Z Rheumatol 2024 · 83 (Suppl 1):S214–S221
https://doi.org/10.1007/s00393-022-01216-2
Accepted: 17 April 2022
Published online: 16 May 2022

Redaktion
Ulf Müller-Ladner, Bad Nauheim
Uwe Lange, Bad Nauheim

Associations between anti-mitochondrial antibodies and cardiac involvement in idiopathic inflammatory myopathy patients

A systematic review and meta-analysis

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Abstract

Objective: The objectives of this study are to analyze the association between anti-mitochondrial antibody (AMA) and cardiac involvement in idiopathic inflammatory myopathy (IIM) and to evaluate the diagnostic value of AMA for cardiac involvement in IIM patients.

Methods: We conducted a comprehensive search in PubMed, Web of Science, EMBASE, and the Cochrane Library to identify English-language studies published before November 19, 2021. Stata 12.0 software (Stata Corp., College Station, TX, USA) was used for the statistical analyses. We used the sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and summary receiver operating characteristic (SROC) curve to evaluate the diagnostic value of AMA for cardiac involvement in IIM patients. Statistical heterogeneity of studies was assessed using the I^2 statistic with 95% confidence intervals (95% CIs).

Results: Seven studies were included in the final analyses, with a total of 2308 IIM patients (including 171 AMA-positive and 2137 AMA-negative patients). The pooled sensitivity of AMA for cardiac involvement in IIM patients was 0.29 (95% CI: 0.19–0.43) and specificity was 0.92 (95% CI: 0.88–0.96). The pooled PLR was 3.9 (95% CI: 2.82–5.38), NLR was 0.76 (95% CI: 0.66–0.88), and the diagnostic odds ratio (DOR) was 5 (95% CI: 3–7). The area under the SROC curve was 0.76 (95% CI: 0.72–0.79).

Conclusion: The overall diagnostic value of AMA may not be very high for cardiac involvement in IIM patients.

Keywords
Idiopathic inflammatory myopathy · Anti-mitochondrial antibody · Cardiac involvement · Meta-analysis · Cardiovascular disease

Supplementary Information

The online version of this article (https://doi.org/10.1007/s00393-022-01216-2) includes Table S1.

Additional information
This article was registered in PROSPERO with registration number CRD42021289813.

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Introduction

Idiopathic inflammatory myopathies (IIM) are a collection of systemic autoimmune connective tissue diseases, with an incidence of 9–14 cases/million people and mainly including dermatomyositis (DM), polymyositis (PM), immune-mediated necrotizing myopathy (IMNM), sporadic inclusion body myositis (IBM), and overlap myositis [12, 25]. Data from recent studies have shown a significant rate of cardiac involvement in individuals with IIM [14], where the incidence of subclinical cardiac involvement in PM/DM patients ranges from 13 to 72%, much higher than other symptoms [21].

Anti-mitochondrial antibody (AMA) is a common autoantibody which is closely related to primary biliary cirrhosis (PBC), but is also noted in other autoimmune diseases, such as scleroderma, autoim-

Table 1 Characteristics of the studies included in the meta-analysis

Author	Year	Region	Inclusion criteria	No. patients	Method of antibodies determination	No. positive for antibodies tested who had cardiac involvement (*n*/*N*)	No. negative for antibodies tested who had cardiac involvement (*n*/*N*)	*P*-value	Specific manifestations of cardiac involvement	Score of quality
Maeda	2012 [18]	Japan	Adult patients diagnosed as inflammatory myopathies using the Bohan and Peter criteria [3, 4] included between November 1999 and April 2009	212	ELISA (MESACUP-2 test)	8/24	17/188	$P < 0.05$	Arrhythmias (supraventricular tachycardia, ventricular tachycardia, atrioventricular block), and decreased ejection fraction (< 50%)	11
Uenaka	2017 [29]	Japan	Adult patients diagnosed as inflammatory myopathies using the Bohan and Peter criteria included between March 2003 to January 2014	41	ELISA (MESACUP-2 test)	5/8	2/33	$P = 0.001$	Arrhythmia (atrial fibrillation, ventricular tachycardia, A-V block, or sick sinus syndrome); left ventricular systolic dysfunction (ejection fraction of < 52% for men and < 54% for women in UCG)	10
Liu, Y	2020 [16]	China	Adult patients diagnosed as IIM using the 2017 European League Against Rheumatism American College of Rheumatology classification criteria [17] included between January 2014 and January 2019	62	Not specified	8/9	23/53	$P = 0.026$	Atrial fibrillation, ventricular arrhythmia, abnormal cTnI, elevated NT-proBNP, and impaired cardiac systolic function	9
Huang, Y	2021 [10]	China	Adult patients diagnosed as inflammatory myopathies using the Bohan and Peter criteria included between 11 October 1997 to April 2019	75	Not specified	17/28	13/47	$P = 0.005$	Ventricular arrhythmia	9
Sabbagh	2021 [22]	America	Adult patients diagnosed as DM, PM, inclusion body myositis (IBM), or amyopathic DM using Bohan and Peter, Griggs [7], or Sontheimer criteria included between 2011 and 2015	619	ELISA (Quanta Lite M2 EP (MIT3))	5/32	49/587	$P = 0.2$	Myocarditis, atrial tachycardia, heart block, and cardiomyopathy	11
Zhang, L	2021 [32]	China	Adult patients diagnosed as IIM using the 2017 European League against Rheumatism/American College of Rheumatology Classification Criteria for Adult Idiopathic Inflammatory Myopathies included between January 2008 and December 2019	145	ELISA (an Anti-M2–3E ELISA kit)	21/29	33/116	$P < 0.001$	ECG, UCG abnormalities: atrial fibrillation; ventricular premature beats; complete right bundle branch block; supraventricular premature beat	11
Lixi Zhang	2021 [33]	China	Adult patients diagnosed as IIM using the 1975 Bohan and Peter criteria or Sontheimer criteria [27] included between January 2017 and May 2019	1154	Not specified	10/41	51/1113	$P < 0.001$	Congestive heart failure, conduction abnormality, supraventricular, or ventricular arrhythmia	10

A-V block auriculo-ventricular block, *DM* dermatomyositis, *ECG* electrocardiogram, *IBM* inclusion body myositis, *IIM* Idiopathic inflammatory myopathies, *PM* polymyositis, *UCG* ultrasound cardiogram

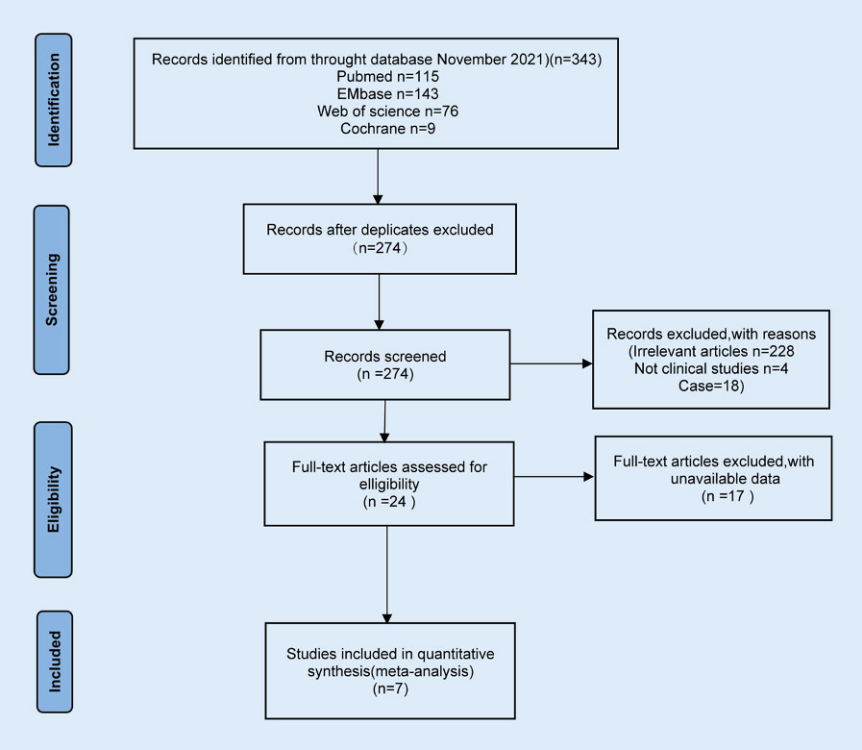

Fig. 1 ▲ Flow diagram of studies selection process

mune thyroid disease, and Sjogren's syndrome [5]. Previously, we have observed 7 patients with AMA-related myositis from North America and found that 71% had cardiac involvement [1]. Due to the fact that most current reports are small sample data or case reports, there is no clear consensus on the association between AMA and heart damage in patients with IIM.

Therefore, in this study, we conducted a systematic review of the literature aiming to analyze the association between AMA and cardiac involvement in IIM patients and evaluate the diagnostic value of AMA for cardiac involvement in patients with IIMs.

Methods

Search strategy

In this meta-analysis, we performed a search independently in PubMed, Web of Science, Embase, and the Cochrane Library to identify studies published in English prior to November 19, 2021. A combination of the following keywords was used to retrieve studies: "idiopathic inflammatory myopathy," "inflammatory muscle diseases," "myositis," "myopathy," "polymyositis," "immune-mediated necrotizing myopathy," "inclusion body myositis," "dermatomyositis," "juvenile dermatomyositis" AND "heart," "pericardial," "pericardium," "ventricular," "valvular," "echocardiography," "cardiac involvement," "myocarditis," "cardiovascular," "arrhythmia," "coronary heart disease," "atherosclerosis" AND "anti-mitochondrial antibody," "anti-AMA antibody." The reference lists of the retrieved articles were also manually screened independently to identify potentially relevant articles. The inclusion criteria were well specified and no discrepancies in search results were found.

Study selection

Studies were selected according to the following inclusion criteria: (1) patients with IIMs fulfilled the Bohan and Peter criteria [10, 16], the 2017 European League Against Rheumatism American College of Rheumatology classification criteria [7], Griggs [7], or Sontheimer [27] criteria; (2) availability of data pertaining to the AMA autoantibody status of patients with IIMs; (3) availability of adequate data to calculate true-positive (tp), false-positive (fp), true-negative (tn), false-negative (fn) rates; studies were excluded if they (1) were reviews, case reports, or letters; or (2) lacked a control group of AMA-negative IIM patients. For similar studies conducted by one research group, we gave priority to articles with a larger sample size.

Main outcome variables

Two reviewers independently browsed the potentially eligible articles and extracted the relevant data from each study. The following information was recorded: the first author's name, publication year, country, disease type, detection method, the total number of cases and controls, frequency of AMA in cases and controls, and detailed information about cardiac involvement, if available. Disagreements were resolved by discussion.

Risk of bias assessment

Two reviewers independently assessed the quality of the studies included using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool [29]. They performed the following assessment procedure: patient selection, index test, reference standard, and flow and timing. Each key domain includes two sections: risk of bias and applicability. If answers to all signaling questions for a domain are "yes," then we could judge the risk of bias as low. If any question is answered with "no," potential bias exists. Concerns about applicability are judged as "low," "high," or "unclear." We define "yes" as one score.

Analysis

We used Stata 12.0 software to statistically analyze sensitivity (Sen), specificity (Spe), diagnostic ratio (DOR), positive likelihood ratio (PLR), and negative likelihood ratio (NLR), finally calculating the overall odds ratios (ORs) with 95% confidence intervals (CIs) and the summary receiver operating characteristic (SROC) curve. We used the *P*-value and I^2 statistic to test for heterogeneity in every result. The selected studies are considered to be homogeneous if the *P*-value is greater than 0.1. When the *P*-

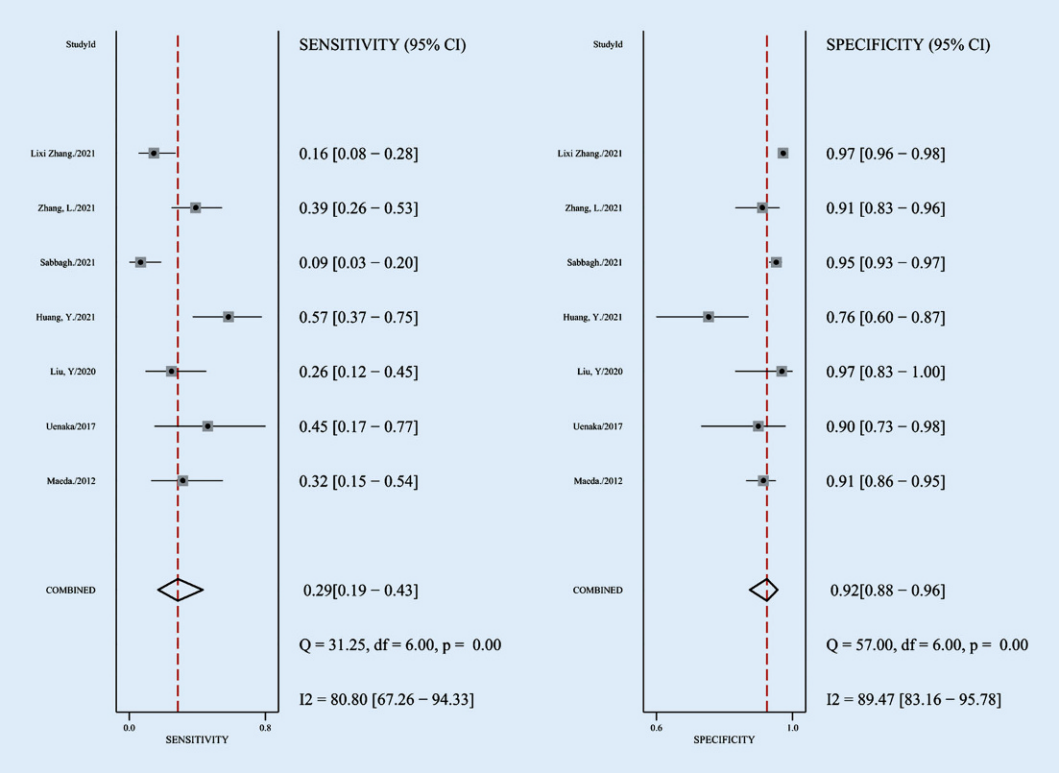

Fig. 2 ◄ Forest plots of estimated sensitivity and specificity of anti-mitochondrial autoantibody testing for cardiac involvement in idiopathic inflammatory myopathies

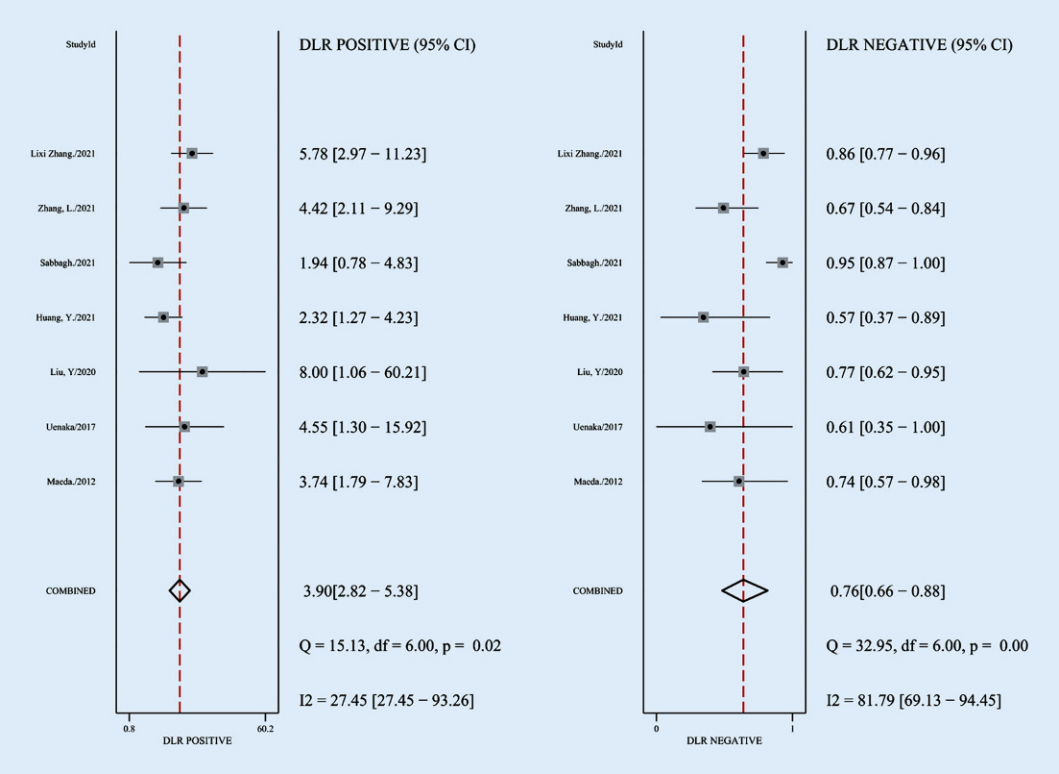

Fig. 3 ◄ Forest plots of estimated PLR and NLR of anti-mitochondrial autoantibody testing for cardiac involvement in idiopathic inflammatory myopathies

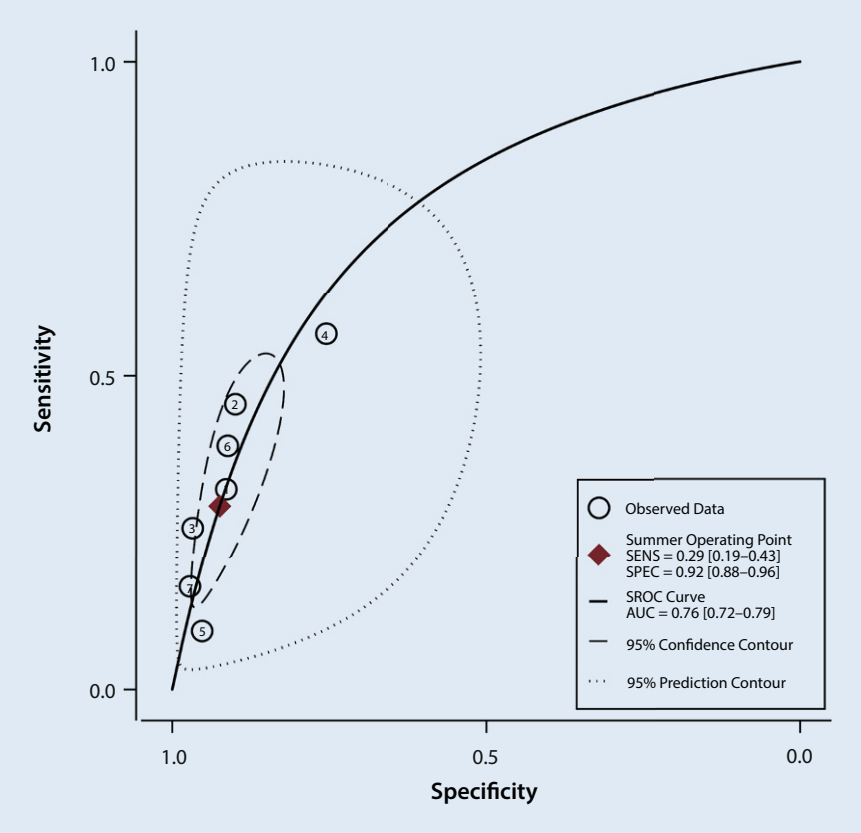

Fig. 4 ▲ Summary receiver operating characteristic (*SROC*) curve of anti-mitochondrial autoantibody testing. *Numbered circles* show sensitivity (*SENS*) and specificity (*SPEC*) estimates for individual studies. *Circle 1* represents the study by Maeda et al. [18]; *circle 2*, the study by Uenaka et al. [29]; *circle 3*, the study by Liu, Y et al. [16]; *circle 4*, the study by Huang, Y et al. [10]; *circle 5*, the study by Sabbagh. et al. [22]; *circle 6*, the study by Zhang, L et al. [32]; *circle 7*, the study by Lixi Zhang et al. [33]. The *diamond* represents the summary operating point (summary values for sensitivity and specificity) and the *broken line* delimits the 95% confidence region for the summary operating point. The numbers in brackets are the 95% confidence intervals. *AUC* area under the curve

value was >0.1 or I^2 was $<50\%$, a fixed-effects model was adopted. If P was <0.1 or I^2 was $>50\%$, we used a random-effects model. In addition, we performed a Deek's funnel plot for the assessment of publication bias.

Results

Literature search and study characteristics

A total of 343 related articles were obtained following a search of the four databases, with 69 replicated studies. After the titles and abstracts were screened, 250 studies were excluded. Seven studies were included after the final evaluation, with a total of 2308 IIM patients (including 171 AMA-positive and 2137 AMA-negative patients). The flow diagram of the search is shown in ◘ **Fig. 1**. The detailed characteristics of the eligible studies are depicted in ◘ **Table 1**. The studies included were conducted in three different countries, with four studies [10, 16, 32, 33] conducted in China, two [18, 29] in Japan, and one [22] in the USA. Moreover, three studies [18, 22, 32] described the demographics, clinical symptoms, and laboratory tests of AMA-positive patients.

Quality assessment

The quality score of each study is presented in Supplementary Table S1. Each study was assigned a score from 0 to 11 points, and higher scores indicated higher quality. The score of each study was more than 9 points. All the included studies received moderately high scores from the QUADAS-2 quality assessments [30].

Findings of the selected studies

In the meta-analysis, we use the random-effects model to pool the sensitivity and specificity because the I^2 value was over 50%. The overall pooled sensitivity and specificity were 0.29 (95% CI: 0.19–0.43) and 0.92, respectively (95% CI: 0.88–0.96; ◘ **Fig. 2**). The pooled PLR was 3.9 (95% CI: 2.82–5.38), NLR was 0.76 (95% CI: 0.66–0.88; ◘ **Fig. 3**), and DOR was 5 (95% CI: 3–7). The overall SROC curve is shown in ◘ **Fig. 4**, and the area under the SROC curve was 0.76 (95% CI: 0.72–0.79). The diagnostic accuracy of cardiac involvement in idiopathic inflammatory myopathy patients was not very high.

Publication bias

The Deek's funnel plot shows $t=0.77$, $P=0.48$ (◘ **Fig. 5**), so we consider there was no publication bias.

Discussion

In this meta-analysis, the pooled OR showed that AMA are associated with an increased risk of cardiac involvement in patients with IIM (OR = 5.07, 95% = 3.43–7.50). We also found that AMA autoantibody achieved the overall pooled sensitivity of 0.29 (95% CI: 0.19–0.43) and specificity 0.92 (95% CI: 0.88–0.96), and AUC was 0.76 (95% CI: 0.72–0.79). The results show that the diagnostic accuracy is not high, with low sensitivity and high specificity. The DOR represents the value that combines sensitivity and specificity, with a higher value meaning better diagnostic ability. The DOR in our study was 5 (95% CI: 3–7), suggesting the overall pooled accuracy was not high.

Although cardiac involvement in patients with IIM mainly presents subclinical symptoms, it has attracted increasing attention because it occurs frequently and even significantly worsens the prognosis [6, 9, 28]. Current research has found there is a correlation between cardiac involvement and the type of autoantibodies. For example, Behan et al. analyzed 55 patients with PM and found that 69% of PM patients complicated with cardiac involvement were anti-Ro antibody positive,

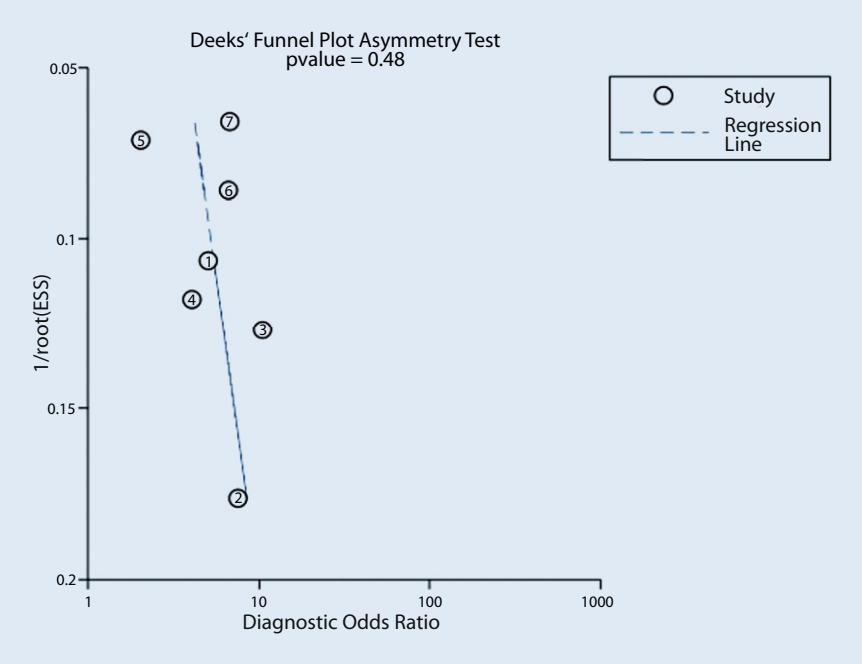

Fig. 5 ▲ Deek's funnel plot to evaluate the publication bias. *Circle 1* represents the study by Maeda et al. [18]; *circle 2*, the study by Uenaka et al. [29]; *circle 3*, the study by Liu, Y et al. [16]; *circle 4*, the study by Huang, Y et al. [10]; *circle 5*, the study by Sabbagh. et al. [22]; *circle 6*, the study by Zhang, L et al. [32]; *circle 7*, the study by Lixi Zhang et al. [33]

and the main manifestation was complete heart block [2]. Gupta et al. revealed that 25% of patients had arrhythmias in 12 patients with anti-SRP-positive PM [8]. Albayda et al. showed that 71% of the 7 patients with AMA-positive myositis had myocarditis, arrhythmia, and cardiomyopathy [1]. Therefore, further research in this field may help us identify IIM patients who are prone to cardiovascular damage and perform timely interventions.

AMA are autoantibodies against a variety of mitochondrial antigens, which can be detected in the IIM patient's serum by western blot and enzyme-linked immunosorbent assay. Although the positive rate of AMA in IIM is very low, it plays a role in cardiac involvement, including arrhythmia, myocarditis, heart failure, and cardiomyopathy [11, 13, 15, 19, 31]. At present, the role of AMA in the pathogenesis of cardiac involvement in IIM patients remains to be further elucidated; however, several theories have cast light upon possible mechanisms. Previous findings have shown that in dilated cardiomyopathy, the most enriched protein in the mitochondrial inner membrane is an organ-specific autoantigen [23], and the functionally active antibody–antigen complex of this structure reduces the rate of ADP/ATP exchange in cardiac mitochondria by blocking the substrate-binding site of the carrier protein [24], leading to an imbalance between energy supply and demand. This may be regarded as one of the mechanisms of AMA in cardiomyocyte dysfunction. Furthermore, AMA-related cardiac involvement may be related to mitochondrial dysfunction caused by cellular autoimmunity and humoral autoimmunity maintained by autoreactive T cells [19, 26].

We strictly followed the PRISM guidelines [20] to conduct the meta-analysis. However, there are still several limitations in the meta-analysis. First, despite making every effort to search for relevant studies, we may have ignored some studies not published online. Second, the present studies are mainly from the Asian population, which may lead to some population selection bias. Third, different ELISA kits were used, and the differences between the tests needs to be further confirmed. Finally, the small sample size of overall studies and the low positive rate for AMA could over- or underestimate the predictive ability of AMA for cardiac involvement of IIM patients. Therefore, further studies are required to obtain more definitive evidence.

Conclusion

Our findings indicate that the AMA autoantibody has a low sensitivity and high specificity for the diagnosis of cardiac involvement of IIM patients. Thus, the overall diagnostic value may not be very high. However, AMA still has a warning effect regarding cardiovascular damage in patients with IIM.

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Declarations

Conflict of interest. H. Wang, Y. Zhu, J. Hu, J. Jin, J. Lu, C. Shen, and Z. Cai declare that they have no competing interests.

For this article no studies with human participants or animals were performed by any of the authors. All studies mentioned were in accordance with the ethical standards indicated in each case.

References

1. Albayda J, Khan A, Casciola-Rosen L, Corse AM, Paik JJ, Christopher-Stine L (2018) Inflammatory myopathy associated with anti-mitochondrial antibodies: A distinct phenotype with cardiac involvement. Semin Arthritis Rheum 47:552–556. https://doi.org/10.1016/j.semarthrit.2017.06.004
2. Behan WM, Behan PO, Gairns J (1987) Cardiac damage in polymyositis associated with antibodies to tissue ribonucleoproteins. Brit Heart J 57(2):176–180. https://doi.org/10.1136/hrt.57.2.176
3. Bohan A, Peter JB (1975) Polymyositis and dermatomyositis (first of two parts). N Engl J Med 292(7):344–347. https://doi.org/10.1056/NEJM197502132920706
4. Bohan A, Peter JB (1975) Polymyositis and dermatomyositis (second of two parts). New Engl J Med 292(8):403–407. https://doi.org/10.1056/NEJM197502202920807
5. Dahlqvist G, Gaouar F, Carrat F, Meurisse S, Chazouillères O, Poupon R, Johanet C, Corpechot C (2017) Large-scale characterization study of patients with antimitochondrial antibodies but nonestablished primary biliary cholangitis. Hepatology 65:152–163. https://doi.org/10.1002/hep.28859

6. Dankó K, Ponyi A, Constantin T, Borgulya G, Szegedi G (2004) Long-term survival of patients with idiopathic inflammatory myopathies according to clinical features: a longitudinal study of 162 cases. Medicine 83(1):35–42. https://doi.org/10.1097/01.md.0000109755.65914.5e
7. Griggs RC, Askanas V, DiMauro S, Engel A, Karpati G, Mendell JR, Rowland LP (1995) Inclusion body myositis and myopathies. Ann Neurol 38(5):705–713. https://doi.org/10.1002/ana.410380504
8. Gupta R, Wayangankar SA, Targoff IN, Hennebry TA (2011) Clinical cardiac involvement in idiopathic inflammatory myopathies: a systematic review. Int J Cardiol 148(3):261–270. https://doi.org/10.1016/j.ijcard.2010.08.013
9. Højgaard PA-OX, Witting N, Rossing K, Pecini R, Hartvig Lindkær Jensen T, Hasbak P, Diederichsen LP (2021) Cardiac arrest in anti-mitochondrial antibody associated inflammatory myopathy. Oxf Med Case Rep. https://doi.org/10.1093/omcr/omaa150
10. Huang Y, Liu H, Wu CA-O, Fang L, Fang Q, Wang Q, Fei YA-O, Guo X, Zhang S (2021) Ventricular arrhythmia predicts poor outcome in polymyositis/dermatomyositis with myocardial involvement. Rheumatology 60:3809–3816. https://doi.org/10.1093/rheumatology/keaa872
11. Kadosaka T, Tsujinaga S, Iwano H, Kamiya K, Nagai A, Mizuguchi Y, Motoi K, Omote K, Nagai T, Yabe I, Anzai T (2020) Cardiac involvement with anti-mitochondrial antibody-positive myositis mimicking cardiac sarcoidosis. ESC Heart Fail 7:4315–4319. https://doi.org/10.1002/ehf2.12984
12. Khadilkar SV, Dhamne MC (2020) What is new in idiopathic inflammatory myopathies: mechanisms and therapies. Ann Indian Acad Neurol 23:458–467. https://doi.org/10.4103/aian.AIAN_400_19
13. Konishi H, Fukuzawa K, Mori S, Satomi-Kobayashi S, Kiuchi K, Suzuki A, Yano Y, Yoshida A, Hirata KI (2017) Anti-mitochondrial M2 antibodies enhance the risk of supraventricular arrhythmias in patients with elevated hepatobiliary enzyme levels. Intern Med 56:1771–1779
14. Lilleker JA-O, Vencovsky JA-O, Wang G, Wedderburn LR, Diederichsen LA-O, Schmidt J, Oakley P, Benveniste O, Danieli MA-O, Danko K, Thuy NTP, Vazquez-Del Mercado M, Andersson H, De Paepe B, deBleecker JL, Maurer B, McCann LJ, Pipitone N, McHugh N, Betteridge ZE, New P, Cooper RG, Ollier WE, Lamb JA, Krogh NS, Lundberg IE, Chinoy H (2018) The EuroMyositis registry: an international collaborative tool to facilitate myositis research. Ann Rheum Dis 77:30–39. https://doi.org/10.1136/annrheumdis-2017-211868
15. Liu XH, Feng XJ, Shi JY, Jia FW, Liu YX, Zhu YL, Li X, Wang YN, Huo L, Wang Q, Chen W (2020) The quest for diagnostic approaches of cardiac involvement in polymyositis and dermatomyositis. Ann Palliat Med 9:2256–2270. https://doi.org/10.21037/apm-19-650
16. Liu Y, Fang L, Chen W, Zhu Y, Lin X, Wang Y, Li X, Wang Q, Liu Z (2020) Identification of characteristics of overt myocarditis in adult patients with idiopathic inflammatory myopathies. Cardiovasc Diagn Ther 10:405–420. https://doi.org/10.21037/cdt.2020.03.04
17. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, de Visser M, Alfredsson L, Amato AA, Barohn RJ, Liang MH, Singh JA, Aggarwal R, Arnardottir S, Chinoy H, Cooper RG, Dankó K, Dimachkie MM, Feldman BM, Garcia-De La Torre I, Gordon P, Hayashi T, Katz JD, Kohsaka H, Lachenbruch PA, Lang BA, Li Y, Oddis CV, Olesinska M, Reed AM, Rutkowska-Sak L, Sanner H, Selva-O'Callaghan A, Song YW, Vencovsky J, Ytterberg SR, Miller FW, Rider LG (2017) 2017 European league against rheumatism/American college of rheumatology classification criteria for adult and juvenile idiopathic inflammatory Myopathies and their major subgroups. Ann Rheum Dis 76:1955–1964. https://doi.org/10.1136/annrheumdis-2017-211468
18. Maeda MH, Tsuji S, Shimizu J (2012) Inflammatory myopathies associated with anti-mitochondrial antibodies. Brain 135:1767–1777. https://doi.org/10.1093/brain/aws106
19. Matsumoto K (2012) Successful steroid therapy for heart failure due to myocarditis associated with primary biliary cirrhosis. Can J Cardiol 28:515.e3–515.e6. https://doi.org/10.1016/j.cjca.2011.12.010
20. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. https://doi.org/10.1371/journal.pmed.1000097
21. Opinc AA-O, Makowski MA-O, Łukasik ZA-O, Makowska JA-OX (2021) Cardiovascular complications in patients with idiopathic inflammatory myopathies: does heart matter in idiopathic inflammatory myopathies? Heart Fail Rev 26:111–125. https://doi.org/10.1007/s10741-019-09909-8
22. Sabbagh SA-O, Pinal-Fernandez I, Casal-Dominguez M, Albayda J, Paik JJ, Miller FW, Rider LG, Mammen AL, Christopher-Stine L (2021) Anti-mitochondrial autoantibodies are associated with cardiomyopathy, dysphagia, and features of more severe disease in adult-onset myositis. Baillieres Clin Rheumatol 40:4095–4100
23. Schultheiss HP, Bolte HD (1985) Immunological analysis of auto-antibodies against the adenine nucleotide translocator in dilated cardiomyopathy. J Mol Cell Cardiol 17(6):603–617. https://doi.org/10.1016/s0022-2828(85)80029-8
24. Schulze K, Becker BF, Schultheiss HP (1989) Antibodies to the ADP/ATP carrier, an autoantigen in myocarditis and dilated cardiomyopathy, penetrate into myocardial cells and disturb energy metabolism in vivo. Circ Res 64(2):179–192. https://doi.org/10.1161/01.res.64.2.179
25. Selva-O'Callaghan A, Pinal-Fernandez I, Trallero-Araguás E, Milisenda JC, Grau-Junyent JM, Mammen AL (2018) Classification and management of adult inflammatory myopathies. Lancet Neurol 17:816–828. https://doi.org/10.1016/S1474-4422(18)30254-0
26. Shimizu J (2013) Clinical and histopathological features of myositis associated with anti-mitochondrial antibodies. Rinsho Shinkeigaku 53:1114–1116. https://doi.org/10.5692/clinicalneurol.53.1114
27. Sontheimer RD (2002) Would a new name hasten the acceptance of amyopathic dermatomyositis (dermatomyositis siné myositis) as a distinctive

Zusammenfassung

Zusammenhang zwischen antimitochondrialen Antikörpern und kardialer Beteiligung bei Patienten mit idiopathischer inflammatorischer Myopathie. Systematischer Überblick und Metaanalyse

Ziel: Ziel der vorliegenden Studie war es, den Zusammenhang zwischen antimitochondrialen Antikörpern (AMA) und Herzbeteiligung bei idiopathischer inflammatorischer Myopathie (IIM) zu untersuchen und die diagnostische Aussagekraft der AMA für eine Herzbeteiligung bei Patienten mit IIM zu ermitteln.
Methoden: Eine umfassende Suche in den Datenbanken PubMed, Web of Science, EMBASE und Cochrane Library wurde durchgeführt, um englischsprachige Studien zu ermitteln, die vor dem 19. November 2021 publiziert worden waren. Für die statistische Auswertung wurde die Software Stata 12.0 benutzt. Zur Bestimmung der diagnostischen Aussagekraft der AMA für eine kardiale Beteiligung bei IIM-Patienten verwendeten die Autoren die Sensitivität, Spezifität, positive Likelihood-Ratio (PLR), negative Likelihood-Ratio (NLR) und Summary-Receiver-Operating-Characteristic(SROC)-Kurve. Die statistische Heterogenität der Studien wurde unter Verwendung der I^2-Statistik mit 95 %-Konfidenzintervallen (95 %-KI) ermittelt.
Ergebnisse: In die endgültige Analyse wurden 7 Studien mit 2308 IIM-Patienten (inklusive 171 AMA-positiver und 2137 AMA-negativer Patienten) eingeschlossen. Die gepoolte Sensitivität der AMA für eine kardiale Beteiligung bei IIM-Patienten betrug 0,29 (95 %-KI: 0,19–0,43) und die Spezifität 0,92 (95 %-KI: 0,88–0,96). Die gepoolte PLR lag bei 3,9 (95 %-KI: 2,82–5,38), die NLR bei 0,76 (95 %-KI: 0,66–0,88) und die diagnostische Odds Ratio (DOR) bei 5 (95 %-KI: 3–7). Die Fläche unter der SROC-Kurve betrug 0,76 (95 %-KI: 0,72–0,79).
Schlussfolgerung: Der diagnostische Gesamtwert der AMA für die Herzbeteiligung bei Patienten mit IIM ist möglicherweise nicht besonders hoch.

Schlüsselwörter
Idiopathische entzündliche Myopathie · Antimitochondriale Antikörper · Herzbeteiligung · Metaanalyse · Herz-Kreislauf-Erkrankungen

subset within the idiopathic inflammatory dermatomyopathies spectrum of clinical illness? J Am Acad Dermatol 46:626–636. https://doi.org/10.1067/mjd.2002.120621
28. Taborda AL, Azevedo P, Isenberg DA (2014) Retrospective analysis of the outcome of patients with idiopathic inflammatory myopathy: a long-term follow-up study. Clin Exp Rheumatol 32(2):188–193
29. Uenaka T, Kowa H, Ohtsuka Y, Seki T, Sekiguchi K, Kanda F, Toda T (2017) Less Limb Muscle Involvement in Myositis Patients with Anti-Mitochondrial Antibodies. Eur Neurol 78(5–6):290–295.https://doi.org/10.1159/000481503
30. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM; QUADAS-2 Group (2011) QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Internal Med 155(8):529–536. https://doi.org/10.7326/0003-4819-155-8-201110180-00009
31. Yamanaka T, Fukatsu T, Ichinohe Y, Hirata Y (2017) Antimitochondrial antibodies-positive myositis accompanied by cardiac involvement. BMJ Case Rep. https://doi.org/10.1136/bcr-2016-218469
32. Zhang L, Yang H, Lei J, Peng Q, Yang H, Wang G, Lu X (2021) Muscle pathological features and extra-muscle involvement in idiopathic inflammatory myopathies with anti-mitochondrial antibody. Semin Arthritis Rheum 51:741–748. https://doi.org/10.1016/j.semarthrit.2021.05.019
33. Zhang L, Zhu H, Yang P, Duan X, Wei W, Wu Z, Fang Y, Li Q, Liu S, Shi X, Li H, Wu C, Zhou S, Leng X, Zhao J, Xu D, Wu Q, Tian X, Li M, Zhao Y, Wang QA-O, Zeng X (2021) Myocardial involvement in idiopathic inflammatory myopathies: a multi-center cross-sectional study in the CRDC-MYO Registry. Baillieres Clin Rheumatol 40:4597–4608. https://doi.org/10.1007/s10067-021-05828-y