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Pain, depression and anxiety in acute stroke patients

An observational study

Graduate thesis in medicine

Trondheim, December 2015

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Preface and acknowledgements

This graduate thesis in medicine is written using data from an observational study performed in the stroke unit at St. Olavs Hospital in 2012 and 2013. The statistical analyses and the scientific writing have been performed during autumn 2015.

I want to acknowledge everyone who has contributed in making this thesis possible.

First I want to thank my inspiring supervisor Torunn Askim for guiding me and providing constructive feedback throughout this period. You have encouraged me to strive for independent thinking, but your door has always been open for constructive discussions and reassurance in times of doubt.

Thanks to my co-supervisor Bent Indredavik for good advices and help in planning this student thesis, and useful feedback in completing this work.

I also want to acknowledge the nurses Turid Aasbø, Sølvi Åsvold, Pia Olsen and Maren Uppheim, who have made a great contribution in gathering data for this thesis, and Hild Fjærtoft from the Norwegian Stroke Register who have supported us with important data.

At last I want to thank all the patients who have taken the time to participate in this study; this would not have been possible without you.

Thank you.

Martina Reiten Bovim

Trondheim, December 2013

Abstract

Background

Pain is shown to be quite common in the chronic phase after stroke. Psychological symptoms of depression and anxiety are also considerable problems in the chronic phase, and are associated with impaired functional outcome. However, there are ambiguous results on the prevalence of pain and symptoms of depression and anxiety in the very early phase, and to which extend post stroke pain can be prescribed to the stroke. The primary aim of the present study was to assess the frequency of pain and symptoms of depression and anxiety during the first two weeks after stroke in a group of unselected stroke patients treated in a comprehensive stroke unit with both acute care and early rehabilitation. The secondary aims were to investigate the most common sites for the pain, how pain, depression and anxiety were related to stroke severity and to assess the association between pain, depression and anxiety during the same period.

Material and method

Acute stroke patients admitted to the stroke unit at St. Olavs Hospital in Trondheim were eligible for inclusion in this prospective observational study. Patients were followed for two weeks after the stroke. Pain, depression and anxiety were assessed through simple questionnaires once a week. Pain was assessed by the first three items of the Brief Pain Inventory questionnaire, and it was distinguished between pain that occurred prior to the stroke and novel pain that occurred after onset of stroke. Symptoms of depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS). Patients with an early discharge from hospital were contacted by telephone and asked to respond to the questionnaires during follow-up.

Results

A total of 222 patients were screened for inclusion and 185 patients were included in the study. Mean (SD) age was 76.9 (8.51), 88 (47.6%) of the patients were women, and mean (SD) score on the Scandinavian Stroke Scale (SSS) was 37.0 (16.40). Of these, 136 were able to respond to the pain questionnaire, and 115 responded to HADS in both weeks. Pain was present in 31 patients (22.8 %) during the first week; 16 patients (11.8 %) claimed that the

pain had occurred subsequent to the stroke, while 15 patients (11.0 %) said that the pain had been present before the stoke. A total of 47 patients (34.6 %) experienced pain in the second week, which was significantly more patients compared to the first week, $p<0.001$. During the first week, 4 patients experienced novel pain in their affected arm. Otherwise pain was most often localized to the head or the neck.

Twelve (10.4 %) and 13 (11.3 %) patients scored above cutoff for symptoms of respectively depression and anxiety during the first week. During the second week the numbers were 11 (9.6 %) and 13 (11.3 %) patients.

Conclusion

The present study showed that 23% of patients treated in an evidence-based stroke unit experienced pain during the first week after stroke. Half of the reported pain was pain that had occurred before the stroke and the frequency of pain increased significantly from the first to the second week after stroke. New pain was most frequently localized to head or neck. Symptoms of depression and anxiety were also present, but were not more frequent than in the general elderly population reported in other studies. The frequency remained stable during the first two weeks. Few patients with severe strokes were able to respond to the questionnaires; which made it difficult to investigate the association between stroke severity and pain, symptoms of depression or symptoms of anxiety in this study. Future research should explore the relationship between pain, depression and anxiety after stroke more thoroughly, and identify ways of preventing these complications after stroke in the future.

Contents

Background

Stroke is the second leading cause of death worldwide (Lozano et al., 2012), and causes serious disability in many of those affected (Bonita, Solomon, & Broad, 1997). Mortality after stroke is declining in almost all age groups, and today approximately 13 % of stroke patients in Norway dies within 30 days after stroke (Helsenorge, 2013; Vaartjes, O'Flaherty, Capewell, Kappelle, & Bots, 2013). Because more people survive having experienced a stroke, also among elderly people (Ellekjaer & Selmer, 2007), more patients live with the physical and psychological consequences of having had a stroke.

Incidence of stroke differ around the world, and increases with age. Incidence of stroke in people aged 55 years or more ranges between 4.3-6.5 per 1000 person-year (Feigin, Lawes, Bennett, & Anderson, 2003). Prevalence of stroke also increases with age, and ranges from 46.1 to 73.3 per 1000 population in people aged 65 years or more (Feigin et al., 2003). In Norway, it is estimated that 15.000 strokes occur each year (Ellekjaer, Holmen, Indredavik, & Terent, 1997). Of these, 11.000 are first-time ever strokes, while the remaining are relapsing strokes (Ellekjaer & Selmer, 2007). Mean age in female first-ever stroke patients is 77.7 years and 75.3 years in men (Ellekjaer et al., 1997) and 89 % of first-ever stroke occurs in patients aged ≥65 years (Ellekjaer et al., 1997). There are only small differences between men and women below 75 years in the risk of experiencing stroke, but in older patients the risk is higher in men. However, since women live longer than men, there are more women than men experiencing stroke in absolute numbers (Ellekjaer & Selmer, 2007).

Stroke may have great socioeconomically impact on the society, with considerable costs. The first year after a stroke is estimated to cost about 150 000 to 170 000 NOK, and a lifetime expense after stroke is 600 000 NOK (Fjærtoft & Indredavik, 2007). If the age related incidence remains stable, the number of new stroke patients each year is estimated to increase towards 2030 due to the increasing percentage of elderly people in the population (Waaler, 1999). And since mortality after stroke decreases, the morbidity and the socioeconomic burden that a stoke adds to the person's life and to the society may become an increased challenge in the future as the amount of elderly people in the western world is increasing.

According to the Norwegian guidelines on treatment and rehabilitation after stroke, Norwegian stroke patients should be treated in comprehensive stroke units (SU) with both acute care and early rehabilitation (Health, 2010). Stroke units are the most favourable

treatment of stroke patients, with an increased likelihood of surviving the stroke, returning home and regain independency ("Organised inpatient (stroke unit) care for stroke," 2013). Some of the most important features of SU care are acute management to ensure that physiological homeostasis is maintained, the early mobilization, management of complications and skilled nursing. Multidisciplinary teams and careful management of food and fluid intake are other important characteristics of stroke unit care (Indredavik, Bakke, Slordahl, Rokseth, & Haheim, 1999; Langhorne, Pollock, & Stroke Unit Trialists, 2002).

Reduction of certain complications, especially immobility related complications like infections and pressure sores, has shown to be one of the achievements from treating stroke patients in SUs with focus on early mobilization (Govan, Langhorne, Weir, & Stroke Unit Trialists, 2007). Complications, particularly pneumonia, are associated with an increased length of stay in hospital. Even though SU treatment seems to reduce the frequency of complications, a considerable amount of patients still experience complications after an acute stroke (Indredavik, Rohweder, Naalsund, & Lydersen, 2008). Some of the most common complications are fever, urinary tract infections, pneumonias, progressing stroke and falls (Indredavik et al., 2008; Ingeman, Andersen, Hundborg, Svendsen, & Johnsen, 2011). A recent study from St. Olavs Hospital in Trondheim has shown that the frequency of complications has decreased over the past 10 years, indicating that the SU treatment continuously improves in managing complications (Bovim, Askim, Lydersen, Fjærtoft, & Indredavik, 2015)

In addition to the abovementioned complications, patient reported complications such as pain, and also psychological complications such as depression and anxiety may occur in stroke patients.

Post-stroke pain

The reported frequency of post stroke pain seems to vary considerably. A study on stroke patients during the first 4 days after admission to a neurologic department found, by asking participants if they experienced pain in temporal relation to stroke onset, that 37.8 % experienced newly developed pain (Hansen et al., 2012). This number increased towards 3 and 6 months, particularly in shoulder pain which increased from 1 % in the acute phase to 12 % at 6 months. Headache, on the other side, was most frequent in the acute phase, decreasing from 33 % in the acute phase to 13 % at 6 months. Another study on complications after

stroke found an increase of diffuse pain, from 12 % to 24 % during the first week after stroke, and even further increase to more than 50 % at 3 months (Indredavik et al., 2008). There seem to be a considerable risk of developing chronic pain; In a study from Bergen, 44.6 % of stroke patients reported pain at 1 year after the stroke (Naess, Lunde, Brogger, & Waje-Andreassen, 2010). Hansen, Marcussen, Klit, Andersen, Finnerup and Jensen (2012) found that 45.8 % of patients experience pain defined as "newly developed" within 6 months after stroke. Another study found the prevalence of pain one year after the stroke to be 49%, but it was related to the stroke in only 21 % (Lundstrom, Smits, Terent, & Borg, 2009). Appelros (2006) found that 11 % of stroke patients have pain that they relate to the stroke after one year. As these studies show, there are some inconsistencies in the literature investigating stroke-related pain in the acute and chronic phase after stroke.

Traditionally, shoulder pain has been considered as a common type of pain after stroke, but particularly headache, and also central pain and other types of pain are seen after stroke (Hansen et al., 2012). At least one-fifth of patients are reported to have painful shoulder in the first 6 months after stroke (Warlow et al., 2008). Many factors have been associated with painful shoulder, for instance spasticity, severe weakness of the arm, neglect, sensory loss and others, but their role is unclear. Central post-stroke pain is described as a superficial burning, lacerating or pricking sensation related to damage in the sensory tracts of the central nervous system caused by the stroke, and many studies find the frequency of such pain to be around 10 % (Ob & Seo, 2015). Examining other types of pain shows that headache, shoulder pain, muscle stiffness and other pain, except joint pain, is more common in a stroke population than the general population (Klit, Finnerup, Overvad, Andersen, & Jensen, 2011). One study found that 39% of stroke patient reported pain after the stroke, while the frequency in a reference group was 28.9 %. Thus the stroke patients experienced significantly more pain than the non-stroke population. (Klit et al., 2011). Another population based study (HUNT) found that chronic pain, defined as moderate, severe or very severe pain on 3 or more of 4 consecutive measures 3 months apart, from baseline to 9 months follow-up, was present in 26 % of the general population in Nord-Trøndelag, Norway (Landmark, Romundstad, Dale, Borchgrevink, & Kaasa, 2012). The use of analgesics for shoulder pain during hospitalization after stroke is below 10 %, while one third uses analgesics for other kinds of pain (Davenport, Dennis, Wellwood, & Warlow, 1996; Langhorne et al., 2000).

Methods of measuring pain

Pain is a subjective unpleasant sensation, which is difficult to measure objectively. There are different methods for assessing pain in a population. It is interesting distinguish between pre-stroke pain and stroke-related pain when discussing frequency of pain after stroke. Some studies examine how much analgesics are used for pain in stroke patients and do not give account for whether the patients were taking analgesics before the stroke (Langhorne et al., 2000); hence it is difficult to determine if the pain actually had anything to do with the stroke. Others use different questionnaires and scales to assess and grade the pain (Naess et al., 2010). Some of the discrepancy in the literature is probably caused by the use of different schemes and methods when measuring pain, and there is a need of a consensus on which methods that most properly reflect the real prevalence of pain in the stroke population.

Post-stroke depression

Psychological complications after stroke are common; studies on post-stroke depression show great discrepancies, with frequencies ranging from one in 7 to one in 3 stoke patients within 2 weeks after stoke, and post-stroke depression is associated with increased mortality and reduced social function (Everson, Roberts, Goldberg, & Kaplan, 1998; Fure, Wyller, Engedal, & Thommessen, 2006; Kouwenhoven, Gay, Bakken, & Lerdal, 2013; Robinson, Starr, Kubos, & Price, 1983). Most of these patients are classified as mild depression according to Kouwenhoven, Gay, Bakken and Lerdal (2013), while Astrom, Adolfsson ans Asplund (1993) found major depression in 1 of 4 in the first week after hospitalization. Patients experiencing post-stroke depression are less likely to achieve independence in activities of daily living after 6 months than non-depressed stroke patients (Lai, Duncan, Keighley, & Johnson, 2002), and there is a consensus that depressed stroke patients have higher mortality than nondepressed stroke patients with severity of the depression being independently associated to mortality (Robinson & Spalletta, 2010). Patients with acute post stroke depression were 3.4 times more likely to die during 10 years after stroke than patients not experiencing depression in the acute phase, and were more likely to develop depression in the long term as self-reported depressive symptoms during inpatient rehabilitation were predictive for post stroke depression six months after discharge (Lewin-Richter, Volz, Jobges, & Werheid, 2015; Robinson & Spalletta, 2010). A pooled estimate from population based studies found that long term prevalence of depression after stroke was 34 %, which was similar to what was found in the acute phase (Hackett, Yapa, Parag, & Anderson, 2005). A systematic review of observational

studies found that depression in stroke survivors resolved spontaneously within several months (Hackett et al., 2005), although others argue that depression is actually more common 5 years after the stroke than at 6 months, and that depression at six month is a determinant for depression at five years (Lincoln et al., 2013). Astrom et al. (1993) suggested a time line where major depression in stroke patients increases towards 3 months poststroke, then turns and declines towards 1 year, but increases again after one year.

There might be different reasons that post-stroke depression occurs in some patients and not in others. Personality traits may influence the risk of developing post stroke depressive symptoms, as one study found that more helplessness, passive coping and less acceptance and perceived benefits were independently associated with the presence of post stroke depressive symptoms (van Mierlo, van Heugten, Post, de Kort, & Visser-Meily, 2015). It has also been hypothesized that stroke location might influence the risk of developing depression, but there are no definite results on this (Bhogal, Teasell, Foley, & Speechley, 2004; Carson et al., 2000; Kouwenhoven et al., 2013).

A review of the literature concluded that the strongest single correlate of depression was severity of impairment in activities of daily living (Robinson & Spalletta, 2010). Eighty-three % of the studies in this review support this finding; however there were some conflicting results. One reason for the inconsistency might be that the impact of stroke severity in emotional and psychological distress is difficult to investigate, especially in the acute phase, as patients suffering from very severe strokes often have problems with communication because of aphasia, reduced consciousness or tiredness. There exist some instruments constructed to assess depression in stroke patients with aphasia, but none of these are sufficiently validated, as the studies investigating the consistency and reliability of these instruments are postponed to small samples sizes and selection bias (van Dijk, de Man-van Ginkel, Hafsteinsdottir, & Schuurmans, 2015). As for the patients with low consciousness, it is even more difficult to get information about emotions and thoughts. These patients are often excluded in studies examining depression after stroke (Robinson & Spalletta, 2010).

The relationship between age and frequency of depression after stroke has been discussed (Hadidi, Treat-Jacobson, & Lindquist, 2009).Younger age, below 75 years, is shown to be a predictor for depression, but there are also studies finding no association (Kouwenhoven, Kirkevold, Engedal, & Kim, 2011). A review of the literature did not find any consistent support of the relationship between depression after stroke and psychiatric history; some

studies found a strong relationship, but there have also been studies reporting no association. This could be due to different approaches when gathering information on previous psychiatric illness (looking in journals, asking family), and different thresholds for defining illness (Hadidi et al., 2009).

A systematic review of factors associated with risk of cognitive decline in elderly people found that there was an association between depression and cognitive decline in later life (Plassman, Williams, Burke, Holsinger, & Benjamin, 2010). This relationship seems to be present also among stroke patients and it increases with severity of the depression, as moderate to severe depressive symptoms demonstrate three times more cognitive impairments than patients with no or mild depressive symptoms in the acute phase after stroke (Nys et al., 2005). This association is considered to be complex, and dependent of factors such as lesion location, time after the stroke and functional outcome. It is also unclear to what degree the cognitive impairment is due to depression or a result of brain damage after stroke (Hadidi et al., 2009).

Post-stroke anxiety

There exists a lot of research on depression after stroke, and even though anxiety appears to be quite common after stroke as well, the amount of literature on this topic is sparse. A review found that one in five stroke patients experience generalized anxiety disorder in the acute phase after stroke, but the results of the studies contributing to this review vary a lot, both in frequency of anxiety, time poststroke, methods and cut-offs for measuring anxiety (Campbell Burton et al., 2013). It is shown that patients with anxiety in the acute phase have a high risk of developing chronic anxiety disorder (Astrom, 1996). Dependence in activities of daily living and reduced social network in years after the stroke is associated with general anxiety disorder (Astrom, 1996). Even though anxiety seems to be quite common after stroke, anxiety symptoms prior to stroke are also associated with increased risk of actually experiencing a stroke, independent of other risk factors (Lambiase, Kubzansky, & Thurston, 2014).

Methods of measuring depression and anxiety

There are different ways of examine for psychological disorders in patients. In order to diagnose patients with a specific psychiatric disease, the diagnostic criteria (ICD-10 or DSM-V) are used in a clinical setting. But in a research setting, it might be more suitable to use

other tools like questionnaires and scoring systems. Hence; many studies measure symptoms of depression or anxiety by questionnaires rather than diagnostic criteria (Campbell Burton et al., 2013; Kouwenhoven et al., 2011). It is important to distinguish between these two features, as questionnaires make it possible to grade the symptoms at the time of the assessment, but they are not eligible as diagnostic tools of the diagnosis of psychiatric diseases like anxiety or depression. A systematic review of observational studies on depression after stroke demonstrates great variation in frequency in different studies, where many different questionnaires have been used (Hackett et al., 2005). Several standardized questionnaires exist, and the use of different mood assessment scales influence the frequency of depressive symptoms, e.g. with the Montgomety Åsberg Depression Rating Scale (MADRS) reporting higher frequencies than other questionnaires (Hackett et al., 2005).

The Hospital Anxiety and Depression Scale (HADS) is a brief questionnaire developed to identify symptoms of depression and anxiety in hospital medical outpatient clinics (Zigmond & Snaith, 1983), with seven questions in each category. All of the uneven numbers in the questionnaire are questions about anxiety (HADS-A), and all the even numbers are about depression (HADS-D). A copy of the questionnaire is attached. Higher scores indicate more symptoms of depression and/or anxiety. HADS is validated for use in hospital setting (Zigmond & Snaith, 1983) and in primary care patients, with a sensitivity and specificity of ~ 0.8 when using a cut-off at 8 for each sub-score (Bjelland, Dahl, Haug, & Neckelmann, 2002), and is often used as a screening tool in stroke patients (Hackett et al., 2005). A score of ≥ 8 in HADS-A (anxiety) and –D (depression) subscale during the first two weeks after stroke is associated with anxiety, depression and apathy after four months, hence it could be used in the acute phase to predict patients at risk (Sagen et al., 2010).

Association between pain, depression and anxiety

Experiencing pain after stroke is related to increased emotional distress, and it is found to be associated with depression or dysphoria (van Almenkerk, Depla, Smalbrugge, Eefsting, & Hertogh, 2015). Another study support this assertion by showing that stroke-related pain is associated with depression and sensorimotor impairments (Lundstrom et al., 2009). A study from Bergen investigated the triad of fatigue, pain and depression and found that fatigue was linked to both pain and depression in stroke patients, but they did not find any association between pain and depression when fatigue was absent (Naess, Lunde, & Brogger, 2012).

Hence, the relationship between pain and depression in stroke patients is complex and even though some studies have looks into the relationship it is far from properly given account for.

Anxiety is often seen in company with other psychological disorders, especially depression. During a 10 year-period after stroke, it is shown that 2-3 of 4 patient with anxiety also experience depression (Ayerbe, Ayis, Crichton, Wolfe, & Rudd, 2014), showing that there is a great overlap between these disorders. Association between anxiety disorders and pain is established, and might even be more pronounced than the relationship between depression and pain (Casten, Parmelee, Kleban, Lawton, & Katz, 1995). One study also found an association between pain and anxiety in chronic stroke patient in a long term care facility (van Almenkerk et al., 2015), but there is a lack in literature exploring this association more thoroughly.

Summary of introduction

In summary, stroke unit treatment has shown to reduce the frequency of complications after stroke. Still patient reported complications like pain and symptoms of depression and anxiety seem to be common both in the early and chronic stages after stroke. However, frequencies reported in previous research vary a lot due to lack of consensus on how to define and measure these complications. Hence, there is a need for more research using standardized measures to assess the frequency of pain and symptoms of depression and anxiety in an unselected group of patients early after stroke. There is also a need to distinguish between stroke related pain and general pain that might have other causes than the stroke and all that comes with it. Furthermore, there seem to be an association between pain and depression, at least when fatigue also is present. Few studies have been investigating the association between pain, and symptoms of depression and anxiety as early as the first two weeks after the stroke.

Aims

The primary aim of the present study was to assess the frequency of pain and symptoms of depression and anxiety during the first two weeks after stroke in a group of unselected stroke patients treated in a comprehensive stroke unit with both acute care and early rehabilitation.

The secondary aims were to investigate the most common locations of the pain, how pain, depression and anxiety were related to stroke severity and also to assess the association between pain, depression and anxiety early after stroke.

Research questions

1. What is the frequency of pain, symptoms of depression and symptoms of anxiety among acute stroke patients treated in a comprehensive stroke unit in the first and second week after stroke?
2. Where on the body do the patients most often localize pain after stroke?
3. Is there a relationship between severity of stroke and pain, symptoms of depression and symptoms of anxiety?
4. Is there an association between pain and symptoms of depression or between pain and symptoms of anxiety in the acute phase after stroke

Material and method

Study design and setting

This study was part of a larger study on complications in the acute phase after stroke. It was a prospective observational study carried out in the stroke unit at St. Olavs Hospital, The University Hospital of Trondheim, Norway.

Sample

The World Health Organization has defined stroke as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin" (Sacco et al., 2013). Patients with acute stroke according to this definition (except from subarachnoid hemorrhage), treated in the SU in Trondheim and admitted to hospital within 48 hours after onset of symptoms were eligible for inclusion. Patients were fit for inclusion if they were able to understand Norwegian language and willing to sign informed consent. In keeping with Norwegian consent procedures for patients unable to consent for themselves, such patients were also included if their next of kin did not oppose participation. Patients were excluded if they were transferred to another unit during the first days or given palliative care (i.e. not receiving standard SU treatment), or if they already had been included to the project due to an earlier stroke.

For this sub study patients were required to respond to the questionnaires on pain, depression and anxiety in both weeks in order to be included in the analyses exploring each of these variables. This means that we only analyzed data on pain from patients responding to questions on pain in both weeks, and we only analyzed data on symptoms of depression and anxiety in patients completing HADS both the first and second week. The project was approved by the Regional Committee for Medical and Health Research Ethics in Norway (REK no 2012/1236).

Measures and variables

Baseline information about gender, age, type of stroke and length of stay in hospital was assessed in all patients. Severity of stroke was measured at admission using the Scandinavian

Stroke Scale (SSS), and the score was divided into five different categories; very severe (score 0-14), severe (15-29), moderate (30-44), mild (45-51) and very mild (52-59) stroke.

Patients were observed for 2 weeks after hospitalization to register if any complications occurred. The medical complications that were monitored were recurrent and progressing stroke, fever, seizures, falls, thromboembolism, acute myocardial infarction, pressure sores and infections of the urinary tract or in the chest. Registrations were done every day while the patients were staying in hospital. The results are presented elsewhere (Bovim et al., 2015).

Registration of pain and symptoms of depression and anxiety was performed once in each week. Information on pain was gathered using the first three items of the Brief Pain Inventory (Cleeland & Ryan, 1994). Participants were asked if they felt any pain other than the normal day-to-day pain and if the pain had occurred after the stroke, and they were asked to localise the pain on a body map. In this thesis, *pre-stroke pain* is used to describe pain that were present also before the stroke, *novel pain* describes new pain occurring after the stroke, and *total post-stroke pain* contains both of these features. Symptoms of depression and anxiety were assessed using the HADS. A score of ≥ 8 in each category (HADS-D and HADS-A) was considered as symptoms of depression or anxiety respectively (Bjelland et al., 2002).

Procedure

In addition to the author of this thesis, four trained assessors screened and included patients arriving at the SU and performed all the necessary registrations. Meetings were held during the period of data collection, making sure everyone followed the same procedure. Patients who were discharged from hospital earlier than two weeks after inclusion were contacted by telephone and asked about pain and the HADS questionnaire.

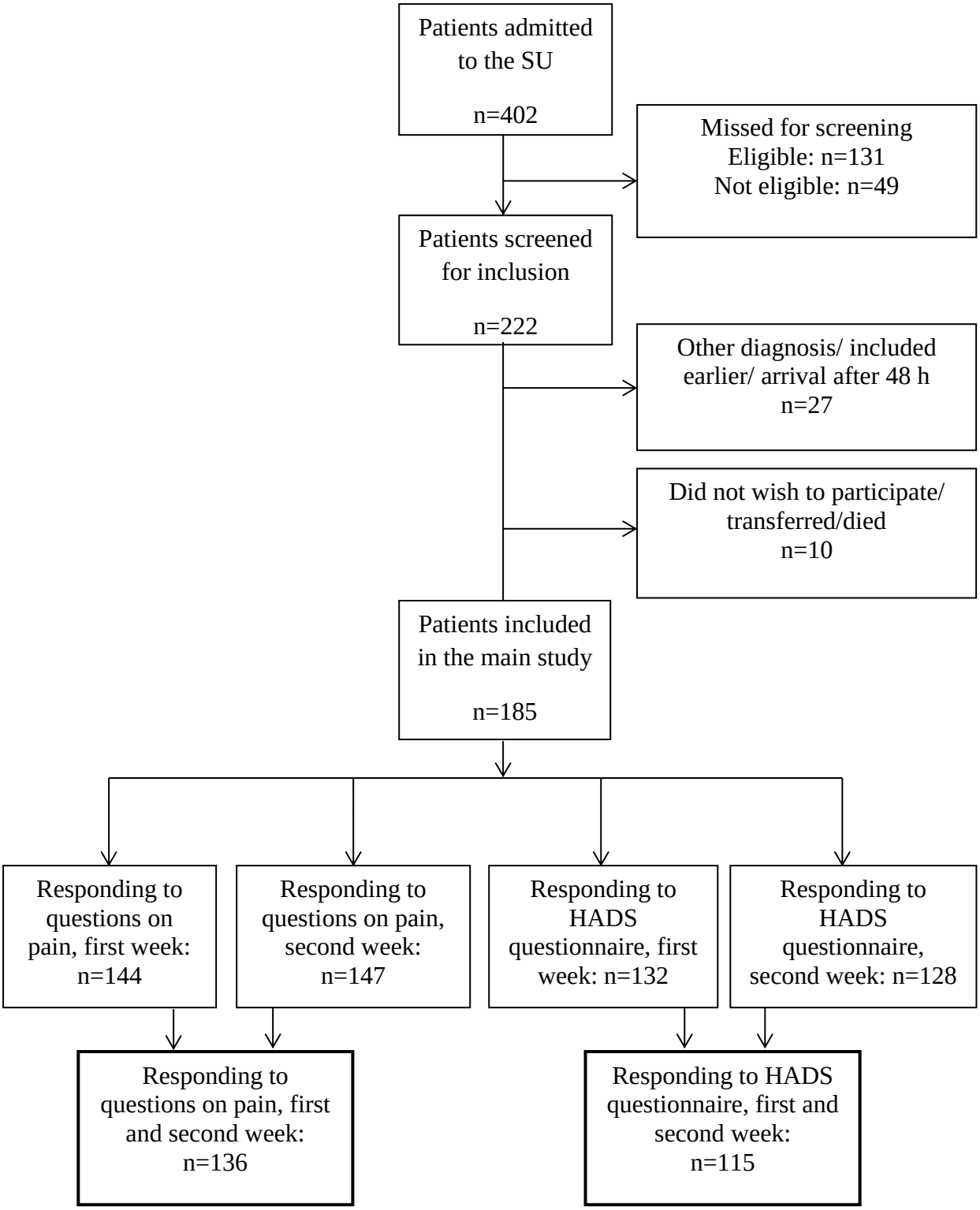
Statistics

Statistical analyses were performed in SPSS 21. Most of the data is presented using descriptive statistics. Proportions were analysed and p-values generated using the Pearson Chi-Square test for dichotomous proportions, and Mann-Whitney test for continuous variables. P-value < 0.05 was considered significant in the analyses.

Results

Inclusion of patients lasted from the 17th September 2012 to 13th December 2013, with two planned brakes in the inclusion between the 14th December 2013 to 7th January 2013 and 5th June to 12th August 2013; hence the inclusion period covered 13 months. Four hundred and two patients with suspected stroke were admitted to the SU during this period. Some were missed for inclusion, others were not eligible for inclusion, and a final group of 185 patients contributed to the data sample. Of these, 158 (85.4 %) arrived in hospital within 24 hours after symptom onset. Ninety-four patients (50.8 %) were discharged during the first week, and were contacted by telephone to complete the registration. Two patients (1.1 %) were not reached by telephone and considered lost to follow-up, and they were taken out of the analyses in this thesis. Some of the included patients were not able to respond to questions about pain, depression and anxiety in the first and/or second week after the stroke; neither of these patients have been contributing to the analyses. The flowchart of patients is shown in Figure 1.

Figure 1. Flowchart of the patient group



As shown in Figure 1, 131 eligible patients were missed for screening and inclusion to the study. Data from the Norwegian Stroke Register enabled information and comparison of these patients with the 185 patients included in the study. Those missed for inclusion were in mean (SD) aged 79.9 (8.8) years, which was significantly older than those included, $p = 0.004$. They also had a shorter length of stay in hospital, with a mean (SD) of 6.3 (6.7) days, $p < 0.001$. Their mean (SD) SSS-score was higher, 39.8 (16.5) points, which was borderline significant, $p = 0.055$. There were significantly more patients in the group of very mild stroke among those missed for inclusion compared with those included, 39 (29.8 %) versus 28 (15.1 %), $p = 0.002$. They did not differ significantly from those included concerning gender and type of stroke.

Table 1. Descriptive presentation of baseline information in all patients

	All patients n = 185	Responding to pain questions n = 136	Not responding to pain questions n = 49	p-value[a]	Responding to HADS n = 115	Not responding to HADS n = 70	p-value[b]
Women, n (%)	88 (47.6)	66 (48.5)	22 (44.9)	0.66**	54 (47.0)	34 (48.6)	0.83**
Age, mean (SD)	76.9 (8.51)	75.26 (8.23)	81.6 (7.57)	<0.001*	74.51 (8.07)	80.93 (7.72)	<0.001*
Infarction, n (%)	161 (87.0)	121 (89.0)	40 (81.6)	0.19**	101 (87.8)	60 (85.7)	0.68**
Scandinavian Stroke Scale, mean (SD)	37.0 (16.40)	42.40 (11.80)	21.8 (17.95)	<0.001*	44.59 (10.16)	24.41 (17.03)	<0.001*
Days of hospital stay, mean (SD)	8.5 (8.07)	6.24 (4.28)	14.80 (11.96)	< 0.001*	5.92 (3.86)	12.76 (10.93)	< 0.001*

HADS = Hospital Anxiety and Depression Scale
[a] P-value compares baseline of those responding and those not responding to question on pain
[b] p-value compares baseline of those responding and those not responding to HADS
*Mann-Whitney U test
**Pearsons Chi-Square Test

Baseline information on all patients included in the study is demonstrated in Table 1. All strokes not classified as infarctions were haemorrhages. Not all patients included in the study were able to respond to questions about pain, depression and anxiety. This matter particularly to those affected by very severe strokes, suffering from tiredness, reduced consciousness or aphasia, making it difficult to expresses themselves. Patients responding to the questionnaires during both the first and second week had a significantly higher SSS-score, were significantly younger and spent shorter time in hospital than those not able to respond.

Table 2. All patients divided into stroke severity groups

	All patients n=185 n (%)	Responding to pain questions n=136 n (%)*	Responding to HADS n=115 n (%)*
Very severe	26 (14.1)	5 (19.2)	2 (7.7)
Severe	24 (13.0)	12 (50)	7 (29.2)
Moderate	58 (31.4)	51 (87.9)	41 (70.7)
Mild	49 (26.5)	42 (85.7)	40 (81.6)
Very mild	28 (15.1)	26 (92.9)	25 (89.3)

HADS = Hospital Anxiety and Depression Scale
Very severe: Scandinavian stroke scale (SSS)=0-14, severe: SSS=15-29, moderate: SSS=30-44, mild: SSS=54-51, very mild: SSS=52-59
*Percent of all patients in that stroke severity group

Pain

Table 3. Frequency of pain during the first and second week according to stroke severity

	First week N=136			Second week N=136
	Pre-stroke pain n (%)*	Novel pain n (%)*	Total post-stroke pain n (%)*	Total post-stroke pain n (%)*
Very severe n = 5	2 (1.5)	1 (0.7)	3 (2.2)	2 (1.5)
Severe n = 12	2 (1.5)	1 (0.7)	3 (2.2)	2 (1.5)
Moderate n = 51	5 (3.7)	5 (3.7)	10 (7.4)	16 (11.8)
Mild n = 42	4 (2.9)	7 (5.2)	11 (8.1)	17 (12.5)
Very mild n = 26	2 (1.5)	2 (1.5)	4 (2.9)	10 (7.4)
Total	15 (11.0)	16 (11.8)	31 (22.8)	47 (34.6)

Very severe: Scandinavian Stroke Scale (SSS)=0-14, severe: SSS=15-29, moderate: SSS=30-44, mild: SSS=54-51, very mild: SSS=52-59
* Percent of all 136 patients responding to questions about pain

Forty-nine patients (26.5 %) were unable to respond to questions about pain, mainly due to aphasia, tiredness or reduced consciousness. Thirty-one (22.8 %) of the 136 responding patients experienced pain during the first week, and 15 (11.0 %) characterized the pain as pre-stroke pain. Sixteen patients (11.8%) characterized the pain as novel pain occurring subsequent to the stroke.

During the second week, the number of patients experiencing pain had increased to 47 patients (34.6 %). Significantly more patients experienced pain in the second week compared to the first week, $p > 0.001$.

The distribution of pain across the body is displayed in Table 4. Four (12.9%) of the patients reporting novel pain the first week located it to the arm on affected side of the body. A broad part of those reporting novel pain subsequent to the stroke located it to the head or neck. Old pain was more evenly distributed all over the body. Patients could report pain from more than one location; hence the number of pain in different locations in Table 4 exceeds the number of patients experiencing pain.

Table 4. Localization of self-reported pain

	Week 1 N=136			Week 2 N=136
	Pre-stroke pain n (%)*	Novel pain n (%)*	Total post-stroke pain n (%)*	Total post-stroke pain n (%)*
Head/neck	2 (1.5)	8 (5.9)	10 (7.4)	22 (16.2)
Arm on affected side	0	4 (2.9)	4 (2.9)	6 (4.4)
Arm on unaffected side	0	0	0	3 (2.2)
Leg on affected side	3 (2.2)	3 (2.2)	6 (4.4)	11 (8.1)
Leg on unaffected side	7 (5.1)	2 (1.5)	9 (6.6)	13 (9.6)
Back	8 (5.9)	1 (0.7)	9 (6.6)	10 (7.4)
Chest	1 (0.7)	0	1 (0.7)	2 (1.5)
Abdomen	1 (0.7)	0	1 (0.7)	3 (2.2)

* Percentages of all 136 patients responding to questions on pain

Depression and anxiety

A total of 115 patients (62.2 %) responded to HADS during both the first and second week. As with pain, the reason for not responding was mainly aphasia, tiredness or reduced consciousness. Mean (SD) score on HADS was 7.12 (5.99) and 5.98 (5.68) during the first and second week respectively, which is a nonsignificant reduction in total score, p = 0.101.

Table 5. Symptoms of depression and anxiety according to severity of stroke

	First week N=115		Second week N=115	
	Depression n (%)*	Anxiety n (%)*	Depression n (%)*	Anxiety n (%)*
Very severe n = 2	0	0	1 (50)	0
Severe n = 7	0	0	1 (14.3)	1 (14.3)
Moderate n = 41	6 (14.6)	7 (17.1)	6 (14.6)	6 (14.6)
Mild n = 40	4 (10.0)	5 (12.5)	1 (2.5)	5 (12.5)
Very mild n = 25	2 (8.0)	1 (4.0)	2 (8.0)	1 (4.0)
Total	12 (10.4)	13 (11.3)	11 (9.6)	13 (11.3)

Very severe: Scandinavian Stroke Scale (SSS)=0-14, severe: SSS=15-29, moderate: SSS=30-44, mild: SSS=54-51, very mild: SSS=52-59
*Percent of all patients in that stroke severity group

Twelve patients (10.4 %) experiences symptoms of depression during the first week, and 11 patients (9.6) during the second week. Thirteen patients (11.3 %) experienced symptom of anxiety in the first and second week.

Three out of the 12 patients with depressive symptoms during the first week had depressive symptoms during the second week. Five out of the 13 patients with symptoms of anxiety during the first week had such symptoms also during the second week.

One hundred and twelve patients replied to both questions about pain and HADS in the first and second week. Table 6 shows the association between pain and symptoms of depression or anxiety during the first and second week, respectively.

Table 6. Association between total post-stroke pain and depression or anxiety

a) First week

		Depression (n)		Anxiety (n)		Total
		Yes	No	Yes	No	
Total post-stroke pain	Yes	2	23	6	19	25
	No	9	78	6	81	87
p-value*		0.728		0.015		

*) The Pearson chi-squared test

b) Second week

		Depression (n)		Anxiety (n)		Total
		Yes	No	Yes	No	
Total post-stroke pain	Yes	6	31	6	31	37
	No	5	70	7	68	75
p-value*		0.110		0.285		

*) The Pearson chi-squared test

Association was significant for pain and anxiety in the first week, p = 0.015, but not in the second week between in pain and depression.

Discussion

This study showed that 23 % of stroke patients experienced pain, other than everyday kinds of pain, in the acute phase after stroke. Furthermore the results showed that 1 out of 10 patients experienced novel pain in the first week after a stroke, and this number increased significantly in the second week. Novel pain was mainly localized to head or neck, while pre-stroke pain was more evenly distributed across the body. Furthermore, about 1 of 10 patients experienced symptoms of depression or anxiety, and this frequency was quite stable during the first and second week. Despite a temporarily significant association between pain and symptoms of anxiety during the first week, there were no other clear associations between pain and symptoms of depression or anxiety in the acute phase after stroke.

Method

A strength of this study was the prospective design, and the fact that all patients were treated in the same stroke unit which offers evidence-based treatment according to the Norwegian guidelines (The Norwegian Directorate of Health, 2010). Another strength was that patients missed for inclusion were accounted for using data from the Norwegian Stroke Register, which also has made it possible to report the baseline characteristics of those not included.

Pain and symptoms of depression and anxiety are variables that, in some cases, are difficult to measure in acute stroke patients. Patients have to be alert, able to concentrate and to respond to questions, and some of the questions concerning symptoms of depression and anxiety also require that they are able to reflect on their own behaviour and reactions, which is quite a demanding task during acute illness. Patients with aphasia or reduced consciousness also have difficulties responding to the questionnaires. This might have led to an inclusion bias, and we know from our data that patients responding to these questions generally have less severe strokes, measured by the Scandinavian Stroke Scale, than those not responding. It might not be relevant to measure symptoms of depression and anxiety in unconscious patients, but it should be taken into consideration in patients not able to express themselves, e.g. patients with aphasia.

When examining pain, patients were asked if the pain had occurred after the stroke, which introduce a recall bias, as they have to consider if they have had the current pain before the

stroke. It may be difficult to remember and to distinguish between pre-stroke pain and novel pain, and it could be valuable to do an even more thorough examination to differentiate between these two classifications of pain.

The questions used in HADS are supposed to display symptoms of depression and anxiety. When depression and anxiety are diagnosed in the clinic, diagnostic criteria including other features like the time perspective are used. Having a stroke might be an acute, life changing situation, and it is possible to imagine that it may cause terrified thoughts and feeling presenting as transient symptoms of depression or anxiety in some patients. One should have this in mind when interpreting the results of HADS performed in the acute phase.

The study had some limitations to be considered. HADS is validated for use in both hospitalized (Zigmond & Snaith, 1983) and primary care patients (Bjelland et al., 2002), but the correlation with other commonly used questionnaires is ranging from 0.49 to 0.83, which could explain some if the discrepancy in findings between studies using different questionnaires. Hence, our findings should be compared to other studies also using the HADS for assessing symptoms of depression and anxiety. The HADS-A is found to have a good level of sensitivity in detecting present generalized anxiety disorder, while the depression-subscale is found to be a poorer screening instrument in stroke patients (Johnson et al., 1995). Still, the HADS is commonly used to estimate symptoms of depression and anxiety in stroke patients (Campbell Burton et al., 2013).

Even though assessment of the HADS during the first two weeks after stroke is found to be useful in predicting depression and anxiety at 4 months (Sagen et al., 2010), others find that HADS has a low sensitivity, but good specificity in predicting depression and anxiety at one month when assessed in the acute phase (Lees, Stott, Quinn, & Broomfield, 2014). It may take time before symptoms of depression and anxiety develops in some patients, which might explain the low sensitivity of HADS in predicting the risk of developing depression and anxiety 1 month after it has been performed. We may expect that even more patients in our cohort would experience symptoms of depression or anxiety within a month.

The number of patients included in this study was relatively low, especially considering those contributing to the analyses. This is partly caused by the fact that some stroke patients had reduces consciousness or difficulties responding to questions about pain, depression and anxiety. These patients had a lower mean SSS-score, implying that they had more severe strokes than those responding to the questionnaires. They were older and stayed in hospital

for significantly longer time, which supports the assertion that those not able to respond to questionnaires had a more severe medical situation. Another reason for the low sample size is that a considerable amount of eligible patients were missed for inclusion. The baseline characteristics of these patients were quite similar to the patients included, but eligible patients missed for inclusion had borderline significantly milder strokes and stayed in hospital for significantly shorter time. This might also explain why many of them were missed, as they left hospital as soon as the diagnostics were completed.

Results

Thirty one patients (22.8 %) experienced pain during the first week. Half of these patients reported the pain to be novel pain subsequent to the stroke, which means that a considerable amount reported pre-stroke pains. Compared to what was found in the HUNT-study in Nord-Trøndelag, where 26 % of the general population experienced chronic pain (Landmark et al., 2012), the frequency of pain in our study is not increased from the general population. A study from Denmark found a larger frequency of pain in chronic stroke patients (39 %), but it is also higher in a reference group, with pain occurring in 28.9 % of non-stroke patients (Klit et al., 2011). Hansen, Marcussen, Klit, Andersen, Finnerup and Jensen (2012) found that more than 1 of 3 patients experienced novel pain at stroke onset. In our study, we used the first three items of the Brief Pain Inventory to measure pain. This measure asks the patients to report if they experienced any pain *other than the normal day-to-day pain,* which might, to some extent, explain the low frequency. In addition, many of the patients might have other worries than pain to think about a few days after experiencing a stroke. It may also be that treatment in a specialized stroke unit with attentive personnel preventing and treating pain in the early phase, as in our stroke unit, reduces the frequency of pain compared to studies in other units.

In some previous studies, pain has been defined as being in need of and taking analgesics (Indredavik et al., 2008; Langhorne et al., 2000). Indredavik et al. (2008) found that 24 % had pain during the first week after stroke, which increased to more than 50 % at 3 months, while Langhorne et al. (2000) found a prevalence of pain of 34 % at hospital admission, remaining almost constant at 6 and 30 months. This definition with use of analgesics might overestimate the number of patients suffering from pain, as unconscious patients might get analgesics even though they do not report pain, and some might receive paracetamol with the intention to

reduce fever. Using a questionnaire to assess pain excluded patients not able to express themselves, which as discussed earlier may also be a weakness, but made it possible to distinguish between pre-stroke pain and new pain occurring subsequent to the stroke.

Significantly more patients experienced pain during the second week than the first week. This was similar to what was found in other studies, and implies that post-stroke pain increases over time. One possible explanation might be that patients are less active after a stroke, especially those dependent on help to move around. They might get pain from the pressure of lying in the bed or being immobilized in a chair. Shoulder pain in the paretic arm is thought to develop because of, amongst other, loss of muscle strength and an increased force pulling in the tissue in the shoulder, and the risk of developing such pain also increase over time.

Only 4 (2.9 %) of the responding patients in the present study reported new pain in the arm on the paretic side during the first week, indicating that shoulder pain has not yet developed. In a Swedish study, shoulder pain is said to be quite common after stroke, (Lindgren, Jonsson, Norrving, & Lindgren, 2007) occurring in approximately 20 % at 4 months. Still, the study from Sweden found that one out of three with shoulder pain after 16 months developed the pain during the first two weeks after stroke (Lindgren et al., 2007). Hence, it is relevant to take note of shoulder pain in stroke patients in the early phase as it might become chronic, and considerably more patients will probably develop pain in the long run. Another study found that 17 % experienced shoulder pain at one week after stroke, but only one fifth ascribed it to the stroke (Ratnasabapathy et al., 2003). This outlines the importance of distinguishing between pre-stroke pain and novel pain subsequent to the stroke.

In our study, a great proportion of those experiencing novel pain suffered from head and/or neck pain. This accounts for 5.9 % of all responding patients during the first week, and even more during the second week. A previous study found similar proportion, 10.5 %, of new onset chronic headache two years after stroke (Klit et al., 2011), compared to a frequency of 2.3 % in the reference group. Hence, also other types of pain than shoulder pain needs to be considered in the follow-up after stroke, and especially pain in head or neck in the acute phase.

When asking about pain, we considered if the pain had been present prior to the stroke. This was beneficial in order to identify a possible association between pain and the stroke. However, this was not possible to do with the questions concerning symptoms of depression and anxiety. These were questions considering present thoughts and feelings, and it would be

difficult to perform the whole questionnaire on how they felt before the stroke. Data from the HUNT-study suggest that the prevalence of depressive symptoms in elderly (≥65 years) in the Norwegian population is 12.5 %, measured with a cut off at ≥ 8 in HADS. (Helvik, Engedal, Krokstad, Stordal, & Selbaek, 2012) This is similar to what we found in acute stroke patients, indicating that the symptoms of depression in the first 2 weeks after stroke are similar to the general elderly population.

The frequency of symptoms of depression in our study is somewhat lower than what has been found in other studies on stroke patients. The frequency of depression after stroke ranged from 6 % to 55 %, with a pooled estimate of 33 %, but this review included studies examining depression at very different points in time after the stroke (Hackett et al., 2005). A Norwegian study found a prevalence of symptoms of depression at 14 % which is in accordance with our findings (Fure et al., 2006). The frequency of symptoms of anxiety is also lower than other studies have found. A systematic review reported a frequency of anxiety of 20 % within one month after stroke (Campbell Burton et al., 2013). Fure, Wyller, Engedal and Thommesen (2006) found that 26 % of ischemic stroke patients suffer from symptoms of anxiety, measured with the HADS, during the first week after stroke. Some patients were not able to respond to the questionnaires in our study, and as discussed earlier, these patients suffered from more severe strokes. This might have led to an underestimation of symptoms of depression as it is associated with stroke severity, and maybe also anxiety, although this relation is unclear (Menlove et al., 2015).

Even though the number of patients with symptoms of depression and anxiety was relatively constant from the first to the second week, the patients were not all the same at these two time occasions. Only 5 patients with symptoms of anxiety and 3 patients with symptoms of depression during the first week had symptoms in the second weeks as well. This means that symptoms of depression and anxiety vary a lot in the acute phase after stroke. As discussed earlier, experiencing a stroke is a stressful situation to many patients, as they may experience a sudden decline in functional ability and independence. Hence, it is not surprising that some patients may experience symptoms of depression or anxiety that resolves within days, or that occurs after some days when they realize how extensive their life has been affected by the stoke.

We aimed to investigate the relationship between pain, depression or anxiety and stroke severity, but the majority of the patients with severe or very severe stokes were not able to

respond to the questionnaires and it was difficult to examine this association with such small groups. Looking at Table 5 it seems that, at least for anxiety and perhaps also depression, there are more symptoms in the moderate than in the mild and especially the very mild stroke group, both in the first and second week. This finding is supported by Kouwenhoven, Kirkevold, Engedal and Kim (2011), who found that stroke severity is associated with post stroke depression. Still, few responding patients in the groups of severe and very severe stokes also makes it difficult to say something about association between stroke severity and pain or symptoms of depression and anxiety.

We found a temporary association between pain and symptoms of anxiety during the first week (Table 6), but no association was found during the second week, or between pain and symptoms of depression. In order to show a clear association, if there is one, we would have needed more patients in each of the groups. Hence, we cannot conclude on this association. But it could be interesting and useful to investigate this in later research.

Conclusion

A total of 23 % of responding patients treated in an evidence-based comprehensive stroke unit experienced pain during the first week after stroke, but only 12 % considered the pain to have developed subsequent to the stroke. Half of these patients experienced pain in the head or neck. A few patients experienced novel pain in the affected arm, but the pain was not strictly bound to the affected side of the body. The frequency of pain increased significantly from the first to the second week after stroke indicating that post stroke pain increases along with increasing time from onset of stroke.

Symptoms of depression and anxiety were less frequent and present in approximately 10% of the patients. This finding remained stable for the first two weeks after stroke.

It seems that pain and symptoms of depression and anxiety were most frequent in patients with moderate and severe strokes. However, these results have to be interpreted with caution because of the very low number of severely affected patients included in the present study.

It would be interesting to look further into the association between pain and symptoms of depression and anxiety after stroke, as we found a transient significant association between pain and symptoms of anxiety in the first week. It would also be useful to investigate how to prevent these outcomes more successfully in the future.

References

Appelros, P. (2006). Prevalence and predictors of pain and fatigue after stroke: a population-based study. *International Journal of Rehabilitation Research, 29*(4), 329-333. doi: 10.1097/MRR.0b013e328010c7b8

Astrom, M. (1996). Generalized anxiety disorder in stroke patients. A 3-year longitudinal study. *Stroke, 27*(2), 270-275.

Astrom, M., Adolfsson, R., & Asplund, K. (1993). Major depression in stroke patients. A 3-year longitudinal study. *Stroke, 24*(7), 976-982.

Ayerbe, L., Ayis, S. A., Crichton, S., Wolfe, C. D., & Rudd, A. G. (2014). Natural history, predictors and associated outcomes of anxiety up to 10 years after stroke: the South London Stroke Register. *Age and Ageing, 43*(4), 542-547. doi: 10.1093/ageing/aft208

Bhogal, S. K., Teasell, R., Foley, N., & Speechley, M. (2004). Lesion location and poststroke depression: systematic review of the methodological limitations in the literature. *Stroke, 35*(3), 794-802. doi: 10.1161/01.str.0000117237.98749.26

Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res, 52*(2), 69-77.

Bonita, R., Solomon, N., & Broad, J. B. (1997). Prevalence of stroke and stroke-related disability. Estimates from the Auckland stroke studies. *Stroke, 28*(10), 1898-1902.

Bovim, M., Askim, T., Lydersen, S., Fjærtoft, H., & Indredavik, B. (2015). Complications in the first week after stroke. A 10-year comparison. *Submitted*.

Campbell Burton, C. A., Murray, J., Holmes, J., Astin, F., Greenwood, D., & Knapp, P. (2013). Frequency of anxiety after stroke: a systematic review and meta-analysis of observational studies. *Int J Stroke, 8*(7), 545-559. doi: 10.1111/j.1747-4949.2012.00906.x

Carson, A. J., MacHale, S., Allen, K., Lawrie, S. M., Dennis, M., House, A., & Sharpe, M. (2000). Depression after stroke and lesion location: a systematic review. *Lancet, 356*(9224), 122-126. doi: 10.1016/s0140-6736(00)02448-x

Casten, R. J., Parmelee, P. A., Kleban, M. H., Lawton, M. P., & Katz, I. R. (1995). The relationships among anxiety, depression, and pain in a geriatric institutionalized sample. *Pain, 61*(2), 271-276.

Cleeland, C. S., & Ryan, K. M. (1994). Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore, 23*(2), 129-138.

Davenport, R. J., Dennis, M. S., Wellwood, I., & Warlow, C. P. (1996). Complications after acute stroke. *Stroke, 27*(3), 415-420.

Ellekjaer, H., Holmen, J., Indredavik, B., & Terent, A. (1997). Epidemiology of stroke in Innherred, Norway, 1994 to 1996. Incidence and 30-day case-fatality rate. *Stroke, 28*(11), 2180-2184.

Ellekjaer, H., & Selmer, R. (2007). Hjerneslag - like mange rammes, men prognosen er bedre. *Tidsskr Nor Lægeforening, 6*, 740 - 743.

Everson, S. A., Roberts, R. E., Goldberg, D. E., & Kaplan, G. A. (1998). Depressive symptoms and increased risk of stroke mortality over a 29-year period. *Archives of Internal Medicine, 158*(10), 1133-1138.

Feigin, V. L., Lawes, C. M., Bennett, D. A., & Anderson, C. S. (2003). Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. *Lancet Neurol, 2*(1), 43-53.

Fjærtoft, H., & Indredavik, B. (2007). Kostnadsvurderinger ved hjerneslag. *Tidsskr Nor Lægeforening*(127), 744 - 747.
Fure, B., Wyller, T. B., Engedal, K., & Thommessen, B. (2006). Emotional symptoms in acute ischemic stroke. *Int J Geriatr Psychiatry, 21*(4), 382-387. doi: 10.1002/gps.1482
Govan, L., Langhorne, P., Weir, C. J., & Stroke Unit Trialists, C. (2007). Does the prevention of complications explain the survival benefit of organized inpatient (stroke unit) care?: further analysis of a systematic review. *Stroke, 38*(9), 2536-2540. doi: 10.1161/STROKEAHA.106.478842
Hackett, M. L., Yapa, C., Parag, V., & Anderson, C. S. (2005). Frequency of depression after stroke: a systematic review of observational studies. *Stroke, 36*(6), 1330-1340. doi: 10.1161/01.str.0000165928.19135.35
Hadidi, N., Treat-Jacobson, D. J., & Lindquist, R. (2009). Poststroke depression and functional outcome: a critical review of literature. *Heart and Lung, 38*(2), 151-162. doi: 10.1016/j.hrtlng.2008.05.002
Hansen, A. P., Marcussen, N. S., Klit, H., Andersen, G., Finnerup, N. B., & Jensen, T. S. (2012). Pain following stroke: a prospective study. *Eur J Pain, 16*(8), 1128-1136. doi: 10.1002/j.1532-2149.2012.00123.x
Helsenorge. (2013). Report of Quality Indicators. Retrieved from https://helsenorge.no/kvalitet-seksjon/Sider/Kvalitetsindikatorer-rapporter.aspx?kiid=30_dager_overlevelse_hjerneslag, *assessed 2015*
Helvik, A. S., Engedal, K., Krokstad, S., Stordal, E., & Selbaek, G. (2012). A comparison of depressive symptoms in elderly medical inpatients and the elderly in a population-based health study (the Nord-Trondelag Health Study 3). *Nord J Psychiatry, 66*(3), 189-197. doi: 10.3109/08039488.2011.614958
Indredavik, B., Bakke, F., Slordahl, S. A., Rokseth, R., & Haheim, L. L. (1999). Treatment in a Combined Acute and Rehabilitation Stroke Unit : Which Aspects Are Most Important? *Stroke, 30*(5), 917-923. doi: 10.1161/01.str.30.5.917
Indredavik, B., Rohweder, G., Naalsund, E., & Lydersen, S. (2008). Medical complications in a comprehensive stroke unit and an early supported discharge service. *Stroke, 39*(2), 414-420. doi: 10.1161/STROKEAHA.107.489294
Ingeman, A., Andersen, G., Hundborg, H. H., Svendsen, M. L., & Johnsen, S. P. (2011). In-hospital medical complications, Lenght of Stay, and Mortality Among Stroke Unit Patients. *Stroke*, *42*, 3214-3218.
Johnson, G., Burvill, P. W., Anderson, C. S., Jamrozik, K., Stewart-Wynne, E. G., & Chakera, T. M. (1995). Screening instruments for depression and anxiety following stroke: experience in the Perth community stroke study. *Acta Psychiatr Scand*, *91*(4), 252-257.
Klit, H., Finnerup, N. B., Overvad, K., Andersen, G., & Jensen, T. S. (2011). Pain following stroke: a population-based follow-up study. *PLoS One, 6*(11), e27607. doi: 10.1371/journal.pone.0027607
Kouwenhoven, S. E., Gay, C. L., Bakken, L. N., & Lerdal, A. (2013). Depressive symptoms in acute stroke: a cross-sectional study of their association with sociodemographics and clinical factors. *Neuropsychol Rehabil, 23*(5), 658-677. doi: 10.1080/09602011.2013.801778
Kouwenhoven, S. E., Kirkevold, M., Engedal, K., & Kim, H. S. (2011). Depression in acute stroke: prevalence, dominant symptoms and associated factors. A systematic literature review. *Disabil Rehabil, 33*(7), 539-556. doi: 10.3109/09638288.2010.505997

Lai, S. M., Duncan, P. W., Keighley, J., & Johnson, D. (2002). Depressive symptoms and independence in BADL and IADL. *Journal of Rehabilitation Research and Development, 39*(5), 589-596.

Lambiase, M. J., Kubzansky, L. D., & Thurston, R. C. (2014). Prospective study of anxiety and incident stroke. *Stroke, 45*(2), 438-443. doi: 10.1161/strokeaha.113.003741

Landmark, T., Romundstad, P., Dale, O., Borchgrevink, P. C., & Kaasa, S. (2012). Estimating the prevalence of chronic pain: validation of recall against longitudinal reporting (the HUNT pain study). *Pain, 153*(7), 1368-1373. doi: 10.1016/j.pain.2012.02.004

Langhorne, P., Pollock, A., & Stroke Unit Trialists, C. (2002). What are the components of effective stroke unit care? *Age and ageing, 31*, 365-371.

Langhorne, P., Stott, D. J., Robertson, L., MacDonald, J., Jones, L., McAlpine, C., . . . Murray, G. (2000). Medical Complications After Stroke : A Multicenter Study. *Stroke, 31*(6), 1223-1229. doi: 10.1161/01.str.31.6.1223

Lees, R., Stott, D. J., Quinn, T. J., & Broomfield, N. M. (2014). Feasibility and Diagnostic Accuracy of Early Mood Screening to Diagnose Persisting Clinical Depression/Anxiety Disorder after Stroke. *Cerebrovasc Dis, 37*(5), 323-329. doi: 10.1159/000360755

Lewin-Richter, A., Volz, M., Jobges, M., & Werheid, K. (2015). Predictivity of Early Depressive Symptoms for Post-Stroke Depression. *J Nutr Health Aging, 19*(7), 754-758. doi: 10.1007/s12603-015-0540-x

Lincoln, N. B., Brinkmann, N., Cunningham, S., Dejaeger, E., De Weerdt, W., Jenni, W., . . . De Wit, L. (2013). Anxiety and depression after stroke: a 5 year follow-up. *Disabil Rehabil, 35*(2), 140-145. doi: 10.3109/09638288.2012.691939

Lindgren, I., Jonsson, A. C., Norrving, B., & Lindgren, A. (2007). Shoulder pain after stroke: a prospective population-based study. *Stroke, 38*(2), 343-348. doi: 10.1161/01.STR.0000254598.16739.4e

Lozano, R., Naghavi, M., Foreman, K., Lim, S., Shibuya, K., Aboyans, V., . . . Memish, Z. A. (2012). Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet, 380*(9859), 2095-2128. doi: 10.1016/s0140-6736(12)61728-0

Lundstrom, E., Smits, A., Terent, A., & Borg, J. (2009). Risk factors for stroke-related pain 1 year after first-ever stroke. *Eur J Neurol, 16*(2), 188-193. doi: 10.1111/j.1468-1331.2008.02378.x

Menlove, L., Crayton, E., Kneebone, I., Allen-Crooks, R., Otto, E., & Harder, H. (2015). Predictors of anxiety after stroke: a systematic review of observational studies. *J Stroke Cerebrovasc Dis, 24*(6), 1107-1117. doi: 10.1016/j.jstrokecerebrovasdis.2014.12.036

Naess, H., Lunde, L., & Brogger, J. (2012). The triad of pain, fatigue and depression in ischemic stroke patients: the Bergen Stroke Study. *Cerebrovasc Dis, 33*(5), 461-465. doi: 10.1159/000336760

Naess, H., Lunde, L., Brogger, J., & Waje-Andreassen, U. (2010). Post-stroke pain on long-term follow-up: the Bergen stroke study. *J Neurol, 257*(9), 1446-1452. doi: 10.1007/s00415-010-5539-y

Nys, G. M., van Zandvoort, M. J., van der Worp, H. B., de Haan, E. H., de Kort, P. L., & Kappelle, L. J. (2005). Early depressive symptoms after stroke: neuropsychological correlates and lesion characteristics. *Journal of the Neurological Sciences, 228*(1), 27-33. doi: 10.1016/j.jns.2004.09.031

Ob, H., & Seo, W. (2015). A Comprehensive Review of Central Post-Stroke Pain. *Pain Management Nursing, 16*(5), 804-818.
Organised inpatient (stroke unit) care for stroke. (2013). *Cochrane Database Syst Rev, 9*, Cd000197. doi: 10.1002/14651858.CD000197.pub3
Plassman, B. L., Williams, J. W., Jr., Burke, J. R., Holsinger, T., & Benjamin, S. (2010). Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life. *Ann Intern Med, 153*(3), 182-193. doi: 10.7326/0003-4819-153-3-201008030-00258
Ratnasabapathy, Y., Broad, J., Baskett, J., Pledger, M., Marshall, J., & Bonita, R. (2003). Shoulder pain in people with a stroke: a population-based study. *Clin Rehabil, 17*(3), 304-311.
Robinson, R. G., & Spalletta, G. (2010). Poststroke depression: a review. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie, 55*(6), 341-349.
Robinson, R. G., Starr, L. B., Kubos, K. L., & Price, T. R. (1983). A two-year longitudinal study of post-stroke mood disorders: findings during the initial evaluation. *Stroke, 14*(5), 736-741.
Sacco, R. L., Kasner, S. E., Broderick, J. P., Caplan, L. R., Connors, J. J., Culebras, A., . . . Vinters, H. V. (2013). An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke, 44*(7), 2064-2089. doi: 10.1161/STR.0b013e318296aeca
Sagen, U., Finset, A., Moum, T., Morland, T., Vik, T. G., Nagy, T., & Dammen, T. (2010). Early detection of patients at risk for anxiety, depression and apathy after stroke. *General Hospital Psychiatry, 32*(1), 80-85. doi: 10.1016/j.genhosppsych.2009.10.001
The Norwegian Directorate of Health (2010). Norwegian guidelines on management and rehabilitation of stroke. Retrieved from http://www.helsebiblioteket.no/Retningslinjer/Hjerneslag/Forord-og-innledning, *assessed 2015*
Vaartjes, I., O'Flaherty, M., Capewell, S., Kappelle, J., & Bots, M. (2013). Remarkable decline in ischemic stroke mortality is not matched by changes in incidence. *Stroke, 44*(3), 591-597. doi: 10.1161/strokeaha.112.677724
van Almenkerk, S., Depla, M. F., Smalbrugge, M., Eefsting, J. A., & Hertogh, C. M. (2015). Pain among institutionalized stroke patients and its relation to emotional distress and social engagement. *Int J Geriatr Psychiatry, 30*(10), 1023-1031. doi: 10.1002/gps.4256
van Dijk, M. J., de Man-van Ginkel, J. M., Hafsteinsdottir, T. B., & Schuurmans, M. J. (2015). Identifying depression post-stroke in patients with aphasia: A systematic review of the reliability, validity and feasibility of available instruments. *Clin Rehabil*. doi: 10.1177/0269215515599665
van Mierlo, M. L., van Heugten, C. M., Post, M. W., de Kort, P. L., & Visser-Meily, J. M. (2015). Psychological factors determine depressive symptomatology after stroke. *Arch Phys Med Rehabil, 96*(6), 1064-1070. doi: 10.1016/j.apmr.2015.01.022
Waaler, H. (1999). Scenario 2030, Sykdomsutvikling for eldre fram til 2030. *Statens helsetilsyn*.
Warlow, C., van Gijn, J., Dennis, M., Wardlaw, J., Bamford, J., Hankey, G., . . . Rothwell, P. (2008). STROKE, Practical Management.
Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatr Scand, 67*(6), 361-370.

Attachments

1. The Brief Pain Inventory – first 3 items

Kartlegging av smerte etter hjerneslag

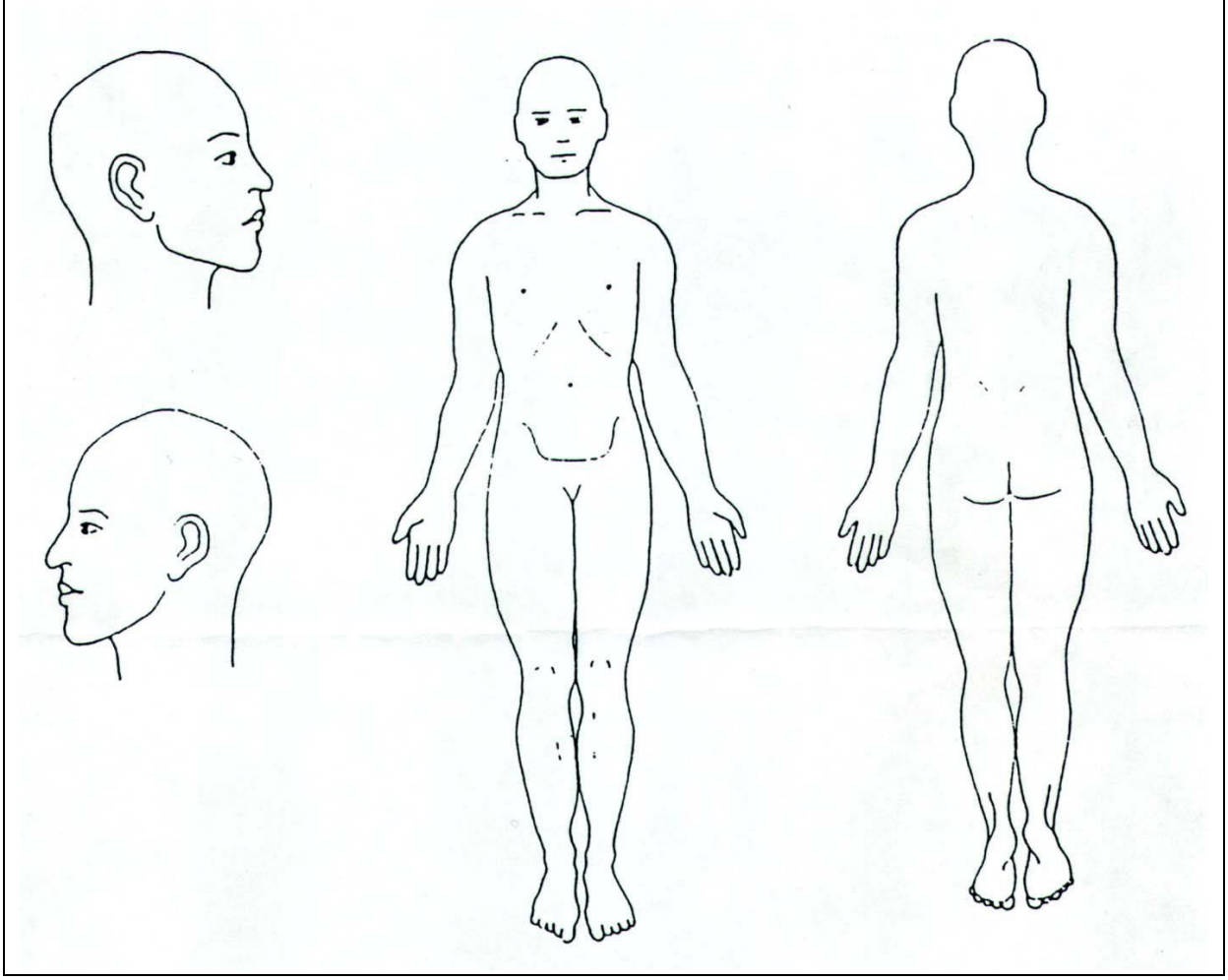
1. Gjennom livet har de fleste av oss hatt smerter (som lett hodepine, forstuelser eller tannpine). Har du i dag smerter av et annet slag enn slike dagligdagse smerter?

Ja ☐ Nei ☐

2. Hvis ja: Har denne smerten tilkommet etter hjerneslaget?

Ja ☐ Nei ☐

3. Vil du skravere de områdene på kroppen hvor du har smerter. Marker med et kryss der du har mest vondt.



2. The Hospital Anxiety & Depression Scale
(January 1999)

Rettledning
Legen er klar over at følelser spiller en stor rolle ved de fl este sykdommer. Hvis legen vet mer om følelser, vil han/hun bli bedre i stand til å hjelpe deg.
Her kommer noen spørsmål om hvorledes du føler deg. For hvert spørsmål setter du kryss for ett av de fire svarene som best beskriver dine følelser den siste uken. Ikke tenk for lenge på svaret – de spontane svarene er best.

1. Jeg føler meg nervøs og urolig
❏ 3 Mesteparten av tiden
❏ 2 Mye av tiden
❏ 1 Fra tid til annen
❏ 0 Ikke i det hele tatt

2. Jeg gleder meg fortsatt over tingene slik jeg pleide før
❏ 0 Avgjort like mye
❏ 1 Ikke fullt så mye
❏ 2 Bare lite grann
❏ 3 Ikke i det hele tatt

3. Jeg har en urofølelse som om noe forferdelig vil skje
❏ 3 Ja, og noe svært ille
❏ 2 Ja, ikke så veldig ille
❏ 1 Litt, bekymrer meg lite
❏ 0 Ikke i det hele tatt

4. Jeg kan le og se det morsomme i situasjoner
❏ 0 Like mye nå som før
❏ 1 Ikke like mye nå som før
❏ 2 Avgjort ikke som før
❏ 3 Ikke i det hele tatt

5. Jeg har hodet fullt av bekymringer
❏ 3 Veldig ofte
❏ 2 Ganske ofte
❏ 1 Av og til
❏ 0 En gang i blant

6. Jeg er i godt humør
❏ 3 Aldri
❏ 2 Noen ganger
❏ 1 Ganske ofte
❏ 0 For det meste

7. Jeg kan sitte i fred og ro og kjenne meg avslappet
❏ 0 Ja, helt klart
❏ 1 Vanligvis
❏ 2 Ikke så ofte
❏ 3 Ikke i det hele tatt

8. Jeg føler meg som om alt går langsommere
❏ 3 Nesten hele tiden
❏ 2 Svært ofte
❏ 1 Fra tid til annen
❏ 0 Ikke i det hele tatt

9. Jeg føler meg urolig som om jeg har sommerfugler i magen
❏ 0 Ikke i det hele tatt
❏ 1 Fra tid til annen
❏ 2 Ganske ofte
❏ 3 Svært ofte

10. Jeg bryr meg ikke lenger om hvordan jeg ser ut
❏ 3 Ja, jeg har sluttet å bry meg
❏ 2 Ikke som jeg burde
❏ 1 Kan hende ikke nok
❏ 0 Bryr meg som før

11. Jeg er rastløs som om jeg stadig må være aktiv
❏ 3 Uten tvil svært mye
❏ 2 Ganske mye
❏ 1 Ikke så veldig mye
❏ 0 Ikke i det hele tatt

12. Jeg ser med glede frem til hendelser og ting
❏ 0 Like mye som før
❏ 1 Heller mindre enn før
❏ 2 Avgjort mindre enn før
❏ 3 Nesten ikke i det hele tatt

13. Jeg kan plutselig få en følelse av panikk
❏ 3 Uten tvil svært ofte
❏ 2 Ganske ofte
❏ 1 Ikke så veldig ofte

❏ 0 Ikke i det hele tatt

14. Jeg kan glede meg over gode bøker, radio og TV
❏ 0 Ofte
❏ 1 Fra tid til annen
❏ 2 Ikke så ofte
❏ 3 Svært sjelden

Takk for utfyllingen!

Sum A:
1+3+5+7+9+11+13= _____

Sum D:
2+4+6+8+10+12+14=_____

Sum A + D: _____