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PAIN RELATED ASPECTS OF NECK MUSCLE PERFORMANCE, FUNCTIONING AND PSYCHOSOCIAL FACTORS IN INDIVIDUALS WITH CERVICAL RADICULOPATHY

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Pain related aspects of neck muscle performance, functioning and psychosocial factors in individuals with cervical radiculopathy
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"No matter how hard the past,
you can always begin again."
-Buddha

ABSTRACT

Aim: The overall aim of the work presented in this thesis was to describe and explore pain-related aspects of neck muscle performance, functioning and psychosocial factors in individuals with cervical radiculopathy (CR).

Methods: Participants were 157 patients with CR. Also *Study II* included 33 asymptomatic age-and gender-matched controls. *Study I,* a prospective randomized controlled pilot trial, investigated outcomes after anterior cervical discectomy and fusion (ACDF) with interbody cage with (n=17) or without (n=16) cervical collar in CR. In *Study II and III,* ventral and dorsal neck muscle fatigue was recorded with surface electromyography (EMG) during isometric endurance (NME) tests. *Study II* compared a CR group (n=46) with healthy controls (n=34). In *Study III*, results after neck-specific training or prescribed physical activity (n=50) were analyzed. Pain was estimated using visual analogue scales (VAS) and perceived fatigue rated with Borg CR-10 scales before, during and after the tests. Cross-sectional, *Study IV*, identified dimensions underlying measures of impairments, disability, personal factors, and health status in patients with CR (n=124).

Results: *Study I,* Both groups improved in all outcome measures, with a significant improvement from baseline to two years after surgery. Cervical collar worn for six weeks postoperatively, were associated with enhanced neck function and less neck pain even at long-term. *Study II* showed altered neck muscle endurance investigated with greater negative median frequency slope, variability, side imbalance, lower endurance time, and higher experience of fatigue among in the CR group compared to the healthy controls. Patients with CR had significantly shorter endurance time. In *Study III,* significant improvement in flexor NME was found after training, but with no difference between training groups. For the neck-specific training group only, there less activation of the splenius capitis during neck flexion after 14 weeks and one year, indicating reduced co-activation of the neck muscles. In *Study IV,* the PCA model provided three-components: Pain and functioning, Health, beliefs, and kinesiophobia, and Mood state and catastrophizing. These accounted for 73% of the cumulative percentages.

Conclusions: Cervical collar post-surgery can help deal with initial post-operative pain and reduce disability. Shorter endurance and higher experience of fatigue was perceived among patients with CR compared to healthy subjects. Exercises increased flexor NME regardless of exercise group. The neck-specific group indicated reduced compensation of antagonist muscles during flexion contraction. To capture a broad picture of patients with CR pain, their functioning, fear avoidance beliefs, and anxiety are important factors in a clinical perspective.

Keywords: activity limitations, asymptomatic subjects, cervical radiculopathy, disability, electromyography, endurance, fatigue, health, neck muscles, pain, psychosocial factors

SAMMANFATTNING

Det övergripande syftet med denna avhandling var att beskriva och undersöka smärtrelaterade aspekter av nackmusklernas egenskaper, funktion och psykosociala faktorer hos personer med cervikal radikulopati (CR). Metod: 157 patienter med CR deltog i studierna. *Studie II* inkluderade också 33 friska personer som hade samma ålders-och könsfördelning som CR gruppen och mot vilka CR gruppen jämfördes. *Studie I*, en liten framåtblickande studie där behandlingen lottades, så kallad prospektiv randomiserad kontrollerad studie undersökte resultaten från opererade patienter med halsryggsdiskbråck, operative åtgärd med diskutrymning med steloperation (ACDF), med (n = 17) och utan (n = 16) nackkrage i efterförloppet. I *studie II och III*, mättes muskeltrötthet i främre och bakre nackmusklerna med elektromyografi (EMG) där elektroder på huden registrerade den elektriska aktiviteten i muskeln under det att ett nackmuskel-uthållighetstest (NME) utfördes. *Studie II*, CR gruppen (n = 46) jämfördes med friska kontrollpersoner (n = 34). *Studie III*, effekten av två olika träningsprogram jämfördes; A) nack-specifika övningar respektive B) fysisk aktivitet på recept (n = 50). Skattad smärta utvärderades med hjälp av visuell analog skala (VAS) och upplevd skattad trötthet med Borg CR-10 skalan före, under och efter testet. *Studie IV*, en tvärsnittsstudie där dimensioner som underliggande mått på funktionsnedsättning, funktionsförmåga, personliga faktorer och hälsotillstånd hos patienter med CR (n = 124) identifierades. Resultat: *Studie I*, båda grupperna förbättrades i samtliga utfallsmått, med statistiskt signifikant förbättring från start till 2 år efter operationen. Användningen av nackkrage sex veckor efter operationen, medför högre skattning av nackfunktion och lägre nivåer av nacksmärta även vid långtidsuppföljningarna. *Studie II* visade mer muskeltrötthet, obalans mellan höger och vänster sida, signifikant kortare uthållighetstid och högre skattning av trötthet hos patienter med CR jämfört med de friska kontrollerna. I *Studie III*, var det signifikant förbättring i nack-flexor uthållighet efter träning, för båda träningsgrupperna. Patienter nack- specifik träning hade minskad aktivitet av splenius capitis vid flexion efter 14 veckor och ett år, vilket tyder på minskad samaktivering av nackmusklerna. I *Studie IV*, identifierade PCA-analysen tre komponenter 1) smärta och funktion 2) hälsa, övertygelse och rörelserädsla, samt 3) stämningsläge och katastroftankar. Dessa stod för 73 % av förklaringsvärdet.

Slutsatser: Halskrage efter operation kan hjälpa vissa patienter att hantera initiala post-operativ smärta och minska funktionsnedsättningen. Patienter med CR hade kortare uthållighetstid och högre skattad trötthet av jämfört med friska försökspersoner. Träning ökade halsmusklernas uthållighetstid oavsett träningsgrupp. Patienter i nack-specifika träningsgruppen hade indikationer på minskad kompensation av antagonist musklerna under flexionskontraktion. Smärta, funktion, rörelserädsla och ångest är viktiga faktorer som bör ingå i utvärderingen av patienter med CR.

LIST OF SCIENTIFIC PAPERS

I. Abbott A, **Halvorsen M**, Dedering Å.
Is there a need for cervical collar usage post anterior cervical decompression and fusion using interbody cages? A randomized controlled pilot trial.
Physiotherapy Theory and Practice, 29 (4): 290-300, 2013

II. **Halvorsen M**, Abbott A, Peolsson A, Dedering Å
Endurance and fatigue characteristics in the neck muscles during sub-maximal isometric test in patients with cervical radiculopathy.
European Spine Journal, 23 (3):590-8, 2014

III. **Halvorsen M**, Falla D, Gizzi L, Harms-Ringdahl K, Peolsson A, Dedering Å.
Short and long term effects of exercise on neck muscle function in patients with cervical radiculopathy.
Manuscript

IV. **Halvorsen M**, Kierkegaard M, Harms-Ringdahl K, Peolsson A, Dedering Å.
Dimensions underlying measures of disability, personal factors and health status in cervical radiculopathy: a cross-sectional study.
Medicine (Baltimore), 94 (24): e999, 2015 [11]

CONTENTS

LIST OF ABBREVIATIONS

ACDF	Anterior Cervical Decompression Fusion
ARV	Average Rectified Value
BMI	Body Mass Index
CR	Cervical Radiculopathy
CROM	Cervical Range of Motion
CSQ	Coping Strategies Questionnaire
DHI	Dizziness Handicap Inventory
EMG	Electromyography
ESES	Exercise Self-efficacy Scale
FABQ	Fear Avoidance Beliefs Questionnaire
FES	Falls Efficacy Scale
HADS	Hospital Anxiety and Depression Scale
IASP	The International Association for the Study of Pain
IPAQ	International Physical Activity Questionnaire
ICF	International Classification of Functioning, Disability and Health
MDF	Median Frequency
MRI	Magnetic Resonance Imaging
NDI	Neck Disability Index
NME	Neck Muscle Endurance
SCM	Sternocleidomastoid muscle
SES	Self-efficacy Scale
SENIAM	Surface Electromyography for the Non-Invasive Assessment of Muscles
SF-36	Short form 36 health survey
TSK	Tampa Scale of Kinesiophobia
VAS	Visual Analogue Scale
WHO	World Health Organization

1 INTRODUCTION

Cervical radiculopathy (CR) causes neck pain and/-or arm pain. CR is, by definition, a disease of the cervical spinal nerve root (Ellenberg, 1994) and is most commonly caused by cervical disc herniation and spondylotic changes (Wolff & Levine, 2002). The consequences of neck pain stretch beyond the pain experience and often affect daily living and quality of life, and further incur a burden on society (Cote, Cassidy, & Carroll, 1998; Hogg-Johnson et al., 2008).

General neck pain encompasses numerous diagnosed health conditions which include inflammatory, systemic and degenerative disorders. Specifically, within the degenerative neck disorders, CR is the most common condition referred in Sweden for physiotherapy prior to deciding whether surgical intervention is required (SweSpine). CR affects muscle performance possibly due to nerve root compression, which in turn affects functioning. The effect of muscle performance cannot alone explain the negative effect on functioning, and it is therefore important to explore psychosocial factors in order to design patient-specific intervention programs. CR is considered an important subgroup of neck disorders, and although less prevalent than general neck pain, it is associated with severe pain and disability (Childs et al., 2008; Manchikanti, Singh, Datta, Cohen, & Hirsch, 2009; Rubinstein, Pool, van Tulder, Riphagen, & de Vet, 2007).

As a physiotherapist, working at the Neurological section, Department of Physiotherapy at Karolinska University Hospital, I meet patients with CR at our in-and outpatients clinic. These patients have often described how debilitating the disease was, interfering with work, social obligations and emotional states. It was therefore of great interest to me as a clinician to do research on factors of importance for rehabilitation because they influence the patients' and physiotherapists' choice of treatment.

This thesis focuses on pain-related aspects of neck muscle performance, functioning and psychosocial factors in individuals with CR.

2 BACKGROUND

2.1 PAIN

Pain has been defined by the International Association for the Study of Pain (IASP) as "*an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage*" (Merskey, 2007; Merskey, Bogduk, 1994).

Pain is probably the most common reason why people seek health care (Loeser & Melzack, 1999). Always subjective, pain is the experience we associate with actual or potential tissue damage. It is unquestionably a physical sensation in one or several parts of the body. Further, it is always unpleasant and therefore also an emotional experience. Pain has long been considered as a complex experience, including sensory-discriminatory aspects (pain intensity, duration and localization), emotional-motivational aspects (behavior, emotional), and cognitive-evaluative dimensions (earlier experiences, thoughts and ideas) (Melzack, 1999; Melzack & Wall, 1965).

2.1.1 Definitions of neck pain

The International Association for the Study of Pain (IASP) in its classification of chronic pain defines "*cervical spinal pain as pain perceived anywhere in the posterior region of the cervical spine, from the superior nuchal line to the first thoracic spinous process*". This is a topographic definition (Merskey, 1994). Bogduk and McGuirk also suggested that neck pain may be subdivided into upper-cervical spinal pain and lower-cervical spinal pain (McGuirk, Bogduk, 2007). The Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders describes neck pain as *"pain located in the anatomical region of the neck with or without radiation to the head, trunk, and upper limbs* (Guzman et al., 2008).

2.2 CERVICAL RADICULOPATHY

2.2.1 Definition of Cervical Radiculopathy

The following definitions have been proposed for CR. This thesis is based on the first definition.

CR, resulting from degenerative disorders, can be defined as "*pain in a radicular pattern in one or both upper extremities related to compression and/or irritation of one or more cervical nerve roots. Frequent signs and symptoms include varying degrees of sensory, motor and reflex changes as well as dysesthesias and paresthesia related to nerve root(s) without evidence of spinal cord dysfunction (myelopathy)"* North American Spine Society (NASS), 2009.

There are other definitions and to date there is no consensus on one only (Kuijper, Tans, Beelen, Nollet, & de Visser, 2009; Ragonese, 2008). Cervical radicular pain is defined by the

IASP as "*distinguished from nociception by the axons being stimulated along their course; their peripheral terminals are not the site of stimulation. Ectopic activation may occur as a result of mechanical deformation of the dorsal ganglion root, mechanical root"* (IASP).

2.2.2 Pathology

CR is clinically described as pain and neurological symptoms resulting from any type of condition that irritates a nerve in the cervical spine. Several pathologies can cause pain deriving from the cervical spine (Roth, Mukai, Thomas, Hudgins, & Alleva, 2009). Eight cervical-spinal nerves (C1-C8) exit the cervical spine vertebrae (C1-C7). When any nerve root in the cervical spine is irritated through compression or inflammation, the symptoms can radiate along the dermatome of a specific nerve. One condition is herniated disc. This is characterized by sequestration of the central part of an intervertebral disc. The neck pain is caused by the inflammatory response or nerve dysfunction arising from either inflammation or mechanical compression of the spinal nerves (Wolff & Levine, 2002). Spinal stenosis is a condition in which there is a narrowing of one or more regions of a person´s spine. This can result in pressure on the spinal cord and the nerves that travel through the spine. Spinal stenosis can arise from bone spurs or osteophytes, or from ligamentous thickening affecting compression. In patients, specific CR symptoms will depend primarily on the specific nerve affected. The symptoms may also be referred to as radicular pain. Herniated disc, degenerative disc disease and its related pathologies including stenosis, are the most common cervical pathologies causing radicular symptoms. Herniated disc accounts for about 20-25% and degenerative disc disease for about 70-75% of CR (Roth et al., 2009). In rare cases CR can be caused by other conditions such as tumor, fracture or sarcoidosis, resulting in compression or damaging the cervical nerve roots (Radhakrishnan, Litchy, O'Fallon, & Kurland, 1994).

In CR, pain radiates into the arm, and is often followed by one or more neurological symptoms such as numbness, muscle weakness and inhibited reflexes in arms (Bono et al., 2011). Further, a sharp, achy or burning sensation is described, which is commonly experienced in the neck, arms, shoulders and even chest (Abbed & Coumans, 2007). It is not uncommon for patients to experience sensory or motor deficits without pain (Corey & Comeau, 2014). CR may also occur with no identifiable cause. Atypical findings, such as deltoid weakness, scapular winging, chest and deep breast pain (LaBan, Meerschaert, & Taylor, 1979), headache, and weakness of the intrinsic muscles of the hand may be present in a few patients and can be alleviated with treatment (Henderson, Hennessy, Shuey, & Shackelford, 1983).

Diagnostic imaging is used to confirm the presence of a clinically suspected CR. It evaluates the disc herniation with or without nerve root compression. Magnetic resonance imaging (MRI) of the cervical spine generally shows the cause of the radiculopathy, usually spondylosis or a herniated disc (Kuijper, Tans, Schimsheimer, et al., 2009). Radiographic changes such as disc degeneration and osteophyte formation, commonly seen in the cervical spine, are just partly responsible for the reported pain, and are not even considered a risk factor for general neck pain (Boden et al., 1990). MRI findings should be correlated with clinical findings because both false-positive and false-negative rates are high (Kuijper et al., 2011). The reliability of repeated evaluation of MRI in the cervical spine, as summarized from six studies, was generally fair-to-moderate (Nordin et al., 2008). In one study, the intra-observer reliability coefficients for determining anterior disc protrusion, disc degeneration, and foraminal stenosis in the cervical spine were moderate (kappa = 0.51-0.61) (Matsumoto et al., 1998).

Degenerative changes in MRI are common in asymptomatic subjects and increase with age. Since degenerative changes are not well associated with neck pain, the findings may have little to do with neck pain (Guzman et al., 2008).

2.2.3 Epidemiology and risk factors

Incidence rates for CR in an American population-based study indicated an overall rate of 83.2 per 100,000, with a higher incidence in men than women (107.3 per 100,000 versus 63.4 per 100,000, respectively) and peak incidence in the sixth decade of life in both genders (Kuijper, Tans, Schimsheimer, et al., 2009; Radhakrishnan et al., 1994). The Saskatchewan Health and Back Pain Survey reported that 54% of respondents had experienced neck pain in the previous six months, of whom almost 5% said that the pain was highly disabling (Cote, Cassidy, & Carroll, 2000). According to a review by the United States military that included those aged 40 years and above, white ethnicity and female gender were at greater risk of CR (Schoenfeld, George, Bader, & Caram, 2012). Specifically for cervical spondylosis, the incidence increases with age in both genders (Radhakrishnan et al., 1994). Epidemiological studies have shown that women experience chronic neck pain more often than men (O'Leary, Falla, Hodges, Jull, & Vicenzino, 2007; Ylinen et al., 2003). Various causal risk factors have been investigated for the development of CR, which include gender, genetic factors, episodes of neck pain, and occupational or spare-time factors (North American Spine Society (NASS), 2009). Other aspects are smoking, high and persistent load bearing and previous back pain (Ellenberg, Honet, & Treanor, 1994; Radhakrishnan et al., 1994; Roth et al., 2009).

2.2.4 Etiological considerations

In more than 70% of CR or stenosis, pain is the primary presenting feature. The typical patient with CR or stenosis presents with a sudden onset of neck and arm pain that causes discomfort which is often experienced as either a dull ache or a severe burning pain. As the condition progresses, the pain radiates to the arm and into the hand, along the sensory distribution of the involved nerve root(s) (Polston, 2007). Radicular pain is a frequent complaint of patients often attending outpatient primary care and musculoskeletal clinics (Casey, 2011).

Little is known about the natural course of CR. Lee et al followed 51 patients with CR between 2 and 19 years and found that 43% were asymptomatic after a few months, 29% had mild or intermittent symptoms, and 27% had more disabling pain (Lees & Turner, 1963). The results of shorter longitudinal studies (6 months) found similar positive trends of natural recovery (Maigne & Deligne, 1994; Saal, Saal, & Yurth, 1996; Vinas, Wilner, & Rengachary, 2001).

Symptoms related to CR tend to be unilateral, but where there are severe spurs bilateral symptoms may be present (Eubanks, 2010). The distribution of the discomfort and physical findings may vary depending on the nerve root involved. The absence of radiating symptoms does not eliminate CR as a potential diagnosis (Rhee, Yoon, & Riew, 2007). Patients also frequently develop radiculopathy in the absence of a causative or predisposing factor (Ellenberg et al., 1994; Radhakrishnan et al., 1994).

Disc herniation may develop spontaneously, whereas root lesions related to spondylosis may develop more slowly. The natural occurrence of degenerative changes in the spine is often asymptomatic (Roh et al., 2005). Radiculopathies seen in the younger population are most often related to disc herniation resulting from direct pressure on an existing nerve, whereas those in older patients are related to foraminal narrowing due to the formation of osteophytes (spondylosis) (Malanga, 1997). In general, spondylosis accounts for approximately 70% and disc herniation for approximately 30% of all cervical radiculopathies (Polston, 2007; Radhakrishnan et al., 1994).

2.2.5 **Treatment**

Although the symptoms and signs may resolve spontaneously, clinicians need to be aware of persisting symptoms; chronic functional impairment and activity limitations that are predisposing factors for developing chronic neck pain (Childs et al., 2008; Rubinstein et al., 2007). To date, the effectiveness of any specific treatment has not been established definitely. Only two randomized controlled trials (RCT) have identified the effectiveness of surgical versus conservative treatment for these patients CR (Engquist et al., 2015; Hurwitz et al., 2008). Physical therapy has not been demonstrated to alter the natural history of CR (Levine, Albert, & Smith, 1996). Studies have increasingly found changes in the structure of cervical muscles and behavior of patients with chronic pain, compared to healthy subjects (Falla, Bilenkij, & Jull, 2004; A. Peolsson & Kjellman, 2007). Further, evidence suggests that an active, compared to a passive, treatment approach for patients with CR results in better outcome (Saal et al., 1996). For health care providers, an understanding of the natural history of radiculopathy is paramount for accurate diagnosis, recommending the best choice of treatment and providing patients with tailored guidance (Casey, 2011).

First-line treatment for patients with CR is typically conservative (Engquist et al., 2013; L. C. Persson & Lilja, 2001; Thoomes, Scholten-Peeters, Koes, Falla, & Verhagen, 2013; Wolff &

Levine, 2002). In general, radicular symptoms can usually be resolved with simple therapy, at times they disappear spontaneously (Radhakrishnan et al., 1994). Several studies have reported outstanding outcomes with aggressive nonsurgical treatment of CR (Herzog, 1999; Radhakrishnan et al., 1994; Saal et al., 1996; Sampath, Bendebba, Davis, & Ducker, 1999). This treatment included active physical therapeutic exercises in combination with cognitive approaches (Peolsson et al., 2013). In some patients, radiculopathy develops insidiously and becomes chronic; thus, notoriously affects work, social activities, and recreation (Saal et al., 1996). Patients with sub-acute or chronic symptoms (Sampath et al., 1999) are typically referred to a neurosurgeon for the evaluation as to whether surgery is needed.

Several intervention strategies are generally used: either physiotherapy or surgical intervention (Cleland, Fritz, Whitman, & Heath, 2007; Rhee et al., 2007). Numerous physiotherapy interventions are available, despite the lack of evidence for some ‘perceived active ingredients’ (Levine et al., 1996). For example, massage and modalities such as heat, ice, electrical stimulation, and ultrasound have been widely used without proof of favorable long-term effects (Santiesteban, 1983). A graded program of physiotherapy has lately been prescribed after an initial period of short-term rest and/or immobilization. Initially, as pain resolves, isometric exercises are introduced to strengthen the cervical musculature. Additionally, aerobic conditioning may be helpful in alleviating symptoms and to avoid jarring the cervical spine (Rhee et al., 2007). Active range-of-motion and resistive exercises may be added as tolerated (Rhee et al., 2007). In the later stages of the program, the focus is on behavioral change, which includes postural training, ergonomics, and lifestyle modifications (Rhee et al., 2007).

2.2.5.1 Outcome for conservative treatment

Conservative treatment seeks mainly the reduction of pain and improvement of function (van Middelkoop et al., 2013; Wolff & Levine, 2002). Poor response to conservative treatment normally justifies a referral for additional evaluation, typically surgical consultation (Epstein, 2002). Data from randomized controlled trials to address the benefits of surgery versus conservative management are limited (van Middelkoop et al., 2013). A recently updated report from the *Cochrane Database of Systematic Reviews* in 2001 found only two acceptable studies that address this issue. The report suggests that in one study of 81 patients, the subjects improved in the short term (three months), but at one year no differences between the groups could be seen (Fouyas, Statham, & Sandercock, 2002). In the review from Middelkoop et al , there was only poor evidence for the effects of physiotherapy compared to surgery on long-term recovery (van Middelkoop et al., 2013). In another review (Thoomes et al., 2013), the most common conservative interventions for patients with CR were summarized as: pharmacological treatments, physical training, manual therapy, massage, physical exercise, muscle training, heat pack, ergonomic advice, traction, acupuncture and TENS, behavior therapy, treatments using a collar etc.

Physiotherapy can be performed passively or actively (Arnasson, Carlsson, & Pellettieri, 1987). Passive treatment is administered by the treating physiotherapist. In active treatment, the patient is responsible for carrying out the exercises/-training sessions. Conventionally, treatment sessions combine both modalities. To date, physical therapy has not been demonstrated to alter the natural history of CR (Levine et al., 1996), although many treatment approaches such as exercise, mobilization and manipulation have proved effective, but only in the short-term (Rhee et al., 2007; Thoomes et al., 2013).

2.2.6 **Outcome of surgical treatments**

Patients who do not respond to pain management may require surgery, especially where there is significant extremity weakness, severe pain, or unsuccessful response to this treatment (Kim & Kim, 2010; van Middelkoop et al., 2013). Surgical intervention is typically considered for patients with radiographic evidence of nerve compression and more complex pathologies as found on MRI (Corey & Comeau, 2014). Few studies have compared surgical treatment to non-surgical treatment (Persson, Carlsson, & Carlsson, 1997) (Engquist et al., 2015). At three month´s follow-up, surgery gave better results in terms of pain, compared to physical therapy or a hard cervical collar (Persson et al., 1997). However, at one year there were no significant differences between the groups. The results confirmed short-term benefits (three month´s) for sensory loss and paresthesia, but these were not present at the one-year follow-up. The existing small randomized trials do not present reliable evidence on the effects of surgery for cervical radiculopathy or myelopathy (Nikolaidis, Fouyas, Sandercock, & Statham, 2010).

2.2.6.1 Anterior Decompression Fusion

Depending on the pathology, CR may be surgically addressed either anteriorly or posteriorly. In the present work, anterior cervical discectomy and fusion (ACDF) was used (Cloward, 2007). This is a common surgical intervention for cervical spinal degenerative disease (Jacobs et al., 2011; Smith & Robinson, 1958) and permits direct removal of most lesions that cause CR. In general, anterior pathology such as centrally herniated disc and osteophytes are treated anteriorly (Narayan & Haid, 2001). Anterior cervical discectomy (ACD) may be performed in conjunction with fusion (allograft, auto graft, or bone substitutes) and fixation (plates) (Matz et al., 2009). A combination of discectomy and fusion is recommended in all patients especially when several levels are involved (Rhee, Park, Yang, & Riew, 2005; Samartzis et al., 2003). Several long-term follow-up studies have shown that the outcomes of ACDF are favorable in terms of success of surgery and pain severity (Gore & Sepic, 1998; Hermansen, Hedlund, Vavruch, & Peolsson, 2011; Sugawara, Itoh, Hirano, Higashiyama, & Mizoi, 2009) and neurological deficits (Hacker, Cauthen, Gilbert, & Griffith, 2000). After cervical spinal surgery, health status was reported to be worse in women, than in men (Peolsson & Kjellman, 2007; A. Peolsson, Vavruch, & Oberg, 2006a).

2.2.6.2 *Post operative neck collar*

The use of a cervical collar reduces pain by limiting active motion and nerve root irritation (Dillin et al., 1986; Dreyer & Boden, 1998; Levine et al., 1996). Passive therapy consists of collar immobilization and rest from activities that aggravate the condition. Three studies that compared immobilization to active therapy showed no difference in long-term outcome, but those treated more aggressively tended to improve more quickly (Herzog, 1999; Saal et al., 1996; Sampath et al., 1999). There is widespread indication that prolonged use of the collar leads to deconditioning of the neck musculature and tissue damage and should be avoided (Carette & Fehlings, 2005; Levine et al., 1996). Active interventions are more favored in the literature (Dreyer & Boden, 1998; Jette & Jette, 1996; Tan & Nordin, 1992). Immobilization of the neck with a cervical collar is thought to reduce inflammation around an irritated nerve root and to reduce muscle spasm (Naylor & Mulley, 1991). Further, the warmth provided by the cervical collar is often reported as therapeutic. The effect of cervical collars in limiting the duration of CR has not been demonstrated (Naylor & Mulley, 1991). Although short-term use of cervical collars may helpful, extended immobilization of more than one to two weeks should be avoided to prevent hypo-atrophy of the cervical musculature (Rhee et al., 2007). A postoperative collar is commonly used after treatment for degenerative conditions of the cervical spine, primarily to immobilize the spine (Connolly, 1998). A semi-hard cervical collar resulted in a reduction of neck and arm pain in the early phase of CR (Kuijper, Tans, Beelen, et al., 2009). In the anterior cervical spine, the use of bracing compared to the collar is preferred after fusion if more vertebral segments are affected, (Bible et al., 2009). The duration of collar use is proportionate to the number of operative segments, and is shorter for a single-level ACDF (Bible et al., 2009; Persson et al., 1997). However, Persson et al highlighted that no significant differences in outcomes were found between subgroups of patients with CR who either received physiotherapy alone, soft cervical collar alone or surgery alone (Persson et al., 1997). Unfortunately, up-to-date support is lacking for the effectiveness of any non-surgical treatment, including cervical collar, physiotherapy or wait-and-see (Kuijper, Tans, Beelen, et al., 2009).

2.3 NECK MUSCLE PERFORMANCE

The neck muscles are responsible for directing the head and maintaining its posture. An optimal combination of all muscles is necessary for normal function, while a dysfunction can lead to pain and disability (Dvir & Prushansky, 2008). Different studies indicate, that muscular dysfunction in the cervical spine refers to change in structure (Elliott et al., 2008; Uhlig, Weber, Grob, & Muntener, 1995) and function (Falla, Bilenkij, et al., 2004; Falla, Jull, & Hodges, 2004; Falla, Jull, & Hodges, 2004). Neck muscle endurance reportedly decreases with age in both genders (Peolsson, Almkvist, Dahlberg, Lindqvist, & Pettersson, 2007), women being weaker than men (Domenech, Sizer, Dedrick, McGalliard, & Brismee, 2011; Dvir & Prushansky, 2008). Further discussion of two other factors that may affect the result placement of the load and thoracic support is needed in order to standardize test protocols (Dvir & Prushansky, 2008).

Lower endurance of the neck muscles is common in patients with neck pain, chronic cervicobrachial syndrome and headache (Falla, Jull, Rainoldi, & Merletti, 2004; Jull, Barrett, Magee, & Ho, 1999). Deficits in isometric strength and endurance have been frequently documented in the craniocervical flexors (O'Leary, Jull, Kim, & Vicenzino, 2007), cervical flexor (Barton & Hayes, 1996; Parazza et al., 2014; Peolsson, Hedlund, & Oberg, 2001) and cervical extensor muscles (Parazza et al., 2014), in connection with neck disorders.

The strength of the cervical muscles may be measured using either isometric or dynamic techniques. The isometric method is so far the most common, used in clinical settings without complicated tools. Muscle strength has been widely described, measured using equipments such as handheld dynamometer, fixed dynamometer (O'Leary, Falla, Jull, & Vicenzino, 2007), and by graded head load (Peolsson & Kjellman, 2007) or no specific equipment attached to the head (Grimmer, 1994). Tests for cervical muscles have been used, such as the cranio-cervical flexion test (CCF), the neck flexor muscle test (NFME) and the neck extensor endurance test (NEE) (Edmondston et al., 2008; Lee, Nicholson, & Adams, 2005; Peolsson & Kjellman, 2007). These tests have been defined in different ways in the literature.

Neck strength training is effective in improving neck muscle strength and function among patients with neck disorders (Falla, Jull, Hodges, & Vicenzino, 2006; Peolsson & Kjellman, 2007; Salo, Hakkinen, Kautiainen, & Ylinen, 2010). Neck muscle endurance in female patients with non-specific pain improved and male patients with ACDF showed improvement after treatment (Peolsson & Kjellman, 2007). The endurance time for patients with postural neck pain compared to a control group was characterized by greater variability in neck flexor and extensor muscle endurance (Edmondston et al., 2011).

It has been recommended that general strengthening and endurance training for the cervical flexor muscles should be prescribed for people with neck pain to reduce their fatigability and to strengthen their neck muscles (Garces, Medina, Milutinovic, Garavote, & Guerado, 2002; Ylinen et al., 2003). Further studies are needed to evaluate training effects in a long-term perspective and also neck-specific exercises protocols in order to better understand the influence of both extension muscles and flexor muscles (Leggett et al., 1991; Peolsson et al., 2013).

At seven-week follow-up, an endurance training group demonstrated a greater increase in maximum voluntary contraction (MVC) force than a cranio-cervical flexion training group (Falla et al., 2006).

2.3.1 EMG recordings

Surface electromyography (EMG) is a non-invasive method for evaluating muscle function. The most general way to quantify muscle fatigue is by the change in mean or median frequency (MF) of the power spectrum of the EMG signal (Phinyomark et al., 2012). Mean frequency (MNF) and median frequency (MDF) are the most useful and accepted frequency-domain features, and are often used for assessing muscle fatigue in surface EMG signals. The signals are obtained with surface electrodes placed on the skin over the targeted muscle (Phinyomark et al., 2012). During maintained muscular contraction, a compression of the MF EMG power spectrum towards a lower frequency has been observed to follow a linear relationship with muscular fatigue (De Luca, 1984).

EMG studies have confirmed that neck pain is associated with inhibition of the deep cervical flexor muscles (Falla et al., 2004). However, there is extensive variability of muscle activation between individuals with neck pain during functional upper-limb tasks (Falla, Bilenkij, et al., 2004).

2.3.2 Perceived fatigue

Muscle fatigue is an exercise-induced reduction in maximal voluntary muscle force. Voluntary activation usually diminishes during maximal voluntary isometric tasks, that is when central fatigue increases and motor unit firing rates decline (Gandevia, 2001). The capacity to sustain aerobic exercise is very important for endurance training whereas poor exercise tolerance is strongly associated with disability (Newman, 2006, Gulati, 2005).

In a study comparing patients with lumbar disc herniation and healthy subjects, perceived fatigue level correlated with endurance time (Dedering, Nemeth, & Harms-Ringdahl, 1999), as assessed on the Borg CR-10 scale (Borg, 1990). Further, in patients, a strong correlation was found between lumbar muscle fatigue ratings and applied force (Elfving, Nemeth, Arvidsson, & Lamontagne, 1999). Greater fatigability was observed in the cervical flexor muscles, especially in the sternocleidomastoid (SCM) and the anterior scalene (AS) muscles of patients with chronic neck pain (Falla, Rainoldi, Merletti, & Jull, 2003). In helicopter pilots, a reduction in the prevalence of the neck pain was reported for the exercise group, and this was significant for pain rating during the previous week and previous three months (Äng, Monnier, & Harms-Ringdahl, 2009).

2.4 FUNCTIONING AND PSYCHOSOCIAL FACTORS

Understanding unique individual factors on patient reported measures of functioning has become a standard for evaluating treatment effectiveness in spine surgery (McCormick, Werner, & Shimer, 2013). Psychological and social factors affect mental state and quality of life (Soderlund & Lindberg, 1999; Burton & Waddell, 1998). Both physical impairment and psychosocial factors are associated with higher neck disability index (NDI) scores in patients with CR (Wibault et al., 2014). In a study that controlled for potential confounders, psychological distress was reported and considered a long-term predictor of unfavorable outcome (Peolsson, Vavruch, & Oberg, 2006b). It is important for clinicians to have an understanding of the interplay of these factors on functioning. Activity limitations in CR influence quality of life, and are associated with sick leave, disability and loss of productivity (www.nikkb.dk).

Ariens et al. examined various psychosocial factors in a working population, and grouped them into categories (Ariens et al., 2001). The results of their systematic review verified poor social support, low job control, and low job satisfaction as risk factors for high level of neck pain (Ariens et al., 2001). Patients with high levels of pain developed more clinical depression, as assessed with HADS, than the pain-free did (Blozik et al., 2009).

2.5 MODELS

Psychosocial factors have been suggested to influence the perception of pain, as well as to play an important role in the development of pain chronicity and disability (Gatchel, Peng, Peters, Fuchs, & Turk, 2007). Their questionnaires for a population with neck pain could provide information concerning neck pain, patients' functional performance, psychosocial status and health, allowing a holistic perspective on factors influencing function.

2.5.1 The Bio-psychosocial model

The bio-psychosocial model has replaced the earlier biomedical model of disease in order to better understand the influence of the contextual paradigm on functioning (Manchikanti, Boswell, et al., 2009). Further, the bio-psychosocial model claims that biological, psychological and social factors all play a sufficient role in human functioning in the context of disease or illness (Alonso, 2004). In this model, health professionals need to recognize the biomedical and psychosocial components when developing treatments strategies aimed at improving patients´ situation. The integration of these two components is important for the physiotherapists' reference framework (Main & Watson, 1999). In the bio-psychosocial model, the focus is not only on pain, but also on disability in daily activities, how patients cope with pain (Smith, Fortin, Dwamena, & Frankel, 2013), and other factors of importance for understanding how patients respond to treatment.

2.5.2 Fear-avoidance beliefs

Pain-related fear is well known in the general population (Buer & Linton, 2002), as well as in various patient groups with persistent musculoskeletal and neuropathic pain (Buitenhuis, Jaspers, & Fidler, 2006; de Jong et al., 2005). Linton et al (2000) describe fear of pain and re-injury as an important part of the understanding of disability in patients with persistent musculoskeletal pain (Linton, Buer, Vlaeyen, & Hellsing, 2000). Fear-avoidance in the context of pain refers to the avoidance of movement or activities based on fear.

The fear-avoidance model identifies two behavioral responses to pain: confrontation and avoidance (Vlaeyen, Haazen, Schuerman, Kole-Snijders, & van Eek, 1995). Confrontation is considered an adaptive response leading to carrying out all activities, and avoidance as a maladaptive response in which activity avoidance can lead to continued disability (Lethem, Slade, Troup, & Bentley, 1983). The fear-avoidance model suggests that patients with fear-avoidance beliefs will avoid physical activities that are likely to increase pain (Vlaeyen, Kole-Snijders, Boeren, & van Eek, 1995).

Psychological factors such as fear-avoidance beliefs, fear of movement / re-injury and coping strategies, are thought to play a significant role in the development of chronic pain (Linton, 2000). A weaker relationship between measures of fear and avoidance beliefs and pain/disability among patients with mechanical neck pain has been reported, contrary to a stronger relationship seen in patients with low-back pain (Cleland, Fritz, & Childs, 2008). The term kinesiophobia was introduced in 1990 by Kori et al (Kori, Miller, & Todd., 1990). The term was further elaborated by Vlayen et al (Vlaeyen, Kole-Snijders, et al., 1995), who called the experience “fear of movement / (re) injury”. The Tampa scale of kinesiophobia (TSK-SV) is reportedly reliable for use in patients with chronic low-back pain (Lundberg, Styf, & Carlsson, 2004). Pain catastrophizing is an exaggerated, negative focus on pain and is related to psychological suffering, pain severity and other negative outcomes in the pain experience (Keefe, Brown, Wallston, & Caldwell, 1989). Catastrophizing is defined as: “*an exaggerated negative mental set brought to bear during actual or anticipated painful experience* “(Sullivan et al., 2001). A study of pain acceptance, optimism, and hope found no significant association with pain in patients with chronic musculoskeletal pain (Wright et al., 2011). Self-efficacy mediates a relation between pain-related fear and pain intensity, and between pain-related fear and disability. For example, if self-efficacy is low, pain-related fear is experienced. This is thought to result in greater pain and disability in patients with chronic low-back pain (Woby, Urmston, & Watson, 2007). Self-efficacy beliefs are more important determinants of disability than fear avoidance beliefs in primary health care patients with musculoskeletal pain (Denison, Åsenlof, & Lindberg, 2004).

3 OVERALL AIM

The overall aim of the work presented in this thesis was to describe and explore pain-related aspects of neck muscle performance, functioning and psychosocial factors in individuals with cervical radiculopathy (CR).

3.1 SPECIFIC AIMS

Specific aims were

● to investigate prospective physical, functional, and quality-of-life-related outcomes of patients with CR undergoing anterior cervical decompression with fusion (ACDF) with interbody cage, with and without post-operative cervical collars (Study I),

● to compare myoelectric manifestations in neck-muscle endurance and fatigue characteristics during sub-maximal isometric endurance tests in patients with CR and asymptomatic subjects: further, to explore associations between primary neck muscle endurance, myoelectric fatigability, and self-rated levels of fatigue, pain and subjective health measurements in patients with CR (Study II),

● to compare the short-term and long-term outcomes of dorsal and ventral neck muscle endurance, EMG-fatigue characteristics, and ratings of fatigue and pain after neck-specific training or physical activity on prescription in patients with CR (Study III), and

● to identify dimensions underlying measures of disability, personal factors and health status in patients with CR (Study IV).

4 METHODS

4.1 PARTICIPANTS

For study I, the inclusion criteria were age between 18-65 years with clinical and radiological signs of cervical root compression coupled with corresponding pain distribution for more than three months. The patients were recruited over a one-year period between 2003 and 2004. For studies II-IV, the inclusion criteria were CR verified with magnetic resonance imaging (MRI), and cervical nerve root compression and neck-and/or arm pain confirmed with a positive result on the Spurling sign test. All patients had the diagnosis cervical disc disorders with radiculopathy. The patients were recruited from a Neurosurgery Clinic and were referred for selection to surgery, and thus consisted of the sub-sample that was not eligible for surgery in the larger randomized clinical trial.

Patients who did not match the criteria for selection to surgery or denied surgery were asked to participate in the study (II-IV). The patients received written information about the study from the surgeon at the first visit. An additional 34 asymptomatic subjects with no history of neck pain during the last 6 months were recruited for study II.

Exclusion criteria for studies I-IV included the following: earlier surgery to the cervical spine; former fracture or luxation; myelopathy, malignity or spinal tumor; and spinal infection. Lastly, those who lacked proficiency in the Swedish language were excluded.

For study I, 33 patients (17 allocated to the cervical collar group, 16 to the non-collar group) who were to undergo elective ACDF surgery were assessed by neurosurgeons at the Karolinska University Hospital´s Neurosurgery Clinics, Stockholm, Sweden.

Studies II-IV are based on a sample of 124 patients (mean age 48, range 20-75 years), 59 men and 65 women, who fulfilled the criteria and were included. None of these patients received any active physiotherapy treatment but were examined for participating in a randomized controlled trial to evaluate exercise treatment. For study II, 46 patients with CR (26 women and 20 men) were included. Seventy-five patients with confirmed CR participated in study III (39 women and 36 men).

For study II, 34 healthy volunteer subjects (21 women and 13 men) were recruited by the Neurological and Physiotherapy Departments. They, had no history of neck pain during the previous six months (n=34). These volunteer subjects formed a homogeneous group with respect to gender and age.

4.1.1 Patients characteristics

In study I, neurological examination confirmed one level (n=59), and two levels (n=41) of cervical disc herniation. The mean duration of neck pain was 5.12 (SD 2.5) and mean duration of arm pain was 4.94 (SD 2.7). In study II, neurological examination confirmed one level (n=13), two levels (n=22) and several levels (n=11) of radiculopathy. The mean duration of neck pain was 21.7 months (SD 38.1). The mean duration of arm pain was 20.7 (SD 35.0) months. All patients had clinical findings of neurological symptoms (sensibility disturbance, motor weakness and reflex disturbance) in the arm/hand. Patients MRI and clinical findings confirmed cervical disc herniation (n= 23) and/or spondylosis (foraminal stenosis) (n=23). In study III, pain duration (VAS) median and 25^{th} -75^{th} percentile for all patients (n=75) was 7 (4-24) months.

4.1.2 Drop outs

Figure 1, as presented in study I, illustrates the allocation, drop-out rates, and reasons for non participation during the intervention.

For the healthy subjects in study II, all participants completed the tests and the EMG recordings. Of the 75 patients in study III, 50 completed the follow-up occasions where neck muscle endurance (NME) and EMG recordings were evaluated and captured, respectively. The drop outs were due to EMG mechanical faults or lack of time to participate in the intervention.

4.2 STUDY DESIGN

Four studies are included in the present work. Study I is a prospective randomized, controlled pilot trial, while studies II-IV are from a two-armed-intervention, randomized, controlled trial comparing two interventions: neck-specific training or physical activity. Study II, patients and healthy reference group and III, are of experimental design: in the latter, the patients were randomly allocated to the two different exercise interventions. Study IV is cross-sectional, analyzing and evaluating clinical examinations, test results, and questionnaires in patients with CR. The study designs of Studies I-IV are presented in Table1.

Table 1. Studies and design, number of subjects, data collection

Study	Type of Study	Number of subjects	Data collection
I	Quantitative - Prospective randomized controlled pilot trial	33 patients anterior cervical discectomy fusion candidates	Clinical test Questionnaires
II	Quantitative - Experimental	46 patients with cervical radiculopathy 34 asymptomatic subjects	Clinical tests Questionnaires
III	Quantitative – Randomized controlled trial	75 patients with cervical radiculopathy	Clinical tests Questionnaires
IV	Quantitative - Cross-sectional	124 patients with cervical radiculopathy	Clinical tests Questionnaires

4.3 DATA COLLECTION

All data were collected at the Department of Physiotherapy, Karolinska University Hospital, Sweden. The questionnaires were self-reported. All measures were conducted at baseline and on every test occasion (follow-up). The patients in study I were assessed at baseline, 6 weeks, 3 months, 6 months and 1 and 2 year follow-ups. In study II, the measures took place at baseline in both patients and asymptomatic volunteers. For study III, measures at baseline, at 14 weeks and at 1 year were used. In study IV, the patients were assessed at baseline.

4.3.1 **Clinical examinations**

Before inclusion, all the patients were examined thoroughly with a standardized physical examination carried out by a physiotherapist. The evaluation included background history, pain, sensory and neurological examination, range of motion and muscle-strength tests of the neck muscles and upper extremities. Questionnaires concerning the subjects' socio-demographic and symptomatology aspects were completed. Thereafter the eligible patients took part in the baseline evaluation as described below.

In study I, the clinical measurements were cervical range of motion (Peolsson et al., 2001) and the unipedal standing balance test (Springer, Marin, Cyhan, Roberts, & Gill, 2007). Following the first testing, patients received a sealed envelope with a note indicating the intervention to which they had been randomly assigned.

The clinical measurements in studies II-IV included a neurological examination (sensibility, motor function, reflexes), range-of-motion of the neck in all three planes, measured with a cervical range of motion device (CROM) Capuano-Pucci et al., 1991; Peolsson, Ertzgaard, Öberg, 2000), neck muscle endurance in seconds (Peolsson et al., 2007), and static and dynamic balance (Juul-Kristensen et al., 2013; Kammerlind, Ledin, Odkvist, & Skargren, 2006). Visual analogue scales were used to assess perceived pain (Scott & Huskisson, 1976). The VAS used was a 100-mm horizontal line ranging from 0 (no pain) to 100 mm (worst imaginable pain) (Table 2).

4.3.2 **Neck muscle performance tests**

4.3.2.1 EMG (Studies II-III)

During a test for muscle endurance EMG from the ventral and dorsal neck muscles was recorded bilaterally, i.e. in the cervical paraspinal muscles (abbreviated CPS in study II and SCap in study III-the latter abbreviation is used in this thesis), upper trapezius (UT), middle trapezius (MT) and sternocleidomastoid muscle (SCM). A reference-electrode was placed on the right clavicle.

Disposable surface-ground electrodes (Blue Sensor N-00-S, Medicotest A/S, Denmark) were used. The skin was cleaned with alcohol (to reduce skin impedance) before surface electrode application in pairs with an interelectrode distance of 20 mm in the direction of the muscle fibers, with the patients and subjects sitting erect.The electrodes were placed at the following sites (Figure 1):

SCM: over the belly, about 1/3 cranially to the distance between the sternal notch and the mastoid process.

SCap: positioned over the lower portion of the muscle,

UT: 20% medially to the halfway point between the medial border of the acromion and the cervical vertebra C7.

MT: 50% between the medial border of the scapula and the spine, at level T3 on a line between T5 and acromion.

The SENIAM recommendations for sensor locations in neck or shoulder muscles were followed (Merletti R., Hermens H., 2000).

EMG signals were transmitted telemetrically (Myo Research XP, Master edition, Noraxon, USA). The raw EMG signals were recorded at a sampling rate of 1,000 Hz, band pass filtered (10-500 Hz), analogue-to-digitally converted and stored in a database. Median frequency was calculated for every second using fast fourier transformation.

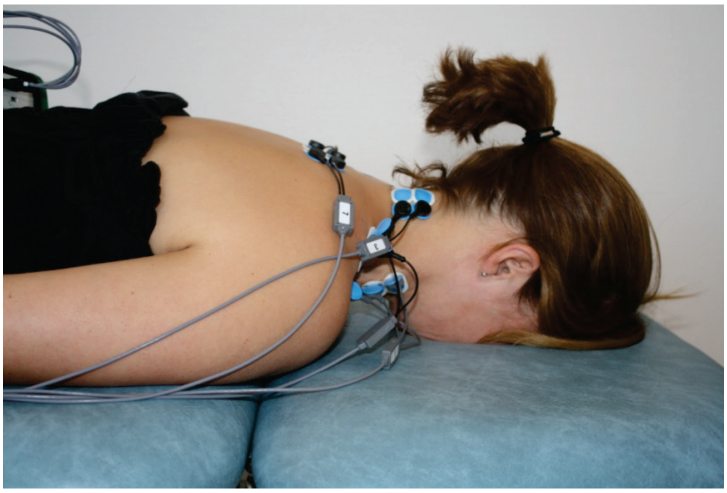


Figure 1. Surface EMG electrodes were placed bilaterally over the splenius capitis (SCap), upper trapezius (UT), middle trapezius (MT) and sternocleidomastoid muscles (SCM).

4.3.2.2 *Ratings of neck muscle fatigue and pain (Studies II-III)*

Subjects rated their perceived fatigue on a Borg CR-10 scale (Borg, 1982) and their neck pain on a visual analogue scale (VAS) before and immediately after the NME tests. Fatigue was also rated every 15 seconds during the NME test in the prone position. During the five-minute recovery period after the prone test, fatigue was rated every minute. During the NME in the supine position fatigue ratings were used. The CR-10 has been used for ratings of fatigue in neck muscles (Strimpakos, Georgios, Eleni, Vasilios, & Jacqueline, 2005; Thuresson, Äng, Linder, & Harms-Ringdahl, 2005; Äng, Monnier, & Harms-Ringdahl, 2009). The scale ranges from 0-10 and the numbers are supported with written expressions. Patients received both verbal and written instructions on how to use the scale. They were asked "how tired are you in the neck", and instructed to use a number appropriate for their perceived fatigue (Borg, 1990).

4.3.2.3 *Endurance test (Study II-IV)*

The patients and asymptomatic subjects in studies II-IV performed a modified neck muscle endurance (NME) test in both prone and supine positions. The modification from the original Peolsson NME test (Peolsson & Kjellman, 2007) was that a cranio-cervical flexion "nod in the chin slightly" should be done before raising the head (Figure 2). Arms and legs were positioned straight, with arms at the sides of the body during the tests. Beforehand, the patients and healthy subjects were instructed in the performance of the NME tests and did a "test trial" in each position to ensure that the test procedure was carried out correctly. They were instructed to maintain the test position for as long as possible, to stop when exhausted or in pain radiating from the neck into the arms. The test was interrupted if the patients/subjects were unable to hold the head in the correct position. No encouragement was given during the tests. EMG and performance time were recorded during the test.

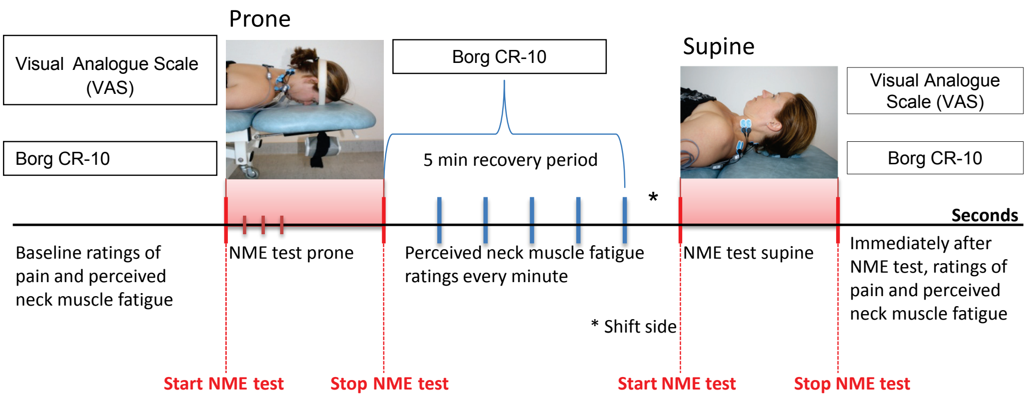


Figure 2. Two sub-maximal isometric endurance tests (NME). Participants rated their perceived fatigue on Borg-CR 10 and neck pain on the 100 mm VAS before and immediately after the NME test. After a 5-minute recovery period the NME test was performed for the supine position.

4.3.3 **Questionnaires**

An overview of used measures in the present work is presented in Table 2.

One set of study-specific questionnaires was completed by the patients in study I. It included the neck disability index (NDI), and the falls efficacy scale (FES). Health-related quality of life was measured with the medical outcome study short form 36 health survey (SF-36), and clinical outcome measures were assessed for pain intensity of the neck, shoulder and arm using the Borg CR-10 scale. Also recorded were subjective pain descriptions (pain drawing), cervical range of motion (CROM) in sitting position, and a unipedal balance test on hard and soft surfaces with eyes open and closed.

4.3.3.1 Neck Disability Index

The neck disability index (NDI), developed from the Oswestry low-back pain disability index (ODI) (Vernon & Mior, 1991), is a disease-specific questionnaire evaluating the influence of neck pain on functioning and disability (Schellingerhout et al., 2012). Its ten item cover; pain intensity, personal care, lifting, sleeping, driving, recreation, headaches, concentration, reading and work. Rating is on a six-point scale, ranging from 0 (no activity limitations) to 5 (major activity limitations). The added scores to a maximum of 50 can also be expressed as a percentage. Higher scores indicate greater disability (Ackelman & Lindgren, 2002; Vernon & Mior, 1991). Disability levels are categorized as follow: 0-4 = none; 5-14 = mild; 15-24 = moderate; 25-34 = severe; over 34 = complete disability (Vernon, 2008). Sterling et al proposed another established recovery categorization as follows: less than 4 = recovered; 5-14 = mild disability; more than 15 = moderate/severe disability (Sterling, 2006). The NDI is a reliable and valid outcome measures for patients with neck pain (Hains, Waalen, & Mior, 1998; Hoving, O'Leary, Niere, Green, & Buchbinder, 2003; Riddle & Stratford, 1998; Vernon & Mior, 1991), and acceptable (ICC = ≥ 0.50) from a validity perspective, as positively correlated with instruments measuring pain and/or physical functioning (r = 0.53-0.70) (Cleland et al., 2008).

4.3.3.2 Dizziness Handicap Inventory

The dizziness handicap inventory (DHI) (Jacobson & Newman, 1990) was used to assess self-perceived disability imposed by dizziness. Its 25 items are rated on a 3-point scale (0, 2 and 4) and summed to a total score. Possible score ranges are 0 to 100. A higher score indicates more disability. The DHI includes three response levels, sub-grouped into three domains: functional, emotional and physical. Sub-scores for each of the tree domains can be calculated, but in this work only the total sum scores were used. Whitney et al proposed that a total score of 0-30 should indicate mild disability, 31-60 moderate, and 61-100 severe. They noted that scores relate well to levels of functional balance impairment (Whitney, Wrisley, Brown, & Furman, 2004).

Table 2. An overview of assessments used in the studies included in this thesis.

Assessment for the data analysis	Study I	Study II	Study III	Study IV
Neurological examination and tests	●	●	●	●
Cervical range of motion (CROM)	●			●
Unipedal standing balance test	●			
Borg CR-10 scale, pain intensity	●			
Visual Analogue Scale (VAS), pain intensity		●	●	●
Borg CR-10 scale, fatigue		●	●	
Neutral head position				●
EMG		●	●	
Rating of neck muscle fatigue		●	●	
Endurance time		●	●	●
Figure of eight test				●
Sharpened Romberg test				●
Neck Disability Index	●			●
Dizziness Handicap Inventory				●
Falls Efficacy Scale	●			
Self Efficacy Scale		●		●
Exercise Self Efficacy Scale				●
International Physical Activity Questionnaire		●		●
Physical Activity level				●
Pain Catastrophizing Scale				●
Coping Strategies Questionnaire				●
Fear-Avoidance Beliefs Questionnaire				●
Tampa Scale of Kinesiophobia		●		●
Hospital Anxiety Depression Scale		●		●
EuroQol-5D Index and EuroQol-5D VAS		●		●
Short-form-36 health survey	●			

4.3.3.3 Falls efficacy scale

The falls efficacy scale (FES) questionnaire was used to measure patients confidence in performing dynamic activities of daily living without falling (Tinetti, Richman, & Powell, 1990). Ten relatively non-risky activities of daily living were scored on a 10-point continuum with a higher score indicating lower confidence or efficacy. Each item is rated from 1 ("very confident") to 10 ("not confident at all"), and the item ratings are added to a summary total score. The possible scores ranged from 10 (best possible) to 100 (worst possible). The lower scores indicate more confidence and higher scores indicate lack of confidence and greater fear of falling. The FES have been shown to be valid and reliable in Swedish conditions (Hellstrom & Lindmark, 1999). The FES has shown adequate test-retest reliability (r = 0.71) (Tinetti et al., 1990), and excellent correlation with the Activities Specific Balance Confidence Scale (ABC) (r = 0.84) (Powell & Myers, 1995). Construct validity was excellent with balance (r = 0.84) (Huang & Wang, 2009).

4.3.3.4 Self Efficacy Scale

The Self Efficacy Scale (SES) (Altmaier, Russell, Kao, Lehmann, & Weinstein., 1993) was used to assess patients ´perceived confidence in performing different activities ("*How confident you are that you can do it now?*" in spite of pain) and consists of 20 items rated on an 11-point scale, ranging from 0 (not at all confident) to 10 (very confident), and summed to a total score. The total range is 0-200, where higher scores indicates greater self-efficacy (Bandura, 1977). The activities covered are: taking out the garbage, concentrating on a project, going shopping, playing cards, shoveling snow, driving the car, eating in a restaurant, watching television, visiting friends, working on the car, raking leaves, writing a letter, doing a load of laundry, working on a house repair, going to a movie, washing the car, riding a bicycle, going on vacation, going to a park, and visiting relatives. The SES was translated into Swedish (Denison et al., 2004) and English checked, showing internal consistency in both samples was good (0.93/0.95). There is increasing support that the level of self-efficacy is a significant contributor to how far a person is disabled by their chronic pain (Arnstein, Caudill, Mandle, Norris, & Beasley, 1999).

4.3.3.5 Exercise Self Efficacy

The Exercise Self efficacy Scale (ESES) (Dzewaltowski, 1989; Johansson & Lindberg, 2000) was used to assess patients' confidence in performing an exercise program despite potential barriers. The six ESES items are rated on a 10-point scale, ranging from 1 (not at all confident) to 10 (very confident), and summed to a total score. The total range is 6-60, where higher scores indicate greater confidence. The activities covered are: work schedule, physical fatigue, boredom related to exercise, minor injuries, other time demands, and family and home responsibilities (Dzewaltowski, 1989). The Exercise Self-efficacy scale was translated into Swedish (Johansson & Lindberg, 2000) and tested for internal consistency ($\alpha = 0.85$) and test-retest reliability ($r = 0.64$). Self-perceptions of efficacy have significantly predicted exercise behavior in several studies (Wurtele & Maddux, 1987), and perceptions of self-efficacy are distinguished from outcome expectations (Bandura, 1977). Cronbach's alpha coefficient for the constructs ranged from .80 to .97 (Dzewaltowski, 1989).

4.3.3.6 International physical activity questionnaire

The International physical activity questionnaire short-form questionnaire (IPAQ) was used to measure patient's self-reported physical activity during the previous seven days (Craig et al., 2003). It consists of questions about time spent sitting, walking, in moderate-intensity physical activity and in vigorous-intensity physical activity. It is used to estimate total weekly physical activity expressed as MET-hours per week (MET=metabolic equivalent, where, 1 MET=resting energy expenditure).

4.3.3.7 Physical activity level

The physical activity levels during the previous summer and winter half-years were evaluated with the Saltin-Grimby physical activity level scale (Frändin & Grimby, 2007). This six-graded scale, ranges from hardly any physical activity to heavy or very heavy exercise regularly and several times a week.

4.3.3.8 Pain catastrophizing scale

The pain catastrophizing scale (PCS) was used to assess catastrophic thoughts or feelings concerning painful experiences. Its13 items are rated on a 5-point scale, ranging from 0 to 4, and summed to produce a total score. Each item is rated on a 5-point Likert scale, ranging from 0 ("not at all") to 4 ("all the time"). The total score ranges from 0 to 52, with a higher score indicating a higher degree of pain catastrophizing (Sullivan, 1995; Sullivan & D'Eon, 1990). The PCS subscales are computed by summing the responses to the following items; rumination (items 8, 9, 10 and 11, sum score 16), magnification (items 6, 7 and 13, sum score 12) and helplessness (items 1, 2, 3, 4, 5 and 12, sum score 24). The PCS is currently one of the most widely used measures of catastrophic thinking about pain. It is a valid and reliable instrument for measuring catastrophizing pain in individuals (Rosenstiel & Keefe, 1983). The moderate correlations between the three components of PCS and the high internal consistency of the scale suggest that rumination, magnification, and helplessness can be viewed as different dimensions of the same underlying construct (Sullivan, 1995).The PCS has adequate-to-excellent internal consistency (total PCS = .87) (Sullivan, 1995).

4.3.3.9 Coping strategies questionnaire

The coping strategies questionnaire (CSQ) was used to measure cognitive coping activity by assessing patients´ use of cognitive and behavioral strategies to cope with pain (Rosenstiel & Keefe, 1983). The CSQ consists of 50 items which are rated on a seven-point scale, ranging from 0 ("*never do"*) to 6 ("*always do"*). The first 48 items are summed to produce a total score varying between 48 and 288. There are six cognitive categories: diverting attention, reinterpreting pain sensations, coping self-statements, ignoring pain sensation, praying and hoping and catastrophizing. Two additional items are reported separately since they evaluate patients' self-perceived control over pain (CSQ-COP) and ability to decrease pain (CSQ-ADP). These items are also scored on a seven-point scale (0-6) measuring how well they control or decrease their pain. These two scales are not thought to measure coping strategies but rather their effectiveness. Two or three dimensions of cognitive coping are embedded in the measure. Robinson et al, found that three factor-dimensions are enough: they include (a) cognitive coping and suppression, (b) helplessness, and (c) diverting attention and praying (Robinson et al., 1997). The CSQ has demonstrated satisfactory internal consistency and test-retest reliability (Rosenstiel & Keefe, 1983).

4.3.3.10 Fear avoidance beliefs questionnaire

The fear avoidance beliefs questionnaire (FABQ) was original developed by Waddell et al (Waddell, Newton, Henderson, Somerville, & Main, 1993) to measure beliefs about possible harm resulting from physical activity and from work-specific activities. The FABQ´s sixteen-items are rated on a verbal seven-point scale, ranging from 0 ("do not agree at all") to 6 ("completely agree"), and summed to a total score. The score ranges from 0-95, higher scores indicate higher levels of fear-avoidance beliefs. The original English version of FABQ is reliable and has evidence of validity (Waddell et al., 1993). The FABQ has been evaluated in patients with cervical pain (Lee, Chiu, & Lam, 2006), and may be recommended for test-retest evaluation in patients with CR (Dedering & Borjesson, 2013). It appears to be the best available measure, in terms of psychometric properties, for measuring the concept "fear-avoidance beliefs".

4.3.3.11 Tampa scale of kinesiophobia

Kinesiophobia was measured using the Swedish version of the Tampa Scale of Kinesiophobia (TSK) (Lundberg, Styf, & Carlsson, 2004), i.e. to assess patients' current pain-related fear of movement/ (re)injury. The TSK has 17 items rated on a four-point Likert scale with scoring alternatives ranging from 0 ("strongly disagree") to 4 ("strongly agree"). A total sum is calculated after inverting the scores for items 4, 8, 12 and 16. Total scores vary between 17 and 68. A high TSK value indicates a higher degree of kinesiophobia (Kori et al., 1990). The TSK appears to be the best available measure of kinesiophobia. The reliability of the Swedish version was high in a group of patients with persistent low-back pain (Lundberg, Styf, & Carlsson, 2004). However, validity was low in all versions. The TSK has moderate test-retest reliability in patients with CR (Dedering & Borjesson, 2013).

4.3.3.12 Hospital anxiety and depression scale

The hospital and anxiety and depression scale (HADS) is a questionnaire developed by Zigmond and Snaith in 1983 to identify possible and probably anxiety disorders and depression among patients in non-psychiatric hospital clinics (Zigmond & Snaith, 1983). The

HADS is a fourteen-item scale, with a short form, easily completed. Seven of the items relate to anxiety and seven relate to depression. It is divided into an anxiety subscale (HADS-A) and a depression subscale (HADS-D). Each item on the questionnaire is scored on a 4-point Likert scale from 0 to 3. The total score can range from 0 to 21 for either of anxiety or depression. A higher score indicates a higher level of anxiety or depression. Symptom severity is indicated by scores 0-7; mild by 8-10; moderate 11-21, and severe (> 21). These cut-offs are those established by HADS developers.

4.3.3.13 Health related quality of life

The EuroQol 5D (EQ-5D) consisting of the EQ-5D Index and EQ VAS was used as a measure of health status (Brooks, 1996). The EQ-5D comprises five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. These are rated on three levels (no problem, some problems or extreme problems). The answers are converted to an index score using the time-trade-off value set. Negative index scores were set to zero and possible scores ranged from 0 to 1 (full health) (Dolan, 1997). The EQ-5D VAS is scored on a 20 cm vertical line, from 0 (worst imaginable) to 100 (best imaginable). The respondent marks his/her own perceived health state 'today'.

4.3.3.14 Short form 36 health survey

Health related quality of life was measured with the Short-form-36 health survey (SF-36) (Ware & Sherbourne, 1992). The SF-36 consists 36 items. The questionnaire contains eight health subscales: physical functioning (PF), role limitations due to physical problems (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), role limitations due to emotional problems (RE) and mental health (MH). Each subscale scores from 0 to 100 (where 0= worst and 100=best health state). Further, there are two subscales, mental composite score (MCS) and physical composite score (PCS) used in the standard calculation. All ten subscales were used in Study I. The SF-36 is a generic form and is considered both valid and reliable.

4.4 INTERVENTIONS

In study I, patients were randomly divided into two groups after they had fulfilled inclusion/exclusion criteria and signed the informed form consent from Group 1 had no post-operative neck movement restrictions and group 2 wore a rigid cervical collar. A random, sealed allocation was used to form the groups.

In study III, after the baseline assessment, each patient was randomized to one of the two interventions: 1) active physical rehabilitation with a neck specific exercise program with a cognitive behavioral approach (neck training); or 2) prescribed, self-mediated and progressive physical activity (physical activity). Randomization was based on a computer-generated sequence list prepared by a statistician not otherwise involved in the study. In the thesis some of the participants from the RCT are used in the baseline data. The researcher (MH) provided the patients with the clinicians of their choice, and patients could choose their rehabilitation clinics close to home or at work. The intervention process precluded blinding the treating physiotherapist who gave the intervention. Several physiotherapy clinics in Stockholm ran the intervention programs. The goal of the neck-specific exercise intervention focused to improve patients' daily function through on sensorimotor training, neck stabilization, and neck muscle endurance and strengthening training in combination with behavioral component. The goal of the physical activity on prescription was to increase the general level of physical activity and general strength (Figure 3).

The treatment period for study I lasted 6 weeks; for study III was 14 weeks. For Study III the following interventions were used (Figure 3).

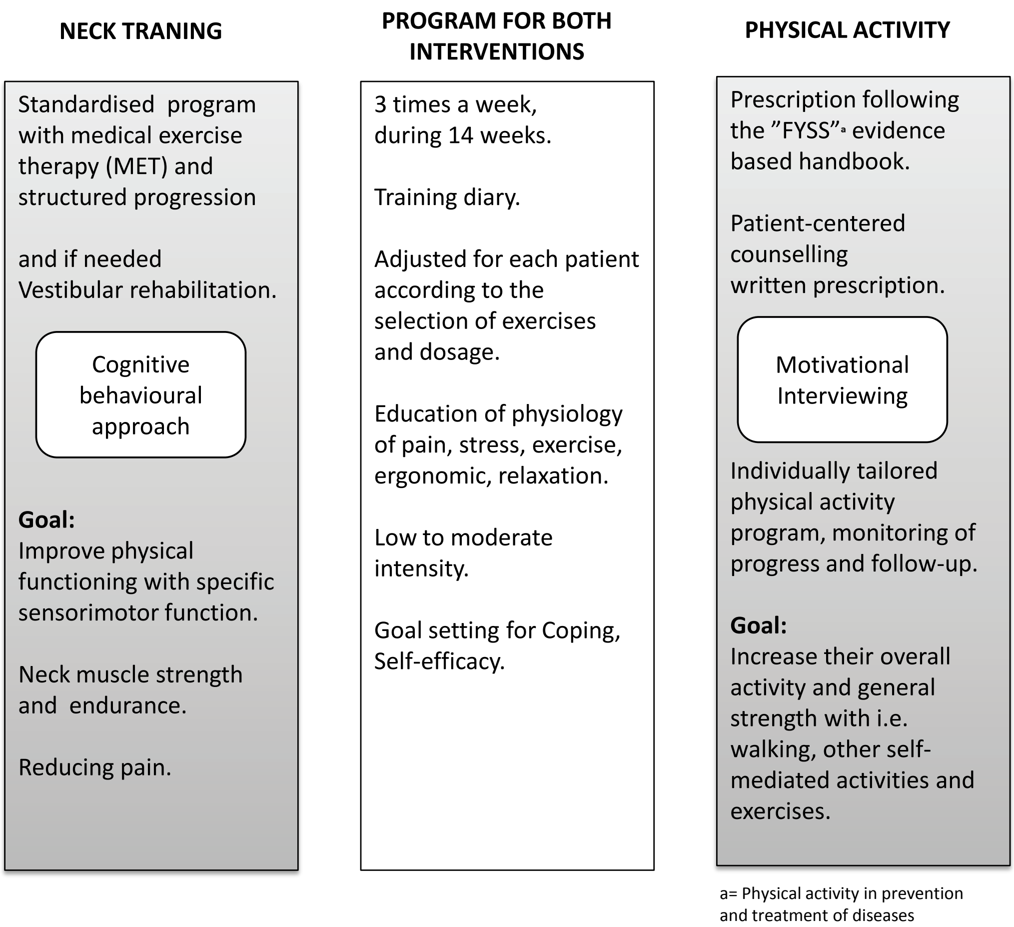


Figure 3. Intervention program for active physical rehabilitation with neck-specific exercise with a cognitive behavioral approach or prescribed physical activity.

4.4.1 **Cervical collar versus no cervical collar (Study I)**

In study I, one group had no post-operative neck-movement restrictions while a second group received a rigid cervical collar. During the first day after surgery, the physiotherapist facilitated respiratory and circulatory exercises, training of transfers, walking and other activities of daily living relevant for the patient.

The patients receiving the rigid cervical collar (C62) (Philadelphia Collar and Camp Scandinavia AB) were instructed to wear it, in the daytime only, for six weeks, both in-and-out of doors. After the first three weeks, the patients could remove the collar when sitting indoors with neck supported.

4.4.1.1 Both intervention groups

Before discharge from the hospital, the patients received instructions for the home program containing general exercises to promote shoulder and thoracic mobility, static stabilizing function of the cervical spine, and walking.

Importantly, for the first three months after the operation, patients were restricted from activities such as contact sports, running, heavy lifting, driving, and outer-range cervical spine movements. At three months they underwent a postoperative visit by the neurosurgeon, and also radiological screening and physiotherapeutic follow-up. Questionnaires and physical measures were assessed at six weeks, three and six months and one and two years after surgery. Six months post-operatively there were no contraindications.

4.4.2 **Neck training versus physical activity on prescription (Study III)**

The neck training and physical activity intervention in the present work is outlined, described and published in the BMC Musculoskeletal Disorders (Dedering, Halvorsen, Cleland, Svensson, & Peolsson, 2014).The intervention programs included two treatment approaches with neck training with a cognitive behavioral approach, or physical activity with motivational interviewing. An overview of the components is given in Figure 3.

Several primary clinicians or private outpatient clinics provided the two physiotherapy interventions. The standardized intervention program was sent to the physiotherapists after a thorough explanation of the study over the telephone. They physiotherapists received the study-specific treatment protocols of each exercise intervention, stating the elements to be included during the early, intermediate and late phases of the interventions. Progression of the intervention program was individually tailored for each patient. Each physiotherapist followed the specific protocol in order to ensure that all patients in the study received the same intervention. For both exercises progression in training intensity and amount depended on the patients´ self- perceived pain. A self-reported diary was used for both physiotherapist and patients during the intervention period of 14 weeks for both exercise interventions. The neck-specific exercises and the physical activity group were performed three times a week at a physiotherapy clinic or an athletic facility.

4.4.2.1 Neck training

The experienced physiotherapists supervised the neck-specific training program on a weekly basis, including three individual follow-ups each week that consisted of neck-specific instructions and manual guidance in the re-learning of motor skills, and neck-muscle endurance training, and postural correction with a behavioral approach regarding pain, strategies etc. The physiotherapist regulated the neck-specific training program for each patient to ensure that the selection of exercise and dosage is suitable for the participant's capacity. These exercises aimed to increase endurance and strength of the muscles that stabilize the neck and the scapula. An example of neck-specific exercise is shown in Figure 4.

The subjects received written instructions with pictures illustrating the neck training exercises. They were required to report pain before and after each session of the medical exercise therapy. Progression went from isolated low-load to synergy exercises and, lastly, to endurance-strength exercises. The progression was based on the patient´s pain and neck movement quality, but also fulfilling the criterion of a certain number of sets and repetitions.

The behavioral approach, which was incorporated in the neck-specific treatment, consisted: of pain physiology, the consequences of stress and how to reduce stress, relaxation techniques, coping strategies and the consequence of regularly increasing exercise intensity; pacing and ergonomics advice to provide postural correction in daily life.

Figure 4. Neck-specific exercise for the neck training group.

4.4.2.2 Physical activity training

Before the physical activity training commenced, the patients had a physical examination and a motivational interview at the physiotherapy clinic. The interview included an exploratory talk, health promotion and evaluation of readiness for change. Each patient received a printed copy of his or her physical activity prescription. Additionally, patients were encouraged, for the duration of the 14 week intervention period, to perform at least 30 minutes of physical activity at-moderate-intensity at least three days per week. They were given a training dairy to record their exercises and other alternative physical activities e.g. walking, running and garden work during their spare time. Throughout the period, the patients were guided by the physiotherapist to increase their overall activity and general strength. An example of exercise is shown in Figure 5. During the 14 weeks of follow-up the patients were allowed and encouraged to contact the physiotherapist as many times as they needed.

Figure 5. General physical activity for the physical activity group.

4.5 STATISTICS

For an overview of the statistical methods used in the four studies see Table 3.

All data were managed and analyzed using the Statistical Package for Social Sciences (SPSS, version 20.0-22.0, Chicago, IL, USA).

For descriptive statistics, mean and standard deviations (SD), median and inter-quartile ranges (IQR) or median and percentiles (25^{th} -75^{th}) were used depending on the data levels or the data distribution. Further, minimum and maximum values, frequencies and percentages were calculated. All reported significance levels were 5% (Study I-IV).

4.5.1 Study I

The study groups at different time points, specifically 6 weeks, 3, 6 and 12 months, and finally 2 years were compared using analysis of covariance adjusted for baseline score, sex, and age.

The effects of surgery next to potential complimentary effects of the post-operative routine at all time points were assessed with repeated-measure analysis of covariance.

Effect sizes of the surgical and post-operative interventions were assessed with Cohen´s *d* (Cohen, 1992). Cohen´s guidelines for interpretation of effect size are as follow: 0.20 = small effect, 0.50 = medium effect, and 0.80 = large effect.

Analyses of statistical differences between groups over time were conducted on an intention-to-treat principle for the continuous and discrete data. Thus, all patients, regardless of their loss to follow-up, drop out, or non-compliance, remained in the analysis of the group to which they had been randomly assigned. The analysis was supplemented with a sensitivity-

Table 3. Statistical methods applied in the different studies.

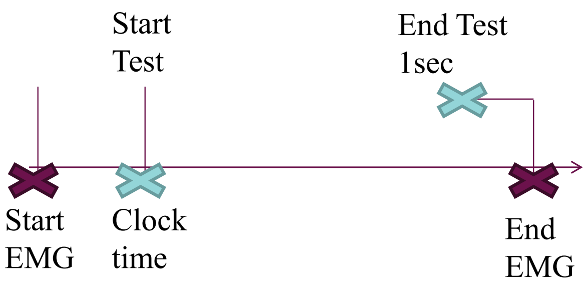
Statistics applied	Study I	Study II	Study III	Study IV
Descriptive statistics				
Mean, standard deviation	●	●	●	●
Median, inter quartile range		●	●	
Frequency (n), percentage (%)	●	●		●
Statistical methods				
Effect size	●			
Repeated measure analysis of covariance	●			
Cohen´s *d*	●			
Mann-Whitney *U* test (Mann-Whitney)		●		
Wilcoxon signed ranked test		●	●	
Pearson´s Chi-Square x^2		●		
Categorical regression (CATREG)		●		
Friedman´s ANOVA			●	
Repeated measures analysis (ANOVA)			●	
Principal component analysis (PCA)				●

of-missing-data imputation and was considered satisfactory after comparing results of the per protocol analysis of data exclusively from patients with completed data sets.

4.5.2 **Study II**

To coordinate the offset of the time between the EMG muscle activation recordings and the NME test start and stop times, the following calculations were used (Figure 6):

1. Total EMG recorded time – total NME test clock time = Start time difference.
2. Start time differences + 2 s = EMG recorded data time withdrawn from the start for analyses.
3. NME test clock time stop – 1 s = EMG recorded data stop time used in analyses.



Start *analysis* = Total EMG time - Clock time =
diff+2 sec (withdraws in the beginning)

End *analysis = Stop – 1 second*

Figure 6. Measuring time between the EMG recordings and test start and stop times.

Linear regression analysis was used to determine the EMG MDF slope during the prone and supine NME tests.

The difference between the two independent groups in Study II was tested with an Independent *t* test; or else the Mann Whitney *U* test was used for continuous or discrete data, respectively, when comparing groups.

Friedman's test or Wilcoxon's rank sign test was used for ordinal data and non-normally-distributed data. Wilcoxon's rank signed tests were used for within-group comparison of right and left side MF EMG.

Imbalance between left-and-right-side MDF EMG slopes was calculated as a ratio for every recorded second (division of right-side value/left-side value). The mean of all the transformed ratios was used to represent the imbalance behavior in the muscle groups.

A categorical regression (Van der Kooij, 2004) method was used to analyze nonlinear relations between dependent variable (NME test time), mean of the bilateral right-and-left-side slope of each muscle group during the NME test, NDI, pain (VAS), TSK and self-rated fatigue at the end of the NME test for the CR group.

4.5.3 **Study III**

Present neck pain intensity (VAS) and self-perceived fatigue (Borg CR-10) were treated as ordinal data, and non-parametric statistical methods were used. For ordinal data, between-groups differences were tested with the Mann Whitney *U* test, using the differences in scores between baseline and each follow-up occasion (Study III).

A one-way repeated measure analysis of variance (ANOVA) tests, the same entities that take part in all conditions of an experiment (Field, 2012). The one-way ANOVA was used due to the study's within-subjects design, which involved repeated measures on the same participants (with several observations over time). To correct for multiple comparison, a Bonferroni post-hoc test was applied.

A four-way repeated measures ANOVA was used to evaluate the changes in the slope of the MDF for the extensor muscles during the NME test in extension, with group (interventions), muscles (SCap, UT, MT), side (ipsilateral, contralateral) and time (baseline, 14 weeks, one year) as factors. Additionally, a three-way repeated ANOVA was used to evaluate changes in the slope of the MDF for the SCM muscle during flexion contraction, with group (interventions), side (ipsilateral, contralateral) and time (baseline, 14 weeks, one year) as factors.

The EMG amplitude (ARV) of the SCM and SCap muscles was expressed as a percentage change relative to the initial epoch.

Significant differences revealed by ANOVA were followed using post-hoc Student Newman-Keuls (SNK) tests pair-wise for comparing flexion and extension.

4.5.4 **Study IV**

Principal component analysis (PCA) with oblique rotation was used in study IV. PCA identifies groups or clusters of variables, and the aim was to understand the structure of the set of variables. Oblique rotation was chosen as it was assumed that the components would be correlated. The PCA was iterated until variables fulfilled the criteria for inclusion. The Kaiser-Meyer-Olkin measure of sampling adequacy (KMO) was used to ascertain whether the sample was appropriate for a factor analysis. In Study IV, three of the most well-established criteria were used: oblique rotation, the Scree-plot, and the percentage of non-redundant residuals values over 0.05. The KMO measure of sampling adequacy and Bartlett's test of sphericity were used as measure of appropriateness of the PCA. The component loadings were as follows: over 0.71 = excellent; 0.63 - 0.70 = very good; 0.55 - 0.62 = good; 0.45 - 0.54 = fair; and below 0.32 = poor (Tabachnik BG, 2013).

4.5.5 Missing values analysis

Missing data in the questionnaires were dealt with in the following way: for missing items less than 30%, an imputation value was calculated; that is, the mean value of the non-missing item. Questionnaires with more than 30% missing data were excluded from the analysis.

4.6 ETHICAL APPROVAL

The projects were approved by the Stockholm Regional Ethical Review Board (Dnr: 01-396, 2009/1756-31/4, 2011/692-32), and were carried out in compliance with the Helsinki Declaration.

5 RESULTS

This section presents the main results of the present work. Detailed results for each study are given in the publications and manuscript at the end of the thesis.

5.1 STUDY I

The non-cervical collar group had a larger effect size in reduction of neck pain (1.57) than the cervical collar group did (1.34). A medium-to-large effect size was observed for the physical outcome for CROM in both groups (Table 2, *study I*) two years post-surgery.

The non-collar group presented a large effect size in NDI (1.75); however, medium effect size differences were shown in favor of the collar group when considering the initial NDI scores. The FES showed a medium-to-large effect size in both groups.

Analysis of covariance and controlling for the combined effects of prospective measurements between the two groups results revealed that the collar group scores for function in terms of NDI improvement were significantly higher than in the non-collar group at different time points after surgery.

Covariance analysis between the two groups showed that the cervical collar group scores for SF-36 PF at various time points (6 weeks, 3, 6 and 12 months) and SF-36 PF and SF-36 BP subscale even at 6 and 12 months improved significantly compared to those for the non-cervical-collar group after surgery.

5.2 STUDY II

During the prone NME test, the analysis comparing the myoelectric manifestations between patients with CR and asymptomatic subjects showed that the right-side SCap had more negative muscle slope (p =0.035) than the left-side SCap in the CR group (Figure 4, *study II).* In addition, both sides of the middle trapezius (MT) muscle slopes were steeper (p= 0.005, p = < 0.001 respectively) in the CR group than in the asymptomatic group (Figure 4, *study II*).

During the supine NME test, the slope of the right SCap muscles was significantly more negative (0.001) than the left-side in the CR group than in the asymptomatic group (p =0.028) (Figure 4, *study II*).

The asymptomatic group results during the supine NME test showed that the slope declined more significantly (p = 0.039) in the left side SCap muscles than in those in the CR group. Further, during both NME tests the slope of the right UT muscle was significantly more negative (p < 0.001) than the left side in the asymptomatic group (Figure 4, *study II*).

Endurance times were significantly shorter for patients in both prone (p <0.001) and in supine positions compared to those in the asymptomatic subjects (p = 0.017) (Figure 7) (Figure 2, *study II*).

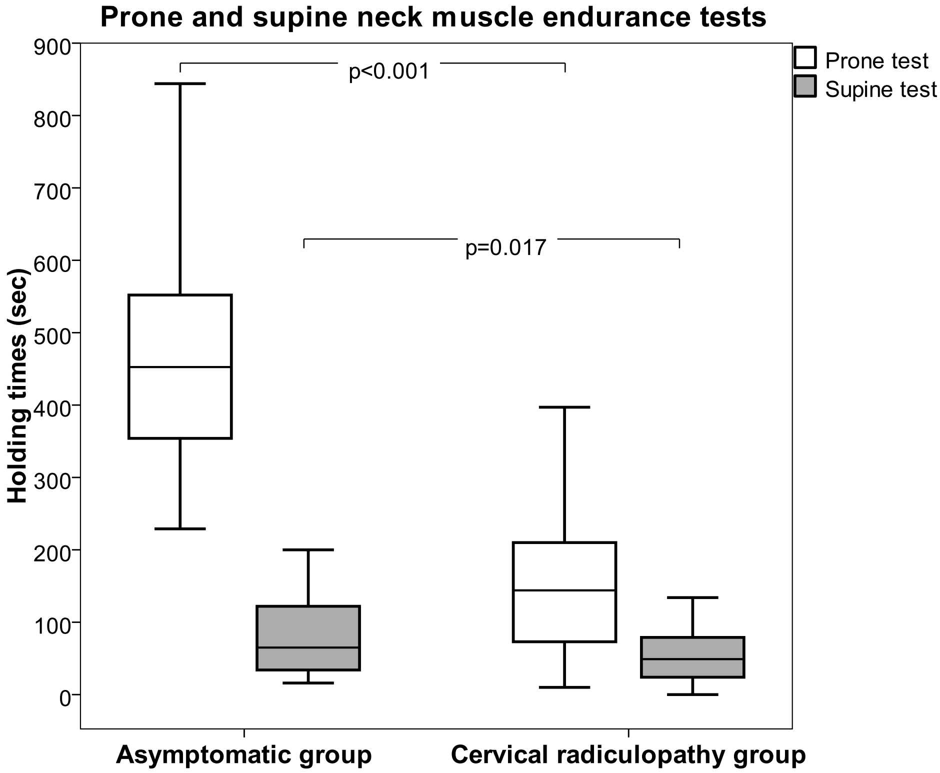


Figure 7. Box-plot of the prone and supine neck muscle endurance tests. From, Halvorsen et al. 2014.

Figure 3 *study II* shows the rating of neck muscle fatigue (Borg CR-10 scale) during prone and supine NME tests in the CR group and the asymptomatic group, respectively. The results show more fatigue among patients with CR than among the asymptomatic subjects. For the modified NME endurance test, the CR group rated significantly more fatigue than the asymptomatic group at all time points ($p < 0.001$). The exception was the end of the prone test, where the asymptomatic group rated more fatigue ($p < 0.001$). The CR group experienced significantly more remaining fatigue ($p = 0.017$) than the asymptomatic group after the five-minute recovery period between the two NMEs. The patient group (CR) and the asymptomatic group had significantly lower ratings of neck muscle fatigue ($p = < 0.001$) after the supine NME test than after the prone NME test (Figure 8) (Figure 3, *study II*).

Moderate correlation between test time and NDI (-0.54) was found in both prone and supine NME tests (Table 2, *study II*). Further results showed that the CR group had significantly lower levels of (p <0.001) SES and IPAQ compared to the asymptomatic group.

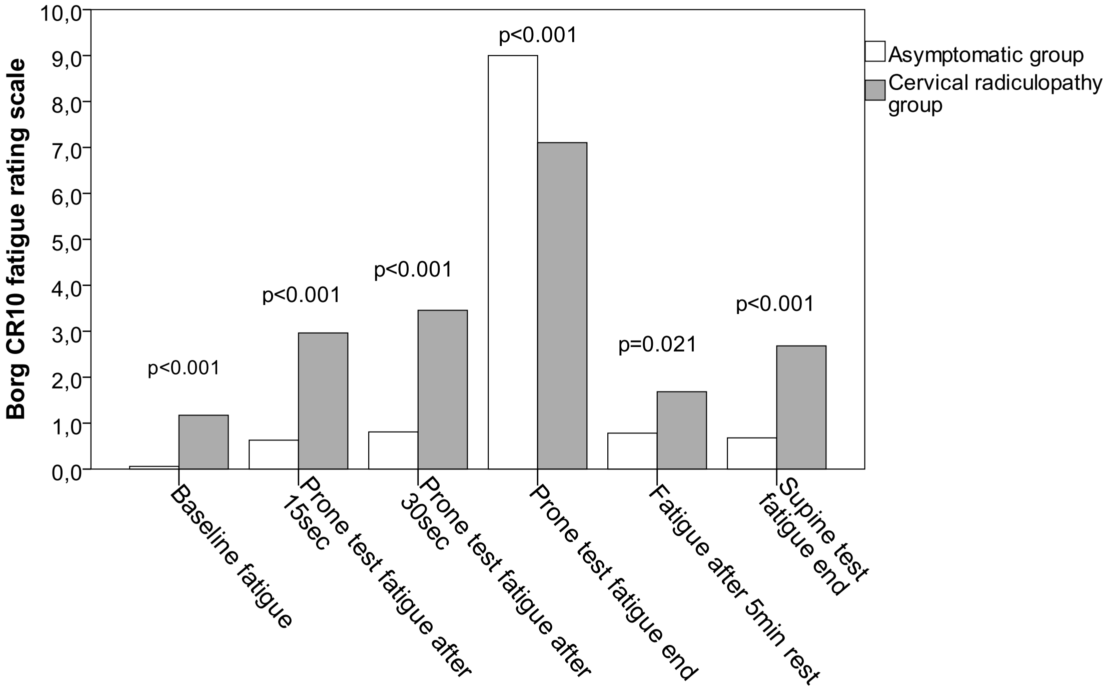


Figure 8. Results of the group differences in Borg CR 10 rating of fatigue (Borg CR 10 scale, 0-10). From Halvorsen et al. 2014.

During the NME test, fatigue in the UT and in the SCM in the prone and supine test positions, respectively, was more important than self-perceived pain, disability or kinesiophobia in predicting neck muscle endurance (NME) for the patients (Table 3 and Table 4, *study II*). The CR groups mean score of TSK 37.4 (SD 8.7) indicated the presence of kinesiophobia.

The CR group had significantly lower levels (p <0.001) of health-related quality of life than the asymptomatic group had.

5.3 STUDY III

The percentage change (relative to the initial 10%) in ARV during the sustained extension contraction of the SCap (agonist) and SCM (antagonist) muscles of both groups showed percentage changes in both SCap (F = 22.17, $p < 0.00001$) and SCM (F = 3.50, $p < 0.001$) Figure 5, study III. Thus ARV increased the contraction regardless of group or time, but did not differ between groups and was not affected by either intervention.

Figure 4, study III shows the percentage change (relative to the initial 10%) in EMG amplitude (ARV) during the sustained flexion contraction of both the SCap (agonist) and SCM (antagonist) muscles for both groups. The percentage change in SCM ARV increased during the contraction regardless of group or time (F = 53.36, $p < 0.000$): and in SCap ARV during the flexion contraction (F = 43.96, $p = 0.000$).

Table 3, study III shows the results of the endurance time of the neck extensor and flexors of the final group. These showed, no significant differences between occasions for extensors endurance time in the prone position ($p = .486$) and no differences between the intervention groups ($p = .609$). In addition, there were no relation effects between occasions and groups ($p = .989$).The endurance time in supine position for the flexor muscles was significantly longer over time; however no differences between the two groups ($p = .187$) were found.

The patients interrupted the endurance tests due to neck muscle fatigue, pain, both fatigue and pain or other reasons at all time points, and the interruptions were associated with fear in 50 %, according to comments from the patients. We identified the patients' explanations as to why they interrupted in a different way than in *study II*. Further, the fatigue rating end of the extension stop was significantly lower at both the 14-weeks follow-up and one-year follow-up for both groups. In addition neck-pain ratings for both groups were lower between the baseline and the 14-week test occasions than at the start and one-year follow-ups (Table 4, *study III*).

5.4 STUDY IV

The majority of participants in study IV were classified as having chronic neck and/or arm pain, with most experiencing pain daily. Men presented 52% and women 39% of unilateral radiating pain (Table 2, *study IV*). Sensory impairments were seen in 67% and motor impairments in 52%. Here too, the average neck flexor muscle endurance was much shorter than that of the neck extensor muscles 169 s (SD 145), 23 s (SD 17), Table 3, study IV). The present and average pain values were considered mild since the VAS was between 36 and 43 mm, respectively even though close-to-moderate in some cases (Table 4, *study IV*).

Of the 14 variables included in the final three-component model, NDI, SES and DHI were represented in the functioning factor. These variables showed that NDI scores were on a severe disability level. SES values (143 points SD 49) were considered as being at a modest self-perceived self efficacy level. The DHI values of 25 points represented a mild level of self-perceived handicap from dizziness. The physical activity levels in the CR group during both summer and winter were low (50/ 40%) and moderate-to-hard (60/ 51%), respectively (Table 2, *study IV*).

The Kaiser-Meyer-Olkin (KMO) value measure of sampling adequacy was 0.89, indicating that the 14 variables were appropriate for PCA. The PCA in study IV indicated a three-factor solution which accounted for 73% of the total variance. The following three dimensions emerged from the analysis in study IV: 1) Pain and functioning, 2) Health, beliefs and kinesiophobia, and 3) Mood state and catastrophizing, shown in Figure 9 (Table 5, *study IV*).

The EQ-5D index and perceived health status (EQ-5D VAS) indicated a low level of health status shown by the patients with CR (Table 4, *study IV*).

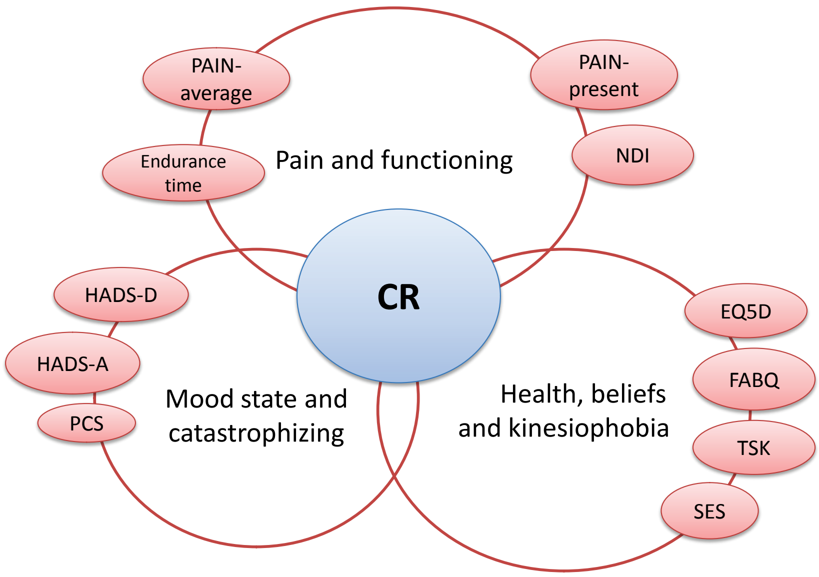


Figure 9. The final principal component model for a 3-component solution.

6 DISCUSSION

The overall purpose of the work presented in this thesis was to describe and explore pain-related aspects of neck muscle performance, functioning and psychosocial factors in individuals with cervical radiculopathy (CR). The thesis comprises four studies, from which the main findings are as follows:

● Comparison of the use and non-use of postoperative cervical collar revealed that patients undergoing ACDF with interbody cages can be helped in the short term by wearing a semi-rigid cervical collar to cope with post-operative pain and disability. Both comparison groups however, improved in all outcome measures from baseline to two years after surgery (*Study I*).

● Several of the neck muscles investigated showed changed endurance with more negative MF slope, greater variability, side differences, shorter endurance time and greater fatigue among the patients compared with asymptomatic individuals (*Study II*).

● Comparison of the outcomes of ventral and dorsal neck muscles endurance tests, electromyographic manifestations of fatigue, and ratings of fatigue and pain 14 weeks and one year after neck-specific training or prescribed physical activity in CR patients, showed increased neck flexion endurance at 14 weeks and at one year compared to baseline and despite to intervention group (*Study III*).

● The cross-sectional study sought to identify dimensions underlying measures of impairment, disability, personal factors, and health status in patients with CR. The dimensions identified resulted in a final model with a three-component solution, categorized in terms of Pain and functioning; Health, beliefs and kinesiophobia, and Mood state and catastrophizing (*Study IV*).

6.1 NECK MUSCLE PERFORMANCE

This is to our knowledge the first study to compare the differences in EMG spectral variables between non-operated patients with CR and asymptomatic subjects. The patients had shorter endurance time in both NME tests. Endurance time differed significantly between the groups. Psychological factors might have affected the patients' motivation and kinesiophobia may have influenced performance during the endurance test (Lindstrom, Schomacher, Farina, Rechter, & Falla, 2011; Vlaeyen, Kole-Snijders, et al., 1995). Even more factors could be influencing the patients during the tests, such as coping with the pain during the test, self-efficacy, earlier experience of physical activity. The score levels of SES and IPAQ were significantly lower in the patient group, and this may confirm their disability. Both patients and asymptomatic subjects ended their NME tests due to neck muscle exhaustion, which was not expected to the same degree from the CR patients in both tests. Lower endurance capacity of the neck muscles is a common finding in patients with neck pain (Strimpakos et al., 2005), whiplash (Ludvigsson, Peterson, O'Leary, Dedering, & Peolsson, 2015), headache (Falla, Jull, Rainoldi, et al., 2004; Jull et al., 1999) and after surgery for CR (Peolsson & Kjellman, 2007). NME tests provide a gross estimation of muscle endurance and self-perceived fatigue, are easily conducted in a clinical setting and do not require specific or expensive instruments. They are, however less common in a clinical setting.

The requirement to sustain contraction until complete fatigue may be contraindicated in many patients because of the possible risk; for this reason we let the patients themselves interrupt the NME tests when they felt the effort was as high as they could cope with. This method has been evaluated differently in Peolsson's study, with higher NME in patients and healthy subjects (Peolsson & Kjellman, 2007). Their method showed good reliability and difference between operated CR patients and healthy individuals.

The results in study II showed changed neck muscle endurance in several of the muscles investigated with more negative MF slope, greater variability, and side imbalance. The MF slope depends on endurance time and therefore is secondarily affected by motivation and kinesiophobia, which can explain the differences in between patients and asymptomatic individuals. A combination of present pain, neck disability, kinesiophobia and fear of exaggerating the pain level during both tests can lower patient motivation (Lindstrom et al., 2011; Vlaeyen, Kole-Snijders, et al., 1995). Our patients´ performance was reduced due to several factors during the NME test, such as endurance capacity, higher fatigue ratings, imbalance. To evaluate the use of EMG and clinical tests that measure time-dependent changes or subjective estimation of fatigue in the NME tests, our results confirmed that myoelectric fatigability was the most important factor (Strimpakos & Oldham, 2001).

Gogia and Sabbahi (Gogia & Sabbahi, 1990) used sustained isometric neck extensions. These authors stressed the importance of test postures with higher IMF and MF slope values observed in prone position. Their findings run contrary to our own study, where we found higher MF slope values in supine position for both patients and asymptomatic subjects. Unfortunately, their MF slope values could not be compared with ours (*Study II*).

Compared to the asymptomatic group, the patients demonstrated greater fatigue at every time points during the NME tests, except for at the end of the prone test, where the asymptomatic group rated more self-perceived fatigue. This has also been seen in healthy subjects compared to lumbar-disc-herniation patients (Dedering, Oddsson, Harms-Ringdahl, & Nemeth, 2002). Their subjects rated fatigue at standard time intervals and were expected to increase their ratings over time. The fatigue level in our patients was already present before they performed the NME test. Fatigue ratings were not very high, although this is a factor to be aware of when training patients and planning an intervention. Fatigue after five minutes´ rest was still evident in the CR group; although; during the rest period they returned nearly to their starting level. Our results suggest asymptomatic subjects dared to push themselves to higher levels of fatigue during the NME test, especially in the prone position, and recovered faster than the CR patients. Both groups had considerably lower ratings of fatigue after the supine NME test compared to the end of the prone NME test. This may have been an effect of general lower capacity in the flexor muscles or the long test in prone position. Differences were seen in the NME test time between the groups, possibly influenced by the positioning. This was also the case with the NME test in prone position. Here the participants had to rate fatigue level every 15 seconds which can be a dissipative factor.

The asymptomatic subjects in study II presented results similar to one other author, with higher NME values in both NME tests (Peolsson et al., 2007). In our study II, the asymptomatic subjects when prone dared to push themselves especially to greater fatigue levels during the NME test. Their motivation influenced both endurance time and fatigue ratings, judging from their own comments during/after the tests.

The endurance time for the flexor muscles in the supine NME test was significantly longer, which may indicate that the intervention program focused more on flexor muscle performance. The increase in endurance time after 14 weeks was expected, because of the regular training during the intervention. This may be the first study to presents data on and long-term effects of increased endurance time at one-year follow-up in patients with CR (*Study III*). Our higher mean values (*Study III*) compared to CR patients (Peolsson & Kjellman, 2007) may be due to the modified support of the forehead before they started: psychological awareness of the support made them feel more secure. But the modified position in the present study can also interfere; a pilot test indicated that the patients did not want to extend their necks. Some of Peolsson's et al, study population had undergone ACDF: that could be another reason for the different lower mean levels in their NME (Peolsson & Kjellman, 2007) where their subjects had no support for the forehead. A further reason may be the exact position of the neck (neutral or not), where a difference activates different muscle lengths (Jordan, 1999; Leggett et al., 1991).

Our results in studies II and III indicates an increase in amplitude of the surface EMG to lower frequencies. This corresponds to results published by Strimpakos et al, who also reported changes in action potential conduction velocities (Strimpakos et al., 2005).

In study III, the patients rated less fatigue and pain at14 weeks and at one year follow-ups irrespective of intervention group. The well-accepted Borg scale of perceived fatigue (Borg, 1990), which assess muscle fatigue, has only been is used in a few studies, but correlates well with the subjective estimation of muscle fatigue with more objective findings e.g. electromyography (Dedering et al., 2002; Elfving et al., 1999; Äng et al., 2009) as in our own EMG studies.

In study III, our results showed that during the extension test the ARV of both SCap and SCM increased during the contraction. Falla et al. showed the same results in their study of chronic pain (Falla, 2004). Other studies have shown a decrease in strength and endurance capacity of the cervical extensor and flexor muscles in patients with neck pain (Barton & Hayes, 1996; Treleaven, Jull, & Atkinson, 1994). In addition, with EMG equipment more complicated instruments have been used to measure fatigability in the cervical muscles (Falla et al., 2003; Gogia & Sabbahi, 1994). This fatigue was also present, in our study, greater myoelectric manifestations of the SCM and SCap during both tests being shown in the CR population.

We found significantly higher endurance of neck extensor compared to flexors. The same results have been presented by Parazza (Parazza et al., 2014), where people with neck pain whether flexors endurance were related to extensor endurance. Further, our extensor endurance time was lower than theirs, but our patients had an additional two kg load during the test, and were also older, which also interfere with performance.

Our results regarding NME test in flexion differ from those of (Edmondston et al., 2008; Harris et al., 2005; Parazza et al., 2014). This could be due to different sample groups or to the examiner´s methodology and we did not do any clinical palpations to instruct the patients. It may also be that our sample had their symptoms much longer: most were chronic subjects, maybe used to coping with this unpleasant feeling when performing demanding activities.

We investigated the ventral and the dorsal neck muscles during a-not-so-functional activity, but even though prompted higher co-activation values of the SCM (agonist) and SCap (antagonist) during the NME test. Our results were similar but in different muscle groups. Their results demonstrated higher co-activation of the upper trapezius muscle in neck-pain patients compared to controls (Falla, Bilenkij, et al., 2004). The increased EMG amplitude for both SCM and SCap throughout our endurance test can be due to the inability to relax the muscles after exertion.

The NME test in extension was always performed first, and in more than half of our sample stopped due to fatigue or pain, associated with fear. Parazza (Parazza et al., 2014) performed the flexion test first, but half their sample also stopped due to pain or pain associated with fatigue or fear; also comments from our patients.

6.2 FUNCTIONING AND PSYCHOSOCIAL FACTORS

At the time when Study I was planned both soft and rigid cervical collars were frequently used after cervical spine surgery to immobilize the cervical spinal column, minimize postoperative pain and reduce rates of non-fusion. This has since changed in Sweden (SweSpine) and (North American Spine Society) and the use of cervical collars has been questioned, especially with the increasing frequency of internal surgery including fixation. The collar is advocated so as to avoid comprising healing after fusion. The support from the cervical collar can be beneficial in the post-operative regime for ACDF with interbody cage, for some patients with more severe conditions and several levels of fusion. Restriction with bracing is more common after fusion procedures and the wear time is often longer (Bible et al., 2009), which was why our patients had immobilization for so long (*Study I*). The collar probably reduces foraminal root compression and keeps the head in a midline and unflexed position, which may relieve pain; but there is still little evidence regarding the mechanism of collars (Ellenberg et al., 1994; Kuijper, Tans, Beelen, et al., 2009). Some studies discuss the counterproductive effects of prolonged immobilization on tissues (Mazanec & Reddy, 2007; Polston, 2007). Our patients wore their collars during daytime only for six weeks, and after 3 weeks they were allowed to sit indoors without collar provided the neck was supported (Heckmann et al., 1999; Polston, 2007; Wainner & Gill, 2000). Some researchers have advocated the use of immobilization for less than two weeks with either a hard or a soft collar to help pain control.

In healthy subjects the rigid cervical collar itself reduces the neck movement on average by 62.9 % which indicates that not all parts of the cervical spine are restricted completely (Whitcroft, Massouh, Amirfeyz, & Bannister, 2011). Hence, movements when wearing cervical collar can have been possible (Miller, Bible, Jegede, Whang, & Grauer, 2010). Some authors have suggested that different cervical collars may hinder different movements especially in extension/flexion (Miller et al., 2010), and this may have been useful in our (*Study I*) (Askins & Eismont, 1997; Schneider, Hipp, Nguyen, & Reitman, 2007). The cervical collar used in this study was the Philadelphia C62, which prevents general movement of the cervical spine in the sagittal plane (Schneider et al., 2007). One study suggested that cervical collars are no more effective than normal behavior or active mobilization (Kongsted et al., 2007), which also strengthens our results in the long-term follow-up in the non-collar group (*Study I*). Miller and colleagues suggested that the rigid collar after surgery including fixation may not be necessary and that the soft collar was satisfactory for restricting motion during daily activities (Miller et al., 2010).

We found no indications that use of a cervical collar for six weeks affected the statistic balance tests results or self-perceived confidence to manage dynamic activities without falling (*Study I*) as suggested by Persson et al., (Persson, Karlberg, & Magnusson, 1996). They showed that CR patients had 50% more complaints of vertigo, and higher body sway velocities than controls; but we did not register any of these parameters in our study I. The difference may also be due to the measurement methods; they used EMG and velocity as provocation, we just the time. Our population had lower cervical root levels, proposed in the literature to be more common in C1-C3, whereas roots are important for postural controls (de Jong, Bles, 1986). The static balance test is clinically easily to perform and permits a quick evaluation for static postural balance disorders. It is functional for normal gait (Springer et al., 2007). The unipedal stance balance test has also been evaluated on healthy individuals in different age groups and genders.

We saw similar results in trials with eyes open vs. eyes closed (test time in seconds). Our group had much lower test times with eyes closed, as also seen in patients with WAD (Juul-Kristensen et al., 2013). Interestingly, comparison with the WAD group showed that our patients with CR had higher NDI scores, at a more severe level; but the physical component (PH) (SF-36) was close to that in their control group. Mental health (SF-36) in our non-collar group was higher than that in their control group, also a small sample. The present results should not be confused with physical composite scores (PCS) and mental composite scores (MCS) in the SF-36, which were very low in our CR group (*Study I*) A further contribution to our results could be that our patients had pain and had undergone a surgical intervention. Comparing right and left leg standing, the time for both groups´ right-legs standing on hard vs. soft surface with eyes closed was decreased. Another factor most probably due to the normal aging process from 40 to 60 years, is that healthy subjects also showed decreased performance with eyes shut as compared to eyes open (Bohannon, Larkin, Cook, Gear, & Singer, 1984). Our results were close to full time on hard surface, which Kammerlind also presented (Kammerlind, 2004). The unipedal stance balance test on soft surface with closed eyes was managed for 30 seconds by most of our patients. This indicates balance difficulties in CR patients both with and without visual support (Springer et al., 2007). The same results are reported for whiplash-associated disorders (Juul-Kristensen et al., 2013). Further, a majority of ACDF patients with dizziness had impaired postural control (Kammerlind, Peolsson 2004).

There were remarkably large effect sizes for the non-collar group in the decrease of neck pain and NDI; similarly for the collar group, decrease of neck pain after two years after surgery. A cervical collar can help healing and reduce the risk of graft/cage migration, and of course reduce post-operative pain and get patients to feel more secure during the first week of daily activities. The reason for not using a collar could be the arguments from Karlberg et al, that their use impairs balance performance (Karlberg, Persson, & Magnusson, 1995): another reason already stated is the deconditioning of the neck muscles (Carette & Fehlings, 2005). A cervical collar group improved significantly more than a non-collar group after surgery

(Kuijper, Tans, Beelen, et al., 2009). Use of a collar or not did not seem to influence radiographic fusion rates as they were 100% in both groups.

In study II, the CR group´s mean score of 37.4 on the TSK indicates borderline kinesiophobia, as also suggested by Lundberg et al, (Lundberg, Styf, & Carlsson, 2004). The TSK questionnaire captures the patient´s fear of pain in relation to physical activity, which is essential information for the intervention. Different values have been presented for the cut-off level, considered to represent a high degree of kinesiophobia in patients with back pain. The measurement error rate is three points i.e. a value between 34 and 40 (37 +/- 3) (Lundberg, 2006). In the present study II, significantly lower levels of SES and IPAQ in the CR group compared to the asymptomatic group were shown. This indicates that the CR group´s confidence in their own ability is an important factor to be aware of during an intervention. Denison et al., reported that self-efficacy refers to the confidence a person has regarding their ability to perform any activity (Denison et al., 2004). Further, Woby et al, 2007, with the same sample size and, background data in our study but in low-back pain patients, evaluated their fear with a different measurement tool, the CSQ, and argued that low self-efficacy lead to greater pain-related fear (Woby et al., 2007).

In our study IV, pain and functioning appeared to be the most important and highly representative components of our model. In other studies, strong correlations between neck disability and pain severity have been presented, for a population followed for 11-14 years after undergone ACDF (Hermansen, Cleland, Kammerlind, & Peolsson, 2014; Hermansen, Hedlund, Vavruch, & Peolsson, 2013). For our patients, the relation appeared already at study baseline and was one reason to seek care. It can be argued that our group represented a population with chronic neck and/or arm pain, with daily experience in many cases, and considered to be at a moderate level of disability (Vernon, 2008). Additionally, the presence of neck pain daily/occasionally could contribute to greater interference during daily activities. This has also been compared in several studies, with other population samples, which showed the same relationship as our study (Hoving et al., 2003; Vernon & Mior, 1991; Wibault et al., 2014). Lower confidence in performing daily activities is a very important variable in our first component and has a relation to disability. Dension et al. showed that when predicting disability, self-efficacy was a more powerful predictor, which maybe is the reason for our result (Denison et al., 2004). There are no cut-off values in the SES so we cannot categorize our population, but the results and also the PCA model indicates that the confidence factor can be important. Further, Arnstein et al have presented similar result, showing correlations between higher pain intensity and lower self-efficacy in chronic-pain patients (Arnstein et al., 1999). Similar results have been presented in other studies, comparing a population with WAD and perceived disability (PDI), using a questionnaire similar to the NDI. Those authors presented a positive relation between VAS and PDI among WAD patients even at the first visit (Kyhlback, Thierfelder, & Soderlund, 2002).

The second component in our model, in study IV, showed fear avoidance and EQ-5D to be good-to-excellent component loadings, and the most important variables in that component. Our results indicate a correlation between the two variables, and if fear of movement is present in daily life this will probably affect and interfere with quality of life. The research group of Lee et al. presented similar results, with moderate correlations between fear-avoidance and with initial six-week disability scores and health measures scores (Lee, Chiu, & Lam, 2007).

Our third component highlights the importance of HADS anxiety, closely followed by HADS depression in our study IV. Similar results have been reported by Wibault et al, whose patients with CR scheduled for surgery showed depressed mood and somatic anxiety associated with higher NDI scores (Wibault et al., 2014).

Unlike other studies on CR, our study presents a comprehensive set of sociodemographic, disease-related and psychosocial factors, several of which have never previously been studied in relation to patients with non-operative interventions due to muscle performance, function and psychosocial factors.

Finally, the PCA model in study IV explained 73% of the total variance, which may imply that information regarding CR patients cannot be captured through questionnaires only. The model illustrates a bio-psychosocial pattern with fear-avoidance beliefs as an important factor, which in another perspective suggests the inclusion of a qualitative research approach in the future. Further, and in a clinical perspective these factors seems important for capturing the broad picture of CR patients.

6.3 METHODOLOGICAL CONSIDERATIONS

The analyses (*Study I*) were based on small, but well-defined, samples of patients with CR recruited via a neurosurgery clinic. The response rate to the questionnaires in Study I at six weeks, three, and six months post-surgery was between 65% and 75%. One reason for non-response could be that the patient's became fatigued and bored doing the same tests so often; another, the very long follow-up period.

Since our patients with cervical degenerative disorders were recruited mainly from primary care and referred to specialized care, they had long-lasting symptoms suggesting selective bias toward more severe CR. This has been proposed as an advantage and can give less changes in studies evaluating the course of disease with reference to the treatment regimen (Heckmann et al., 1999).

In Study III we compared two different treatment strategies. To add a third control group without treatment may have strengthened the results. However, as the trials were performed in a clinical physiotherapy setting it was considered as more problematic for the treating physiotherapist to keep them apart, and not practicable. It could also be regarded as unethically to have a control group without intervention.

The randomized controlled trials included in studies I and III were performed in a clinical outpatients´ physiotherapy setting. One bias in these randomized controlled trials (*Studies I, III*) may be the lack of blinding of the assessor at follow-up. However, at baseline testing the assessor and patients were blinded for allocation, since the allocation took place after the test. The patients were continually told not to reveal their group allocation, but despite all effort they sometimes revealed this by expressing their gratitude at participating in the study and discussing thoughts around their exercise programs.

Several physiotherapists were involved in the training during the intervention period in Study III, and even some patients continued physiotherapy after the 14 weeks of intervention. In a long-term follow-up it is important to know how many participants continue their treatment by the physiotherapist or whether they manage by themselves with how many exercise sessions per week. More specific neck training maybe targeting the neck muscle dysfunction, may be useful in the long term.

In Study II the patients and the asymptomatic subjects were tested in the same positions throughout studies II-IV, which might have affected the test results. Patients and the healthy subjects might be more confident in doing the tests when they know the same order, and of course there can be a training effect involved in this.

Note that in this present study the total FES score was calculated and the results indicated high scores in both groups at baseline. The patients obviously felt confident in doing the daily activities without falling. The FES scale showed a medium to large effect size for improvement in both groups. But maybe the FES scale is not demanding enough for patients after ADCF. The original FES items refer almost entirely to basic activities of daily living which only disabled people would be likely to have trouble with (Tinetti et al., 1990). They, do not include the more demanding activities which may be the main cause for concern among higher-functioning CR sufferers. The Swedish version of the FES added items to the original, and the new scale assesses confidence or concern relating to a wider range of activities (Hellstrom & Lindmark, 1999). The total score was administered and if the single item had been identified due to muscle performance maybe a different result would have been identified.

In general, lying positions give the lowest values, and sitting positions seem to give greater strength values than standing ones do (Strimpakos & Oldham, 2001). In study II, it is reasonable to note that patients and asymptomatic subjects had to raise the weight of their head and in our prone NME test also a weight to counteract the load moment, tiring them faster. A more functional testing position would be appropriate in the future for evaluating endurance time in CR patients.

In study II, the patients and asymptomatic subjects were allowed to practice the movement before performing the NME tests. This was a routine warm-up which can eliminate fear and increase confidence (Berg, Berggren, & Tesch, 1994; Highland, Dreisinger, Vie, & Russell, 1992). It was not the reason for the interruption of the NME tests, which we probably expected in the CR group.

Due to the CR patients´ pain and MRI findings, a maximal strength test was never appropriate, and this could be a limitation of the evaluation during a sub-maximal isometric test, whereas static function of the neck muscles depends on endurance and strength (Strimpakos et al., 2005). Self-perceived fatigue and pain during a test have been measured in several earlier studies of lumbar-back pain (Dedering et al., 2002; Elfving et al., 1999). The Borg scale as a method is easily applicable, although many subjects may have different perceptions of exertion, allowing only a gross estimation of the parameter (Strimpakos, 2011).

A strength in our studies II and III is that the combined data from right and left side are more reliable than analyzing only one side (Gogia & Sabbahi, 1990; Koumantakis, Arnall, Cooper, & Oldham, 2001). In our population patients had problems either on one side or both, and for planning an exercise program both sides of the upper extremities are important, for capture and for possible over-compensation or non-relaxation of the unaffected side. Koumantakis et al., also showed the importance of combining data between sides, which in a general perspective improves reliability and clinical applicability (Koumantakis et al., 2001). The opposite was found by Falla et al. in non-functional tasks (Falla et al., 2004), but the contradiction was also presented by Nederhand et al., who found higher co-activation of the upper trapezius muscle in patients than in controls (Nederhand, Hermens, Baten, & Zilvold, 2000).

In studies II and III, the identified landmarks and placement sites for the electrodes during the follow-up assessments with EMG were never marked or photographed to establish exact placement for each follow-up. This would have given a more accurate test-retest of the same muscle groups, although the same experienced assessor palpated/identified the landmarks on each occasion. In a clinical setting where the effect of exercise is evaluated, it will fail to function, because it disappears when showering. One alternative could be to take a photo at the first opportunity and use this as a benchmark.

We introduced the physiotherapists to an established and well-researched protocol for training the neck muscle groups (Dedering et al., 2014). There is still a feeling among clinicians that strength testing and training of the CR patients could be risky, further aggravating the injury. The same is seen in non-cord-injured cervical-spine subjects (Highland et al., 1992). However, clinical evidence points to the efficacy of muscular strengthening in neck rehabilitation programs in different populations (Highland et al., 1992; Ludvigsson et al., 2015).

Following a limitation in study I, sample size needs to be increased at least fourfold and optimally six fold for sufficient power to investigate causal outcomes when accounting for data loss in prospective follow-ups. One reason for multi-center trials is to be able to include sufficient subjects within a reasonable time. This can increase generalized, external validity, but at the same time is it easier to handle a smaller population which can reduce the drop-out rate (*Studies I, III*). Today´s technology with for example reminder text messages, and evaluation via web-based questionnaires could make the effort easier for the participants.

In study I, we did not identify the patients with coping strategies before surgery. It could have been important to identify these patients, prior to the exercise program and explain that they should increase their daily life activity. This has been suggested in a earlier study by Peolsson et al, who reported that psychological distress was unchanged and predicted poor outcome of surgery (Peolsson et al., 2006b) measured depression with Zung and psychosomatic on DRAM. Wibault et al. used the depressed moods and anxiety score on the Zung and the MSPQ and high pain catastrophizing on the CSQ (Wibault et al., 2014) for explanation.

7 CONCLUSION

Comparing cervical collar or non-collar use after ACDF showed that both groups improved in all outcomes, and were considerably better from baseline to the two year´s follow-up after surgery.

Compared to asymptomatic individuals, patients with CR presented more pronounced signs of muscular fatigue as well as fatigue ratings, and shorter endurance time during a test situation.

A 14-week neck-specific exercise program consisting of a cognitive behavioral approach or physical activity on prescription, resulted in better endurance capacity directly after intervention and was maintained at the present at 1-year follow-up in both groups. The neck-specific training indicated reduced co-activation of antagonist muscles during flexion.

When evaluating CR patients, current neck pain, fear avoidance and anxiety should be considered as important measurements when a broad perspective is needed.

8 CLINICAL IMPLICATIONS

After ACDF wearing a soft cervical collar is sufficient for those subjects in whom psychological factors such as coping, fear avoidance and self-efficacy are present before surgery. Screening for these factors before surgery is important and if needed should be incorporated in the treatment. Our non-cervical-collar group improved in function and had less pain, as did our cervical-collar group after two years of follow-up. This indicates no need for a cervical collar in first-or second-level ACDF.

For evaluating neck muscle endurance and fatigue either clinical methods or more sophisticated EMG methods should be used. The Borg fatigue rating can be a supplement in a clinical setting for evaluating endurance capacity in patients with CR. Have the same test positions between measurements and if possible fixate the torso.

Neck-specific training is a low-load exercise, tolerated by most patients and manageable without provocation of the neck and/ or the arm. Specific neck training or general exercises seem to increase neck flexor endurance, and reduce perceived fatigue and pain regardless of intervention in a long-term perspective.

The complicated nature of the cervical spine requires knowledge of many factors to take into account during one´s evaluation as a clinician or researcher. It is important to evaluate CR patients with a broad perspective of outcome measurements, and pain, fear-avoidance and anxiety may be the most important.

9 FUTURE RESEARCH

There is a need for large, high-quality RCTs with larger sample sizes, comparing the effectiveness of conservative physiotherapy interventions further.

There is also great need for research into established and well-defined protocols of neck-specific training and long-term follow-up of this approach in any patient group with cervical spine-disorders.

Further research is also needed, on the outcome of EMG recordings during neck-muscle endurance tests in different positions, and in different populations with cervical-spinal pain.

The present work advocates exercise training to improve the co-activation of antagonist muscles during flexion contraction. Exercise programs should be developed properly and supervised closely to avoid compensation from other muscles; but this needs to be further explored.

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