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Shoulder pain after stroke

Prevalence, contributing factors and
consequences in daily life

Ingrid Lindgren



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AKADEMISK AVHANDLING

som med vederbörligt tillstånd av Medicinska fakulteten vid Lunds universitet
för avläggande av doktorsexamen i medicinsk vetenskap kommer att offentligent
försvaras i sal H01, Health Science Centre, Baravägen 3, Lund

Fredagen den 6 december 2013, kl. 09.00

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<p>Abstract</p> <p>Post stroke shoulder pain, PSSP, is a common type of pain after stroke, but still further knowledge of this condition is needed. An increased knowledge of prevalence, contributing factors and impact on the individual's life could enhance the possibility to find more effective treatments and therefore more studies are needed. The overall aim of this thesis was to evaluate PSSP with a special focus on prevalence, contributing factors and consequences in daily life.</p> <p>In an unselected stroke population of 327 individuals, the prevalence of PSSP was 22% four months post stroke. Predictors of PSSP (paper I) were shown to be severely affected arm motor function and severe impairments according to the National Institutes of Health Stroke Scale, (NIHSS). About 70% of the individuals with impaired sensorimotor function at stroke onset and PSSP at four months had still pain one year later. Predictors for long-lasting PSSP were left-sided hemiparesis, pain frequency and decreased passive shoulder abduction (paper II). In a group of 49 individuals with mild to moderate sensorimotor impairments post stroke (24 with and 25 without PSSP) and 11 healthy controls, somatosensory abnormalities were assessed with thermal and mechanical thresholds using the Quantitative Sensory Testing (QST) method. No significant difference in QST measurements were found between the groups with and without PSSP, but both stroke groups had generally higher thermal thresholds and more extreme low or high mechanical thresholds than the healthy controls (paper III). The association between PSSP, sensorimotor function, ability to perform daily hand activities, perceived participation and life satisfaction were evaluated in 24 individuals with and 25 individuals without PSSP, all with mild to moderate sensorimotor impairments. PSSP was associated with reduced motor function, but the PSSP had a weak association with daily hand activities, perceived participation and life satisfaction (paper IV). In conclusion, this thesis has shown that PSSP is common in individuals with decreased upper extremity motor function. Left-sided hemiparesis, pain frequency and decreased passive shoulder abduction seem to predict long-lasting PSSP. In individuals with mild to moderate upper extremity paresis, somatosensory impairments seem to have a small impact on the pain and the PSSP appears to have only a small impact on their life situation.</p>	
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Table of contents

Abstract	9
List of papers	10
Abbreviations	11
Preface	12
Introduction	13
Stroke	13
Consequences after stroke	13
Rehabilitation	14
Pain after stroke	15
Definition of pain	16
Post-stroke shoulder pain	17
Prevalence of PSSP	17
Contributing factors to PSSP	18
Treatments for PSSP	19
Consequences of PSSP in daily life	19
Rationale for the thesis/research fields	21
Aims	23
Overall aim	23
Specific aims	23
Methods	25
Participants	25
Assessments and outcome measures	28
Baseline assessments	28
Outcome measures	29
Outcome measures to assess impairments	29
Outcome measures to assess activity limitations	32
Outcome measures to assess participation restrictions	33
Outcome measures to assess self-perceived health and life satisfaction	33
Site of examination and assessors	33

Statistics	34
Ethics	35
Results	37
Prevalence of PSSP	37
PSSP characteristics	37
Contributing factors to PSSP	38
Motor impairments	38
Range of motion	38
Somatosensory impairments	39
Other contributing factors	39
Consequences of PSSP in daily life	39
Activity limitations	39
Perceived participation restrictions	40
Self-perceived health and life satisfaction	40
General discussion	41
Prevalence of PSSP	41
Contributing factors to PSSP	41
Who are at risk of developing PSSP?	42
Who are at risk for long-lasting PSSP?	42
Consequences of PSSP in daily life	43
Methodological considerations	44
Participants	44
Methods	44
Strengths and limitations	46
Clinical implications and future studies	47
Prevention	47
Assessments	47
Treatments	47
Considerations for future studies	48
Conclusions	49
Populärvetenskaplig sammanfattning	51
Acknowledgements	53
Fundings	55
References	57

Abstract

Post stroke shoulder pain, PSSP, is a common type of pain after stroke, but still further knowledge of this condition is needed. An increased knowledge of prevalence, contributing factors and impact on the individual's life could enhance the possibility to find more effective treatments and therefore more studies are needed. The overall aim of this thesis was to evaluate PSSP with a special focus on prevalence, contributing factors and consequences in daily life.

In an unselected stroke population of 327 individuals, the prevalence of PSSP was 22% four months post stroke. Predictors of PSSP (paper I) were shown to be severely affected arm motor function and severe impairments according to the National Institutes of Health Stroke Scale, (NIHSS). About 70% of the individuals with impaired sensorimotor function at stroke onset and PSSP at four months had still pain one year later. Predictors for long-lasting PSSP were left-sided hemiparesis, pain frequency and decreased passive shoulder abduction (paper II). In a group of 49 individuals with mild to moderate sensorimotor impairments post stroke (24 with and 25 without PSSP) and 11 healthy controls, somatosensory abnormalities were assessed with thermal and mechanical thresholds using the Quantitative Sensory Testing (QST) method. No significant difference in QST measurements were found between the groups with and without PSSP, but both stroke groups had generally higher thermal thresholds and more extreme low or high mechanical thresholds than the healthy controls (paper III). The association between PSSP, sensorimotor function, ability to perform daily hand activities, perceived participation and life satisfaction were evaluated in 24 individuals with and 25 individuals without PSSP, all with mild to moderate sensorimotor impairments. PSSP was associated with reduced motor function, but the PSSP had a weak association with daily hand activities, perceived participation and life satisfaction (paper IV). In conclusion, this thesis has shown that PSSP is common in individuals with decreased upper extremity motor function. Left-sided hemiparesis, pain frequency and decreased passive shoulder abduction seem to predict long-lasting PSSP. In individuals with mild to moderate upper extremity paresis, somatosensory impairments seem to have only a small impact on the pain and the PSSP appears to have a small impact on their life situation.

List of papers

I

Lindgren I, Jönsson AC, Norrving B, Lindgren A. Shoulder pain after stroke: a prospective population-based study. *Stroke*. 2007;38:343-348.

II

Lindgren I, Lexell J, Jönsson AC, Brogårdh C. Left-sided hemiparesis, pain frequency, and decreased passive shoulder range of abduction are predictors of long-lasting poststroke shoulder pain. *PM R*. 2012;4:561-568.

III

Lindgren I, Ekstrand E, Lexell J, Westergren H, Brogårdh C. Somatosensory impairments are common after stroke but have only a small impact on post-stroke shoulder pain. *J Rehabil Med*. Accepted for publication.

IV

Lindgren I, Brogårdh C. Post-stroke shoulder pain and its association with upper extremity sensorimotor function, daily hand activities, perceived participation and life satisfaction. Submitted.

Abbreviations

ADL	Activities of Daily Living
BI	Barthel Index
BMI	Body Mass Index
CDT	Cold Detection Threshold
CI	Cerebral Infarction
CI	Confidence Interval
CPT	Cold Pain Threshold
ESD	Early Supported Discharge
HPT	Heat Pain Threshold
IASP	International Association of Pain
ICF	International Classification of Functioning, Disability and Health
LiSat-11	Life Satisfaction check list
MAS	Modified Ashworth Scale
M-MAS	Modified Motor Assessment Scale
NIHSS	National Institutes of Health Stroke Scale
OR	Odds Ratio
P-ADL	Personal Activities of Daily Living
PSSP	Post Stroke Shoulder Pain
QST	Quantitative Sensory Testing
ROM	Range of Motion
SIS	Stroke Impact Scale
VAS	Visual Analogue Scale
VAS-P	Visual Analogue Scale for Pain
WDT	Warm Detection Threshold

Preface

When I was studying to be a physiotherapist, the supervisor physiotherapist in Lund, Kerstin Lundbladh, had innovating and inspiring lectures on the topic of how to analyze and treat persons with stroke. Already at that point I became engrossed with this field of clinical practice and decided to embark upon a physiotherapy career within rehabilitation of persons with stroke and other neurology impairments. It was also Kerstin Lundbladh who recommended me an article about shoulder pain, written by Judith Griffin (Griffin JW. Hemiplegic shoulder pain *Phys Ther.* 1986 Dec;66(12):1884-93); this was the first article I read on the topic. In my clinical work I continuously meet patients with stroke and who suffer from shoulder pain. The questions I get from patients, their next to kin and from staff have been why does the problem exist and how can one treat it. The general opinion in the clinical setting I feel, is that the problem of shoulder pain following stroke is a matter for the physiotherapist to solve. During my clinical years I have many times wondered why stroke patients have pain specifically in the shoulder. Even if there are a lot of studies performed, differences in design and study populations make it difficult to generalize results. My first study aimed to find out the prevalence of shoulder pain in a stroke population. The results were important for the research area and also for the following studies in the thesis. However, my research did not take off at that point, and years passed when I was engaged with other interesting tasks in my profession, such as working with a wide range of neurological diseases and disorders as well as working with healthcare management. I am thus grateful to Associate professor Christina Brogårdh and Professor Jan Lexell for urging me and facilitating for me to take up again and continue with my research on shoulder pain following stroke. Even if the problem with shoulder pain has not been solved as I ideally hoped at the beginning of my doctoral studies, and although of course more interventions are still required, some new knowledge has been added to the area. For the individuals suffering from consequences of stroke, shoulder pain is one of many problems. As healthcare professionals, it is our duty to search for best prevention, treatments and strategies to avoid and minimize the consequences of stroke, to regain function and increase activity, participation and life satisfaction.

Introduction

Stroke

Stroke is the third leading cause of mortality in our society and the most common cause of long-term disabilities in the adult population. According to the World Health Organization (WHO), stroke is defined as an “acute neurological dysfunction of vascular origin with sudden or at least rapid occurrence of symptoms or signs corresponding to involvement of focal areas of the brain” (1). There are two main types of stroke; hemorrhages (10-15%) and ischemic strokes (85%). Every year about 25 000 individuals in Sweden have their first stroke (2).

Consequences after stroke

Stroke often leads to consequences in the individual’s daily life. These consequences can be described in the context of impairments (i.e. problems in body functions and structures), activity limitations (i.e. problems in the execution of a task), participation restrictions (i.e. problems in involvement in life situations) as well as personal and environmental factors according to the International classification of functioning, disability and health (ICF) formulated by the WHO (3) (Fig 1).

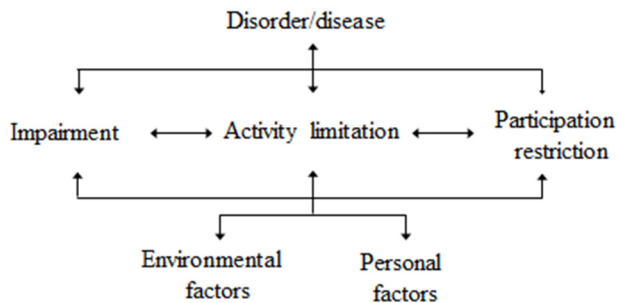


Fig 1.
International Classification of Functioning, Disability and Health (ICF) (WHO 2001).

Common primary impairments in the acute phase are paralysis or paresis, sensory deficits, impaired balance as well as problems with cognition, speech, dysphagia and vision. Secondary complications may also develop and give rise to impairments such as pain and infections. The impairments lead to activity limitations and participation

restrictions. Examples of activity limitations and participation restrictions are difficulties in walking, getting dressed/undressed (P-ADL), carrying out daily routines, doing housework, working, using transportation and taking part in recreational and leisure activities. During the first three months after stroke, impairments, activity limitations and participation restrictions have been shown to lead to reduced health-related quality of life, while in a longer perspective, environmental factors and personal factors are of greater importance for health-related quality of life (4, 5). Motor impairments are the most common impairment after stroke (6). Various impairments in the arm and hand are present in as many as 50 to 80% of the stroke patients in the acute phase (7-9). Recovery of the arm and hand mainly occurs within three months post stroke (9), however after 3-6 months, about 60-80 % of these individuals are reported to have upper extremity impairments (9, 10).

Rehabilitation

According to the World Health Organization, rehabilitation of people with disabilities is defined as “a process aimed at enabling them to reach and maintain their optimal physical, sensory, intellectual, psychological and social functional levels”. Rehabilitation aims to provide disabled people with the tools they need to attain independence and self-determination (11). To optimize rehabilitation, one must evaluate the consequences of the impairments for the individual, and therefore it is important to ascertain how the impairments are associated with the ability to perform daily activities, perceived participation and life satisfaction. The rehabilitation process in the clinical setting aims to find ways to regain and optimize motor function, activity and participation, but also to prevent and minimize the negative consequences of stroke through pain relief, physical activity and coping strategies.

For all types of stroke care and rehabilitation, the team work is essential. Stroke rehabilitation should commence already in the acute care phase. There is evidence that care in a stroke unit, staffed by a multidisciplinary team is beneficial (12). Many persons require further rehabilitation after discharge from the stroke unit, therefore the rehabilitation continues in different forms and at different care levels depending on the individual's needs. In stroke rehabilitation, the interdisciplinary or multidisciplinary team works together with the patient using a process involving goal setting, assessment, intervention and reassessment from the ICF perspective. Early supported discharge (ESD) and continued rehabilitation at home after stroke have been shown to be beneficial (13) and is recommended for individuals with mild or moderate deficits by the Swedish National Board of Health and Welfare (14). The professions represented in an ESD-team can vary, but usually a physiotherapist and an occupational therapist are involved and a physician works either as a team member or as a consultant. Some individuals will benefit from an intense rehabilitation period at a rehabilitation facility, either as inpatient or outpatient. Rehabilitation in primary care, either offered by the primary care centers or in the realms of community care, is for some individuals beneficial

already after the acute care and for others after a rehabilitation period. A well functioning chain of care between the hospital, primary care centers and community care are crucial for an effective rehabilitation.

The physiotherapist's role in the team is to have a special focus on mobility, gait, balance, arm- and hand exercises and physical activity (15, 16). Pain relief is a task for the whole team; while the physician may prescribe medications, administer intra articular corticoid injections or botulinum toxin, the physiotherapist may use of electrical stimulation or programs including careful mobilisations, the occupational therapist tries to find non-painful ways to perform daily activities, the nurse employs non-painful relaxing positions and the social worker ways to cope with the pain.

To be able to evaluate recovery and changes after interventions and functioning over time, reliable and valid outcome measures are required that cover all ICF domains. Assessments must be related to the situation and disability but also time aspects have to be considered. To be able to cover different aspects of a problem and its consequences, a combination of objective measurements, interview methods and self-reported assessments are needed.

Pain after stroke

Pain is a common impairment after stroke and has been reported in more than one third of stroke survivors (17, 18). Shoulder pain, here referred to as PSSP, is one common pain type (18, 19), other types are headache, central pain, spasticity related pain and musculoskeletal pain (18) (Fig 2). While PSSP, headache, spasticity and musculoskeletal pain are reported to occur in around 10-40% (18), central pain is reported to affect about 3-10 % of the stroke population (17, 19). There is a difficulty in differentiating these pain types, as for example PSSP might be caused by as well musculoskeletal pain as spasticity and central pain (Fig 2).

More than one type of pain (for example PSSP and headache) is reported by about one third of the individuals with post-stroke pain and also one third describe a moderate to severe impact on daily life (17). Post-stroke pain is more common in individuals with severe stroke. Low age has been reported to be a risk factor for development of post-stroke pain (18, 20), in contrast to the general population where prevalence of pain increases with age. Also depression is mentioned as a risk factor (18).

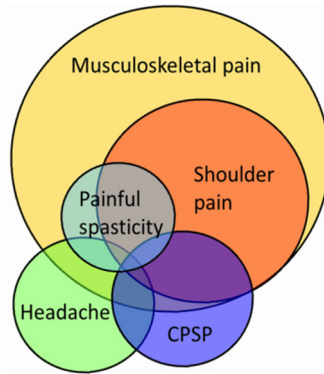


Fig 2.

Common types of chronic pain that can occur after stroke. Diagram of the complexity of PSSP. An individual can have a single pain type or a combination of pain types (overlapping areas). The sizes of the circles are approximate to relative frequency (spasticity 7%, headache 10%, CPSP 10%, shoulder pain 20%, musculoskeletal pain 40%). CPSP=central post-stroke pain. Klit et al. Central post-stroke pain: clinical characteristics, pathophysiology, and management. *Lancet Neurol* 2009 Sep;8(9):857-68 (21).

Definition of pain

According to the International Association of Pain, IASP, pain is defined as “an unpleasant sensation and emotional experience which is associated with actual and potential tissue damage or is described in terms of such damage” (22) and by ICF as “Sensation of unpleasant feeling indicating potential or actual damage to some body structure felt in a specific part, or parts, of the body” (3). Pain impulses transmit in the afferent pain fibers from the periphery via the spinothalamic, spinoreticularic and spinomesencephalic tracts and pain arises when the action potentials finally reach the sensory cortical areas. Different types of fibers conduct the impulses; A- delta, which are myelinated and lead pain, hard pressure and cold and C-fibers which are unmyelinated and lead pain, heat and touch. While A-delta fibers give a sharp well localized pain, C-fibers give a more diffuse located pain and dull aching. Nociceptive neurons in the dorsal horn are of two main types, namely “nociceptive specific” and “wide dynamic range” neurons (WDR). WDR neurons receive input from both noxious and non-noxious afference including afference from A-beta fibres. Normally WDR neurons do not respond to non-noxious stimuli, however they may become sensitized and hyper-responsive under certain conditions to low threshold stimuli such as touch or movement. The WDR neuron becomes hyperactive and therefore can non-painful stimuli be perceived as painful (allodynia) (23).

Peripheral as well as central sensitization develop already after a short period of acute pain stimuli, but as time goes by it becomes more manifest. While peripheral sensitization is a reduction in threshold and an increase in responsiveness of the peripheral ends of nociceptors, central sensitization is a more complex phenomenon. An increased sensitivity in the second neuron and in the surrounding neurons appears. Also

descending systems contribute to the increased excitability. Interaction between nerve cells and glia cells also contribute to central sensitization and repeated activation of C-fibers lead to increased and remaining answer in the second neuron, a phenomenon named wind-up.

Based on origin, pain can be divided into nociceptive, neuropathic and other pain, where the latter includes pain without neurobiological origin (24). Nociceptive pain is defined as an activation of high threshold receptors which are localized in the whole body. Examples are pain raised by an inflammatory processes, ischemia or degenerative processes in for example muscles, nerves or tendons. Neuropathic pain is defined as pain arising as a direct consequence of a lesion or disease in the somatosensory nervous system and can appear weeks or months after the injury. It can arise spontaneously or be triggered by a stimulus. When neuropathic pain exists, an impact of the sensory system is apparent, either as a hypo- or a hyper phenomenon. It is common that the pain- or temperature sensory is affected (25). One type of neuropathic pain is Central Post Stroke Pain, CPSP. The central pain can be spread over smaller or greater areas of the affected side. Stroke in the thalamic area is known as a risk for central pain, but studies have shown that it can arise even if the stroke is localized in other areas (21).

Post-stroke shoulder pain

Even if post-stroke shoulder pain (PSSP) is one of the most common forms of pain after stroke, a precise definition does not exist (26) and consensus has not been reached about a time span for pain onset, pain characteristics and localization. One reason is probably that several underlying causes may contribute to the development and maintenance of PSSP. Another challenge when trying to define PSSP is that shoulder pain and shoulder problems are common in the general population. The reported prevalence in a general population has in studies varied between 7% and 30% (27), with the highest prevalence in the 50-70 years of age (28), ages in which stroke is prevalent. Demarcation of which pain is stroke related or not is in some cases difficult. It is also difficult to evaluate if individuals with shoulder pain prior to stroke are predisposed to PSSP.

Prevalence of PSSP

The prevalence of PSSP varies hugely in previous studies from 5-84% (29-32). Plausible reasons for these wide discrepancies are differences in definitions, time span after stroke, assessments or studied population. Differences in care and rehabilitation may also contribute to the variety in prevalence. The incidence of PSSP has in some studies been reported to be associated with age (33, 34) and one study has reported higher prevalence of PSSP in women (33). Though, differences in PSSP prevalence according to age and sex have not been confirmed in other studies (30, 31).

Contributing factors to PSSP

A variety of underlying causes and contributing factors for PSSP have been suggested in the literature, as motor impairments, decreased range of motion and somatosensory disturbances. These contributing factors may be present separately or exist together.

Motor impairments

Reduced motor function, paresis as measured by the Motor Assessment Scale (35) the NIHSS (30) or the Motricity Index and the Frenchay Arm Test (36), have earlier been described to be related to PSSP. Reduced motor function and muscle imbalance might lead to changes in joint positions and subluxation. Subluxation leads to overstretching of soft tissues around the glenohumeral joint. A causal relationship between subluxation and PSSP has been suggested as measured by palpation (33, 37, 38), or with radiographs (34, 39) but not all authors have found this relationship (40).

Changes in muscle tone lead to lack of normal movements. Therefore increased muscle tone as assessed by the Ashworth or Modified Ashworth Scale has been considered to be associated with post stroke shoulder pain in some studies (41, 42), but other studies have not confirmed these findings (34, 37, 39).

Range of motion

Range of motion is often decreased in individuals with hemiparesis. A relation between decreased range of motion assessed by goniometer and shoulder pain has been found (35, 36, 43). However range of motion decreases over time and the relationship to long-lasting PSSP have rarely been described.

Somatosensory impairments

Recently, studies have suggested that somatosensory impairments can play a role in the development and maintenance of post stroke shoulder pain (44, 45). Measuring light touch and proprioception is in the clinical setting and in research often performed with the participant's eyes closed while trying to localize the touch or movement direction. Several tests exist on this concept (46, 47). To quantify thermal and mechanical impairments, the Quantitative Sensory Testing (QST) method can be used (44, 48, 49). With this method, it is possible to study different functions of the somatosensory system. Analyses of thermal thresholds allow the assessment of A-delta and C-fibres, and analyses of mechanical thresholds allow the assessment of A-beta fibres. The QST is described more in detail in the Method section.

Shoulder pain as an expression of a central pain process has been suggested (21, 50) but this relationship remains. For central pain diagnosis, several criteria have to be fulfilled, as pain within an area of the body corresponding to the lesion of the CNS, and other causes of pain such as nociceptive or peripheral neuropathic pain excluded or considered highly unlikely (21).

Other contributing factors

Stroke laterality might play a role; a stroke in the right hemisphere has been suggested to be a contributing factor for PSSP, (31, 33, 51), but the results in previous studies varies (34, 37). The suggested theory is that stroke in the right hemisphere may lead to neglect, which in turn might lead to lack of attention and less caring of the affected arm.

As most individuals with PSSP have decreased motor function in the shoulder a risk for “learned nonuse”, where movements are suppressed, is evident. This phenomenon may prevent or limit motor recovery (52), which may in turn lead to pain.

Treatments for PSSP

Evidence for PSSP treatments is limited. With the regard to the effect on shoulder pain after three months, only intramuscular neuromuscular electric stimulation (NMES) has been found to be effective in relieving the pain (53), but this is a complicated treatment only suitable for some individuals with stroke and also few studies have been performed to confirm the findings. Due to the fact that there is poor evidence for most of the treatments used in the clinical settings, more studies are needed. Common treatments and regims are pain medication, range of movement exercises, gentle handling, orthoses and other types of support for the arm. While gentle handling, movement exercises and support for the arm are common as preventive measures, pain medication, movement exercises, electrical stimulation and acupuncture are examples of treatments given to individuals who have developed PSSP. Usually, the physiotherapist is responsible for the analysis of the PSSP, and in conjunction with the individual suffering from PSSP and the other team members a decision is made as to which interventions could be actual. Despite these measures, PSSP develops and also remains in many individuals.

Consequences of PSSP in daily life

Even if PSSP is reported to be associated with depression (30) and longer hospital stay (39, 54), very few studies have investigated how PSSP impacts on daily life, i.e. lead to daily activity limitations, participation restrictions and reduced life satisfaction, and also their outcome measurements and results differ.

Activity limitations

One study has reported that individuals with PSSP in the subacute phase have more activity limitations, according to Barthel Index, than individuals without shoulder pain (55), but two other studies using the same outcome measure have not been able to confirm this finding (30, 37). Neither have authors who used other instruments to measure activity, such as Arm Motor Ability Test, Motor Activity Log (MAL) and Nine Hole Peg Test, found a relation between PSSP and activity (56-58). While the Barthel Index assesses daily activities more in general, the Arm Motor Ability Test, MAL and Nine Hole Peg Test are conducted to measure more specifically daily arm and hand activities.

Perceived participation restrictions

Perceived participation is an individual's experience of involvements in life situations. An association between PSSP and decreased participation was found in one study where the Stroke Specific Quality of Life instrument was used (56), whereas another study using the Reintegration to Normal Living Index, did not find such a relationship (57). A suitable measurement for use in a Swedish stroke population is the participation domain in Stroke Impact Scale, SIS (59, 60).

Impact on self-perceived health, life satisfaction and quality of life

Self-perceived health is an indicator of overall health status and has been shown to be associated with change in functioning (61). To get information about the individual's self-perceived health in general, the generic instrument SF-36, a short form health survey, can be used (62). However, no study has been found which has used this instrument in evaluating PSSP and self-perceived health.

Life satisfaction refers to a judgemental process in which individuals assess the quality of their lives on the basis of their own unique set of criteria (63). Judgements of satisfaction are dependent upon a comparison of one's circumstances with what is thought to be an appropriate standard (64). No study, assessing life satisfaction among individuals with PSSP, has been found. An instrument previously used to assess life satisfaction in stroke studies in general is the Life Satisfaction Checklist, LiSat-11, (65, 66).

Life satisfaction should not be confused with the related term quality of life (QOL), which refers to general well-being of individuals and societies and also includes environment. QOL is defined as "the individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns" (67). Only one study has found an association between PSSP and reduced quality of life. In this study, pain-related quality of life was assessed with the Brief Pain Inventory question number 12 (58).

Rationale for the thesis/research fields

Since there is a difference in the reported shoulder pain frequency among individuals suffering from stroke and it is still not clear which factors contribute to the development and maintenance of post-stroke shoulder pain, more studies are needed. New theories have indicated a relationship with somatosensory function, but few studies are done and the evidence is still unclear. Also, few studies have investigated how shoulder pain impacts on daily life. Results from these studies vary about how shoulder pain is related to activity, perceived participation and life satisfaction, i.e. the dignity of the shoulder pain problem among other problems affecting the individual with stroke. An increased understanding can assist the clinicians in the planning of more individually targeted interventions. With this background a general aim and specific aims were developed.

Aims

Overall aim

The overall aim of this thesis was to increase knowledge of PSSP with respect to prevalence, contributing factors and consequences in daily life.

Specific aims

- To provide more detailed data about PSSP, including prevalence, characteristics, influence on daily life, and predictors, in a population-based group of first-ever stroke patients.
- To determine the proportion of persons with PSSP four months after onset of the stroke in whom long-lasting shoulder pain develops and to assess the extent to which age, side of paresis at stroke onset, pain frequency and pain intensity, passive shoulder range of motion, resistance to passive movements, motor function and subluxation at four months after stroke predicts shoulder pain one year later.
- To investigate if somatosensory impairments are more common in individuals with PSSP than individuals without PSSP (non-PSSP) and healthy controls (HC).
- To assess the differences in upper extremity sensorimotor function, daily hand activities, perceived participation and life satisfaction between individuals with and without PSSP and to determine how PSSP is associated with these variables.

Methods

Participants

In Table I, an overview of design, participants, recruitment, inclusion and exclusion criteria and data collection is presented. Participants were recruited from two populations. The first population was included in study I and II and the second population in study III and IV.

Table I.

Overview of the study design, participants, recruitment origin, inclusion and exclusion criteria and data collection for studies I-IV

	Study I	Study II	Study III	Study IV
Design	Prospective study	Prospective study	Cross-sectional study	Cross-sectional study
Sample	327 unselected individuals with stroke	58 individuals with stroke, selected from the 327 individuals in study 1	49 selected community-dwelling individuals with stroke (24 with and 25 without PSSP) and 11 healthy controls	49 selected community-dwelling individuals with stroke (24 with and 25 without PSSP)
Mean age (yrs)	73 ±12	71±14	64±9 (stroke participants) 65±6 (healthy controls)	64±9
Male n (%)	195 (60)	37 (64)	35 (71) (stroke participants) 7 (64) (healthy controls)	35 (71)
Recruitment origin	Lund Stroke Register	Lund Stroke Register	Lund Stroke Register, Departments of Neurology and Rehabilitation Medicine, Skåne University Hospital (stroke participants) Healthy controls recruited from colleagues and friends	Lund Stroke Register, Departments of Neurology and Rehabilitation Medicine, Skåne University Hospital
Inclusion criteria	First-ever stroke	First-ever stroke, affected sensorimotor function at stroke onset and shoulder pain four months post stroke	Stroke with onset at least five months prior to study enrollment, decreased sensorimotor function in the affected arm, but ability to use the arm to some extent in daily activities For PSSP-participants: Pain in the affected shoulder for at least four months after stroke onset, daily or almost daily pain For healthy controls: No shoulder pain	Stroke with onset at least five months prior to study enrollment, decreased sensorimotor function in the affected arm, but ability to use the arm to some extent in daily activities For PSSP-participants: Pain in the affected shoulder for at least four months after stroke onset, daily or almost daily pain
Exclusion criteria	None	None	Difficulty to communicate or to understand test instructions, other conditions causing pain or sensory disturbances (e.g. example fibromyalgia and arthritis), severe depression or other psychiatric conditions	Difficulty to communicate or to understand test instructions, other conditions causing pain or sensory disturbances (e.g. fibromyalgia and arthritis), severe depression or other psychiatric conditions
Data collection	Four and 16 months post stroke	Four and 16 months post stroke	Median 14 months post stroke	Median 14 months post stroke

In Fig 3, a flow chart for study I is presented. In study I, 327 consecutive first-ever stroke patients with stroke onset between March 1, 2001 and February 28, 2002 were included. All patients with a first-ever stroke who accepted to participate in the Lund Stroke Register were included. All but one with a final diagnosis of first-ever stroke underwent computed tomography scan of the brain. The 327 participants were assessed at a median period of four months after stroke and one year later the 305 participants who remained in the study were reassessed. To gain further knowledge about post-stroke shoulder pain, data from 58 of the 71 individuals with PSSP from this population were selected for study II. These participants had sensorimotor impairments at stroke onset and shoulder pain four months after stroke.

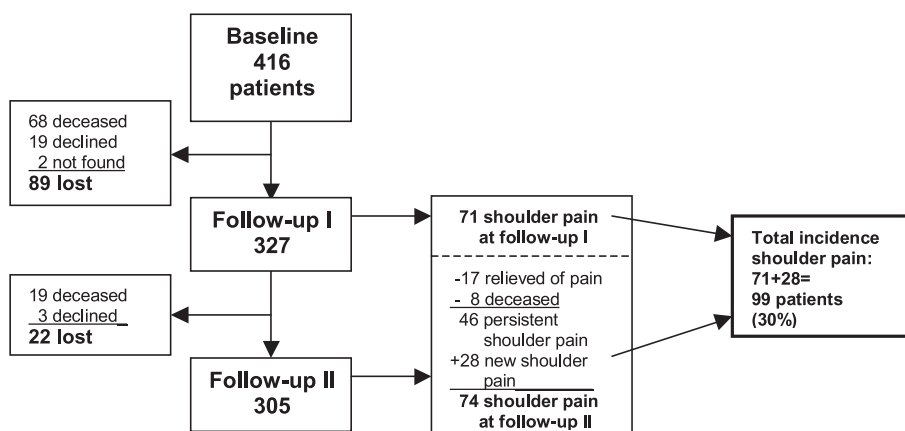


Fig. 3.
Flow chart for study I.

In Fig. 4, a flow chart for study III and IV is presented. For study III and IV, a new population was recruited. This population consisted of 49 community-dwelling individuals (24 with and 25 without PSSP) with mild to moderate sensorimotor impairments after stroke. All but one were independent walkers and all but three were independent in personal activities of daily living (P-ADL). In study III, also 11 healthy sex and age matched controls were included.

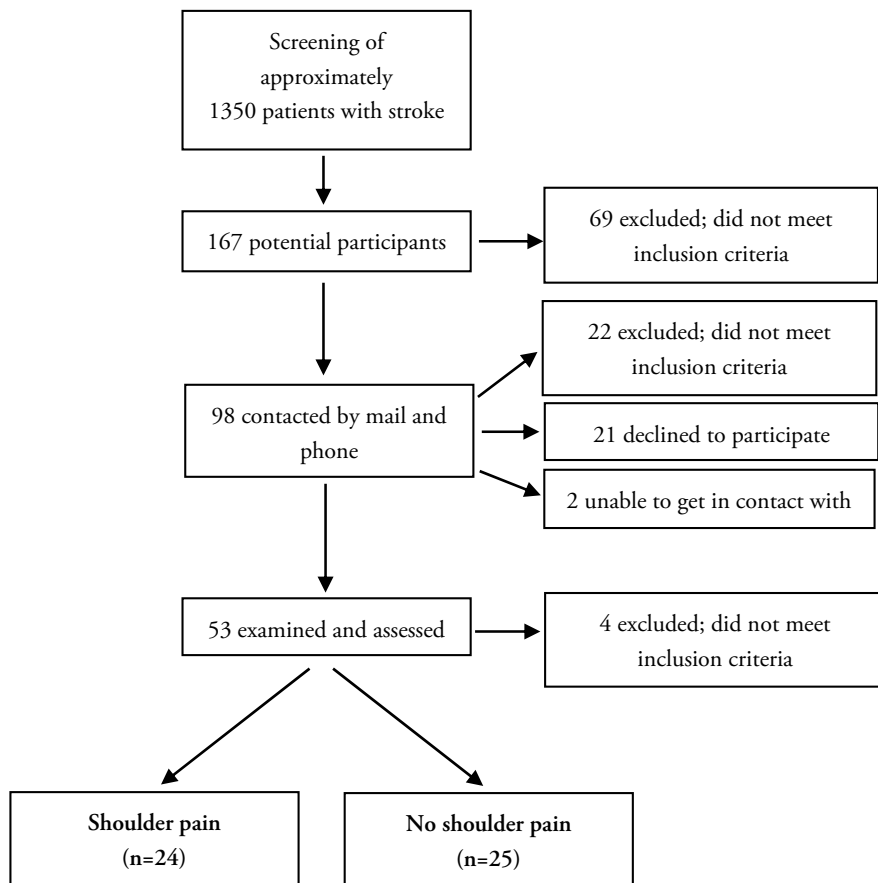


Fig. 4.
Flow chart for study III and IV.

Assessments and outcome measures

Baseline assessments

In all studies descriptives such as age, sex, height and weight are given. Demographic data was also collected before assessments; type of stroke, sub type of stroke, side of paresis, presence of diabetes mellitus (as shoulder pain could be a complication to diabetes mellitus), abnormal sensation, pain in other body parts, and length of post-stroke rehabilitation period. Primary activities of daily living such as walking ability, dressing and toileting, hand dominance and ability to grasp and release an object were also recorded. Furthermore, the participants' main living situation as well as family and

vocational situation were documented. To characterize the shoulder pain the following data were registered; pain onset, location, frequency, quality and situations, medication for shoulder pain, pain during movements and/or at rest and pain at touch.

Outcome measures

The outcome measures used in studies I-IV are given in Table II.

Table II.

Overview of outcome measures

Outcome measures	Study I	Study II	Study III	Study IV
Visual Analogue Scale for Pain (VAS-P)	X	X	X	X
National Institutes of Health Stroke Scale (NIHSS)	X	X		
Modified Motor Assessment Scale (M-MAS)	X	X	X	X
Subluxation (palpation)	X	X		X
Modified Ashworth Scale (MAS)		X	X	X
Range of motion, ROM (goniometer)		X	X	X
Light touch (Fugl-Meyer)	X		X	X
Proprioception (Fugl-Meyer)			X	X
Quantitative Sensory Testing (QST)			X	
Barthel Index (BI)	X			
ABILHAND questionnaire				X
Stroke Impact Scale (SIS)				X
SF-36	X			
Life Satisfaction Check List (LiSat-11)				X

Outcome measures to assess impairments

Shoulder pain intensity

In paper I-IV, the subjects evaluated their shoulder pain intensity during the previous 48 hours by using the 0 to 100 mm Visual Analogue Scale for Pain (VAS-P) marked at one end “no pain” and at the other “worst imaginable pain” (in Swedish) (68). In this method, a scale is presented, and the person has to estimate how much pain he/she

has. VAS-P score zero was defined as no pain, 10-30 as mild pain and 40-100 as moderate to severe pain (69). VAS is commonly used in the clinical setting as well in studies.

Impairment scale

In paper I, the National Institutes of Health Stroke Scale, or NIH Stroke Scale (NIHSS) was used. This is a tool to objectively quantify the impairments caused by a stroke. The NIHSS comprises 11 items, each of which scores a specific ability between a 0 and 4. In the version used in these studies, an item for right and left hand motor function is included (70). For each item, a score of 0 indicates normal function in that specific ability, while a higher score indicates some level of impairment (70). NIHSS is reliable (71) and is recommended for use in the clinical situation as well as in research (72).

Motor function

In paper I-IV, motor function of the upper arm and hand as well as advanced hand activities were assessed with the Swedish version of the Modified Motor Assessment Scale (M-MAS UAS-95) which is a reliable and valid outcome measure (73, 74). In this instrument, the subscales range from 0 to 5, where 5 is normal or almost normal motor function and 0 is no motor function. In paper I and II, only the upper arm was assessed; the maximum total score for each arm was 5 points. In paper III and IV, both upper arm, hand and advanced hand activities were assessed and the maximal total score was therefore 15 points.

Subluxation

In paper I and II, subluxation was registered as present/not present by palpation of the glenohumeral joint, with the participant in an upright sitting position, which has been shown to be a reliable method (38, 75, 76).

Resistance to passive movements

In paper II-IV, the Modified Ashworth Scale, MAS (77, 78) was used to measure resistance to passive movements. This outcome measure has been shown to be reliable (78). In these papers resistance to passive movements was assessed in the elbow. The scale ranges from 0 to 4, where 0 = no increase in muscle tone, 1-3 = some degree of increased muscle tone and 4 = rigidity in flexion or extension.

Range of motion

In paper II-IV, passive range of motion, ROM, was assessed with a hand held goniometer. This is a reliable method (79) and a common assessment in as well the clinical setting as in research (79, 80).

Light touch and proprioception

In paper I, light touch was registered in the arm as normal or diminished/absent. In paper III and IV, proprioception and light touch was assessed according to Fugl Meyer (46, 81). Light touch in the upper arm and forearm, hands and fingers were assessed using a cotton swab and recorded as normal, diminished, increased or absent. Proprioception was assessed in the thumbs and wrists using a 3-point scale, where 2 = all four attempts correct, 1 = 3/4 attempts correct and 0 = <3/4 attempts correct.

Thermal and mechanical thresholds

In paper III, thermal and mechanical thresholds were assessed using the Quantitative Sensory Threshold (QST) equipment (Somedic AB) (82, 83) (Fig. 5a and 5b). Thermal thresholds were assessed with the MSA Thermotest and included cold detection thresholds (CDT), warmth detection thresholds (WDT), cold pain thresholds (CPT) and heat pain thresholds (HPT). The mechanical tests, i.e., pressure pain thresholds (PPT) and pin prick pain thresholds (PPPT) were assessed with the Algometer and the SenseBox Electronic von Frey. The method of limits was used, i.e. the intensity of the stimulus applied to the skin was increased (or decreased) until the subject perceived a stimulus or felt it painful. The detection threshold was defined as the minimum intensity of a stimulus perceived as stimulus, and the pain threshold as the minimum intensity of a stimulus perceived as painful (83).

During the QST, the participants were assessed when sitting upright in a chair. They used a handheld switch in their unaffected/dominant hand and were instructed to press the switch when they felt cold/warm sensations, cold/heat pain or discomfort, and pressure/pin prick pain or discomfort. When the participant pressed the switch, the assessment stopped. All QST assessments were performed by the same examiner and lasted about one hour.

In the thermal tests, a thermode, 25 mm x 50 mm, with an initial temperature of 32° C and a speed of 1°/sec, was applied to the skin. During the cold tests the temperature gradually decreased until a minimum of 10° C. During the warmth/heat tests the temperature gradually increased, with a maximum temperature of 50° C. The thermal test was performed on the unaffected/dominant leg (i.e., reference point), on the unaffected/dominant upper arm and on the affected/non-dominant upper arm.

The PPT was assessed with an electronic algometer, using a probe with a pressure diameter of 1cm² and a slope of 50 kPa/s. The pressure was initiated at 10 kPa, and the examiner gradually increased the pressure until the participant pressed the switch. The maximum pressure was set to 1000 kPa. The unaffected/dominant arm and the affected/non-dominant arm were assessed. The probe was applied on three points: upper, middle and lower part of the middle deltoid muscle.

The PPPT was assessed with an electric von Frey transducer, using a 0.2 mm tip diameter with a speed of 10 g/sec. The PPPT commenced at 10 g and the examiner gradually increased the pressure until the participant pressed the switch. The maximum pressure was set to 400 g. The PPPT was assessed once over three points in the upper, middle and lower part of the deltoid muscle. The unaffected/dominant arm was assessed first and thereafter the affected/non-dominant arm.



Fig 5a.
Quantitative Sensory Test equipment (Somedic AB, Hörby Sweden); MSA thermotest.



Fig 5b.
Quantitative Sensory Test equipment (Somedic AB, Hörby Sweden); computer, sensbox, electronic algometer, electronic von Frey transducer, VAS response unit and hand held switch. The VAS response unit was not used in this study.

Outcome measures to assess activity limitations

In paper I, daily activities were assessed with the Barthel Index (BI) (84). Ten activities of daily living (feeding, bathing, grooming, dressing, bowels, bladder, toilet use, transfers from bed to chair and back, mobility and stairs) are assessed on a three-graded scale, with a scoring of 0, 5 and 10 points, giving a maximum score of 100 points. The scale was divided into three grades of dependency: independency (score 95-100), moderate dependency (score 60-90) and major dependency (score 0-55) (85). In paper IV, ability to perform daily hand activities was assessed with the ABILHAND Questionnaire (86, 87), which is a self-report outcome measure. ABILHAND measures self-perceived ability to perform complex hand activities in 23 daily situations. The participants rate their perceived difficulty in performing each activity based on a three-level response scale: 2 = easy, 1 = difficult or 0 = impossible. Activities not performed during the past three months are scored as missing responses. The ABILHAND is Rasch analysed (86, 87) and has been shown to be valid and reliable in persons with chronic strokes (87, 88).

Outcome measures to assess participation restrictions

In paper IV, perceived participation was assessed by the participation domain in Stroke Impact Scale (SIS) 3.0, domain 8 (59, 60); this domain can be analyzed separately and addresses the impact of stroke on work, social activities, quiet recreations, active recreations, role as a family member, religious activities, life control and ability to help others. The participants responded to the items in each domain using a 5-point rating scale from 5 = none of the time to 1 = all of the time. For each subject, the mean score of the items was calculated and converted into a percentage value. Higher scores indicate low restrictions in perceived participation, whereas low values indicate more restrictions in participation. The SIS is a stroke specific outcome measure developed from persons with mild to moderate stroke. SIS has been Rasch analysed (60), is reported to be reliable, valid and sensitive to change (59, 60) and is frequently used in clinical stroke studies (89).

Outcome measures to assess self-perceived health and life satisfaction

In paper I, self-perceived health status was assessed by SF-36 (62). SF-36 consists of 8 health domains. It is a common instrument and also suitable for use in older adults (90). In paper I, only two questions were used; 1. In general, how would you say your health is? (Excellent, very good, good, fair, poor), and 2. Compared to one year ago, how would you rate your health in general now? (Much better than a year ago, somewhat better than a year ago, about the same as one year ago, somewhat worse now than one year ago, much worse now than one year ago). In paper IV, life satisfaction was assessed with the Life satisfaction Checklist, LiSat-11 (65), which is a self-administered questionnaire that assesses global satisfaction with life in one item and domain-specific satisfaction in 10 items. Only the item assessing level of global satisfaction with life (i.e., life as a whole) was used here. LiSat-11 uses a six-step ordinal self-rating scale ranging from 6 = very satisfying to 1 = very dissatisfying. The response options were dichotomized, with scores of 5-6 meaning 'satisfied', and scores 1-4 meaning 'dissatisfied' as described by Fugl-Meyer et al. (65). The questionnaire has previously been used for individuals after stroke using the global question (life as a whole) as a measure of life satisfaction (66).

Site of examination and assessors

In paper I and II, approximately 70% of the participants examined were able to come to the outpatient clinic at the Department of Neurology, whereas the remaining were examined in primary care centers (approximately 10%) nursing homes (approximately 10%) and their own homes (approximately 10%). All assessments of shoulder pain and upper extremity were performed by the author. General assessments, as baseline data were performed in collaboration with a registered nurse. In paper III and IV all participants were assessed at the Department of Rehabilitation Medicine. Assessments in paper III were performed by two physiotherapists; one therapist performed the QST-

assessments and the author the rest of the assessments. Assessments in paper IV were performed by the author.

Statistics

Several statistical methods were used in the papers (Table III). The Mann-Whitney U-test and the independent sample t-test were used for continuous variables and the chi-square test and the Fisher's exact test for categorical variables. For pairwise comparisons, the Wilcoxon's sign rank test was used. Correlations between different variables were tested with the Spearman's rank correlation coefficient and Pearson's correlation coefficients. Logistic and linear regression analyses (univariate and multiple) were used for dichotomous and continuous dependent variables, respectively. Forward logistic analyses was used in paper I and in paper III and IV the enter method was used. The statistical program used was SPSS versions 12-21. P-values <0.05 were considered significant (paper I-IV).

Table III.

Overview of statistical methods

	Study I	Study II	Study III	Study IV
Wilcoxon signed rank test	X		X	
Mann-Whitney U-test	X	X	X	X
Independent sample t-test				X
Chi-2 test/Fisher's exact test	X		X	X
Spearman's rank correlation coefficient		X		X
Pearson's correlation coefficient				X
Univariate logistic regression analysis				X
Univariate linear regression analysis				X
Multivariate logistic regression analysis	X	X		X
Multivariate linear regression analysis				X

Ethics

Study I and II were approved by the Ethics Committee of the Faculty of Medicine, Lund University (Dnr LU 602-00) and study III and IV by the Regional Ethical Review Board in Lund, Sweden (Dnr 2011/471). The principles of the Helsinki Declaration were followed.

In all studies, participants received both written and verbal information about the purpose of the studies, the test procedure and their right to withdraw from the study at any time without giving any reason. Before the assessments, the participants gave their written informed consent.

In study I and II, all individuals with first-ever stroke were invited to take part in the study. Some individuals were severely affected by their stroke, for example by dysphasia and also by other impairments. For these individuals, assistance with assessments from spouses or persons were needed. Special caution had to be taken when measuring passive range of motion in individuals with PSSP because of discomfort when the arm was moved. Follow-ups were offered at the hospital, at the primary care center or in the participant's home, according to personal preferences. Visiting persons in their own home required respect for individual integrity. The overall impression was that individuals were satisfied to participate and also regarded it as an advantage to take part in the study.

In study III and IV, assessments were rather time-consuming and presupposed concentration from the participants. Also, the participants should be able to come to the Department of Rehabilitation Medicine as the QST equipment was not portable. Some potential participants found it difficult to come to the hospital, mainly due to their medical condition, and therefore they declined to participate. During the design of study III, we considered consequences for the participants with QST assessments as these might result in some discomfort for a short period after the assessment. Prior to the study, the researchers performed several assessments on each other, and also on healthy students as well as healthy retired persons to get familiar with the equipment, estimated the time required and calculated risk for pain. None of the test persons reported complaints of significance and thus planning for the assessments continued. The presumed participants were informed both verbally and writing about the risk for pain. As far as we know, no participant had complaints about pain due only to the assessments.

In study IV, the participants were asked about perceived participation and life satisfaction. Such questions may lead to a number of serious reflections and concerns. The participants therefore responded to the questions in a calm and quiet environment.

Results

Prevalence of PSSP

In the unselected stroke population with first-ever stroke (paper I), PSSP onset within four months after stroke was reported by 71 individuals (22%). Of these, 17 were pain free one year later (16 months follow-up), while a further 28 individuals had onset of PSSP during the same year period. At the 16 months follow-up, 305 individuals remained and among these, shoulder pain was reported by 74 individuals (24%). Taken together, during the first 16-months period, 99 (30%) of the 327 participants in the unselected stroke population developed PSSP. In the group of 58 individuals (paper II), 42 (72%) still had shoulder pain at 16 months.

For 55% of the individuals, PSSP occurred within two weeks after stroke and within two months, the percentage of PSSP had increased to 85% (paper I). Similar percentages are presented in paper II. In the selected population presented in paper III and IV, 18 (75%) of the participants reported onset of shoulder pain within two months after stroke.

PSSP characteristics

Moderate to severe pain intensity scored as ≥ 40 according to VAS-P was found in a majority of the PSSP participants in both populations; in 79% among the 71 PSSP participants presented in paper I and in 67% of the 24 PSSP participants presented in paper III and IV. Among participants with pain at both the four and 16-months follow-ups (paper I), the pain intensity was reduced at the second follow-up 16 months post stroke ($p=0.003$). Also in paper I, frequent shoulder pain (daily or constant) was reported by 84% of the PSSP participants at the four months follow-up, but at the 16-months follow-up, the earlier reported pain frequency had significantly decreased ($p=0.007$).

In both study populations, a majority of the PSSP participants experienced pain while the arm was moved voluntarily or passively. In paper I, 69 (97%) reported pain during arm movements four months after stroke and in the second population (paper III and IV) pain during arm movements was reported by 63%, while 33% reported pain both during movements and at rest.

Contributing factors to PSSP

Motor impairments

Reduced arm motor function was the main contributing factor to PSSP in both populations. In the population presented in paper I, shoulder pain was present in 83% of the participants with no motor function or severe motor impairments, while 50% of the participants with moderate motor impairments had shoulder pain. Among participants with normal motor function, only 5% had shoulder pain. Logistic regression analysis showed that two variables at baseline significantly related to PSSP four months post stroke. These two variables were i) severe impairments at baseline according to NIHSS ($p=0.008$) and ii) severely affected arm motor function at baseline (NIHSS item 5) ($p=0.03$). At the 16 months follow-up post stroke, only severely affected arm motor function at baseline (NIHSS item 5) was an independent predictor of shoulder pain ($p<0.001$).

In the population presented in paper III and IV, a significant difference was found in motor function between participants with and without PSSP ($p=0.03$) and in paper IV, PSSP was associated with decreased upper extremity motor function in the univariate regression analysis ($p=0.03$; OR 3.82; 95% CI 1.13-12.87).

The number of participants with subluxation differed significantly between participants with and without PSSP ($p<0.001$) in paper I, but in the population described in paper II, no significant difference was seen between the groups.

Though resistance to passive movements according to the modified Ashworth Scale was more frequently found among PSSP participants in both populations, no significant difference was found between PSSP and non-PSSP participants ($p=0.55$ in paper II and $p=0.20$ in paper III and IV).

Range of motion

Decreased passive range of motion was a contributing factor to PSSP in both populations. In the population presented in paper II, a low degree of passive range of abduction four months post stroke was a predictor for long-lasting PSSP ($p=0.05$; OR 4.46; 95% CI 0.99-20.10) and in the population presented in paper III and IV, participants with shoulder pain had significantly decreased passive shoulder abduction ($p<0.001$) in comparison to participants without shoulder pain. In the multivariate analysis presented in paper IV, decreased passive shoulder abduction was associated with upper extremity motor function ($p=0.02$; OR 1.03; 95% CI 1.00-1.05) but not with PSSP.

Somatosensory impairments

A significant difference in light touch between participants with and without PSSP was found in the population presented in paper I ($p < 0.001$). In the population presented in paper III, neither perception of light touch nor proprioception differed between the PSSP and non-PSSP participants. Moreover, no significant differences were found in thermal or mechanical thresholds between the participants with and without PSSP, though participants with PSSP had higher cold perception thresholds. Also, more PSSP participants reported abnormal cold sensation in the affected side ($p = 0.02$). Both stroke groups had generally higher thermal thresholds and more extreme low or high mechanical thresholds than the healthy controls. Thus, the relation between PSSP and thermal thresholds was weak and no relation was found between PSSP and mechanical thresholds.

Other contributing factors

Left-sided hemiparesis was shown to be a further risk factor for individuals with long-lasting shoulder pain ($p = 0.01$; OR 10.47; 95% CI 1.92-57.05) (paper II). Also pain frequency four months after stroke was found to be a predictor for long-lasting PSSP ($p = 0.02$; OR 6.85; 95% CI 1.46-32.14).

Consequences of PSSP in daily life

Activity limitations

The impact of PSSP on the ability to perform daily activities were described in both paper I and IV. In paper I, shoulder pain while dressing was reported by 36 individuals (51%) four months after stroke, but a significant reduction in shoulder pain while dressing was present at the second follow-up 16 months post stroke ($p = 0.025$). In study IV shoulder pain while eating and dressing was reported by 54%.

In the unselected population (paper I), individuals with PSSP had a reduced ability to perform daily activities as assessed by the Barthel Index ($p < 0.001$) four months after stroke, in comparison to individuals without PSSP. In the second, selected population (median 14 months post stroke) (paper IV), no significant differences were found between participants with and without PSSP in daily hand activities, as assessed by the ABILHAND questionnaire, even if the PSSP participants scored lower than the non-PSSP participants. In the regression analyses, PSSP was not associated with daily hand activities. Instead, proprioception ($p = 0.01$; $B = 1.16$; 95% CI = 0.26-2.05), passive shoulder abduction ($p = 0.03$; $B = 0.01$; 95% CI = 0.001-0.02) and resistance to passive movements ($p = 0.03$; $B = 0.85$; 95% CI = 0.09-1.62) explained 44% of daily hand activities in the linear multivariate analysis.

Perceived participation restrictions

Even if mean perceived participation was scored lower by the PSSP participants than the non-PSSP participants in paper IV, perceived participation was however in the multivariate analyses explained by other factors than PSSP. In the final model, daily hand activities ($p < 0.001$; $B = 5.23$; 95% CI = 2.55-7.90), vocational situation ($p = 0.003$; $B = 14.48$; 95% CI = 5.32-23.64) and sex ($p = 0.03$; $B = 10.77$; 95% CI = 1.19-20.35) explained 41% of perceived participation. So in short, this study did not reveal a significant relation between PSSP and the individuals perceived participation.

Self-perceived health and life satisfaction

In paper I, self-perceived health assessed by the two questions in SF-36 “In general, how would you say your health is?” and “Compared to one year ago, how would you rate your health in general now?” was scored significantly lower by the individuals with PSSP in comparison to individuals without PSSP ($p < 0.001$).

In paper IV, only 33% of the PSSP participant rated their life satisfaction (life as a whole) as satisfied compared to 56% of the non-PSSP participants, but the difference was not significant. In the multivariate analyses, no specific association between life satisfaction and PSSP was found. In the final model, perceived participation was the only variable associated with life satisfaction ($p = 0.001$; OR 1.08; 95% CI 1.03-1.13).

General discussion

The studies in this thesis have focused on evaluating the prevalence of PSSP, contributing factors and consequences in daily life. The results showed that PSSP is common in individuals with reduced upper extremity motor function. Left-sided hemiparesis, pain frequency and decreased passive shoulder abduction four months after stroke are predictors for long-lasting PSSP. In individuals with mild to moderate upper extremity paresis, somatosensory impairments seem to have only a small impact on the pain and the PSSP appears to have only a small impact on their life situation.

Prevalence of PSSP

In paper I, the prevalence of PSSP (22% four months post stroke and 24% 16 months post stroke) was in agreement with Ratnasabapathy et al. who included a similar population and reported a prevalence of 23 % six months after stroke (31). Langhorne et al. (32) reported a prevalence of 9%, but their study had a different design as it was retrospective and based on medical records. Moreover, 75-85% of the participants in the present studies reported onset of shoulder pain within two months, which is rather similar to 87% reported by Gamble et al. (30).

Within a one-year perspective post-stroke (paper I) the pain was resolved in around 20% of the individuals, mainly among individuals with mild to moderate upper extremity impairments. Furthermore, among individuals able to score VAS-P at both follow-ups, pain intensity was significantly relieved. Also another study found that shoulder pain was resolved or relieved over time (30). It is unclear why PSSP decreased over time, but suggestions are that the individuals might have regained improved upper extremity motor function, learned how to use the extremity in pain free positions or have become accustomed to the pain.

Contributing factors to PSSP

According to the results from this thesis and previous studies (30, 35, 36, 43), some shoulder impairments seem to be present in a majority of the individuals with PSSP such as moderate to severe pain intensity, frequent pain, pain when moving the arm, reduced upper arm motor function and decreased passive range of shoulder motion. These impairments need attention, because they could be contributing factors to PSSP.

An association between shoulder pain and somatosensory impairments has been shown by previous authors (44, 48, 49) but could not be confirmed in this thesis (paper III).

A small but non-significant difference in cold detection thresholds was found between PSSP and non-PSSP participants. Even if the PSSP participants had a significantly increased self-reported cold sensitivity in everyday life in comparison to the non-PSSP participants, somatosensory differences in general were small between PSSP and non-PSSP participants, indicating that PSSP in the present population is mainly nociceptive. Roosink et al. found increased abnormal cold sensation, allodynia, hyper- and hypoalgesia to pressure as well as higher thresholds for touch and electrical stimuli among PSSP participants (48). In another study by Roosink et al. widespread pain was found among individuals with PSSP (91). Zeilig et al. reported also higher thermal thresholds in the affected side in the PSSP group compared to the non-PSSP group (44). These three studies suggest that neuropathic mechanisms may play a role in PSSP. Furthermore, Soo Hoo et al. reported lower PPT thresholds in the PSSP group than in the non-PSSP group and concluded that this indicate a hypersensitivity for pressure (49). However, the study populations and the differences in somatosensory between PSSP and non-PSSP participants in these studies were small. Therefore, their conclusion that neuropathic mechanisms may play a role in PSSP must be interpreted with great caution. Sensitization might be present in a subpopulation of individuals with PSSP, but a larger study population is definitely required to confirm this.

Who are at risk of developing PSSP?

In study I, a relationship between shoulder pain and reduced upper extremity motor function was found. This has been reported by several others (30, 31, 35, 92). However, in our study we were also able to differentiate between individuals with no or severely affected arm motor function where shoulder pain was evident in more than 80%. Moreover, in individuals with moderately affected arm motor function shoulder pain was found in 50%.

Interestingly, a recently published study has reported a lower prevalence of upper extremity impairments at stroke onset (50%) (8) in comparison to earlier studies (70-80%) (7, 9). This might be due to more effective treatment with thrombolysis and a more structured stroke care and rehabilitation (8). These figures indicate a development in stroke treatment which probably can decrease the prevalence of PSSP. However, for those individuals developing PSSP, more knowledge is needed to enhance the development of more effective treatments.

Who are at risk for long-lasting PSSP?

In paper II, left-sided hemiparesis, frequently reported pain and decreased range of abduction were found to be predictors for long-lasting shoulder pain. An association between long-lasting shoulder pain and left-sided hemiparesis is described also in other studies (31, 33, 51). The underlying mechanism behind is not clear, but suggestions from previous studies are that neglect might influence these findings, as individuals with neglect might have a greater tendency to avoid using their arm (93). They might also

have an increased risk for trauma of the shoulder because of lack of proper selfcare and positioning (51).

Also pain frequency turned out to be of importance for long-lasting PSSP. This highlights the question of how to assess pain; different qualities, such as intensity, frequency and mode, needs to be taken into consideration when assessing PSSP. Assessing only pain intensity is not enough to gain a thorough picture of the pain and in the clinical setting as well as in research, several qualities are needed to describe the total pain situation.

Decreased passive range of abduction as a predictor for long-lasting shoulder pain corresponds with the results from Roosink et al. who found that restricted range of abduction was associated with PSSP six months post stroke (43). In addition, other authors have described decreased range of motion in the shoulder six months post stroke in individuals with PSSP (30, 35). However, the underlying relation remains unclear. The question is if the decreased range of motion is a consequence of decreased upper extremity motor function, or if the decreased range of motion itself causes pain.

Consequences of PSSP in daily life

Participants in paper I described that shoulder pain constantly or often had an impact on activities in daily life such as dressing (50%) and during ambulation (30%), and in paper IV, about 50% of the participants described shoulder pain when eating and dressing. In paper I, the activity level as assessed with the Barthel Index (BI), was significantly lower in PSSP participants than those without PSSP four months post stroke. Also another study with a similar population, found that a majority of PSSP participants had significantly lower BI scores two months post stroke than those without PSSP (55). However, two other studies found no significant differences in BI scores between PSSP and non-PSSP participants (30, 37) six months post stroke. Even if a reduced upper extremity motor function was found in the PSSP participants in comparison with the non-PSSP participants in paper IV, no significant difference was found in the ability to perform daily hand activities as measured by ABILHAND. Other authors who have assessed activity in upper extremity have not found an association to PSSP (56-58). One explanation might be that individuals over time adapt to the pain and use compensatory strategies where the affected arm is less involved in daily activities. Another explanation could be that ABILHAND consists of bimanual tasks where the individuals do not have to raise their arm over the horizontal plane – a position where shoulder pain often occurs. To summarize, a significant difference in overall activity between PSSP and non-PSSP participants was seen in the unselected population, but in the selected population of individuals with mild to moderate upper extremity impairments, PSSP seems to have limited impact on daily hand activities.

In study IV, two-thirds of the PSSP participants reported frequent pain and moderate to severe pain intensity. Despite that, no significant difference was found between the PSSP and non-PSSP participants in perceived participation. Instead, daily hand activities were associated with perceived participation in the multivariate analyses. Harris & Eng did not find an association between PSSP and participation, but showed that arm and hand activity measures were related to participation (57). Contrary to these results, Faria-Fontini et al. found a relation between PSSP and participation when the Stroke Specific Quality of Life instrument was used (56). Thus, further studies about the relationship between PSSP and participation are needed.

In paper I, a significant difference in self-perceived health was seen between participants with and without PSSP, but as the PSSP individuals also had other severe impairments in comparison to the non-PSSP individuals, other impairments than the shoulder pain might have contributed to the difference. The PSSP participants in paper IV scored a lower life satisfaction than the non-PSSP participants, but the difference was not significant. Perceived participation, rather than shoulder pain, seemed to be an important contributing factor for life satisfaction. No previous study investigating the relationship between PSSP and life satisfaction has been found, but one study reported an association between PSSP and pain-related quality of life in persons with chronic stroke (58). One explanation for the results in paper IV might be that several impairments following stroke could lead to different activity limitations and participation restrictions. Shoulder pain is only one impairment among several which have to be considered when evaluating the life situation. Also, a majority of the participants were mildly to moderately affected in the upper extremity after their stroke. As individuals with severe impairments were not included in this study, the results can not be generalized to the whole stroke population in its entirety.

Methodological considerations

Participants

To be able to recruit participants for study III and IV, individuals with stroke onset within a period of 2,5 years from a large area had to be sought. A large number of medical records were screened, however, due to the specific inclusion- and exclusion criteria, only 49 participants could finally be included in the study. These figures reflect difficulties in recruitment when studying post-stroke shoulder pain in a selected population.

Methods

In this thesis, several objective and self-report outcome measurements covering different domains according to ICF have been used which strengthens the studies. Other authors have also pointed out the need to cover different aspects when describing consequences

after stroke (94, 95). The intention was to use only valid and reliable instruments. However, to find translated, reliable and valid outcome measures is a challenge. For example, when searching for measurements to assess daily activity limitations, instruments covering relevant activities for both sexes, updated for the culture and demands of the present time are needed. Another challenge is to find instruments that could be used in different settings, such as in the participant's home and at the hospital. Other instruments could have been used, but not all measures used in earlier studies for assessing motor function and pain, as for example Frenchay Arm Test and the Brief Pain Inventory, are available in Swedish.

In paper I, activity limitation was assessed with the Barthel Index, which is a more general instrument describing ability to perform daily activities as eating, grooming and mobility and not as specific as the ABILHAND questionnaire used in paper IV, which describes the ability to use the arm and hand in daily activities. The advantage with Barthel Index is that it is simple, while in ABILHAND, several aspects have to be considered for the participants when answering the questions. Therefore, studies using these different instruments make direct comparisons difficult, even if both represent activity according to ICF.

Even if the ABILHAND questionnaire is a Rasch analysed instrument, with good psychometric properties (87) and recommended for stroke studies (88), it was developed more than ten years ago and in another context. Some items, such as shelling hazel nuts and sharpening a pencil might not be relevant, and further more, some items such as threading a needle and wrapping up gifts might be gender specific activities.

The methods used to assess self-perceived health (96), perceived participation (59, 60) and life satisfaction (66) have all been used in other stroke studies and were therefore considered suitable for our populations. While the SIS participation domain contains questions about self-perceived participation in different situations, the questions used in these studies in SF-36 such as "In general, how would you say your health is?" and "Compared to one year ago, how would you rate your health in general now?" together with the Life satisfaction checklist (life as a whole) cover more general aspects.

Pain intensity, frequency, localisation and quality were recorded and assessed. All these aspects contribute to the total experience of the pain and to the impact on daily life. The instruments used in our studies have however some limitations. According to a previous study (97) many individuals who have had a stroke are unable to successfully complete visual analogue scales, related to hemi-neglect and visuospatial impairment. This was actually the case in the population used in study I and II, where VAS-P was difficult to assess for some individuals.

Pain drawing and an extended examination of neuropathic pain, for example by using the neuropathic pain diagnostic questionnaire Doleur Neuropathic 4 (DN4) (98), or by assessing allodynia using a brush in a structured way (Brush Stroke allodynia), could

have been added in paper III to give more aspects to the pain situation. Moreover, instruments assessing other consequences of PSSP could also have been used in our studies, for example depression, sleep disturbances and anxiety. However, in study III and IV individuals with severe depression were excluded because they had to be alert and concentrated during the QST assessments.

In paper III, the QST method was used, which is a relatively new method to assess somatosensory impairments in individuals with stroke. The QST method has earlier mainly been used for other diagnoses. Experiences from studies investigating chronic pain, for example fibromyalgia, showed decreased QST thresholds for stimuli, i.e. hypersensitivity. Previously hyposensitivity has been demonstrated in individuals with stroke (44, 48). Stroke in itself might lead to somatosensory impairments, and therefore it might be difficult to evaluate if they are related to the stroke or to the pain. Also, when assessing somatosensory function with QST using the method of limits, the reaction time is included. If stroke patients in general have a prolonged reaction time, there might be a bias in the assessments. When analyzing the results, it was shown that many participants did not experience pain even at the lowest limit (10°) in the Cold Pain Threshold test nor at the highest limits (1000 kPa in PPT and 400 g in PPPT) in the mechanical tests. Whether this was due to reaction time or due to a changed somatosensory status, needs to be further studied. An alternative protocol could have been used; the method of levels, in which a series of predefined stimuli are applied to the skin, and where the subject is asked to report for each stimulus whether the stimulus is perceived or not, or whether it is painful or not (83). Overall, more studies with larger study populations are needed to be able to draw conclusions if somatosensory impairments are related to PSSP. Even if QST is an established method to assess somatosensory changes, few studies have been done in stroke populations, and reliability is lacking.

Strengths and limitations

There are several strengths and limitations in the studies in this thesis. The first study is based on a large unselected population with few drop-outs. One disadvantage was that detailed assessments were difficult to use, due to the fact that some participants had severe impairments and fatigue. An example is that motor function was assessed only in the shoulder and not in the whole upper extremity. Moreover, there was a difficulty to deal with pre-morbid status, i.e. shoulder pain before stroke onset. In study III and IV, the advantage was a well-defined study population and the use of established outcome measures. However, the population was small and the exclusion of individuals with severe upper extremity impairments, makes results difficult to generalize to the whole stroke population.

Clinical implications and future studies

Prevention

Results from studies in this thesis show that reduced upper extremity motor function is associated with PSSP, and that a majority of the individuals develop PSSP within two months after stroke onset. This emphasizes the importance of regaining upper extremity motor function and stability around the shoulder to reduce the risk for shoulder pain. Therefore, motor training of the upper extremity should be a priority from the early stages of rehabilitation. The individual should be encouraged to use the affected arm and hand as much as possible in daily activities. This thesis has also shown that decreased range of motion is common in individuals with PSSP, which requires gentle passive and active movement to maintain range of motion in the affected shoulder. But, these suggested interventions need to be further evaluated in future research. To evaluate if early intensive treatment, consisting of motor training and passive and active movements, will prevent PSSP is an important area, but needs to be further investigated.

Assessments

In all stages of the rehabilitation, individuals who are at risk of developing PSSP are important to identify. In those individuals, it is important that physiotherapists and other health professionals conduct a thorough examination of the upper extremity function including motor function, somatosensory status and range of motion, and a thorough examination of the pain including intensity, frequency, distribution, pain quality and additionally pain in other locations of the body. To be able to evaluate how PSSP impacts on the individual's life, the pain needs to be described in several ways according to the ICF. Therefore, there is a need to develop protocols that could be used in the clinical settings as well as in research. Furthermore, even if the results from studies in this thesis suggest that neuropathic pain is not so common after stroke, it is important to identify individuals with widespread pain to provide proper treatment.

Treatments

Today, several treatments for PSSP are used in the clinic, for example transcutaneous electrical stimulation (99, 100), active movements (15), passive or active range of motions exercises (101), slings/supportive devices or strappings to reduce subluxation (102, 103), analgesics or anti inflammatory medication (101), intraarticular corticoid injections and botulinumtoxin (53).

As PSSP is suggested to have multifactorial causes, single treatment methods might be difficult to evaluate at a group level. To be able to reduce long-lasting PSSP, a combination of pain treatment and movement exercises might be needed in conjunction. However, the effects need to be evaluated in future research. So far, only intramuscular NMES has been shown to be effective in a three months perspective (53),

but this method is usually not available in the clinical setting. As there is no evidence that neuropathic mechanisms play a role in PSSP, treatments for the nociceptive pain, as is commonly used today seems to be the most effective. In future research, there is a great need to evaluate the effects of existing treatments as well as new novel treatments or treatment strategies.

Considerations for future studies

When designing future studies, several considerations have to be taken into account. Even if large study populations are of importance, it might be difficult to conduct studies that use strict exclusion- and inclusion criteria. Another difficulty when studying PSSP, is that individuals with no or almost complete loss of arm motor function are often severely disabled and therefore might have limited possibility to participate in studies. Multicenter studies are a plausible solution, but cultural factors as well as differences in stroke care must then be considered.

The lack of a precise definition of PSSP is a problem when recruiting participants for studies. In the future, it would be desirable with some form of consensus between researchers to get a more uniform definition; a time span for onset and a set of criteria based on established clinical findings and previous research. Also, in future studies pain has to be measured in a variety of ways, covering various aspects of pain and all the ICF domains. A consensus about which measurements that should be recommended to use for the PSSP population is needed. To be able to compare the results, the same or very similar outcome measures are warranted. However, one drawback is that all instruments are not validated in languages other than English. Another research area is therefore to translate instruments into different languages and assess their validity and reliability.

Increased knowledge about which QST methods that should be used in persons after stroke to optimally assess the somatosensory impairments are needed. This require large study populations. Also, more knowledge about pain mechanisms is needed to be able to identify individuals at risk for long lasting pain. Studies from chronic pain diseases have suggested that genetic factors might play a role in pain development (104). Moreover, after being exposed to stressful life events, some individuals tend to get chronic pain (105). A suggestion is therefore that some individuals might be predisposed to develop chronic pain.

Future studies should also focus on increasing the knowledge of how individuals with PSSP adapt to the pain situation, maybe by using qualitative research designs. When measuring consequences in daily life – self-reports alone might not cover all aspects according to ICF – and they might be too obtuse since the questions are predetermined. Thus, qualitative research might offer a deeper understanding of the consequences following PSSP.

Conclusions

In response to our initial research questions, we found the following results:

In the unselected population of 327 individuals, 22% developed PSSP within four months and almost one third developed PSSP within the first 16 months after stroke onset. The majority had moderate to severe pain. The increased risk of PSSP for individuals with a severely affected arm motor function (>80%) needs close attention in post-stroke care. PSSP is associated with upper extremity motor function also in individuals with mild to moderate upper extremity impairments, which indicates that upper extremity motor function is an important contributing factor to PSSP.

A high proportion of persons with shoulder pain four months after stroke are at risk of having persistent PSSP one year later. Left-sided hemiparesis, pain reported frequently and decreased passive shoulder abduction at four months are predictors for long-lasting PSSP and require increased attention in the rehabilitation setting.

Somatosensory impairments are common among individuals with mild to moderate upper extremity impairments after stroke compared to healthy controls, but the non-significant differences in QST thresholds between the PSSP and non-PSSP participants indicate that somatosensory impairments have only a small impact on PSSP.

Pain in daily activities is common in individuals with PSSP. Self-perceived health was associated with PSSP in an unselected population, but in individuals with mild to moderate upper extremity impairments after stroke, a weak association with daily hand activities, perceived participation and life satisfaction was seen. This indicates that PSSP may selectively only have a small impact on a their life situation.

Populärvetenskaplig sammanfattning

Det övergripande syftet med denna avhandling var att öka kunskapen om skuldersmärta efter stroke avseende förekomst, bidragande faktorer och konsekvenser i det dagliga livet.

Stroke är i Sverige den vanligaste orsaken till funktionsnedsättning hos vuxna. Vanliga funktionsnedsättningar vid insjuknandet är nedsatt rörelseförmåga i ena kroppshalvan, känselnedsättning, balansstörning, synfältsbortfall och talsvårigheter. Smärta är vanligt efter stroke och har uppgetts drabba mer än en tredjedel av personerna. Skuldersmärta i den svaga sidan är en av de vanligaste typerna av smärta. Orakerna till skuldersmärta efter stroke är fortfarande inte klarlagda, men anses vara multifaktoriella. Skuldersmärthan kan inverka på det dagliga livet, men på vilket sätt är ofullständigt kartlagt.

I delarbete I studerades förekomsten av skuldersmärta, liksom bidragande faktorer, i en grupp bestående av 327 personer som insjuknat i stroke för första gången. Vid uppföljning fyra månader efter insjuknandet, hade ca 20 % utvecklat skuldersmärta. Skuldersmärthan debuterade vanligen inom några veckor eller någon månad efter insjuknandet och hade samband med graden av rörelseförmåga i axeln och armen. Vanligast var smärta i samband med rörelser och smärtan påverkade därför dagliga aktiviteter såsom påklädning och förflyttning.

I delarbete II studerades vilka faktorer som bidrog till långvarig skuldersmärta. I studien ingick 58 personer från den första studien, som alla hade nedsatt rörelseförmåga i ena sidan vid insjuknandet och skuldersmärta fyra månader efter insjuknandet. Vid uppföljning ett år senare hade 70% kvarstående smärta i skuldran. Faktorer associerade med långvarig skuldersmärta var nedsatt rörelseförmåga i vänster kroppshalva, frekvent smärta liksom nedsatt ledrörlighet i axeln.

I det tredje och fjärde delarbetet undersöktes 49 personer med stroke, 24 med och 25 utan skuldersmärta, och som hade lätt till måttlig nedsättning av rörelseförmågan i den drabbade armen och handen. I det tredje delarbetet ingick dessutom 11 ålders- och könsmatchade friska kontrollpersoner som inte hade någon skuldersmärta.

I delarbete III studerades om känsel förändringar har betydelse för skuldersmärthan. Quantitative Sensory Testing, QST, användes för att mäta trösklar för temperatur, tryck och stick. Mätning av beröring och ledkänsl utfördes och personerna tillfrågades hur de upplevde sin känsel. Resultaten visade ingen statistisk säkerställd skillnad mellan personerna med och utan skuldersmärta gällande trösklar för temperatur, tryck och

stick. Däremot hade personerna som drabbats av stroke, både med och utan skuldersmärta, högre trösklar för temperatur, dvs reagerade senare på stimuli än kontrollgruppen. De hade också i större utsträckning extremt höga eller låga trösklar för tryck- och stickstimuli jämfört med kontrollgruppen. Upplevelse av förändrad känsel för kyla var vanligare i gruppen med skuldersmärta jämfört med gruppen utan skuldersmärta.

I delarbete IV studerades hur skuldersmärthan efter stroke påverkar funktions- och aktivitetsförmågan, upplevd delaktighet och livstillfredsställelse. Smärtekaraktäristika registrerades och rörelseförmåga, ledrörlighet och känsel i armen bedömdes. Undersökning av aktivitetsförmåga gjordes med ABILHAND, ett frågeformulär som mäter självskattad förmåga att utföra vardagliga handaktiviteter. Upplevd delaktighet skattades med Stroke Impact Scale och livstillfredsställelse med LiSat-11. Resultaten visade att personerna som drabbats av skuldersmärta hade sämre rörelseförmåga och ledrörlighet i armen än de som inte hade skuldersmärta. Däremot påverkade inte skuldersmärthan förmågan att utföra vardagliga handaktiviteter, upplevd delaktighet eller livstillfredsställelse.

Sammanfattningsvis visar studierna i denna avhandling att skuldersmärta efter stroke är vanligt bland personer som har nedsatt rörelseförmåga i armen. Vänstersidig svaghet, frekvent smärta och nedsatt ledrörlighet i axeln fyra månader efter insjuknandet är faktorer associerade med långvarig skuldersmärta. Förändrad känsel efter stroke tycks endast ha en liten inverkan på skuldersmärthan hos personer med lätt till måttlig nedsättning av rörelseförmågan i armen. Skuldersmärthan hos dessa personer tycks inte begränsa det dagliga livet i någon större utsträckning, möjligen på grund av en anpassning till att inte använda armen i situationer där smärtan förekommer. Resultaten i avhandlingen kan leda till en bättre förståelse för hur vanligt skuldersmärta efter stroke är. Genom att bidragande faktorer beskrivits kan personer med risk att drabbas av skuldersmärta lättare identifieras och omhändertagandet förbättras.

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