# The Diagnostic Yield of Antiacetylcholine Receptor Antibodies Versus Antimuscle Kinase Antibodies in Ocular Myasthenia Gravis: A Meta-Analysis

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**Background:** Ocular myasthenia gravis (OMG) is an autoimmune disease characterized by autoantibodies targeting postsynaptic proteins at the neuromuscular junction, leading to weakness and fatigability of the levator palpebrae superioris, orbicularis oculi and extraocular muscles. Although OMG is primarily a clinical diagnosis, serological antibody testing, predominantly acetylcholine receptor (AChR) antibodies, is usually performed. The clinical utility of muscle-specific kinase (MuSK) antibodies is less well established in OMG. This meta-analysis evaluates the use of anti-AChR and anti-MuSK in patients with OMG and the relative costs of simultaneous vs sequential testing.

**Methods:** Studies were extracted from Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase (Ovid), Medline (Ovid), and additional gray literature. A systematic review was conducted using Covidence with 2 independent reviewers for study selection and data extraction. The meta-analysis was conducted with R version 4.4.1 on RStudio, and the *meta* package. Depending on the level of heterogeneity, either a fixed-effects or random-effects model was used to pool the data. Funnel plots were used to assess publication bias.

**Results:** The pooled analysis of 44 studies (n = 4,937 patients with OMG) revealed 59% (95% confidence interval [CI]: 52%–66%) positivity for anti-AChR, whereas the pooled analysis of 34 studies with (n = 3,380) showed 5% (95% CI: 2%–9%) positivity for anti-MuSK. From 62 studies (n = 5,180), 4 patients (0.1%) were doubly seropositive for anti-AChR and anti-MuSK. In patients with OMG positive for AChR antibodies, 5 studies (n = 527) reported a thymoma prevalence of 35% (95% CI: 3%–90%), underscoring the clinical value of anti-AChR testing. Four studies (n= 259) showed that anti-AChR positive patients had a 1.82 (95% CI: 1.15–2.88) times greater risk of progressing from OMG to generalized myasthenia gravis.

**Conclusions:** Almost two-thirds (59%) of the patients with OMG tested positive for AChR antibodies, but MuSK antibodies were only detected in 5% of patients. Positivity for anti-AChR in OMG was associated with a worse prognosis, including a higher prevalence of thymomas and an increased risk of disease generalization. Given the relatively low prevalence of anti-MuSK and the higher cost of anti-MuSK testing, clinicians could consider a stepwise approach to the serological diagnosis of OMG, where anti-MuSK is ordered only if the initial anti-AChR returns negative.

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Ocular myasthenia gravis (OMG) is an autoimmune disease that results from the production of autoantibodies targeting postsynaptic proteins in the neuromuscular junction.[1] These antibodies are directed against acetylcholine receptors (AChR) or muscle-specific kinase (MuSK), disrupting the normal transmission of nerve signals and leading to muscle weakness and fatigue.[2] The levator palpebrae superioris, extraocular muscles, and orbicularis oculi are usually affected, resulting in ptosis and ophthalmoplegia.[3] The diagnosis of OMG can be challenging, as it can mimic other conditions such as involutional ptosis, isolated cranial nerve palsies, internuclear ophthalmoplegia, or conjugate gaze palsy.[3]

The absence of standardized diagnostic criteria and evidence-based guidelines adds to the difficulty of diagnosing OMG, which typically relies on a combination of clinical and laboratory tests. These include investigations such as antibody testing, single-fiber electromyography (SFEMG), or diagnostic treatments involving cholinesterase inhibitors and immunosuppressants. However, SFEMG lacks specificity for OMG and can yield positive results in other conditions.[4] Pyridostigmine bromide carries risks, including hypotension and bradycardia.[5] Edrophonium chloride testing is largely unavailable in North America and carries risks of severe complications, including seizures and respiratory failure.[6] Therefore, serology testing remains a safe and simple method for diagnosing OMG.

The primary antibodies associated with myasthenia gravis are anti-AChR, anti-MuSK, and anti–low-density lipoprotein receptor–related protein 4 (LRP4).[7] Anti-LRP4 and anti-titin antibodies are poorly understood, and

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testing is not routinely performed,[8] so they are not included in this review. AChR antibodies disrupt neuromuscular transmission by blocking acetylcholine binding, promoting AChR internalization, and activating complement.[9] MuSK antibodies impair AChR clustering by disrupting MuSK-LRP4 interactions and may form monovalent "Fab-exchange" variants that exacerbate this effect.[10]

AChR antibodies are found in approximately 85% of patients with generalized myasthenia gravis (GMG).[11] Of the remaining 15% of patients with GMG who are seronegative for anti-AChR antibiodies, 50% will test positive for anti-MuSK antibodies.[11] Although the prevalence of autoantibodies in GMG is well established, it is less understood in OMG. AChR testing is believed to be less sensitive for OMG than GMG, as suggested by the last systematic review in 2006, which included few studies.[12] Advances in diagnostic antibody testing highlight the need to update the proportion of patients with OMG who test positive for AChR and MuSK antibodies to clarify their clinical utility and refine diagnostic algorithms. This meta-analysis investigates the diagnostic utility of AChR and MuSK antibodies in OMG.

## METHODS

### Search Strategy

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, with the PRISMA checklist provided in **Supplemental Digital Content** (see **Appendix A**, http://links.lww.com/WNO/A954). We conducted searches across multiple databases including CINAHL, Embase (Ovid), and Medline (Ovid) to investigate the use of AChR and MuSK antibodies in OMG. Our search strategy included terms for AChR and MuSK antibodies, along with terms for OMG (see **Supplemental Digital Content**, **Appendix B**, http://links.lww.com/WNO/A955). We also included gray literature sources, searching ClinicalTrials.gov and ProQuest Dissertations and Theses Global. Conferences from the Association for Research in Vision and Ophthalmology, the American Academy of Ophthalmology, and the Canadian Ophthalmological Society were manually reviewed to identify any relevant poster presentations or abstracts. The study was entered on PROSPERO #607881.

### Inclusion Criteria and Exclusion Criteria

The study population included adult patients aged 18 and older diagnosed with both OMG and GMG. We evaluated studies to assess the proportion of patients with OMG who tested positive for either AChR or MuSK antibodies. A subgroup analysis was conducted on patients with OMG positive for AChR antibodies to determine the proportion with thymoma and the risk of disease generalization. This systematic review and meta-analysis included observational studies, cohort studies, multicenter studies, randomized controlled trials, and clinical trials. Conference abstracts were considered if they provided adequate data. Publications from all years and geographical locations were included.

Case reports, commentaries, letters to the editor, narrative reviews, systematic reviews, and meta-analyses were excluded. Studies that were not available in English were also omitted to avoid potential translation errors.

### Study Selection

The screening process was conducted in 3 stages: title review, abstract review, and full-text review. Literature was first imported into COVIDENCE, where an automated duplicate check was performed, followed by a manual review to ensure that all duplicates were removed. Screening of titles (Level 1) and abstracts (Level 2) was conducted based on predefined inclusion and exclusion criteria. Full-text screening (Level 3) was then performed. Cohen kappa ($\kappa$) was calculated to evaluate the level of agreement between the 2 reviewers (E.T. and G.N.) during the study selection process. Figure 1 outlines the studies included and excluded at each screening stage. A list of citations for all studies included in this review are available in Supplementary Digital Content, Appendix C. (see **Supplementary Appendix C – Included Articles,** http://links.lww.com/WNO/A958).

### Risk of Bias

The risk of bias assessment was performed using the modified Downs and Black checklist (see **Supplemental Digital Content**, **Appendix D**, http://links.lww.com/WNO/A956). Studies with a score of 20 or higher were classified as high quality, those scoring between 15 and 19 were considered medium quality, and studies with scores below 15 were categorized as low quality.

### Statistical Analysis

Using R version 4.4.1 on Windows and RStudio, we conducted the meta-analysis with the *meta* package. Meta-analyses of proportions were performed using logit transformation and the inverse variance method to account for the variability in proportions across studies.

To compare the event rates between the seropositive and seronegative groups, risk ratios were calculated for each study based on the number of events and the total number of participants in each group. The risk ratios were defined as the ratio of the event risk in 1 group to the event risk in the other group.

A random-effects model was employed to pool the risk ratios across studies, yielding an overall estimate of the relative risk between the groups. Statistical analysis was performed using the *metabin* function from the *meta* package in R.

We quantified the heterogeneity between the studies using the $I^2$ value. The $\chi^2$ test was utilized to assess whether

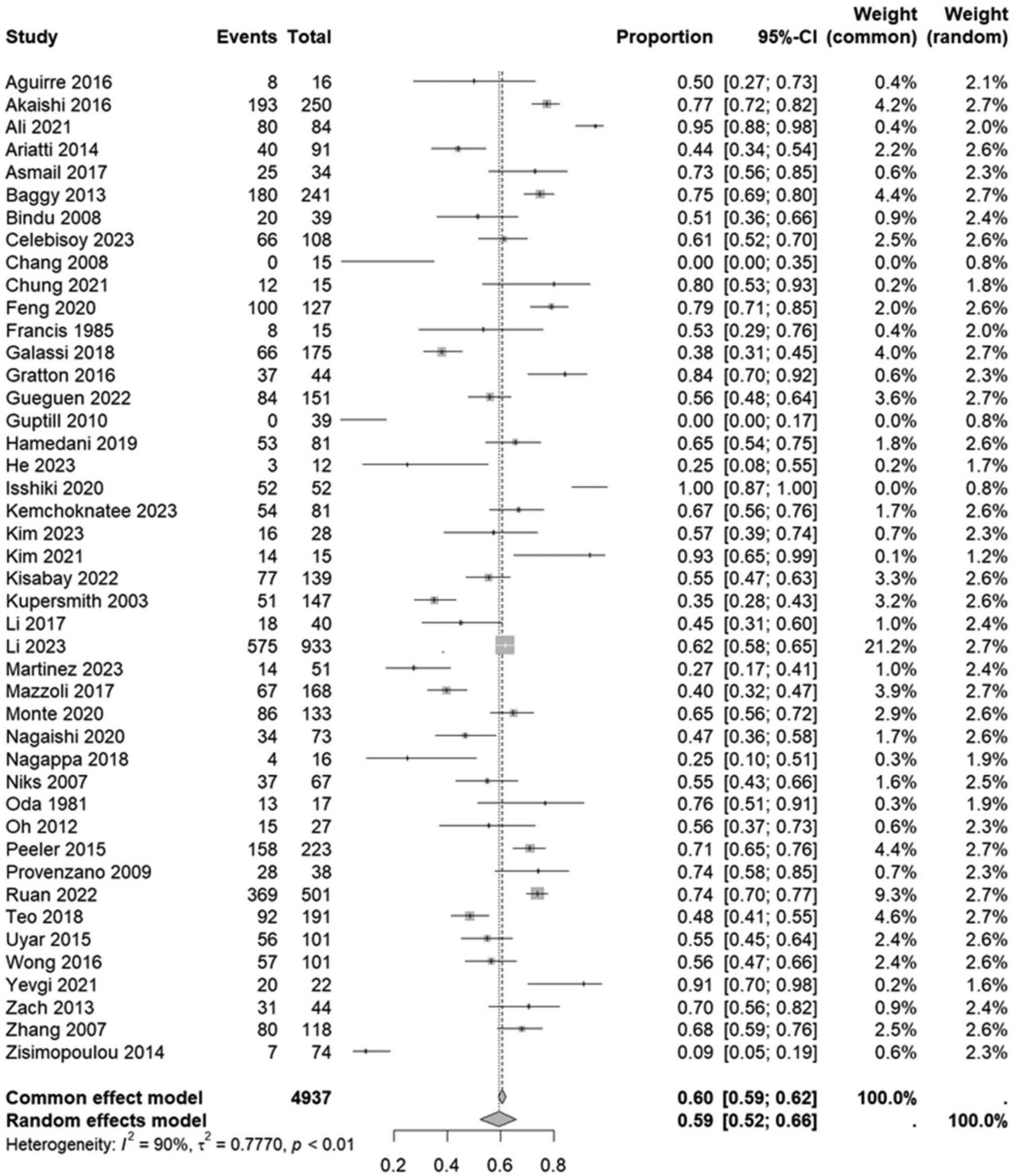


**FIG. 1.** Forest plot depicting the prevalence of antiacetylcholine receptor antibodies in patients with ocular myasthenia gravis from 44 different studies (N = 4,937). There was significant heterogeneity among the studies ($I^2$ = 90%, $P$ <0.01); therefore, a random effects model was employed, which yielded a prevalence of 0.59 (95% CI [0.52–0.66]). CI, confidence interval.

the observed variability between studies was due to random chance. A significant $\chi^2$ result, along with a low $P$-value compared to its degrees of freedom, indicated the presence of heterogeneity. Based on the level of heterogeneity identified, appropriate models were applied. A random-effects model was applied to account for between-study variance, and a fixed-effect model was also calculated for comparison. The results were presented using forest plots.

To assess potential publication bias, funnel plots were generated by plotting standard error against the logit-transformed proportion. Each point represents an individual study in the meta-analysis. The logit transformation was used to stabilize variance and improve symmetry in the distribution of proportions, especially when values are near 0 or 1. This adjustment makes the data more normally distributed, enhancing interpretability and allowing for a clearer assessment of publication bias in the funnel plot. A symmetric funnel shape indicates minimal publication bias, as studies are expected to be symmetrically distributed around the mean effect size. Asymmetry in the funnel plot could suggest the presence of publication bias or other small-study effects, with smaller studies potentially showing more variability around the effect size.

## RESULTS

### Search Results

In total, 1,294 studies were imported into COVIDENCE following searches in online databases and gray literature. After removing 372 duplicates, 786 studies were excluded based on their titles and abstracts, leaving 136 for full-text review. Of these, 62 articles were selected for data extraction and included in the meta-analysis, whereas 74 were excluded for being irrelevant or failing the screening criteria. Although 62 articles were included for data extraction in the meta-analysis, specific subsets of these studies contributed to different analyses. These results are summarized by **Supplemental Digital Content** (see **Figure S1**, http://links.lww.com/WNO/A951). Inter-rater reliability during the screening process was assessed using Cohen kappa (k) coefficients, which were 0.50 for title/abstract screening and 0.94 for full-text screening.

### Study Demographics

Table 1 outlines the study demographic characteristics of this meta-analysis. This review includes 62 studies, all of which were retrospective cohort studies. The mean age was 47 years, and 56% of the participants were female. Most studies were conducted in the United States, Italy, and China, with the remaining studies originating from various countries, including Japan, Turkey, Korea, and India. For studies that investigated the risk of generalization, the median follow-up time was 40 months (range 24–96 months).

### Serologic Assays in Myasthenia Gravis

Radioimmunoprecipitation assays (RIPA) were the most commonly used method for detecting both AChR (29.5%) and MuSK (35.2%) antibodies. ELISA was the next most common for AChR (20%), whereas cell-based assays (CBAs) were used in 26.8% of MuSK cases. Additional details are provided in the **Supplemental Digital Content** (see **Table S1**, http://links.lww.com/WNO/A953).

### Diagnostic Utility of Acetylcholine Receptor Antibodies vs Muscle Specific Kinase Antibodies in Patients With Ocular Myasthenia Gravis

Among 4,937 patients in 44 studies, the prevalence of AChR antibodies in OMG was 0.59 (95% confidence interval [CI]: 0.52–0.66), with significant heterogeneity ($I^2$ = 90%, $P < 0.01$) (Fig. 2). In contrast, among 3,380 patients in 34 studies, the prevalence of MuSK antibodies in patients with OMG was much lower, at 0.05 (95% CI: 0.02–0.09; Fig. 3). Significant heterogeneity was also found ($I^2$ = 80%, $P < 0.01$).

### Clinical Utility of Antiacetylcholine Receptor Positivity in Patients With Ocular Myasthenia Gravis

Figure 4 illustrates the proportion of patients with anti-AChR positive OMG with a thymoma. Across 5 studies, significant heterogeneity was observed ($I^2$ = 88%, $P < 0.01$). Pooled data from 527 patients with OMG indicated that 35% (95% CI: 3%–90%) of anti-AChR positive patients had a thymoma. Of 226 patients with seronegative OMG, 2 cases (0.88%) had thymoma. Among 10 Anti-MuSK positive patients, 1 case (10%) of thymoma was documented.

Figure 4 highlights the risk of generalization in patients with OMG with positive AChR antibodies. The risk ratio compares the likelihood of disease generalization between anti-AChR positive vs anti-AChR negative patients. In 4 studies, moderate heterogeneity was observed ($I^2$ = 51%, $P$ = 0.10). Analysis of 259 patients revealed that anti-AChR positivity was linked to a 1.82-fold increased risk (95% CI: 1.15–2.88) of progressing from OMG to GMG.

### Publication Bias and Risk of Bias Assessment

The funnel plots for the prevalence of AChR antibodies in patients with OMG, MuSK antibodies in patients with OMG, thymomas in patients with anti-AChR positive OMG, and the risk of generalization in patients with anti-AChR positive OMG revealed no significant asymmetry, suggesting a low likelihood of publication bias (see **Supplemental Digital Content**, **Figure S2**, http://links.lww.com/WNO/A952). For the Risk of Bias assessment, 34 studies were classified as high quality, scoring 20 or higher on the risk of bias assessment. Twenty-eight studies were considered medium quality, with scores ranging between 15 and 19, whereas no studies were categorized as low quality, as none scored below 15.

## DISCUSSION

This meta-analysis of 62 studies (N = 5,180) evaluated the diagnostic utility of AChR and MuSK antibodies by assessing their prevalence in patients with OMG. In this systematic review, 59% (95% CI: 52%–66%) of OMG tested positive for AChR antibodies, whereas only 5% (95% CI: 2%–9%)

**TABLE 1.** Study demographics of the publications included in this meta-analysis. All studies were retrospective in design.

| Author | Year | Location | N (overall) | Age | SD | Female (%) |
|---|---|---|---|---|---|---|
| Abukhalil | 2015 | United States | 44 | 45.54 | 15.78 | 65.9 |
| Aguirre | 2016 | Argentina | 130 | — | — | 64.6 |
| Akaishi | 2016 | Japan | 923 | 47.3 | 18.8 | 65.4 |
| Ali | 2021 | Egypt | 147 | 34.2 | 16.6 | 72.8 |
| Ariatti | 2014 | Italy | 91 | 70 | 11.6 | 40.6 |
| Asmail | 2017 | Israel | 126 | 56.9 | 19.11 | 48.4 |
| Baalbaki | 2023 | Lebanon | 17 | — | — | 70 |
| Baggy | 2013 | Italy | 677 | — | — | 68.7 |
| Bindu | 2008 | India | 165 | 37.8 | 16.5 | — |
| Celebisoy | 2023 | Turkey | 108 | 57 | — | 49.1 |
| Chan | 2007 | United States | 569 | 51.9 | — | 46 |
| Chang | 2008 | Sri Lanka | 113 | — | — | — |
| Chung | 2021 | Australia | 114 | — | — | — |
| Damato | 2022 | Italy | 82 | 38.5 | — | 62 |
| Farrugia | 2006 | United States | 26 | 33.23 | 18.02 | 73.1 |
| Feng | 2020 | China | 127 | 45.33 | 16.06 | 57.48 |
| Francis | 1985 | Australia | 15 | 56 | — | 40 |
| Galassi | 2018 | Italy | 175 | 64 | — | 41.1 |
| Gratton | 2016 | United States | 44 | — | — | — |
| Gueguen | 2022 | Germany | 151 | 49.3 | — | 41.1 |
| Guptill | 2010 | United States | 110 | 36.6 | — | 85 |
| Hamedani | 2019 | United States | 81 | 59.73 | 13.21 | 43.21 |
| He | 2023 | China | 34 | — | — | 76.5 |
| Huang | 2008 | Taiwan | 44 | 48.6 | 13.5 | 72.7 |
| Isshiki | 2020 | Japan | 52 | 61.1 | 14.7 | 48.1 |
| Kemchoknatee | 2023 | Thailand | 81 | 49.7 | 13.71 | 67.9 |
| Kim | 2022 | Korea | 28 | 55.39 | 14.49 | 57.1 |
| Kim | 2021 | Korea | 36 | 56.87 | 13.36 | 46.7 |
| Kisabay | 2022 | Turkey | 139 | 49.8 | — | 50.3 |
| Kupersmith | 2003 | United States | 147 | 50 | 21 | 42.9 |
| Kwon | 2023 | Korea | 160 | 48 | | 53.8 |
| Lavrnic | 2004 | Serbia | 55 | 37.47 | | 70.91 |
| Li | 2017 | China | 116 | 38.76 | 20.86 | 59.5 |
| Li | 2023 | China | 2272 | 43.3 | 22.5 | 55.8 |
| Martinez | 2023 | Canada | 153 | 60 | 14 | 58.2 |
| Mazzoli | 2017 | Italy | 168 | 65 | — | 40.5 |
| McConville | 2004 | United Kingdom | 84 | — | — | — |
| Monte | 2020 | Italy | 133 | 48.5 | — | 27.8 |
| Nagaishi | 2020 | Japan | 73 | 51 | — | 36 |
| Nagappa | 2018 | India | 85 | 39.29 | 17.3 | 47 |
| Niks | 2007 | Netherlands | 253 | — | — | — |
| Oda | 1981 | Japan | 54 | — | — | 55.6 |
| Oh | 2012 | United States | 235 | 49.9 | 19.7 | 51.9 |
| Park | 2018 | Korea | 87 | — | — | — |
| Pasnoor | 2010 | United States | 53 | 37.8 | 19.5 | 85 |
| Peeler | 2015 | United States | 223 | 59.2 | 16.4 | 37.7 |
| Provenzano | 2009 | Italy | 240 | | | 59 |
| Ricciardi | 2024 | Italy | 202 | 40.3 | 15.6 | 80.7 |
| Romi | 2006 | Norway | 51 | 36 | 18 | 52.9 |
| Ruan | 2022 | China | 501 | 44.7 | 19.5 | 47.7 |
| Samal | 2020 | India | 87 | 43 | — | 49.43 |
| Teo | 2018 | Singapore | 191 | 59 | | 48.4 |
| Tsonis | 2014 | Greece | 633 | 54.4 | 14.5 | — |
| Uyar | 2015 | Turkey | 101 | 40 | — | 80 |
| Wong | 2016 | United Kingdom | 101 | 48 | 17.1 | 56.4 |
| Yevgi | 2021 | Turkey | 53 | 38.5 | 15.1 | 52.8 |

(Continued)

| Author | Year | Location | N (overall) | Age | SD | Female (%) |
|---|---|---|---|---|---|---|
| Zach | 2013 | Austria | 44 | 54 | 17 | 45.4 |
| Zhang | 2007 | China | 291 | — | — | 56 |
| Zhao | 2021 | China | 18 | 40.28 | 18.57 | 0.778 |
| Zhou | 2004 | United States | 25 | 43 | 15.99 | 68 |
| Zhou | 2022 | China | 69 | 44.7 | 15.84 | 79.71 |
| Zisimopoulou | 2014 | Greece | 404 | 33.4 | — | — |

All studies were retrospective in design.

of patients were positive for anti-MuSK. Rarely were patients seropositive for both anti-AChR and anti-MuSK. This suggests that routine anti-AChR antibody testing remains warranted in OMG due to its relatively high prevalence, whereas routine anti-MuSK testing has a more limited diagnostic yield. In keeping with prior studies, patients with OMG were more likely to be seronegative than anti-MuSK positive,[13] and double seropositivity was exceedingly rare.

Approximately 10%–20% of patients with myasthenia gravis have an anterior mediastinal tumor or thymoma.[14] A delayed thymoma diagnosis poses a high mortality risk due to local invasion, whereas timely surgical resection can improve symptoms and increase the chances of remission.[15] The presence of a thymoma may also complicate myasthenia gravis (MG) management, as it is associated with more severe disease and a higher risk of myasthenic crisis.[16] Of

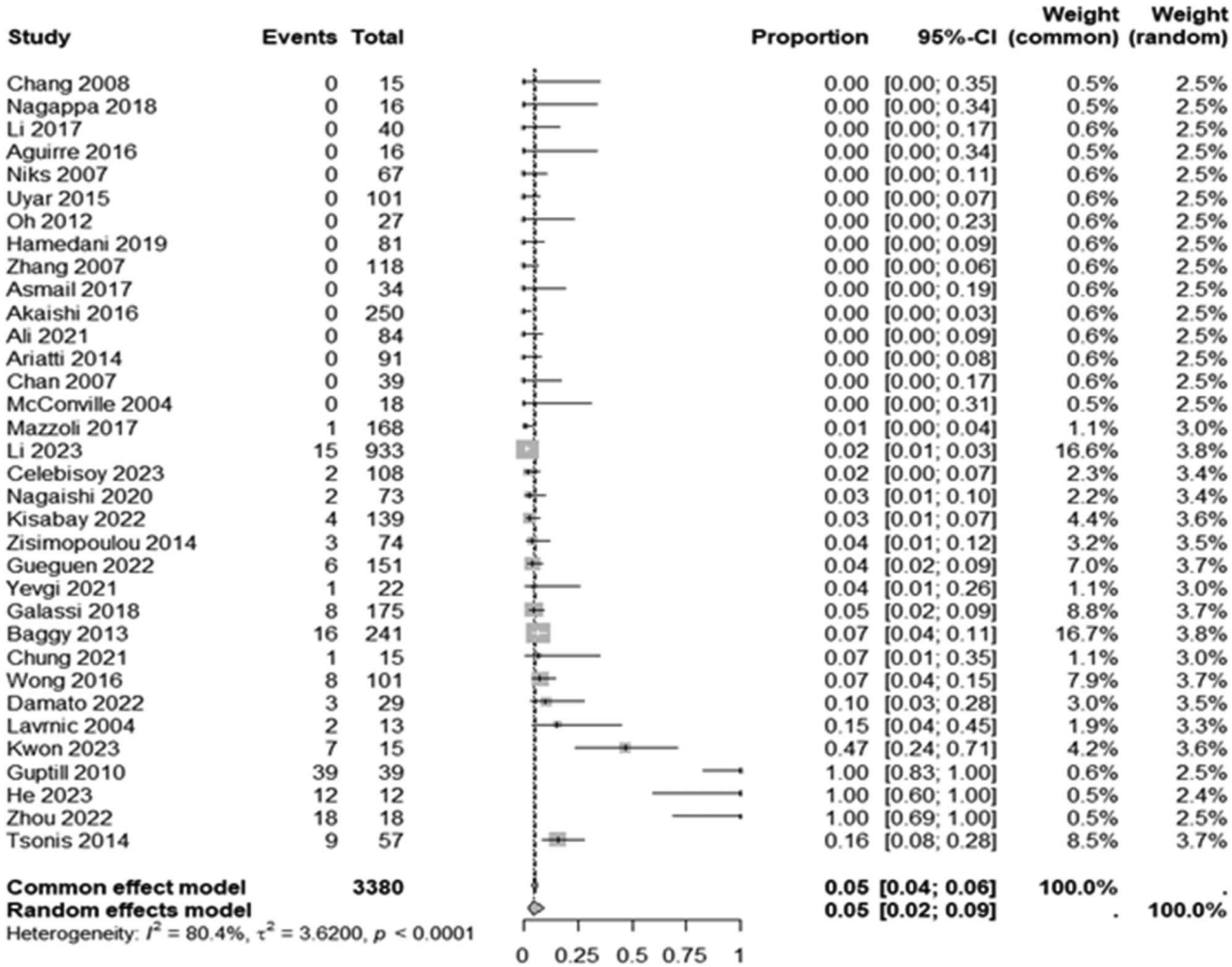


**FIG. 2.** Forest plot depicting the prevalence of anti-muscle specific kinase (MuSK) antibodies in patients with ocular myasthenia gravis from 34 different studies (N = 3,380). There was significant heterogeneity among the studies ($I^2$ = 80%, $P$ <0.01). The random effects model yielded a prevalence of 0.05 (95% CI [0.02–0.09]). CI, confidence interval.

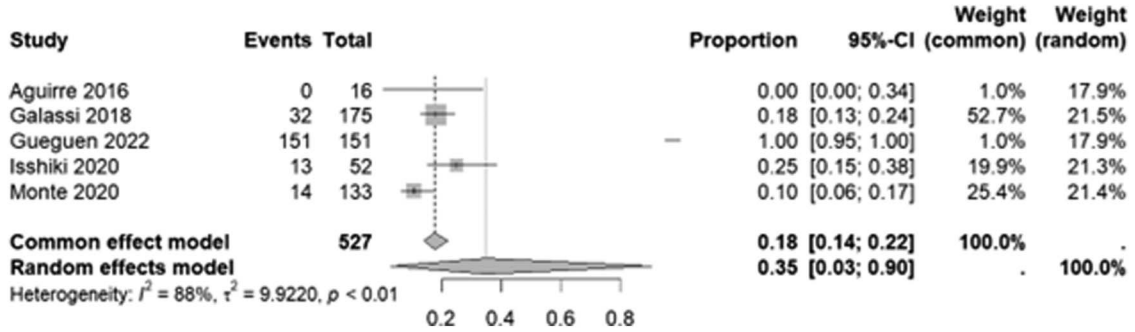


**FIG. 3.** Forest plot depicting the proportion of patients with ocular myasthenia gravis with positive antiacetylcholine receptor antibodies and a thymoma from 5 different studies (N = 527). There was significant heterogeneity among the studies ($I^2$ = 88%, $P$ <0.01). The random effects model yielded a prevalence of 0.35 (95% CI [0.03–0.90]). CI, confidence interval.

the patients positive for anti-AChR, our meta-analysis found that 35% (95% CI: 3%–90%) had a thymoma. Thymomas were rare in seronegative OMG, with 2 cases (0.88%), and in anti-MuSK positive OMG, with 1 case (10%). Current diagnostic guidelines recommend that all patients with MG undergo chest computed tomography to rule out thymoma.[17] Our findings suggest that anti-AChR serology testing might help identify a more targeted population of patients with OMG to be screened for a thymoma.

Patients with anti-AChR positive OMG were 1.82 times (95% CI: 1.15–2.88) more likely to progress to GMG compared to patients with seronegative OMG. Antibody-positive patients have been previously found to be more likely to experience disease progression, leading to more severe symptoms like generalized muscle weakness and respiratory involvement.[18] Early identification allows for closer monitoring and more aggressive treatment to prevent or mitigate progression to GMG, highlighting the prognostic value of anti-AChR antibody testing in OMG.

The prognostic value of MuSK antibodies for generalization risk in OMG is unclear. There is debate about whether a purely OMG-MuSK subtype exists, given its rarity and the tendency of many patients to progress to GMG.[18] In MuSK-positive GMG, the onset is typically acute and muscle involvement is more selective, affecting facial, bulbar, neck, and respiratory muscles.[15] However, in patients who remain purely MuSK-positive OMG, the clinical course tends to be more benign yet heterogeneous. Patients may experience mild ocular symptoms, progressive extraocular muscle atrophy, or spontaneous remission.[15] In summary, for patients who are anti-MuSK positive and remain purely OMG, the clinical course appears more benign, whereas those who progress to include facial, bulbar, and respiratory symptoms likely represent early-detected GMG. Anti-MuSK serological testing may add value to risk stratification in OMG by helping identify patients at greater risk of generalization.

MuSK antibodies were only detected in 5% of patients with OMG, so routine testing for anti-MuSK is low yield. Sequential serologic testing, beginning with anti-AChR (RIPA) and proceeding to anti-MuSK only if negative. If arrangements can be made with the laboratory to hold serum from the initial blood draw for testing for anti-MuSK antibodies if anti-AChR antibody testing is negative. This will also save the patient's time and transportation costs. Although anti-MuSK seropositivity is relatively low and adds health care expenses, its presence supports continued glucocorticoid therapy in suspected myasthenia gravis cases and may help identify patients at higher risk for bulbar symptoms and respiratory failure on generalization.

This meta-analysis has some limitations. Variability in serological testing methods including fixed vs live CBA, RIPA, and

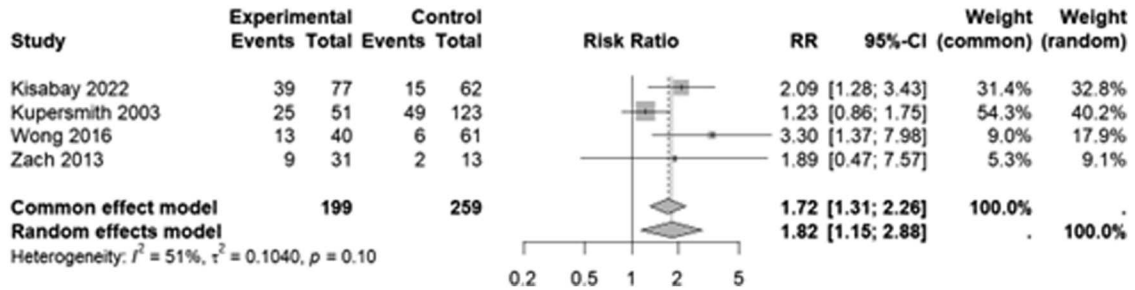


**FIG. 4.** Forest plot depicting the risk ratio of generalization in patients with ocular myasthenia gravis with positive antiacetylcholine receptor antibodies from 4 different studies (N = 259). There was no significant heterogeneity among the studies ($I^2$ = 51%, $P$ <0.10). A common effects model yielded a risk ratio of 1.72 [95% CI: 1.31–2.26]. A random effects model was also employed, which yielded a risk ratio of 1.82 [95% CI: 1.15–2.88]. CI, confidence interval.

ELISA may contribute to inconsistent antibody positivity rates.[19] Variations in assay accuracy, along with the potential for false positives,[20] could affect the consistency of our results. Another limitation is that the inclusion of only patients with established myasthenia gravis means the observed seroprevalence may not accurately reflect the true sensitivity and specificity of anti-AChR and anti-MuSK testing. The absence of a control group with similar clinical presentations but without OMG further limits our ability to assess the true diagnostic accuracy of these antibodies. These limitations highlight the challenges in accurately assessing the diagnostic value of serological tests for myasthenia gravis.

In conclusion, the routine testing for AChR antibodies in patients with suspected OMG is reasonable due to its higher prevalence and potential prognostic value. Instead of routinely requisitioning anti-AChR and anti-MuSK simultaneously in the initial work-up of patients with suspected OMG, consideration should be given to using anti-MuSK as a second-line test that is obtained after anti-AchR is negative.

STATEMENT OF AUTHORSHIP
Conception and design: E. Tran, E. Ing; Acquisition of data: E. Tran, G. Nair; Analysis and interpretation of data: E. Tran. Drafting the manuscript: L. Bursztyn, J. A. Fraser, E. Ing; Revising the manuscript for intellectual content: L. Bursztyn, J. A. Fraser, E. Ing. Final approval of the completed manuscript: L. Bursztyn, J. A. Fraser, E. Ing.

## REFERENCES

1. **Nair AG**, Patil-Chhablani P, Venkatramani DV, Gandhi RA. Ocular myasthenia gravis: a review. Indian J Ophthalmol. 2014;62:985–991.
2. **Dresser L**, Wlodarski R, Rezania K, Soliven B. Myasthenia gravis: epidemiology, pathophysiology and clinical manifestations. J Clin Med. 2021;10:2235.
3. **Behbehani R**. Ocular myasthenia gravis: a current overview. Eye Brain. 2023;15:1–13.
4. **Milone M**, Monaco M, Evoli A, Servidei S, Tonali P. Ocular myasthenia: diagnostic value of single-fibre EMG in the orbicularis oculi muscle. J Neurol Neurosurg Psychiatry. 1993;56:720–721.
5. **Khan M**, Tiwari A, Khan Z, et al. Pyridostigmine induced prolonged asystole in a patient with myasthenia gravis successfully treated with hyoscyamine. Case Rep Cardiol. 2017;2017:6956298.
6. **Ing EB**, Ing SY, Ing T, Ramocki JA. The complication rate of edrophonium testing for suspected myasthenia gravis. Can J Ophthalmol. 2000;35:141–145; discussion 145.
7. **Koneczny I**, Herbst R. Myasthenia gravis: pathogenic effects of autoantibodies on neuromuscular architecture. Cells. 2019;8:671.
8. **Zisimopoulou P**, Evangelakou P, Tzartos J, et al. A comprehensive analysis of the epidemiology and clinical characteristics of anti-LRP4 in myasthenia gravis. J Autoimmun. 2014;52:139–145.
9. **Gomez AM**, Van Den Broeck J, Vrolix K, et al. Antibody effector mechanisms in myasthenia gravis-pathogenesis at the neuromuscular junction. Autoimmunity. 2010;43:353–370.
10. **Koneczny I**, Stevens JA, De Rosa A, et al. IgG4 autoantibodies against muscle-specific kinase undergo Fab-arm exchange in myasthenia gravis patients. J Autoimmun. 2017;77:104–115.
11. **Meriggioli MN**, Sanders DB. Autoimmune myasthenia gravis: emerging clinical and biological heterogeneity. Lancet Neurol. 2009;8:475–490.
12. **Benatar M**. A systematic review of diagnostic studies in myasthenia gravis. Neuromuscul Disord. 2006;16:459–467.
13. **Evoli A**, Alboini PE, Iorio R, Damato V, Bartoccioni E. Pattern of ocular involvement in myasthenia gravis with MuSK antibodies. J Neurol Neurosurg Psychiatry. 2017;88:761–763.
14. **Aydemir B**. The effect of myasthenia gravis as a prognostic factor in thymoma treatment. North Clin Istanbul. 2016;3:194–200.
15. **Rodolico C**, Bonanno C, Toscano A, Vita G. MuSK-associated myasthenia gravis: clinical features and management. Front Neurol. 2020;11:660.
16. **Nelke C**, Stascheit F, Eckert C, et al. Independent risk factors for myasthenic crisis and disease exacerbation in a retrospective cohort of myasthenia gravis patients. J Neuroinflammation. 2022;19:89.
17. **Lorenzoni PJ**, Augusto LP, Kay CSK, Scola RH, Werneck LC. Myasthenia gravis and thymus: long-term follow-up screening of thymectomized and non-thymectomized patients. Arq Neuropsiquiatr. 2013;71:462–464.
18. **Guo RJ**, Gao T, Ruan Z, et al. Risk factors for generalization in patients with ocular myasthenia gravis: a multicenter retrospective cohort study. Neurol Ther. 2022;11:73–86.
19. **Li Z**, Zhang C, Chang T, et al; SCREAM Study Investigators. A multicentre, prospective, double-blind study comparing the accuracy of autoantibody diagnostic assays in myasthenia gravis: the SCREAM study. Lancet Reg Health West Pac. 2023;38:100846.
20. **Maddison P**, Sadalage G, Ambrose PA, Jacob S, Vincent A. False-positive acetylcholine receptor antibody results in patients without myasthenia gravis. J Neuroimmunol. 2019;332:69–72.