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Title

Cervical Spine Radiculopathy Epidemiology. Systematic Review

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Category of submission:

Systematic review

PROSPERO Registration Number

CRD42019138903

Funding & Acknowledgement:

Nil funding.

This study forms part of Michael Mansfield's PhD study programme.

Prof. Lesley Haig's valuable support in Michael Mansfield's research journey.

Conflict of Interest statement

There is no conflict of interests across all authors (MM, TS, NS and MT)

Author Contributions:

Conceptualisation: Michael Mansfield and Mick Thacker

Formal analysis: Michael Mansfield, Toby Smith, Nicolas Spahr and Mick Thacker

Investigation: Michael Mansfield, Toby Smith and Mick Thacker

Methodology: Michael Mansfield, Toby Smith, Nicolas Spahr and Mick Thacker

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Writing, review and editing: Michael Mansfield, Toby Smith, Nicolas Spahr and Mick Thacker

ABSTRACT

Background & Objective

Cervical spine radiculopathy (CSR) is a disabling condition which has significant negative impacts on a person's mental health, physical functioning and social participation. Research has reported variable CSR incidence and prevalence among different populations. To date no systematic review has been completed investigating the prevalence or incidence of CSR, therefore our objective was to determine the incidence and/or prevalence of CSR in adults.

Design and Method

A systematic review was conducted including searches of PubMed (MEDLINE), EMBASE and CINAHL from inception to February 25th 2020. Studies including data on incidence and/or prevalence of CSR were included. Methodological quality was assessed using a modified Hayden, Cote and Bombardier (2006) appraisal checklist. Data was analysed narratively.

Results

Nine low to high-quality studies were included in the final review. Incidence ranged between 0.832 to 1.79 per 1000 person-years from two high quality and one low quality study. Prevalence values ranged from 1.21 to 5.8 per 1000 from four medium to high quality studies. Prevalence values of 1.14% (95% CI 0.45-1.82) and 1.31% (95% CI 0.66-1.96) for males and females respectively were

reported from one medium quality study. One medium quality study reported an unadjusted prevalence value of 6.3% for males and females.

Conclusions

This is the first systematic review investigating the epidemiology of CSR in an adult population. This review reports a variable incidence rate and prevalence of CSR among specific populations, however, this was based on nine studies. There is a priority to investigate CSR epidemiology across other populations globally and standardising CSR diagnostic criteria.

Key Words

Cervical Spine Radiculopathy; Epidemiology; Prevalence; Incidence;

MANUSCRIPT (TEXT)

INTRODUCTION

Cervical Spine Radiculopathy (CSR) is a disabling condition which has significant negative impacts on a person's mental health, physical functioning and social participation (Iyer & Kim, 2016). CSR is a complex presentation, associated with increased dependence on healthcare systems (Hogg-Johnson et al., 2009; Iyer & Kim, 2016). CSR poses a substantial challenge for clinicians and patients as it does not always respond to conventional therapies (Rice & Hill, 2006; Woods & Hilibrand, 2015).

CSR is defined as an objective loss of sensory and/or motor function from a conduction compromise to a spinal nerve or its root (Finnerup et al., 2016). This can occur with or without pain (Finnerup et al., 2016). Pain associated with radiculopathy is referred to as painful radiculopathy, which may fit the criteria of *definite* neuropathic pain if impaired sensory symptoms are reported (Treede et al., 2008). The criteria of *probable* neuropathic pain is based on motor signs only (Treede et al., 2008). The conduction compromise in CSR can be a direct compression or indirectly through the interruption of blood supply or nutrition to a nerve axon or its root (Treede et al., 2008). Mechanical deformation, inflammation or ischemic damage of a dorsal root ganglion and/or mechanical stimulation of nerve roots may result in ectopic activation and is a typical feature

of radicular pain (Backonja et al., 2013; Haanpaa et al., 2011). People with radicular pain describe symptoms such as lancinating along narrow bands, which is similar but not identical to “dermatomal distribution” (Haanpaa et al., 2011; Smyth & Wright, 1958). Radiculopathy and radicular pain are distinct diagnostic entities. However there is inconsistency of definition used across observational studies (Lin et al., 2014; Thoomes et al., 2012). The inconsistent reporting and subsequent diagnostic criteria employed may under- or over-estimate the incidence and/or prevalence of CSR.

There is no definitive reference test to diagnose CSR. Diagnosis is made by a detailed patient interview and physical assessment. Subjective complaints of paraesthesia, hyperaesthesia, dysaesthesia and/or allodynia, substantiated by neurological examination, quantitative sensory testing and/or electrodiagnostic testing are typical findings (Backonja et al., 2013; Dillingham, 2013; Siller, Kasem, Witt, Tonn, & Zausinger, 2018; Treede et al., 2008). Painful or restricted neck movements, diminished deep tendon reflex and/or upper limb weakness are characteristic examination outcomes (Iyer & Kim, 2016; Rubinstein, Pool, van Tulder, Riphagen, & de Vet, 2007). However, CSR diagnostic testing procedures vary considerably in clinical practice (Thoomes et al., 2012). This variability may result in over- or under-reporting of CSR in observational studies. Imaging modalities such as Magnetic Resonance Imaging (MRI) can be utilised to diagnose CSR (Aanem, 2015; Dillingham, 2013; Iyer & Kim, 2016). However, “abnormal” cervical spine imaging findings in individuals who are asymptomatic is common (Kato, Yukawa, Suda, Yamagata, & Ueta, 2012).

Therefore relying on imaging in isolation to identify CSR should be used with caution and may distort epidemiological data (Bono et al., 2011; Nardin, Patel, Gudas, Rutkove, & Raynor, 1999; Thoomes et al., 2018).

To date, no systematic review has been undertaken to determine the epidemiology (incidence and/or prevalence) of CSR. Accordingly, the aim of this review is to determine the incidence and/or prevalence of CSR in adults.

METHODS

The systematic review was registered with PROSPERO review database (Ref: CRD42019138903). The PRISMA guidelines of reporting (Moher, Liberati, Tetzlaff, Altman, & Group, 2009) were followed.

Search Strategy

One reviewer (MM) conducted the systematic search of electronic databases PubMed (MEDLINE), EMBASE and CINAHL from inception to February 25th 2020. Unpublished (grey) literature and trial registry search was also completed of the databases: OpenGrey, ClinicalTrials.gov, NIHR portfolio and WHO International Clinical Trials Registry Platform. As an authorship team we agreed on the search terms collaboratively through discussion. The lead author (MM) adopted Radhakrishnan et al (1994) as the search strategy framework across electronic databases. Figure I reports an example of the search strategy used in MEDLINE. Hand searches of references lists and contacting lead authors of included articles was completed to determine if there were any pending article publications or unpublished work.

Eligibility Criteria

Studies were included if they met the following criteria:

a) Adult participants (over 18 years) with a diagnosis of CSR. Diagnosis was made by using a modified version of the International Association of Pain (IASP; Scholz et al., 2019) *painful* radiculopathy and radicular pain classifications detailed in **Figure II**.
b) Incidence or prevalence data reported. Prevalence referring to the proportion of persons who have a condition at or during a particular time period. Incidence referring to the proportion or rate of persons who develop a condition during a particular time period. Studies will be considered if they sample from open population, primary, secondary or tertiary healthcare sectors.
c) Studies must be in the English language (or can be translated to English) and be either be case control, cross- sectional, or cohort study design.

It was anticipated that studies may use different CSR diagnostic criteria. CSR may not always be associated with pain (i.e. a painless radiculopathy) (Siller et al., 2018) and often there is a combination of clinical findings or outcomes, which can be attributed to clinical examination techniques utilised (Thoomes et al., 2018). Our inclusion criteria reflected this anticipated variation. Therefore, a subgroup analysis of eligible studies was undertaken to determine *definite* or *probable* CSR diagnosis (**Figure II**). No publication date or study setting restriction was applied. Studies were excluded if the study population of CSR were related to systemic pathology, metabolic diseases such as diabetes

(including pre-diabetes), radiculitis, post-surgery, fracture, myelopathy or upper motor neurone pathology.

Study Identification

Based on the eligibility criteria, titles and abstracts of all search results were independently screened by two reviewers (MM, MT). From this, full-text studies from potentially eligible studies were retrieved and independent assessment was completed by the same two reviewers. Final eligibility was based on a full-text assessment. Assessment of reliability (between-reviewer) for the eligibility criteria was performed for a random sample of 10 potentially eligible papers using a weighted Kappa statistic (Cohen, 1968). The between-reviewer agreement ranged from 90-100% across the criteria, with 90% (Kappa: 0.62) for overall agreement on eligibility of individual papers (available on request).

Data Extraction

Data were extracted into a pre-defined data extraction table independently by one reviewer (MM). Data extracted included: study characteristics, participants (number, age and gender), population setting, CSR definition and incidence and/or prevalence data. This was verified independently by a second reviewer (TS). Corresponding authors were contacted to seek clarification or to request additional information on the datasets.

Quality Assessment (Risk of bias)

Two authors (MM, TS) independently assessed the quality of each included study using a modified quality appraisal tool by Hayden et al (2006) (Hayden, Cote, & Bombardier, 2006). This tool was applicable to our included studies because it assessed case definition, response rates to surveys, definition of radiculopathy and precision estimates to prevalence/incidence data. Any disagreement between reviewers in respect of study eligibility, data extraction or critical appraisal was firstly discussed between the two reviewers (MM, TS). If a consensus could not be reached a third reviewer (MT) acted as adjudicator.

The quality appraisal assessed the appropriateness and reporting of study population, CSR definition, response rate and information about non-responders and data precision. `High quality' was judged when four or five criteria where met; ‘medium quality’ two or three criteria met and ‘low quality’ was judged when one or no criteria met. Scoring between the two reviewers had an agreement of 91% (42 out of 45). Disagreements were around the item “If appropriate, was information about non-responders described?” which was resolved through discussion and consensus was achieved.

Data Analysis

The study heterogeneity of the included studies was assessed by the two reviewers (MM, TS) through examination of the data extraction table. This

demonstrated heterogeneity with data collection methods and subsequent incidence and prevalence data. It was therefore inappropriate to pool data in a meta-analysis. Accordingly, a descriptive analysis was performed.

RESULTS

Search Strategy

3,898 studies were identified and screened, 3,721 were excluded and 177 full-text articles were retrieved. One hundred and sixty seven full-text articles were excluded, the main reasons for exclusion included no incidence or prevalence data and cervical spine radiculopathy was not a diagnostic inclusion criteria. Ten studies met the inclusion criteria (**Figure III**). One study was excluded as the authors failed to respond to our request for CSR data (Choi, Kim, Lee, & Kim, 2017). Accordingly, nine studies were included in the final review (Bharucha, Bharucha, & Bharucha, 1991; Braddom, Spitz, & Rivner, 2009; Brooks, Fuller, Kemp, & Reddin, 2005; Kandil, Darwish, Khedr, Sabry, & Abdulah, 2012; Khedr et al., 2018; Radhakrishnan, Litchy, O'Fallon, & Kurland, 1994; Salemi et al., 1996; Sandoughi et al., 2013; Schoenfeld, George, Bader, & Caram, 2012).

Study Characteristics – Population and location

The characteristics of the included studies are presented in **Table I**. Three studies were based in the United States of America (USA) (Braddom et al., 2009; Radhakrishnan et al., 1994; Schoenfeld et al., 2012). Two studies were based in Egypt (Kandil et al., 2012; Khedr et al., 2018), one from Iran (Sandoughi et al., 2013), India (Bharucha et al., 1991), United Kingdom (UK) (Brooks et al., 2005) and Italy (Salemi et al., 1996) respectively.

A total of 13,869,818 subjects were recruited. Six studies analysed participants from general population (Bharucha et al., 1991; Kandil et al., 2012; Khedr et al., 2018; Radhakrishnan et al., 1994; Salemi et al., 1996; Sandoughi et al., 2013), one study analysed participants recruited from elite sport (rugby union) (Brooks et al., 2005). One study analysed participants from a neurology department in a tertiary hospital (Braddom et al., 2009) and one study analysed participants from the military (Schoenfeld et al., 2012).

Study characteristics - Cervical Spine Radiculopathy (CSR) Diagnostic Criteria

In a military setting, one study used sensory (including radicular pain) and motor disturbances to confirm CSR (Schoenfeld et al., 2012). Two studies utilised a combination of sensory, diminished reflexes and/or and motor disturbances with EMG, MRI or CT confirmation (Braddom et al., 2009; Khedr et al., 2018). Two studies used a combined of sensory and motor disturbances with imaging correlation when confirming CSR (Bharucha et al., 1991; Kandil et al., 2012). Salemi et al confirmed CSR through combined sensory and motor disturbances with or without imaging correlation (Salemi et al., 1996). Bharucha et al confirmed CSR with pain or stiffness in the cervical spine with sensory or motor disturbances in an arm (Bharucha et al., 1991). Sandoughi et al relied on an “expert” rheumatology consultant examination when confirming CSR in a study population from Iran (Sandoughi et al., 2013). Despite contacting the authors, no further details were confirmed. One study used an Orchard Sports Injury Classification retrospectively to determine CSR (Brooks et al., 2005). No further

details were provided on their CSR definition, despite contacting Brooks et al. [28]

Quality Assessment (Risk of bias)

The quality assessment is presented in **Table II**. Four studies were deemed "high quality", four studies were deemed "medium quality" and one "low quality". All studies met Criteria 1, "*The study sample represents the population of interest on key characteristics*". Following this, the most frequent criteria satisfied were "*The CSR diagnosis specific and is it reproducible?*". The least most frequent criteria satisfied were "*Was there an adequate response rate?(>75%)*" and "*If appropriate, was information about non-responders described*

Analysis 1: Epidemiology of CSR

Incidence

Incidence ranged between 0.83 (converted from 83.2 per 100,000) to 1.79 per 1000 person-years (Brooks et al., 2005; Radhakrishnan et al., 1994; Schoenfeld et al., 2012).

Three studies collected incidence data, one from UK elite level rugby (Brooks et al., 2005), one from USA military (Schoenfeld et al., 2012) and one from retrospective analysis of medical records in USA (Radhakrishnan et al., 1994). Over two sporting seasons, retrospective data was collected from 502 sportsmen (mean age of 25.4 years, Standard Deviation (SD) 4.2) and the unadjusted prevalence was 2% (Brooks et al., 2005). Schoenfeld et al included 13,813,333 subjects between 2000-2009 with an age range of 18-40 years (Schoenfeld et al., 2012). In total, 20,806 and 3,936 males and females respectively were diagnosed with CSR. An unadjusted incidence rate of 1.76 per 1000 person-years for males and an adjusted incidence rate of 1.36 per 1000 person-years (95% Confidence Interval (CI): 1.30-1.42) for females. The total incidence rate was 1.79 per 1000 person-years. Radhakrishnan et al (Radhakrishnan et al., 1994) analysed 561 patients, 332 were male (47.6 years of age; SD: 13.1) and 229 cases were female (48.2 years of age; SD: 13.8). Male incidence was 107.3 per 100,000 person-years adjusted incidence rate (age adjusted 95% CI: 95.4-119.2). Female adjusted incidence was 63.5 per 100,000 person-years (age adjusted 95% CI: 55.1-71.8). The combined male

and female incidence were 83.2 per 100,000 person-years (age adjusted 95% CI: 77.0-91.1).

Prevalence

Prevalence values ranged from 1.21 (converted from 121 per 100,000) to 5.8 per 1000 from four studies (Bharucha et al., 1991; Kandil et al., 2012; Khedr et al., 2018; Salemi et al., 1996). Prevalence values of 1.1% (95% CI: 0.45-1.82) and 1.3% (95% CI: 0.66-1.96) for males and females respectively were reported by one study (Sandoughi et al., 2013). One study reported an unadjusted prevalence value of 6.3% (Braddom et al., 2009).

Three studies utilised a door-to-door survey to report prevalence, one in Italy (Salemi et al., 1996), India (Bharucha et al., 1991) and Egypt (Kandil et al., 2012). Salemi et al reported an unadjusted prevalence of 1.3 per 1000 and 5.8 per 1000 for male and females respectively with a total of 3.5 per 1000 for both sexes (Salemi et al., 1996). Five male cases (50-69 years of age) and 22 female cases (40-79 years of age) were reported from a sample size of 8,782 subjects (Salemi et al., 1996). Bharucha et al sampled 14,010 subjects and 334 cases of peripheral neuropathy were confirmed (Bharucha et al., 1991). The authors reported an unadjusted prevalence of 136 per 100,000. Kandil et al sample size was 42,223 and 51 cases of CSR (35 male and 16 female) were confirmed (Kandil et al., 2012). The combined prevalence for both sexes was 121 per 100,000 (95% CI: 88-154) (Kandil et al., 2012).

Two studies collected prevalence data in hospital neurology departments, one in USA (Braddom et al., 2009) and one in Egypt (Khedr et al., 2018). Braddom et al analysed EMG reports between 1979-2004. 23,317 subjects (mean age 46 years) were recruited consecutively and unadjusted prevalence was 6.3% (1,465 confirmed CSR cases from 23,317) (Braddom et al., 2009). A cross-sectional study of 1057 families in Egypt (Total sample size 9303) reported nine males and two females with CSR (Khedr et al., 2018), resulting in prevalence values of 4.8 and 1.9 per 1000 for male and females respectively (Khedr et al., 2018).

Sandoughi et al conducted a cluster sampling method across multiple Iranian provinces (Sandoughi et al., 2013). From a sample size of 2100, 1204 subjects responded (74% response rate) and were included in their analysis. The male prevalence of CSR was 1.1% (95% CI: 0.45-1.82) and female 1.3% (95% CI: 0.66-1.96) (Sandoughi et al., 2013).

Analysis 2: Sub – Group Analysis of *Definite* CSR incidence and/or prevalence data

From nine included studies, five studies met the modified ‘definitive’ CSR criteria (**Figure II**) (Braddom et al., 2009; Kandil et al., 2012; Khedr et al., 2018; Radhakrishnan et al., 1994; Salemi et al., 1996). Prevalence ranged between 1.21 (converted from 121 per 100,000) to 5.8 per 1000. One study reported a 6.28% prevalence value (Braddom et al., 2009). One study reported an

incidence of 0.83 per 1000 person-years (converted from 83.2 per 100,000 person-years) (Radhakrishnan et al., 1994).

Radhakrishnan et al (1994) utilised a combined definite and probable (i-v) CSR diagnostic criteria (Radhakrishnan et al., 1994). The authors were contacted to delineate this diagnostic criteria but there was no response. Radhakrishnan et al reported a 107.3 per 100,000 person-years adjusted incidence rate (age adjusted 95% CI: 95.4-119.2) for males. The adjusted incidence rate for females was 63.5 per 100,000 person-years (age adjusted 95% CI: 55.1-71.8). The combined male and female incidence was reported as 83.2 per 100,000 person-years (age adjusted 95% CI: 77.0-91.1) (Radhakrishnan et al., 1994).

Braddom et al adopted a 'definite' CSR diagnostic criteria (i) for inclusion, which resulted in an unadjusted prevalence value of 6.28% (1,465 from 23,317 cases) (Braddom et al., 2009). Kandil et al utilised a definite CSR diagnostic criteria (ii) and reported a prevalence value of 1.21 per 1000 (converted from 121 per 100,000) for males and females combined (95% CI: 88-154) (Kandil et al., 2012). Khedr et al utilised a definite CSR diagnostic criteria (i) and (ii) for inclusion (Khedr et al., 2018). The reported prevalence was 4.8 per 1000 and 1.9 per 1000 for male and females respectively (Khedr et al., 2018).

Salemi et al adopted a definite and probable CSR diagnostic criteria (Salemi et al., 1996). Definite criteria were based on subjective sensory disturbances and motor weakness correlating with imaging findings. The authors were contacted

for further details but there was no response. Salemi et al reported an unadjusted prevalence of 1.3 per 1000 and 5.8 per 1000 for males and females respectively with a total of 3.5 per 1000 for both sexes (Salemi et al., 1996).

Analysis 3: Sub – Group Analysis of *Probable* CSR Incidence And/or Prevalence

Four studies from the nine included studies met a 'probable' CSR diagnostic criteria (**Figure II**) (Bharucha et al., 1991; Brooks et al., 2005; Sandoughi et al., 2013; Schoenfeld et al., 2012). Two studies (Radhakrishnan et al., 1994; Salemi et al., 1996) combined definitive and probable CSR diagnosis criteria and have been described in Sub-group Analysis 2 (*Definite* CSR criteria). Schoenfeld et al included subjects with a probable CSR diagnostic criteria (iii) and the combined incidence was 1.79 per 1000 person-years for males and females (Schoenfeld et al., 2012). Bharucha et al adopted probable CSR diagnostic criteria of (vi) or (vii) and reported an unadjusted prevalence value of 1.36 per 1000 (converted from 136 per 100,000) (Bharucha et al., 1991). Two studies provided insufficient CSR diagnosis definition criteria (Brooks et al., 2005; Sandoughi et al., 2013) and subsequently not included in either sub-group analysis. Both sets of authors were contacted for further details but did not response to our requests.

DISCUSSION

Main Results

This is the first systematic review of published and unpublished studies investigating the epidemiology of CSR in an adult population. Nine studies were assessed as low to high quality. Incidence ranged between 0.83 (converted from 83.2 per 100,000) to 1.79 per 1000 person-years from two high quality and one low quality study (Brooks et al., 2005; Radhakrishnan et al., 1994; Schoenfeld et al., 2012). Prevalence values ranged from 1.21 (converted from 121 per 100,000) to 5.8 per 1000 from four medium to high quality studies (Bharucha et al., 1991; Kandil et al., 2012; Khedr et al., 2018; Salemi et al., 1996). Prevalence values of 1.1% (95% CI: 0.45-1.82) and 1.3% (95% CI: 0.66-1.96) for males and females respectively were reported from one medium quality study (Sandoughi et al., 2013). One medium quality study reported an unadjusted prevalence value of 6.3% for males and females (Braddom et al., 2009).

The included studies sampled populations from diverse locations. Three studies sampled populations from USA, two from general population and one from military personnel (Braddom et al., 2009; Radhakrishnan et al., 1994; Schoenfeld et al., 2012). Two studies sampled from urban and sub-urban districts in Egypt (Kandil et al., 2012; Khedr et al., 2018). The remaining studies sampled populations from Sicily (Salemi et al., 1996), India (Bharucha et al.,

1991), Iran (Sandoughi et al., 2013) and UK professional sport (rugby union) (Brooks et al., 2005). The diverse populations included in this review can support the application of results across multiple populations and worldwide geographical areas.

All studies were varied in CSR diagnostic criteria employed, including a combination of sensory disturbances (with or without radicular pain) and/or motor weakness made through imaging or nerve conduction testing. This may be attributed to the utility and availability of CSR diagnostic procedures across global healthcare systems. Clinicians and researchers should continue to use recommended guidelines and expectations when diagnosing CSR (Bono et al., 2011; Haanpaa et al., 2011; Treede et al., 2008). Assessment methods should be clinically reasoned in conjunction with the patient and with clear therapeutic cost: benefit analysis considered.

Comparison with other literature

Contrasting this review's results to other spinal radiculopathies may enhance our understanding of CSR. Lumbar spine radiculopathy is generally characterised by sensory disturbances originating from the lumbar spine and radiating below the knee (Koes, van Tulder, & Peul, 2007). Compared to CSR prevalence findings in this review, the point prevalence is higher at 4.6% to 13.4% and a lifetime prevalence of 1.2% to 43% (Konstantinou & Dunn, 2008). These results were based from a systematic review with 23 included studies

(Konstantinou & Dunn, 2008). However, caution should be taken as these specific values were limited to two studies using physical assessment to confirm lumbar spine radiculopathy.

Discussion of findings

The clinical diagnosis and classification of CSR of the included studies has a bias towards specific pathoanatomical classifications, for example, spondylosis, spinal central or lateral stenosis. Contemporary pain science recognises the complexity of biopsychosocial phenomenon in spinal conditions, with or without radiculopathy, that presents a challenge to both assessment and treatment (Finnerup et al., 2016; Hogg-Johnson et al., 2009; Vardeh, Mannion, & Woolf, 2016). CSR can result in altered afferent and efferent processing at various sites along the neuraxis, which will alter both sensory and motor functioning (Baron et al., 2017). This may contribute to the variance in incidence rates across the included studies. The included studies provided limited details on how the 'sensory' assessment was completed, thereby restricting these results to clinical practice. Previous work has recently demonstrated that detection of these alterations throughout the neuraxis are detectable using detailed screening and rigorous sensory examination of patients within the clinic (Spahr et al., 2017).

Identifying the mechanism-based phenotypes in people with CSR may enhance the diagnosis classification and subsequently enrich our understanding of this

complex presentation (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006; Hogg-Johnson et al., 2009; Holm et al., 2008; Vardeh et al., 2016). Systematic and non-invasive sensory testing through methodologies such as quantitative sensory testing, is well validated (Gierthmuhlen et al., 2019; Rolke et al., 2006; Vollert et al., 2016). This form of psychophysical testing has promising potential to improve CSR diagnosis (and other peripheral neuropathy presentations) by identifying specific mechanisms of pain and sensory experiences alongside our clinical reasoning frameworks (Gierthmuhlen et al., 2019; Spahr et al., 2017; Vardeh et al., 2016). Interestingly, none of the included studies detailed such psychophysical testing paradigms in establishing CSR diagnosis.

Further research is warranted to progress our understanding of CSR. The consistency and transparency of CSR diagnostic criteria should to be strongly encouraged among researchers and clinicians; this will enhance the analysis of future reviews including any updates to this review. Investigating other patient populations across a range of socioeconomic settings and occupations will improve understanding of how this debilitating condition can impact people from a variety of demographic backgrounds. Importantly, there was a paucity of literature investigating young adult populations, future observational studies investigating patients aged between 18-35 years would enhance understanding in this specific age group.

Strengths and weaknesses

Despite a systematic and rigorous approach to our literature searching, which included electronic databases, hand searching, grey literature, citation searching and contacting authors, there are a number of potential limitations to our review. Firstly, we initially identified 10 studies that met our inclusion criteria. One study was excluded as the authors did not respond to our request for further information on data collection methods. Furthermore, the included studies that had insufficient data to complete a meta-analysis. Therefore our narrative analysis was based on the small number of heterogenous studies. Secondly, the geographical location of recruited participants varied between elite sport and general populations in the UK and Italy; urban and non-urban districts in India, Egypt and Iran; and military and general populations in the USA. The largest sample size was in a military population (n=13,813,333), which limits application to general civilian populations. Finally, there was inconsistency on the CSR case definition among the included studies. This may have introduced detection bias across our included studies. Greater transparency and detail of CSR diagnosis may have enhanced the analysis resulting in improved generalisability to other populations and healthcare systems.

Conclusions

There is considerable variability with incidence and prevalence values for CSR. This can be attributed to wide-ranging diagnostic criteria and population sampling methods. There is limited consistency showing females are more likely to experience CSR compared to males. However caution should be taken as the epidemiological data is based on a small number of heterogenous studies with prevalence values ranging from 1.07 to 1.76 per 1000 and 0.63 to 5.8 per 1000 for males and females respectively. Further research is indicated to standard diagnosis classification criteria and analysing other populations globally to further our understanding on this debilitating condition.

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Table I – Study Characteristics

Lead Author & Date	**Population and location**	**Data Collection Methods**	**Sample Size (Age, Gender)**	**Definition of Cervical Spine Radiculopathy (CSR)**	**Prevalence/Incidence of CSR**
Schoenfeld (2012) [34]	USA Military personnel between years 2000-2009	Retrospective analysis of USA military's Defence Medical Epidemiological Database (DMED)	Total sample: 13,813,333 20,806 CSR Diagnosis (Males) 3,936 CSR Diagnosis (Females) Age Range 18-40 Years	***Probable CSR criteria (iii)*** ICD Code M541 "Pain (radicular pain), weakness, numbness, or difficulty controlling specific muscles related to nerve roots"	**Incidence** Males 1.76 per 1000 person-years (unadjusted **incidence**) Females: 1.36 per 1000 person-years (95% CI 1.30-1.42) (adjusted **incidence**) Total: 1.79 per 1000 person-years

Brooks (2005) [28]	Professional UK Club Rugby Football Union (RFU). Elite Level.	Orchard Sorts Injury Classification. Retrospectively analysed over 2 seasons	Total sample: 502 All Male Age: 25.4 years (SD: 4.2)	"Cervical nerve root injury" There was insufficient data presented to retrieve further detail (authors were contacted)	**Incidence** 0.02 per 1000 person-hours
Radhakrishnan (1994) [31]	General population Minnesota, USA	Retrospective population analysis of Mayo Clinic medical records	Total sample: 561 332 Male 47.6 years of age (SD: 13.1) 229 Female 48.2 years of age (SD: 13.8)	***Definite and probable CSR criteria (i)-(v) combined***	**Incidence** Female 63.5 per 100,000 person-years (Age Adjusted, 95% CI 55.1-71.8) Male 107.3 per 100,000 person-years (Age adjusted, 95% CI 95.4-119.2)

					Total – 83.2 per 100,000 person-years (age adjusted 95% CI: 77.0-91.1)
Braddom (2009) [27]	Georgia, USA Consecutive sample through a Neurology Department at the Medical College of Georgia. Individuals following Motor Vehicle Accident (39)	Retrospective analysis EMG reports between 1979 through to 2004.	Total sample 23,317 MVAs Mean age: 46 Years Unknown Male: Female data	***Definite CSR Criteria (i)*** Acute denervation with EMG studies OR Sensory changes in dermatomal distribution AND Weakness, atrophy OR fasciculation in a myotomal distribution *AND* Unilateral diminished deep tendon reflexes	**Prevalence** 1,465 of 23,317 (6.28%)

Khedr (2018) [30]	Qena area, Egypt	Prospective cross sectional sample Interview, Questionnaire, Clinical examination and Imaging Consultant neurologist completed clinical examination and imaging interpretations at	Total sample: 9303 (1057 families) Unknown Male: Female Ages 30-80 years 32 Confirmed cases of combined Lumbar and Cervical radiculopathy 9 males CSR 2 females CSR	***Definite CSR Criterion (i) or (ii)*** (i) Acute denervation with EMG studies OR Sensory changes in dermatomal distribution AND Weakness, atrophy OR fasciculation in a myotomal distribution *AND* Unilateral diminished deep tendon reflexes (ii) Abnormal myelography, CT or MRI correlating with radiculopathy	**Prevalence** Male 4.8 per 1000 Female 1.9 per 1000

		Qena University Hospital	Total – 11 (CPR: 1.2 per 1000 Lumbosacral radiculopathy (CPR: 2.3 per 1000)	WITH Neck pain or combined neck and arm pain OR Paraesthesia, hyperaesthesia or dysaesthesia in a nerve root distribution or muscle weakness in a myotomal distribution or atrophy	
Salemi (1996) [32]	Sicilian Municipality, Italy	Door-to-door survey Stage 1: Questionnaire screening tool	Total Sample: 8792 142 evaluated for CSR	***Definite and probable CSR criteria*** "Bouts of pain in the neck radiating down one or both arms. The pain had to start suddenly and could be associated with weakness,	**Prevalence** 3.5 per 1000 Both sexes 1.3 per 1000 Male 5.8 per 1000 Female

		Neurologists then completed physical assessment on suspicion of CSR	27 definite or probable CSR diagnosis 5 Male cases (50-69 Years of age) 22 Female cases (40-79 years of age)	paraesthesia or numbness in the arms. Stiffness in the neck could be present. Signs or symptoms had to persist for at least one day" ***Definite CSR*** clinical features had to relate to MRI, CT, EMG, Myelogram, X-ray ***Probable CSR***: Reoccurring bouts without neurological signs at the visit	
Bharucha (1991) [26]	Bombay, India	Door-to-door survey	Total sample: 14,010 334 cases of peripheral neuropathy	***Probable CSR criteria (vi or vii)*** Pain or stiffness in the neck associated with paresthesias, numbness, or weakness in an arm.	**Prevalence** 136 per 100,000

			44% over 50 years of age		
Kandil (2012) [29]	Assiut Governorate, Egypt	Door-to-door survey Stage 1: Questionnaire If answers suggested of neuropathy, then Stage 2: Neurological examination at University Hospital	Total sample: 42,223 Rural and urban areas 51 total CSR cases. 35 Male and 16 Female.	***Definite CSR criteria (ii)*** "Pain or stiffness in the neck associated with paresthesias, numbness, or weakness in an arm. Both conditions were confirmed by neurophysiological data and magnetic resonance imaging of cervical regions"	**Prevalence** 121 per 100,000 (95% CI 88-154)
Sandoughi (2013) [33]	Zahedan, Iran	Cluster sampling method across the region	2100 sample size	"Cervical radiculopathy"	**Prevalence** Male 1.14%

		COPCORD Core Questionnaire for initial data collection Where pathology suspected, subject referred to hospital where a Rheumatologist completed an assessment	1204 response rate (77.7%) 921 Male 1179 Female Occupation – 37.5% home-makers, 31.2% university or college students, 17.6% employees, 10.5% unemployed, 5.8% skilled and unskilled manual workers, 5.7% drivers.	There was insufficient data presented to retrieve further detail (authors were contacted)	(95% CI 0.45-1.82) Female 1.31% (95% CI 0.66-1.96)

Key – Cervical Spine Radiculopathy (CSR) Diagnosis Criteria

Definite CSR Diagnosis - *Either (i) or (ii)*

(i) Acute denervation with EMG studies OR Sensory changes in dermatomal distribution

AND

Weakness, atrophy OR fasciculation in a myotomal distribution *AND* Unilateral diminished deep tendon reflexes

(ii) Abnormal myelography, CT or MRI correlating with radiculopathy

WITH

Neck pain or combined neck and arm pain

OR

Paraesthesia, hyperesthesia or dysaesthesia in a nerve root distribution or muscle weakness in a myotomal distribution or atrophy

Probable CSR Diagnosis - *Either (iii), (iv) or (v)*

(iii) Neck pain, neck and arm pain, paraesthesia, hyperaesthesia or dysaesthesia in a nerve root distribution or muscle weakness in a myotomal distribution or atrophy

WITH

Sensory changes in dermatomal distribution or muscle weakness in a myotomal distribution or atrophy or Fasciculation in a myotomal distribution or Unilateral diminished deep tendon reflexes

(iv) Neck pain, neck and arm pain, paraesthesia, hyperaesthesia or dysaesthesia in a nerve root distribution or muscle weakness in a myotomal distribution or atrophy

WITH

Abnormal myelography, CT or MRI correlating with radiculopathy

(v) Neck pain, neck and arm pain with two from:

(v-i) Sensory changes in dermatomal distribution

(v-ii) Muscle weakness in a myotomal distribution or atrophy

(v-iii) Fasciculation in a myotomal distribution

(v-iv) Unilateral diminished deep tendon reflexes

Table II. Quality Appraisal

Lead Author & Year	The study sample represents the population of interest on key characteristics	Was there an adequate response rate? (>75%)	If appropriate, was information about non-responders described?	Was the CSR diagnosis specified and is it reproducible?	Is it clear what was used to determined precision estimates? (E.g. CIs)		Total Score High Quality = 4 and above Medium Quality = 2 and 3 Low Quality = 1 and below
Schoenfeld (2012)	1	1	0	1	1		High
Brooks (2005)	1	0	0	0	0		Low
Radhakrishnan (1994)	1	1	0	1	1		High
Braddom (2009)	1	1	0	1	0		Medium
Khedr (2018)	1	0	0	1	0		Medium
Salemi (1996)	1	1	1	1	0		High
Bharucha (1991)	1	1	0	1	0		Medium
Kandil (2012)	1	1	0	1	1		High
Sandoughi (2013)	1	1	0	0	1		Medium

Y= Yes (1 Point)
N = No (0 points)
NA = Not Applicable

Figure Legends

Figure I – MEDLINE search strategy - Completed on February 25th 2020.

Radiculopathy: Radiculopathy [MESH] OR Nerve* entrapment OR Radicular [MESH] OR Referred pain [MESH] OR Brachialgia [MESH] OR Cervicobrachial [MESH] OR Upper limb radiculopathy [MESH] OR Neck and arm pain [MESH]

AND

Epidemiology: Epidemiology [MESH] OR Incidence [MESH] OR Prevalence [MESH] OR Surveillance [MESH] OR Natural History [MESH] OR Occurrence [MESH] OR Frequency [MESH]

Figure II. Modified Radiculopathy Diagnostic Criteria

Definite CSR Diagnosis - *Either (i) or (ii)*

(i) Acute denervation with EMG studies or sensory changes in dermatomal distribution

AND

Weakness, atrophy or fasciculation in a myotomal distribution *and*

Unilateral diminished deep tendon reflexes

(ii) Abnormal myelography, CT or MRI correlating with radiculopathy *with* neck pain or combined neck and arm pain

OR

Paraesthesia, hyperaesthesia or dysaesthesia in a nerve root distribution or muscle weakness in a myotomal distribution or atrophy

Probable CSR Diagnosis - *Either (iii), (iv) or (v)*

(iii) Neck pain, neck and arm pain, paraesthesia, hyperaesthesia or dysaesthesia in a nerve root distribution or muscle weakness in a myotomal distribution or atrophy

with

Sensory changes in dermatomal distribution or muscle weakness in a myotomal distribution or atrophy or fasciculation in a myotomal distribution or unilateral diminished deep tendon reflexes

(iv) Neck pain, neck and arm pain, paraesthesia, hyperaesthesia or dysaesthesia in a nerve root distribution or muscle weakness in a myotomal distribution or atrophy

with

Abnormal myelography, CT or MRI correlating with radiculopathy

(v) Neck pain or neck and arm pain *with two* from:

(v-i) Sensory changes in dermatomal distribution

(v-ii) Muscle weakness in a myotomal distribution or atrophy

(v-iii) Fasciculation in a myotomal distribution

(v-iv) Unilateral diminished deep tendon reflexes

Figure III. Study Selection - Flow Diagram