary of time intervals between the onset of visual impairment and IVMP (TIOVM) amongst all the afflicted eyes of the 62 patients with isolated anti-myelin oligodendrocyte glycoprotein-IgG (MOG-IgG) antibody-mediated ON (iMOG-ON). A. TIOVM of each afflicted eye. B. Subdivision of all the afflicted eyes based on TIOVM.

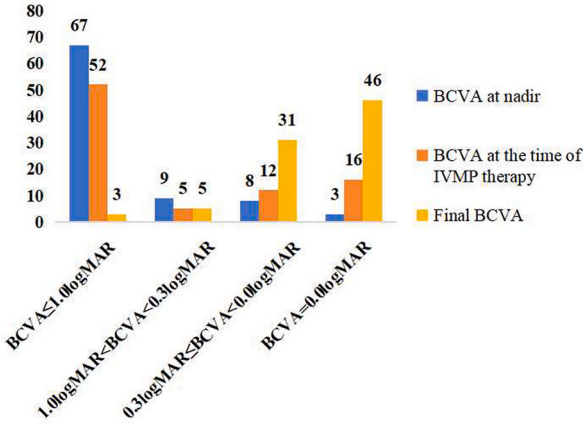


Fig. 3. A summary of best-corrected visual acuity (BCVA) of the 85 afflicted eyes of 62 patients with isolated anti-myelin oligodendrocyte glycoprotein-IgG (MOG-IgG) antibody-mediated ON (iMOG-ON) before and after administration of intravenous methylprednisolone therapy (IVMP).

(P = 0.881), and BCVA at the time of IVMP (P = 0.282) when stratified by a 7-day TIOVM.

A final BCVA of 0.0 logMAR was achieved in 46 (54.12 %) afflicted eyes (Fig. 3). Distribution of final BCVA was displayed with the change of TIOVM in the 85 afflicted eyes of 62 patients with iMOG-ON (Fig. 4). TIOVM was not a predictive factor for the final BCVA of

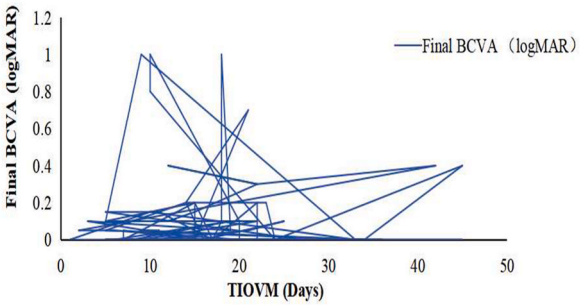


Fig. 4. Distribution of final BCVA was displayed with the change of TIOVM in the 85 afflicted eyes of 62 patients with iMOG-ON. BCVA, best-corrected visual acuity; TIOVM, time intervals between the onset of visual impairment and IVMP; iMOG-ON, isolated anti-myelin oligodendrocyte glycoprotein-IgG (MOG-IgG) antibody-mediated ON (iMOG-ON).

Table 1
The multivariate logistic regression analysis of the predisposing factors for regaining a final BCVA of 0.0 logMAR.

	Model 1				Model 2				Model 3			
	Variance inflation factors	**Odds Ratio**	**95 % CI**	P	**Variance inflation factors**	**Odds Ratio**	**95 % CI**	P	**Variance inflation factors**	**Odds Ratio**	**95 % CI**	P
BCVA at nadir	2.160	1.507	0.963–2.358	0.073	2.239	2.255	0.873–2.173	0.169	2.330	1.383	0.867–2.205	0.173
BCVA at the time of IVMP	2.160	0.325	0.174–0.608	0.000	2.321	2.222	0.176–0.635	0.001	2.351	0.333	0.173–0.641	0.001
Age of onset	–				1.075	1.042	0.934–0.998	0.041	1.150	0.965	0.932–0.999	0.046
Gender	–				–	–	–	–	1.193	1.049	0.354–3.108	0.931

TIOVM, time intervals between the onset of visual impairment and IVMP; BCVA, best-corrected visual acuity; IVMP, intravenous methylprednisolone therapy.

0.0 logMAR in univariable logistic regression (Odds Ratio (OR): 1.014 (0.969–1.062), P = 0.546) (Supplemental Table 1). The multivariate logistic regression analysis revealed that BCVA at the time of IVMP and age of onset were predictive factors for regaining a final BCVA of 0.0 logMAR, while BCVA at nadir and gender distribution had no significant influences (Table 1).

In sensitivity analysis, the association between BCVA at the time of IVMP and final BCVA achieving 0.0 logMAR remained significant when the study population was divided into "MOG-IgG titer ≥100″ group and "MOG-IgG titer <100″ group (Supplemental Table 2). Moreover, after further adjustment for age of onset or gender, the association between BCVA at the time of IVMP and final BCVA achieving 0.0 logMAR remained essentially unchanged (Supplemental Table 2).

An ROC analysis was performed with BCVA at the time of IVMP as the predictor and regaining a final BCVA of 0.0 logMAR vision as the dependent variable. An area under the curve (AUC) of 0.752 was identified, and with a Youden optimal criterion of BCVA at the time of IVMP < 0.175 logMAR, a sensitivity and specificity of 94.87 % and 45.65 %, respectively, were achieved (Fig. 5). A similar analysis revealed a Youden optimal criterion of age of onset < 48.5 years with an AUC of 0.644, sensitivity of 69.57 %, and specificity of 58.97 %.

A total of 77 (90.59 %) afflicted eyes recovered visual acuity to 0.3 logMAR or better, with BCVA at the time of IVMP (P = 0.024) identified as a predictive factor for achieving this outcome in univariate logistic regression analysis (Table 2).

An ROC analysis was performed with BCVA at the time of IVMP as the predictor and regaining a final BCVA of 0.3 logMAR vision as the dependent variable (Fig. 5). An AUC of 0.729 was identified, and with a Youden optimal criterion of BCVA at the time of IVMP was < 2.6 logMAR, a sensitivity and specificity of 62.5 % and 79.2 %, respectively, were achieved.

3.4. Risk of relapse and mycophenolate mofetil therapy

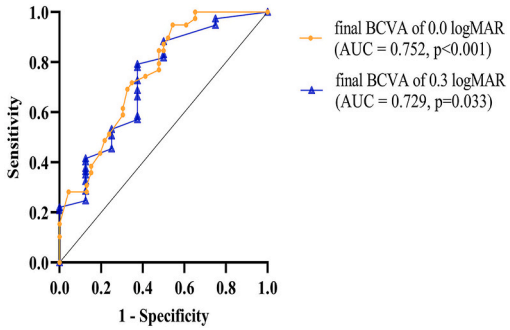
After administration of IVMP, 46 patients were followed up for at least 1 year, with a median follow-up period of 34 (28, 50.75) months (range, 13–62 months). 11 patients had high MOG-IgG serum titers. All patients received the same tapering strategy of oral prednisone for at least 3 consecutive months in the remission stage, which had been withdrawn at the last follow-up except for 1 patient who had maintained oral methylprednisolone at a dose of 4 mg for over 1 year.

12 (26.09 %) patients received oral systemic immunosuppressants (azathioprine, n = 1; mycophenolate mofetil (MMF), n = 11), and no one experienced relapses. MMF therapy was defined as the administration of MMF at a dose of 0.75 g twice per day (1.5 g per day) lasting more than 14 days continuously. It was withdrawn in 7 patients at last follow-up. The remaining 34 (73.91 %) patients did not receive any immunosuppressants, and 4 (8.70 %) experienced relapse of visual impairment. No one experienced relapses of other clinical phenotypes except for ON. The female/male ratio was 10/1 in the MMF + Group and 17/17 in the MMF- Group (P = 0.04). No statistical differences were found in age of onset (P = 0.526), age type (i.e., ages >18–40 years vs ages >40 years) (P = 0.786), and baseline MOG-IgG serum titers (P = 0.879) between MMF + Group and MMF- Group.

The Kaplan-Meier curves of survival free of relapse by the time of last recorded follow-up were shown in Fig. 6. The time-dependent cox proportional hazards regression model indicated that MMF therapy was not associated with a high likelihood of relapse-free survival (HR = 1.099, 95 % CI 0.892–1.354, P = 0.376) after adjusting for age of onset, gender, and baseline MOG serum titers. Similar analysis exhibited evidently negative association between high MOG-IgG serum titers at baseline and relapse-free survival after adjusting for age of onset, gender, and MMF therapy (HR = 0.339, 95 % CI 0.155–0.741, P = 0.007).

4. Discussion

Our study focused on patients with iMOG-ON. Approximately one-third of the patients exhibited high MOG-IgG serum titers, while the remaining patients had low MOG-IgG serum titers along with at least one of the four supporting clinical and MRI features proposed by the international MOGAD panel [1], leading to a diagnosis of MOGAD. Notably, few clinical studies have provided detailed information on the timing of immunotherapy in MOGAD [12,13]. Our findings suggested that visual outcomes were more frequently



IVMP, intravenous methylprednisolone therapy; BCVA, best-corrected visual acuity; AUC, area under the curve

Fig. 5. A receiver operating characteristic curve of best-corrected visual acuity (BCVA) at the time of intravenous methylprednisolone therapy (IVMP) as a predictor of a final BCVA of 0.0 logMAR and 0.3 logMAR, respectively.

Table 2
The univariate logistic regression analysis of the predisposing factors for final BCVA achieving 0.3 logMAR or better.

	Odds Ratio	95 % CI	P
Gender	1.655	0.384–7.131	0.499
Age of onset	0.964	0.916–1.014	0.154
TIOVM	0.949	0.887–1.016	0.133
BCVA at nadir	0.802	0.514–1.252	0.331
BCVA at the time of IVMP	0.546	0.323–0.922	0.024

TIOVM, time intervals between the onset of visual impairment and administration of IVMP; BCVA, best corrected visual acuity; IVMP, intravenous methylprednisolone therapy.

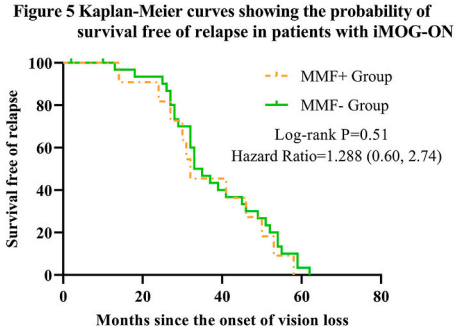


Fig. 6. Kaplan-Meier curves showing the probability of survival free of relapse in patients with isolated anti-myelin oligodendrocyte glycoprotein-IgG (MOG-IgG) antibody-mediated ON (iMOG-ON).

influenced by BCVA at the time of IVMP rather than the timing of IVMP if initiated after 4 days since the onset of visual impairment. Additionally, MMF therapy did not significantly reduce the risk of recurrence after the first episode of ON especially in patients with low MOG-IgG serum titers by the time of last recorded follow-up.

In the acute phase of MOG-ON, high-dose IVMP remains a primary treatment option, although some cases may experience spontaneous recovery [1,8]. The Optic Neuritis Treatment Trial (ONTT) showed that IVMP did not significantly alter the ultimate visual outcome compared to oral prednisone [14,15]. However, this finding may not directly apply to MOG-ON due to the limited focus on this specific condition. Observational studies have suggested the visual recovery was apparently facilitated by the administration of the IVMP therapy [8–10,13,16], but the optimal timing of IVMP administration remains unclear. Stiebel-Kalish et al. found that a 7-day delay in IVMP administration reduced the likelihood of regaining a BCVA of 0.0 logMAR and 0.2 logMAR at the 3-month follow-up [12]. However, their study included only 9 patients with MOG-ON. Rode J et al. demonstrated that failure to regain 0.0 logMAR at the 3-month follow-up was associated with time to first IVMP treatment $\geq$ 10 days in adult MOG-ON, but it was unclear whether some important confounding variables, such as administration of plasma exchange, had been included in multiple linear regression analyses [17]. Another study indicated that early IVMP administration within 2–3 days of the onset of visual impairment might lead to slightly better final visual outcomes. However, analyses using a cutoff of 4 days did not reveal significant associations with a higher chance of achieving a final BCVA of 0.3 logMAR or better [13]. Our study suggested that IVMP initiation after 4 days since the onset of visual impairment may not be associated with improved visual recovery. It could be inferred that even a 2-day delay in IVMP administration might lead to worse visual outcomes. This phenomenon could be explained by the finding that inflammatory cell infiltration occurred within 2 days of visual impairment, inducing demyelination and axonal injury that then led to retinal ganglion cells (RGCs) death in experimental ON models [18,19]. Therefore, potential neuroprotective therapies, such as IVMP, should be initiated before axonal injury to prevent permanent RGC loss from ON [18]. However, the differences observed in Stiebel-Kalish's study were no longer significant after adjusting for the initial BCVA at the time of treatment [13]. Hence, the timing of IVMP may not be the sole prognostic factor for visual outcomes following the first episode of MOG-ON. In essence, time may not always equate vision, and there may be other influencing factors for visual outcomes in MOG-ON.

Before admission to our department, most of our patients had already reached their lowest BCVA during their ON attacks. Some had experienced slow visual recovery, while others had been treated with low-dose oral prednisolone, resulting in better BCVA at the time of IVMP administration compared to the BCVA at nadir during the initial ON attack. Approximately half of the affected eyes achieved a final BCVA of 0.0 logMAR, and the relationship between BCVA at the time of IVMP and the final BCVA of 0.0 logMAR suggested that early IVMP treatment might prevent visual impairment from reaching nadir, and IVMP should be initiated before visual acuity decreasing to 0.175 logMAR, potentially increasing the likelihood of complete visual recovery in MOG-ON. Our present and previous studies observed that a small fraction of patients with MOG-ON may experience severe visual impairment despite appropriate swift administration of IVMP [16,20], and older patients were less likely to fully recover than younger adults. These results were excellent in comparison to previous reports [9,13,16], and they encouraged clinical physicians to implement IVMP as early as possible to prevent

the deterioration of BCVA during acute attacks of MOG-ON, especially in older patients, in order to achieve a better visual outcome. Additionally, Akaishi T et al. found that one of the possible factors for worse visual outcome in MOGAD may include a long ON lesion with chiasmal involvement [16]. Similarly, our previous results showed that the worst final BCVA was observed in afflicted eyes with lesions extending across three segments of the optic nerve [20]. Therefore, visual recovery may also be influenced by the lengths of longitudinally expansive lesions of the optic nerve to a certain extent. Further studies are needed to determine the possible relationships between structural changes and visual prognosis of MOG-ON.

Analyses indicated 90 % of eyes achieved a final BCVA of 0.3 logMAR, consistent with previous findings [9,13]. Akaishi T et al. found that BCVA at 1 and 5 years showed only weak to moderate correlations with BCVA at nadir in patients with MOG-ON [16]. Our study also suggested that visual outcome was influenced more by BCVA at the time of IVMP administration rather than BCVA at nadir. In other words, for patients who had reached their lowest BCVA, if the baseline vision before IVMP could be improved to the level of 2.6 logMAR, visual recovery might be more favorable, despite the challenges in achieving full visual recovery. Based on findings from the Optic Neuritis Treatment Trial (ONTT) and some observational studies, oral corticosteroid therapy may also expedite visual recovery [14], and bioequivalent doses of oral corticosteroids may serve as an alternative to IVMP for treating acute ON [21]. Therefore, for patients unable to receive IVMP therapy promptly under realistic conditions, early administration of appropriate doses of oral corticosteroids may also help improve the visual outcome by reversing the lowest recorded vision. These findings suggested that oral corticosteroid therapy may present an opportunity to enhance visual outcomes even the lowest vision had occurred. Taken together, the main strategies we could adopt to improve visual outcomes involved preventing visual impairment from decreasing to 0.175 logMAR before reaching its natural nadir and sometimes increasing the baseline BCVA before IVMP administration. These findings suggested that the optimal timing of IVMP may not be a specific time point but an individualized timeframe before visual acuity decreasing to 0.175 logMAR, which varied among patients with iMOG-ON.

MOGAD has a 2-year and 5-year recurrence rate of 44.8 % and 61.8 %, respectively [9,22–24], and the predictive factors includes young adult age at disease onset (i.e., ages >18–40 years), isolated ON, a duration of treatment with oral prednisolone less than 3 months, and maintenance of seropositive status in the remission stage of MOGAD [9,25–28]. Consequently, a secondary prevention treatment strategy is recommanded for patients who experience a relapse and persistently positive MOG-IgG -[8,27,29]. However, there is no consensus on whether immunosuppressive therapy is necessary after a first MOGAD attack, especially for patients with the special phenotype of isolated ON [25,30–33]. Some studies found that the risk of future visual disability in the first-episode MOG-ON was as high as 8 %, suggesting that an unsatisfactory recovery from the onset attack may require immunosuppressive therapy [9,33]. A Chinese study suggested that initiation of maintenance therapy after the first attack and before the first relapse was associated with a decreased risk of a second attack of MOGAD, but this became insignificant in the multivariate analysis [27]. In the present study, approximately 90 % of affected eyes experienced a final BCVA of 0.3 logMAR. Some patients received oral immunosuppressants after the first episode of ON based on our experiences extrapolated from AQP4-seropositive NMOSD, and the majority of them remained relapse-free for a considerable period after initial corticosteroid therapy. Hence, it was inferred that visual outcomes were generally favorable in iMOG-ON, and MMF, albeit demonstrated to be effective in reducing relapse risk in relapsing MOGAD [32,33], may not be necessary if MOG-IgG serum titers were low during the first episode of iMOG-ON. Additionally, a dynamic longitudinal analysis of MOG-IgG titers, which was relatively expensive, uneconomical, time-consuming, and practically not feasible for some rural countries, may also not be so pressing in decision-making process to initiate long-term relapse prevention treatment in iMOG-ON. Further studies are needed to demonstrate the necessities of maintenance therapies for the first clinical attack of MOGAD, including low-dose oral corticosteroids, intravenous immunoglobulins, classic steroid-sparing antirheumatic immune suppressants, and B-cell-depleting therapies [8,33].

Our study has several limitations. First, it was a retrospective study, and some of the information was derived by self-report, which may lead to recall bias. Second, this work presented TIOVM was not associated with outcomes. However, 97 % of the afflicted eyes had a delay to IVMP of at least 5 days and 81 % had a delay of at least 7 days. When the vast majority of ON attacks were treated in a delayed fashion, it was difficult to provide a more accurate assessment of the effect of time to treatment on outcomes. Therefore, future research is necessary to enhance public awareness and education on MOG-ON in order to offer patients prompt and efficient treatment, thereby reducing treatment intervals. Third, visual outcomes should be evaluated more comprehensively with structural parameters acquired by optical coherence tomography and functional parameters of visual field. Fourth, because of the limited number of patients with MMF therapy, it is hard to further analyze the effects of oral prednisolone dosage on MMF analysis. Further studies with larger-scale, multi-center, prospective designs should be performed to investigate the timing of immunotherapeutic strategies for the first clinical attack of MOGAD.

Statement of ethics

This study was approved by the ethics committee of Beijing Tongren Hospital, Capital Medical University (Institutional Review Board number: TRECKY2020-053). All participants signed informed consent and they were treated in accordance with the tenets of the Declaration of the Helsinki.

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Data availability statement

The data that support the findings of this study are available from the corresponding author (Dr. Liping Zhu) or the first author (Dr. Juan Zhao) upon reasonable request. Please contact the corresponding author (zlp1742@126.com) or the first author (zhj7509@163.com) for inquiries regarding data access.

CRediT authorship contribution statement

Juan Zhao: Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Chao Meng:** Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation. **Hanqiu Jiang:** Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation. **Chuntao Lai:** Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation. **Yanjun Guo:** Validation, Supervision, Resources, Project administration, Methodology, Investigation. **Liping Zhu:** Writing – review & editing, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jiawei Wang:** Writing – review & editing, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing 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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e33263.

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