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Symptoms and consequences of subarachnoid haemorrhage after 7 years

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Objectives: Short-term follow-up studies after a subarachnoid haemorrhage (SAH) have shown impaired cognition, fatigue, depression and anxiety, but less is known regarding long-term consequences. The aim of this study was to investigate health outcomes in persons 7 years after SAH.

Materials and Methods: This is a descriptive cohort follow-up study of persons with non-traumatic SAH treated at Sahlgrenska University Hospital, Gothenburg, Sweden. The follow-up was conducted 7 years post-treatment and included home visits using forms and questionnaires about health outcomes; the Barthel Index (BI), modified Rankin Scale (mRS), National Institutes of Health Stroke Scale (NIHSS), Hospital Anxiety and Depression Scale (HADS), Montreal Cognitive Assessment (MoCA) and Multidimensional Fatigue Inventory (MFI).

Results: Seven years post-SAH, 33 persons fulfilled the inclusion criteria, of whom 18 (55%) participated (median age 63 years). Cognitive impairment was present in 11 participants, assessed with the MoCA, where the item of delayed recall was most difficult. The majority (n = 16) were independent in activities of daily living (ADL), and few (n = 3) had physical symptoms according to the NIHSS. However, three participants were free from disability according to the mRS. Nearly, half of the participants had symptoms of anxiety (n = 8). Three had symptoms of depression and more than half experienced fatigue.

Conclusion: The physical function and independency in ADL is high among long-term SAH survivors. Despite this, only a few were completely free from disability, and the main problems 7 years after SAH were cognitive impairment and anxiety.

KEYWORDS
cognitive impairment, follow-up studies, subarachnoid haemorrhage

1 | INTRODUCTION

A subarachnoid haemorrhage (SAH) can cause diverse symptoms for the individual, ranging from no to severe consequences,[1-3] which is comparable to other types of stroke. However, the long-term consequences described up to 4 years after SAH differ, and most SAH survivors have few physical symptoms and manage to complete their activities of daily living (ADL),[4-6] but they still have several other symptoms that may affect their quality of life.[7] From

this perspective, independence in ADL is not equal to an experienced "good outcome" for the person. SAH survivors had significant more cognitive deficits as well as depressed moods when compared to controls,[8] and in a follow-up study 4 years after SAH,[5] 43.3% had mild cognitive impairment. One year after SAH, cognitive deficits were present in every domain tested (7%-15%), with the highest scores in visuospatial skill and memory with 15% prevalence.[9] These cognitive impairments lowered the SAH survivors' function in daily life.[4,9]
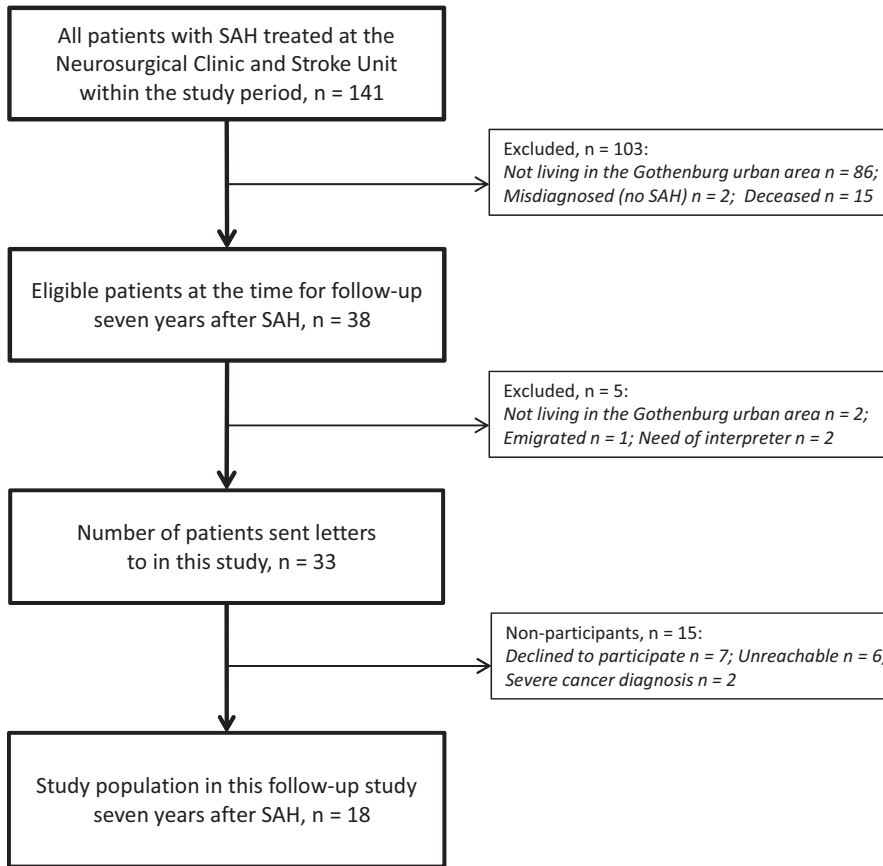
All patients with SAH treated at the Neurosurgical Clinic and Stroke Unit within the study period, n = 141

Excluded, n = 103:
Not living in the Gothenburg urban area n = 86; Misdiagnosed (no SAH) n = 2; Deceased n = 15

Eligible patients at the time for follow-up seven years after SAH, n = 38

Excluded, n = 5:
Not living in the Gothenburg urban area n = 2; Emigrated n = 1; Need of interpreter n = 2

Number of patients sent letters to in this study, n = 33

Non-participants, n = 15:
Declined to participate n = 7; Unreachable n = 6; Severe cancer diagnosis n = 2

Study population in this follow-up study seven years after SAH, n = 18

Nearly, 50% have experienced depression within the first year[10] and within 2 years after SAH, more than 50% have a higher level of anxiety than the normal Swedish population.[6] Even 2-5 years after onset, over half of the persons with SAH presented symptoms of depression and anxiety.[11] Other long-term symptoms that are commonly reported are mental fatigue[5,12] and impaired memory.[12] Several follow-up studies shortly after SAH have been carried out, but less is known regarding long-term outcome and eventual cognitive and mental consequences. An improved knowledge of the long-term consequences of SAH is desirable for tailor-made rehabilitation and for prediction of outcome. The aim of the present study was to investigate health outcomes in persons 7 years after SAH.

2 | MATERIAL AND METHODS

Eligible for this descriptive cohort follow-up study were all surviving persons with SAH treated at the Neurosurgical Clinic or at the Stroke Unit at Sahlgrenska University Hospital, Gothenburg, Sweden, during an 18-month period in 2009-2010.[13,14] The Neurosurgical Clinic covers a catchment area of the western part of Sweden. The inclusion criteria were: first occasion non-traumatic SAH (diagnosis code I60 according to the International Classification of Diseases 10, confirmed by clinical assessment and imaging or lumbar puncture); resident in Gothenburg urban area (within 35 km from the hospital); able to communicate in the Swedish language; ≥18 years old at

the time of SAH. There were no exclusion criteria by other medical conditions.

2.1 | Data collection procedure

Within the study period, 141 patients were treated for SAH at the Neurosurgical Clinic or at the Stroke Unit, see flow chart in Figure 1. At the time of the follow-up, in September 2016, 33 persons from the cohort fulfilled the inclusion criteria and were eligible for the study. An invitation letter was sent to the cohort of SAH survivors, followed by a phone call. If a person was not reachable, a second and third letter was sent, as well as several phone calls. Fifteen persons declined participation for different reasons such as did not want to participate, had no time to spare, no sequelae after SAH or "trying to put this behind me." Six persons that fulfilled the inclusion criteria were unreachable. Eighteen persons agreed to participate in the study.

2.2 | Home visits at the time of follow-up

One of the authors (OW) conducted all home visits in the participants' own homes, and there were no internal dropouts. The home visit included assessment of neurological status and questionnaires regarding the consequences of SAH described below.

To assess neurological status the National Institutes of Health Stroke Scale (NIHSS)[15] was used, range 0-46 points, higher is better.

TABLE 1 Characteristics of the study population at time of SAH (n = 18)

Demographics	
Age at SAH, years	
Mean (SD), years	58.6 (10.24)
Median (minimum-maximum)	56 (45-81)
Sex, n (%)	
Male/female	8 (44.4)/10 (55.6)
Hunt & Hess at admission, n (%)	
1	2 (11.1)
2	11 (61.1)
3	1 (5.6)
4	3 (16.7)
5	1 (5.6)
Glasgow Coma Scale (15-3), grade, n (%)	
15	12 (66.7)
13-14	2 (11.1)
7-12	2 (11.1)
3-6	2 (11.1)

Note: Abbreviations: SAH, Subarachnoid haemorrhage; SD, standard deviation.

Independency in ADL was assessed using the Barthel Index (BI),[16] score 0-100 points, maximum score indicates a high level of independency in ADL. Functional outcome was assessed with the modified Rankin Scale (mRS),[17] range 0-6, lower is better.

The Montreal Cognitive Assessment (MoCA),[18] is a screening tool for mild cognitive impairment which includes tests in eight domains: Visuospatial/executive, Naming, Memory, Attention, Language, Abstraction, Delayed recall and Orientation. The maximum score is 30 and a score <26 indicates cognitive impairment.[5,18]

To detect symptoms of anxiety and/or depression within the last week, the Hospital Anxiety and Depression Scale (HADS)[19] was used. The HADS is a 14-item questionnaire, with a 7-item subscale for anxiety (HADS-A) and depression (HADS-D), respectively. The maximum score of each subscale is 21, where a higher score indicates anxiety/depression. The cut-off used in the present study for each subscale indicating depression and anxiety was >7.[19,20]

Level of consciousness was assessed using the Glasgow Coma Scale (GCS),[21] score 3-15, where a higher score corresponds to a higher level of consciousness. The level of fatigue was investigated using the Multidimensional Fatigue Inventory (MFI-20).[22,23] The MFI-20 comprises 20 items, subdivided into five dimensions of fatigue (general fatigue, physical fatigue, mental fatigue, reduced activity and reduced motivation), with four items per dimension. In each dimension, the score ranges from 4 to 20, where a higher score indicates greater fatigue. The total score ranges from 20 to 100.

Two assessments from the initial neurological examinations at admission to hospital at the time of SAH were used. Severity of SAH rated with the Hunt and Hess (H&H),[24,25] grade III-V corresponds to a severe clinical state, while grades I-II are considered as less severe.

The study was approved by the Regional Ethical Review Board in Gothenburg, (no. 225-08, T801-10, 400-13). Oral and written informed consent was obtained from all participants. The STROBE guideline for observational studies was followed.

2.3 | Statistical methods

Non-parametric descriptive statistics were used when presenting data. Differences between groups were analysed using Fisher's exact test and Mann-Whitney *U* test, and *P*-values <.05 were regarded as significant. The MoCA sum score was dichotomized using the cut-off at ≥26 points. The MoCA items where ≥60% of the participants did not score the maximum score were classified as problematic and were further described. All statistical analysis was performed in IBM Statistical Package for Social Sciences (SPSS version 22.0).

3 | RESULTS

A total of 18 (55%) of the eligible 33 persons participated in this study, Figure 1. There was no significant difference between participants and non-participants in age (*P* = .126), sex (*P* = .386) or H&H (*P* = .355). The median age in the participant group was slightly higher 63 (52-87) compared with the non-participants median age 58 (41-85). The home visits took place at a mean of 7 years after the SAH.

As seen in Table 1, the majority of participants were female (n = 10) and 72% had less severe symptoms at admittance to hospital (H&H grade I-II). At the time of follow-up, the median age was 63 years and most lived in a household with others (Table 2). Three participants did not have detectable disability, neither physical nor cognitive. Among the three participants who were dependent on others (mRS > 2), one had suffered an additional stroke, whereas the two others did not report any comorbidity causing the high mRS score. Three persons had higher score than 0 in NIHSS at 7 years (2, 2 and 6 points) and the correlation between mRS and NIHSS was ρ 0.572, indicating that high grades in mRS did not necessarily correlate with high NIHSS score.

The MoCA showed that nine of the participants had mild cognitive impairment (<26) and two moderate cognitive impairment (total score 15, 17), Table 2. There were no significant differences in level of cognition (dichotomized MoCA at 7 years) depending on SAH severity at admission (H&H; *P* = .676).

The top five most difficult items in MoCA were the two visuospatial items (copy a cube and draw a clock), one attention item (subtraction series 100-7-7-7-7), the abstraction item (comprehend similarity between two words) and the delayed recall item (remember five words after approximately 5 minutes), Table 3. Lowest results were scored in the item of delayed recall where only two of the 18 participants received the maximum score. Four of the participants' difficulties to perform the visuospatial item to copy a cube are shown in Figure 2.

Seventeen of the participants scored ≥41 (minimum-maximum 41-81) in the MFI indicating some symptoms of fatigue, while one participant scored 23 points indicating no symptoms of fatigue. According to HADS, half of the study population experienced

TABLE 2 Characteristics of the study population at time of follow-up at home visit (n = 18)

Demographics	
Age, years median (minimum-maximum)	63 (52-87)
Living situation, n	
Living together with spouse/alone	11/7
Accommodation, home	18
Work/Retired or sick-leave	10/8
Time since SAH to follow-up, years mean (SD)	6.9 (0.57)
Barthel index, score, n	
65	1
90	1
95	4
100	12
MoCA, score, n	
>26/≤26	7/11
NIHSS, score, n	
0/2/6	15/2/1
mRS, score, n	
0-2/>2	15/3

Note: Abbreviations: MoCA, The Montreal Cognitive Assessment; mRS, modified Rankin Scale; NIHSS, the National Institutes of Health Stroke Scale; SAH, Subarachnoid haemorrhage; SD, standard deviation.

TABLE 3 Top five list of most difficult items in the Montreal Cognitive Assessment, scored by the participants (n = 18)

Item	Participants that did not obtain maximum score[a] (%)
Delayed recall	16 (89)
Abstraction	10 (56)
Visuospatial, clock	7 (39)
Visuospatial, cube	6 (32)
Attention, subtraction	6 (32)

[a]Maximum score corresponds to better performance.

anxiety (median 6, minimum-maximum 0-13) and three depression (median 3, minimum-maximum 0-11).

At the open-ended question of self-experienced consequences of the SAH, eight of the participants reported memory deficits after the SAH, six participants mentioned difficulties to concentrate and four participants described difficulties in "finding words." Five participants reported difficulty to maintain normal balance. Ten participants stated increased fatigue after SAH. One participant said: "You cannot tell it by looking at me, I wish it was more visible on the outside."

4 | DISCUSSION

The major findings of this study were that 7 years after SAH, participants had high physical function and in general high independency in ADL. However, only a few were completely free from disability. The majority of the participants had remaining cognitive impairment, more than half experienced fatigue and nearly half of the participants (n = 8) had symptoms of anxiety.

Half of the participants had mild cognitive impairment. The highest prevalence of impairment was in delayed recall, abstraction and visuospatial tasks, which is consistent with a previous study[9] carried out 1 year after SAH, where deficits in visuospatial skill and memory were most prevalent. The assessed grade of severity at acute stage of SAH did not correlate with the cognitive outcome at 7 years post-SAH. Cognitive impairment was most notable in the delayed recall MoCA item, where only two participants received the maximum score. For that matter, according to the original MoCA paper, the delayed recall item was the item with highest impairment among patients with mild cognitive impairment.[18]

What causes the impaired delayed recall is not clearly understood. In the open-ended question of self-experienced current SAH residual symptoms, four participants declared they have "difficulty finding words," six mentioned having concentration difficulties and eight stated memory deficits. It could be speculated that deficits in concentration and/or attention contributed to the high occurrence of impairment in delayed recall, in addition to memory deficits. Attention deficits have been reported in previous follow-up studies after SAH, as a common self-reported cognitive complaint 3 months after SAH.[26] Furthermore, attention deficits have been shown to be a common symptom (58%) demonstrated in a pilot study in a test of attention 7 months after SAH.[27]
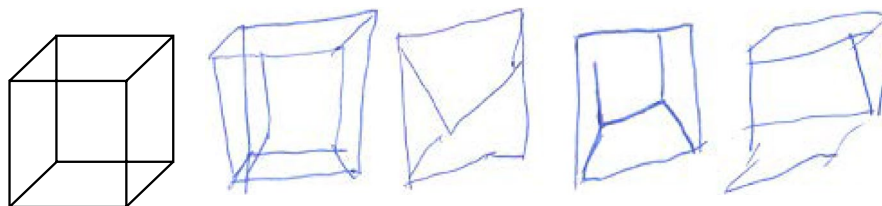

FIGURE 2 The Visuospatial cube item in the Montreal Cognitive Assessment (MoCA). To the left, the cube that the participant was asked to copy, and thereafter, examples of cubes drawn by four of the six participants who received a score of 0 in the item

In general, higher scores in the NIHSS correlated with higher mRS grades. However, in this study populations, participants that scored 0 in the NIHSS could have either high or low score in the mRS. This indicates a disability, though not necessarily a physical one. For example, the cognitive impairment found in the majority of the participants may contribute to this disability. A ceiling effect has been observed in the NIHSS,[28] indicating that residual neurological symptoms of the SAH may remain undetected. For instance, sense of balance is not included in the NIHSS, and difficulty in maintaining normal balance was reported by five participants in the open-ended question of residual symptoms. The high physical function and independency in ADL found in this study is consistent with findings in previous studies.[5,6,29]

The finding that nearly half (n = 8) of the participants had symptoms of anxiety is consistent with findings in another follow-up study carried out 2-5 years after SAH.[11] Three participants had symptoms of depression, which is a lower proportion than what has been found in previous long-term follow-up studies.[6,11] In a follow-up study, 2-5 years after SAH[11] over half of the participants had symptoms of depression. A follow-up study[6] 2 years after SAH, reported that about 30% of the participants had symptoms of depression, and increased fatigue was reported by more than half of the participants. However, this finding of fatigue might be explained by the rather high mean age of the study population, as increased age might contribute to increased fatigue.[30]

This study was carried out 7 years after SAH onset, and therefore, other occurrences during that time, for example, comorbidity and ageing may have affected the study result. There were no exclusion criteria by comorbidity or age, which complicates the assessment of causality, however, also increasing the number of eligible patients. A sex-, age- and geographically matched control group could have improved the study concerning causality, and differences in characteristics of the survivors of SAH compared with the general population or other stroke diagnoses.

The study population (n = 18) was rather small, which is to be expected as SAH is an uncommon disease with high mortality, and findings need to be confirmed in larger studies. A consecutive sampling was used and the non-participants did not differ significantly from the participants in age, sex or severity of SAH. It could not be ruled out that non-participants may have fewer consequences of their SAH, which may have led to an overrepresentation of consequences among participants.

To be able to answer the questionnaires the participants need to be attentive, concentrated and alert. Lack of attention and concentration in addition to impaired cognition and fatigue may have contributed to errors while answering the questionnaires. Some of the participants may have concealed their disability by not asking for explanation if they did not understand the question and this strategy might have affected their performance. The fact that the questionnaires were administered in the same order to all participants and were all assessed by the same person is a strength of this study.

4.1 | Further research

Findings from the present study could be followed up with a longitudinal study with a sex-, age- and geographically matched control group from the population census. There is a need of further research about the cognitive impairment among SAH survivors, including studies that compare the cognitive status of individuals after SAH over time, to gain knowledge of their prognosis. In order to improve our knowledge about cognitive impairments, more specific neuropsychological questionnaires and tests, which are able to detect more subtle cognitive deficits such as concentration, attention and difficulties in "finding words" need to be used. Further research may also be done in the qualitative domain by doing unstructured interviews to be able to acquire information of different individual symptoms.

5 | CONCLUSIONS

The long-term consequences of SAH, 7 years after onset, were dominated by cognitive and emotional symptoms rather than physical. Over half of the SAH survivors had impaired cognition and around half of the study population reported symptoms of anxiety. This knowledge is of importance for clinicians and SAH survivors, as they need to be aware of the often hidden long-term symptoms of SAH, and that even in absence of physical disabilities, the patients may be in need of rehabilitation and support, and information about the prognosis of SAH.

CONFLICT OF INTEREST

None declared.

DATA AVAILABILITY STATEMENT

The data sets analysed during the current study are not publicly available due to ethical restrictions. According to the Swedish regulation http://www.epn.se/en/start/regulations/, the permission to use data is only for what has been applied for and then approved by the Ethical board. Data are available from the authors (contact Professor KS Sunnerhagen, email: ks.sunnerhagen@neuro.gu.se) upon reasonable request.

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