INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Duration of symptoms before diagnosis in Degenerative Cervical Myelopathy: protocol for a systematic review

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Review question / Objective: **The aim of this systematic review is to describe and measure the duration of symptoms prior to diagnosis of DCM, as reported in primary studies of people with this condition, with a view to informing further research on diagnostic delay. To this end, the systematic review will focus on the primary question: What is the typical duration of symptoms prior to diagnosis in people with Degenerative Cervical Myelopathy?**
Condition being studied: **DCM represents a collection of pathological entities including spondylosis, degenerative disk disease, ossification of the posterior longitudinal ligament (OPLL), and ossification of the ligamentum flavum which individually, or in combination, cause compression of the cervical spinal cord, resulting in a clinical syndrome typified by gait imbalance, loss of hand dexterity and sphincter dysfunction (Tetreault et al., 2015a). It is the most common cause of spinal cord dysfunction in adults worldwide (Kalsi-Ryan et al, 2013).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 June 2021 and was last updated on 22 June 2021 (registration number INPLASY202160079).

INTRODUCTION

Review question / Objective: **The aim of this systematic review is to describe and measure the duration of symptoms prior to diagnosis of DCM, as reported in primary studies of people with this condition, with a view to informing further research on diagnostic delay. To this end, the systematic review will focus on the primary question: What is the typical duration of symptoms prior to diagnosis in people with Degenerative Cervical Myelopathy?**

Rationale: **Degenerative cervical myelopathy (DCM) is the most serious**

degenerative cervical spine pathology, causing potentially devastating and irreversible neurological disturbance, and the most common cause of spinal cord dysfunction in adults worldwide (Kalsi-Ryan et al., 2013). DCM represents a collection of pathological entities including spondylosis, degenerative disk disease, ossification of the posterior longitudinal ligament (OPLL), and ossification of the ligamentum flavum which individually, or in combination, cause compression of the cervical spinal cord, resulting in a clinical syndrome typified by gait imbalance, loss of hand dexterity and sphincter dysfunction (Tetreault et al., 2015a). It has been described as "a spinal cord injury in slow motion". The detection and diagnosis of DCM is fraught with difficulty, with many patients reporting lengthy and convoluted pathways to diagnosis after first onset of symptoms. Once diagnosed, surgical decompression is the only evidence-based treatment demonstrated to arrest DCM progression and has been shown to offer significant but often incomplete gains in functional impairment, disability and pain in patients with moderate or severe DCM (Fehlings et al, 2017). A shorter duration of symptoms and less severe myelopathy preoperatively are both important predictors of achieving a good outcome (Tetreault et al., 2015b). Therefore, there is an urgency in detecting DCM. However, although delayed diagnosis and prolonged symptom duration are commonly reported by patients, and despite the importance of duration of symptoms as a prognostic indicator, there is little quantitative evidence on the extent of this problem in the literature. This systematic review will measure the pre-diagnosis duration of symptoms in people with DCM in primary studies, giving an indication of the problem of diagnostic delay.

Condition being studied: DCM represents a collection of pathological entities including spondylosis, degenerative disk disease, ossification of the posterior longitudinal ligament (OPLL), and ossification of the ligamentum flavum which individually, or in combination, cause compression of the cervical spinal cord, resulting in a clinical syndrome typified by gait imbalance, loss of hand dexterity and sphincter dysfunction (Tetreault et al., 2015a). It is the most common cause of spinal cord dysfunction in adults worldwide (Kalsi-Ryan et al, 2013).

METHODS

Search strategy: The following databases will be consulted for this review: Medline (OVID), Pubmed, Cochrane library, EBSCO, Scopus, Embase, Web of Science, CINAHL, Google Scholar. There is no time restriction. Studies will be restricted to English language. Search will be conducted using following keywords: cervical stenosis AND spinal cord compression, OR degenerative cervical myelopathy, OR cervical spondylotic myelopathy, OR cervical myelopathy, OR spinal cord compression AND cervical canal stenosis, OR atraumatic spinal cord injury AND degenerative.

Participant or population: Adults enrolled in studies of Degenerative Cervical Myelopathy (or its alternative names, Cervical Myelopathy or Cervical Spondylotic Myelopathy) will be eligible for this review. Diagnosis must be confirmed against standard criteria and exclude other possible or concomitant causes of neurological dysfunction. Where studies report a mixed population of individuals with degenerative cervical spine pathology, including but not limited to myelopathy (cord compression), the participants with DCM must be reported as a distinct subgroup.

Intervention: Not applicable.

Comparator: Not applicable.

Study designs to be included: The review will include all primary studies of people with DCM, be they observational or intervention studies, including case reports, case series, cross-sectional studies, cohort studies and randomised controlled trials.

Eligibility criteria: Inclusion criteria: • Study includes participants with DCM or its

synonyms or subtypes (cervical spondylotic myelopathy, ossification of the posterior longitudinal ligament, spinal cord compression, cervical myelopathy) • DCM diagnosed using standard criteria • Studies reporting and presenting clear description of symptoms duration prior to diagnosis or intervention. • Full text articles. • Published in, or translated to, the English language. Exclusion criteria: • Non-human studies. • Studies including participants with other spinal conditions. • Studies of people with radiculopathy, or with a mixed population of myelopathy and radiculopathy without distinction between them. • Studies of people with non-degenerative causes of non-traumatic spinal cord injury, such as tumours or vascular injuries. • Studies of people with traumatic spinal cord injury • Studies with participants younger than 18 years (paediatric studies). • Studies not in the English language or translated into English.

Information sources: The following databases will be searched: Medline (OVID), PubMed, EBSCO, Scopus, EMBASE, Web of Science, CINAHL, Google Scholar.

Main outcome(s): The primary outcome is the duration of symptoms prior to diagnosis of DCM, or prior to intervention (if date of diagnosis is not reported), whether reported as a continuous variable or dichotomously (greater than or less than a pre-specified period of time). Data extraction will also include participant demographic information, sample size, type of study, and severity of DCM, measured using a standardised scale (such as the modified Japanese Orthopaedic Association score or the Nurick score).

Data management: Two reviewers will independently search the databases and, upon retrieving study titles and abstracts, identify studies to be screened for inclusion. Two reviewers will then independently screen the full texts of these papers for inclusion. Any discrepancies will be will be resolved by a third author.

Quality assessment / Risk of bias analysis: Methodological quality will be assessed using the Crowe Critical Appraisal Tool (CCAT) (Crowe et al, 2015), a 22-item checklist with a maximum score of 40. The CCAT can be applied to all research designs eligible for inclusion in this review. Two authors, both with expertise in the clinical problem and one with methodological expertise, will independently undertake quality assessment. Differences will be resolved by discussion.

Strategy of data synthesis: Data will be presented in tabular format, including categories for study design, country, participant cohort descriptor (DCM, CSM, OPLL or other synonyms), sample size, method used to assess and report severity of myelopathy, presentation of severity data (mean / median, range or cut-scores), and pre-diagnosis symptom duration (as reported, whether as a continuous variable, namely mean and standard deviation, or dichotomised with a cut-score, such as greater than / less than one year). A narrative synthesis will be provided. We will also consider a random effects meta-analysis, depending on the heterogeneity of the found results and study types. For studies reporting the primary outcome, symptom duration, as a continuous variable with a measure of dispersion (standard deviation, standard error or 95% confidence interval), the average will be estimated by meta-analysis, with 95% confidence interval to indicate precision. We will consider imputation methods for other results reported as medians or categorical values, and conduct sensitivity analyses as relevant.

Subgroup analysis: No subgroup analysis is planned.

Sensitivity analysis: Some studies in DCM may report symptom duration prior to intervention (typically surgery), rather than date of diagnosis. A sensitivity analysis will adjust the reported symptom durations based on the typical time from diagnosis to surgery, and repeat the analysis a) with these adjustments and b) without these

studies, to determine the effect of this method of reporting. Sensitivity analysis will be considered if any of the results are imputed (e.g. medians substituted for mean values).

Language: English.

Country(ies) involved: Ireland (review will include studies from all countries).

Keywords: Spinal cord injury; degenerative cervical myelopathy; spinal cord compression; duration of symptoms.

Dissemination plans: Results will be disseminated via publication in a peer-reviewed journal in spine care and as an abstract at a spine conference.

Contributions of each author:

Author 1 - Ailish Malone - contributions: concept and design, coordination of review, supervision of data collection and management, analysis and interpretation
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