

**Evidence-Based Practice Group Answers to Clinical
Questions**

**“Development of (Peripheral) Nerve
Neuropathies as a Sequelae of COVID-19”**

A Rapid Systematic Review

By

WorkSafeBC Evidence-Based Practice Group

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Clinical Services – Worker and Employer Services

About this report

Development of (Peripheral) Nerve Neuropathies as a Sequelae of COVID-19

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About the Evidence-Based Practice Group

The Evidence-Based Practice Group was established to address the many medical and policy issues that WorkSafeBC officers deal with on a regular basis. Members apply established techniques of critical appraisal and evidence-based review of topics solicited from both WorkSafeBC staff and other interested parties such as surgeons, medical specialists, and rehabilitation providers.

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Objective

To determine whether there is any evidence to support an association between the development of (peripheral) nerve neuropathies, such as median nerve neuropathy or brachial plexopathy, as sequelae of COVID-19 infection.

Methods

- A comprehensive, systematic literature search was conducted on September 17, 2020.
- The search was done on commercial medical literature databases, including Embase® (1974 to 2020 September 16) , Medline Epub Ahead of Print®, Medline In-Process & Other Non-Indexed Citations®, Medline Daily Update® and Medline® (1946 to September 16, 2020), Joanna Briggs Institute EBP Database® (Current to September 09, 2020) and Cochrane Clinical Answers® (August 2020), that are available through the Ovid® platform.
The Evidence-Based Practice Group decided not to search pre-print databases, such as medRxiv® and bioRxiv® (<https://connect.medrxiv.org/relate/content/181>), due to the fact that articles hosted within these databases have not been peer-reviewed, and poses a high potential of retraction in the near future (<https://retractionwatch.com/retracted-coronavirus-COVID-19-papers/>); as of July 2020, there has already been a large number of peer-reviewed publications on COVID-19⁽⁶⁷⁷⁾ available from which to source more substantiated evidence.
- In order to identify studies on COVID-19, we followed the search criteria (keywords) developed by Canadian Agency for Drugs and Technologies in Health (CADTH) (<https://COVID.cadth.ca/literature-searching-tools/cadth-COVID-19-search-strings/#COVID-19-medline>). These keywords include:
 1. (coronavirus **OR** betacoronavirus **OR** (coronavirus **ADJ** infection) **AND** ((disease **ADJ** outbreaks) **OR** epidemics **OR** pandemics)
 2. (nCoV* **OR** 2019nCoV **OR** 19nCoV **OR** COVID19* **OR** COVID **OR** SARS-COV-2 **OR** SARSCOV-2 **OR** SARSCOV2 **OR** (Severe Acute Respiratory Syndrome Coronavirus 2) **OR** (Severe Acute Respiratory Syndrome Corona Virus 2))
 3. ((new **OR** novel **OR** "19" **OR** "2019" **OR** Wuhan **OR** Hubei **OR** China **OR** Chinese) **ADJ** (coronavirus* **OR** (corona virus*) **OR** betacoronavirus* **OR** CoV **OR** HCoV))

4. ((coronavirus* **OR** corona virus* **OR** betacoronavirus*) **ADJ** (pandemic* **OR** epidemic* **OR** outbreak* **OR** crisis))
5. ((Wuhan **OR** Hubei) **ADJ** pneumonia)
6. 1 **OR** 2 **OR** 3 **OR** 4 **OR** 5
7. limit 6 to yr="2019 -Current"

These keywords were then combined with the keywords: "neuropathy" in order to identify the relevant studies

- No limitations, such as on the language or country of publication, were implemented in any of the searches.
- Manual searches were also conducted on the references of the studies that were retrieved in full, as well as from the Evidence-Based Practice Group collection of studies on COVID-19 (literature surveillance on COVID-19 in March 2020).

Results

- Search results:
 - o 140⁽¹⁻¹⁴⁰⁾ published studies were identified from the systematic literature search. An additional four⁽¹⁴¹⁻¹⁴⁴⁾ articles were identified from the manual search.
 - o Upon examination of the titles and abstracts of these 144⁽¹⁻¹⁴⁴⁾ studies, twenty-five^(2,12,14,18,25,29,36,41,42,43,58,70,93,98,101,103,105,113,114,117,131,141-144) studies were thought to be relevant and were retrieved in full for further appraisals.
- Of the twenty-five^(2,12,14,18,25,29,36,41,42,43,58,70,93,98,101,103,105,113,114,117,131,141-144) studies that were retrieved in full, no study provided any data on median nerve neuropathy, while two^(105,117) studies reported two cases (one within each study) of brachial plexopathy.
- In a pre-print format reporting on the emerging spectrum of COVID-19 neurological symptoms, Paterson et al⁽¹⁰⁵⁾ reported neurological symptoms of 43 patients diagnosed with COVID-19. Of these 43 COVID-19 patients with neurological symptoms, one reported the onset of brachial plexopathy two weeks after COVID-19 symptoms. No further information was available with regards to this patient.
- Sanchez-Soblechero et al⁽¹¹⁷⁾ reported a case of brachial plexopathy as a consequence of prone positioning in the first 27 hours of a patient's admission to an intensive care unit (ICU), due to acute respiratory distress syndrome (ARDS) as a result of COVID-19. The authors further reported that, at 1-month follow-up, the patient had completely recovered from COVID-19 but the previous hypoesthesia and partial right arm weakness still persisted.

Summary

- At present, there is no evidence on the development or association between the development of median nerve neuropathy and the diagnosis of COVID-19.
- At present, there is one case of brachial plexopathy reported in a patient with COVID-19. It should be noted that brachial plexopathy in this case, was attributed to the patient's prone positioning during the first 72 hours of the admission to the ICU, due to ARDS.
- At present, there is an interesting hypothesis, supported by an animal study, showing that SARS-CoV-2's spike protein was preventing VEGF-A/NRP-1 signaling, hence working as an antiallodynic in neuropathic pain. This study was still in pre-print⁽¹⁴⁴⁾.

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Appendix 1

WorkSafeBC - Evidence-Based Practice Group Levels of Evidence

(adapted from 1,2,3,4)

1	Evidence from at least 1 properly randomized controlled trial (RCT) or systematic review of RCTs.
2	Evidence from well-designed controlled trials without randomization or systematic reviews of observational studies.
3	Evidence from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.
4	Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

References

1. Canadian Task Force on the Periodic Health Examination: The periodic health examination. CMAJ. 1979;121:1193-1254.
2. Houston TP, Elster AB, Davis RM et al. The US Preventive Services Task Force Guide to Clinical Preventive Services, Second Edition. AMA Council on Scientific Affairs. American Journal of Preventive Medicine. May 1998;14(4):374-376.
3. Scottish Intercollegiate Guidelines Network (2001). SIGN 50: a guideline developers' handbook. SIGN. Edinburgh.
4. Canadian Task Force on Preventive Health Care. New grades for recommendations from the Canadian Task Force on Preventive Health Care. CMAJ. Aug 5, 2003;169(3):207-208.