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# Quality of Life After Poor-Grade Aneurysmal Subarachnoid Hemorrhage

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**BACKGROUND:** Poor-grade aneurysmal subarachnoid hemorrhage (aSAH) is associated with high mortality and poor disability outcome. Data on quality of life (QoL) among survivors are scarce because patients with poor-grade aSAH are underrepresented in clinical studies reporting on QoL after aSAH.

**OBJECTIVE:** To provide prospective QoL data on survivors of poor-grade aSAH to aid clinical decision making and counseling of relatives.

**METHODS:** The herniation World Federation of Neurosurgical Societies scale study was a prospective observational multicenter study in patients with poor-grade (World Federation of Neurosurgical Societies grades 4 & 5) aSAH. We collected data during a structured telephone interview 6 and 12 months after ictus. QoL was measured using the EuroQoL - 5 Dimensions - 3 Levels (EQ-5D-3L) questionnaire, with 0 representing a health state equivalent to death and 1 to perfect health. Disability outcome for favorable and unfavorable outcomes was measured with the modified Rankin Scale.

**RESULTS:** Two hundred-fifty patients were enrolled, of whom 237 were included in the analysis after 6 months and 223 after 12 months. After 6 months, 118 (49.8%) patients were alive, and after 12 months, 104 (46.6%) patients were alive. Of those, 95 (80.5%) and 89 (85.6%) reached a favorable outcome with mean EQ-5D-3L index values of 0.85 (±0.18) and 0.86 (±0.18). After 6 and 12 months, 23 (19.5%) and 15 (14.4%) of those alive had an unfavorable outcome with mean EQ-5D-3L index values of 0.27 (±0.25) and 0.19 (±0.14).

**CONCLUSION:** Despite high initial mortality, the proportion of poor-grade aSAH survivors with good QoL is reasonably large. Only a minority of survivors reports poor QoL and requires permanent care.

**KEY WORDS:** Aneurysmal subarachnoid hemorrhage, EQ-5D, Outcome, Poor grade, Prospective observational study, Quality of life, WFNS grades IV and V

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Data on quality of life (QoL) among survivors of poor-grade aneurysmal subarachnoid hemorrhage (aSAH) are scarce. Despite a general association with high mortality and unfavorable outcomes, the proportion of poor-grade aSAH survivors has increased in recent years.[1,2] Besides physician-reported outcome measures, patient-reported QoL is gaining importance because it reflects the subjective view of patients on their personal health. This is particularly important in conditions such as poor-grade aSAH, where survivors must cope with high rates of neurological deficits. Poor-grade patients are often mixed with good-grade patients, are subject to missing data issues, and are underrepresented in studies reporting on QoL after aSAH.[3-10] Here, we present novel prospective data on QoL in survivors of poor-grade aSAH from the herniation World Federation of Neurosurgical Societies (WFNS) scale study.[11]

**ABBREVIATIONS: ACA,** anterior cerebral artery; **AICA,** anterior inferior cerebellar artery; **ACOM,** anterior communicating artery; **Ant,** anterior; **aSAH,** aneurysmal subarachnoid hemorrhage; **BNI,** Barrow Neurological Institute; **EQ-5D-3L,** EuroQoL - 5 Dimensions - 3 Levels; **ICA,** internal carotid artery; **ICH,** intracerebral hemorrhage; **MCA,** middle cerebral artery; **mRS,** modified Rankin Scale; **PCA,** posterior cerebral artery; **PCOM,** posterior communicating artery; **PICA,** posterior inferior cerebellar artery; **Prox,** proximal; **SCA,** superior cerebellar artery; **WFNS,** World Federation of Neurosurgical Societies.

## METHODS

We conducted a prospective observational study in 1 German and 7 Swiss neurosurgical departments,

which act as exclusive neurovascular referral centers for patients with aSAH patients in their responsible region. This study included patients with aSAH, 18 years or older, Glasgow coma scale ≤12 points (WFNS grades 4 & 5), and excluded patients with SAH because of any other cause or structural abnormality (arteriovenous malformation, dural arteriovenous fistula, cavernous malformation, dissection, tumor, or trauma) of the brain or foreseeable difficulties during follow-up.

This study was approved by the local ethics committee of each center and was registered under https://ClinicalTrials.gov (unique identifier: NCT02304328). Reporting is in accordance with the Strengthening the Reporting of Observational studies in Epidemiology guideline for cohort studies.

All patients with poor-grade aSAH, fulfilling the inclusion criteria, were enrolled in this study regardless of further clinical management or therapy. Written informed consent was obtained from all patients or patients' next of kin. SAH was confirmed by computed tomography, magnetic resonance imaging, or lumbar puncture. Treatment was according to current guidelines and included immediate neurological resuscitation (external cerebrospinal fluid drainage in case of hydrocephalus, seizure treatment, and general intensive care measures), early angiography, and transfer to an intensive care unit.[11-13] Clinical status after neurological resuscitation was used for WFNS grading. Further details on study design, clinical management, and primary end point results are published elsewhere.[11]

Data on QoL, disability outcome, and home status were collected 6 and 12 months after ictus during a structured telephone interview conducted by an independent trained investigator or study nurses blinded to the clinical course. QoL was measured using the EuroQoL - 5 Dimensions - 3 Levels (EQ-5D-3L) questionnaire, reporting health profiles in 5 dimensions (mobility, self-care, usual activities, pain and discomfort, anxiety, and depression), each of which has 3 response levels (no problems, some problems, and extreme problems). The response levels "some problems" and "extreme problems" were further summarized as reporting "any problem." EQ-5D-3L index values are calculated from individual health profiles using a Germany-specific reference value set (values range from 0 to 1, where 0 is a health state equivalent to death and 1 to perfect health).[14] Index values were sex-matched and age-matched for comparison with the German population norm.[15] Disability outcome was measured with the modified Rankin Scale (mRS). In those alive, favorable outcome was defined as mRS 0 to 3 and unfavorable outcome as mRS 4 to 5. Home status was defined as being home, in a rehabilitation clinic, or under constant care in a nursing home.

Statistical analysis was performed using Stata version 16.1 (StataCorp LLC). Descriptive statistics were performed to illustrate frequencies and percentages. EQ-5D-3L index values are displayed as mean (±SD) and were calculated using the Stata eq5d command (StataCorp LLC).[16]

The data supporting this study's findings are available from the corresponding author on reasonable request.

**TABLE 1. Baseline Characteristics of 237 Patients**

| Variable | n (%)/mean (±SD) |
|---|---|
| Total | 237 (100%) |
| Age | 61.7 (±13.4) |
| Female sex | 154 (65%) |
| WFNS grade | |
| IV | 35 (14.8%) |
| V | 202 (85.2%) |
| BNI grading scale | |
| 1 | 7 (3%) |
| 2 | 23 (9.7%) |
| 3 | 72 (30.4%) |
| 4 | 71 (30%) |
| 5 | 61 (25.7%) |
| Unclassified | 3 (1.2%) |
| ICH | 89 (37.6%) |
| Aneurysm location | |
| Prox ICA | 3 (1.3%) |
| Ant choroidal | 3 (1.3%) |
| PCOM | 19 (8%) |
| ICA terminus | 13 (5.5%) |
| MCA | 40 (16.9%) |
| ACOM/ACA | 82 (34.6%) |
| Pericallosal | 8 (3.4%) |
| Basilar tip | 22 (9.3%) |
| Basilar trunk | 3 (1.3%) |
| PCA | 6 (2.5%) |
| SCA | 1 (0.4%) |
| AICA | 2 (0.8%) |
| PICA | 17 (7.2%) |
| Vertebral artery | 8 (3.4%) |
| Unclassified | 10 (4.1%) |
| Aneurysm therapy | |
| Surgical | 50 (21.1%) |
| Endovascular | 114 (48.1%) |
| Combined | 4 (1.7%) |
| None | 69 (29.1%) |
| Withdrawal of care | 102 (43%) |

ACA, anterior cerebral artery; AICA, anterior inferior cerebellar artery; ACOM, anterior communicating artery; Ant, anterior; BNI, Barrow Neurological Institute; ICA, internal carotid artery; ICH, intracerebral hemorrhage; MCA, middle cerebral artery; PCA, posterior cerebral artery; PCOM, posterior communicating artery; PICA, posterior inferior cerebellar artery; Prox, proximal; SCA, superior cerebellar artery; WFNS, World Federation of Neurosurgical Societies.

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## RESULTS

Between December 2015 and November 2019, 250 patients were enrolled in this study. Thirteen patients were excluded from the analysis (1 angio-negative SAH, 9 withdrew consent, and 3 were lost to follow-up), leaving 237 patients included in the analysis at 6 months. After 12 months, 14 additional patients were lost to follow-up, leaving 223 patients for the analysis. Baseline characteristics are presented in Table 1.

After 6 months, 118 (49.8%) patients were alive and 119 (50.2%) were dead. After 12 months, 104 (46.6%) patients were alive and 119 (53.4%) were dead. Of those alive after 6 months, 95 (80.5%) had a favorable outcome (mRS 0-3) and 23 (19.5%) had an unfavorable outcome (mRS 4-5). Of those alive after 12 months, 89 (85.6%) had a favorable outcome and 15 (14.4%) had an unfavorable outcome. The distribution of the mRS is presented in Table 2 and Figure.

EQ-5D-3L health profiles were available for all patients alive. Four patients declined to answer the anxiety and depression question after 6 months, leading to 114 instead of 118 responses in this dimension. The most affected dimension was usual activities with 68 (57.6%) patients reporting any problem after 6 months and 64 (61.5%) patients after 12 months. In all other dimensions, the proportion of patients reporting any problem ranged between 40.3% and 46.6% after 6 months and 33.7% and 45.2% after 12 months. The proportion of patients reporting extreme problems was smallest in the dimensions pain and discomfort as well as anxiety and depression, with values ranging between 3.5% and 5.9% after 6 months and 2.9% and 4.8% after 12 months.

The proportion of patients reporting no problem in each dimension, equivalent to a state of perfect health, was 22 of 114 (19.3%) after 6 months and 21 of 104 (20.2%) after 12 months.

Details on health profiles are listed in Table 3.

EQ-5D-3L index values could be calculated for 114 patients after 6 months and 104 patients after 12 months. The mean age-matched and sex-matched index values of the normal German population were 0.91 (±0.04) for both time points. The overall calculated mean index values were 0.75 (±0.3) after 6 months and 0.76 (±0.3) after 12 months. When stratified by mRS, a decline in index values (decreasing QoL) was observed with increasing mRS, which was most prominent between mRS 3 and 4. The mean index value of patients with a favorable outcome was 0.85 (±0.18) after 6 months and 0.86 (±0.18) after 12 months. By contrast, the mean index value of patients with an unfavorable outcome was 0.27 (±0.25) after 6 months and 0.19 (±0.14) after 12 months. Stratification according to mRS is presented in Table 2 and Figure.

Of those alive after 6 months, information about home status was available for 117 patients: 82 (70.1%) were at home, 16 (13.7%) were in a rehabilitation clinic, and 19 (16.2%) were in a nursing home. After 12 months, information about home status was available for 103 patients: 82 (79.6%) were at home, 5 (4.9%) were in a rehabilitation clinic, and 16 (15.5%) were in a nursing home.

## DISCUSSION

In this study, we found that despite high initial mortality, approximately 80% of poor-grade aSAH survivors have a favorable outcome, can return home, and have good QoL. Approximately 20% reported no restriction of any health domain of the EQ-5D-3L. Stratification by mRS showed that patients with favorable outcomes (mRS 0-3) had EQ-5D-3L index values of 0.85 (±0.18) after 6 months and 0.86 (±0.18) after 12 months. On a scale from 0 to 1, where 1 is equivalent to a state of perfect health and 0.91 (±0.04) is the matched population norm, this can be considered a reasonably good outcome after such a potentially devastating disease. A minority of poor-grade aSAH survivors were in a state of

**TABLE 2. EQ-5D-3L Index Values Stratified by mRS**

| | 6 mo | | | 12 mo | | |
|---|---|---|---|---|---|---|
| Variable | % of total cohort (n) | % of those alive (n) | Mean EQ-5D-3L index value (±SD) | % of total cohort (n) | % of those alive (n) | Mean EQ-5D-3L index value (±SD) |
| Total | *100% (237)* | *100% (118)* | *100% (114)* | *100% (223)* | *100% (104)* | *100% (104)* |
| mRS 0 | 9.7% (23) | 19.5% (23) | 0.97 (±0.06) | 9.9% (22) | 21.2% (22) | 0.98 (±0.04) |
| mRS 1 | 11.8% (28) | 23.7% (28) | 0.91 (±0.12) | 11.2% (25) | 24% (25) | 0.90 (±0.17) |
| mRS 2 | 8.9% (21) | 17.8% (21) | 0.76 (±0.26) | 7.6% (17) | 16.4% (17) | 0.87 (±0.15) |
| mRS 3 | 9.7% (23) | 19.5% (23) | 0.75 (±0.16) | 11.2% (25) | 24% (25) | 0.71 (±0.2) |
| mRS 4 | 5.5% (13) | 11% (13) | 0.35 (±0.24) | 4.5% (10) | 9.6% (10) | 0.2 (±0.18) |
| mRS 5 | 4.2% (10) | 8.5% (10) | 0.12 (±0.19) | 2.2% (5) | 4.8% (5) | 0.16 (±0.03) |
| mRS 6 | 50.2% (119) | | | 53.4% (119) | | |
| mRS 0-3 | 40.1% (95) | 80.5% (95) | 0.85 (±0.18) | 39.9% (89) | 85.6% (89) | 0.86 (±0.18) |
| mRS 4-5 | 9.7% (23) | 19.5% (23) | 0.27 (±0.25) | 6.7% (15) | 14.4% (15) | 0.19 (±0.14) |
| Matched population norm | | | 0.91 (±0.04) | | | 0.91 (±0.04) |

mRS, modified Rankin Scale.

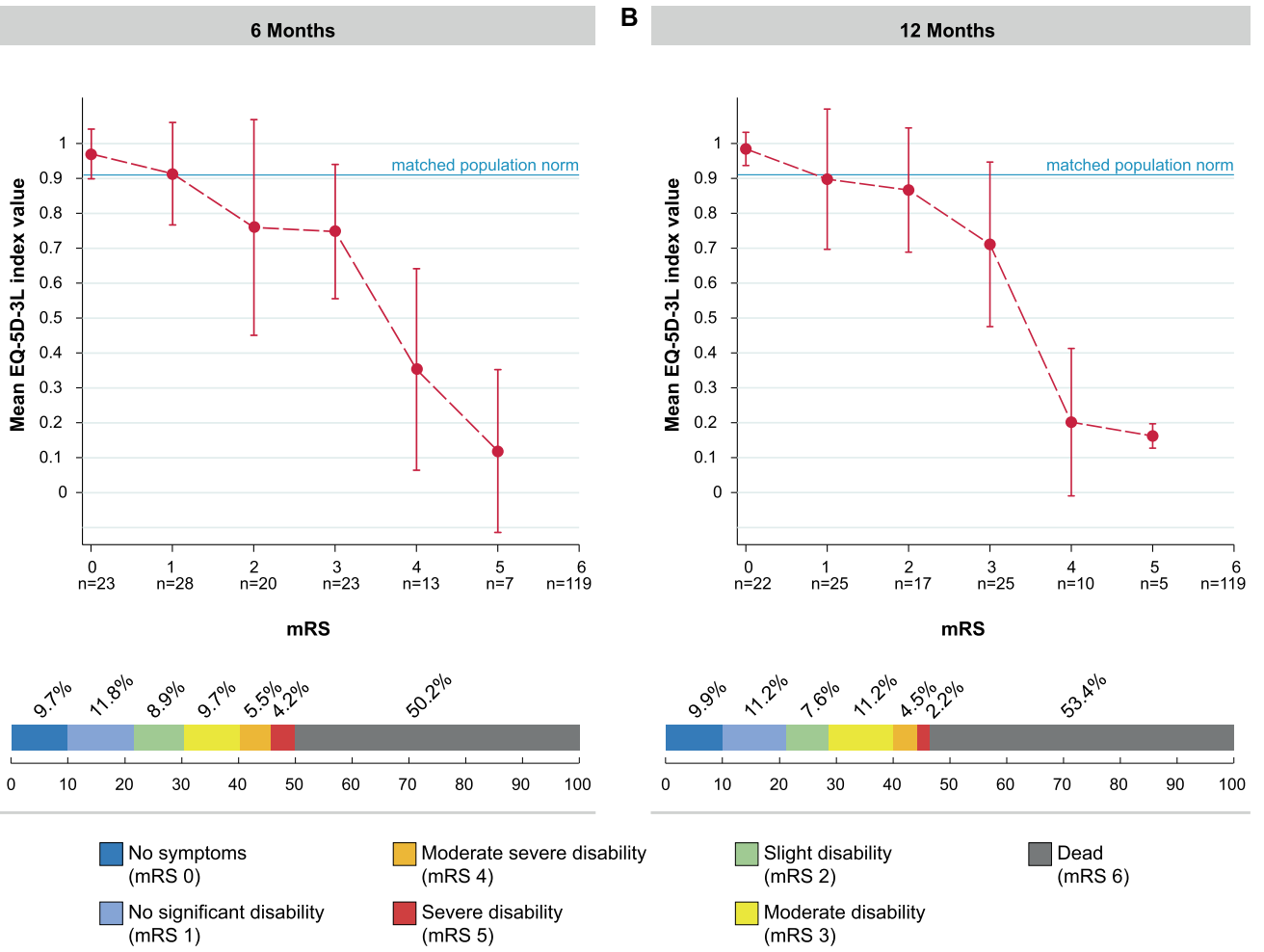


**FIGURE.** *Mean EQ-5D-3L index values (±SD) stratified by mRS and distribution of mRS after* **A**, *6 and* **B**, *12 months. Blue line indicates age-matched and sex-matched population norm (0.91 ± 0.04). mRS, modified Rankin Scale.*

moderate severe disability (mRS 4) or severe disability (mRS 5) after 6 and 12 months (19.5% and 14.4%). These patients had corresponding low EQ-5D-3L index values < 0.3. We found only subtle changes between QoL after 6 and 12 months.

The debate around treatment of patients with aSAH and its potential consequences is mainly centered around poor-grade cases because of the fear of increasing the proportion of dependent patients with severe disabilities. Besides physician-reported

**TABLE 3. EQ-5D-3L Health Profiles After 6 and 12 Months**

| | Mobility % (n) | | Self-care % (n) | | Usual activities % (n) | | Pain/discomfort % (n) | | Anxiety/depression % (n) | |
|---|---|---|---|---|---|---|---|---|---|---|
| EQ-5D-3L response | 6 mo | 12 mo | 6 mo | 12 mo | 6 mo | 12 mo | 6 mo | 12 mo | 6 mo | 12 mo |
| Total | 100 (118) | 100 (104) | 100 (118) | 100 (104) | 100 (118) | 100 (104) | 100 (118) | 100 (104) | 100 (114) | 100 (104) |
| No problems | 53.4 (63) | 54.8 (57) | 58.5 (69) | 66.3 (69) | 42.4 (50) | 38.5 (40) | 56.8 (67) | 64.4 (67) | 59.7 (68) | 57.7 (60) |
| Some problems | 33.9 (40) | 33.7 (35) | 24.5 (29) | 20.2 (21) | 36.4 (43) | 44.2 (46) | 37.3 (44) | 32.7 (34) | 36.8 (42) | 37.5 (39) |
| Extreme problems | 12.7 (15) | 11.5 (12) | 17 (20) | 13.5 (14) | 21.2 (25) | 17.3 (18) | 5.9 (7) | 2.9 (3) | 3.5 (4) | 4.8 (5) |
| Reporting any problem | 46.6 (55) | 45.2 (47) | 41.5 (49) | 33.7 (35) | 57.6 (68) | 61.5 (64) | 43.2 (51) | 35.6 (37) | 40.3 (46) | 42.3 (44) |

EQ-5D-3L, EuroQoL - 5 Dimensions - 3 Levels.

outcome parameters, analysis of patient-reported QoL has become an important adjunct to inform this discussion. Outcomes after aSAH are very heterogeneous and largely depend on the initial clinical presentation.[17] Therefore, it seems useful to report QoL separately for patients with good-grade and poor-grade aSAH, which are also categories that drive clinical decision making. Most studies reporting on QoL after aSAH share the limitation of mixing good-grade and poor-grade patients or analyzing cohorts in which poor-grade patients are underrepresented.[3-8] Others are limited by relatively small cohort sizes[18-22] or are subject to missing data issues.[9]

In our study, survivors reported mainly impairment during usual activities, whereas anxiety and depression, as well as pain and discomfort, were less often affected. This is in line with other studies mainly reporting an impairment of social life rather than physical or somatic constraints.[5,9,18] However, comparability with other studies is often limited due to using different instruments to measure QoL. Two other more recent studies reported QoL after aSAH using the EQ-5D-3L.[3,5] In both of them, patients with poor-grade aSAH are underrepresented (n = 39; 2.4%)[3] (n = 55; 21.5%),[5] and therefore, their relevance for patients with poor-grade aSAH is limited.

To fill this data gap, the results of this study serve as additional information in the complex clinical decision making around patients with poor-grade aSAH and when counseling their families. The good QoL in most patients surviving the initial phase of poor-grade aSAH implies that treatment continues to be justified in this challenging subgroup and leads to reasonably good outcomes in carefully selected patients. Nevertheless, this study shows a high mortality rate during the initial phase of the disease, with a withdrawal of care rate of 40% and a mortality rate of 50% after 6 months. This underscores the need for good clinical judgment during the initial phase after poor-grade aSAH to distinguish cases with a reasonable prognosis from those for which no further treatment seems adequate.

The strengths of our study include its prospective multicentric design and a follow-up of 1 year. Furthermore, it is the largest cohort reporting prospective QoL data in patients with poor-grade aSAH. Timing of the clinical assessment for WFNS grading is a known potential source of misclassification if performed before neurological resuscitation. Therefore, patients in this study were examined and graded after neurological resuscitation.

### Limitations

Our study has certain limitations. Nine patients withdrew consent, and 17 patients were lost to follow-up. Assuming that this is more likely associated with lower QoL, the true results might be skewed toward the negative. Furthermore, the EQ-5D-3L does not collect information about working status and neuropsychological outcomes. Mortality after 6 and 12 months might partially be caused by the known impact of excess mortality due to cardiovascular disease in patients with aSAH.[23,24]

## CONCLUSION

Despite high initial mortality, up to 80% of poor-grade aSAH survivors report reasonably good QoL and can return home. In total, 20% report no restriction of any health domain of the EQ-5D-3L. Only a small number of patients report poor QoL and require permanent care.

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### Disclosures

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