

INPLASY PROTOCOL

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Corresponding author:
Xiangqi Tang

txq6633@csu.edu.cn

Author Affiliation:
The Second Xiangya Hospital

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The authors declare that they have no conflict of interest.

Explore the correlation between IgG4 antibodies against (para)nodal proteins and prognosis of patients with chronic inflammatory demyelinating polyradiculoneuropathy via meta-analysis

Tang, X¹; Guo, X²; Tang, L³; Huang, Q⁴.

Review question / Objective: Is there any statistical correlation between IgG4 antibodies against (para)nodal proteins and prognosis of patients with chronic inflammatory demyelinating polyradiculoneuropathy? We aim to integrate all published evidence systematically in this review to evaluate the use of IgG4 antibodies to nodal and paranodal proteins as potential diagnosis and prognosis biomarkers for CIDP.

Condition being studied: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a rare immune-mediated heterogeneous disease characterized by demyelination of the peripheral nervous system. Over the past 6 years, autoantibodies against nodal and paranodal proteins were reported in about 10% of patients diagnosed with CIDP. These patients have atypical clinical phenotypes and impaired response to the standard CIDP treatments. These IgG4 autoantibodies include the paranodal proteins neurofascin isoform 155 (NF155), contactin-1 (CNTN1), contactin-associated protein-1 (CASPR10), and to the nodal proteins neurofascin isoforms 140 and 186 (NF140 and NF186). We want to explore the relationship between IgG4 autoantibodies positive and prognosis of patients with CIDP.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 June 2020 and was last updated on 21 June 2020 (registration number INPLASY202060078).

INTRODUCTION

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METHODS

Search strategy: This review will be reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. We have searched the following electronic bibliographic databases: PubMed (MEDLINE), EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), as well as Web of Science for all published work from 1st January 1974 to 23th May 2020. The search string have been built similar as follows: (chronic inflammatory demyelinating polyneuropathy OR CIDP) AND (autoantibody OR neurofascin 155 OR contactin-1). The studies have been restricted to human and English. Reference lists and articles citing the relevant publication will be reviewed for all articles that are relevant after full-text screening. Citations alerts will be set up using Web of Science service. Grey literature will be searched by searching the databases <http://www.greylit.org> and <http://www.opengrey.eu>. Google Scholar will be screened for any additional relevant references.

Participant or population: Patients with chronic inflammatory demyelinating polyradiculoneuropathy (as diagnosed by a clinician, or using any recognized diagnostic criteria) will be included.

Intervention: IgG4 antibodies against (para)nodal proteins positive in serum, cerebrospinal fluid (CSF), and plasma exchange (PE) is the main exposure. The exposure arm will be CIDP patients with positive antibody screening.

Comparator: The comparator arm will be patients with negative antibody screening.

Study designs to be included: Cohort studies; case control studies.

Eligibility criteria: Inclusion criteria: 1) We only include published or unpublished case control studies or cohort studies in English with the data we concern available. 2) IgG4 antibodies against (para)nodal proteins are detected in serum, cerebrospinal fluid or plasma exchange in patients with CIDP. 3) The studies involve the measurement of one or more variable that describes survival and/or prognostic factors in patients with CIDP. Exclusion criteria: 1) Studies that are considered with unclear diagnosis or mis diagnosis will be excluded.

Information sources: PubMed (MEDLINE); EMBASE; Cochrane Central Register of Controlled Trials (CENTRAL); Web of Science.

Main outcome(s): Overall survival; recurrence; adverse event. Results will be shown with HR, OR or standard mean difference (SMD) and 95% confidence intervals.

Quality assessment / Risk of bias analysis: Two reviewers will be independently assess the quality of the selected studies according to the Newcastle-Ottawa scale (NOS). Total NOS score ranges from 0 to 9 stars and higher scores stand for better quality. Only articles which are scored 5 or

higher stars through the system can be included in this review.

Strategy of data synthesis: The software Revman 5.3 and Stata 16.0 will be applied for analyzing. Results will be shown with HR, OR or standard mean difference(SMD). Heterogeneity of results will be assessed by using the Cochrane Q test and I² test. Egger's test will be used to assess publication bias. If publication bias is confirmed, a trim-and-fill method developed by Duval and Tweedie will be implemented to adjust for these bias.

Subgroup analysis: Adult only and pediatric only data will be analyzed separately (18 years). Patients with different antibodies will also be analyzed separately (anti-NF155 antibodies/ anti-NF186 antibodies/ anti-NF140 antibodies/ anti-CNTN1 antibodies/ anti-CASPR1 antibodies).

Sensibility analysis: Not applicable.

Language: English.

Country(ies) involved: China.

Keywords: Meta-analysis; prognosis; chronic inflammatory demyelinating polyradiculoneuropathy; autoantibody; neurofascin 155; neurofascin 186; contactin-1; contactin-associated protein 1.

Dissemination plans: A paper will be submitted to a leading journal in this field.

Contributions of each author:

Author 1 - Xiangqi Tang.

Author 2 - Xiaoqian Guo.

Author 3 - Lisha Tang.

Author 4 - Qianyi Huang.