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Nerve Conduction Study in the Diagnosis of Vasculitic Neuropathy: A Systematic Review

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Abstract: Vasculitic Neuropathy (VN) requires early diagnosis to prevent permanent nerve damage. While Nerve Conduction Studies (NCS) are essential non-invasive diagnostic tools, the specific electrophysiological patterns associated with VN vary, and their effectiveness in guiding clinical decisions remains a subject of study.
Objective: This systematic review aims to synthesize current evidence regarding the utility of NCS in the diagnosis of VN and to identify characteristic electrophysiological patterns in biopsy-confirmed cases. A systematic literature search was conducted on PubMed and Scopus databases using the keywords "nerve conduction study" and "vasculitic neuropathy". The review included four eligible articles involving 296 patients comprising Systemic Vasculitis (SV), Non-Systemic Vasculitis (NSV), and Peripheral Vasculitic Neuropathy (VNP). The analysis reveals that VN is consistently dominated by axonal neuropathy. While mononeuritis multiplex is the classic presentation, asymmetric polyneuropathy and diffuse polyneuropathy are frequently observed, likely due to delayed clinical evaluation. Asymmetry in NCS findings serves as a feature that may increase clinical suspicion for VN. Conversely, normal NCS results, primary demyelination patterns, or pure motor presentations are findings that may reduce clinical suspicion, making a VN diagnosis highly unlikely. The review found no significant differences in NCS patterns between Systemic Vasculitis Neuropathy (SVN) and Non-Systemic Vasculitis Neuropathy (NSVN). NCS is a vital diagnostic tool for VN. Clinicians should look for asymmetric axonal neuropathy as a key indicator. While NCS helps support the diagnosis and rule out other conditions, it cannot distinguish between systemic and non-systemic etiology.

Keywords: vasculitic neuropathy; nerve conduction study; axonal neuropathy; mononeuritis multiplex

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Introduction

Neuropathy that occurs as a result of vasculitis is referred to as vasculitic neuropathy (VN). This type of neuropathy may occur when vasculitis affects the entire body, a condition known as systemic vasculitic neuropathy (SVN), or when it affects only the peripheral nerves in a localized area, referred to as non-systemic vasculitic neuropathy (NSVN) (Collins et al., 2024). Peripheral vasculitic neuropathy (PVN) is caused by inflammation of the blood vessels, which subsequently leads to damage to the peripheral nerves (Castiglione et al., 2021). The diagnosis of VN relies on the clinical

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history, neurological examination, laboratory investigations, electrodiagnostic studies, and nerve biopsy. Early diagnosis is essential to initiate appropriate treatment and prevent permanent nerve damage (Davalos et al., 2023).

Nerve conduction study (NCS) is an important non-invasive diagnostic tool for the evaluation of peripheral neuropathy. NCS is sometimes used to assist clinicians in selecting the appropriate nerve for biopsy; however, there is currently no standardized or universally accepted approach, and the effectiveness of NCS in guiding decisions regarding nerve biopsy remains uncertain (Becker et al., 2024). Therefore, determining the most common and frequently observed patterns of NCS abnormalities in vasculitic neuropathy (VN) requires a synthesis of the current evidence.

This review aims to synthesize the current evidence regarding the utility of NCS in the diagnosis of VN. The review will focus on identifying the characteristic electrophysiological patterns observed in cases of PVN confirmed by nerve biopsy.

Materials and Methods

This systematic review was conducted to evaluate the available evidence regarding the role of NCS in the diagnosis of VN. The review methods and reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.

A systematic literature search was conducted using PubMed and Scopus. The search strategy combined terms related to nerve conduction studies and vasculitic neuropathy. The search terms included "nerve conduction study," "electrodiagnostic study," "vasculitic neuropathy," and "vasculitis-associated neuropathy." The complete search strategy for each database, including Boolean operators, filters, and the date of the last search, should be reported in the supplementary material or within the Methods section.

Studies were eligible if they were peer-reviewed publications written in English, included patients with suspected or confirmed vasculitic neuropathy, and reported NCS findings relevant to the diagnosis or characterization of the neuropathy. Observational studies, retrospective studies, comparative studies, and case series were considered eligible when they provided sufficient patient-level or group-level data. Studies reporting only a single case, editorials, and non-systematic reviews were excluded. Studies without sufficient information on diagnostic ascertainment or NCS findings were excluded from the qualitative synthesis, with the reasons documented during full-text assessment.

Records retrieved from the databases were combined, and duplicate records were removed. Titles and abstracts were screened against the eligibility criteria, followed by full-text assessment of potentially relevant articles. The number of records identified, duplicates removed, records screened, full-text reports assessed, exclusions, and studies included in the review were documented in a PRISMA 2020 flow diagram. The number of reviewers involved in screening and the procedure used to resolve disagreements should be specified.

Data were extracted using a structured form. The extracted variables included the first author, publication year, study design, study setting, sample size, diagnostic criteria for vasculitic neuropathy, method of diagnostic confirmation, systemic or non-systemic classification, NCS protocol, affected nerves, motor and sensory response amplitudes, conduction velocities, electrophysiological classification, and distribution of abnormalities. Where available, data on the comparison group and diagnostic accuracy measures were also extracted.

Studies were assessed according to the method used to establish vasculitic neuropathy. Cases with histopathological confirmation from nerve biopsy, with or without muscle biopsy, were distinguished from cases diagnosed on clinical, laboratory, or electrodiagnostic grounds without histopathological confirmation. The diagnostic criteria used in each primary study were recorded, and findings from biopsy-confirmed and clinically suspected cases were interpreted separately whenever the available data permitted.

The methodological quality and risk of bias of the included studies were assessed using a tool appropriate to each study design. For observational studies or case series, an appropriate JBI critical appraisal checklist were used. The assessment should consider patient selection, reference standards, ascertainment of NCS findings, completeness of outcome reporting, and applicability to the review question. The appraisal results should be presented in a table, and their implications for the interpretation of the evidence should be discussed.

Because of potential heterogeneity in study designs, diagnostic criteria, NCS protocols, and outcome definitions, findings were synthesized narratively. The synthesis focused on the frequency and distribution of axonal abnormalities, asymmetry, multifocal involvement, mononeuritis multiplex, sensorimotor involvement, and demyelinating features. Differences between systemic and non-systemic vasculitic neuropathy and between biopsy-confirmed and clinically suspected cases were examined when

supported by the available data. A meta-analysis was not undertaken unless the studies provided sufficiently comparable populations, reference standards, and outcome measures.

Classification of Diagnostic Certainty

The diagnostic status of vasculitic neuropathy was classified according to the reference standard reported in each included study. Biopsy-confirmed cases were defined as patients in whom histopathological findings from nerve biopsy, with or without concomitant muscle biopsy, supported the diagnosis of vasculitis. Clinically suspected cases were defined as patients evaluated for possible vasculitic neuropathy on the basis of clinical presentation, laboratory investigations, and electrodiagnostic findings, without documented histopathological confirmation.

These categories were analyzed separately whenever the published data allowed. Studies enrolling patients with suspected vasculitic neuropathy were considered particularly relevant to the evaluation of diagnostic predictors, whereas studies restricted to biopsy-confirmed cases were used primarily to characterize the electrophysiological phenotype. The distinction was maintained to reduce the risk of interpreting findings from a selected biopsy-confirmed population as estimates of diagnostic performance in an unselected population.

Result and Discussion

Result

The literature search process is summarized in **Figure 1.** Initially, 65 articles were identified through searches of the electronic databases PubMed and Scopus. Of these, 5 duplicate articles were removed, leaving 60 articles for screening. The articles were then screened according to the predefined inclusion criteria. Following the screening process, 49 articles were excluded because they were single case reports, editorials, or non-systematic reviews, leaving 11 articles for further assessment. Subsequently, 7 articles were excluded because they lacked biopsy data and/or had incomplete NCS findings. Ultimately, 4 articles involving a total of 296 patients were included in the review. The study population comprised patients with systemic vasculitis (SV), non-systemic vasculitis (NSV), and peripheral vasculitic neuropathy (PVN). The characteristics of the included patients are presented in **Table 1.**

The included studies differed in their approaches to diagnostic ascertainment. Some studies evaluated patients with suspected vasculitic neuropathy and compared clinical or electrodiagnostic findings with subsequent histopathological outcomes, whereas others primarily described patients with biopsy-confirmed disease. This distinction is important because studies restricted to biopsy-confirmed cases characterize the electrophysiological phenotype of established disease but cannot, by themselves, determine the diagnostic accuracy of NCS in patients presenting with undifferentiated peripheral neuropathy. The diagnostic reference standard and the extent of histopathological confirmation should therefore be considered when interpreting the findings of each study.

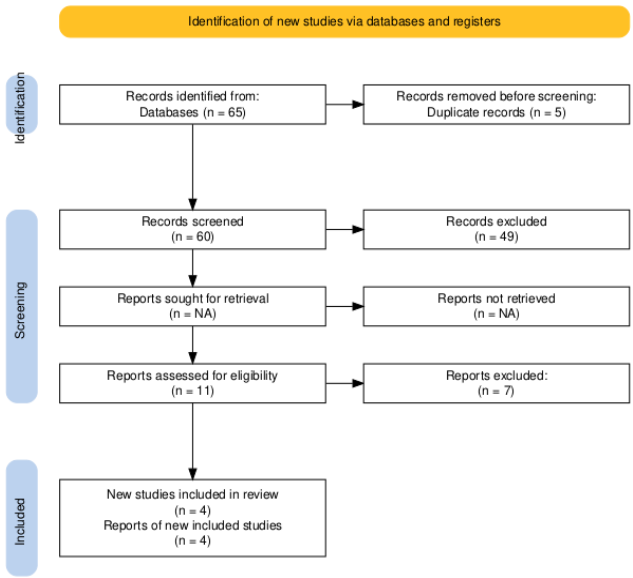


Figure 1. Literature search flowchart

Discussion

Peripheral nervous system involvement in systemic vasculitic neuropathy (SVN) is often associated with poor functional outcomes and increased morbidity, with sensorimotor deficits that may sometimes be irreversible (Rodrigues et al., 2020). Vasculitic neuropathy (VN) is a distinct group of immune-mediated axonal neuropathies that occurs in the setting of vasculitis. Inflammation of the vasa nervorum leads to fibrinoid necrosis, resulting in multifocal nerve infarction and cumulative nerve damage (Tulbă et al., 2021). VN may occur as part of systemic vasculitis, referred to as systemic vasculitic neuropathy (SVN), or as vasculitis confined to the peripheral nerves, referred to as non-systemic vasculitic neuropathy (NSVN) (Collins et al., 2024).

Tabel 1. Research Characteristic

Study	Desain Studi	Sample Size	Type of Vasculitis	Diagnostic Confirmation	Clinical Manifestation	NCS Finding
Ramineni et al., (2019)	Retrospective study	67	- SV (n= 21) - NSV (n= 46)	Biopsy-proven definite/probable VN	- paresthesia (68,7%) - paresthesia with weakness (28,4%) - Onset of neuropathy symptoms occurs in the lower limbs (86,6%)	Predominantly axonal neuropathy (95.52%); sensorimotor involvement (83.58%); mononeuritis multiplex (32.84%); polyneuropathy (67.16%). Asymmetric findings were observed in 71.05% of patients with bilateral NCS data.
Hui et al., (2019)	Retrospective study	126	- SV (n= 61) - NSV (n= 65)	Nerve-biopsy cohort; definite, probable, or possible VN	- pain, paresthesia, and burning sensation (65,07%). - Symptoms occur more frequently in the lower limbs	Mononeuritis multiplex (55.56%) and asymmetric polyneuropathy (23.80%) were the most frequently reported patterns.
Nathani et al., (2019)	Retrospective study	78	- SV (n= 13) - NSV (n= 8) - Pathological Unlikely (n= 55)	Clinically suspected VN evaluated by nerve biopsy	- sensorimotor symptoms and signs with gradual progression	Among pathologically confirmed cases, sensorimotor involvement (81.8%), predominantly axonal neuropathy (76.2%), and asymmetric/multifocal involvement (66.7%) were observed. Normal NCS was reported in 8.1% of the cohort, all without pathological confirmation of vasculitis.
Castiglione et al., (2021)	Case Series	25	- SV (n= 10) - NSV (n= 15)	Final diagnosis of vasculitic peripheral neuropathy; biopsy findings classified as definite, probable, or possible	- Neuropathic pain and gait disturbances are the most frequently occurring symptoms	Multiple mononeuropathy (23/25); axonal pattern (88%), secondary axonal pattern (8%), and demyelinating pattern (4%). No significant electrophysiological differences were observed between systemic and non-systemic VN.

The diagnosis of PVN can be challenging in daily neurological practice, often resulting in significant diagnostic delays or inappropriate treatment (Castiglione et al., 2021). The diagnosis of peripheral neuropathy is based on a thorough medical history and physical and neurological examinations, followed by appropriate investigations. NCS typically demonstrate a sensorimotor or purely sensory axonal neuropathy involving multiple peripheral nerves, often with an asymmetric or multifocal distribution. EMG may reveal diffuse denervation in the affected nerves or muscles. Electrodiagnostic studies may also detect subclinical asymmetry and can be used to identify an appropriate site for nerve biopsy (Anne Møller Witt et al., 2024).

Nerve biopsy remains important in the diagnosis of non-systemic vasculitic neuropathy (NSVN), particularly in cases where vasculitic neuropathy is suspected but systemic manifestations have not yet developed. Nerve biopsy is one of the recommended investigations in selected patients with peripheral neuropathy. The sensitivity of nerve and/or muscle biopsy for detecting vasculitis is estimated to be approximately 60–70%. Definitive histological evidence of vasculitic neuropathy may be difficult to obtain because of the patchy nature of the disease process, characterized by "skip lesions," and because the pathological changes may be located in areas distant from the biopsy site. Currently, many cases of peripheral neuropathy can be diagnosed through non-invasive approaches, including genetic and autoimmune blood testing, which can be combined with nerve conduction studies (NCS) (Ginsberg, 2020).

A study by Ramineni et al. (2019) showed that patients with vasculitic neuropathy exhibited the following NCS findings: diffuse polyneuropathy (67.16%), axonal neuropathy (95.52%), asymmetric neuropathy (71.05%), sensorimotor neuropathy (79.1%), and pure sensory neuropathy (20.9%). In this study, non-systemic vasculitic neuropathy (NSVN) was more frequently observed (46/67; 68.66%) than systemic vasculitis (SV) (21/67; 31.34%). The study also noted that although the classical neuropathic pattern associated with vasculitis is mononeuritis multiplex, the relative frequency of polyneuropathy compared with mononeuritis multiplex varies considerably across studies. One possible explanation for this variation is a delay in patients seeking initial evaluation, resulting in confluent mononeuropathies that may eventually resemble a diffuse polyneuropathy.

A study by Hui et al. (2019), a retrospective analysis conducted at a single tertiary care center, examined 126 patients diagnosed with vasculitic neuropathy based on nerve biopsy between January 2012 and June 2017. The study aimed to correlate clinical features with pathological findings. The majority of patients (55.56%) demonstrated mononeuritis multiplex on nerve conduction studies (NCS), followed by asymmetric polyneuropathy (23.80%). A smaller proportion of patients presented with mononeuropathy, distal symmetric polyneuropathy, or sensory ganglionopathy. The study noted that the NCS findings of mononeuritis multiplex and asymmetric polyneuropathy were consistent with findings reported in other studies. The authors also reported that distal symmetric polyneuropathy was an uncommon presentation of vasculitic neuropathy.

Nathani et al. (2019) retrospectively analyzed pre-biopsy clinical, laboratory, and neurophysiological parameters in 78 patients with suspected vasculitic neuropathy to identify predictors of positive pathological findings. The study found that NCS was rarely normal in patients with vasculitis, consistent with previous literature. Among the 78 patients, 8.1% had normal NCS findings, and none of these patients had pathologically confirmed vasculitis. Patients with pathologically confirmed vasculitis frequently demonstrated sensorimotor abnormalities (81.8%), purely axonal neuropathy (76.2%), and asymmetric or multifocal patterns (66.7%) on NCS. In contrast, vasculitis was considered unlikely in patients with normal NCS findings or those with predominantly demyelinating abnormalities. The study also reported that a pure motor presentation, both clinically and electrophysiologically, was a strong negative predictor of vasculitis.

The study by Castiglione et al. (2021) was a case series and biopsy study that retrospectively reviewed the medical records of 25 patients with peripheral vasculitic neuropathy (PVN). The study aimed to compare the clinical characteristics, biopsy findings, and disease outcomes between patients with systemic vasculitic neuropathy (SVN) and non-systemic vasculitic neuropathy (NSVN). Electrophysiological studies demonstrated abnormalities in all patients, and all patients showed a similar degree of axonal neuropathy. The study classified neuropathy subtypes based on NCS patterns, identifying multiple mononeuropathy in 23 patients, asymmetric polyneuropathy in 1 patient, and symmetric polyneuropathy in 1 patient. The authors concluded that NCS patterns did not differ significantly between the SVN and NSVN groups.

Across the included studies, axonal injury emerged as the most consistent electrophysiological feature of vasculitic neuropathy. However, the distribution of nerve involvement varied, ranging from mononeuritis multiplex and asymmetric polyneuropathy to more diffuse patterns. Ramineni et al.

(2019) reported frequent axonal abnormalities, with asymmetric and sensorimotor patterns among the common findings. Hui et al. (2019) similarly identified mononeuritis multiplex as the most frequent presentation, followed by asymmetric polyneuropathy. These findings suggest that the electrophysiological phenotype of vasculitic neuropathy is broader than the classical description of mononeuritis multiplex.

The variation in reported patterns may reflect differences in disease duration, referral characteristics, patient selection, and the extent of nerve conduction testing. Early vasculitic nerve injury may affect individual nerves in a multifocal distribution, whereas cumulative ischemic injury involving multiple nerves may produce a more diffuse polyneuropathic pattern. This explanation is clinically plausible, but the available studies do not establish delayed presentation as the sole cause of the observed differences.

The findings also need to be interpreted in relation to diagnostic ascertainment. Studies restricted to biopsy-confirmed cases are useful for describing the electrophysiological characteristics of established vasculitic neuropathy. In contrast, studies enrolling patients with suspected vasculitic neuropathy and comparing NCS findings with histopathological outcomes are more informative for evaluating the potential diagnostic value of individual NCS features. These study populations address related but distinct questions and should not be considered interchangeable.

Another important limitation is the lack of specificity of axonal abnormalities. Reduced CMAP and SNAP amplitudes, sensorimotor involvement, and even asymmetric abnormalities may occur in non-vasculitic neuropathies. Consequently, the presence of an axonal pattern alone cannot establish vasculitic neuropathy. The combination of an asymmetric or multifocal distribution, a compatible clinical course, pain, and relevant systemic or laboratory findings may provide stronger grounds for further investigation, but its diagnostic performance requires validation in appropriately designed comparative studies.

Regarding systemic and non-systemic vasculitic neuropathy, the study by Castiglione et al. (2021) reported broadly similar electrophysiological patterns between the two groups. This finding suggests that NCS may be more useful for characterizing the pattern and extent of nerve injury than for determining whether the underlying vasculitis is systemic or restricted to peripheral nerves. Nevertheless, the absence of a reported statistically significant difference in an individual study does not establish equivalence between the groups, particularly when sample sizes are small.

Overall, the evidence supports NCS as an important component of the diagnostic evaluation of vasculitic neuropathy, but not as an independent diagnostic test. Its principal contributions are to characterize axonal injury, identify multifocal or asymmetric involvement, assess the distribution of affected nerves, and potentially guide nerve biopsy. The strength of these conclusions remains limited by the small number of included studies, heterogeneous study designs and diagnostic criteria, and limited evidence directly comparing vasculitic with non-vasculitic neuropathies.

A limitation of these studies is that NCS patterns alone are insufficient to reliably distinguish between systemic and non-systemic vasculitic neuropathy. In addition, it is important to note that the lack of bilateral nerve testing in some cases may limit the ability of NCS to detect characteristic patterns of asymmetry in patients with PVN.

Conclusion

Nerve conduction studies (NCS) are an important diagnostic tool, although not a standalone method, for the diagnosis of vasculitic neuropathy. NCS consistently demonstrates that vasculitic neuropathy is predominantly axonal in nature. Although mononeuritis multiplex is classically recognized as the typical presentation, diffuse and asymmetric polyneuropathy may be more frequently observed, potentially reflecting delayed diagnosis and presentation. The presence of an asymmetric pattern is a a feature that may increase clinical suspicion of vasculitic neuropathy. Conversely, certain NCS findings may serve as finding that may reduce clinical suspicion and help avoid unnecessary nerve biopsies. Vasculitis is unlikely in patients with normal NCS findings or those demonstrating a predominantly demyelinating pattern. In addition, a pure motor presentation, both clinically and electrophysiologically, is a significant negative predictor of vasculitic neuropathy. However, NCS patterns alone are insufficient to reliably distinguish between systemic vasculitic neuropathy (SVN) and non-systemic vasculitic neuropathy (NSVN). Therefore, NCS findings should be interpreted in conjunction with the clinical presentation, laboratory investigations, and, when indicated, nerve biopsy.

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