Quality of Life after aneurysmal subarachnoid haemorrhage

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Quality of Life after aneurysmal subarachnoid haemorrhage

Kwaliteit van leven na aneurysmale subarachnoïdale bloeding

(met een samenvatting in het Nederlands)

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in het openbaar te verdedigen op
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door

Patricia Elisabeth Constance Agnes Passier
geboren op 14 juli 1966, te Maastricht

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Quality of life after aneurysmal subarachnoid haemorrhage

(General Introduction)

ANEURYSMAL SUBARACHNOID HAEMORRHAGE

Subarachnoid haemorrhage (SAH) accounts for approximately 5% of all strokes, occurs at relatively young age compared to those who have other stroke subtypes, with a mean age of 62 years, and still carries a poor prognosis for survival.[1,2] Ruptured aneurysms are the cause in 85% of SAH, whereas 10% fit into the pattern of so-called non-aneurysmal perimesencephalic haemorrhage, a relatively benign condition. The remaining 5% have other causes.[3]

Aneurysm

Intracranial aneurysms are not congenital, as was once believed, but develop in the course of life. Besides a familial predisposition, environmental risk factors of SAH are hypertension, smoking and excessive alcohol intake, all of which more-or-less double the risk.[3]

Saccular aneurysms arise at sites of arterial branching, usually at the base of the brain, either on the circle of Willis itself or at a nearby branching point (figure 1).[3]

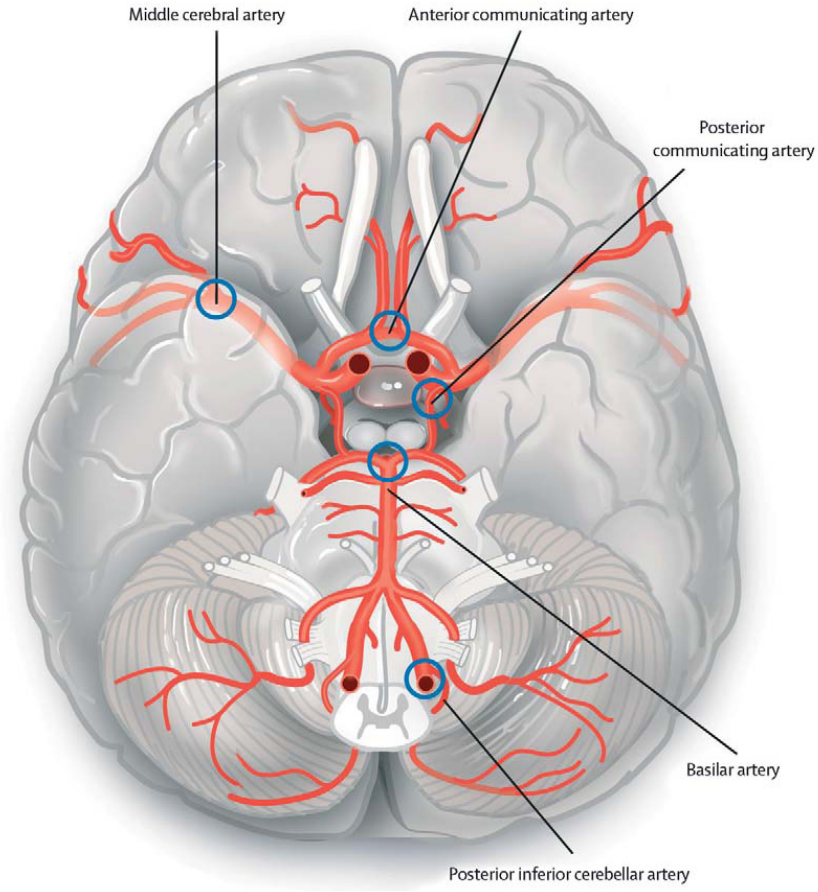

Figure 1. Base of brain, with most common sites of aneurysms (circles).[3]

Symptoms

Sudden headache is the most characteristic symptom of SAH: in three out of four patients, the onset is within a split second or a few seconds. On admission two-thirds of all patients have depressed level of consciousness, of whom half are in coma. Neck stiffness is a common symptom, caused by the inflammatory response to blood in the subarachnoid space.[3]

Focal neurological deficits occur when an aneurysm compresses a cranial nerve or bleeds into the brain parenchyma, or from focal ischemia due to acute vasoconstriction immediately after aneurysmal rupture.[3]

Treatment

During the past decades, endovascular occlusion by means of detachable coils (coiling) of aneurysms has become an accepted method of aneurysm occlusion in addition to surgical occlusion (clipping). The technique of coiling consists of packing the aneurysm with platinum coils, with a system for controlled detachment. The aneurysms of the middle cerebral artery are often unfavourable for coiling, because of the anatomical configuration.[3]

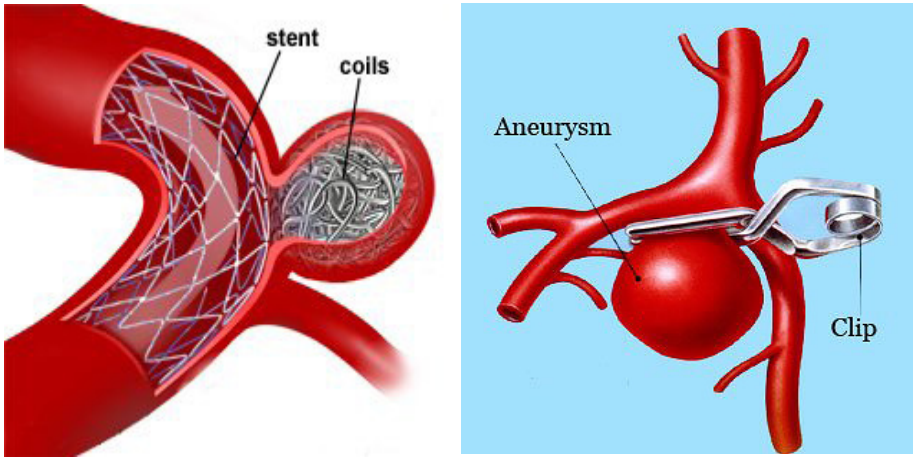

Figure 2. Left aneurysm coiled and right one clipped (www.nvvn.org)

Complications

Rebleeding

In the first hours after the initial haemorrhage, up to 15% of patients have a sudden deterioration of consciousness that suggests rebleeding. After rebleeding the prognosis is poor: 80% of patients die or remain disabled. To prevent rebleeding aneurysms are treated with coiling or clipping.[3]

Secondary ischemia

Unlike thromboembolic stroke, cerebral ischemia after SAH has a gradual onset and often involves more than the territory of a single cerebral artery or one off its branches. The clinical manifestations evolve gradually, over several hours, and consist of hemispheric focal deficits in a quarter of patients, a reduction in the level of consciousness in another quarter, and of both signs in the remaining half.[3]

Hydrocephalus

The typical presentation of acute hydrocephalus is that of a patient who is initially alert, followed by a gradual reduction in consciousness in the next few hours, or consciousness is impaired from the onset. If hydrocephalus occurs, drainage is often indicated, by lumbar puncture or an external catheter.[3]

Long-term problems after aneurysmal SAH

Up to 55% of the patients with aneurysmal SAH recover to functional independence, but nevertheless many patients experience psychosocial problems.[5] High proportions of persons with impairments in cognitive functioning are reported, with memory (14 to 61%), executive function (3 to 75%), and language (0 to 76%) as the most often affected cognitive domains.[4] Furthermore, symptoms of anxiety and depression are common (in up to half of the patients) after aneurysmal SAH.[5] The high prevalence of depression may be attributed to the life-threatening experience of aneurysmal SAH or to the fear of rebleeding. Fatigue is also frequently reported (in up to two-thirds of patients) after SAH, and only partly related to mood disturbances.[5] Also, many SAH patients experience sleep disturbances.[4]

Besides these neuropsychological and psychosocial consequences of aneurysmal SAH anosmia is reported in almost one-thirds of patients, often after operation and with aneurysms of the anterior communicating artery. Anosmia has an important effect on eating, drinking, social functioning, sex, and psychosocial wellbeing.[5]

Furthermore, new aneurysms can develop and existing aneurysms can enlarge in the years after aneurysmal SAH. Risk factors for recurrent aneurysmal SAH are younger age, verified history of familial aneurysmal SAH, current smoking, and presence of more than one aneurysm at the time of the initial aneurysmal SAH.[5]

All these long term problems negatively affect quality of life (QoL), life satisfaction, and participation e.g. return to work. A recent meta-analyses of determinants of Health-Related QoL (HRQoL) in patients with SAH revealed only physical disability as a consistent predictor, but 57% of the variance of physical HRQoL and 94% of the variance of mental HRQoL was left unexplained.[6] However, that review did not take psychosocial aspects into account, whereas psychosocial aspects of HRQoL appear more heavily affected than physical aspects.[7]

AIMS OF THIS THESIS

General aim

To increase our understanding of QoL after aneurysmal SAH, and the most important determinants of QoL, in order to tailor appropriate rehabilitation programs and thereby enhance their effectiveness.

Specific aims

- To review the literature regarding the determinants of QoL after aneurysmal SAH.
- To validate the Stroke Specific Quality of Life scale (SS-QoL) as a measure of HRQoL in patients with aneurysmal SAH.
- To identify determinants of cognitive complaints, fatigue, HRQoL and life satisfaction using cross-sectional and longitudinal designs.

SETTING OF THIS THESIS: THE SAH-OUTPATIENT CLINIC IN THE UNIVERSITY MEDICAL CENTRE UTRECHT

The various physical and cognitive deficits, mood problems and other long-term problems, called for a multidisciplinary outpatient clinic dedicated to patients with aneurysmal SAH and their proxies to improve the care for these group of patients. At the University Medical Centre Utrecht this outpatient clinic was started in September 2006.

Before visiting the outpatient clinic, all patients receive by mail, with the confirmation of their appointment, questionnaires including standardized self-report measures of anxiety, depression and coping, and are asked to bring the completed questionnaire with their visit to the clinic.

At our multidisciplinary SAH-outpatient clinic, patients are seen 6 weeks after discharge, by

a) a specialized SAH nurse who interviews the patient about restrictions that they encounter in day-to-day life and provides information about management of risk factors, in particular smoking and hypertension, familial aneurysmal SAH, long-term prognosis, and restrictions on car driving, and who assesses the Checklist for Cognitive and Emotional consequences following stroke (CLCE-24).

b) a neuropsychologist for a brief neuropsychological examination (45 minutes).

c) a rehabilitation physician who uses all of the collected information by nurse and neuropsychologist and assesses physical restrictions to develop a rehabilitation programme if needed that is tailored to an individual patient's needs on the basis of all information received.

Patients who visited our SAH-outpatient clinic between October 2006 and September 2008 were included in this study.

DATA USED IN THIS THESIS

Cross-sectional study

To study the long term life satisfaction and employment status after aneurysmal SAH, we used data from a previously conducted cross-sectional study of patients who were living at home 3 years after SAH.[7] A questionnaire was sent by mail to patients who had been treated by clipping or coiling after aneurysmal SAH between January 2003 and July 2005. This questionnaire included standardized self-report measures of depression, anxiety, cognitive complaints, fatigue, coping, and neuroticism and questions about employment status. Life satisfaction was measured with the Life Satisfaction questionnaire (LiSat-9), a valid measure of life satisfaction.[14]

Data collected in the outpatient clinic

Neuropsychological examination

The brief neuropsychological screening addressed the following cognitive domains; *Memory* included verbal working memory assessed by the Backward Digit Span of the Wechsler Adult Intelligence Scale III (WAIS-III) and Category Fluency (semantic memory) using animal naming (2 minutes). The Rey Auditory Verbal Learning Task (RAVLT) was used to measure verbal learning, revealing scores for immediate and delayed recall and recognition. Non-verbal recall, incidental, was evaluated using the delayed Rey-Osterrieth Complex Figure Test (CFT). *Executive functioning* was measured with the Brixton spatial Anticipation Test for strategic thinking and with phonological fluency ("N" and "A") for concept generation. *Attention* was measured by Forward Digit Span of the WAIS III and the Stroop Colour Word test. To obtain an indication of *visuospatial functioning*, the copy score of the Rey-CFT was used.[8]

Questionnaires

The questionnaires, which were completed before the visit to the outpatient clinic, included standardized self-report measures of anxiety, depression and coping:

Depressive symptoms were measured with the Beck Depression Inventory-II-NL.[9] We accepted a score of 10 or higher as cut-off point for possible depression.[9]

We measured anxiety with the state part of the State-Trait Anxiety Inventory (STAI-DY-1).[10] A higher sum score implicates a higher level of anxiety, with different cut-off points based on age (above 40 versus up to 40), gender and educational level (high versus low).[11]

Passive coping strategy was measured using the passive coping subscale (7 items) from the Utrecht Coping List (UCL-P).[12] Higher scores indicate more use of passive coping styles.

Interview

The CLCE-24 was assessed by the specialized SAH nurse, and consists of 13 cognitive items (for instance problems with 'doing two things at once' or 'attending to

things') and 9 emotional items (for instance being 'depressed' or 'faster or more often tired') and 2 open-ended questions which allow to add other problems, but which are not included in the scores.[13] The interviewer scores a '0' for absence and a '1' for presence of complaints; the sum score indicates the number of experienced complaints.

Follow-up measurement

One year after SAH, a postal questionnaire about HRQoL and fatigue was sent to all patients who had visited the SAH-outpatient clinic and were living in the community.

Outcome measurements

HRQoL was evaluated with the SS-QoL.[16] The SS-QoL is a disease specific quality of life measure and contains 12 domains with altogether 49 items. The domains are: self-care, mobility, upper-extremity function, language, vision, work, thinking, family roles, social roles, personality, mood and energy. Items are averaged to obtain domain scores and a total SS-QoL score. The possible range of all summary scores is from 1 (poor HRQoL) up to 5 (good HRQoL).

Fatigue was assessed using the Fatigue Severity Scale (FSS).[17] This scale consists of nine statements about the impact of fatigue on daily life, each scored on a 7-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree). The total FSS score is the mean of the item scores. The FSS is a reliable scale distinguishing patients from controls.[17] Fatigue was scored as present if the FSS score was above 4.[17] A score above 4 indicates a moderate to high impact of fatigue on daily living.

OUTLINE OF THIS THESIS

Chapter one represents the general introduction.

Review

Chapter two reviews the literature regarding the determinants of HRQoL in patients with aneurysmal subarachnoid haemorrhage, and used the International Classification of Functioning, Disability, and Health (ICF) model of the World Health Organization to classify these determinants.

Cross-sectional part

Chapter three describes a validation study of the SS-QoL scale and explores different options to merge the 12 SS-QoL domains into a limited number of subtotal scores in a SAH population.

Chapter four reports the prevalence of cognitive complaints in patients who are living at home 3 months after SAH and whether these cognitive complaints are related with cognitive impairments, demographic characteristics (age, sex, level of education), disability (GOS) and emotional problems (depressive symptoms, anxiety).

Chapter five evaluates the long term life satisfaction and the employment status of patients with SAH who were living at home 3 years after SAH. The relationships are explored between life satisfaction and global outcome, employment status, socio-demographic characteristics, subjective complaints and personality characteristics.

Longitudinal part

Chapter six describes whether demographic characteristics, SAH characteristics in the acute stage and outcome (disability, discharge destination), cognitive and emotional complaints, emotional problems (depressive symptoms, anxiety), cognitive impairments and passive coping, assessed three months after SAH predict the HRQoL one year after SAH.

Chapter seven reports the occurrence of fatigue in patients with SAH who are living at home one year after SAH, and whether physical or cognitive impairments, passive coping, emotional problems (anxiety, depressive symptoms), or a combination of these factors, assessed three months after SAH predict the post-SAH fatigue, one year after the SAH.

General discussion

Chapter eight discusses the combined results of the previous chapters, and reflects on the clinical application of the studies for patients with aneurysmal SAH. Recommendations for future research are presented.

REFERENCES

1. Nieuwkamp DJ, Setz L, Algra A, Linn FHH, Rooij de NK, Rinkel GJE. Changes in case-fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex and region: a meta-analysis. Lancet Neurology 2009; 8:635-42.
2. Rooij de NK, Linn FHH, Plas van der JA, Algra A, Rinkel GJE. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. J Neurol Neurosurg Psychiatry 2007;78: 1365-1372.
3. Gijn van J, Kerr RS, Rinkel GJE. Subarachnoid haemorrhage. Lancet 2007; 369: 306-218, Copyright Elsevier.
4. Al-Khindi T, MacDonald RL, Schweizer TA. Cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. Stroke 2010;41: e519-e536.
5. Rinkel GJE, Algra A. Long-term outcomes of patients with aneurysmal subarachnoid haemorrhage. Lancet Neurol 2011;10:349-356.
6. Noble AJ, Schenk T. Which variables help explain the poor health-related quality of life after subarachnoid hemorrhage? A meta-analysis. Neurosurgery 2010;66:772-783.
7. Visser-Meily JMA, Rhebergen ML, Rinkel GJE, Zandvoort van MJ, Post MWM. Long-term health related quality of life after aneurysmal subarachnoid hemorrhage; relationship with psychological symptoms and personality characteristics. Stroke 2009; 40:1526-9.
8. Lezak MD, Howieson DB, Loring DW. Neuropsychological assessment, (4th edition). New York; Oxford University Press, 2004.
9. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-571.
10. Spielberger CD, Gorsuch RL, Lushene PR, Vagg PR, Jacobs AG. Manual for the Stat-Trait Anxiety Inventory (form Y). Consulting Psychologists Press 1983, Inc.: Palo Alto.
11. Ploeg van der HM. Handleiding bij de Zelf-beoordelings vragenlijst, een Nederlandse bewerking van de Spielberger Stait-Trait Anxiety Inventory, STAI-DY. Lisse, Swets en Zeitlinger, 2000.
12. Eriksen HR, Olff M, Ursin H. The CODE, a revised battery for coping and defense and its relation to subjective health. Scand J Psychol 1997;38: 175-182.
13. Heugten van C, Rasquin S, Winkens I, Beusmans G, Verhey F. Checklist for cognitive and emotional consequences following stroke (CLCE-24): development, usability and quality of the self-report version. Clin Neurol and Neurosurg 2007; 109:257-262.
14. Fugl-Meyer AR, Melin R, Fugl-Meyer KS. Life satisfaction in 18- to 64-year-old Swedes in relation to gender, age, partner and immigrant status. J Rehabil Med 2002; 34:239-246.
15. Spilker B, Revicki DA. Taxonomy of quality of life. In: Spilker B ed. Quality of life and pharmacoeconomics in clinical trials, second edition. New York: Lippincott-Raven, 1996.
16. Williams LS, Weinberger M, Harris LE, Clark DO, Biller J. Development of a stroke specific quality of life scale. Stroke 1999;30:1362-9.
17. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale: Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46:1121-1123.

Based on:

Determinants of health-related quality of life after aneurysmal subarachnoid haemorrhage: a systematic review

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Submitted

Determinants of health-related quality of life after aneurysmal subarachnoid haemorrhage: a systematic review

ABSTRACT

Background and purpose: Many patients with subarachnoid haemorrhage (SAH) from a ruptured intracranial aneurysm who recover to functional independence have a reduced quality of life (QoL). The aim of this study was to identify determinants of reduced QoL.

Methods: Databases PubMed, PsychINFO, and CINAHL were used to identify articles about QoL of aneurysmal SAH survivors. We selected all studies which reported relationships between possible determinants and QoL in aneurysmal SAH, and used the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization to classify these determinants. We described all reported associations between these determinants and QoL.

Results: Twenty studies met pre-defined inclusion criteria for this review, in which 13 different QoL questionnaires were used. Based on the ICF model, determinants related to Body Structure & Function (e.g. fatigue and mood), Activity (e.g. physical disability and cognitive complaints) and Personal factors (e.g. female gender, higher age, neuroticism and passive coping) are consistently related to worse QoL after aneurysmal SAH.

Conclusion: QoL after aneurysmal SAH is mainly determined by fatigue, mood problems, physical disability, cognitive complaints and personal characteristics, which is important information to tailor the rehabilitation program to the needs of these patients. Further research is needed to investigate participation in relation to QoL after SAH.

INTRODUCTION

Subarachnoid haemorrhage (SAH) from a ruptured intracranial aneurysm accounts for approximately 5% of all strokes, occurs at relatively young age, and still carries a poor prognosis for survival.[1] Many patients who recover to functional independence experience a reduced quality of life (QoL).[1,2]

QoL is a broad and ill-defined concept.[3] QoL has been taken to be synonymous with health status, physical functioning, perceived health status, subjective health, health perception, symptoms, need satisfaction, individual cognition, functional disability, psychiatric disturbance, well-being, and, often, several of these at the same time.[4] Three broad approaches to the operationalisation of QoL can be found in the literature: (1) by equating quality of life with health, (2) by equating it with well-being, and (3) by treating QoL as a super-ordinate construct.[5] Health-related quality of Life (HRQoL) is seen as a subset of the overall concept of QoL, and as a multidimensional construct including those parts of quality of life that directly relate to an individual's health, in which at least physical, psychological and social dimensions are represented.[6] Aspects of HRQoL can be framed according to the International Classification of Functioning, Disability, and Health (ICF).[5] This ICF model allows the integration of several perspectives regarding the consequences of a health condition, e.g. SAH, and offers a helpful framework to order different predictors of HRQoL.

A recent meta-analyses of determinants of HRQoL in patients with SAH revealed only physical disability as a consistent predictor, but 57% of the variance of physical HRQoL and 94% of the variance of mental HRQoL was left unexplained.[7] However, this review included only studies using a HRQoL questionnaires Short Form-36 or Sickness Impact Profile, excluding studies using different questionnaires, and the analyses concerned only "traditional" predictors: demographic and SAH characteristics, and physical and cognitive impairment, and did not take psychosocial aspects into account.[7] Further, this review included also studies describing patients with non-aneurysmal SAH. Some of these patients with non-aneurysmal SAH might have had a perimesencephalic haemorrhage, which has a good HRQoL, and might have influenced the results.[8] Another review was primarily focused on the description of HRQoL and did not provide a comprehensive description of determinants of HRQoL.[2] Consequently, the factors associated with reduced quality of life are still unclear. A better understanding of these factors is required in order to develop interventions to improve QoL of patients with SAH.

The objective of this review is to provide an in-depth analysis of the determinants of QoL, focusing on survivors of aneurysmal SAH. Based on the ICF[9], we hypothesized that determinants in the category body structures and functions (e.g. SAH grade) will show weaker relationships with QoL than determinants in the categories activities (e.g. outcome) and participation.

METHODS

Search strategy

Electronic searches of the literature published from 1994 to January 2011 were performed in PubMed, PsychINFO, and CINAHL. The year 1994 was chosen because by that time endovascular treatment of ruptured aneurysms started to become an accepted procedure. The search terms were: subarachnoid haemorrhage, subarachnoid hemorrhage

and SAH in combination with quality of life, including the related terms happiness, life satisfaction, health-related quality of life, perceived health, health status, wellbeing, well-being, sanctity of life, value of life and livability. Reference lists of included studies were scrutinized for additional articles.

Selection criteria

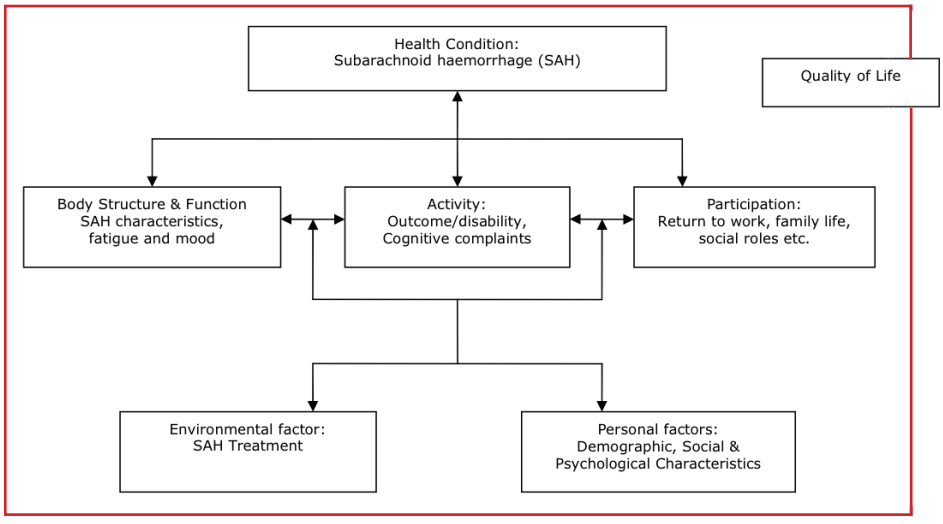
All studies were included that met the following criteria: (1) the study population exclusively concerned aneurysmal SAH; (2) the study described QoL with one or more standardized QoL questionnaires; (3) the study reported on quantitative relationships between possible determinants and QoL, regardless of the type of determinant (5) the article was a report (e.g. not an abstract or letter) published in English, and (6) the study was published in a peer-reviewed journal.

Data collection and analysis

After removing duplicates, two authors (PECAP and MWMP) independently checked the abstracts, or the hard copy in case the abstract was inconclusive, on inclusion and exclusion criteria, and compared their results. In case of disagreement, both authors reassessed and discussed that abstract until consensus was reached.

Information was collected regarding the study setting, and design (cross-sectional, patient-control or cohort), number of participants, sex distribution, the time of assessment since SAH onset, the QoL measure used, and the assessed determinants of QoL. All reported associations between a predictor and a QoL outcome were taken into account. Univariate associations and multivariate associations were described separately. All relevant studies and determinants were included, so a meta-analysis was not possible.

Figure 1. International Classification of Functioning, Disability, and Health (ICF) model for SAH



Application of the ICF model

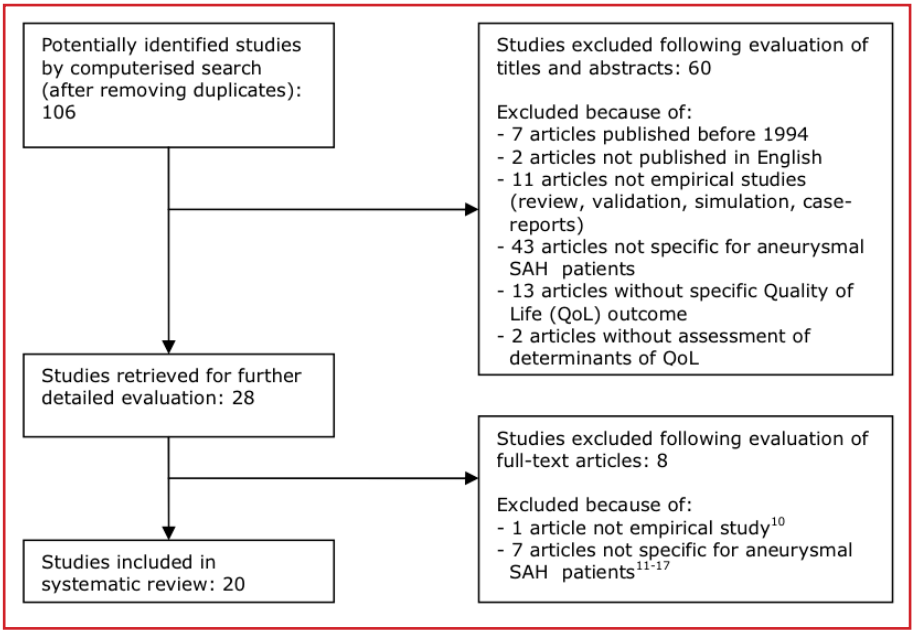
In the ICF model (figure 1), *Body Structure & Functions* are anatomical parts and physiologic functions of body systems.[9] This category covers SAH characteristics e.g. SAH

grade and site of aneurysm, fatigue, mood and neuropsychological functioning representing an impairment. *Activity* is the execution of a task or action by an individual, and activity limitations are the difficulties an individual may have in executing activities. For the purposes of this review, this category contains physical functioning, cognitive complaints and global outcome scores. *Participation* is defined as the involvement in a life situation and participation restrictions as problems in involvement, e.g. return to work. *Environmental factors* are defined as external features of the physical, social, and attitudinal world, including characteristics of treatment, and support. *Personal factors* are defined as individual features which can have an impact on an individual's performance and covers demographic, and psychological characteristics.

RESULTS

Literature searches were performed in PubMed (84 hits), PsychINFO (10 hits), CINAHL (33 hits) and reference lists (2 hits). After removing 23 duplicates, the remaining 106 abstracts were checked for inclusion. There was agreement about inclusion or exclusion for 93 (88%) of these abstracts. The remaining 13 articles were agreed upon in- or exclusion after discussion. The flow chart of the study selection is shown in figure 2.

Figure 2. Study selection process.



Twenty studies met the inclusion criteria. Most studies had a prospective cohort design and were conducted in Europe. The number of subjects ranged from 18 up to 538, and the percentage of females ranged from 43 to 82%. Mean time after SAH of QoL assessment varied from 3 months up to 8 years. Other study characteristics are shown in table 1.

A total of 13 different Quality of Life questionnaires were used, which were all HRQoL measures, containing only 2 to as many as 136 questions. The most often used questionnaire was the SF-36 (table 2).

Determinants of QoL (table 3).

Body Structure & Function

Severity of the SAH. Associations between the clinical condition on admission (usually assessed by means of the Hunt&Hess (H&H) scale) were reported in six studies. Inconsistent results were found; one study found an association between good clinical condition on admission (lower H&H grade) and worse QoL[18], whereas other studies found no association[21,27,31] or found an association between poor clinical condition on admission (higher H&H grade) and worse QoL.[26,35] Poor clinical condition on admission (higher World Federation Neurological Surgeons grade) was predominantly associated with worse QoL[27,35,36], and a higher Glasgow Coma Score was associated with better QoL.[35] Only one study found an association between higher Fisher grade and worse QoL[26], whereas another study found no such association.[27]

Site of the aneurysm was a determinant in two studies, in which patients with aneurysms in middle cerebral artery and/or anterior communicating artery/anterior cerebral artery had worse QoL.[26,37] In two other studies no association was found between aneurysm location and QoL.[18,22] One study has examined *hormone levels* in relation to QoL, and showed higher basal cortisol levels to be associated with part of the QoL subscales, and showed growth hormone deficiency and stimulated adrenocorticotrophine levels to be associated with one out of six QoL subscales.[30] Furthermore, an association was found between complications and worse QoL in one study[36], whereas two other studies found no association.[28,37] There was an association between the number of additional illnesses and worse QoL.[26]

Fatigue and mood problems were associated with lower QoL in three studies.[21,31,37] *Cognitive functioning*: One study[34] showed an association between decreased cognitive functioning and worse QoL, whereas another study showed this association only in one of two QoL measurements.[31]

Environmental factor: SAH treatment

Four studies associated type of treatment of SAH (e.g. surgical, endovascular or medical) and QoL[19,31,32,37], of whom one showed an association between aneurysm treatment by coiling and better QoL[37], whereas another study found coiling to be associated to worse QoL at discharge, but not at 12 months follow-up.[31] Duration of treatment (clipping) was associated with QoL in one study.[26] No associations were found between time to treatment[31], early hemicraniectomie[20], or hypertensive treatment.[18,29] One study[24] reported an association between treatment with acetylsalicylic acid and worse QoL (domain sleep and rest), and one study found an association between pravastatin treatment and better QoL.[36] Screening for new aneurysm was not associated to QoL.[33]

Activity

Two *global outcome scales* have been investigated as determinants of QoL after SAH. Three studies[23,27,31] showed less disability (lower scores on the Modified Rankin Scale (mRS)) to be associated with better QoL, and one study reported improvement of

mRS to be associated with better QoL on several domains.[25] In all 3 studies in which the Glasgow Outcome Scale (GOS) was used, a good clinical condition (higher GOS score) was associated with better QoL.[27,30,37]

Cognitive complaints: One study showed an association between cognitive complaints and worse QoL.[37]

Personal factors

Demographic and social characteristics: All 5 studies found associations between gender and QoL, females reporting worse QoL.[27,30,31,36,37] Four studies reported associations between higher age and worse QoL[26,27,36,37], whereas three other studies did not find a relationship[18,30,31], and one reported an association between higher age and better QoL on one of the six NHP domains.[30] Being single or divorced was associated with worse QoL in one study.[31] One study found lower education to be associated with worse QoL[31], whereas another study found no such association.[37]

Psychological characteristics: Neuroticism and passive coping were both associated with worse QoL after SAH in one study.[37]

DISCUSSION

This review shows that fatigue and depressed mood, physical disability and cognitive complaints, female gender and higher age, neuroticism and passive coping are consistently related to worse HRQoL after aneurysmal SAH.

Concerning *Body Structure & Function* limitations, mood and fatigue have shown to be important determinants of HRQoL after SAH, and we expect these determinants to have also a direct influence on the activity level. In addition, fatigue was measured with the Fatigue Severity Scale, which investigates the impact of fatigue on daily life, and therefore probably already represents the activity level. Mood problems, which are very common after SAH, are also expected to influence activity in daily life. Regarding the *Activity* limitations in this review, we found a strong association between physical disability and physical HRQoL after SAH as well as significant, but weaker, associations with mental HRQoL, which is in line with the meta analysis.[7] Furthermore, a strong association was found between cognitive complaints and HRQoL[37], whereas objective cognitive dysfunction was less strong related to HRQoL.[31,34] In a previous study, we showed cognitive complaints to be predominantly associated with depressive symptoms and the level of (physical) disability.[68] In this review, *Personal factors* passive coping and neuroticism showed strong associations with worse QoL, although only reported in one study.[37]

Participation has not been studied as a determinant of QoL after SAH. We showed that inability to return to work was strongly related to dissatisfaction with life after SAH.[69] Other aspects of participation like, having meaningful leisure activities and satisfying social relations have never been subject of research in survivors of SAH. Further research is needed to investigate participation in relation to QoL after SAH.

There are some limitations of this review to be mentioned. First, the number of studies that could be included was small because many studies, report about QoL of the total SAH population, including those without aneurysm, which might have influenced the

results.[8] Second, the included studies were very heterogeneous with respect to instruments and statistical analyses used. Most of the studies used validated but generic instruments, but there is no gold standard for measuring QoL in SAH. Concerning the analyses, each study adjusted for a different set of factors, and the sample sizes of most studies were small, so the power to detect QoL differences was low. A final limitation is that the results might in part be ascribed to conceptual overlap between the predictors and the outcomes. For example, physical disability was a predictor of physical HRQoL, but the latter concept includes physical disability, e.g. the physical functioning scale of the SF-36 and the mobility scales of the SIP and ALQI. The same is true for fatigue and psychosocial HRQoL. This problem is hard to avoid, because most HRQoL measures include a wide range of consequences of a health condition like SAH. One would need to use either QoL measures that do not include aspects of health, such as measures of over-all subjective well-being, or use only disease characteristics, personal or environmental factors as determinants of HRQoL.[70] Both options have obvious disadvantages, but this overlap between determinant and outcome has to be taken into account while interpreting the results.

Conclusion

HRQoL after aneurysmal SAH is mainly determined by fatigue, mood problems, physical disability, cognitive complaints, passive coping and neuroticism. Information about these determinants in an individual SAH patient can be very important to tailor the rehabilitation program to the needs of this patient. A structured screening of physical, cognitive and emotional functioning early after discharge, for example at an outpatient clinic, can be important to detect these problems. When information is available about the patients functioning, education can be given to patients and their relatives. Also, an occupational therapy program on maintaining a balance between capacity and load in their daily activities may help patients. Similarly, a passive coping style and/or emotional problems may be improved by rehabilitation therapy from physical or mental health professionals. Whether focused interventions result in better HRQoL after aneurysmal SAH should be investigated in future studies. Further, more research is needed into determinants of fatigue and mood problems, issues of social participation and psychological determinants of HRQoL, and their relation to one another.

Table 1. Study characteristics

Author(s), year, nationality	Method	participants		time since SAH	QoL Measurement	Determinants
		n	women (%)			
Barth et al, 2009, Germany/ Japan.[18]	case-control	11 NPRI 7 conservative treatment	61	10- 20 months	Short-Form Health Survey (SF-36)	Nicardipine prolonged-release implants (NPRI)
Bellebaum et al, 2004, Germany.[19]	case-control	16 coiled 16 clipped 16 controls	75	22.7 months (SD 14.6) 28.4 months (SD 11.2)	German version of the Quality of Life index	treatment (coiling vs clipping)
D'Ambrosio et al, 2005, USA.[20]	case-control	12 hemicraniectomy 10 conservative treatment	75 90	3 and 12 months	Euro Quality of Life -5D	hemicraniectomy
Fertl et al, 1999, Austria.[21]	cross-sectional	40	60	21.7 months (SD 3)	German modification of the Lancaster Quality of Life Profile	depression, Hunt &Hess
Haug et al, 2009, Norway.[22]	cohort	46	63	12 months	General Health Questionnaire SF-36	aneurysm location
Hop et al, 1998, Netherlands.[23]	cohort	64	70	4 months (SD 1), (range 2.5 – 7)	SF-36 Sickness Impact Profile Visual analog scale	modified Rankin Scale
Hop et al, 2000, Netherlands.[24]	randomized controlled trial (RCT)	24 ASA 26 placebo	67 81	4 months	SF-36 Sickness Impact Profile Visual analog scale	acetylsalicylic acid (ASA)
Hop et al, 2001, Netherlands.[25]	cohort	49	70	18 months (SD 2), range 13-21 months	Sickness Impact Profile SF-36 Visual analog scale	modified Rankin Scale

Author(s), year, nationality	Method	participants		time since SAH	QoL Measurement	Determinants
		n	women (%)			
Hütter et al, 2001, Germany.[26]	cross-sectional	116	66	52.2 months (SD 5.2) range 41-63 months	Aachen Life Quality Inventory	initial Hunt & Hess, Fisher CT grade, duration of temporary clipping, mean blood flow velocity, number of additional illnesses
Katati et al, 2007, Spain.[27]	cohort	70	43	4 months	SF-36	sex, age, World Federation of neurological surgeons scale, Hunt & Hess, Fisher, Glasgow Outcome Scale (GOS) on release, Rankin
Komotar et al, 2006, USA.[28]	case control	16 Cerebrospinal fluid (CSF) hypovolemia 32 no CSF hypovolemia	63 78	3 months	Sickness Impact Profile	brain sag
Kreitschmann et al, 2001, Germany.[29]	case-control	41 catecholamine 30 no catecholamine	73	28 months	Aachen Life Quality Inventory	hypertensive treatment (catecholamine)
Kreitschmann et al, 2007, Germany. [30]	cohort	40	65	27.3 months (SD 15)	SF-36 Nottingham Health Profile (NHP) Quality of Life Assessment of growth hormone deficiency in adults (QoL-AGHDA)	basal and highest stimulated cortisol level,basal and highest stimulated adreno-cortico-trophine (ACTH) level, basal and highest stimulated growth hormone (GH) level, area under the curve for cortisol. ACTH and GH, presence of any hormone deficit, corticotroph insufficiency and GH deficiency, Hunt & Hess, Fisher CT score, GOS, age, sex

Author(s), year, nationality	Method	participants		time since SAH	QoL Measurement	Determinants
		n	women (%)			
Meyer et al, 2010, Germany. [31]	cohort	113	67	12 months	SF-36 EuroQol-5D EuroQol-VAS	age, gender, marital status, income, educational level, Hunt &Hess, modified Rankin scale, treatment (coiling/clipping), time to treatment, Barthel Index, cognitive impairment (Mini Mental State Examination), depression (Beck Depression Inventory).
Mocco et al, 2006, USA.[32]	cohort	35	73	12 months	Sickness Impact Profile (SIP)	coiling vs clipping
vd Schaaf et al, 2006, Netherlands.[33]	case-control	35 with aneurysm 34 without aneurysm	71 62	9.1 years 7.1 years	SF-36 EuroQol-5D EuroQol-VAS	untreated aneurysm
Scott et al, 2008 United Kingdom.[34]	trial	538	NR	NR	Functional Limitations Profile	Cognitive deficits, based on a cognitive test battery
Soehle et al, 2007, Germany/ United Kingdom.[35]	cohort	29	59	12 months	SF-36	Hunt &Hess, WFNS, Fisher, Glasgow Coma Scale, hemodynamic and Transcranial Doppler derived parameters
Tseng et al, 2007 United Kingdom.[36]	trial	40 pravastatin 40 placebo	55	6 months	SF-36	age, gender, WFNS, immediate postoperative deficits, sepsis, hydrocephalus, ventriculitis, pravastatin treatment

Author(s), year, nationality	Method	participants		time since SAH	QoL Measurement	Determinants
		n	women (%)			
Visser- Meily et al, 2009, Netherlands.[37]	cross-sectional	141	67	36.1 months (SD 7.9) range 23-52 months	Stroke Specific Quality of Life (SS-QoL)	sex, educational level, age, complications, GOS, aneurysm location, coiling vs clipping, Hospital Anxiety and Depression Scale, Fatigue Severity Scale, Cognitive Failure Questionnaire, Eysenck Personality Questionnaire, Utrecht Coping List

Table 2. Quality of Life (QoL) Measurements

QoL measurement	with physical and psychosocial aspects	range	references
Short Form (36) Health Survey (SF-36).[38-41]	contains 36 items in 8 health-related domains: physical Function, physical role, bodily pain, general health, vitality, social function, emotional role, mental health.	score 0 maximum reduction of QoL score 100 no reduction in QoL validated among stroke patients	18,23-25,27,30, 31,33,35,36
Sickness Impact Profile (SIP).[42]	contains 136 items about sickness-related dysfunction in 12 domains of daily life: ambulation, mobility, body care and movement (together *physical subscore*) social interaction, alertness behavior, emotional behavior and communication (together *psychosocial subscore*) sleep and rest, eating, work, recreation and pastimes, and home management (independent categories)	score 100 maximum reduction in QoL score 0 no reduction in QoL	23-25,28,32
Aachen Life Quality Inventory (ALQI) derived from the German version of the SIP.[43,44]	contains 117 items focused on illness-related restrictions in daily life: mobility, housework, ambulation, autonomy, and activation, (together *physical function summary score*); free-time activities, family relations, social contact, communication, and cognition (together *psychosocial summary score*); work.	ALQL enables the calculation of 11 subscale impairment scores and 3 summary scores (total impairment score, physical and psychosocial summary score)	26,29
Functional Limitations Profile; UK version of SIP.[42]	contains 136 items about sickness-related dysfunction in 12 domains of daily life: ambulation, mobility, body care and movement (together *physical subscore*) social interaction, alertness behavior, emotional behavior and communication (together *psychosocial subscore*) sleep and rest, eating, work, recreation and pastimes, and home management (independent categories)	score 100 maximum reduction in QoL score 0 no reduction in QoL	34
German modification of the Lancaster Quality of Life Profile.[45]	contains 100 items in 9 QoL domains : work/education, leisure, religion, finances, living situation, safety, family relations, social relations, and health. data analysis[21] was performed on 6 domains relevant for SAH patients: life in general, physical health, mental health, partnership, social life at home, and social relations with friends and neighbors.	range on a 7-point rating scale in each domain from 1 overall discontent 7 complete satisfaction score < 5 equivalent for dissatisfaction	21
Stroke Specific Quality of Life (SS-QoL).[46,47]	contains 49 items in 12 subscales merged into 4 domains: *physical* (self-care, mobility, upper extremity), *cognitive* (language, thinking and vision), *emotional* (personality, mood, energy) and *social* (work, family roles, social roles).	score 1 to 5 a higher score is associated with a better QoL	37

QoL measurement	with physical and psychosocial aspects	range	references
German version of the QL-index.[48]	contains 5 dimensions: activity, daily activities, general health, social support, outlook on life	score 0 severe impairment score 2 normal score the sum score of all dimensions reflects QoL.	19
Euro-QoL (EQ-5D).[49,50]	contains 5 questions addressing: mobility, self-care, daily activities, pain, anxiety/depression	score 0 representing death score 1 representing perfect health	20, 31, 33
Nottingham Health Profile (NHP).[51]	contains 38 yes/no statements in 6 domains: physical mobility, pain, sleep, energy, emotional reactions, social isolation.	score 0 – 100. a higher score signifies a worse QoL subscale scores are calculated as a weight mean of the associated items and expressed as a value between.	30
QoL measurement	**with psychosocial aspects only**	**range**	**references**
General Health Questionnaire-30 (GHQ).[52]	contains 30 items in 5 health-related domains: anxiety, depression, well-being, coping, social functioning	a higher score is associated with a worse QoL	22
QoL measurement	**with general aspects**	**range**	**references**
Quality of Life Assessment of growth hormone deficiency in adults (QoL-AGHDA).[53]	contains 25 yes/no items that were constructed based on in- depth interviews of adult patients with growth hormone deficiency.	sum score consists of the number of ´yes´ answers a higher score is associated with a worse QoL	30
EuroQol-VAS.[49]	contains subjective rating of health status on a Visual Analog Scale	score 0 representing worst score 100 representing best imaginable health state	31
Visual analog scale.[54]	contains following questions: - how did you do before the haemorrhage? (for caregivers; how did you do before your partner's hemorrhage ?) - how are you now? patients were asked to respond by putting a mark on the scale, taking into account their overall physical, psychological, and social wellbeing.	score 0 poor score 100 excellent	23-25

Table 3. Determinants found to influence Quality of Life in Subarachnoid Haemorrhage

Body Structure & Function		author	univariate	multivariate
SAH grading	Hunt and Hess scale (H&H).[55]	Barth[18]	association between lower grade H&H and worse QoL on SF-36 scores (not specified)	NR
		Fertl[21]	no association between H&H and QoL.	NR
		Hütter[26]	no association between H&H and QoL on ALQI Total score association between higher H&H grade and worse QoL on 4/10 ALQI subscales: Mobility (r=0.22), Free-time activities (0.21), Ambulation (0.22), Autonomy (0.26)	association between higher H&H grade and worse QoL on ALQI Total score (β=-0.19) no association between H&H and QoL on median ALQI Total score
		Katati[27]	NR	no association between H&H and QoL on SF-36 Total Score association between H&H 2 and better QoL on 1/8 SF-36 subscales: Vitality
		Meyer[31]	no association between H&H and QoL on EQ5D or EQ VAS	association between H&H 3-5 and worse QoL on EQ VAS (β= -7.03)
		Soehle[35]	association between higher H&H grade and worse QoL on Physical component summary (r= -0.79) and on 5 subscales of SF-36: Physical functioning (r= -0.63) , Physical Role (-0.71), Bodily Pain (-0.57), Social Functioning (-0.63), Role Emotional (-0.44)	NR
	World Federation of neurological surgeons scale (WFNS).[56]	Katati[27]	NR	no association between WFNS and QoL on SF-36 Total Score association between WFNS 4-5 and worse QoL on 2/8 SF-36 subscales: Physical function, Physical role. association between WFNS 1 and better QoL on 1/8 SF-36 subscale: Physical function

Body Structure & Function		author	univariate	multivariate
SAH grading	World Federation of neurological surgeons scale (WFNS).[56]	Soehle[35]	association between higher WFNS grade and worse QoL on Physical component summary (r= -0.62) association between higher WFNS grade and worse QoL on 4 subscales of SF-36: Physical functioning (r= -0.44), Physical Role (-0.66), Bodily Pain (-0.64), Social Functioning (-0.57)	NR
		Tseng[36]	NR	association between higher WFNS grade and worse QoL on SF-36 Physical score (-0.04) and Psychosocial score (-0.02)
	Fisher CT grade.[57]	Hütter[26]	no association between Fisher CT grade and QoL on ALQI Total / subscales association between Fisher grade 3-4 and worse QoL on ALQI subscales Autonomy (t= -2.41), Physical functions subscale (t= -1.91)	no association between Fisher CT grade and median ALQI Total score
		Katati[27]	NR	no association between Fisher CT grade and QoL on SF-36 Total Score / subscales
	Glasgow Coma Scale (GCS).[58]	Soehle[35]	association between higher GCS and better QoL on Physical component summary (r= 0.48) association between higher GCS and better QoL on 3 subscales of SF-36: Physical Role (r= 0.53), Bodily Pain (0.61), Role Emotional (0.63)	NR

Body Structure & Function		author	univariate	multivariate
localisation	site of aneurysm	Barth[18]	no association between site of aneurysm and QoL on SF-36 scores	NR
		Haug[22]	no association between site of aneurysm and QoL on SF-36 or GHQ-30. worse QoL compared to reference population on - SF-36 domains: Role physical, Bodily pain, General health. - GHQ-30 domains: Well-being, Social functioning. worse QoL anterior communicating artery (AcomA) aneurysm location compared to reference population on - SF-36 domains: Physical functioning, Social functioning, Role emotional - GHQ-30 domain Anxiety	NR
		Hütter[26]	association between middle cerebral artery (MCA) aneurysm location and worse QoL on ALQI domain Communication (not specified). association between left-sided MCA aneurysms location and more restrictions on ALQI-subscales (compared to right-sided): Social contact (t=1.71), Communication (t=2.04), Cognition(t=1.79)	NR
		Visser-Meily[37]	NR	association between MCA aneurysm location and worse QoL on SS-QoL Total (β=-0.16) and SS-QoL Emotional (β=-0.13) association between AcomA/ anterior cerebral artery (ACA) aneurysm location and worse QoL on SS-QoL Cognitive (β=-0.15) association between Vertebrobasilar aneurysm location and better QoL on SS-QoL Cognitive (β=0.23)

Body Structure & Function		author	univariate	multivariate
hormone level	basal cortisol level	Kreitschmann[30]	association between higher basal cortisol level and better QoL on 2/6 NHP subscales: Energy (r= -0.44), Social isolation (-0.50) association between higher basal cortisol level and better QoL on QOL-AGHDA (r= -0.55) no association between basal cortisol level and QoL on SF-36 Physical Function	association between higher basal cortisol level and better QoL on - QoL-AGHDA, - 4/ 6 subscales of NHP: Mobility, Social isolation, Emotional reaction, Energy, - SF-36 mental health subscore.
	growth hormone deficiency (GHD)	Kreitschmann[30]	NR	association between GHD and QoL on 1/6 subscales of NHP (Energy)
	stimulated adreno-corticotrophine (ACTH)	Kreitschmann[30]	NR	association between stimulated ACTH level and QoL on 1/6 subscales of NHP: Sleep
		Kreitschmann[30]	NR	association between area under the curve for ACTH and QoL on 1/6 subscales of NHP: Mobility
	corticotroph insufficiency	Kreitschmann[30]	NR	no association between corticotroph insufficiency and QoL
	presence of any hormone deficit	Kreitschmann[30]	NR	no association between presence of any hormone deficit and QoL
complication	increased blood flow	Hutter[26]	no association between duration of increased blood flow velocities and QoL on ALQI Total score association between duration of increased blood flow velocities and QoL on ALQI Physical function score (r=0.26)	association between increased blood flow velocities and QoL on ALQI Total score (λ=0.90)
	brain sag	Komotar[28]	no association between brain sag and QoL on SIP	NR
	immediate postoperative deficits	Tseng[36]	NR	association between immediate postoperative deficits and worse QoL on SF-36 Physical score (-0.31) and Psychosocial score (-0.26)
	sepsis	Tseng[36]	NR	association between sepsis and worse QoL on SF-36 Physical score (-0.23) and Psychosocial score (-0.23)

Body Structure & Function		author	univariate	multivariate
complication	ventriculitis	Tseng[36]	NR	no association between ventriculitis and QoL on SF-36 Physical score association between ventriculitis and worse QoL on SF-36 Psychosocial score (-0,15)
	hydrocephalus	Tseng[36]	NR	association between hydrocephalus and worse QoL on SF-36 Physical score (-0.07) no association between hydrocephalus and QoL on SF-36 Psychosocial score
	presence	Visser-Meily[37]	NR	no association between presence of complications and QoL on SS-QoL
number of additional illnesses		Hutter[26]	association between no. additional illnesses and worse QoL on ALQI Total score (r= 0.25), Psychosocial function score (0.21) and Physical function score (0.26) association between no. additional illnesses and worse QoL on 9/10 ALQI subscales: Activation (r= 0.22), Mobility (0.29), Housework (0.21), Social contact (0.21), Free-time activities (0.23), Ambulation (0.21), Communication (0.24), Autonomy (0.25), Cognition (0.23)	NR
screening for new aneurysms		vd Schaaf[33]	no association between screening for new aneurysms and QoL on SF-36, EQ5D or EQ VAS	NR
fatigue	Fatigue Severity Scale (FSS).[59]	Visser-Meily[37]	association between fatigue and worse QoL on SS-QoL total score (0.73)	association between fatigue and worse QoL on SS-QoL total score (β=-0.38) and subscales Physical (β=-0.40), Cognitive (β=-0.24), Social (β=-0.25), Emotional (β=-0.32)
depression	Beck Depression Inventory (BDI).[60]	Fertl[21]	association between presence of depression and worse HRQoL on 2/6 LQLP subscales: Social relations (r=-0.44), life in general (-0.46)	NR
		Meyer[31]	association between depressive symptoms and worse HRQoL on EQ5D and EQ VAS (not specified)	association between depressive symptoms and worse HRQoL on EQ VAS (β = -1.80)

Body Structure & Function		author	univariate	multivariate
depression	Hospital Anxiety and Depression Scale (HADS).[61]	Visser-Meily[37]	association between mood problems and worse QoL on SS-QoL total score (0.73)	association between mood problems and worse QoL on SS-QoL total score (β=-0.38), and subscales Physical (β=-0.18), Cognitive (β=-0.30), Social (β=-0.42), Emotional (β=-0.28)
cognitive functioning	Cognitive test battery	Scott[34]	NR	association between cognitive deficits and worse QoL on FLP Total score (15.24 versus 8.16 in patients without cognitive deficits), Physical score (score 11.29 vs 4.63) and Psychosocial score (score 19.59 vs 12.18)
	Mini Mental State Examination (MMSE).[62]	Meyer[31]	association between MMSE score < 24 and worse HRQoL on EQ5D no association between MMSE score < 24 and EQ VAS	no association between MMSE score < 24 and QoL on EQ5D or EQ VAS
Environmental Factors SAH treatment		**author**	**univariate**	**multivariate**
intervention	aneurysm treatment (clipping vs coiling)	Bellebaum[19]	no association between aneurysm treatment and QoL on QL index	NR
		Meyer[31]	no association between aneurysm treatment and QoL at discharge on 6/8 SF-36 domains, EQ5D or EQ VAS. association between coiling and worse QoL at discharge on SF-36 domains Vitality and Role emotional no association between aneurysm treatment and QoL at 12 months after SAH on SF-36, EQ5D or EQ VAS.	NR
		Mocco[32]	no association between aneurysm treatment and QoL on SIP scores	NR
		Visser-Meily[37]	NR	association between aneurysm treatment by coiling and better QoL on SS-QoL Physical (β=0.11) and SS-QoL Social (β=0.12)

Environmental Factors SAH treatment		author	univariate	multivariate
intervention	(early) hemicraniectomy	D'Ambrosio[20]	no association between (early) hemicraniectomy and QoL on EQ5D or QALY.	NR
medication	Nicardipine prolonged-release implants (NPRI)	Barth[18]	no association between NPRI treatment and QoL on SF-36 domains worse QoL compared to reference population on SF-36 domains: Role-Physical functioning, Vitality, and Role- Emotional functioning.	NR
	acetylsalicylic acid (ASA)	Hop[24]	association between treatment with ASA and better QoL on SIP domain Sleep and rest no association between treatment with ASA and QoL on SF-36 or VAS	NR
	hypertensive treatment (catecholamine)	Kreitschmann[29]	no association between hypertensive treatment and QoL on ALQI Total score /subscores	NR
	pravastatin treatment	Tseng[36]	no association between pravastatin treatment and better QoL on SF-36 Physical or Psychosocial score	association between pravastatin treatment and better QoL on SF-36 Physical score (0.06) and Psychosocial score (0.19)
other	duration of clipping	Hütter[26]	association between duration of clipping and QoL on ALQI Total score (r= 0.22), and Physical function score (0.26) association between duration of clipping and QoL on 5/10 ALQI subscales: Activation (r= 0.22), Mobility (0.24), Free-time activities (0.23), Ambulation (0.23), Autonomy (0.30)	no association between duration of clipping and QoL on median ALQI Total score
	time to treatment	Meyer[31]	between time to treatment and QoL on EQ5D or EQ VAS	NR

Activity	Outcome characeteristics	author	univariate	multivariate
disability	modified Rankin Scale (mRS).[63]	Hop[25]	association between improvement in mRS between 4 and 18 months after SAH and better QoL on SF-36 domains: Physical functioning, Physical role limitations, Emotional role limitations, Mental health, Vitality association between improvement in mRS between 4 and 18 months after SAH and worse QoL on SIP domain Household management no association between change in mRS and QoL on VAS scores	NR
		Hop[23]	association between higher mRS and worse QoL on SIP psychosocial domains, physical domains, physical and psychosocial subscore and total score (Somers'D 0.2-0.6) association between lower mRS and better QoL on SF-36 scores, Somers' D between 0.2 (pain) and 0.6 (role limitations due to physical problem). Significance of Somers' D not reported association between Rankin grade 0 and better QoL on VAS	NR
		Hop[23]	no marked difference between Rankin 0 and reference population on SIP, and better scores on 7/8 SF-36 domains.	NR
		Katati[27]	NR	association between mRS and QoL on 7/8 SF-36 subscores
		Meyer[31]	association between mRS 3-5 and worse QoL on EQ5D* no association between mRS and QoL on EQ VAS	association between mRS 3-5 and worse QoL on EQ5D (β = -0.22)

Activity Outcome characeteristics		author	univariate	multivariate
disability	Glasgow outcome scale (GOS).[64]	Katati[27]	NR	association between GOS 5 and better QoL on SF-36 Total Score association between GOS 5 and better QoL on 3/8 SF-36 subscales (Physical Role, Physical Pain, General Health)
		Kreitschmann[30]	association between higher GOS and better QoL on SF-36 Physical function (r= 0.52)	association between higher GOS and better QoL on 1/6 subscales of NHP (Pain; R^2=0.23) association between higher GOS and better QoL on SF-36 Physical function (R^2=0.26)
		Visser-Meily[37]	NR	association between lower GOS and worse QoL on SS-QoL Physical score (β=-0.22*)
cognitive functioning	Cognitive Failure Questionnaire (CFQ).[65]	Visser-Meily[37]	association between cognitive complaints and worse HRQoL on SS-QoL total score (0.56)	association between cognitive complaints and worse HRQoL on SS-QoL total score (β=-0.28) and subscales Physical (β=-0.16), Cognitive (β=-0.46), Social (β=-0.20), Emotional (β=-0.17)
Personal factors		**author**	**univariate**	**multivariate**
demographic	sex	Katati[27]	NR	association between male gender and better QoL on SF-36 Total Score and on 7/8 SF-36 scales.
		Kreitschmann[30]	NR	association between gender (direction not specified) and QoL on 1/6 subscales of NHP: Social Isolation
		Meyer[31]	no association between sex and QoL on EQ5D or EQ VAS score	association between female gender and worse QoL on EQ VAS (β=-15.9)
		Tseng[36]	NR	association between female gender and worse QoL on SF-36 Physical score (-0.12) and Psychosocial score (-0.15)
		Visser-Meily[37]	NR	association between female gender and worse QoL on SS-QoL Total score (β= 0.10) association between female gender and worse QoL on SS-QoL Cognitive subscale (β= 0.16)

Personal factors		author	univariate	multivariate
demographic	age	Barth[18]	no association between age and QoL on SF-36 scores	NR
		Hütter[26]	association between higher age and worse QoL on ALQI Total score (0.23), Physical function score (0.26), and 3/10 subscales: Housework (0.23), Free-time activities (0.24), Ambulation (0.33).	association between higher age and worse QoL on ALQI total score (β=0.22) association between higher age and worse QoL on median ALQI total score (λ=0.92)
		Katati[27]	NR	no association between age and QoL on SF-36 Total Score association between age >60 years and worse QoL on SF-36 Physical Function score
		Kreitschmann[30]	NR	association of higher age and better QoL 1/6 subscales of NHP: Social Isolation no association between age and 5/6 NHP subscales, SF-36 or QoL-AGHDA.
		Meyer[31]	no association between age and QoL on EQ5D or EQ VAS score	NR
		Tseng[36]	NR	association between higher age and worse QoL on SF-36 Physical score (-0.11) no association between hydrocephalus and QoL on SF-36 Psychosocial score
		Visser-Meily[37]	NR	association between higher age and worse QoL on SS-QoL Total score (β= -0.12) association between higher age and worse QoL on SS-QoL Physical subscale (β=-0.23)

Personal factors		author	univariate	multivariate
social	marital status	Meyer[31]	no association between marital status and QoL on EQ5D or EQ VAS score	association between being single/ divorced /widowed and worse QoL on EQ5D (β= -0.17) score
	education level	Meyer[31]	association between < 12 years education and worse QoL on EQ5D and EQ VAS	association between > 12 years education and worse QoL on EQ VAS score (β= 17.1)
		Visser-Meily[37]	NR	no association between education level and QoL on SS-QoL Total score
	income	Meyer[31]	no association between income and EQ5D and QoL on EQ VAS score.	NR
neuroticism	Eysenck Personality Questionnaire (EPQ-N).[66]	Visser-Meily[37]	association between neuroticism and worse QoL on SS-QoL total score (r=0.55)	association between neuroticism and lower QoL on SS-QoL subscale Emotional (β=-0.21)
passive coping	Utrecht Coping List (UCL-p).[67]	Visser-Meily[37]	association between passive coping and worse HRQoL on SS-QoL total score (r=-0.53)	association between passive coping and lower QoL on SS-QoL subscale Cognitive (β=0.13)
Participation		**author**	**univariate**	**multivariate**
No studies found				

NR: not reported; QoL: Quality of Life; ALQI: Aachen Life Quality Inventory; FLP: Functional Limitations Profile; GHQ: General Health Questionnaire-30; NHP: Nottingham Health Profile; QoL-AGHDA: Quality of Life Assessment of growth hormone deficiency in adults; SF-36: Short Form (36) Health Survey; SIP: Sickness Impact Profile; SS-QoL: Stroke Specific Quality of Life.

REFERENCES

1. Rinkel GJE, Algra A. Long-term outcomes of patients with aneurysmal subarachnoid haemorrhage. Lancet Neurol 2011;10:349-356.
2. Al-Khindi T MacDonald RL, Schweizer TA. Cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. Stroke 2010;41:e519-e536.
3. Hill MR, Noonan VK, Sakakibara BM, Miller WC. Quality of life instruments and definitions in induviduals with spinal cord injury: a systematic review. Spinal Cord 2010;48:438-50.
4. Hunt SM. The problem of quality of life. Qual Life Res 1997; 6:205-212.
5. Post MWM, Witte de LP, Schrijvers AJP. Quality of life and the ICIDH: towards an integrated conceptual model for rehabilitation outcomes research. Clin Rehabil 1999;13:5-15
6. Spilker B, Revicki DA. Taxonomy of quality of life. In: Spilker B ed. Quality of life and pharmacoeconomics in clinical trials, second edition. New York: Lippincott-Raven, 1996.
7. Noble AJ, Schenk T. Which variables help explain the poor health-related quality of life after subarachnoid hemorrhage? A meta-analysis. Neurosurgery 2010;66:772-783.
8. Brilstra EH, Hop JW, Rinkel GJ. Quality of life after perimesencephalic haemorrhage. J Neurol Neurosurg Psychiatry 1997;63:382-4.
9. World Health Organization. International Classification of Functioning, Disability and Health: ICF. Geneva, Switzerland: World Health Organization;2001.
10. Bardach NS, Olson SJ, Elkins JS, Smith WS, Lawton MT, Johnston C. Regionalization of treatment for subarachnoid hemorrhage. A cost-utility analysis. Circulation 2004;109:2207-2212.
11. Claassen J, Peery S, Kreiter KT, Hirsch LJ, Du EY, Connolly ES, Mayer SA. Predictors and clinical impact of epilepsy after subarachnoid hemorrhage. Neurology 2003;60:208-214.
12. Frontera JA, Fernandez A, Schmidt JM, Claassen J, Wartenberg KE, Badjatia N, Connolly ES, Mayer SA. Defining vasospasm after subarachnoid hemorrhage. What is the most clinically relevant definition. Stroke 2009;40:1963-1968.
13. Hackett MI, Anderson CS. Health outcomes 1 year after subarachnoid hemorrhage. An international population-based study. Neurology 2000;55:658-662.
14. Kowalski RG, Claassen J, Kreiter KT, Bates JE, Ostapkovich ND, Connolly ES, Mayer SA. Initial misdiagnosis and outcome after subarachnoid hemorrhage. JAMA 2004;291:866-869.
15. Mayer SA, Kreiter KT, Copeland D, Bernardini GL, Bates JE, Peery S, Claassen J, Du YE, Connolly ES. Global and domain-specific cognitive impairment and outcome after subarachnoid hemorrhage. Neurology 2002;59:1750-1758.
16. Noble AJ, Baisch S, Mendelow AD, Allen L, Kane P, Schenk T. Posttraumatic stress disorder explains reduced quality of life in subarachnoid hemorrhage patients in both the short and long term. Neurosurgery 2008;63:1095-1105.
17. Schuiling WJ, Rinkel GJE, Walchenbach R, Weerd de AW. Disorders of sleep and wake in patients after subarachnoid hemorrhage. Stroke 2005;36:578-582.
18. Barth M, Thomé C, Schmiedek P, Weiss C, Kasuya H, Vajkoczy P. Characterization of functional outcome and quality of life following subarachnoid hemorrhage in patients treated with and without nicardipine prolonged/released implants. J. Neurosurg 2009;110:955-960.
19. Bellebaum C, Schäfers L, Schoch B, Wanke I, Stolke D, Forsting M, Daum I. Clipping versus coiling: Neuropsychological follow-up after aneurysmal subarachnoid haemorrhage. J Clin Exp Neuropsychol 2004;26:1081-1092.
20. D'Ambrosio AL, Sughrue ME, Yorgason JG, Mocco JD, Kreiter KT, Mayer SA, McKhann GM, Connolly ES. Decompressive hemicraniectomy for poor-grade aneurysmal subarachnoid hemorrhage patients with associated intracerebral hemorrhage: clinical outcome and quality of life assessment. Neurosurgery 2005;56:12-20.

21. Fertl E, Killer M, Eder H, Linzmayer L, Richling B, Auff E. Long-term functional effects of aneurysmal subarachnoid haemorrhage with special emphasis on the patient's view. Acta Neurochir 1999; 141:571-577.
22. Haug T, Sorteberg A, Sorteberg W, Lindegaard K, Lundar T, Finset A. Cognitive functioning and health related quality of life after rupture of an aneurysm on the anterior communicating artery versus middle cerebral artery. Br J Neurosurg 2009;23:507-515.
23. Hop JW, Rinkel GJE, Algra A, Gijn van J. Quality of life in patients and partners after aneurysmal subarachnoid hemorrhage. Stroke 1998;29:789-804.
24. Hop JW, Rinkel GJE, Algra A, Berkelbach van der Sprenkel JW, Gijn van J. Randomized pilot trial of postoperative aspirin in subarachnoid hemorrhage. Neurology 2000;54:872-8.
25. Hop JW, Rinkel GJE, Algra A, Gijn van J. Changes in functional outcome and quality of life in patients and caregivers after aneurysmal subarachnoid hemorrhage. J Neurosurg 2001;95:957-963.
26. Hütter BO, Kreitschmann-Andermahr I, Gilsbach JM. Health-related quality of life after aneurysmal subarachnoid hemorrhage: impacts of bleeding severity, computerized tmography findings, surgery, vasospasm, and neurological grade. J neurosurg 2001;94:241-251.
27. Katati MJ, Santiago-Ramajo S, Pérez-García M, Meersmans-Sanchez Jofré M, Vilar-Lopez R, Coín-Mejias MA, Caracuel-Romero A, Arjona-Moron V. Description of quality of life and its predictors in patients with aneurysmal subarachnoid hemorrhage. Cerebrovasc Dis 2007;24:66-73.
28. Komotar RJ, Ransom ER, Mocco J, Zacharia BE, McKhann GM, Mayer SA, Connolly ES. Critical postcraniotomy cerebrospinal fluid hypovolemia: risk factors and outcome analysis. Neurosurgery 2006;59:284-290.
29. Kreitschmann-Andermahr I, Hütter BO, Gilsbach JM. Antiischemic therapy of severe prolonged vasospasm after aneurysmal SAH: effects on quality of life. Acta Neurochir 2001;77:251-254.
30. Kreitschmann-Andermahr I, Poll E, Hütter BO, Reineke A, Kristes S, Gilsbach JM, Saller B. Quality of life and psychiatric sequelae following aneurysmal subarachnoid haemorrhage: does neuroendocrine dysfunction play a role? Clin Endocrinology 2007;66:833-837.
31. Meyer B, Ringel F, Winter Y, Spottke A, Gharevi N, Dams J, Balzer-Geldsetzer M, Mueller IK, Klockgether T, Schramm J, Urbach H, Dodel R. Health-Related Quality of Life in patients with subarachnoid haemorrhage. Cerebrovasc Dis 2010;30:423-431.
32. Mocco J, Connolly ES. Long-term domain-specific improvement following poor grade aneurysmal subarachnoid hemorrhage. J Neurol 2006;253:1278-1284.
33. Schaaf van der IC, Wermer MJH, Velthuis BK, Buskens E, Bossuyt PMM, Rinkel GJE. Psychosocial impact of finding small aneurysms that are left untreated in patients previously operated on for ruptured aneurysms. L Neurol Neurosurg Psychiatry 2006;77:748-752.
34. Scott RB, Eccles F, Lloyd A, Carpenter K. From multidimensional neuropsychological outcomes to a cognitive complication rate: The international subarachnoid aneurysm trial. Trials 2008;9:13.
35. Soehle M, Chatfield DA, Czosnyka M, Kirkpatrick PJ. Predictive values of initial clinical status, intracranial pressure and transcranial Doppler pulsatility after subarachnoid haemorrhage. Acta Neurochir 2007;149:575-583.
36. Tseng MY, Hutchinson PJ, Czosnyka M, Richards H, Pickard JD, Kirkpatrick PJ. Effects of acute pravastatin treatment on intensity of rescue therapy, length of inpatient stay, and 6-month outcome in patients after aneurysmal subarachnoid hemorrhage. Sttroke 2007;38:1545-1550.
37. Visser-Meily JMA, Rhebergen ML, Rinkel GJE, Zandvoort van MJ, Post MWM. Long-term health related quality of life after aneurysmal subarachnoid hemorrhage; relationship with psychological symptoms and personality characteristics. Stroke 2009;40:1526-1529.

38. Anderson C, Laubscher S, Burns R. Validation of the Short Form 36 (SF-36) health survey questionnaire among stroke patients. Stroke 1996;27:1812-1816.
39. Deane M, Pigott T, Dearing P. The value of the Shot-Form 36 score in the outcome assessmnt of subarachnoid haemorrhage. Br J Neurosurg 1996;10:187-191.
40. McHorney CA, Ware JE, Raczek AE. The MOS 36-item Short-Form Health Survey (SF-36): II Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31:247-263.
41. Ware JH, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): I conceptual framework and item selection. Med Care 1992;30:473-483.
42. Bergner M, Bobbitt RA, Carter WB, Gilson BS. The Sickness Impact Profile: development and final revision of a health status measure. Med Care 1981;29:787-805.
43. Hütter BO, Gilsbach JM. Das Aachener Lebensqualitätsinventar für patienten mit Hirnschädigung: Entwicklung und methodische Gütekriterien, in Möllers HJ, Engel RR, Hoff P: Befunderhebung in der Psychiatric: Lebensqualität, Negativsymptomatik und andere aktuelle Entwicklungen. Vienna: Springer-Verlag 1996:83-101.
44. Hütter BO, Würtemberger G. Reliability and validity of the German version of the Sickness Impact Profile in patients with chronic obstructive pulmonary disease. Psychol Health 1997;12:149-159.
45. Oliver JPJ. The social care directive: development of a quality of life profile for use in community services for the mentally ill. Soc Work Soc Sci Rev 1991;3:5-45
46. Williams LS, Weinberger M, Harris LE, Clark DO, Biller J. Development of a Stroke-Specific Quality of Life Scale. Stroke 1999;30:1362-1369.
47. Boosman H, Passier PE, Visser-Meily JM, Rinkel GJ, Post MW. Validation of the Stroke-Specific Quality of Life Scale (SS-QoL) in patients with aneurysmal subarachnoid haemorrhage. J Neurol Neurosurg Psychiatry 2010;81(5):485-9.
48. Spitzer WO, Dobson AJ, Hall J, Chesterman E, Levi J, Shepherd R, Battista RN, Catchlove BR. Measuring the quality of life of cancer patients: A concise QL-index for use by physicians. J Chronic Dis 1981;34:585-597.
49. The EuroQoL Group: EuroQoL: A new facility for the measurement of health-related quality of life- The EuroQoL Group. Health Policy 1990;16:199-208.
50. Brooks R. EuroQoL: the current state of play. Health policy 1996;37:53-72.
51. Hinz A, Klaiberg A, Schumacher J, Brahler E. The psychometric quality of the Nottingham Health Profile (NHP) in the general population (in German). Psychotherapie, Psychosomatik, medizinische Psychologie 2003;53:353-358.
52. Goldberg DP. The manual of the General Health Questionnaire. NFER, Windsor, 1978.
53. McKenna SP, Doward LC, Alonso J, Kohlmann T, Niero M, Prieto L, Wiren L. The QoL-AGHDA: an instrument for the assessment of quality of life in adults with growth hormone deficiency. Quality of Life Research 1999;8:373-383.
54. Brass LM. Trial design issues: endpoints and sample size. Cerebrovasc Dis 1995;5:3-11
55. Hunt WE, Hess RM. Surgical risk as related to time of intervention in the repair of intracranial aneurysms. J Neurosurg 1968;28:14-20.
56. Teasdale GM, Drake CG, Hunt W, Kassel N, Sano K, Pertuiset B, De Villiers JC. A universal subarachnoid haemorrhage scale: report of a committee of the World Federation of Neurosurgical Societies. J Neurol Neurosurg Psychiatry 1988;51:1457.
57. Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. Neurosurgery 1980;6:1-9.
58. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974;2:81-4.
59. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46:1121-1123.

60. Beck A.T., Ward C.H., Mendelson M., Mock J., Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-571.
61. Spinhoven PH, Ormel J, Sloekers PPA, Kempen GIJM, Speckens AEM, van Hemert AM. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. Psych Med 1997;27:363-70.
62. Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state': a practical method for grading the cognitive state of patients for the clinician. J Psychiatry Res 1975;12:189-198.
63. Rankin J. Cerebral vascular accidents in patients over the age of 60. Scott Med J 1957;2:200-215.
64. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet 1975;1:480-484.
65. Broadbent DE, Cooper PJ, Fitzgerald PF, Parkes KR. The Cognitive Failure Questionnaire (CFQ) and its correlates. Br J Clin Psychol 1982;21:1-16.
66. Eysenck HJ, Eysenck SBG. Manual of the Eysenck Personality Scales. London. Hodder and Stoughton, 1991.
67. Eriksen H.R., Olff M., Ursin H. The CODE: a revised battery for coping and defense and its relation to subjective health. Scan J Psych 1997;38:175-182.
68. Passier PECA, Visser-Meily JMA, van Zandvoort MJE, Post MWM, Rinkel GJE, van Heugten C. Prevalence and determinants of cognitive complaints after aneurysmal Subarachnoid Haemorrhage. Cerebrovasc Dis 2010;29:557-563.
69. Passier PECA, Visser-Meily JMA, Rinkel GJE, Lindeman E, Post MWM. Life satisfaction and return to work after aneurysmal subarachnoid haemorrhage. J Stroke Cerebrovasc Dis 2011;20:324-329.
70. Jacobsson LJ, Westerberg M, Malec JF, Lexell J. Sense of coherence and disability and the relationship with life satisfaction 6-15 years after traumatic brain injury in northern Sweden. Neuropsychol Rehabil. 2011;21:383-400.

Based on:

Validation of the Stroke Specific Quality of Life scale in patients with aneurysmal subarachnoid haemorrhage

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Validation of the Stroke Specific Quality of Life scale in patients with aneurysmal subarachnoid haemorrhage

ABSTRACT

Background and purpose: Disease specific quality of life measures have been validated for patients with ischaemic stroke and intracerebral haemorrhage, but not for patients with aneurysmal subarachnoid haemorrhage (SAH). The aim of this study was to validate the Stroke Specific Quality of Life (SS-QoL) scale for patients with SAH.

Methods: Cross sectional survey of 141 aneurysmal SAH patients. Construct and criterion validity were studied and various ways to merge the 12 SS-QoL domains into a limited number of subtotal scores were explored. Statistics included assessing score distributions, Cronbach's α, principal components analysis (PCA) and Spearman correlations between SS-QoL and the Glasgow Outcome Scale (GOS), Cognitive Failures Questionnaire (CFQ), Life Satisfaction-9 (LiSat-9) and Hospital Anxiety and Depression Scale (HADS).

Results: PCA revealed two components reflecting physical health and psychosocial health with a mutual correlation of 0.73. A ceiling effect was present for 10 out of 12 domains and for the physical component. Internal consistency was good for all 12 domains ($\alpha \geq 0.80$), two components ($\alpha \geq 0.95$) and the total score (0.97). Physical SS-QoL scores showed weak to moderate correlations (0.24 - 0.32) with the GOS. All SS-QoL scores showed moderate to strong correlations (0.35 - 0.72) with the CFQ, LiSat-9 and HADS.

Conclusions: The SS-QoL is a valid measure to assess quality of life in patients after aneurysmal SAH. Using physical and psychosocial SS-QoL summary scores simplifies the use of this measure without concealing differences in outcomes on different quality of life domains.

INTRODUCTION

Subarachnoid haemorrhage (SAH) from a ruptured intracranial aneurysm accounts for approximately 5% of all strokes,[1] occurs at a relatively young age[2] and carries a poor prognosis of survival, despite improvements in medical care for these patients.[3] The 50 - 70% of patients who survive an aneurysmal SAH often experience a decrease in their health related quality of life (HRQoL).[4,5] Thus far, HRQoL after SAH has only been assessed with generic HRQoL measures. Generic measures can be administered to a broad range of populations. Hence they do not concentrate on disease specific problems. For outcome research, a combination of generic and disease specific measures is therefore recommended.[6]

The Stroke Specific Quality of Life (SS-QoL) scale is a well known stroke specific HRQoL measure.[7,8] The SS-QoL consists of 49 items and results in 12 domain scores and a total score. The SS-QoL has been extensively validated in patients with ischaemic stroke and intracerebral haemorrhage[9-11] but not in patients who survived SAH. The effects on HRQoL may differ between SAH and ischaemic stroke or intracerebral haemorrhage as SAH results in diffuse or multifocal brain damage whereas the other types of stroke result more often in focal damage. Whether the SS-QoL is also a valid instrument to investigate HRQoL following SAH is therefore uncertain. Furthermore, its structure of 12 domains is less practical for research into correlates of HRQoL, leaving a choice to use all 12 domain scores as dependent variables or to use the total SS-QoL score with a risk of concealing differences between HRQoL domains. In an earlier study,[12] we therefore merged the 12 domains into four dimensions (physical, cognition, social and emotion) to reflect the four basic HRQoL dimensions.[13] Hence the objectives of the current study were: (1) to study the construct validity and criterion validity of the SS-QoL in an SAH population; and (2) to explore different options to merge the 12 SS-QoL domains into a limited number of subtotal scores in this population.

MATERIALS AND METHODS

Subjects

This cross sectional study was part of a larger study on HRQoL after SAH.[12] We studied all patients who had been treated by clipping or coiling after aneurysmal SAH between January 2003 and July 2005 at the University Medical Centre Utrecht (UMC Utrecht). Patients living in a nursing home and patients with severe comorbidity, reduced life expectancy or an insufficient command of the Dutch language were excluded. All eligible patients who were willing to participate were asked to complete a mailed questionnaire. The medical ethics committee of the UMC Utrecht approved the study protocol.

Measures

Data on demographic characteristics, location and treatment of ruptured aneurysm, and complications after SAH were obtained from the SAH database of the Department of Neurology and Neurosurgery, UMC Utrecht.

Stroke Specific Quality of Life scale

The SS-QoL contains 12 domains with 49 items in total. The domains are: self-care, mobility, upper extremity function, language, vision, work, thinking, family roles, social roles, personality, mood and energy. All items are rated on a 5 point Likert Scale. Higher scores indicate better functioning. Items are averaged to obtain domain scores and a total SS-QoL score. The possible range of all summary scores is therefore from 1 (poor HRQoL) to 5 (good HRQoL). The SS-QoL was previously translated into Dutch using a forward-backward procedure.[14]

Criterion variables

As a measure of physical functioning at discharge of the hospital we used the Glasgow Outcome Scale (GOS).[15]

As a measure of perceived cognitive functioning, we used the Cognitive Failures Questionnaire (CFQ).[16] The CFQ consists of 25 items measuring self-reported failures of memory, attention, motor function and perception. Items are rated on a 5 point scale. Scores range from 0 to 100 and a high CFQ score indicates poor cognitive function.

As a measure of perceived social functioning, we used the Life Satisfaction questionnaire (LiSat-9).[17] It consists of one question about satisfaction with life as a whole and eight questions about satisfaction with life domains: self-care ability, leisure time, vocational situation, financial situation, sexual life, partnership relations, family life and contacts with friends. Each question is rated on a 6 point scale. The total LiSat-9 score is the average of all item scores and has a 1-6 range. Higher scores indicate higher levels of satisfaction.

As a measure of emotion, we used the total score of the Hospital Anxiety and Depression Scale (HADS).[18] The HADS contains seven items about depression and seven items about anxiety . Each question is rated on a 4 point scale. Higher scores indicate more emotional problems.

Statistical analysis

SS-QoL score distributions were examined. Skewness was considered present if this statistic was below -1.0 or above 1.0. Floor or ceiling effects were considered present if more than 15% of all respondents chose the lowest or highest possible score.[19]

Construct validity was examined using several methods. For internal consistency, Cronbach's α and mean inter-item correlations were assessed. Internal consistency requires a Cronbach α coefficient of at least 0.70.[19]

Spearman correlations between the 12 domains were investigated to assess whether the individual domains measure different constructs. Principal components analyses (PCA) were used to explore possible groupings of the 12 domains into a limited number of components. Selection of the number of components was based on a plot of the eigenvalues of all components (the screeplot) and the number of components that had an eigenvalue more than 1. In addition, a theory driven four dimensional structure was examined.[13] In these PCAs, the 12 domains were used as variables instead of the 49 items because of the limited sample size and very good internal consistency of all 12 domains (see results section). Oblimin rotation was performed as we expected correlations between components of HRQoL.

Criterion validity was assessed by examining the degree to which SS-QoL scores were related to scores on domain specific instruments. Spearman correlation coefficients

between 0.30 and 0.60 were considered as moderate and correlations exceeding 0.60 as strong.[20]

As complications following SAH (eg, secondary ischaemia) could cause additional and more focal brain damage, we also performed all analyses including only SAH patients without rebleeding, secondary ischaemia or hydrocephalus. These analyses revealed only marginal differences between the results of this group and those of the total patient group. Therefore, we present only the results of the total patient group.

RESULTS

Table 1. Characteristics of patients with subarachnoid haemorrhage (N = 141)

Demographic characteristics	
Women (%)	66.7
Mean age in years (SD)	51.4 (12.3)
Educational level at least high school (%)	31.9
Living with partner (%)	64.9
Pre SAH employment (%)	62.4
Hospital data	
Mean follow up time after SAH in months (SD)	36.1 (7.9)
Range in months	23-52
Location of aneurysm (%)	
ICA	23.4
MCA	21.3
AcomA/ACA	42.6
Vertebrobasilar	12.8
Type of aneurysm occlusion (%)	
Coiling	48.2
Surgery	51.8
Complications after SAH (%)	45.4
Re-bleeding	5.7
Secondary ischemia	16.3
Hydrocephalus	19.9
Hydrocephalus and ischemia	3.5
GOS at discharge (%)	
Dependent from others (III)	21.2
Disability but independent (IV)	32.1
Good outcome (V)	46.7
CFQ (range 0-100) [a] Mean (SD)	36.8 (16.8)
LiSat-9 (range 1-6) [b] Mean (SD)	4.8 (0.8)
HADS (range 0-56) [a] Mean (SD)	10.8 (7.0)

[a]: Higher value reflects worse condition [b]: Higher value reflects better condition

ACA, anterior cerebral artery; AComA, anterior communicating artery; CFQ, Cognitive Failure Questionnaire; GOS, Glasgow Outcome Scale; HADS, Hospital Anxiety and Depression Scale; ICA, internal carotid artery; LiSat-9, Life Satisfaction Checklist; MCA, middle cerebral artery; SAH, subarachnoid haemorrhage; Vertebrobasilar, arteries of the vertebrobasilar system.

Population characteristics

Between January 2003 and July 2005, a total of 212 SAH patients underwent aneurysm occlusion by means of clipping or coiling. Of this group, 21 died, eight were discharged to a nursing home, five were living abroad and four had severe comorbidity. Hence a questionnaire was sent to 174 patients. The response rate was 81% (n=141). No relevant differences between patients who responded and those who declined to participate were found regarding demographic and SAH characteristics.[12] Table 1 presents the population characteristics.

Dimensionality of the SS-QoL

Investigation of correlations between SS-QoL domains (table 2) showed moderate to strong significant correlations between nearly all domains. Expected strong correlations between SS-QoL domains belonging to the same hypothesised dimension were observed but strong correlations were also present between domains that were not expected to be strongly associated, such as 'mood' and 'work'.

PCA without constraints revealed two components with eigenvalues exceeding 1, together explaining 69.7% of the variance (table 3). The screeplot (not displayed) showed a clear break between components 1 and 2. Based on this PCA solution, two subtotal scores were computed, reflecting 'physical' and 'psychosocial' HRQoL. The mutual correlation between both subtotal scores was strong (0.73). A subsequent forced 4 factor PCA resulted in substantial loadings on the first three components only (table 3). Mutual correlations between the four dimension scores were strong, ranging from 0.62, between the physical and emotional dimensions, up to 0.87 between the social and emotional dimensions. These results do not support a four dimensional structure of the SS-QoL, and this structure was therefore not further analysed.

Descriptive statistics of the SS-QoL

We assessed skewness and floor and ceiling effects (table 4). Substantial ceiling effects were observed for 10 of the 12 domains, most strongly for the domains 'self-care' and 'vision' on which more than half of all respondents chose the highest possible score.

Table 2. Spearman correlations between SS-QoL domains in patients with subarachnoid haemorrhage (N=141)

	1	2	3	4	5	6	7	8	9	10	11	12
1. Self-care	1											
2. Mobility	0.71	1										
3. Upper extremity	0.70	0.80	1									
4. Language	0.48	0.56	0.57	1								
5. Vision	0.56	0.58	0.60	0.52	1							
6. Work	0.66	0.72	0.71	0.56	0.61	1						
7. Thinking	0.33	0.39	0.46	0.61	0.46	0.60	1					
8. Family roles	0.48	0.53	0.49	0.46	0.48	0.57	0.47	1				
9. Social roles	0.39	0.53	0.50	0.44	0.38	0.58	0.50	0.73	1			
10. Personality	0.41	0.44	0.46	0.50	0.45	0.54	0.58	0.71	0.61	1		
11. Mood	0.44	0.57	0.50	0.48	0.47	0.61	0.51	0.82	0.79	0.76	1	
12. Energy	0.47	0.57	0.54	0.47	0 .51	0.66	0.55	0.67	0.66	0.57	0.67	1

Note: All correlations are significant after Bonferroni correction ($p < 0.00076$; 2-tailed).

A ceiling effect was also found for the physical subtotal score but not for the other summary scores.

Internal consistency

Internal consistency was good for all 12 domains, Cronbach's α coefficients ranging from 0.80 to 0.92. Reliability of the two subtotal scores and the total score was excellent (table 4).

Criterion validity

Table 5 shows the correlations between SS-QoL domain scores and the domain specific instruments. Of the 12 domains, only 'self-care', 'mobility' and 'upper extremity function' were significantly, but only weakly to moderately, related to the GOS scores. All but one domain scores showed moderate to strong correlations with the CFQ, LiSat-9 and HADS. Expected strong correlations were found. The strongest correlation between SS-QoL and CFQ was observed for 'thinking'. The strongest correlation between SS-QoL and LiSat-9 was observed for 'social roles'. The HADS showed the strongest correlations with 'mood', 'energy' and 'personality' but showed also moderate to strong correlations (0.44 -0.61) with all other SS-QoL domains.

Only the physical subtotal score was significantly correlated with the GOS. Both subtotal scores and total score showed weak or non-significant correlations with the GOS and moderate to strong correlations with the CFQ, LiSat-9 and the HADS.

Table 3. Results of Principal Components Analyses with oblimin rotation of SS-QoL domains in patients with subarachnoid haemorrhage (n=141)

	Initial solution		Forced 4-factor solution			
	1 *psychosocial*	2 *physical*	1	2	3	4
Eigenvalue	6.81	1.56	6.81	1.56	0.76	0.54
% of variance	56.7	13.0	56.7	13.0	6.4	4.5
Loading patterns						
Self care	-0.16	**0.97**	-0.00	**0.91**	0.02	0.11
Mobility	-0.03	**0.90**	0.14	**0.87**	-0.09	0.01
Upper extremity	-0.02	**0.90**	0.06	**0.84**	0.01	-0.07
Language	0.23	**0.56**	0.02	**0.40**	0.72	0.24
Vision	0.14	**0.67**	-0.07	**0.54**	0.23	**-0.43**
Work	0.35	**0.60**	0.20	**0.52**	0.13	-0.39
Thinking	**0.72**	0.01	0.21	-0.16	**0.75**	-0.28
Family roles	**0.88**	-0.02	**0.92**	0.04	-0.03	0.04
Social roles	**0.87**	-0.04	**0.87**	0.02	-0.05	-0.07
Personality	**0.85**	-0.02	**0.71**	-0.04	0.35	0.11
Mood	**0.88**	0.03	**0.91**	0.09	-0.02	0.03
Energy	**0.73**	0.13	**0.54**	0.10	0.04	**-0.47**

Factor loadings of 0.40 or higher are printed in bold

Table 4. Descriptive Statistics of the SS-QoL in patients with subarachnoid haemorrhage (N=141)

	Items	Mean(SD)	Median	IQR	Range	Skewness	% score 1	% score 5	Mean inter-item correlation	Cronbach's α
12 domains										
Self care	5	4.7 (.58)	5.0	0.4	2.00 – 5	-2.3	0	56	0.58	0.85
Mobility	6	4.4 (.75)	4.8	0.8	2.00 – 5	-1.3	0	38.6	0.68	0.92
Upper extremity	5	4.5 (.69)	4.8	0.9	2.40 – 5	-1.3	0	43.3	0.59	0.86
Language	5	4.4 (.69)	4.6	1.0	2.00 – 5	-1.6	0	31.2	0.64	0.90
Vision	3	4.6 (.68)	5.0	0.7	2.00 – 5	-2.1	0	54.6	0.60	0.80
Work	3	4.0 (.99)	4.3	1.7	1.00 – 5	-0.8	0.7	31.9	0.77	0.92
Thinking	3	2.8 (1.19)	2.7	2.0	1.00 - 5	0.4	5	8.5	0.61	0.82
Family roles	3	3.9 (1.08)	4.0	2.0	1.33 – 5	-0.6	0	38.3	0.59	0.82
Social roles	5	3.4 (1.15)	3.1	1.9	1.20 – 5	0	0	15.6	0.58	0.87
Personality	3	3.6 (1.15)	3.7	2.3	1.00 – 5	-0.2	0.7	25.5	0.74	0.90
Mood	5	3.9 (.99)	4.0	2.0	1.80 – 5	-0.4	0	25.5	0.53	0.85
Energy	3	3.0 (1.38)	3.0	2.3	1.00 – 5	0.1	12.8	14.2	0.78	0.92
2 subtotal scores										
Physical	27	4.4 (.60)	4.6	0.9	2.23 -5	-1.3	0	15.7	0.64	0.96
Psychosocial	22	3.4 (.96)	3.4	1.5	1.46 – 5	0	0	4.3	0.62	0.95
Total SS-QoL	49	4.0 (.68)	4.0	1.0	2.29 - 5	-0.4	0	2.8	0.63	0.97

[a]: Physical component: Self care, mobility, upper extremity, language, vision, work
[b]: Psychosocial component: Thinking, family roles, social roles, personality, mood, energy

Table 5. Criterion validity of the SS-QoL scores in patients with subarachnoid haemorrhage (N=141)

	Outcome GOS	Cognition CFQ	Satisfaction LiSat-9	Mood HADS
12 domains				
Self-care	0.42	-0.30	0.56	-0.42
Mobility	0.26	-0.39	0.55	-0.50
Upper-extremity	0.33	-0.44	0.56	-0.48
Language	0.10	-0.53	0.42	-0.44
Vision	0.08	-0.38	0.41	-0.48
Work	0.14	-0.49	**0.60**	**-0.61**
Thinking	0.03	**-0.65**	0.40	-0.45
Family Roles	0.08	-0.40	0.57	**-0.61**
Social Roles	0.10	-0.40	**0.62**	**-0.63**
Personality	0.05	-0.43	0.51	**-0.65**
Mood	0.09	-0.43	0.57	**-0.71**
Energy	0.03	-0.42	0.44	**-0.64**
2 subtotal scores				
Physical	0.25	-0.52	**0.64**	-0.59
Psychosocial	0.07	-0.53	**0.61**	**-0.73**
Total SS-QoL	0.18	-0.56	**0.68**	**-0.73**

Correlations above 0.24 were significant at a p value of 0.0033 (two tailed) using a Bonferroni correction for 15 simultaneous tests. Correlations of 0.60 or higher are printed in bold.
CFQ, Cognitive Failure Questionnaire; GOS, Glasgow Outcome Scale; HADS, Hospital Anxiety and Depression Scale; LiSat-9, Life Satisfaction Checklist; SS-QoL, Stroke Specific Quality of Life.

DISCUSSION

In this study we validated the SS-QoL in an SAH population. Our results showed the SS-QoL to be a valid measure in assessing HRQoL after aneurysmal SAH. The 12 SS-QoL domains showed good internal consistency, which was also found in other types of stroke.[7,10] The SS-QoL showed ceiling effects for all domains except 'thinking' and 'energy'. The physical subtotal score also showed a ceiling effect but the psychosocial subtotal score and the total SS-QoL score did not. One explanation may be that patients with SAH experience few physical impairments after SAH. However, more than half of our patients showed suboptimal outcome on the GOS and previous SS-QoL studies, including patients with ischaemic and haemorrhagic stroke, found similar ceiling effects.[7,8,10,21] This ceiling effect is a problem from the psychometric point of view and may limit the usefulness of the SS-QoL in clinical practice if the SS-QoL lacks sensitivity for minor physical health problems. However, the mobility scale, for example, includes broad questions such as 'did you have problems with walking?', so, if the patient experiences no problems at all, it is not very likely that clinically relevant problems will be missed.

As expected, we found moderate to strong correlations between the domain-specific measures CFQ, LiSat-9 and HADS and corresponding SS-QoL domain scores. In previous studies in patients with other types of stroke, using other criterion measures, for the most part somewhat lower correlations were found.[7-10,22] The physical domains showed only weak to moderate correlations with GOS in our study. In our patient group, only three

levels of the GOS were used which decreases its discriminative ability. Furthermore, the GOS was administered at discharge from hospital, about 3 years before the other measures in this study. Finally, the GOS is not an ideal reference measure for physical disability. Previous studies found higher correlations of 0.41- 0.62 between 'mobility' and the SF-36 physical functioning scale but found correlations of only 0.18 - 0.26 between 'upper extremity function' and the Barthel Index,[9,11] which is similar to what we found using the GOS. Our results show that the SS-QoL has a stronger focus on emotional and social health than on physical health.

Correlations between the 12 SS-QoL domains were moderate to strong and PCA revealed a 'physical' and a 'psychosocial' component. The theoretically driven clustering in four dimensions was not supported by the PCA, the main problem being very high correlations between scores on the 'emotional' and 'social' scales and dimensions. It is not clear how the 12 SS-QoL domains were selected.[7] Previous studies in patients with other types of stroke also did not support the 12 domain structure of the SS-QoL.[9,22] In these studies, PCA was executed on all 49 items and one study found eight components[9] and another study did not specify this number.[22] We refrained from these analyses because of a limited sample size. The use of 49 item scores as variables unavoidably leads to a greater number of identified components than was found in our study using 12 scale scores as variables. Our results nevertheless show that a clustering of the SS-QoL scores in less than 12 domains is possible. One total score might be useful as outcome measure in clinical trials but might obscure differences between different aspects of HRQoL. The 0.73 correlation between the physical and psychosocial subtotal score components shows that one component explains about half of the variance of the other. Using the two SS-QoL subtotal scores for physical and for psychosocial HRQoL might be a good compromise between the simplicity and a need to provide a profile of different aspects of health. The very high Cronbach's α values of these components further indicates that it could be possible to develop a short version of the SS-QoL to facilitate its use in a clinical setting and as an outcome measure in clinical studies.

Our patient group was similar with respect to location of aneurysm, neurological outcome, return to work and mean HADS scores to a large earlier Dutch follow-up study, which increases the external validity of our results.[23] Some potential limitations of this study should be noted. Firstly, we excluded eight patients living in a nursing home and four patients with serious comorbidity. Including these patients might have resulted in slightly less ceiling effects of the physical health scores. Secondly, although our criterion measures are well known and were used in various diagnostic groups, they have not been validated in populations with SAH either. Thirdly, measuring physical health with a measure other than the GOS and at the same time as the SS-QoL might have revealed stronger associations between both measures. Fourthly, our study sample was too small to perform PCA on item level for which a sample size of at least 300 is recommended.[24] Finally, we did not examine other psychometric properties, such as test-retest reliability and agreement between patients and significant others. Further studies are needed to establish these properties in SAH populations.

REFERENCES

1. Donnan GA, Fisher M, Macleod M, et al. Stroke. Lancet 2008;371: 1612-23.
2. Rooij de NK, Linn FHH, van der Plas JA, et al. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. J Neurol Neurosurg Psychiatry 2007;78:1365-72.
3. Van Asch CJ, Luitse MJ, Rinkel GJ, et al. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. Lancet Neurology 2010;9:167-76.
4. Hop JW, Rinkel GJE, Algra E, et al. Quality of life in patients and partners after aneurysmal subarachnoid hemorrhage. Stroke 1998;29:798-804.
5. Hackett ML, Anderson CS. ACROSS Study. Health outcomes 1 year after subarachnoid hemorrhage. An international population-based study. Neurology 2000;55:658-62.
6. Patrick DL, Deyo RA. Generic and disease-specific measures in assessing health status and quality of life. Med Care 1989;27:217-32.
7. Williams LS, Weinberger M, Harris LE, et al. Development of a stroke specific quality of life scale. Stroke 1999;30:1362-9.
8. Williams LS, Weinberger M, Harris L, et al. Measuring quality of life in a way that is meaningful to stroke patients. Neurology 1999;53:1839-43.
9. Ewert T, Stucki G. Validity of the SS-QOL in Germany and in survivors of hemorrhagic or ischemic stroke. Neurorehabil Neural Repair 2007;21:161-8.
10. Muus I, Williams LS, Ringsberg KC. Validation of the Stroke Specific Quality of Life scale (SS-QOL): test of teliability and validity of the Danish version (SS-QOL-DK). Clin Rehabil 2007;21:620-7.
11. Lima RCM, Texeira-Salmela LF, Magalhaes LC, et al. Psychometric properties of the Brazlian versoin of the Stroke Specific Quality of Life Scale: application of the Rasch model. Rev Bras Fisioter 2008;12:149-56.
12. Visser-Meily JMA, Rhebergen ML, Rinkel GJE, et al. Long-term health related quality of life after aneurysmal subarachnoid hemorrhage; relationship with psychological symptoms and personality characteristics. Stroke 2009;40:1526-9.
13. Turner RR. Rehabilitation. In: Spilker B, ed. Quality of life and pharmacoeconomics in clinical trials. New York: Lippincott-Raven, 1990.
14. Nys GMS, van Zandvoort MJE, van der Worp HB, et al. Early cognitive impairment predicts long-term depressive symptoms and quality of life after stroke. J Neurol Sci 2006;247:149-56.
15. Jennett B, Bond M. Assessment of outcome after severe brain damage: a practicale scale. Lancet 1975;7905:480-4.
16. Broadbent DE, Cooper PF, FitzGerald P, et al. The Cognitive Failures Questionnaire (CFQ) and its correlates. Br J Clin Psychol 1982;21:1-16.
17. Fugl-Meyer A, Bränholm IB, Fugl-Meyer K. Happiness and domain-specific life satisfaction in adult northern Swedes. Clin Rehabil 1991;5:25-33.
18. Spinhoven P, Ormel J, Sloekers PP, et al. A validation study of the hospital anxiety and depression scale (HADS) in different groups of Dutch subjects. Psychol Med 1997;27:363-70.
19. Terwee CB, Bot SDM, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol 2007;60:34-42.
20. Visser-Meily JMA, Post MWM, Riphagen II, et al. Measures used to assess burden among caregivers of stroke patients: a review. Clin Rehabil 2004;18:601-23.
21. Czechowsky D, Hill MD. Neurological outcome and quality of life after stroke due to vertebral artery dissection. Cerebrovasc Dis 2002;13:192-7.
22. Hilari K, Byng S, Lamping DL, et al. Stroke and aphasia quality of life scale-39 (SAQOL-39). Evaluation of acceptability, reliability, and validity. Stroke 2003;34:1944-50.

23. Wermer MJH, Kool H, Albrecht KW, et al. Subarachnoid hemorrhage treated with clipping: long-term effects on employment, relationships, personality, and mood. Neurosurgery 2007;60:91-8.
24. Tabachnick BG, Fidell LS. Using multivariate statistics, 5th edn. Boston: Pearson Education Inc, 2007.

Based on:

Prevalence and determinants of cognitive complaints after aneurysmal subarachnoid haemorrhage

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Prevalence and determinants of cognitive complaints after aneurysmal subarachnoid haemorrhage

ABSTRACT

Background: To investigate the prevalence of cognitive complaints after subarachnoid haemorrhage (SAH) and the relationships between cognitive complaints and cognitive impairments, disability and emotional problems.

Methods: Cognitive complaints were assessed with the Checklist for Cognitive and Emotional Consequences following stroke (CLCE-24) in 111 persons who visited our outpatient clinic 3 months after SAH. Associations between cognitive complaints and cognitive functioning, demographic characteristics, disability and emotional problems were examined using Spearman correlations and linear regression analysis.

Results: In this study group, 105 patients (94.6%) reported at least one cognitive or emotional complaint that hampered everyday functioning. The most frequently reported cognitive complaints were mental slowness, short-term memory problems and attention deficits. All cognitive domains, disability, depressive symptoms and feelings of anxiety were significantly associated with the CLCE-24 cognition score. In the final regression model, memory functioning (β value –0.21), disability (–0.28) and depressive symptoms (0.40) were significant determinants of cognitive complaints, together explaining 35.4% of the variance.

Conclusion: Cognitive complaints are common after SAH and associated with memory deficits, disability and depressive symptoms. Rehabilitation programs should focus on these symptoms and deficits.

INTRODUCTION

Subarachnoid haemorrhage (SAH) from a ruptured intracranial aneurysm accounts for approximately 5% of all strokes[1], occurs at a relatively young age[2], and carries a poor prognosis for survival despite improvements in medical care for these patients.[3] Although a large proportion of the patients with SAH who resume living at home show functional independence, many of them have impairments in visual perception and construction, information processing speed, memory and executive functioning.[4]

From a patient's perspective, not the cognitive impairments as assessed by neuropsychological tests, but their experience of cognitive and emotional dysfunction in everyday life matters most. Previous studies in patients with SAH on associations between cognitive impairments and cognitive complaints revealed only weak associations[5] or no significant associations at all.[6] Physical functioning and emotional problems such as depression and anxiety might influence the perceived cognitive dysfunction.[7] Psychological and social problems occur often in patients with SAH and reduce health-related quality of life[8], life satisfaction[9], returning to work[9,10], and engagement in social activities.[10] The contribution of disability and emotional problems to the cognitive complaints in patients with SAH is however still unclear. Knowledge of the factors underlying cognitive complaints in patients with SAH is important to tailor rehabilitation programs with respect to the specific needs in this patient population.

We investigated the prevalence of cognitive complaints in patients living at home 3 months after SAH, and assessed whether cognitive impairments, demographic characteristics (age, sex, level of education), disability (Glasgow Outcome Scale, GOS) and emotional problems (depressive symptoms, anxiety) are related to the cognitive complaints of patients with SAH.

METHODS

SAH Patients and Procedure

Patients who visited the SAH outpatient clinic of the University Medical Centre Utrecht (UMCU) between November 2006 and September 2008 were included if they had had an SAH from a ruptured aneurysm, and were living at home at the time of their visit. At our multidisciplinary SAH outpatient clinic, patients are seen by a neuropsychologist for a brief neuropsychological examination (45 min), a specialized SAH nurse who interviews the patient and assesses the Checklist for Cognitive and Emotional consequences following stroke (CLCE-24), and, finally, patients are seen by a rehabilitation physician who performs a physical examination and evaluates the necessity of any form of therapy. All patients were approached by mail and asked to complete a questionnaire before their visit to the clinic. All patients gave informed consent. The study was approved by the Medical Ethics Committee of the UMCU.

Outcome Measurement

The CLCE-24[11] is assessed by an interviewer asking the patient whether he/she has cognitive and/or emotional complaints since the SAH and consists of 13 cognitive items (for instance problems with 'doing two things at once' or 'attending to things') and 9 emotional items (for instance being 'depressed' or 'faster or more often tired') and 2 open-

ended questions which allow addition of other problems but which are not included in the scores. The interviewer scores a '0' for absence and a '1' for presence of complaints; the sum score indicates the number of experienced complaints. The CLCE-24 was validated[11] using the Mini Mental State Examination and the Dutch CAMCOG, part of the Cambridge Examination of Mental Disorders in the elderly, as reference instruments.

Possible Determinants

Demographic data, the clinical condition on admission (Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage scale[12]), location of the ruptured aneurysm and complications were obtained from the database of the Department of Neurology and Neurosurgery of the UMCU. The level of disability 3 months after SAH was assessed by means of the GOS[13] , obtained either from the neurology database or the outpatient clinic.

The concise neuropsychological examination covered four major cognitive domains. *Memory* included verbal working memory as assessed by the Backward Digit Span of the Wechsler Adult Intelligence Scale III (WAIS-III) and Category Fluency (semantic memory) using animal naming.[14] The Rey Auditory Verbal Learning Task was used to measure verbal learning, revealing scores for immediate and delayed recall and recognition.[14] Non-verbal recall, incidental, was evaluated using the delayed Rey-Osterrieth Complex Figure Test (Rey-CFT).[14] *Executive functioning* was measured with the Brixton Spatial Anticipation Test for strategic thinking and with phonological fluency ('N' and 'A') for concept generation.[14] *Attention* was measured by Forward Digit Span of the WAIS-III and the Stroop Color Word Test.[14] To obtain an indication of *visuospatial functioning*, the copy score of the Rey-CFT was used.[14] A control group, containing 62 subjects with a mean age of 57.8 years and 58.1% women, was studied to obtain reference data for the neuropsychological examination.[15]

To study depressive symptoms, we administered the Beck Depression Inventory-II-NL (BDI), a 21-item screening instrument for depression. The total score ranges between 0 and 63. A high score indicates the severity of depressive symptoms[16] , and we accepted a score of 10 or higher as suggestive of possible depression.[17] We measured anxiety with the state part of the State- Trait Anxiety Inventory (STAI-DY-1), with a sum score between 20 and 80.[18] A higher sum score implicates a higher level of anxiety, with different cutoff points based on sex and educational level.

Statistical Analyses

Descriptive statistics were used to describe the SAH population, the cognitive and emotional complaints, cognitive impairments and emotional problems. We recorded the patients' level of education using the Dutch classification system ranging from 1 (did not finish primary school) to 7 (university education), which was dichotomized as low (0–5) and high (6–7).[19] GOS was dichotomized as 'disability' (GOS < V) and 'no disability' (GOS V). The CLCE-24 cognition score was computed, which showed satisfactory internal consistency in the present study (Cronbach's α 0.7).

Raw neuropsychological test scores of patients on all individual tests were transformed into z scores based on the means and standard deviations of the control group. Subsequently, z scores were averaged per cognitive domain. Based on the z scores, patients could be stratified into 'normal' (within 1.5 standard deviations from the control mean), 'mildly impaired' (between 1.5 and 2 standard deviations from the control mean) or 'severely impaired' (more than 2 standard deviations from the control mean).[14]

Bivariate associations of cognitive domains (memory, attention, executive and visuospatial functioning), demographic characteristics (age, sex, education), disability (GOS) and emotional problems (BDI and STAI) with the CLCE-24 cognition score were tested using Spearman correlations. Differences in the number of cognitive complaints (range 0–13) and emotional complaints (range 0–9) between groups of persons with SAH were tested using Mann-Whitney test. After that, backward multiple regression analyses were performed to examine associations between joint predictors and cognitive complaints. We first used only the cognitive domain scores as independent variables to study the amount of variance of cognitive complaints explained by the cognitive impairments alone. Subsequently, we added the demographic characteristics, disability and emotional problems to the regression models in cumulative steps. We considered $p < 0.05$ as statistically significant.

RESULTS

SAH Population

From September 2006 until August 2008, 268 patients with SAH were admitted to the Department of Neurology and Neurosurgery of the UMCU. Within this group, 68 died, 27 were discharged to a nursing home, 38 to a rehabilitation center, and 136 were discharged home. At a mean time of 3 months after SAH 150 patients were living at home, of whom 129 visited the outpatient clinic. Eighteen of these 129 patients (14%) were excluded because of missing CLCE-24 cognition scores (n = 8), no neuropsychological examination (n = 4) or incomplete BDI and/or STAI (n = 6). The 111 patients with SAH who were included in this study did not differ substantially from the 39 patients who did not visit the outpatient clinic (n = 21) or were excluded from the study (n = 18) in terms of age, sex, education, clinical condition on admission, complications or GOS score at discharge. The characteristics of the 111 included patients are displayed in table 1. Besides the lesions based on the SAH itself and the complications of the SAH, no other cerebral lesions were found.

Cognitive and Emotional Complaints

In this study group, 105 patients (94.6%) reported at least one cognitive or emotional complaint that hampered everyday functioning as assessed by the CLCE-24. In 89 patients (80.2%) this concerned at least one cognitive complaint and in 103 (92.8%) at least one emotional complaint. The proportions of patients with cognitive and emotional complaints are shown in table 2 . The most reported cognitive complaints were mental slowness, short-term memory problems and attention problems, whereas the most reported emotional complaints were fatigue, feelings of anxiety and being emotionally less stable. The number of cognitive complaints showed a median of 3 (IQR from 1 to 5) and the number of emotional complaints showed a median of 3 (IQR from 1 to 4).

Cognitive Functioning and Emotional Problems

Fifty-two patients (46.8%) showed mild and 28 (25.2%) severe cognitive impairments on one or more neuropsychological tests. Results of the separate cognitive tests are shown in table 3.

Table 1. Characteristics of SAH patients (N=111)

		n	*%*
Demographic characteristics			
Sex (women %)		91	82.0
Mean age in years (SD)		52.8 ± 13.0	
Education level (%)			
	Low	9	8.1
	Intermediate	82	73.8
	High	20	18.0
SAH characteristics			
Mean follow up time after SAH in weeks (SD)		11.2 ± 4.0	
PAASH			
	I, GCS 15 (%)	73	65.8
	II, GCS 11-14 (%)	29	26.1
	III, GCS 8-10 (%)	2	1.8
	IV, GCS 4-7 (%)	3	2.7
	V, GCS 3 (%)	3	2.7
	Missing	1	0.9
Aneurysm location			
	Anterior cerebral and anterior communicating	48	43.2
	Middle cerebral	24	21.6
	Internal carotid	26	23.4
	Posterior circulation	13	11.7
Treatment received			
	Coiling (%)	70	63.1
	Surgery (%)	41	36.9
Complications (yes %)		45	40.5
	Rebleeding	5	4.5
	Secondary ischaemia	23	20.7
	Hydrocephalus	14	12.6
	Hydrocephalus and ischaemia	3	2.7
GOS at 3 months after SAH			
	III dependent from others (%)	4	3.6
	IV disability, but independent (%)	26	23.4
	V good recovery (%)	81	73.0
Emotional characteristics			
STAI-DY-1	Anxious (%)	58	52.3
BDI-II-NL	Mean	8.6 ± 6.9	
	No depressive symptoms (score 0-9)	67	60.4
	Minor – moderate depression (score 10-18)	35	31.5
	Severe depression (score >30)	2	1.8

SAH = subarachnoid haemorrhage; PAASH = Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage; GCS = Glasgow Coma Scale; GOS = Glasgow Outcome scale; STAI-DY-1 = State Trait Anxiety Inventory; BDI-II-NL = Beck Depression Inventory.

On the whole, 44 patients (39.6%) had depressive symptoms; most of whom (n = 35) had scores in the minor to moderate depression range (score 10–18). Based on the STAI sum score, feelings of anxiety were present in 58 patients (52.3%).

Table 2. Cognitive and emotional complaints in patients with SAH, as assessed with the CLCE-24.

Complaints since SAH	n	%
Cognitive complaints		
Keeping up; has become slower	67	60.4
Remembering new information	54	48.6
Attending to things	49	44.1
Doing two things at once	41	36.9
Taking initiative	26	23.4
Planning and organizing things	25	22.5
Remembering old information	23	20.7
Performing daily activities	23	20.7
Speaking or writing	9	8,1
Perceiving time	6	5.4
Orientating to places or persons	3	2.7
Social aspects of language	2	1.8
Attending to a part of the body or space	2	1.8
Emotional complaints		
Faster and more often tired	100	90.1
In fear of things to come	47	42.3
Emotional, crying faster	41	36.9
Irritable	36	32.4
Depressed	34	30.6
Less oriented socially	31	27.9
Indifference	18	16.2
Not realistic about things	8	7.2
Less in control of his own behaviour	7	6.3

CLCE: Checklist for Cognitive and Emotional consequences following stroke, SAH: subarachnoid haemorrhage.

Relationships with Cognitive Complaints

Table 4 shows bivariate and multivariate relationships with the CLCE-24 cognition score. All cognitive domains, disability (GOS), depressive symptoms (BDI) and feelings of anxiety (STAI) were significantly associated with the CLCE-24 cognition score. There were no differences in the amount of cognitive complaints ($p = 0.90$) or emotional complaints ($p = 0.14$) between persons with SAH due to an aneurysm at the anterior circulation compare to those having an aneurysm at the posterior circulation. Furthermore, there were no differences in the amount of cognitive ($p = 0.35$) and emotional complaints ($p = 0.67$) between persons with SAH without complications compared to those having complications.

In the regression analyses, step 1 (cognitive domains only) explained 6.9% of the variance of the CLCE-24 cognition score. Adding demographic characteristics in step 2 did not increase the percentage of variance. Step 3, adding the level of disability (GOS), increased the explained variance to 22.8%. In the final regression model, memory, disability (GOS), and depressive symptoms (BDI) were significant independent determinants, together explaining 35.4% of the variance in the CLCE-24 cognition score. The presence of depressive symptoms was the strongest predictor.

DISCUSSION

Our study showed that most patients who are living at home after SAH have one or more cognitive or emotional complaints 3 months after SAH, and half of these patients showed mild or severe cognitive impairments, predominantly in memory and visuospatial functioning. In addition, more than half of the patients had feelings of anxiety and one third of the patients had depressive symptoms. Cognitive impairments were significantly related to cognitive complaints in the bivariate analysis, whereas in combination with other determinants only memory was a significant predictor in the regression analyses. The presence of depressive symptoms was the strongest predictor of cognitive complaints.

All patients in our study group were living at home at the time of the assessment and had a moderate to good physical recovery. Nevertheless, the prevalence of cognitive complaints, cognitive impairments, and emotional problems was high. Only one third of the cognitive complaints found in our study could be explained by underlying cognitive impairments, the presence of depressive symptoms, and the level of (physical) disability. Other factors, such as social support, personality characteristics, physical function, and fatigue might also be considered as predictors of these cognitive complaints in future studies.[6,7]

Mental slowness, memory problems for new information and attention problems were the most reported cognitive complaints in our study. Similarly, cognitive impairments most often concerned memory, and less often executive and visuospatial functioning[20,21], and rarely attention, which is in line with previous findings in SAH.[6,20–22]

Table 3. Neuropsychological screening in patients with SAH (n=111)

Domain	task		Mildly impaired		Severely impaired		Impaired Total
		N	n	%	n	%	%
Memory							
	RAVLT- immediate recall	111	7	6.3	6	5.4	11.7
	RAVLT- delayed recall	110	14	12.7	10	9.1	21.8
	RAVLT- recognition	104	9	8.7	9	8.7	17.4
	Digit span backward	111	0	0	0	0	0
	Semantic fluency	110	8	7.3	4	3.6	10.9
	Rey-CFT- delayed recall	102	12	11.8	3	2.9	14.7
Attention							
	Digit span forward	111	8	7.2	0	0	7.2
	Stroop	96	1	1.0	3	3.1	4.1
Executive functioning							
	Brixton	107	5	4.7	2	1.9	6.6
	Letter fluency	110	15	13.6	2	1.8	15.4
Visuospatial functioning							
	Rey-CFT- copy	107	9	8.4	11	10.3	18.7

SAH: subarachnoid haemorrhage; RAVLT: The Rey Auditory Verbal Learning Task; Rey-CFT: Rey-Osterrieth Complex Figure Test Some patients were not able to complete one or more tests, predominantly due to problems finding words or visual problems.

In this study only weak associations between cognitive complaints and potentially underlying cognitive impairments were found, which has been described earlier for SAH[5,6], ischemic stroke[23], and patients with traumatic brain injury.[7] The discrepancy between cognitive complaints and impairments might be due to different factors. First, our concise neuropsychological examination did not cover the complete spectrum of cognitive functioning. Second, neuropsychological examinations in general are aimed to detect cognitive impairments and, as such, are less sensitive to subtle cognitive changes. Third, subtle cognitive changes might force patients, with good functional outcome, to use additional cognitive resources in order to perform within normal limits, which may lead to the experience of cognitive failure and, as such, give rise to cognitive complaints.[7] Fourth, an overestimation of cognitive complaints might be due to attribution, which means patients are more observant after their SAH and attribute cognitive problems related to normal aging or stress to the SAH.[24] Finally, an overrating of cognitive complaints might be caused by depressive symptoms, which were frequent in our study sample.

Although this is a large-scale study on cognitive complaints and impairments in patients with SAH and good neurological recovery, some limitations should be mentioned. The neuropsychological data set did not cover all relevant domains and was not completed by all patients, and some selection bias might have taken place. However, when all available data were put into the regression analyses the significant predictors of cognitive complaints did not change (data not reported). Furthermore, the CLCE-24 was not compared to an age-matched control group. However, with a mean age of 52.8 (SD 13.0) years in our patient group, a substantial age-related cognitive decline is not to be expected.

Table 4. Bivariate and multivariate analyses of independent variables and CLCE-24 cognition score after SAH. (N = 111)

Determinant	Bivariate analysis		Multivariate analysis β value (p value)			
	Spearman	p-value	Step 1	Step 2	Step 3	Step 4
Cognitive functions						
memory	-0.323	0.001	-0.279 (0.004)	-0.279 (0.004)	-0.338 (0.001)	-0.213 (0.009)
executive functioning	-0.190	0.047	-	-	-	-
attention	-0.222	0.019	-	-	-	-
visuospatial functioning	-0.333	0.000	-	-	-	-
Demographic characteristics						
Gender	0.061	0.527	Not entered	-	-	-
Age	0.001	0.996	Not entered	-	-0.156 (0.099)	-
Education level	0.008	0.929	Not entered	-	-	-
SAH characteristics						
GOS at 3 months	-0.361	0.000	Not entered	Not entered	-0.385 (0.000)	-0.277 (0.001)
Emotional problems						
STAI-DY-1	0.484	0.000	Not entered	Not entered	Not entered	-
BDI-II-NL	0.589	0.000	Not entered	Not entered	Not entered	0.399 (0.000)
Explained variance			*6.9*	*6.9*	*22.8*	*35.4*

SAH: subarachnoid haemorrhage; CLCE-24: Checklist for cognitive and emotional consequences following stroke; GOS: Glasgow Outcome Scale; STAI-DY-1: State Trait Anxiety Inventory, BDI-II-NL: Beck Depression Inventory.

Our study shows that, in patients who recovered enough after SAH to live at home, structured screening at an outpatient clinic will often reveal emotional and cognitive problems that are otherwise easily overlooked. The rehabilitation program for patients with SAH should focus on these problems and include cognitive therapy or psychological education dependent on whether cognitive impairment or emotional problems are most prominent. Additionally, anti-depressive treatment should be considered when depressive symptoms are present. Furthermore, physiotherapy and occupational therapy can be of some importance in patients with persisting disability. When making the rehabilitation program, the weak relationships between the cognitive problems as experienced by the patients and the cognitive impairments should be taken into account. Personality characteristics and fatigue might also be important determinants of cognitive complaints which need to be examined in future.

REFERENCES

1. Donnan GA, Fisher M, Macleod M, Davis SM: Stroke. Lancet 2008; 371: 1612–1623.
2. Rooij de NK, Linn FHH, Plas van der JA, Algra A, Rinkel GJE: Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. J Neurol Neurosurg Psychiatry 2007; 78: 1365–1372.
3. Nieuwkamp DJ, Setz L, Algra A, Linn FHH, Rooij de NK, Rinkel GJE: Case-fatality of aneurysmal subarachnoid haemorrhage: a meta-analysis with emphasis on time trends, age, sex and region. Lancet Neurology 2009; 8: 635–642.
4. Wilde MC: Neuropsychological outcome in subarachnoid hemorrhage due to aneurysm. Crit Rev Physic Rehab Med 2006; 18: 117–131.
5. Ravnik J, Starovasnik B, Šešok S, Pirtošek Z, Švigelj V, Bunc G, Bošnjak R: Long-term cognitive deficits in patients with good outcomes after aneurysmal subarachnoid hemorrhage from anterior communicating artery. Croat Med J 2006; 47: 253–263.
6. Toomela A, Pulver A, Tomberg T, Orasson A, Tikke A, Asser T: Possible interpretation of subjective complaints in patients with spontaneous subarachnoid haemorrhage. J Rehabil Med 2004; 36: 63–69.
7. Stulemeijer M, Vos PE, Bleijenberg G, Werf van der AP: Cognitive complaints after mild traumatic brain injury: things are not always what they seem. J Psychosom Res 2007; 63: 637–645.
8. Visser-Meily JMA, Rhebergen ML, Rinkel GJE, Zandvoort van MJ, Post MWM: Longterm health related quality of life after aneurysmal subarachnoid hemorrhage; relationship with psychological symptoms and personality characteristics. Stroke 2009; 40: 1526–1529.
9. Fertl E, Killer M, Eder H, Linzmayer L, Richling B, Auff E: Long-term functional effects of aneurysmal subarachnoid haemorrhage with special emphasis on the patient's view. Acta Neurochir 1999; 141: 571–577.
10. Morris PG, Wilson JTL, Dunn L: Anxiety and depression after spontaneous subarachnoid hemorrhage. Neurosurgery 2004; 54: 47–54.
11. Heugten van C, Rasquin S, Winkens I, Beusmans G, Verhey F: Checklist for cognitive and emotional consequences following stroke (CLCE-24): development, usability and quality of the self-report version. Clin Neurol Neurosurg 2007; 109: 257–262.
12. Heuven van AW, Dorhout Mees SM, Algra A, Rinkel GJE: Validation of a prognostic subarachnoid hemorrhage grading scale derived directly from the Glasgow Coma Scale. Stroke 2008; 39: 1347–1348.
13. Jennett B, Bond M: Assessment of outcome after severe brain damage. Lancet 1975;i: 480–484.
14. Lezak MD, Howieson DB, Loring DW: Neuropsychological Assessment, ed 4. New York,Oxford University Press, 2004.
15. Nys GMS, Zandvoort van MJE, Kort de PLM, Jansen BPW, Haan de EHF, Kapelle LJ: Cognitive disorder in acute stroke: prevalence and clinical determinants. Cerebrovasc Dis 2007; 23: 408–416.
16. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J: An inventory for measuring depression. Arch Gen Psychiatry 1961; 4: 561–571.
17. Aben I, Verhey F, Lousberg R, Lodder J, Honig A: Validity of Beck Depression Inventory, Hospital Anxiety and Depression Scale,SCL-90, and Hamilton Depression Rating Scale as screening instruments for depression in stroke patients. Psychosomatics 2003; 43: 386–393.
18. Spielberger CD, Gorsuch RL, Lushene PR, Vagg PR, Jacobs AG: Manual for the Stat-Trait Anxiety Inventory (Form Y). Palo Alto,Consulting Psychologists Press, 1983.
19. Verhage F: Intelligentie en leeftijd: Onderzoek bij Nederlanders van twaalf tot zevenenzeventig jaar [Intelligence and Age: Study with Dutch People from Age 12 to 77]. Assen,Van Gorcum, 1964.

20. Mayer SA, Kreiter KT, Copeland D, Bernardini GL, Bates JE, Peery S, Claassen J, Du YE, Conolly ES: Global and domain-specific cognitive impairment and outcome after subarachnoid hemorrhage. Neurology 2002; 59: 1750–1758.
21. Ogden JA, Mee EW, Henning M: A prospective study of impairment of cognition and memory and recovery after subarachnoid hemorrhage. Neurosurgery 1993; 33: 572– 557.
22. Powell J, Kitchen N, Heslin J, Greenwood R: Psychosocial outcomes at three and nine months after good neurological recovery from aneurysmal subarachnoid haemorrhage: predictors and prognosis. J Neurol Neurosurg Psychiatry 2002; 72: 772–781.
23. Duits A, Munnecom T, Heugten van C, Oostenbrugge van RJ: Cognitive complaints in the early phase after stroke are not indicative for cognitive impairment. J Neurol Neurosurg Psychiatry 2008; 79: 143–146.
24. Wenzel HG, Haug TT, Mykleltun A, Dahl AA: A population study of anxiety and depression among persons who report whiplash traumas. J Psychosom Res 2002; 53: 831–835.

Based on:

Life satisfaction and return to work after aneurysmal subarachnoid haemorrhage

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Life satisfaction and return to work after aneurysmal subarachnoid haemorrhage

ABSTRACT

Background: This study was conducted to investigate life satisfaction and employment status after aneurysmal subarachnoid haemorrhage (SAH) and to explain the associations between life satisfaction and demographic, disease-related, psychological, and personality characteristics.

Methods: Subjects with SAH (n = 141) living at home 2-4 years after the SAH responded to a mailed questionnaire. Outcomes were life satisfaction, as measured with the Life Satisfaction Questionnaire 9 (LiSat-9), and employment status. Determinants in multiple regression analysis were demographic and SAH characteristics, subjective complaints (eg, mood disorder, fatigue, cognitive complaints), and personality characteristics (eg, neuroticism, passive coping style).

Results: Of the 141 subjects, 64 (46.7%) had a Glasgow Outcome Scale score of V (good outcome) at discharge. Mean subject age was 51.4 $\pm$ 12.3 years, and mean time after SAH was 36.1 $\pm$ 7.9 months. Of the 88 subjects who were working at the time of the SAH, 54 (61.4%) returned to work, but only 31 (35.2%) resumed their work completely. The subjects were least satisfied with their vocational situation (51.9% satisfied) and sexual life (51.7%) and were most satisfied with their relationships (75.2% - 88.7%) and selfcare ability (88.6%). Age (β value = 0.17), return to work after SAH (0.19), disability at hospital discharge (0.25), worsened mood (-0.37), and passive coping (-0.25) together accounted for 47.2% of the life satisfaction scores.

Conclusion: Our data indicate that return to work is a major issue for individuals who survive an SAH. Not returning to work, disability, depression, and passive coping are associated with reduced life satisfaction. Thus, vocational reintegration after SAH merits more attention during rehabilitation.

INTRODUCTION

Many individuals who survive an episode of aneurysmal subarachnoid haemorrhage (SAH) experience longterm mood disturbances, personality changes,[1-5] and impaired reintegration into their social situation.[6] Several studies on the quality of life of SAH survivors are available,[2,4,7-9] but these studies report only on health-related quality of life (HRQoL), and there is a difference between the more objective HRQoL and the subjective quality of life or life satisfaction.[10] Whereas HRQoL includes physical, mental, and social aspects of health, life satisfaction concerns a person's feelings regarding functioning and life circumstances.[10] Rehabilitation attempts to secure or restore life satisfaction in persons with chronic disabilities.[11] Life satisfaction in SAH survivors has been reported in only one previous study, which took only depression and clinical symptomatology into account.[1] In addition, more than one-third of persons who survive SAH are unable to return to their work.[1,5,6,12,13] Research into long-term life satisfaction and employment status is important to identify support needs and provide recommendations to improve aftercare. Consequently, we investigated the long-term life satisfaction and employment status of SAH survivors living at home after the episode. We also examined associations among global outcomes, employment status, sociodemographic characteristics, subjective complaints, and personality characteristics related to life satisfaction after SAH.

METHODS

Subjects

The study group comprised individuals who had experienced SAH from a ruptured aneurysm that had been treated by clipping or coiling between January 2003 and July 2005 in the University Medical Center Utrecht (UMCU) and who were living at home at the time of the study. Excluded were individuals with nonaneurysmal SAH, severe comorbidity, or reduced life expectancy, and those who could not speak Dutch. Those who agreed to participate were asked to complete a mailed questionnaire. The UMCU's Medical Ethics Committee approved the study design.

Outcome Measurement

Life satisfaction was measured with the Life Satisfaction questionnaire (LiSat-9), a validated tool for evaluating life satisfaction.[14-18] The LiSat-9 includes 1 question about satisfaction with life as a whole and 8 questions regarding satisfaction with the following life domains: self-care ability, leisure time, vocational situation, financial situation, sexual life, partnership relations, family life, and contacts with friends. Each question is scored on a 6-point scale: 1 = very unsatisfied, 2 = unsatisfied, 3 = rather unsatisfied, 4 = rather satisfied, 5 = satisfied, and 6 = very satisfied. The subjects were also asked questions about their employment status before and after the SAH episode. For a subject who had been working before SAH, the type of job and the total hours worked were recorded. For a subject who had returned to his or her original job after the SAH episode, whether they worked fewer hours or had less responsibility was noted. Employment status was evaluated as a nominal variable comprising 3 categories: having no paid work either before or after SAH, having paid work before but not after SAH, and having paid work both before and after SAH.

Possible Determinants

Data on age, sex, time after SAH, location of the ruptured aneurysm, and clinical condition on admission (World Federation of Neurological Surgeons (WFNS) scale),[19] data on complications and level of disability at discharge (the Glasgow Outcome Scale (GOS)),[20] were obtained from the SAH database of UMCU's Department of Neurology and Neurosurgery. All other measurements were obtained through the questionnaire. Mood was evaluated using the Hospital Anxiety and Depression Scale (HADS), which contains 14 items assessing anxiety and depression with a total score of 0-42, with a higher score indicating lower mood.[21] Fatigue was evaluated using the Fatigue Severity Score (FSS),[22] which comprises 9 statements regarding the impact of fatigue. The Total FSS score is the mean of the 9 item scores and ranges from 1 to 7, with a higher score indicating greater fatigue. Cognition was assessed using the Cognitive Failure Questionnaire (CFQ),[23] which comprises 25 items measuring the frequency of self-reported failures of memory, attention, motor function, and perception. The CFQ has a maximum score of 100, with higher scores indicating poorer perceived cognitive function. Passive coping strategy was measured using the 7-item passive coping subscale of the Utrecht Coping List (UCL-P),[24] with higher scores indicating greater use of passive coping styles. The neuroticism subscale of the Eysenck Personality Questionnaire (EPQ-N)[25] contains 12 items with "yes/no" answers, with each "yes" answer worth 1 point. Persons with a high score tend to be quickly worried and mentally unstable.

Statistical Analysis

Descriptive statistics were used to describe the SAH population and their work situation and life satisfaction. LiSat-9 item scores were dichotomized as dissatisfied (1-4, "very dissatisfied" to "rather satisfied") or satisfied (5, "satisfied," or 6, "very satisfied").[26] A total LiSat-9 score was computed as the average of all item scores, and thus also had a range of 1–6.[14,17,18] This total score satisfied the normal distribution (skewness, - 0.8) and demonstrated good internal consistency and reliability in the present study (Cronbach's $\alpha = 0.87$). Relative risk with corresponding 95% confidence interval (CI) was used to compare life satisfaction in subjects with disability at discharge (GOS < V) and those without disability at discharge (GOS of V) and in subjects who returned to work and those who did not return to work. Bivariate associations of demographic characteristics (eg, age, sex, education, work before and after SAH), SAH-related factors (eg, GOS and complications), subjective complaints (as assessed by the FSS, HADS, and CFQ) and personality characteristics (as assessed by the EPQ-N and UCL-P) with the LiSat-9 total score were tested using Spearman correlations. Variables that were significantly associated with the LiSat-9 total score using an a value of 0.10 were entered as independent variables in a backward multiple regression analysis. The very high correlation between HADS and EPQ-N scores precluded using both of these variables in the same regression analysis; thus, only the HADS was used. Employment status was defined by 2 dummy variables (paid work before and after SAH), both of which were entered into the regression analysis.

RESULTS

Between January 2003 and July 2005, a total of 212 SAH survivors were treated by aneurysm coiling or clipping at UMCU. Of this group, 21 died in the hospital, 8 were discharged to a nursing home, 5 lived in a foreign country, and 4 had severe comorbidity.

Table 1. Characteristics of persons with SAH (n = 141)

Demographic characteristics	
Female sex , n (%)	94 (66.7)
Age, years, mean (SD)	51.4 (12.3)
Higher education level, n (%)	45 (31.9)
Living with partner, n (%)	108 (76.6)
Pre SAH employment , n (%)	88 (62.4)
SAH characteristics	
Follow up after SAH, months, mean (SD)	36 (7.9)
Aneurysm location, n (%)	
Internal carotid artery	33 (23.4)
Middle cerebral artery	30 (21.3)
Anterior communicating artery / anterior cerebral artery	60 (42.6)
Vertebrobasilar arteries	18 (12.8)
WFNS, n (%)	
I, GCS 15, no focal lesions	86 (61.0)
II, GCS 13-14, no focal lesions	28 (19.9)
III, GCS 13-14, focal lesions	5 (3.5)
IV, GCS 7-12, focal lesions or not	17 (12.1)
V, GCS 3-6, focal lesions or not	1 (0.7)
Type of intervention, n (%)	
Coiling	68 (48.2)
Clipping	73 (51.8)
Complications, n (%)	77 (54.6)
Rebleeding	8 (5.7)
Secondary ischemia	23 (16.3)
Hydrocephalus	28 (19.9)
Hydrocephalus and ischemia	5 (3.5)
GOS at discharge, n (%)	
V no disability	64 (46.7)
IV disability, but independent	44 (32.1)
III disability, dependent from others	29 (21.2)
Subjective complaints, mean (SD)	
HADS	10.8 (7.0)
FSS	4.6 (1.4)
CFQ	36.8 (16.8)
Personality characteristics, mean (SD)	
EPQ-N	4.5 (3.4)
UCL-p	10.6 (3.0)

Abbreviations: WFNS, World Federation of Neurological Surgeons scale; GOS, Glasgow Outcome Scale; HADS, Hospital Anxiety and Depression Scale; FSS, Fatigue Severity Scale; CFQ, Cognitive Failure Questionnaire; EPQ, Eysenck Personality Questionnaire; UCL, Utrecht Coping List.
Demographic data and SAH characteristics were gathered from a database. Psychological and personality characteristics were obtained from the questionnaires.
* Higher value denotes worse condition

Thus, a total of 174 subjects were eligible for the survey and received a questionnaire; of these, 141 (81%) agreed to participate in this study. The 141 subjects with SAH who chose to participate and the 33 individuals with SAH who declined to participate did not differ significantly in terms of age, sex, time after SAH, clinical condition on

admission, occurrence of complications during the clinical course, and clinical condition at discharge. Demographic data, SAH characteristics, and psychological and personality test scores are summarized in table 1.

Life Satisfaction

The mean LiSat-9 total score was 4.8 ± 0.8 (range, 1.56 – 6.00), which is between "rather satisfied" (4) and "satisfied" (5), and the median LiSat-9 total score was 5.0. Self-care ability, partner relationship, and family life were the highest-rated life domains, and vocational situation and sexual life were the lowest-rated domains (table 2). The LiSat-9 total score was higher in subjects without disability at discharge compared with those with disability at discharge (5.03 ± 0.7 vs 4.56 ± 0.9; P= .001). On individual LiSat-9 items, the proportion of subjects reporting good satisfaction with life as a whole, self-care ability, financial situation, and sexual life was significantly higher in the group without disability at discharge (table 2).

Table 2. Total SAH population and comparison of GOS V and GOS < V in relationship to satisfaction according to LiSat-9. (N = 141)

LiSat 9	Total SAH population		GOS				Relative Risk GOS V/<V	
			GOS V		GOS <V			
	n	% satisfied	n	% satisfied	n	% satisfied	RR	95% CI
Life as a whole	141	61.7	64	71.9	77	53.2	1.35	1.04 -1.75
Self care ability	140	88.6	64	96.9	76	81.6	1.19	1.06 -1.33
Leisure situation	141	66.0	64	68.8	77	63.6	1.08	0.85 -1.37
Vocational situation	79	51.9	40	57.5	39	46.2	1.25	0.81 -1.92
Financial situation	139	66.2	64	75.0	75	58.7	1.28	1.01 -1.62
Sexual life	120	51.7	56	66.1	64	39.1	1.69	1.81 -2.42
Partner relationship	115	88.7	54	92.6	61	85.2	1.09	0.96 -1.24
Family life	141	83.7	64	85.9	77	81.8	1.05	0.91 -1.21
Contact friends	141	75.2	64	81.3	77	70.1	1.60	0.96 -1.40

SAH: subarachnoid haemorrhage; GOS: Glasgow Outcome Scale; CI: confidence interval

Table 3. Patients with SAH who had work before the SAH (n=88); comparison of patients with and without work after SAH in relationship to satisfaction according to LiSat-9.

LiSat 9	Work before SAH				Relative Risk : Work/ no work after SAH	
	Work after SAH		No work after SAH			
	n	% satisfied	n	% satisfied	RR	95% CI
Life as a whole	54	79.6	34	52.9	1.5	1.07-2.12
Self care ability	54	96.3	34	79.4	1.2	1.01-1.45
Leisure situation	54	68.5	34	61.8	1.1	0.81-1.53
Vocational situation	53	67.9	14	-	-	-
Financial situation	54	74.1	34	50.0	1.5	1.02-2.15
Sexual life	52	63.5	30	46.7	1.4	0.88-2.10
Partner relationship	47	93.6	28	92.9	1.0	0.89-1.15
Family life	54	85.2	34	85.3	1.0	0.84-1.19
Contact friends	54	75.9	34	67.6	1.1	0.85-1.48

SAH: subarachnoid haemorrhage; CI: confidence interval

Return to Work and Life Satisfaction

A total of 88 subjects were employed at the time of the SAH episode, and 53 were not employed. In the latter group, 23 subjects were retired, 18 were full-time housekeepers, 2 were students, 4 could not work due to health problems unrelated to SAH, and 6 did not work for other or unknown reasons. Three years after the SAH episode, 54 of the 88 (61.4%) subjects who were employed before the episode had returned to work, but only 31 (35.2%) had completely resumed their former work. The others were working fewer hours per week or had shifted to a less-demanding position. In the subjects who were employed before the SAH episode, those who resumed work after the episode had a higher LiSat-9 total score than those who did not (5.00 ± 0.7 vs 4.63 ± 0.9; P =.007). On individual LiSat-9 items, a significantly higher percentage of those with work after SAH reported good satisfaction with life as a whole, selfcare ability, and financial situation (table 3).

Relationships With Life Satisfaction

Table 4 reports bivariate and multivariate associations with the LiSat-9 total score. Age, resumption of work after SAH, disability at discharge (as assessed by the GOS), and all subjective complaints and personality characteristics were significantly associated with life satisfaction and were entered as independent variables in the regression analysis. In the final regression model, age, employment after SAH, disability at discharge (GOS), mood (HADS), and passive coping (UCL-P) were significant independent variables, together explaining 47% of the LiSat-9 variance.

Table 4. Bivariable and multivariable analyses of independent variables and LiSat-9 (total score) long term after SAH.(N = 141)

Determinant	Bivariate analysis		Multivariate analysis	
	Spearman	p-value	β-value	p-value
Demographic characteristics				
Gender	-0.001	0.986	Not entered	
Age	0.175	0.038	0.170	0.032
Education level	0.021	0.809	Not entered	
Employment				
Work before SAH*	0.043	0.615	-0.045	0.593
Work after SAH	0.208	0.013	0.185	0.027
SAH characteristic				
GOS	0.291	0.000	0.251	0.000
Complications	-0.127	0.134	Not entered	
Time after SAH	0.071	0.404	Not entered	
Psychological symptoms				
FSS	-0.504	0.000	-	-
HADS	-0.566	0.000	-0.374	0.000
CFQ	-0.355	0.000	-	-
Personality characteristics				
EPQ-N	-0.428	0.000	Not entered	
UCL-P	-0.558	0.000	-0.250	0.003

SAH: subarachnoid haemorrhage; GOS: Glasgow Outcome Scale; HADS: Hospital Anxiety and Depression Scale; FSS: Fatigue Severity Scale; CFQ: Cognitive Failure Questionnaire; EPQ: Eysenck Personality Questionnaire; UCL-P: Utrecht Coping List.

* Employment after SAH was defined by two dummy variables and therefore we kept the nonsignificant dummy variable having paid work before SAH in the analysis.

DISCUSSION

In this study, more than one-third of the subjects who were living at home after an episode of SAH were not satisfied with their life as a whole, and about half of the subjects were not satisfied with their employment situation and sexual life. Age, employment (especially after SAH), level of disability at hospital discharge, mood, and passive coping together explained almost half of the variance in life satisfaction. Our results generally are in line with those of previous studies of HRQoL in SAH survivors.[2,4,10,11] Only one previous study has reported on life satisfaction in persons with SAH; that study found that these individuals had high levels of satisfaction with their life in general and were very content with their relationships, which is in line with our findings.[1] Compared with our study, that study was rather small, focused on a subsection of a quality-of-life instrument developed to measure the impact of chronic psychiatric disease, and reported only 2 possible determinants of life satisfaction (depression and the Hunt and Hess scale). In agreement with our findings, a correlation between life satisfaction and the prevalence of depression was noted.[1] But no correlation was found between the Hunt and Hess scale score on admission and life satisfaction, whereas we detected a relationship between disability at discharge and life satisfaction, which may take complications during admission into account. We previously examined determinants of HRQoL in this same study group, using the Stroke Specific Quality of Life scale (SS-QoL).[4] Some of the results were similar to our present findings, especially regarding the predictive value of mood; however, sex, fatigue, and cognitive complaints were found to determinants of HRQoL but not of life satisfaction, whereas global outcome and passive coping were determinants of well being but not of HRQoL. Two previous studies on life satisfaction of persons with ischemic stroke or intracerebral haemorrhage used the LiSat-9[27,28] and were comparable to our study in terms of age of the study population and duration of follow-up after stroke (1–3 years). In those studies, compared with our subjects, fewer subjects were satisfied with life as a whole and with all other life domains except vocational situation,[27] partner relationship,[27] and family life.[27,28] This difference might be the result of better functional outcomes in SAH survivors compared with survivors of ischemic stroke or intracerebral haemorrhage.[7,27] The previous studies also reported a negative correlation between life satisfaction on the one hand and depression and participation on the other hand, in line with our findings. In the present study, almost two-thirds of the subjects who had worked before the SAH episode returned to work, but only one-third resumed their work completely. These proportions are comparable to those reported in several previous European studies.[1,5,12,13] In one of those studies, two-thirds of the subjects with SAH returned to full-time employment. We have no ready explanation for this higher percentage compared with our study, except for probable cultural differences.[6] Return to work after SAH has been shown to depend mainly on age, initial neurologic condition, residual physical disability and depression,[6] and the preservation of cognitive and sensorimotor functions.[13] Our subjects who returned to work after SAH reported higher levels of satisfaction with life as a whole, self-care ability, and financial situation compared with subjects who did not work after SAH. A previous study of patients with ischemic stroke or intracerebral haemorrhage found that those who returned to work also had higher levels of life satisfaction,[29] confirming the importance of vocational rehabilitation to life satisfaction.[30,31] Our study has some limitations. We used only a selfreport measure for cognitive functioning; however, the subjective experience of cognitive dysfunction is important from a life satisfaction perspective. Because the study was limited

to those subjects who survived the SAH and were discharged to home, the results cannot be generalized to persons who do not resume living at home after SAH but rather live in, for instance, a nursing home or sheltered housing program. Our cross-sectional study design precludes an analysis of causality. Our findings demonstrate that a substantial proportion of SAH survivors have decreased satisfaction with life as a whole, their vocational situation, and their sexual life. In this group, life satisfaction is negatively influenced by moderate disability, older age, unemployment, mood problems, and a passive coping style. There is a relationship between suboptimal outcome and satisfaction with self-care ability and sexual life. It is important to take these factors into account when assessing for potential vulnerability for reduced life satisfaction. Furthermore, mood problems might be related to satisfaction with sexual life and leisure situation, which merits examination in future studies. Only one-third of the subjects returned to their original job, and returning to work was strongly related to satisfaction with life overall and also to satisfaction with vocational situation and financial situation. Increased attention to vocational rehabilitation may lead to increased life satisfaction, especially in persons without disability at hospital discharge.

REFERENCES

1. Fertl E, Killer M, Eder H, et al. Long-term functional effects of aneurysmal subarachnoid haemorrhage with special emphasis on the patient's view. Acta Neurochir 1999; 141:571-577.
2. Katati MJ, Santiago-Ramajo S, Pérez-García M, et al. Description of quality of life and its predictors in patients with aneurysmal subarachnoid hemorrhage. Cerebrovasc Dis 2007;24:66-73.
3. Ogden JA, Utley T, Mee EW. Neurological and psychosocial outcome 4 to 7 years after subarachnoid hemorrhage. Neurosurgery 1997;41:25-34.
4. Visser-Meily JMA, Rhebergen ML, Rinkel GJE, et al. Long-term health-related quality of life after aneurysmal subarachnoid hemorrhage: Relationship with psychological symptoms and personality characteristics. Stroke 2009;40:1526-1529.
5. Wermer MJH, Kool H, Albrecht KW, et al. Subarachnoid hemorrhage treated with clipping: Long-term effects on employment, relationships, personality, and mood. Neurosurgery 2007;60:91-98.
6. Carter BS, Buckley DRN, Ferraro RMSOT, et al. Factors associated with reintegration to normal living after subarachnoid hemorrhage. Neurosurgery 2000;46:1326-1334.
7. Hop JW, Rinkel GJE, Algra A, et al. Quality of life in patients and partners after aneurysmal subarachnoid hemorrhage. Stroke 1998;29:798-804.
8. Hütter BO, Kreitschmann-Andermahr I, Gilsbach JM. Health-related quality of life after aneurysmal subarachnoid hemorrhage: Impacts of bleeding severity, computerized tomography findings, surgery, vasospasm, and neurological grade. J Neurosurgery 2001;94:241-251.
9. McKenna P, Willison JR, Phil B, et al. Cognitive outcome and quality of life one year after subarachnoid haemorrhage. Neurosurgery 1989;24:361-367.
10. Veenhoven R. The four qualities of life: Ordering concepts and measures of the good life. J Happiness Studies 2000;1:1-39.
11. Fuhrer MJ. Subjectifying quality of life as a medical rehabilitation outcome. Disabil Rehabil 2000;22:481-489.
12. Powell J, Kitchen N, Heslin J, et al. Psychosocial outcomes at 18 months after good neurological recovery from aneurysmal subarachnoid haemorrhage. J Neurol Neurosurg Psychiatry 2004;75:1119-1124.
13. Vilkki JS, Juvela S, Siironen J, et al. Relationship of local infarctions to cognitive and psychosocial impairments after aneurysmal subarachnoid hemorrhage. Neurosurgery 2004;55:790-803.
14. Post MWM, Dijk van AJ, Asbeck van FWA, et al. Life satisfaction of persons with spinal cord injury compared to a population group. Scand J Rehabil Med 1998; 30:23-30.
15. Fugl-Meyer AR, Bränholm IB, Fugl-Meyer KS. Happiness and domain-specific life satisfaction in adult northern Swedes. Clin Rehabil 1991;5:25-33.
16. Melin R, Fugl-Meyer KS, Fugl-Meyer AR. Life satisfaction is 18- to 64-year-old Swedes in relation to education, employment situation, health and physical activity. J Rehabil Med 2003;35:84-90.
17. Koppenhagen van CF, Post MW, Woude van der LH, et al. Changes and determinants of life satisfaction after spinal cord injury: A cohort study in the Netherlands. Arch Phys Med Rehabil 2008;89:1733-1740.
18. Visser-Meily A, Post M, Schepers V, et al. Spouses' quality of life one year post-stroke: Prediction at the start of clinical rehabilitation. Cerebrovasc Dis 2005; 20:443-448.
19. Report of World Federation on Neurological Surgeons committee on universal subarachnoid hemorrhage grading scale. J Neurosurg 1988;68:985-986.
20. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet 1975;1:480-484.

21. Spinhoven P, Ormel J, Sloekers PPA, et al. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. Psychol Med 1997;27:363-370.
22. Krupp LB, LaRocca NG, Muir-Nash J, et al. The fatigue severity scale: Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46:1121-1123.
23. Broadbent DE, Cooper PF, FitzGerald P, et al. The Cognitive Failures Questionnaire (CFQ) and its correlates. Br J Clin Psychol 1982;21:1-16.
24. Eriksen HR, Olff M, Ursin H, The CODE. a revised battery for coping and defense and its relation to subjective health. Scand J Psychol 1997;38:175-182.
25. Eysenck HJ, Eysenck SBG. Manual of the Eysenck Personality Scales. London: Hodder and Stoughton, 1991.
26. Fugl-Meyer AR, Melin R, Fugl-Meyer KS. Life satisfaction in 18- to 64-year-old Swedes in relation to gender, age, partner and immigrant status. J Rehabil Med 2002; 34:239-246.
27. Carlsson GE, Möller A, Blomstrand C. Consequences of mild stroke in persons ,75 years: A 1-year follow-up. Cerebrovasc Dis 2003;16:383-388.
28. Hartman-Maeir A, Soroker N, Ring H, et al. Activities, participation and satisfaction one-year post-stroke. Disabil Rehabil 2007;29:559-566.
29. Vestling M, Tufvesson B, Iwarsson S. Indicators for return to work after stroke and the importance of work for subjective well-being and life satisfaction. J Rehabil Med 2003;35:127-131.
30. Fugl-Meyer AR, Eklund M, Fugl-Meyer KS. Vocational rehabilitation in northern Sweden III. Scand J Rehabil Med 1991;23:83-87.
31. Bränholm IB, Eklund M, Fugl-Meyer KS, et al. On work and life satisfaction. J Rehabil Sci 1991;4:29-34.

Based on:

Predictors of long-term health-related quality of life in patients with aneurysmal subarachnoid haemorrhage

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Predictors of long-term health-related quality of life in patients with aneurysmal subarachnoid haemorrhage

ABSTRACT

Objective: To determine the predictive value of physical and psychological factors assessed three months after aneurysmal subarachnoid haemorrhage (SAH) for health-related quality of life (HRQoL) one year after the SAH.

Design: Prospective cohort study.

Subjects: Patients with SAH (n=113) who visited our SAH-outpatient clinic three months after SAH and who were living independently in the community one year after SAH.

Methods: HRQoL was evaluated using the Stroke Specific Quality of Life scale (SS-QoL). We used Spearman correlations, Somers'd, and linear regression analyses. Independent variables were demographic and SAH characteristics, cognitive and emotional complaints, depressive symptoms, anxiety, cognitive functioning, and passive coping style.

Results: In the regression analysis, female gender (β value -0.17), cognitive complaints (-0.31), cognitive functioning (0.40) and passive coping style (-0.23) were independent predictors, and together explained 45.9 % of the variance of the SS-QoL total score.

Conclusion: Female gender, cognitive complaints, cognitive functioning and passive coping style assessed at 3 months after SAH are important predictors of HRQoL 1 year after SAH. Early interventions to improve cognitive and emotional functioning should be evaluated for their ability to improve long-term HRQoL after SAH.

INTRODUCTION

Subarachnoid haemorrhage (SAH) from a ruptured intracranial aneurysm accounts for approximately 5% of all strokes, occurs at relatively young age, and still carries a poor prognosis for survival.[14,21] Around 65% of the SAH patients survive[20] and of those who recover to functional independence many experience residual physical deficits, cognitive complaints and deficits, decreased long-term health-related quality of life (HRQoL) and working capacity.[2,18-20,26,27]

Health-related quality of life (HRQoL) is seen as a subset of the overall concept of quality of life, and as a multidimensional construct including those parts of quality of life that directly relate to an individual's health, in which at least physical, psychological and social dimensions are represented.[24] If it would be possible to identify early after discharge those patients who are at risk for reduced HRQoL in the long-term, interventions could be targeted at these patients to prevent or reduce negative consequences of SAH for long-term HRQoL.

Previous longitudinal studies revealed several predictors for poor long-term HRQoL: female sex[10,13]; clinical condition on admission[10,13,22]; high cortisol levels[11]; and physical disability at discharge.[8,10,11,13] A recent meta-analysis showed that, of these traditional predictors, only physical disability was a consistent predictor of HRQoL, and that 60% of the variance of physical HRQoL and 90% of the variance of psychosocial HRQoL was left unexplained.[15] Inclusion of psychological factors might therefore contribute to better predictions of HRQoL after SAH. Only few longitudinal studies have taken psychological predictors of long-term HRQoL into account. One recent longitudinal study found depression, assessed at discharge, as one of the predictors of HRQoL after SAH.[13] Another longitudinal study reported post traumatic stress, assessed after 3 months, as the best predictor of HRQoL in SAH.[16] In a cross-sectional design, 48%-64% of the variance of various HRQoL domains could be explained by adding psychological symptoms (fatigue, mood, cognitive complaints) and personality characteristics (neuroticism, passive coping) to the traditional predictors.[26] However, longitudinal studies are needed to show that such factors are predictive of long-term HRQoL of persons with SAH. With a better understanding of the determinants of HRQoL after aneurysmal SAH, interventions could be targeted at these patients to prevent or reduce negative consequences of SAH for long-term HRQoL.

The objective of this study is to determine whether physical factors (acute SAH characteristics, disability, discharge destination), cognitive functioning, emotional functioning (depressive symptoms, anxiety), cognitive and emotional complaints, and passive coping, assessed three months after SAH are predictors of HRQoL one year after SAH.

METHODS

SAH Patients and procedure

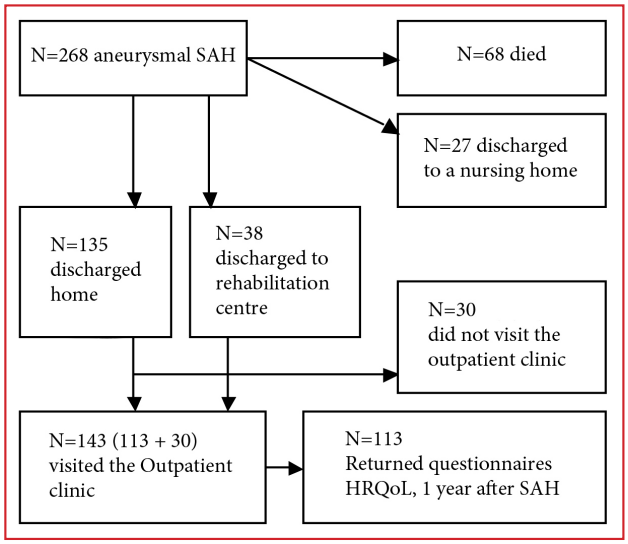
Patients were included who visited our SAH-outpatient clinic at the University Medical Centre Utrecht, which is a large urban specialized tertiary care centre with a catchment area of 2 million people, for a regular follow-up visit three months after SAH between October 2006 and September 2008, if they had had an SAH from a ruptured

aneurysm, and if this aneurysm had been treated by means of clipping or coiling. Preceding the 3 months SAH-outpatient clinic visit, all patients received by mail a questionnaire including standardized self-report measures of anxiety, depression and passive coping, and were asked to bring the completed questionnaire with their visit to the clinic. At our clinic, all patients were administered a brief neuropsychological screening by a neuropsychologist and a specialized SAH nurse administered the Checklist for Cognitive and Emotional consequences following stroke (CLCE-24) as part of an oral interview. All this information was collected to be used by the rehabilitation physician during this follow-up visit.

One year after SAH, a postal questionnaire about quality of life was sent to all patients who had visited the SAH-outpatient clinic. Patients were only excluded if they resided in a nursing home. The study was approved by the Medical Ethics Committee of the UMCU and all patients gave informed consent.

A total of 268 patients with SAH were admitted to our Department of Neurology and Neurosurgery during the study period of 24 months. Of the 173 patients discharged at home or to a rehabilitation centre, 143 visited the outpatient clinic 3 months after the SAH, of whom 113 returned the questionnaire on HRQoL (response rate 79%) one year after SAH (figure 1).

Figure 1. Flow diagram



SAH, subarachnoid haemorhage; HRQoL, Health Related Quality of Life.

These 113 patients did not differ substantially from the 60 patients who did not visit the outpatient clinic (n=30), or who did not return the questionnaire (n=30). On formal testing, there were no significant differences in terms of age (p=0.392), sex (0.292), education (0.292), clinical condition on admission (0.406), complications (0.112), location of aneurysm (0.491) or GOS-score at 3 months (0.603).

Of the 113 SAH patients included in this study, 83% was female, 64% was treated by coiling, 47% had one of more complications (rebleeding, delayed cerebral ischemia, hydrocephalus, or systemic complications) during the clinical course (table 1).

Table 1. Characteristics of SAH patients (N=113)

		n	%
Demographic characteristics			
Women		94	83
Mean age in years (SD)		53.6 (12.2)	
High education level		19	17
Living with partner		71	63
SAH characteristics			
Discharged at home		92	81
PAASH			
	I, GCS 15	71	62.8
	II, GCS 11-14	32	28.3
	III, GCS 8-10	3	2.7
	IV, GCS 4-7	3	2.7
	V, GCS 3	3	2.7
	Missing	1	0.9
Aneurysm location			
	Anterior cerebral and anterior communicating	51	45
	Middle cerebral	23	21
	Internal carotid	25	22
	Posterior circulation	14	12
Treatment received			
	Coiling	72	64
	Clipping	41	36
Complications		53	47
	Rebleeding	6	5
	Secondary ischemia	26	23
	Hydrocephalus	18	16
	Hydrocephalus and ischemia	3	3

SAH: subarachnoid haemorrhage; PAASH: Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage; GCS: Glasgow Coma Scale.

Outcome measurement

HRQoL was evaluated with the Stroke Specific Quality of Life scale version 2 (SS-QoL).[4,28] The SS-QoL is a disease specific HRQoL measure and contains 12 domains with altogether 49 items. The domains are: self-care, mobility, upper-extremity function, language, vision, work, thinking, family roles, social roles, personality, mood and energy. Items are averaged to obtain domain scores and a total SS-QoL score. The possible range of all summary scores is from 1 (poor HRQoL) up to 5 (good HRQoL). The SS-QoL was earlier translated into Dutch using a forward-backward procedure and validated in patients with SAH.[4,17] In an earlier study, we showed the 12 domain scores can be merged in two subtotal scores, the first six domains in a physical subtotal score and the last six domains in a psychosocial subtotal score.[4]

Possible Determinants

Data on demographics, the clinical condition (assessed by means of the Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage (PAASH) scale)[7], site of the

ruptured aneurysm, method of aneurysm occlusion and complications during the clinical course were obtained from the prospectively collected database of the Department of neurology and neurosurgery of the UMC Utrecht. Based on the Glasgow Coma Scale (GCS) on admission, patients were divided into the 5 categories of the PAASH: I) GCS 15; II) GCS 11 to 14; III) GCS 8 to 10; IV) GCS 4 to 7; V) GCS 3. All other data were assessed at 3 months after SAH. Disability was assessed with the Glasgow Outcome Scale (GOS).[9]

We measured depressive symptoms with the Beck Depression Inventory-II-NL, a 21-item screening instrument for depression.[3] The total score ranges between 0 and 63. A high score indicates severity of depressive symptoms. A score of 10 or higher was considered to be suggestive for possible depression, conform Beck's guidelines.[1,3] We measured anxiety with the state part of the State-Trait Anxiety Inventory (STAI-DY-1)[23], consisting of 20 items with a sum score between 20 and 80. A higher sum score implicates a higher level of anxiety, with different cut-off points based on age (up to 40 versus above 40), gender and educational level (high versus low).[23] Passive coping strategy was measured using the passive coping subscale (7 items) from the Utrecht Coping List (UCL-P).[5] Higher scores indicate more use of passive coping styles. The Checklist for Cognitive and Emotional consequences following stroke (CLCE-24) consists of 13 cognitive items (for instance problems with 'doing two things at once' or 'attending to things') and 9 emotional items (for instance being 'depressed' or 'faster or more often tired') and 2 open-ended questions which allow to add other problems, but which are not included in the scores.[6] The interviewer scores a '0' for absence and a '1' for presence of complaints; the sum score indicates the number of experienced complaints.

The brief neuropsychological screening addressed the following cognitive domains; *Memory* included verbal working memory assessed by the Backward Digit Span of the Wechsler Adult Intelligence Scale III (WAIS-III) in which the patient is presented with a sequence of digits (4, 7, 2, etc.) and then has to repeat these in reversed order, and Category Fluency (semantic memory) in which patients have to say as many as possible animal names within 2 minutes.[12] The Rey Auditory Verbal Learning Task (RAVLT)-Dutch version was used to measure verbal learning.[12] This test comprises a list of 15 unrelated words, presented to the patient at 5 consecutive trials. Recall is tested immediately after each trial and the total number of correctly remembered words in all 5 trials is taken as a score for immediate recall. After a delay of 20 minutes the patient is asked to recall again as many words as possible (delayed recall), followed by a recognition test in which the 15 words have to be recognized between 15 distractors. Non-verbal incidental memory, was evaluated using the delayed Rey-Osterrieth Complex Figure Test (CFT).[12] For this test patients were asked to reproduce the CFT from memory without having been asked to memorize the figure. *Executive functioning* was measured with the Brixton spatial Anticipation Test for strategic thinking. In this test patients were presented with a 56-page stimulus booklet. Each page contains 2 rows of 5 circles, one of which is blue. The tests measures the patient's ability to detect rules in changes of the position of the blue circle form one page to the next, expressed in a 1-10 score. Also, executive functioning was tested with the phonological fluency for concept generation test[12], a test in which patients have to say as many words as possible in one minute that begin with the letters "N" and "A". *Attention* was measured by Forward Digit Span of the WAIS III, in which a sequence of digits is presented (4, 7, 2, etc.) and then the patient has to repeat them in forward order, and the Stroop Color Word test.[12] This Stroop test consists of a series of sheets with color names printed in incongruent colors (for example, the word "blue" is printed in red). In the first trial patients were asked to read all

the words as quickly and accurately as possible. In the second trial patients are asked to name the color of the boxes. In the third trial, patients have to name the color of each word, ignoring the word name itself. To obtain an indication of *visuospatial functioning*, the copy score of the Rey-CFT was used.[12] In this test patients are asked to copy a figure consisting of a design with lines and geometric figures.

A control group was assembled as a reference sample for the neuropsychological examination, consisting of 62 persons (mean age of 57.8 years (SD 15.6); 58% women; 27.4% high education level) living in the community.[17] The controls were either spouses or family of stroke patients. Control subjects were less often women than patients, but were highly comparable with respect to age and level of education.

Statistical analysis

Descriptive statistics were used to describe the SAH population and the HRQoL. For level of education we used the Dutch classification ranging: from 1: did not finish primary school to 7: university and dichotomized this as low (0-4) and high education (5-7: finished high school, college or university).[25] Furthermore, PAASH was dichotomized as good (PAASH I) and reduced (PAASH>I), aneurysm location as anterior and posterior, treatment as clipping and coiling, and complications as absence or presence of complications. The GOS was dichotomized as disability (GOS <V) and no disability (GOS V) and the discharge destination as to a rehabilitation centre and at home. Chi-square and t-tests were used to look for differences between in- and excluded patients. For the neuropsychological data we transformed crude test scores of patients on individual tasks into z-scores based on scores of a matched control group.[17,18] Subsequently, we averaged z-scores of tests belonging to the same cognitive domain and computed a total cognition score as the average of the four cognitive domain scores. Based on the z-scores, patients were classified as "normal cognition" (z-score > -1.5), "mildly impaired cognition" (z-score between -2 and -1.5) or "severely impaired cognition" (z-score < -2).[12] Bivariate correlations between all possible predictor variables and the SS-QoL scores (SS-QoL total score, psychosocial and physical subtotal score) were tested using Somers'd for nominal, and Spearman correlations for ordinal determinants. For all analyses, continuous scores were used if available. Variables that were significantly correlated with the SS-QoL scores using an alpha level of 0.20 were entered as independent variables in a backward multiple regression analysis. This liberal criterion was used to find a balance between maximizing power (ratio of number of participants and number of variables in the analyses), and minimizing the risk to miss relevant predictor variables. Collinearity (correlation coefficients > 0.7) between BDI, STAI and emotional complaints prohibited the use of all three variables in the same regression analysis. We choose to use the BDI because this variable showed the highest correlation coefficient with the SS-QoL scores. The correlations between "cognitive and emotional complaints" and "cognitive functions" were small. Two different backward multiple regression analyses were performed to examine correlations between predictors and each of three different SS-QoL scores (total, psychosocial and physical score). First, we looked whether general cognitive functioning (total cognition score) was of influence on the amount of variance of SS-QoL scores. Subsequently, we studied the influence of the domain specific cognitive functioning (four separate cognitive domains) to assess which of the domains was of some importance. The SS-QoL total score and the SS-QoL psychosocial score were normally distributed, whereas the SS-QoL physical score was not. We also performed the regression analysis with a log-transformed SS-QoL physical score,

but this did not change the results so that we only present the results with the raw data. We considered $p<0.05$ as statistically significant.

RESULTS

Table 2. Characteristics of SAH patients at initial assessment (N=113)

		n	mean (SD)	%
Characteristics 3 months post-SAH				
Time after SAH, in weeks (SD)			11.5 (4.1)	
GOS				
	III dependent on others	5		4
	IV disability, but independent	36		32
	V good recovery	72		64
STAI-DY-1	mean	109	0.54 (0.5)	
	anxious	59		54
	non-anxious	50		46
BDI-II-NL	mean	109	9 (7)	
	no depressive symptoms (score <10)	64		59
	minor-moderate depression (score 10-18)	35		32
	moderate-severe depression (score 19->30)	10		9
CLCE-24	mean number of cognitive complaints	107	3.2 (2.4)	
	≥ 1 cognitive complaint	89		83
	mean number of emotional complaints	111	3.0 (1.9)	
	> 1 emotional complaint	107		96
UCL-p	Mean	108	10.8 (2.9)	
	passive coping style	38		35.2
Memory§		110	-0.41 (0.7)	
	no impairment	104		94.5
	impairment §§	6		5.5
Attention§		109	-0.08 (0.7)	
	no impairment	104		95.4
	impairment §§	5		4.8
Executive functioning§		109	-0.40 (0.7)	
	no impairment	102		93.6
	impairment §§	7		6.4
Visuoconstruction§		104	-0.62 (1.2)	
	no impairment	84		80.8
	impairment §§	20		19.2
Total cognitive functioning		110	-0.38 (0.62)	

GOS: Glasgow Outcome Scale; STAI-DY-1: State Trait Anxiety Inventory; BDI-II-NL: Beck Depression Inventory; CLCE-24: Checklist for Cognitive and Emotional consequences following stroke;
§ z-score; §§ z-score ≤ -1.5.

SAH population

Of the 113 SAH patients included in this study, most patients (64%) had a good recovery based on the GOS. However, 54% of the patients was anxious, 41% had depressive symptoms, and 83% had at least 1 cognitive and 96% at least one emotional complaint (table 2).

Qualify of life

The mean SS-QoL total score was 4.2 (SD 0.7), indicative for a relative satisfactory HRQoL (table 3). The physical subtotal SS-QoL score (mean 4.5; SD 0.5) was higher than the psychosocial subtotal score (mean 3.8; SD 1.0), indicating that patients experienced lower psychosocial than physical HRQoL. The HRQoL score was lowest for the domain thinking (3.3; SD 1,3) and highest for the domain self- care (4.7; SD 0.4).

Table 3. HRQoL measured by SS-QoL in persons with SAH (N=113)

Domain	Score (minimum – maximum)	Mean score (SD)
Physical domains		4.5 (0.5)
Self-care	3.0 – 5.0	4.7 (0.4)
Mobility	1.5 – 5.0	4.5 (0.7)
Upper extremity	2.8 – 5.0	4.6 (0.6)
Language	2.6 – 5.0	4.6 (0.6)
Vision	2.7 – 5.0	4.6 (0.6)
Work	2.0 – 5.0	4.2 (0.8)
Psychosocial domains		3.8 (1.0)
Thinking	1.0 – 5.0	3.3 (1.3)
Family roles	1.7 – 5.0	4.1 (1.0)
Social roles	1.4 – 5.0	3.8 (1.2)
Personality	1.0 – 5.0	3.8 (1.2)
Mood	1.6 – 5.0	4.1 (1.0)
Energy	1.0 – 5.0	3.5 (1.3)
Total score	2.3 – 5.0	4.2 (0.7)

HRQoL, Health Related Quality of Life; SS-QoL, Stroke Specific Quality of Life; SAH, subarachnoid haemorrhage.

Relationships with HRQoL

Table 4 shows bivariate relationships with the different SS-QoL scores. Female gender (Somers'd = 0.12), GOS (d= -0.31) and discharge destination (d= 0.18), anxiety (Spearman r= -0.39) and depressive symtoms (r= -0.42), cognitive (r= -0.53) and emotional complaints (r= -0.39), cognitive domains (memory r= 0.42, attention 0.32, executive functioning 0.34, visuoconstruction 0.37, cognition total score 0.51) and passive coping (r= -0.38) were related to the SS-QoL total score.

Also, female gender (d= 0.14), GOS (d= -0.26), anxiety (Spearman r= -0.44) and depressive symtoms (r= -0.48), cognitive (r= -0.53) and emotional complaints (r= -0.45), cognitive domains (memory r= 0.35, attention 0.24, executive functioning 0.26, visuoconstruction 0.32, cognition total score 0.41) and passive coping (r= -0.44) were related to the SS-QoL psychosocial score.

Furthermore, GOS (d= -0.36) and discharge destination (d= 0.26)), anxiety

(Spearman r= -0.22) and depressive symtoms (r= -0.24), cognitive (r= -0.46) and emotional complaints (r= -0.22), cognitive domains (memory r= 0.45, attention 0.40, executive functioning 0.37, visuoconstruction 0.39, cognition total score 0.58) and passive coping (r= -0.20) were related to the SS-QoL physical score.

Table 4. Bivariate analyses of determinants and SS-QoL-total score, physical and psychosocial score, one year after SAH.

Determinant	n	SS-QoL total	SS-QoL psychosocial	SS-QoL physical
Gender (women)	113	-0.12*	-0.14*	-0.06
Age	113	0.06	0.08	-0.03
Education	113	0.10†	0.09	0.09†
PAASH‡	112	0.03	0.05	-0.02
Aneurysm location (posterior)	113	-0.07	-0.08†	-0.02
Complications‡ (presence)	113	-0.07	-0.05	-0.08
Treatment (coiling)	113	-0.06	-0.08	-0.02
GOS 3 months‡	113	-0.31*	-0.26*	-0.36*
discharge destination (at home)	113	0.18*	0.11†	0.26*
STAI-DY-I#	109	-0.39*	-0.44*	-0.22*
BDI-II-NL#	109	-0.42*	-0.48*	-0.24*
CLCE-24 cognition#	107	-0.53*	-0.53*	-0.46*
CLCE-24 emotion#	111	-0.39*	-0.45*	-0.22*
Memory§	110	0.42*	0.35*	0.45*
Attention§	109	0.32*	0.24*	0.40*
Executive functioning§	109	0.34*	0.26*	0.37*
Visuoconstruction§	104	0.37*	0.32*	0.39*
Cognition total score§	119	0.51*	0.41*	0.58*
UCL-P#	108	-0.38*	-0.44*	-0.20*

SS-QoL, Stroke Specific Quality of Life; SAH, subarachnoid haemorrhage; PAASH, Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage; GOS, Glasgow Outcome Scale; STAI-DY-1, State Trait Anxiety Inventory; BDI-II-NL, Beck Depression Inventory; CLCE-24, Checklist for cognitive and emotional consequences following stroke; UCL-P, Utrecht Coping List.
Correlations based on Somers'd for nominal, and Spearman correlations for ordinal determinants;
*p<0.05, † p<0.20; ‡ higher value means worse condition; # continuous variable, higher value means worse condition; § z-score.

In the regression analysis, using the four cognition domain scores, female gender (β= 0.17), cognitive complaints (-0.34), cognitive domains executive (0.23) and visuoconstructive (0.22) functioning and passive coping style (-0.23) together explained 46.1% of the variance (adjusted R^2) in the SS-QoL total score. Female gender (0.21), cognitive complaints (-0.35), cognitive domain executive functioning (0.27) and passive coping style (-0.33) explained 42.7% of the variance in the SS-QoL psychosocial score. In the SS-QoL physical score 45.1% of the variance is explained by discharge destination (0.20), cognitive complaints (-0.19) and cognitive domains attention (0.21) and visuoconstriction (0.45). (table 5).

In the regression analyses with the cognition total scores, female gender (0.16), cognitive complaints (-0.31), cognition total score (0.40) and passive coping (-0.23) together explained 45.9% of the variance in the SS-QoL total score. Also, female gender

(0.16), cognitive complaints (-0.33), cognition total score (0.27) and passive coping (-0.31) together explained 41.9% of the variance in the SS-QoL psychosocial score. In the SS-QoL physical score 44.8% of the variance is explained by discharge destination (0.25), cognitive complaints (-0.16) and cognition total score (0.51).

DISCUSSION

Cognitive complaints, cognitive functioning and passive coping measured at 3 months after SAH have shown to be the most relevant independent predictors of HRQoL 1 year after SAH; these determinants explained almost half of the variance in SS-QoL scores.

This study added a longitudinal perspective to our previous cross-sectional study in which we found mood, fatigue and cognitive complaints to be associated with HRQoL at three years after SAH.[26] Similar to our earlier cross-sectional study, lower scores were reported on the psychosocial SS-QoL domains than on the physical SS-QoL domains.[26] In the current study SS-QoL scores were slightly higher (0.1-0.5 points on a 1-5 scale) than those reported in the previous study, which is probably explained by the higher proportion of patients with good outcome in our study (64%) than in the previous study (47%).

In our study, symptoms of anxiety and depression were highly prevalent, which is in line with two recent reviews.[2,20] The most frequently impaired cognitive domain was executive functioning, which is also found previously[2], although in our study the number of patients with impaired cognitive domains was rather low, probably due to the exclusion of patients residing in a nursing home. However, many patients had cognitive and emotional complaints.

In a recent meta-analysis on predictors of HRQoL after SAH, about 40% of the Physical HRQoL and only 10% of the variance of the Mental HRQoL could be explained, both predominantly by physical disability.[15] This meta-analysis however studied only "traditional" predictors: demographic and SAH characteristics, and physical and cognitive impairment[15], and did not take psychological aspects into account. Moreover, in only 3 out of the 10 included studies cognitive impairment were measured. In our study, we included some psychosocial aspects (anxiety and depression, cognitive and emotional complaints, and passive coping style) and found discharge destination (probably related to physical disability), cognitive complaints and cognitive functioning (especially domains attention and visuoconstruction) to explain almost half of the variance in Physical HRQoL. For psychosocial HRQoL, almost half of the variance could be explained by female gender, cognitive complaints, cognitive functioning (especially executive functioning) and passive coping. So, by introducing these psychosocial aspects, we were able to predict HRQoL of patients with SAH much better than can be done using only traditional predictors. Still, further research is needed to increase our understanding of HRQoL after aneurysmal SAH, because this will be helpful to tailor appropriate rehabilitation programs and thereby, enhance their effectiveness. More information is needed into issues of social participation and psychological determinants of HRQoL.

Although this was a large scale prospective study on HRQoL in patients with SAH, some limitations should be mentioned. The neuropsychological data set did not cover all cognitive domains, particularly a test on mental speed was not included. Furthermore, this neuropsychological data set was not completed by all patients mainly because some patients

Table 5. Multivariate backward analyses of determinants and SS-QoL-total score, physical and psychosocial score, one year after SAH.

	SS-QoL total β-value (p-value)		**SS-QoL Psychosocial** β-value (p-value)		**SS-QoL Physical** β-value (p-value)	
Determinant	cognitive domains¦	cognition total score##	cognitive domains¦	cognition total score##	cognitive domains¦	cognition total score##
gender (women)	-0.17 (0.04)*	-0.16 (0.03)*	-0.21 (0.01)*	-0.16 (0.04)*	NE	NE
education level	-	-	NE	NE	-	-
aneurysm location (posterior)	NE	NE	-	-	NE	NE
GOS 3 months ‡	-	-	-	-	-	-
discharge destination (at home)	-	-	-	-	0.20 (0.02)*	0.25 (0.002)*
BDI-II-NL##	-	-	-	-	-	-
CLCE-24 cognition##	-0.34 (0.00)*	-0.31 (0.00)*	-0.35 (0.00)*	-0.33 (0.00)*	-0.19 (0.02)*	-0.16 (0.049)*
Memory§	-	NE	-	NE	-	NE
Attention§	-	NE	-	NE	0.21 (0.01)*	NE
Executive functioning§	0.23 (0.01)*	NE	0.27(0.001)*	NE	-	NE
Visuoconstruction§	0.22 (0.03)*	NE	-	NE	0.45 (0.00)*	NE
Cognition total score§	NE	0.40 (0.00)*	NE	0.27 (0.001)*	NE	0.51 (0.00)*
UCL-P##	-0.23 (0.01)*	-0.23(0.004)*	-0.33 (0.00)*	-0.31 (0.00)*	-	-
R^2 / adjusted R^2	49.0/ 46.1	48.1/ 45.9	45.2/ 42.7	44.3/ 41.9	47.5/45.1	46.5/ 44.8
F, degrees of freedom, p-value	16.9/5/ 0.00*	22.0/4/0.00*	18.3/4/0.00*	18.9/4/0.00*	20.1/4/0.00*	27.8/3/0.00*

SS-QoL, Stroke Specific Quality of Life; SAH, subarachnoid haemorrhage; GOS, Glasgow Outcome Scale; STAI-DY-1, State Trait Anxiety Inventory; BDI-II-NL, Beck Depression Inventory; CLCE-24, Checklist for cognitive and emotional consequences following stroke; UCL-P, Utrecht Coping List; NE, not entered.
*p<0.05; ‡ higher value means worse condition; # continuous variable, higher value means worse condition;§ z-score; ¦ n= 93, ## n=99.

had problems finding words or visual problems. This might have lead to an underestimation of the influence of the predictive value of cognitive impairments on long-term HRQoL. Additionally, this study did not include patients with SAH who resided in a nursing home three months after discharge, because these patients usually do not visit our outpatient clinic. It is likely that these patients have showed more physical and cognitive deficits. Thus, the results of our study only apply to patients who live at home or undergo rehabilitation three months after discharge. This is however by far the largest group of patients; less than 15% of patients had been discharged to a nursing home during our study period. Finally, we could explain only half of the variance of HRQoL. Considering the time span, we think this amount of explained variance is good.

In patients who recover to living at home after SAH, structured screening of cognitive and emotional functioning early after discharge, for example at an outpatient clinic, is important to detect cognitive and emotional complaints, emotional problems, cognitive impairments and passive coping. Patients with few cognitive complaints or impairments and an active coping, can be informed about their good expectance in HRQoL and stimulated to resume their activities. In patients with these risk factors present, it can be very important to tailor the rehabilitation program to their needs. It is important to screen all patients, because reduced HRQoL after SAH is not limited to those patients who were discharged to a rehabilitation centre. Whether focused interventions from rehabilitation or mental health professionals result in improved quality of life for patients in the first year after their SAH should be investigated in future studies.

REFERENCES

1. Aben I, Verhey F, Lousberg R, Lodder J, Honig A. Validity of Beck Depression Inventory, Hospital Anxiety and Depression Scale, SCL-90, and Hamilton Depression Rating Scale as screening instruments for depression in stroke patients. Psychosomatics 2003;43:386-393.
2. Al-Khindi T, MacDonald RL, Schweizer TA. Cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. Stroke 2010;41: e519-e536.
3. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-571.
4. Boosman H, Passier PECA, Visser-Meily JMA, Rinkel GJE, Post MWM. Validation of the Stroke Specific Quality of Life Scale (SS-QoL) in patients with aneurysmal subarachnoid haemorrhage. J Neurol Neurosurg Psychiatry 2010;81(5):485-9.
5. Eriksen HR, Olff M, Ursin H. The CODE: a revised battery for coping and defense and its relation to subjective health. Scan J Psych 1997;38:175-182.
6. Heugten van C, Rasquin S, Winkens I, Beusmans G, Verhey F. Checklist for cognitive and emotional consequences following stroke (CLCE-24): development, usability and quality of the self-report version. Clin Neurol and Neurosurg 2007;109:257-262.
7. Heuven AW van, Dorhout Mees SM, Algra A, Rinkel GJE. Validation of a prognostic subarachnoid hemorrhage grading scale derived directly from the Glasgow Coma Scale. Stroke 2008;39:1347-1348.
8. Hop JW, Rinkel GJE, Algra A, Gijn van J. Quality of life in patients and partners after aneurysmal subarachnoid hemorrhage. Stroke 1998;29: 798-804.
9. Jennett B, Bond M. Assessment of outcome after severe .brain damage. Lancet 1975;1:480-484.
10. Katati MJ, Santiago-Ramajo S, Pérez-García M, Meersmans-Sánchez Jofré M, Vilar-Lopez R, Coín-Mejias MA, Caracuel-Romero A, Arjona-Moron V. Description of quality of life and its predictors in patients with aneurysmal subarachnoid hemorrhage. Cerebrovasc Dis 2007;24:66-73.
11. Kreitschmann-Andermahr I, Poll E, Hütter BO, Reineke A, Kristes S, Gilsbach JM, Saller B. Quality of life and psychiatric sequelae following aneurysmal subarachnoid haemorrhage: does neuroendocrine dysfunction play a role? Clin Endocrinology 2007;66: 833-837.
12. Lezak MD, Howieson DB, Loring DW. Neuropsychological assessment, (4th edition). New York; Oxford University Press, 2004.
13. Meyer B, Ringel F, Winter Y, Spottke A, Gharevi N, Dams J, Balzer-Geldsetzer M, Mueller IK, Klockgether T, Schramm J, Urbach H, Dodel R. Health-Related Quality of Life in patients with subarachnoid haemorrhage. Cerebrovasc Dis 2010;30:423-431.
14. Nieuwkamp DJ, Setz L, Algra A, Linn FHH, Rooij de NK, Rinkel GJE. Changes in case-fatality of aneurysmal subarachnoid haemorrhage over time, according to age, sex and region: a meta-analysis. Lancet Neurology 2009;8:635-42.
15. Noble AJ, Schenk T. Which variables help explain the poor health-related quality of life after subarachnoid hemorrhage? A meta-analysis. Neurosurgery 2010;66:772-783.
16. Noble AJ, Baisch S, Mendelow AD, Allen L, Kane P, Schenk T. Posttraumatic stress disorder explains reduced quality of life in subarachnoid hemorrhage patients in both the short and long term. Neurosurgery 2008;63:1095-1105.
17. Nys GMS, van Zandvoort MJE, van der Worp HB, de Haan EHF, de Kort PLM, Jansen BPW, Kapelle LJ. Early cognitive impairment predicts long-term depressive symptoms and quality of life after stroke. J Neurol Sci 2006;247:149-156.
18. Passier PECA, Visser-Meily JMA, Zandvoort van MJE, Post MWM, Rinkel GJE, van Heugten C. Prevalence and determinants of cognitive complaints after aneurysmal Subarachnoid Haemorrhage. Cerebrovasc Dis 2010;29:557-563.

19. Passier PECA, Visser-Meily JMA, Rinkel GJE, Lindeman E, Post MWM. Life satisfaction and return to work after aneurysmal subarachnoid haemorrhage. J Stroke Cerebrovasc Dis 2011;20:324-329.
20. Rinkel GJE, Algra A. Long-term outcomes of patients with aneurysmal subarachnoid haemorrhage. Lancet Neurol 2011;10:349-356.
21. Rooij de NK, Linn FHH, Plas van der JA, Algra A, Rinkel GJE. Incidence of subarachnoid haemorrhage: a systematic review with emphasis on region, age, gender and time trends. J Neurol Neurosurg Psychiatry 2007;78:1365-1372.
22. Soehle M, Chatfield DA, Czosnyka M, Kirkpatrick PJ. Predictive value of initial clinical status, intracranial pressure and transcranial Doppler pulsatility after subarachnoid haemorrhage. Acta Neurochir 2007;149: 575-583.
23. Spielberger CD, Gorsuch RL, Lushene PR, Vagg PR, Jacobs AG. Manual for the Stat-Trait Anxiety Inventory (form Y). Consulting Psychologists Press, Inc.: Palo Alto, 1983.
24. Spilker B, Revicki DA. Taxonomy of quality of life. In: Spilker B ed. Quality of life and pharmacoeconomics in clinical trials, second edition. New York: Lippincott-Raven, 1996.
25. Verhage F. Intelligentie en leeftijd: Onderzoek bij Nederlanders van twaalf tot zevenenzeventig jaar [Intelligence and age: Study with Dutch people from age 12 to 77]. Assen: Van Gorcum, 1964.
26. Visser-Meily JMA, Rhebergen ML, Rinkel GJE, Zandvoort van MJ, Post MWM. Long-term health related quality of life after aneurysmal subarachnoid hemorrhage; relationship with psychological symptoms and personality characteristics. Stroke 2009;40:1526-9.
27. Wermer MJH, Kool H, Albrecht KW, Rinkel GJE. Subarachnoid hemorrhage treated with clipping: long-term effects on employment, relationships, personality, and mood. Neurosurgery 2007;60:91-98.
28. Williams LS, Weinberger M, Harris LE, Clark DO, Biller J. Development of a Stroke Specific Quality of Life Scale. Stroke 1999;30:1362-1369.

Based on:

Predicting fatigue 1 year after aneurysmal subarachnoid haemorrhage

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Predicting fatigue 1 year after aneurysmal subarachnoid haemorrhage

ABSTRACT

Background: Fatigue is an important contributor to quality of life in patients who survive aneurysmal subarachnoid haemorrhage (SAH), but the determinants of this fatigue are unclear.

Methods: We assessed the occurrence of fatigue 1 year after SAH and its relation to physical or cognitive impairment, passive coping, and emotional problems, measured 3 months after SAH. This was a prospective cohort study of 108 patients who visited our SAH outpatient clinic 3 months after SAH and who were living independently in the community 1 year after SAH. Fatigue was evaluated using the Fatigue Severity Scale (FSS). Analysis of variance was used to analyze the data.

Results: Fatigue (FSS>4) was present in 77 patients (71%). Mean FSS scores were 4.1 (SD 1.6) in the group of patients having 'neither physical nor cognitive impairment,' 5.2 (1.4) having 'either physical or cognitive impairment,' and 5.9 (0.9) having 'both physical and cognitive impairments.' Mean FSS scores were higher in patients scoring high on passive coping (85 vs. 58%; RR 1.46, 95% CI 1.13–1.87), anxiety (84 vs.55%; RR 1.53, 95% CI 1.17–2.02), or depression (85 vs.62%; RR 1.36, 95% CI 1.08–1.72) than in patients without these complaints. Relationships between these complaints and FSS scores were higher in patients having neither physical nor cognitive impairments than in patients having physical or cognitive impairments.

Conclusion: Fatigue is common after SAH and is related to physical and cognitive impairments. In patients with neither physical nor cognitive impairments, passive coping style and emotional problems are important predictors of fatigue.

INTRODUCTION

Many SAH patients recover to functional independence, but nevertheless experience fatigue[1,2], and this fatigue is related to reduced health-related quality of life.[3] The mechanisms underlying fatigue after SAH are unclear. Diffuse neuronal damage might contribute to post-SAH fatigue.[4] Furthermore, post-traumatic stress, personality changes, and memory deficits have been suggested to play a role in fatigue in patients with SAH.[4,5] Whether impaired physical functioning or emotional problems such as depression and anxiety contribute to post-SAH fatigue is unclear. Knowledge of the factors underlying post-SAH fatigue is important, because this may yield possibilities for treatment of fatigue.

We investigated the occurrence of fatigue in patients with SAH who were living at home 1 year after SAH, and assessed relationships among physical or cognitive impairments, passive coping, emotional problems (anxiety, depressive symptoms), or a combination of these factors with post-SAH fatigue.

METHODS

SAH patients and procedure

Patients who visited our SAH outpatient clinic for a regular follow-up visit 3 months after SAH between October 2006 and September 2008 were included if they had had an SAH from a ruptured aneurysm and if this aneurysm had been occluded by means of clipping or coiling. All patients were asked to complete a questionnaire before their visit to the clinic. At our clinic, all patients were administered a brief neuropsychological screening by a neuropsychologist. One year after SAH, a postal questionnaire about fatigue was sent to all patients who were living in the community. The study was approved by the Medical Ethics Committee of the UMCU, and all patients gave informed consent.

Outcome measurement

Fatigue 1 year after SAH was assessed using the fatigue severity scale (FSS).[6] This scale consists of nine statements about the impact of fatigue on daily life, each scored on a 7-point Likert scale, ranging from 1 (strongly disagree) to 7 (strongly agree). The total FSS score is the mean of the item scores. The FSS is a reliable scale distinguishing patients from controls.[6] Fatigue was scored as present if the FSS score was above 4.[6] A score above 4 indicates a moderate to high impact of fatigue on daily living.

Possible determinants

Data on demographics, the clinical condition assessed by means of the prognosis on admission of the Aneurysmal Subarachnoid Haemorrhage (PAASH) Scale[7], site of the ruptured aneurysm, method of aneurysm occlusion, and complications during the clinical course were obtained from the prospectively collected database of the Department of Neurology and Neurosurgery of the UMC Utrecht, The Netherlands.

All other data were assessed at 3 months after SAH. Physical disability was assessed with the Glasgow Outcome Scale (GOS).[8] Passive coping strategy was measured using the seven-item passive coping subscale from the Utrecht Coping List (UCL-P).[9] Higher scores indicate more use of passive coping styles. Using the median score as the cutoff value, passive coping strategy was dichotomized as 'passive coping' and 'no passive coping.' We

measured anxiety with the state part of the State-Trait Anxiety Inventory (STAI-DY-1).[10] A higher sum score indicates a higher level of anxiety, with different cutoff points based on age (above 40 vs. up to 40), gender, and educational level (high vs. low).[11] We measured depressive symptoms with the Beck Depression Inventory II-NL, an instrument for measuring symptoms suggestive of the presence of depression.[12,13] We accepted a score of 10 or higher as suggestive of possible depression.[13]

The brief neuropsychological screening addressed the following cognitive domains: memory included verbal working memory assessed by the Backward Digit Span of the Wechsler Adult Intelligence Scale III (WAIS-III) and category fluency (semantic memory) using animal naming.[14] The Rey Auditory Verbal Learning Task (RAVLT) was used to measure verbal learning, revealing scores for immediate and delayed recall and recognition.[14] Non-verbal recall was evaluated using the delayed Rey-Osterrieth Complex Figure Test (CFT).[14] Executive functioning was measured with the Brixton Spatial Anticipation Test for strategic thinking and with phonological fluency ("N" and "A") for concept generation.[14] Attention was measured by Forward Digit Span of the WAIS III and the Stroop Color Word test.[14] To obtain an indication of visuospatial functioning, the copy score of the Rey-CFT was used.[14] A control group of 62 persons (mean age of 57.8 years; 58% women) living in the community was studied to obtain reference data for the neuropsychological examination.[15]

Statistical analysis

Descriptive statistics were used to describe the SAH population and post-SAH fatigue. For level of education, we used the Dutch classification ranging from 1, did not finish primary school to 7, university, and dichotomized this as low (0–4) and high education (5–7: pre-university secondary education—university).[16] The GOS was dichotomized as physical disability (GOS V) and no physical disability (GOS V). For the neuropsychological data we transformed crude test scores of patients on individual tasks into z scores based on scores of a matched control group.[2,15] Subsequently, we averaged z scores of tests belonging to the same cognitive domain. Based on the z scores, for each domain patients were classified as "normal cognition" (z score>-1.5) or "impaired cognition" (z score $\leq$-1.5)[14], and a total cognition score was computed as the number of impaired cognitive domains. We computed a "level of impairment" variable with three levels: neither physical nor cognitive impairment, either physical disability or cognitive impairment, and both physical disability and cognitive impairment. The relative risk with corresponding 95% confidence interval (95% CI) was used to compare fatigue in patients with GOS<V to those with GOS V, and to compare those with passive coping, anxiety, or depressive symptoms to those without these characteristics. Bivariate relationships between FSS and the dichotomous independent variables were tested using independent t tests. Associations between FSS and the three levels of impairment were tested with analysis of variance (ANOVA) with Scheffe´ correction for pairwise comparisons. Three separate ANOVAs were performed to analyze relationships between combinations of level of impairment and coping style, anxiety, or depression with fatigue. Separate ANOVAs were performed because of strong intercorrelations among the three psychological variables. Both main effects and the interaction effect were tested for significance. We considered $p<0.05$ as statistically significant.

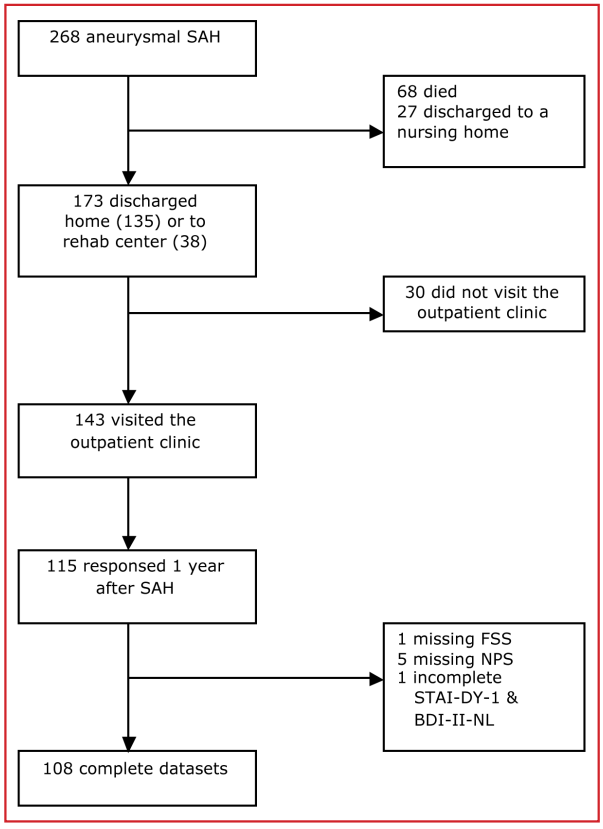
RESULTS

SAH population

Two hundred sixty-eight patients with SAH were admitted to our Department of Neurology and Neurosurgery. Of the 173 patients discharged at home or to a rehabilitation center, 143 visited the outpatient clinic 3 months after the SAH, of whom 115 returned the questionnaires (response rate 80%) 1 year after SAH. Seven of these 115 patients (6%) were excluded because of missing or incomplete data (figure 1).

The 108 patients who were included in this study did not differ essentially from the 65 patients who did not visit the outpatient clinic (n = 30), did not return the questionnaire (n = 28) or were excluded from the study (n = 7) in terms of age, sex, education, clinical condition on admission, complications, location of aneurysm or GOS score at 3 months. The characteristics of the 108 included patients are displayed in table 1.

Figure 1. Flow diagram



SAH: subarachnoid haemorrhage; GOS; FSS: Fatigue Severity Scale; NPS: neuropsychological screening; STAI-DY-1: State Trait Anxiety Inventory; BDI-II-NL: Beck Depression Inventory.

Table 1. Characteristics of SAH patients (N=108).

Demographic characteristics		*n*	*%*
Women		89	82.4
Mean age in years		53.4 (12.3)	
Education level	low/intermediate	91	83.5
	high	18	16.5
SAH characteristics			
PAASH			
	I, GCS 15	67	62.6
	II, GCS 11-14	31	29.0
	III, GCS 8-10	3	2.8
	IV, GCS 4-7	3	2.8
	V, GCS 3	3	2.8
	missing	1	
Aneurysm location			
	Anterior cerebral and anterior communicating	49	45.4
	Middle cerebral	20	18.5
	Internal carotid	25	23.1
	Posterior circulation	14	13.0
Treatment received			
	Coiling	70	64.8
	Surgery	38	35.2
Complications, yes		50	46.3
	Rebleeding	6	5.6
	Secondary ischemia	26	24.1
	Hydrocephalus	15	13.9
	Hydrocephalus and ischemia	3	2.8
Characteristics at 3 months post-SAH			
Mean time after SAH in weeks		11.3 (4.1)	
Glasgow Outcome Scale (GOS)			
	III dependent from others	5	4.6
	IV disability, but independent	35	32.4
	V good recovery	68	63.0
Cognitive impairment (z-score ≤-1.5)			
	no impaired cognitive domains	79	73.1
	1 impaired cognitive domain	21	19.4
	2 impaired cognitive domains	6	5.6
	3 impaired cognitive domains	2	1.9
STAI-DY-1	Anxious	57	52.8
BDI-II-NL	Mean (SD)	9.0 (6.9)	
	No depressive symptoms (score 0-9)	65	60.2
	Minor – moderate depression (score 10-18)	33	30.6
	Moderate -severe depression (score >30)	10	9.3

SAH: subarachnoid haemorrhage; PAASH: Prognosis on Admission of Aneurysmal Subarachnoid Haemorrhage; GCS: Glasgow Coma Scale; STAI-DY-1: State Trait Anxiety Inventory; BDI-II-NL: Beck Depression Inventory; UCL-p: Utrecht Coping List.

Fatigue in SAH

The mean FSS score was 4.8 (SD 1.6), and fatigue (FSS >4) was present in 77 patients (71%). Table 2 shows mean FSS scores for patients with different demographic and SAH characteristics. The frequency of fatigue (FSS >4) was higher among patients with GOS<V than with GOS V (93 vs. 57%; RR 1.61, 95% CI 1.29–2.02), with passive coping than without passive coping (85 vs. 58%; RR 1.46, 95% CI 1.13–1.87), with anxiety than without anxiety (84 vs. 55%; RR 1.53, 95% CI 1.17–2.02), and with depressive symptoms than without depressive symptoms (85 vs. 62%; RR 1.36, 95% CI 1.08–1.72).

Table 2. Bivariate analyses of determinants and FSS scores, one year after SAH.

Bivariate analyses		n	mean FSS (SD)	t-test	p-value
Age					
	< 52 (median)	50	4.9 (1.5)	-1.13	0.262
	≥ 52	58	4.6 (1.6)		
Sex					
	male	19	4.5 (1.2)	-0.58	0.562
	female	89	4.8 (1.7)		
Education level					
	high	18	4.2 (1.8)	1.56	0.121
	low	90	4.8 (1.5)		
Aneurysm location					
	anterior	94	4.7 (1.6)	-1.073	0.286
	posterior	14	5.2 (1.4)		
Treatment					
	surgery	38	4.6 (1.8)	-0.872	0.385
	coiling	70	4.8 (1.5)		
Complications					
	no complications	58	4.7 (1.6)	-0.485	0.629
	complications	50	4.8 (1.6)		
Physical impairment					
	no impairments (GOS V)	68	4.3 (1.6)	-4.15	0.000
	impairment (GOS <V)	40	5.5 (1.2)		
Cognitive impairment					
	no impairments	79	4.4 (1.6)	-3.33	0.001
	impairments	29	5.5 (1.3)		

SAH: subarachnoid haemorrhage; GOS: Glasgow Outcome Scale.

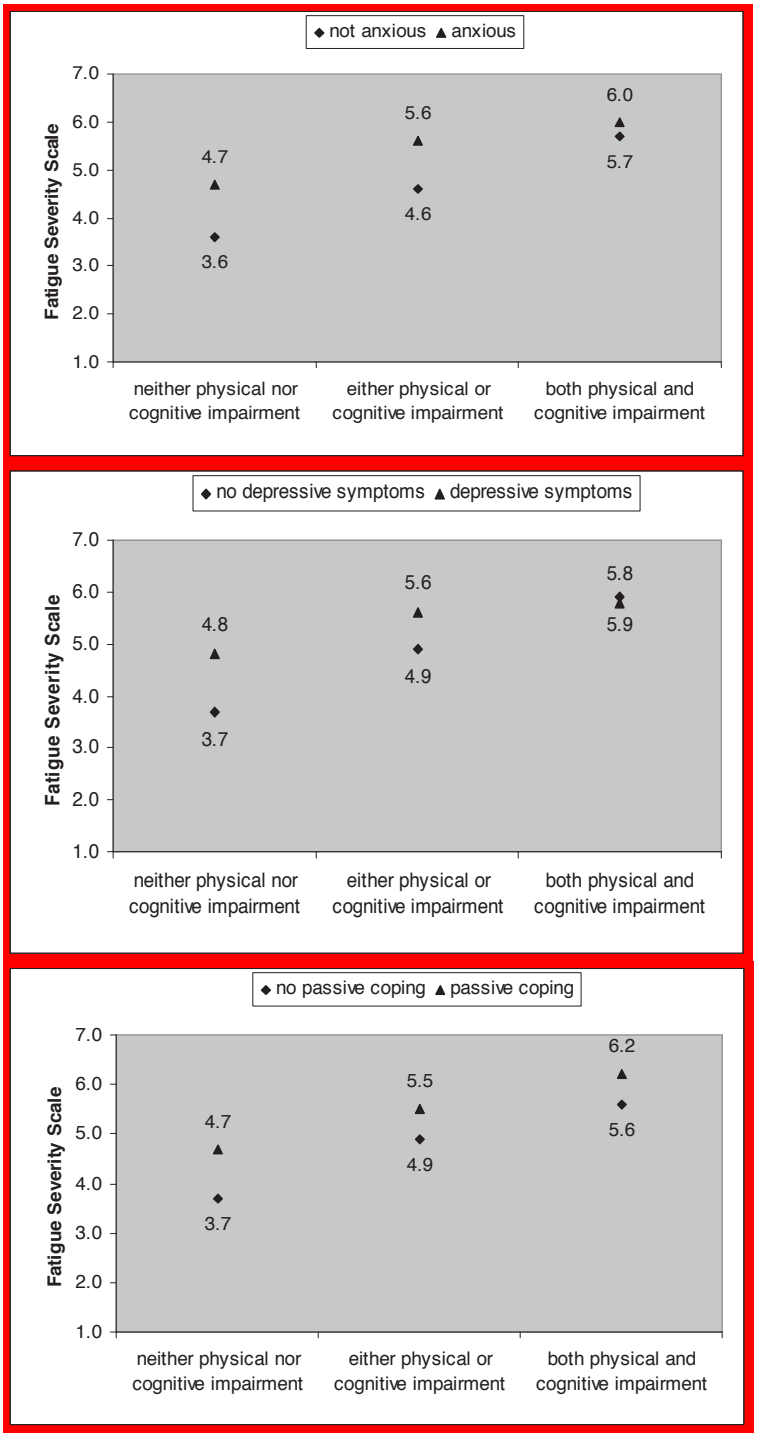
The mean FSS scores in the three levels of impairment are shown in table 3. Mean FSS scores differed among the groups of patients having neither physical nor cognitive impairment (4.1 SD 1.6), patients having either physical or cognitive impairment (5.2 SD 1.4), and patients having both physical and cognitive impairment (5.9 SD 0.9) ($F = 13.33$; $p<0.001$). Post-hoc comparisons with Scheffe´ correction showed that the "neither" group differed from both the "or" and the "both" groups, but that the "or" and the "both" groups did not significantly differ from each other. Table 3 shows mean FSS scores in relation to coping style and emotional problems (anxiety, depressive symptoms) in relation to the different levels of impairment. In the group of patients having 'neither physical nor cognitive impairment,' there was a significant difference among patients with passive coping, anxiety, or depressive symptoms and those without these characteristics.

Table 3. Bivariate analyses of determinants and FSS scores in different levels of impairment, one year after SAH.

	total group			neither physical nor cognitive impairments			either physical or cognitive impairments			both physical and cognitive impairments		
	n	mean FSS (SD)	t-test (p- value)	n	mean FSS (SD)	t-test (p- value)	n	mean FSS (SD)	t-test (p- value)	n	mean FSS (SD)	t-test (p- value)
	108	4.7 (1.6)		54	4.1 (1.6)		39	5.2 (1.4)		15	5.9 (0.9)	
UCL-p												
no passive coping	57	4.2 (1.6)	-3.58 (0.001)	34	3.7 (1.5)	-2.57 (0.013)	16	4.9 (1.5)	-1.21 (0.233)	7	5.6 (0.8)	-1.32 (0.210)
passive coping	51	5.3 (1.4)		20	4.7 (1.5)		23	5.4 (1.2)		8	6.2 (0.9)	
STAI-DY-1												
not anxious	51	4.1 (1.6)	-4.26 (0.000)	31	3.6 (1.5)	-2.84 (0.006)	14	4.6 (1.7)	-2.31 (0.027)	6	5.7 (0.7)	-0.63 (0.540)
anxious	57	5.3 (1.3)		23	4.7 (1.5)		25	5.6 (1.1)		9	6.0 (1.0)	
BDI-II-NL												
no depressive symptoms	65	4.3 (1.6)	-3.36 (0.001)	37	3.7 (1.4)	-2.55 (0.014)	20	4.9 (1.4)	-1.55 (0.130)	8	5.8 (0.9)	-0.22 (0.829)
depressive symptoms	43	5.3 (1.4)		17	4.8 (1.7)		19	5.6 (1.3)		7	5.9 (0.9)	

SAH: subarachnoid haemorrhage; UCL-p: Utrecht Coping List ; STAI-DY-1: State Trait Anxiety Inventory; BDI-II-NL: Beck Depression Inventory.

Figure 2. Relationships between impairments after SAH and fatigue in the presence or absence of passive coping, anxiety and depression



In the group having 'either physical or cognitive impairment,' a significant difference was found only between patients with and without anxiety, whereas no significant differences were found in the patients having 'both physical and cognitive impairment.' No interactions were found between the determinants in the analyses of variance (figure 2). The three separate ANOVAs show significant main effects of the level of impairment, passive coping, anxiety, and depressive symptoms on the FSS score. No interactions were found between the level of impairment and the three different determinants (table 4).

Table 4. Analyses of variance of determinants and FSS scores, one year after SAH.

Analyses of variance		ANOVA (F)	p-value
UCL-p	Model	7.90	0.000
	UCL-p	5.91	0.017
	Level of impairment	10.93	0.000
	interaction Level of impairment- UCL-p	0.41	0.663
STAI-DY-1	Model	8.87	0.000
	STAI-DY-1	7.07	0.009
	Level of impairment	11.23	0.000
	interaction Level of impairment- STAI-DY-1	0.57	0.569
BDI-II-NL	Model	7.66	0.000
	BDI-II-NL	4.10	0.046
	Level of impairment	9.94	0.000
	interaction Level of impairment- BDI-II-NL	0.82	0.443

SAH: subarachnoid haemorrhage; GOS: Glasgow Outcome Scale; UCL-p: Utrecht Coping List ; STAI-DY-1: State Trait Anxiety Inventory; BDI-II-NL: Beck Depression Inventory.

DISCUSSION

Our study showed that most patients experience fatigue 1 year after SAH, which is strongly correlated to physical and cognitive impairment, a passive coping style, and emotional problems. In particular in patients without physical or cognitive impairments, passive coping, anxiety, and depression play an important role in the presence of fatigue.

The baseline measurement of this study was 3 months after SAH. This was not only for practical reasons since it is the regular follow-up time of our SAH outpatient clinic. More importantly, the clinical condition after SAH is more stabilized at 3 months after SAH than during hospitalization or at discharge. In the acute phase all kinds of complications can occur, which may change the clinical condition of the patient. It is uncertain whether the determinants measured at 4–6 weeks after the SAH will have the same predictive power; this should be assessed in future studies.

All patients in our study group were living at home at the time of the assessment and had a moderate to good physical recovery. Nevertheless, the occurrence of post-SAH fatigue was very high, with mean scores above the cutoff point in all categories of patients. Earlier studies show that post-SAH fatigue occurs often[1,2], which is in line with our study. This post-SAH fatigue is also very persistent over time[5,17], which makes it a substantial problem with great impact on daily life.[3] In patients who have had a SAH, sleep and wake disturbances might contribute to post-SAH fatigue and depression.[18] Several reports have suggested that also pituitary-hypothalamic insufficiency may play a role after SAH[19], but

in a recent study, including the largest reported cohort of SAH patients to date, with early and late endocrine evaluation, none of the patients had chronic hypopituitarism.[20] One earlier prospective study in SAH included psychological factors (maladaptive coping, post-traumatic stress disorder) in the analyses, and reported post traumatic stress as the best predictor of post-SAH fatigue, while maladaptive coping was the best predictor of post-traumatic stress.[5] Furthermore, in another study 4–7 years after SAH, fatigue was correlated with difficulties maintaining sleep at night, personality changes, and complaints of poor memory.[4]

It is uncertain whether the determinants we studied, including coping and emotional problems, were influenced by the SAH itself. Passive coping strategy represents the tendency not to take any action when problems occur. Being anxious after SAH is strongly related to the personality factor neuroticism.[3] We found that these personal factors were most strongly related to fatigue in patients without physical or cognitive impairments. Further studies should address whether coping style can be improved in these patients and if this improves fatigue.

Although this was a large-scale study on fatigue in patients with SAH, some limitations should be mentioned. The neuropsychological data set did not cover all cognitive domains, and this data set was not completed by all patients, mainly because some patients had problems finding words or visual problems. Although this concerned only a few patients, it might have led to an underestimation of the influence of the cognitive impairments on post-SAH fatigue. Additionally, this study included only those persons with SAH who had visited the outpatient clinic 3 months after SAH and were living at home 1 year after SAH. The group of patients discharged to a nursing home do not belong to our study domain, because these patients usually do not visit our outpatient clinic. Thus, the results of our study only apply to patients who are discharged home or to a rehabilitation center. This is, however, by far the largest group of patients; <15% of patients had been discharged to a nursing home during our study period. It is possible that some of the patients discharged to a nursing home were living at home 1 year after SAH, but our results cannot be extrapolated to these patients. Finally, factors we did not take into account, such as disorders in sleep and post-traumatic stress disorder, might be relevant for post-SAH fatigue as well. Additional research is needed to clarify the impact of such factors on post-SAH fatigue.

Fatigue is an important issue after SAH, even in those patients with good clinical outcome. Education on fatigue should be given to patients and their relatives, explaining the accumulating effect of the physical and cognitive impairments, and the psychosocial aspects such as coping and emotional problems. An occupational therapy program on maintaining a balance between capacity and load in their daily activities may help patients with post-SAH fatigue. Similarly, a passive coping style and/or emotional problems may be improved by rehabilitation therapy from physical or mental health professionals. Whether focused interventions result in reduced impact of fatigue in the first year after their SAH should be investigated in future studies.

REFERENCES

1. Al-Khindi T, MacDonald RL, Schweizer TA (2010) Cognitive and functional outcome after aneurysmal subarachnoid hemorrhage. Stroke 41:e519–e536
2. Passier PECA, Visser-Meily JMA, van Zandvoort MJE, Post MWM, Rinkel GJE, van Heugten C (2010) Prevalence and determinants of cognitive complaints after aneurysmal subarachnoid haemorrhage. Cerebrovasc Dis 29:557–563
3. Visser-Meily JMA, Rhebergen ML, Rinkel GJE, van Zandvoort MJ, Post MWM (2009) Long-term health related quality of life after aneurysmal subarachnoid hemorrhage; relationship with psychological symptoms and personality characteristics. Stroke 40:1526–1529
4. Ogden JA, Utley T, Mee EW (1997) Neurological and psychosocial outcome 4 to 7 years after subarachnoid hemorrhage. Neurosurgery 41:24–34
5. Noble AJ, Baisch S, Mendelow AD, Allen L, Kane P, Schenk T (2008) Posttraumatic stress disorder explains reduced quality of life in subarachnoid hemorrhage patients in both the short and long term. Neurosurgery 63:1095–1105
6. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD (1989) The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 46:1121–1123
7. van Heuven AW, Dorhout Mees SM, Algra A, Rinkel GJE (2008) Validation of a prognostic subarachnoid hemorrhage grading scale derived directly from the glasgow coma scale. Stroke 39:1347–1348
8. Jennett B, Bond M (1975) Assessment of outcome after severe brain damage. Lancet 1:480–484
9. Eriksen HR, Olff M, Ursin H (1997) The CODE: a revised battery for coping and defense and its relation to subjective health. Scan J Psychol 38:175–182
10. Spielberger CD, Gorsuch RL, Lushene PR, Vagg PR, Jacobs AG(1983) Manual for the state-trait anxiety inventory (form Y). Consulting Psychologists Press, Palo Alto
11. Ploeg van der HM (2000) Handleiding bij de Zelf-beoordelings vragenlijst, een Nederlandse bewerking van de Spielberger Stait-Trait Anxiety Inventory, STAI-DY, Swets en Zeitlinger, Lisse
12. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J (1961) An inventory for measuring depression. Arch Gen Psychiatry 4:561–571
13. Aben I, Verhey F, Lousberg R, Lodder J, Honig A (2003) Validity of beck depression inventory, hospital anxiety and depression scale, scl-90, and Hamilton depression rating scale as screening instruments for depression in stroke patients. Psychosomatics 43:386–393
14. Lezak MD, Howieson DB, Loring DW (2004) Neuropsychological assessment, 4th edition. Oxford University Press, New York
15. Nys GMS, van Zandvoort MJE, van der Worp HB et al (2006) Early cognitive impairment predicts long-term depressive symptoms and quality of life after stroke. J Neurol Sci 247:149–156
16. Verhage F (1964) Intelligentie en leeftijd: Onderzoek bij Nederlanders van twaalf tot zevenenzeventig jaar (Intelligence and age: study with Dutch people from age 12 to 77). Van Gorcum, Assen
17. Hellawell DJ, Taylor R, Pentland B (1999) Persisting symptoms and carers' views of outcome after subarachnoid haemorrhage. Clin Rehabil 13:333–340
18. Schuiling WJ, Rinkel GJE, Walchenbach R, de Weerd AW (2005) Disorders of sleep and wake in patients after subarachnoid hemorrhage. Stroke 36:578–582
19. Kreitschmann-Andermahr I, Poll E, Hütter BO, Reineke A, Kristes S, Gilsbach JM (2007) Quality of life and psychiatric sequelae following aneurysmal subarachnoid haemorrhage: does neuroendocrine dysfunction play a role? Clin Endocrin 66:833–837

20. Klose M, Brennum J, Poulsgaard L, Kosteljanetz M, Wagner A, Feldt-Rasmussen U (2010) Hypopituitarism is uncommon after aneurysmal subarachnoid haemorrhage. Clin Endocrinol 73:95–101

General Discussion

This chapter discusses the main conclusions, strength and limitations of our study, as well as possible implications for rehabilitation programs. Finally, some suggestions for future research are provided.

MAIN FINDINGS OF THIS THESIS

Findings of the systematic review

We reviewed the literature on the determinants of Quality of life (QoL) among aneurysmal subarachnoid haemorraghe (SAH) patients. Based on the International Classification of Functioning, Disability, and Health (ICF) model of the World Health Organization[1], we found determinants related to *Body Structure & Function* (e.g. fatigue and mood), *Activity* (e.g. physical disability and cognitive complaints) and *Personal factors* (e.g. female gender, higher age, neuroticism and passive coping) to be consistently related to worse QoL after aneurysmal SAH. *Participation* has not been studied as a determinant of QoL after SAH.

Only four studies took psychological problems (fatigue and mood problems, cognitive functioning and personality characteristics) into account[2-5], in which mood problems[2,3,5] and cognitive impairments[3,4] have shown to be related to worse QoL. Fatigue, cognitive complaints, neuroticism and passive coping were also associated with worse QoL after aneurysmal SAH, but were only reported in one study.[5]

Findings of our empirical studies

Cognitive functioning

At three months after SAH, about half the patients showed mild and a quarter severe cognitive impairments on one or more neuropsychological tests, predominantly in the domains of memory and visuospatial functioning.

In the follow-up study of cognitive functioning one year after SAH almost half of the patients showed persistent cognitive impairments. In particular, impairments in visuoconstruction and visuoperception remained present over time.[6]

Anxiety and depression

At three months after SAH, half the patients reported symptoms of anxiety, whereas one third had depressive symptoms. Most of the patients with depressive symptoms (80%) had a minor to moderate depression, whereas the rest had a moderate to severe depression.

In the cross-sectional study three years after SAH, one third was anxious and a quarter had depressive symptoms.

Fatigue

One year after SAH, the mean Fatigue Severity Scale (FSS) score was 4.8 and fatigue (FSS >4) was present in 71%. The frequency of fatigue was higher among patients with physical impairment (93%) than among those without physical impairment (57%), in patients with passive coping (85%) than without passive coping (58%), in patients with anxiety (84%) than without anxiety (55%), and in patients with depressive symptoms (85%) than without depressive symptoms (62%).

In the group of patients having 'neither physical nor cognitive impairments' those with passive coping, anxiety or depressive symptoms more often reported fatigue than those without these characteristics.

In the cross-sectional study three years after SAH, two thirds of the patients reported fatigue.

Disability

At three months after SAH, about three quarter of the patients showed good recovery (Glasgow Outcome Scale (GOS) V), whereas a quarter was disabled but independent (GOS IV) and a small group (5%) was dependent on others (GOS III).

Of the patients studied three years after SAH, half of the patients showed good recovery (GOS V) at discharge, whereas one third was disabled but independent (GOS IV) and one fifth was dependent on others (GOS III).

Cognitive complaints

At three months after SAH, almost all patients (95%) reported at least one cognitive or emotional complaint that hampered everyday functioning, assessed with the Checklist for Cognitive and Emotional consequences following stroke (CLCE-24). At least one cognitive complaint was reported in 80% of the patients and at least 93% reported one emotional complaint. The most often reported cognitive complaints were mental slowness, short-term memory problems and attention problems, whereas the most reported emotional complaints were fatigue, feelings of anxiety, and being emotionally less stable.

All cognitive domains, disability, depressive symptoms, and feelings of anxiety were significantly associated with the CLCE-24 cognition score. In the final regression model, memory, disability, and depressive symptoms together explained 35% of the variance in the CLCE-24 cognition score. Presence of depressive symptoms was the strongest predictor.

Return to work

Three years after SAH, almost two thirds of the patients with employment before the SAH had returned to work, but only half of them had completely resumed their former job. The others worked less hours a week than before SAH or had shifted to a less demanding position.

Health-Related Quality of Life (HRQoL)

The mean Stroke Specific Quality of Life (SS-QoL) total score was 4.2, indicating a relative satisfactory HRQoL. However, a diverging pattern between the subscales of the SS-QoL appeared with the highest scores for the physical subtotal (mean 4.5) and the lowest scores in the psychosocial subtotal (mean 3.8), indicating that patients experienced lower psychosocial than physical HRQoL. The HRQoL score was lowest for the domain thinking (mean 3.3) and highest for the domain self-care (mean 4.7).

Female gender, cognitive complaints, cognitive impairments, and passive coping style explained almost half (46%) of the variance in the SS-QoL total scores and almost half (43%) of the psychosocial scores. Regarding the SS-QoL physical score, almost half (45%) of the variance was explained by discharge at home, cognitive complaints and cognitive impairments.

Life Satisfaction

Three years after SAH, the mean total Life satisfaction (LiSat-9) score was 4.8, which is between ´rather satisfied (4)´ and ´satisfied (5)´. SAH patients were least satisfied with their vocational situation and sexual life, and most satisfied with their relationships and self-care ability. Not returning to work, disability, depression, and passive coping were associated with reduced life satisfaction. Life satisfaction was better in persons without disability at discharge (5.0) than in persons with disability at discharge (4.6). Also, life satisfaction was better in those patients who resumed work after SAH (5.0) than in those who did not resume work after SAH (4.6).

Age, employment after SAH, disability at discharge, mood and passive coping together explained half (47%) of the variance in life satisfaction.

LESSONS LEARNED FROM THIS THESIS

In our review we showed that psychological determinants play an important role in HRQoL after SAH. We found no studies on the relationship between participation and HRQoL after SAH.

Thus far, predominantly generic QoL measurements have been used. The results of this thesis show that the SS-QoL scale is valid in SAH patients, and can be used in a multi-disciplinary (rehabilitation) care setting as well as in research.

Cognitive complaints occur often after SAH and are related to cognitive impairments, physical impairment and depressive symptoms, of which depressive symptoms were the strongest predictor. The association between cognitive complaints and underlying cognitive impairments is weak, which had already been suggested in earlier studies in SAH[7,8], ischemic stroke[9], and traumatic brain injury.[10]

Also fatigue occurs very often after SAH and is persisting over time.[11,12] Passive coping, anxiety or depressive symptoms are important determinants of fatigue.

Almost half of the variance of HRQoL can be explained with cognitive complaints, cognitive impairments and passive coping. Thus, by introducing the psychological aspects (cognitive complaints and impairments, and passive coping), we were able to predict HRQoL after SAH much better than a previous meta-analysis.[13] SAH patients experience lower psychosocial than physical HRQoL. Return to work is a very important determinant for life satisfaction after SAH. Return to work after SAH depends mainly on age, initial neurologic condition, residual physical disability and depression[14], and the preservation of cognitive and sensorimotor functions.[15]

Based on the information of this thesis, cognitive domains language, visuoperception and mental speed were added to the neuropsychological examination assessed at the multidisciplinary SAH-outpatient clinic. Furthermore, questionnaires about activities of daily living, QoL, participation, perceived stress and post traumatic stress have been added to the set of questionnaires that patients receive before visiting the outpatient clinic. Also, evaluation of the SAH patients' situation at the long-term is standardised, with

the same questionnaires as assessed at the outpatient clinic, sent by mail at 6 and 12 months after SAH. Finally, nowadays, patients discharged to a nursing home who might benefit from a rehabilitation program later on, are invited to the multidisciplinary SAH-outpatient clinic.

STRENGTH AND LIMITATIONS

Strengths

This thesis is based on two relatively large studies, with more than one hundred patients included. In comparison, in our review we found only four studies with large (n > 100) patient groups [3-5,16], of which only two were prospective.[3,4]

Also, the data of our study were quite complete, since basic information was prospectively collected at the department of neurology and neurosurgery of the UMC Utrecht for both study samples, and further information was assessed at the outpatient clinic for the prospective study. Additionally, the response rate was very high (about 80% in both studies).

Furthermore, we used information based on a combination of interviews, questionnaires and a neuropsychological screening. Therefore, we studied a broad range of outcomes and determinants, which makes it a comprehensive study.

Finally, by using the ICF model to order the different determinants of HRQoL, we were able to make clear which information is present and which is still lacking in literature.

Limitations

Our studies apply only to patients who are discharged home or to a rehabilitation centre and who return home after rehabilitation. The group of patients discharged to a nursing home (less than 15% of our SAH population) did not belong to our study domain. It is possible that some of the patients discharged to a nursing home were living at home one year after SAH, but our results cannot be extrapolated to these patients.

The neuropsychological data set did not cover all cognitive domains, and this data set was not completed by all patients, mainly because some patients could not complete the tests due to word finding problems or visual problems. Although this concerned only a few patients, it will have led to a slight underestimation of the prevalence of cognitive impairments and of the influence of the cognitive impairments on outcome variables.

POSSIBLE CLINICAL IMPLICATIONS FOR REHABILITATION TREATMENT

With the information reported in this thesis, we increased our understanding of QoL after aneurysmal SAH, and the most important determinants of QoL, and now are able to tailor appropriate rehabilitation programs and thereby enhance their effectiveness.

In this thesis, I have shown the importance of gathering information about fatigue, mood problems, physical impairment, cognitive impairments and complaints, neuroticism and passive coping style in an individual SAH patient, because these factors all are related to HRQoL and well-being after SAH, and are therefore important to tailor the rehabilitation

program to the needs of this patient.

A structured screening of this physical, cognitive and emotional functioning early after discharge, as in our outpatient clinic, could be an important way to detect these problems. As a clinician, I would recommend every medical centre specialised in treatment of SAH patients to arrange such a multidisciplinary outpatient clinic. Then, after collecting information about the patients physical, cognitive and emotional functioning, a tailored rehabilitation program can be recommended by the rehabilitation physician, which can be carried out at the rehabilitation department of a hospital or at a rehabilitation centre in the patients' neighbourhood. For research, such a specialised multidisciplinary outpatient clinic also offers a great opportunity to collect information about patients with SAH, and therefore can further increase our understanding of long-term problems after SAH.

The tailored rehabilitation program can contain different kind of therapies. When information is available about the patients functioning, education about cognitive and emotional problems (including fatigue) can be given to patients and their relatives. Additionally, physiotherapy and occupational therapy can be of some importance in patients with persisting disability. Also, an occupational therapy program on maintaining a balance between capacity and load in their daily activities may help patients. Furthermore, anti-depressive treatment should be considered when depressive symptoms are present. Similarly, a passive coping style and/or emotional problems may be improved by rehabilitation therapy from physical or mental health professionals.[17,18] Finally, vocational reintegration after SAH needs (more) attention during rehabilitation programs.

The location of this rehabilitation program depends on the severeness of the patients' impairments and can be offered clinical in a rehabilitation centre or at an outpatient clinic in a rehabilitation centre or hospital. Unfortunately, the most severely impaired patients might need a rehabilitation program in a nursing home first, before transfer to a rehabilitation centre is possible.

In the rehabilitation program, the weak relationships between the cognitive problems as experienced by the patients and the cognitive impairments should also be taken into account. Thus, both neuropsychological examination of cognitive functioning as assessment of the patient's experience of cognitive problems are necessary.

SUGGESTIONS FOR FUTURE RESEARCH

In this thesis I showed that problems related to cognitive and emotional functioning are highly prevalent after SAH, and more information about these factors and their relationships is needed to further tailor the rehabilitation programme.

First, it is important to gather more information about determinants of fatigue and mood problems, social support, social participation problems including social relations, and psychological determinants of HRQoL, and their relation to one another. Also, more research is needed on personality characteristics and fatigue because these might be important determinants of cognitive complaints, whereas disorders in sleep and post-traumatic stress disorder have to be taken into account in future research of post-SAH fatigue.

Additionally, the effectiveness of psychological interventions from rehabilitation or

mental health professionals and whether these interventions result in improved QoL, less cognitive complaints or reduced impact of fatigue should be investigated in future studies.

Finally, more information is needed about the internal relationships between the different determinants, based on the ICF model, and their relationship with QoL after SAH. I suppose that determinants in the category personal factors and participation have stronger relationships with QoL than determinants in the category body structure and function. The latter covers the impairments, but the way a patient can handle his/her impairments results in the individually perceived health. Therefore, I expect personal factors e.g. coping style to be of great influence.

In conclusion, research in patients with aneurysmal SAH is of great importance, because our understanding of the long-term problems after SAH can still be increased, and the results of rehabilitation programmes remain unknown. In this thesis we have improved our knowledge about determinants of cognitive complaints, fatigue, HRQoL and life satisfaction after aneurysmal SAH, but we also have to evaluate the long-term effects of the tailored rehabilitation programme, based on the gathered information about the physical, cognitive and emotional functioning of the SAH patient.

REFERENCES

1. World Health Organization. International Classification of Functioning, Disability and Health: ICF. Geneva, Switzerland: World Health Organization;2001.
2. Fertl E, Killer M, Eder H, Linzmayer L, Richling B, Auff E. Long-term functional effects of aneurysmal subarachnoid haemorrhage with special emphasis on the patient's view. Acta Neurochir 1999;141:571-577.
3. Meyer B, Ringel F, Winter Y, Spottke A, Gharevi N, Dams J, Balzer-Geldsetzer M, Mueller IK, Klockgether T, Schramm J, Urbach H, Dodel R. Health-Related Quality of Life in patients with subarachnoid haemorrhage. Cerebrovasc Dis 2010;30:423-431.
4. Scott RB, Eccles F, Lloyd A, Carpenter K. From multidimensional neuropsychological outcomes to a cognitive complication rate: The international subarachnoid aneurysm trial. Trials 2008;9:13.
5. Visser-Meily JMA, Rhebergen ML, Rinkel GJE, Zandvoort van MJ, Post MWM. Long-term health related quality of life after aneurysmal subarachnoid hemorrhage; relationship with psychological symptoms and personality characteristics. Stroke 2009;40:1526-9.
6. Penninx JF, Visser-Meily JMA, Passier PECA, Rinkel GJE, Post MW, Zandvoort van MJE. The prognostic value of neuropsychological examination after SAH. Behavioural Neurology 2010; 23: 173-175.
7. Ravnik J, Starovasnik B, Šešok S, Pirtošek Z, Švigelj V, Bunc G, Bošnjak R: Long-term cognitive deficits in patients with good outcomes after aneurysmal subarachnoid hemorrhage from anterior communicating artery. Croat Med J 2006; 47: 253–263.
8. Toomela A, Pulver A, Tomberg T, Orasson A, Tikke A, Asser T: Possible interpretation of subjective complaints in patients with spontaneous subarachnoid haemorrhage. J Rehabil Med 2004; 36: 63–69.
9. Duits A, Munnecom T, Heugten van C, Oostenbrugge van RJ: Cognitive complaints in the early phase after stroke are not indicative for cognitive impairment. J Neurol Neurosurg Psychiatry 2008; 79: 143–146.
10. Stulemeijer M, Vos PE, Bleijenberg G, Werf van der AP: Cognitive complaints after mild traumatic brain injury: things are not always what they seem. J Psychosom Res 2007; 63: 637–645.
11. Hellawell DJ, Taylor R, Pentland B. Persisting symptoms and carers' views of outcome after subarachnoid haemorrhage. Clin Rehabil 1999;13:333–340.
12. Noble AJ, Baisch S, Mendelow AD, Allen L, Kane P, Schenk T. Posttraumatic stress disorder explains reduced quality of life in subarachnoid hemorrhage patients in both the short and long term. Neurosurgery 2008;63:1095–1105.
13. Noble A.J., Schenk T. Which variables help explain the poor health-related quality of life after subarachnoid hemorrhage? A meta-analysis. Neurosurgery 2010;66:772-783.
14. Carter BS, Buckley DRN, Ferraro RMSOT, Rordorf GMD, Ogilvy CS. Factors associated with reintegration to normal living after subarachnoid hemorrhage. Neurosurgery 2000;46:1326-1334.
15. Vilkki JS, Juvela S, Siironen J, Ilvonen T, Varies J, Porras M. Relationship of local infarctions to cognitive and psychosocial impairments after aneurysmal subarachnoid hemorrhage. Neurosurgery 2004;55:790-803.
16. Hütter BO, Kreitschmann-Andermahr I, Gilsbach JM. Health-related quality of life after aneurysmal subarachnoid hemorrhage: impacts of bleeding severity, computerized tomography findings, surgery, vasospasm, and neurological grade. J Neurosurg 2001;94:241-251.
17. Joo HM, Lee SJ, Chung YG, Shin IY. Effects of mindfulness based stress reduction program on depression, anxiety and stress in patients with aneurysmal subarachnoid haemorrhage. J Korean Neurosurg Soc 2010;47:345-351.

18. Rasquin SMC, Bouwens SFM, Dijcks B, Winkens I, Bakx WGM, Heugten van CM. Effectiveness of a low intensity outpatient cognitive rehabilitation programme for patients in the chronic phase after acquired brain injury. Neuropsychological Rehabilitation 2010; 20: 760-777.

Summary

The main objective of this thesis was to gain more knowledge about quality of life (QoL) after aneurysmal subarachnoid haemorrhage (SAH), in order to tailor appropriate rehabilitation programs and thereby, enhance their effectiveness. A cohort of 143 aneurysmal SAH patients, who visited our multidisciplinary SAH-outpatient clinic 3 months after SAH, between October 2006 and September 2008, was followed up to one year after SAH. Besides, we used data from a previous cross-sectional study in patients with aneurysmal SAH, three years after SAH.

In *chapter 2* we reviewed the determinants of QoL among aneurysmal SAH patients. Based on the International Classification of Functioning, Disability, and Health model, determinants related to Body Structure & Function (e.g. fatigue and mood), Activity (e.g. physical disability and cognitive complaints) and Personal factors (e.g. female gender, higher age, neuroticism and passive coping) are consistently related to worse QoL after aneurysmal SAH. Participation has not been studied as a determinant of QoL after aneurysmal SAH.

In *chapter 3* we described a validation study of the Stroke Specific Quality of Life (SS-QoL) scale for patients with aneurysmal SAH, which has shown to be a valid measure to assess QoL after SAH. Using physical and psychosocial SS-QoL summary scores simplifies the use of this measure without concealing differences in outcomes on different quality of life domains.

In *chapter 4* we investigated the prevalence of cognitive complaints after aneurysmal SAH and the relationships between cognitive complaints and cognitive impairments, disability and emotional problems. Patients were 111 persons who visited our outpatient clinic 3 months after SAH. In this study group, 105 patients (95%) reported at least one cognitive or emotional complaint that hampered everyday functioning. The most frequently reported cognitive complaints were mental slowness, short-term memory problems and attention deficits. All cognitive impairments, disability, depressive symptoms, and feelings of anxiety were significantly associated with cognitive complaints. Significant determinants of cognitive complaints in regression analysis were memory deficits, disability and depressive symptoms. Rehabilitation programs should focus on these symptoms and deficits.

In *chapter 5* we investigated life satisfaction and employment status after aneurysmal SAH and the associations between life satisfaction and demographic, disease-related, psychological, and personality characteristics, at a mean time of 3 years after SAH. Included patients were 141 persons living at home 2-4 years after the SAH. In this study group, 64 patients had a Glasgow Outcome Scale score of V (good outcome) at discharge. Out of the 88 patients who were working at the time of the SAH, 54 returned to work, but only 31 resumed their work completely. The other 23 were working fewer hours per week or had shifted to a less-demanding position. The SAH patients were least satisfied with their vocational situation and sexual life, and were most satisfied with their relationships and self-care ability. Our data indicate that return to work is a major issue for individuals who survive aneurysmal SAH. Not returning to work, disability, depression, and passive coping were associated with reduced life satisfaction. Thus, vocational reintegration after SAH merits specific attention during rehabilitation.

In *chapter 6* we investigated the predictive value of physical, emotional and cognitive

factors for long-term health-related quality of life (HRQoL) in patients who survived aneurysmal SAH. This was a prospective cohort study of 113 patients with aneurysmal SAH who visited our SAH-outpatient clinic three months after SAH and who were living independently in the community one year after SAH. HRQoL was evaluated using the SS-QoL. Regards the SS-QoL total score, 46% of its variance was explained by female gender, cognitive complaints, executive and visuoconstructive functioning, and passive coping style. Regards the SS-QoL psychosocial score, 43% of its variance was explained by female gender, cognitive complaints, executive functioning and passive coping style. Regards the SS-QoL physical score, 45% of the variance was explained by discharge destination, cognitive complaints, and attention and visuoconstriction. Early interventions to improve cognitive and emotional functioning should be evaluated for their ability to improve long-term HRQoL after aneurysmal SAH.

In *chapter 7* we investigated the occurrence of fatigue 1 year after aneurysmal SAH and its relation to physical or cognitive impairment, passive coping, and emotional problems, measured 3 months after SAH. This was a prospective cohort study of 108 patients who visited our SAH outpatient clinic 3 months after aneurysmal SAH and who were living independently in the community 1 year after SAH. Fatigue was evaluated using the Fatigue Severity Scale (FSS). Fatigue was present in 77 patients. Mean FSS scores were higher in patients scoring high on passive coping, anxiety or depression than in patients without these complaints. Relationships between these complaints and FSS scores were higher in patients having neither physical nor cognitive impairments than in patients having physical or cognitive impairments. In patients with neither physical nor cognitive impairments, passive coping style and emotional problems are important predictors of fatigue. This knowledge can be used for education on fatigue given to patients and their relatives, and for tailoring the rehabilitation program, especially to the psychosocial aspects such as coping and emotional problems.

In *chapter 8*, the main conclusion, strengths and limitations of our study, as well as possible implications for rehabilitation programs and future directions for research are discussed for the central themes of this thesis: quality of life after aneurysmal SAH, return to work, and relationships with psychosocial characteristics in SAH patients e.g. cognitive complaints and fatigue.

Dutch summary

Dit proefschrift heeft als onderwerp de kwaliteit van leven (KvL) van mensen die een subarachnoïdale bloeding (SAB) hebben doorgemaakt. Een SAB is een bloeding tussen de hersenen en de schedel, die meestal ontstaat uit een gebarsten vaatafwijking (aneurysma; aSAB). SAB is een levensbedreigende aandoening en komt voornamelijk voor bij relatief jonge mensen, met een gemiddelde leeftijd van 62 jaar. Het aneurysma kan behandeld worden door de radioloog middels coilen of door de neurochirurg middels clippen. Ruim de helft van de patiënten die een aSAB hebben overleefd herstellen fysiek vrij goed, maar velen van hen houden wel psychosociale problemen die van invloed kunnen zijn op hun KvL. De onderzoeken die in dit proefschrift worden beschreven richten zich vooral op het identificeren van fysieke en psychosociale problemen die invloed hebben op de KvL na een aSAB. Het uiteindelijke doel van het onderzoek is om met de opgedane kennis de begeleiding van deze patiënten door het multidisciplinaire revalidatieteam te verbeteren en de effectiviteit van de revalidatiebehandeling te vergroten. Het gaat om een prospectief onderzoek, waarbij 143 aSAB patiënten die de multidisciplinaire SAB poli hebben bezocht, 3 maanden na de doorgemaakte SAB, in de periode van september 2006 – oktober 2008, en die tot 1 jaar na SAB werden gevolgd. Daarnaast zijn data gebruikt van een eerder uitgevoerde cross-sectionele studie bij patiënten met een aSAB, 3 jaar na SAB.

Hoofdstuk 2 geeft een overzicht van de literatuur betreffende de determinanten van KvL na een aSAB. Gebaseerd op de Internationale Classificatie van het menselijk Functioneren (ICF), bleken vooral determinanten gerelateerd aan Lichaamsfuncties (vermoeidheid en stemming), Activiteiten (fysieke beperkingen en cognitieve klachten) en Persoonlijke factoren (vrouwelijk geslacht, hogere leeftijd, neuroticisme en passieve coping stijl) geassocieerd met slechtere KvL na aSAB. Participatie bleek niet te zijn bestudeerd in relatie tot KvL na aSAB.

In *hoofdstuk 3* beschrijven we een validatie studie van de Stroke Specific Quality of Life scale (SS-QoL). De SS-QoL bleek een valide schaal voor gebruik bij mensen die een aSAB hebben doorgemaakt. Verder bleek het mogelijk om de 12 schalen van de SS-QoL samen te voegen tot een fysieke en een psychosociale subscore, wat deze KvL maat eenvoudig te gebruiken maakt.

In *hoofdstuk 4* hebben we de prevalentie van cognitieve klachten na aSAB onderzocht, en de relaties tussen deze cognitieve klachten enerzijds en cognitieve functies, fysieke beperkingen en emotionele problemen anderzijds. Het onderzoek betrof 111 patiënten die de SAB poli bezochten 3 maanden na de doorgemaakte aSAB. In deze studiegroep rapporteerden 105 (95%) patiënten minimaal één cognitieve of emotionele klacht die hen beperkte in het dagelijkse leven. De meest voorkomende cognitieve klachten waren het hebben van moeite om alles bij te houden, om nieuwe informatie te onthouden en om de aandacht ergens bij te houden. Cognitieve stoornissen, fysieke beperkingen, depressieve symptomen en gevoelens van angst waren significant geassocieerd met de cognitieve klachten. In de regressie analyse bleken geheugenstoornissen, fysieke beperkingen en depressieve symptomen significante determinanten van deze cognitieve klachten. Het is van belang dat revalidatieprogramma's aandacht besteden aan deze gevolgen van aSAB.

In *hoofdstuk 5* wordt het algemeen welbevinden (levens satisfactie) en de situatie rondom werk beschreven bij patiënten gemiddeld 3 jaar na aSAB. Tevens is gekeken naar de

associaties tussen het welbevinden enerzijds en demografische, ziekte gerelateerde, psychologische en persoonlijkheidsfactoren anderzijds. De studie bestond uit 141 zelfstandig wonende patiënten, 2-4 jaar na de doorgemaakte SAB. In deze studiegroep hadden 64 patiënten geen fysieke beperkingen toen zij uit het ziekenhuis werden ontslagen. Van de 88 patiënten die werkten ten tijde van het ontstaan van de aSAB, keerden er 54 terug naar hun werk, maar slechts 31 waren in staat om volledig terug te keren naar hun oude functie. De overige 23 patiënten waren na de aSAB minder uren gaan werken of hadden een functie met minder verantwoordelijkheden. In de totale studie populatie waren patiënten het minst tevreden over hun arbeidssituatie en hun seksuele leven, en het meest tevreden over hun relaties en zelfzorg. Terugkeer naar werk is een belangrijk issue gebleken na het doormaken van een SAB. Niet kunnen terugkeren naar werk, fysieke beperkingen, depressie en een passieve coping stijl waren geassocieerd met een verlaagd welbevinden. Het is dus van groot belang om binnen het revalidatieprogramma van aSAB patiënten aandacht te besteden aan re-integratie naar werk.

In *hoofdstuk 6* hebben we de voorspellende waarde onderzocht van fysieke, emotionele en cognitieve factoren voor de lange termijn KvL bij patiënten met een aSAB. Het ging om een prospectieve studie van 113 patiënten met een aSAB, die 3 maanden later de SAB poli hadden bezocht, en 1 jaar na de SAB zelfstandig woonden. KvL werd gemeten met de SS-QoL. In totaal 46% van de variantie van de totaalscore van de SS-QoL kon worden verklaard door de factoren: vrouwelijk geslacht, cognitieve klachten, executieve en visuoconstructieve functiestoornissen, en een passieve coping stijl. Van de SS-QoL psychosociale subscore werd 43% van de variantie verklaard door vrouwelijk geslacht, cognitieve klachten, executieve functiestoornissen en passieve coping stijl. Van de SS-QoL fysieke subscore werd 45% van de variantie verklaard door de ontslagbestemming, cognitieve klachten, en stoornissen in aandacht en visuoconstructie. Vroege interventies om het cognitieve en emotionele functioneren te doen verbeteren moeten verder worden onderzocht, om na te gaan of deze ook de KvL na aSAB kunnen verbeteren.

In *hoofdstuk 7* hebben we gekeken naar het voorkomen van vermoeidheid 1 jaar na aSAB. Onderzocht werd de relatie tussen vermoeidheid 1 jaar na aSAB enerzijds en fysieke of cognitieve beperkingen, passieve coping, en emotionele problemen 3 maanden na SAB anderzijds. Het ging hierbij om een prospectieve studie van 108 patiënten die 3 maanden na de SAB de SAB poli hadden bezocht, en 1 jaar na de SAB zelfstandig woonden. Vermoeidheid werd gemeten met de Fatigue Severity Scale (FSS). Bij 77 patiënten was er sprake van vermoeidheid. Gemiddelde FSS scores waren hoger bij patiënten die hoog scoorden op gebied van passieve coping, angst en depressie, vergeleken met patienten zonder deze klachten. Deze relaties waren sterker bij die patienten zonder fysieke of cognitieve beperkingen, vergeleken met patienten die wel fysieke of cognitieve beperkingen hadden. Bij die patiënten zonder fysieke of cognitieve beperkingen waren passieve coping en emotionele problemen belangrijke voorspellers van vermoeidheid. Deze kennis kan gebruikt worden voor voorlichting over vermoeidheid aan patiënten en partners en geeft richting aan het revalidatieprogramma, met name voor de psychosociale factoren zoals coping en emotionele problemen.

In *hoofdstuk 8* worden de belangrijkste bevindingen en de methodologische problemen, implicaties voor revalidatieprogramma's en suggesties voor toekomstig onderzoek

beschreven aan de hand van de thema's van dit proefschrift: kwaliteit van leven na aSAB, terugkeer naar werk, en relaties met psychosociale factoren zoals cognitieve klachten en vermoeidheid.

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List of publications

Swaen GMH, Passier PECA, Attekum van ANMG.
De prevalentie van silicose in de Nederlandse fijn-keramische industrie.
Tijdschrift voor Sociale Gezondheidszorg 1987; 65: 668-669.

Swaen GMH, Passier PECA, Attekum van ANMG.
Prevalence of silicosis in the Dutch fine-ceramic industry.
International Archives of Occupational and Environmental Health 1988; 60: 71-74.

Passier PECA, Twijnstra A, Geest van der S.
Wat is de neurologische prognose van patiënten, die na een hart- en/of ademstilstand comateus zijn ?
Nederlands Tijdschrift voor Cardiologie 1992; 6: 52-56.

Passier PECA, Vredeveld JW, Krom de MCTFM.
Basilar migraine or viral meningo-encephalitis with severe EEG abnormalities.
Electroencephalography and clinical Neurophysiology 1993; 86: 12P (abstract).

Passier PECA, Vredeveld JW, Krom de MCTFM.
Basilar Migraine with severe EEG abnormalities.
Headache 1994 ; 34 : 56 - 58.

Steen van der JT, Adèr HJ, Assendelft van JHM, Kooistra M, Passier PECA, Ooms ME.
Retrospectieve afname van de Nederlandse versie van de Discomfort Scale - Dementia of Alzheimer Type (DS-DAT): is inschatten achteraf voldoende valide en betrouwbaar?
Tijdschrift voor Gerontologie en Geriatrie 2003; 34: 254 - 259.

Passier PECA, Visser-Meily JMA, Zandvoort van MJE, Post MWM, Rinkel GJE, Heugten van C.
Prevalence and determinants of cognitive complaints after aneurysmal subarachnoid haemorrhage.
Cerebrovascular Diseases 2010; 29: 557-563.

Passier PECA, Visser-Meily JMA, Zandvoort van MJE, Post MWM, Rinkel GJE, Heugten van C.
Prevalence and determinants of cognitive complaints after aneurysmal subarachnoid haemorrhage.
Revalidata 2010; 32: 15 (abstract).

Boosman H, Passier PE, Visser-Meily JM, Rinkel GJ, Post MW.
Validation of the Stroke Specific Quality of Life Scale (SS-QoL) in patients with aneurysmal subarachnoid haemorrhage.
J Neurol Neurosurg Psychiatry 2010; 81: 185-9.

Passier PECA, Visser-Meily JMA, Rinkel GJE, Lindeman E, Post MWM.
Life satisfaction and return to work after aneurysmal subarachnoid haemorrhage.
J Stroke Cerebrovasc Dis 2011; 20: 324-329.

Post MWM, Boosman H, Rinkel GJE, Zandvoort van MJE, Passier PECA, Visser-Meily JMA.
Development and validation of a short version of the Stroke Specific Quality of Life Scale.
J Neurol Neurosurg Psychiatry 2011; 82: 283-6.

Boosman H, Post MWM, Zandvoort van MJE, Passier PECA, Rinkel GJE, Visser-Meily JMA.
Development and validation of a short version of the Stroke Specific Quality of Life Scale.
Revalidata 2010; 32: 12 (abstract).

Passier PECA, Visser-Meily JMA, Zandvoort van MJE, Rinkel GJE, Lindeman E, Post MWM.
Predictors of long-term Health-Related Quality of Life in patients with aneurysmal subarachnoid hemorrhage.
Revalidata 2010; 32; 42 (abstract).

Penninx JF, Visser-Meily JMA, Passier PECA, Rinkel GJE, Post MW, Zandvoort van MJE.
The prognostic value of neuropsychological examination after SAH.
Behavioural Neurology 2010; 23: 173-175.

Passier PECA, Post MWM, Zandvoort van MJE, Rinkel GJE, Lindeman E, Visser-Meily JMA.
Predicting fatigue 1 year after aneurysmal subarachnoid hemorrhage.
J Neurol 2011; 258: 1091-1097.

Passier PECA, Visser-Meily JMA, Zandvoort van MJE, Rinkel GJE, Lindeman E, Post MWM.
Predictors of long-term Health-Related Quality of Life in patients with aneurysmal subarachnoid hemorrhage.
Neurorehabilitation, accepted for publication.

Passier PECA, Visser-Meily JMA, Zandvoort van MJE, Rinkel GJE, Lindeman E, Post MWM.
Determinants of health-related quality of life after aneurysmal subarachnoid haemorrhage: a systematic review.
Submitted.

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CURRICULUM VITAE

Patricia Passier is geboren op 14 juli 1966 in Maastricht. In 1984 deed zij eindexamen atheneum B op de scholengemeenschap Stella Maris te Meerssen. Zij studeerde Geneeskunde van 1984 tot 1991 aan de Rijksuniversiteit Limburg te Maastricht. Gedurende haar opleiding was zij betrokken bij het verrichten van wetenschappelijk onderzoek, veelal in combinatie met een student-assistentschap. Zij begon haar loopbaan als arts-assistent neurologie op verschillende locaties, maar koos uiteindelijk voor het meer holistische vak verpleeghuisgeneeskunde (thans specialist ouderengeneeskunde genaamd). Van 1996 – 1998 deed zij de opleiding tot verpleeghuisarts aan de Vrij Universiteit te Amsterdam. Vervolgens ging zij binnen het verpleeghuisartsenvak op zoek naar uitdagingen, die zij onder andere vond in het voorzitterschap van de commissie ethiek en het opleiderschap. Daarvoor volgde zij onder andere de postdoctorale opleiding Ethiek in de zorgsector. Vanwege de grote interesse voor de revalidatie binnen het vak, startte zij met de kaderopleiding gerontorevalidatie, doch vóór de afronding hiervan koos zij ervoor over te stappen naar een ander vak: revalidatiegeneeskunde. Van maart 2007 – maart 2011 deed zij de opleiding tot revalidatiearts binnen het circuit De Hoogstraat / UMCU / Antonius Ziekenhuis in Utrecht. Het onderzoek in het kader van de opleiding liep in positieve zin uit de hand en heeft uiteindelijk geleid tot dit boekje. Aan het eind van haar opleiding kreeg zij de LIVIT trofee, als aanmoediging tot het doen van verder wetenschappelijk onderzoek. Sinds april 2011 is zij werkzaam als revalidatiearts bij Merem Trappenberg, locatie Flevoziekenhuis te Almere. Zij is de partner van Marcel van Nes, waarmee zij haar passie voor wandelen en natuur deelt, en met wie zij sinds kort samenwoont.

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En de ander die hef 'm van lood

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