World Neurosurgery: X 22 (2024) 100305

Contents lists available at ScienceDirect

World Neurosurgery: X

journal homepage: www.journals.elsevier.com/world-neurosurgery-x

Original article

Quality of life in patients with unruptured intracranial aneurysms treated conservatively, before and after occlusion. A single center cohort study

Francis J. Kissling [a,#], Johannes Goldberg [b], Andreas Raabe [a,b], David Bervini [a,b,*,#]

[a] Bern University, Bern, Switzerland
[b] Department of Neurosurgery, Inselspital, Bern University Hospital, Bern, Switzerland

ARTICLE INFO

Keywords:
Clip
Coil
Intracranial aneurysm
Neurosurgery
Quality of life
QoL

ABSTRACT

Introduction: Rupture of intracranial aneurysms is the most frequent cause of subarachnoid hemorrhage and is associated with high morbidity. Recommendations for preventive treatment of unruptured aneurysms (UIAs) remain controversial due to inconsistent data on their natural history and the risks associated with treatment. The awareness of being diagnosed with one or more UIAs can provoke feelings of anxiety and psychosocial distress. Therefore, the impact of management on a patients' health perception and quality of life (QoL) is an essential factor to be considered in the treatment decision-making process.

Objective: The aim of this study was to assess and compare QoL in patients diagnosed with one or more UIAs depending on their treatment as well as their pre- or postoperative status.

Material and methods: Demographic and clinical data as well as results of the 15D quality of life (15D QoL) questionnaire of 189 patients were prospectively collected and retrospectively analyzed. Patients were categorized into different subgroups, depending on their treatment modalities (conservative, microsurgery or endovascular treatment) and their pre- or postoperative status at the time of completion of the questionnaire. Statistical analysis was performed to compare the different subgroups.

Results: Conservatively treated patients had similar mean 15D QoL scores as preoperative patients. Despite an initial postoperative QoL reduction and a trend towards recovery and even an improvement of QoL in the long term after UIA occlusion, neither clinically relevant nor statistically significant differences between preoperative and postoperative mean 15D QoL scores were observed.

Conclusions: Health-related QoL does not significantly change after treatment of UIAs when compared to the preoperative period. Further studies are needed to confirm long-term postoperative quality of life changes as well as treatment-related influencing factors on patients' quality of life.

1. Introduction

Unruptured intracranial aneurysms (UIAs) are the most frequently diagnosed vascular malformations of the brain with an overall adjusted prevalence of approximately 2.3 percent in a population with a mean age of 50 years, a men-to-women-ratio of 1:1 and no comorbidities.[1] Rupture of an intracranial aneurysm is associated with high morbidity and mortality.[2,3] The purpose of elective intracranial aneurysm treatment is the prevention of aneurysmal rupture and subarachnoid hemorrhage (aSAH).

The indication for preventive treatment of UIAs remains controversial due to inconsistent data about their natural history and the morbidity associated with microsurgical or endovascular treatment. The decision for preventive therapy mainly depends on four essential aspects: the risk of aneurysmal rupture, the risk associated with the intervention, life expectancy and patient preferences. These aspects need to be carefully weighed to advise the best treatment in individual patients.[4–11]

1.1. Quality of life

The awareness of harbouring an UIA can provoke anxiety and psychosocial distress because of the fear of a potentially life-threatening hemorrhage. Therefore, this may have an important impact on quality of life (QoL). On the other hand, the decision to undergo a preventive

* Corresponding author. Department of Neurosurgery Bern University Hospital (Inselspital) 3010 Bern, Switzerland.
E-mail address: david.bervini@insel.ch (D. Bervini).
participated equally to the study.

https://doi.org/10.1016/j.wnsx.2024.100305
Received 26 June 2023; Accepted 21 February 2024
Available online 29 February 2024

List of abbreviations

aSAH	aneurysmal subarachnoid hemorrhage
UIA or RIA	unruptured or ruptured intracranial aneurysm
(hr)QoL	(health-related) quality of life
SD	standard deviation
no	number
CI	confidence interval
MD	mean difference
ANOVA	analysis of variance
Acom	anterior communicating artery
ACA	anterior cerebral artery
MCA	medial cerebral artery
Pcom	posterior communicating artery
ICA	internal carotid artery
PICA	posterior inferior cerebellar artery
PCA	posterior cerebral artery

operative repair as well as the postoperative course can also be stressful and thus have an effect on QoL.[12,13]

In the last decades, subjective measures of functional outcome and health-related QoL after treatment have gained importance. However, the availability of data on QoL is still sparse. Most studies focus on the QoL after treatment and on comparison with QoL values of the general population.[14–19] Only few studies include preoperative QoL measures.[20,21] We collected both pre- and postoperative QoL data of patients undergoing microsurgical (clipping) or endovascular (coiling) treatment of one or more UIAs, as well as QoL scores of conservatively treated patients.

2. Objective

This study aimed to assess and compare the health-related QoL scores in patients diagnosed with one or more UIAs, comparing: 1) the different treatment modalities (conservative versus microsurgical clipping versus endovascular coiling) and 2) differentiating between the time before and after treatment.

3. Methods

3.1. Study design

We conducted a retrospective analysis of a prospective cohort of consecutive patients diagnosed with one or more UIAs referred to the Department of Neurosurgery at Inselspital, Bern University Hospital between October 2016 and July 2019. Starting from October 2016, every patient was asked to fill in the questionnaire, independent from the treatment status or time of diagnosis.

3.2. Patient selection and cohorts

A total of 422 consecutive patients diagnosed with one or more UIAs were asked to fill in the 15D questionnaire assessing QoL. All patients were recruited for the analysis, irrespective of the management plan.

Exclusion criteria

Patients who refused a general consent, patients without a medical record on the recommended management of the aneurysm, patients in whom an initially suspected aneurysm was not confirmed in later diagnostic imaging and patients who did not answer all of the 15 questions of the 15D QoL questionnaire were excluded. Also, patients without intradural UIAs (e.g. extradural aneurysms only) were excluded. One patient diagnosed with a concomitant high-grade glioma was equally excluded. As the experience of a subarachnoid hemorrhage most probably affects the QoL of patients, patients with a history of previous aSAH were excluded, too. Finally, patients who answered only one questionnaire between two or more operative interventions were excluded as well. Fig. 1 shows a flow chart of the patient selection process.

Additional patient recruitment

After the initial patient inclusion timeframe, in July 2019, patients diagnosed with intracranial aneurysms were kept being asked to fill in the 15D QoL questionnaire. These questionnaires were reviewed and checked until June 2020 for patients who had filled in questionnaires both before and after treatment (surgery or endovascular). Five out of

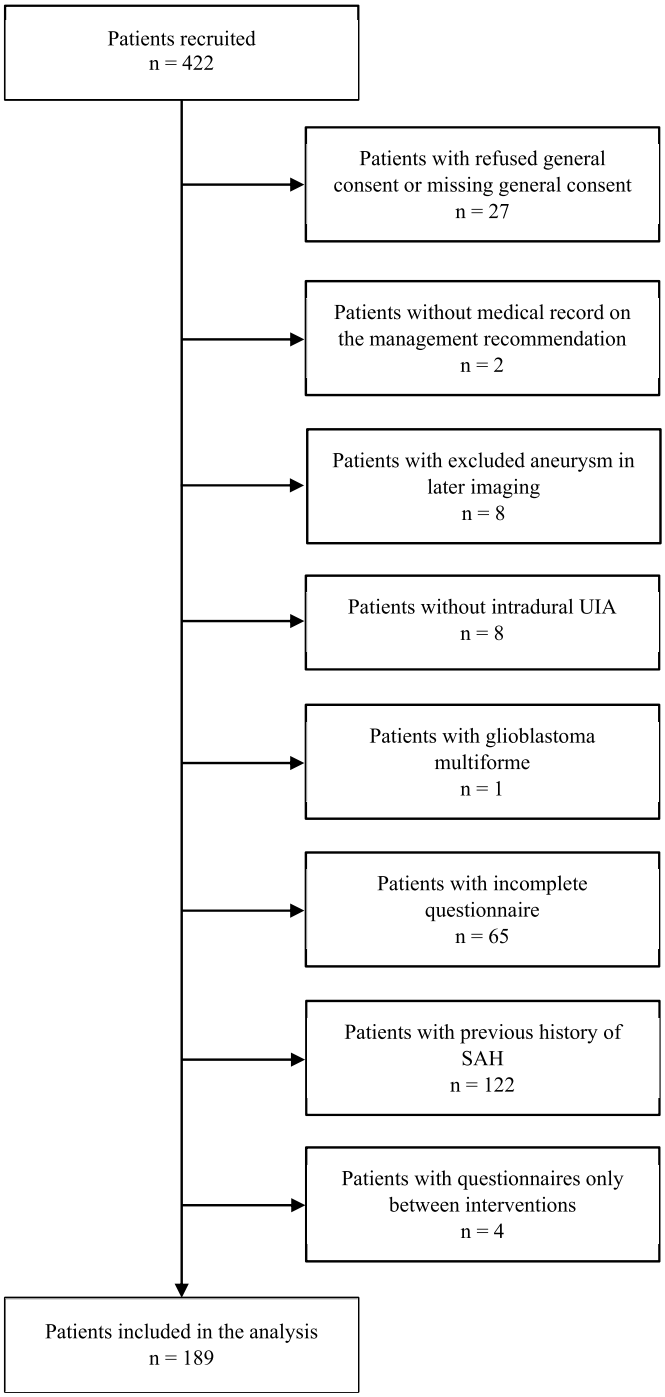

Fig. 1. Flow chart of the patient selection process.

the 189 initially included patients were identified to fulfil this condition. Their questionnaires from the more recent time period from July 2019 to June 2020 (1 year) were only included in the subgroup analysis of patients with questionnaires both before and after treatment.

Subgroups

Cases were categorized into different subgroups depending on their treatment (i.e. conservative vs. UIA occlusion) as well as their pre- or postoperative status at the time of filling the 15D QoL questionnaire.

For the purpose of the analysis and comparison of the QoL scores between treatment modalities but also between different time-points, the following groups were considered: conservative group (best medical treatment), preoperative group (either microsurgery and/or endovascular) or the postoperative group (either microsurgery and/or endovascular). The preoperative group included those patients for whom at least one intervention was planned or recommended but not yet performed. The postoperative group included all patients who had undergone at least one operative intervention (i.e. microsurgical clipping, endovascular coiling, or both).

After identifying those patients who filled in the questionnaires both before and after an intervention (as described above), this particular 'before-and-after-treatment' subgroup was further analysed separately.

Whenever patients had filled in more than one questionnaire in a certain 'time category' (i.e. more than one questionnaire before an intervention, after an intervention or during conservative treatment), only one questionnaire in that particular category was included in the calculation of means. For preoperative questionnaires as well as for questionnaires with conservative treatment, only the very first questionnaire was considered. For postoperative questionnaires, only the last questionnaire after treatment was considered in the analysis.

3.3. 15D questionnaire (15D QoL)

The quality of life was measured by use of the standardized 15D instrument of health-related quality of life questionnaire (15D QoL), which can either be used as a profile or as a single index score measure. The 15 dimensions are: mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity. For each dimension, the respondent chooses from 5 ordinal levels, based on whatever level describes his/her present state of health best. The index score (so-called 15D score) is represented on a continuous scale from 0 to 1 (0 being the worst and 1 the best) and is calculated based on the level values of each dimension using a series of population-based utility weights.[22] A change or difference in the 15D score of $\pm$ 0.015 is clinically important.[23] A change of $>$0.035 is considered to be a large improvement or deterioration in the health-related QoL.[23] Further properties of the instrument are described at http://15d-instrument.net/15d/.

Patients filled in the 15D questionnaire by themselves, without the help or interaction with the attending physician.

3.4. Data collection

In August 2019, in addition to the results of the questionnaires, a number of variables were collected from medical records of all patients: number of intracranial aneurysms, date of diagnosis, history of previous aSAH, treatment modality, date of treatment(s) and number of untreated aneurysms. The date of diagnosis was taken as the first radiological image confirming the diagnosis of UIA. Additionally, for the conservatively as well as preoperative patient group, the following variables were collected: hypertension, family history of ruptured or unruptured intracranial aneurysm (RIA/UIA), smoking status, size of the largest aneurysm and location of the largest aneurysm. The family history was considered positive when at least one first-degree relative had been diagnosed with a ruptured or unruptured intracranial aneurysm. Reason for the collection of these additional variables was the possible impact that these factors might have had on the way of informing and advising the patients on their diagnosis and the recommended treatment during the decision-making process. This by itself could have influenced the perception of the aneurysm by the patients and therefore also their QoL.

Data collection was performed retrieving radiological and clinical data stored in single's patient digital radiological and medical history.

3.5. Statistical analysis

All statistical analyses were performed using IBM® SPSS® Statistics Subscription software. Descriptive statistics were used to report frequencies, means, ranges, standard deviation (SD) as well as 95% confidence intervals (CI). Continuous variables such as age were presented as mean $\pm$ SD. The mean 15D QoL scores were presented as means with 95% CI and compared by use of independent samples *t*-tests (for the overall analysis), paired samples *t*-tests (for the 'before-and-after-treatment' subgroup analysis) or ANOVA (analysis of variance; for comparison of $>$2 groups) as appropriate. The baseline demographic variables 'sex', 'total number of aneurysms', 'location of the aneurysm', 'hypertension', 'family history of UIA or RIA' and 'smoking status' were compared using the chi-square test or Fisher's exact test for small samples. For comparison of mean age and mean size of the largest aneurysm, independent samples *t*-tests or ANOVA were performed. For the 15D profile analysis, the level values were assumed to not be normally distributed and were therefore compared by use of the Mann–Whitney *U* test (for comparison of two groups) or the Kruskal–Wallis test (for comparison of $>$2 groups). An alpha level of $p < 0.05$ was considered statistically significant.

3.6. Ethical considerations

The analysis was conducted according to the International Declaration of Helsinki and was approved by the local ethics committee (number KEK 2019–02415).

4. Results

4.1. Response to questionnaires

189 patients completed a total of 255 questionnaires, met the inclusion criteria and were considered eligible for the analysis (Fig. 1).

4.2. Pre- and postoperative subgroups

Table 1 shows the synopsis of the 189 patients regarding their pre- or postoperative status as well as the number of questionnaires per patient. 131 patients filled in one questionnaire, 52 patients filled in two, 4 patients filled in three and 2 patients filled in four questionnaires throughout the time period of the analysis.

Fig. 2 shows the categorization of all patients in the different groups.

Table 1
Pre- and postoperative cohorts and number of questionnaires.

Variable	Total n (%)
Total no. of patients	189 (100)
Conservative treatment	74 (39.2)
Intervention (surgical or endovascular repair)	115 (60.8)
Pat. with preoperative questionnaire(s) only	30 (15.9)
Pat. with postoperative questionnaire(s) only	60 (31.7)
Pat. with questionnaires before and after intervention(s)	25 (13.2)
No. of questionnaires per patient (% of all patients)	
Pat. with 1 questionnaire	131 (69.3)
Pat. with 2 questionnaires	52 (27.5)
Pat. with 3 questionnaires	4 (2.1)
Pat. with 4 questionnaires	2 (1.1)

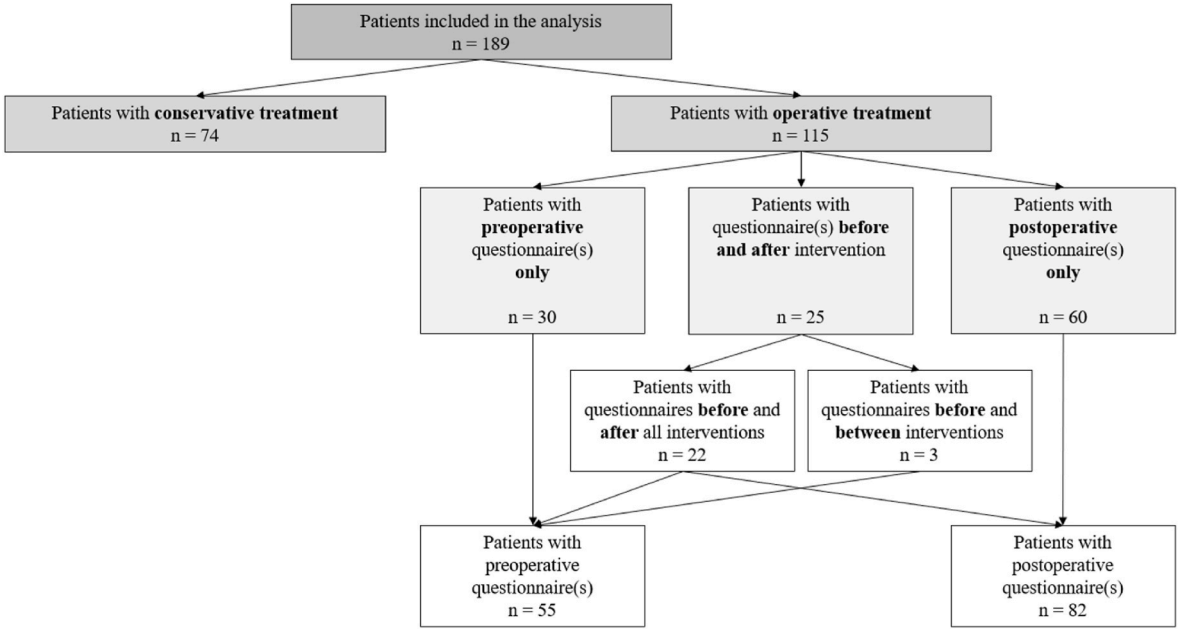

Fig. 2. Group categorisation.

4.2.1. Baseline characteristics

Out of the 189 included patients, 120 were women and 69 were men; their mean age at the time of completion of the questionnaire was 56.6 years (SD, 11.8 years) for women and 57.1 years (SD, 12.0 years) for men, respectively. 148 patients had one UIA and 41 patients had two or more UIAs.

Table 2 summarises the demographic characteristics and the number of UIAs of all patients as well as the conservative, preoperative and postoperative subgroups. Additionally, the mean size and location of their largest aneurysm, diagnosis of hypertension, family history of UIA or RIA as well as the smoking status for the conservative and the preoperative group are displayed. The only statistically significant difference was found in mean size of the largest aneurysm between the conservative and the preoperative group (conservative 4.8 ± 3.4 mm vs. preoperative 7.2 ± 2.9 mm, $p < 0.01$).

Table 2
Baseline characteristics for pre- and postoperative subgroups.

Variable	Total n (%)	Conservative (%)	Preoperative (%)	Postoperative (%)	*p* value
Total no. of patients	189 (100)	74 (100)	55 (100)	82 (100)	
Sex					
Male	69 (36.5)	30 (40.5)	17 (30.9)	28 (34.1)	0.50[b]
Female	120 (63.5)	44 (59.5)	38 (69.1)	54 (65.9)	
Mean age at time of questionnaire ± SD (years)	56.8 ± 11.9	57.7 ± 12.3	57.9 ± 10.5	55.2 ± 12.3	
Male	57.1 ± 12.0	58.0 ± 13.5	57.1 ± 10.4	56.2 ± 11.5	0.86[a]
Female	56.6 ± 11.8	57.5 ± 11.5	58.2 ± 10.7	54.6 ± 12.8	0.29[a]
Total no. of aneurysms					
Pat. with 1 aneurysm	148 (78.3)	61 (82.4)	45 (81.8)	61 (74.4)	0.40[b]
Pat. with ≥2 aneurysms	41 (21.7)	13 (17.6)	10 (18.2)	21 (25.6)	
		Conservative (%)	Preoperative (%)		*p* value
Mean size of largest aneurysm ± SD (mm)		4.8 ± 3.4	7.2 ± 2.9		0.000039[a]
Location of largest aneurysm					
ACOM		20 (27.0)	15 (27.3)		0.11[b]
ACA		6 (8.1)	4 (7.3)		
MCA		34 (45.9)	17 (30.9)		
Pcom		1 (1.4)	5 (9.1)		
ICA other than Pcom		8 (10.8)	8 (14.5)		
Basilar artery		3 (4.1)	1 (1.8)		
Vertebral artery (incl. PICA)		1 (1.4)	5 (9.1)		
PCA		1 (1.4)	0 (0.0)		
Hypertension					
Yes		42 (56.8)	35 (63.6)		0.43[b]
No		32 (43.2)	20 (36.4)		
Family history of UIA or RIA					
Yes		3 (4.1)	6 (10.9)		0.17[b]
No		71 (95.9)	49 (89.1)		
Smoking status					
Ever smoked		44 (59.5)	41 (74.5)		0.074[b]
Never smoked		30 (40.5)	14 (25.5)		

[a] Independent samples *t*-test or one-way ANOVA with post-hoc test.
[b] Chi-square test or Fisher's exact test.

4.3. Number of interventions and treatment modalities

Table 3 shows an outline of the treatment modalities and the number of interventions. 74 patients (39.2%) were treated conservatively and 115 patients (60.8%) were treated either by microsurgical clipping (61 patients, 53.0%), endovascular coiling (45 patients, 39.1%) or both clipping and coiling (9 patients, 7.8%). 96 patients (83.5%) were treated once, while 19 patients (16.5%) underwent ≥2 operative interventions (for either one UIA or multiples UIAs). Patients treated by endovascular coiling more often had multiple interventions (20.0%) compared to patients treated by microsurgical clipping (1.6%).

4.3.1. Baseline characteristics

Table 4 shows the baseline characteristics for the different treatment modalities.

4.4. Quality of life: mean 15D scores

The mean 15D QoL scores were compared between different cohorts and subgroups. Table 5 shows an overview of these comparisons.

4.4.1. Conservative treatment vs. preoperative patients

Patients treated conservatively had a similar mean 15D QoL score as patients that were in their preoperative status at the time of completion of the questionnaire (0.9020, 95% CI 0.8793–0.9247 versus 0.9057, 95% CI 0.8798–0.9316, $p = 0.83$).

4.4.2. Preoperative vs. postoperative patients

The mean 15D QoL score of patients who filled in their questionnaire after an intervention showed no statistically significant difference in quality of life compared to preoperative patients (preoperative 0.9057, 95% CI 0.8798–0.9316 versus postoperative 0.9063, 95% CI 0.8845–0.9281, $p = 0.97$). On average, postoperative patients filled in the questionnaire about two years after their treatment (mean 761 days, SD 920 days). Preoperative patients were operated after a mean of 85 days (SD 79 days) after filling in the questionnaire.

There was an improvement over time in the mean 15D score after UIA occlusion. After a transient reduction in the mean 15D QoL score, QoL scores returned to and exceeded preoperative scores (preoperative 0.9057, 95% CI 0.8798–0.9316 versus postoperative <1 year after treatment 0.8809, 95% CI 0.8383–0.9236 versus postoperative 1–3 years after treatment 0.9106, 95% CI 0.8810–0.9402 versus postoperative >3 years after treatment 0.9446, 95% CI 0.9184–0.9708). However, the mean differences between those subgroups were not statistically significant.

Table 3
Treatment modalities and number of operations.

Variable	Total n (%)	1 Operative intervention, n (%)	≥ 2 Operative interventions, n (%)
Treatment category			
Conservative	74 (39.2)	–	–
Interventional	115 (60.8)	96 (83.5)	19 (16.5)
Interventional modalities (% of all interventions)			
Microsurgical clipping	61 (53.0)	60 (98.4)	1 (1.6)
Endovascular coiling	45 (39.1)	36 (80.0)	9 (20.0)
Microsurgical clipping and endovascular coiling	9 (7.8)	0 (0.0)	9 (100)

* In parentheses: % of total number of each variable.

4.4.3. Microsurgical clipping and endovascular coiling

Patients treated by microsurgical clipping only had a reduced quality of life after treatment compared to preoperative patients (preoperative 0.9176, 95% CI 0.8874–0.9478 versus postoperative 0.8885, 95% CI 0.8566–0.9204). This mean difference was clinically relevant (i.e. difference in mean scores >0.015 [1]), but not statistically significant (MD 0.029, 95% CI -0.016 - 0.074, $p = 0.20$). (Table 6).

Patients treated by endovascular coiling showed a trend toward higher postoperative QoL compared to preoperative levels (preoperative 0.8972, 95% CI 0.8490–0.9454 versus postoperative 0.9426, 95% CI 0.9134–0.9719; MD -0.045, 95% CI -0.097 - 0.0061). Nonetheless, this mean difference was not statistically significant ($p = 0.10$).

Post-clipping patients filled in the questionnaire approximately one year after surgery, on average (mean 371 days, SD 669 days), while post-coiling patients had undergone their treatment more than three years prior to the questionnaire, on average (mean 1371 days, SD 1024 days).

4.5. Quality of life: 15D profile

Fig. 3 shows the mean level values of the 15 dimensions for the following cohorts: 'conservative', 'preoperative', 'conservative and preoperative' (combination of the conservative and the preoperative cohort), 'postoperative'. When comparing the values of postoperative to preoperative patients, the mean level values for the dimensions *hearing*, *breathing*, *sleeping*, *depression*, *distress*, and *vitality* were higher in postoperative patients. On the other hand, the mean values for the dimension *mobility*, *vision*, *speech*, *excretion*, *usual activities*, *mental function*, and *sexual activity* were lower in the postoperative cohort. For comparison of two groups, Mann–Whitney *U* tests were performed and for comparison of more than two groups, Kruskal–Wallis tests were performed as appropriate. However, these differences were not statistically significant.

Fig. 4 shows the mean level values for postoperative patients after clipping and after coiling respectively, compared to the 'conservative and preoperative' cohort. In about half of the dimensions, clipping and coiling had similar postoperative trends, A statistically significant difference was found in the dimensions *usual activities*, *mental function*, *vitality*, and *sexual activity* (p values < 0.05).

4.6. Quality of life: 'before-and-after-treatment' subgroup analysis

In total, 30 patients filled the questionnaires before their first and after their last operation and were eligible for the analysis. 21 were women (70.0%) and 9 were men (30.0%). Table 7 shows the baseline characteristics for all 30 patients.

Table 8 shows the mean preoperative and postoperative 15D scores. There was no clinically relevant difference in the preoperative and postoperative mean scores ($p = 0.73$). These findings correspond to the results of the overall analysis. However, the mean 15D QoL scores of the 30 patients in this specific subgroup were higher than the overall scores (i.e. mean 0.9333 in the subgroup compared to mean 0.9063 in the overall analysis).

5. Discussion

Health-related quality of life and functional outcome in patients with intracranial aneurysms have so far been measured by different outcome scales such as modified Rankin Scale (mRS), Short Form 36 (SF-36), EuroQoL-5D and others in the literature. In our analysis with the 15D questionnaire, the findings were comparable to those of other authors. We found that the mean 15D scores did not significantly differ between conservatively and operatively treated patients. This is consistent with findings of Buijs et al[14] and Li et al,[16] showing that QoL was comparable in patients with and without treatment. The awareness of having an operation performed on an unruptured aneurysm can either be reassuring and therefore reduce levels of anxiety or unsettling (due to

Table 4
Baseline characteristics for treatment modalities.

Variable	Total n (%)	Conservative (%)	Clipping (%)	Coiling (%)	Clipping and coiling (%)	*p* value
Total no. of patients	189 (100)	74 (100)	61 (100)	45 (100)	9 (100)	
Sex						
Male	69 (36.5)	30 (40.5)	21 (34.4)	15 (33.3)	3 (33.3)	0.85[b]
Female	120 (63.5)	44 (59.5)	40 (65.6)	30 (66.7)	6 (66.7)	
Mean age at time of questionnaire ± SD (years)	56.8 ± 11.9	57.7 ± 12.3	55.5 ± 13.1	57.6 ± 9.2	56.1 ± 10.1	
Male	57.1 ± 12.0	58.0 ± 13.5	54.8 ± 12.4	58.6 ± 8.9	61.7 ± 0.9	0.62[a]
Female	56.6 ± 11.8	57.5 ± 11.5	55.8 ± 13.6	57.2 ± 9.4	53.3 ± 11.6	0.80[a]
Total no. of aneurysms						
Patients with 1 aneurysm	148 (78.3)	61 (82.4)	49 (80.3)	35 (77.8)	3 (33.3)	0.02[b]
Patients with ≥2 aneurysms	41 (21.7)	13 (17.6)	12 (19.7)	10 (22.2)	6 (66.7)	

[a] One-way ANOVA with post-hoc test.
[b] Chi-square test or Fisher's exact test.

Table 5
QoL scores in conservative, preoperative and postoperative patients.

Patient subgroups	No. of patients	Mean 15D score (95% CI)	*p* value
a Conservative treatment	74	0.9020 (0.8793–0.9247)	
b Preoperative patients	55	0.9057 (0.8798–0.9316)	a vs. b: 0.83[a]
c Postoperative patients	82	0.9063 (0.8845–0.9281)	b vs. c: 0.97[a]
Time after treatment			
d *< 1 year* postoperative	36	0.8809 (0.8383–0.9236)	b vs. d: 0.70[b]
e *1–3 years* postoperative	25	0.9106 (0.8810–0.9402)	b vs. f: 0.48[b]
f *> 3 years* postoperative	21	0.9446 (0.9184–0.9708)	d vs. f: 0.13[b]

[a] Independent samples *t*-test.
[b] One-way ANOVA with post-hoc test.

Table 6
QoL scores in patients treated by clipping and by coiling.

Patient subgroup	No. of patients	Mean 15D score (95% CI)	*p* value
Clipping			
a Preoperative	33	0.9176 (0.8874–0.9478)	
b Postoperative	48	0.8885 (0.8566–0.9204)	a vs. b: 0.20[a]
Coiling			
c Preoperative	19	0.8972 (0.8490–0.9454)	
d Postoperative	28	0.9426 (0.9134–0.9717)	c vs. d: 0.10[a]

[a] Independent samples *t*-test.

possible complications) and thus increase feelings of anxiety. In our study, these phenomena seemed either not to play a relevant role or compensate each other.

It is important to differentiate between patients with unruptured intracranial aneurysms and patients that previously suffered from an aSAH as the experience of such a devastating event potentially has a major psychological impact and thus reduces QoL. For this reason, patients with a history of aSAH were excluded from our study.

Overall, postoperative QoL was comparable to preoperative measures. Our results confirm previous studies showing that treatment of unruptured intracranial aneurysms has a negative impact on QoL in the short term, but that eventually, QoL returns to preoperative levels or even improves after about one to three years.[18,20,21] The analysis of those patients with both 'before-and-after-treatment' QoL assessments confirmed this trend. Small numbers preclude the comparison between different treatment modalities over time.

One of the limitations of the present study is the lack of data on working status and ability to return to work, postoperative complications and treatment-related symptoms. Adverse events have a big impact on the well-being and the health-perception of a patient and therefore play a vital role in QoL evaluation. Hence, the actual impact on our postoperative results remains unclear.

Another confounding factor is the way patients are informed and advised on their aneurysm and the recommended treatment. As there was no unified education on the diagnosis, this might have been a source of bias on patient's perception and QoL. Depending on different variables such as patient age, location and size of the aneurysm, family history of ruptured or unruptured intracranial aneurysms, smoking status as well as other possible risk factors, the life-time risk of rupture of a particular aneurysm potentially differs. This could have affected the discussion between physician and patient and impact on the QoL for single patients. Comparing the distribution of these possible confounding variables between the conservative and the preoperative group, we only found a significant difference in mean size of the aneurysm.

Another limitation is the generic nature of the 15D questionnaire. Besides neuropsychological and psychosocial functions such as 'mental function', 'depression' or 'distress', several dimensions focus on more physical aspects of QoL such as 'mobility', 'eating' or 'breathing'. As intracranial aneurysms presumably have bigger impact on psychological compared to physical functions, psychological effects on QoL may be understated by unaltered dimensions which are unrelated to the aneurysm. However, the 15D profile (see chapter 4.5. 'Quality of life: 15D profile') partly accounts for this by itemizing the different dimensions and giving each dimension a comparable value so that changes in QoL can be attributed more precisely.

The independence of the patients in the preoperative and the postoperative cohort places a limitation on the comparability of the mean scores of these cohorts. Ideally, all patients would have filled in questionnaires before and after their treatment and pairwise statistical analysis could have been performed like in the 'between-and-after-treatment' subgroup analysis in chapter 4.6. However, possible dissimilarities in our cohorts are a potential source of bias. We tried to account for this by comparing the variables 'sex', 'age' and 'total number of aneurysms' between the different cohorts. No statistically significant difference was found.

Microsurgical clipping seems to have a negative impact on QoL in the short term, whereas patients who underwent endovascular coiling showed a clinically relevant improvement in postoperative scores compared to preoperative levels. However, both mean differences were not statistically significant. This may be related to the small number of patients in the different subgroups. Furthermore, institutional guidelines on post-interventional follow-up at the study center recommend a longer follow-up after endovascular coiling due to higher risk of aneurysm relapses after endovascular coiling compared to microsurgical clipping.[4,23] Hence, the post-coiling subgroup had a notably longer mean postoperative follow-up time compared to the post-clipping subgroup (1371 vs. 371 days), which presumably contributed to the higher mean QoL scores in the coiling cohort. Whether this is due to the reassurance of patients by periodic postoperative examination after endovascular coiling, due to the longer recovery time or related to the

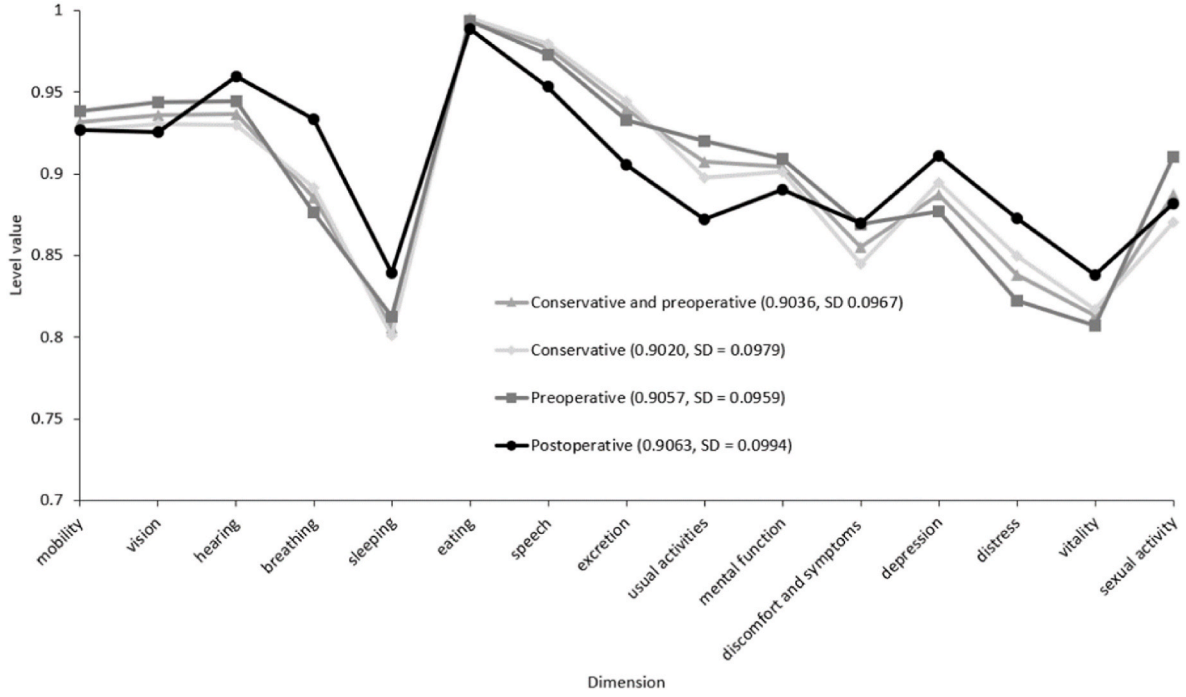

Fig. 3. 15D profile of different cohorts – 'conservative', 'preoperative', 'conservative and preoperative', and 'postoperative'
p values for all 15 variables >0.05.

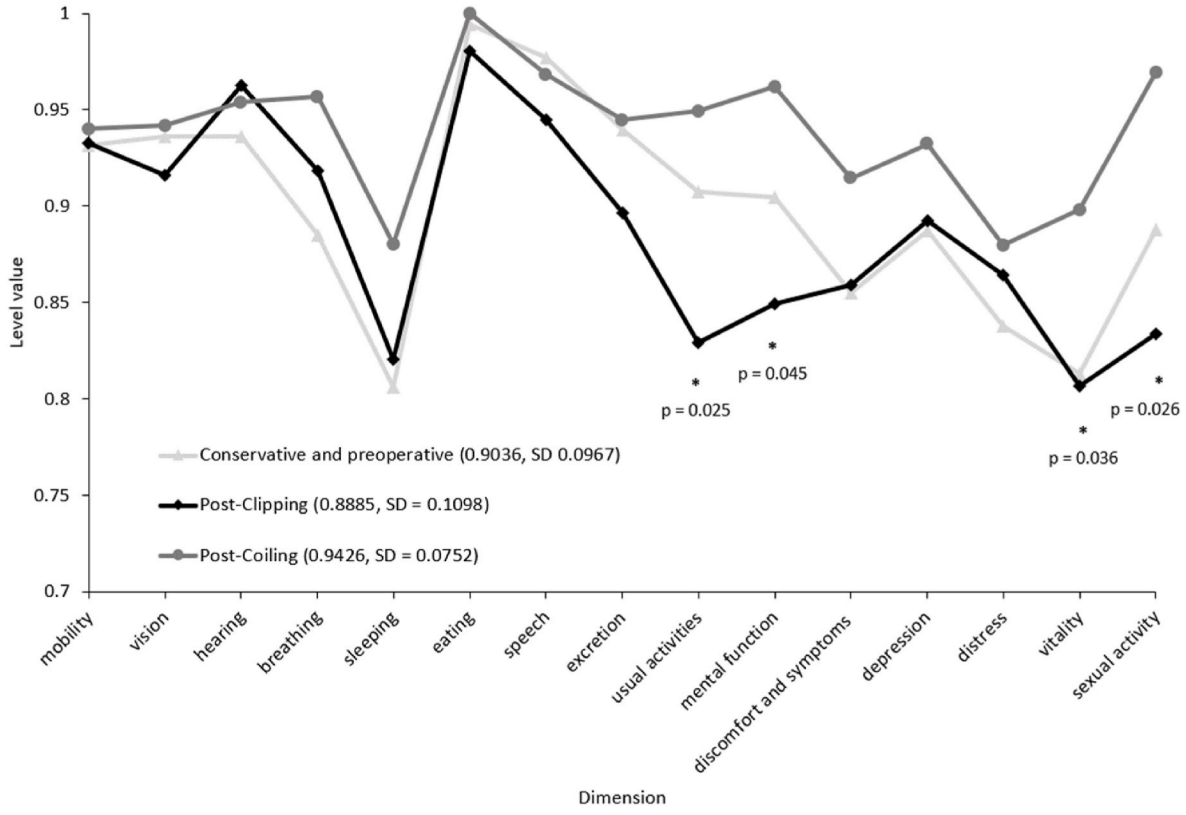

Fig. 4. *15D profile of different cohorts – 'conservative and preoperative', 'post-clipping', and 'post-coiling'*
* Statistically significant differences are indicated with asterisks.

different treatment modality, remains unclear.

The 15D profile showed a more itemised comparison of the treatment methods. The statistically significant differences in the dimension *usual activities*, *mental function*, *vitality*, and *sexual activity* between treatment modalities can possibly be attributed to the nature and the associated prolonged recovery of surgery compared to the endovascular treatment. Here as well, the post-coiling subgroup had a notably longer mean postoperative follow-up time compared to the post-clipping subgroup,

Table 7
Baseline characteristics for the 'before-and-after-treatment' subgroup.

Variable	Total n (%)
Total no. of patients	30 (100)
Sex	
Male	9 (30.0)
Female	21 (70.0)
Mean age at time of questionnaire ± SD (years)	57.2 ± 12.0
Male	54.5 ± 11.5
Female	58.4 ± 12.1
Total no. of questionnaires	69
Total no. of aneurysms	
Pat. with 1 aneurysm	24 (80.0)
Pat. with ≥2 aneurysms	6 (20.0)

Table 8
Preoperative and postoperative QoL scores.

Variable	No. of patients	Mean 15D score (95% CI)	*p* value
a Preoperative	30	0.9288 (0.9053–0.9522)	
b Postoperative	30	0.9333 (0.9076–0.9590)	a vs. b: 0.73[a]

[a] Paired samples *t*-test.

which presumably contributed to the higher scores for these specific modalities in the coiling cohort. For the dimensions *sleeping*, *depression*, *distress*, and *vitality*, the observed trend for improvement after treatment could potentially be reconducted to the fact that patients no longer have to fear a possible UIA rupture.

Controversial findings can be found in the literature regarding influence of both open microsurgery and endovascular treatment on the QoL.[17,20,24]

Our results underline the need to conduct prospective multicentric studies incorporating socio-professional data, medical comorbidities, treatment modalities, complications and long-term follow-up. Despite the existing extensive published data about UIA natural history and morbidity associated with UIAs treatment, the impact of the different treatment pathways on QoL should be considered when advising single patients for treatment.

6. Conclusion

Health-related quality of life does not change significantly before and after occlusion of unruptured intracranial aneurysms. Patients treated with either microsurgical clipping or endovascular coiling experienced similar quality of life scores compared to conservatively treated patients. Despite not being statistically significant, we observed a trend towards short-term reductions and long-term recovery or even improvement in quality of life after aneurysm occlusion. Further studies are needed to confirm long-term postoperative quality of life changes as well as treatment-related influencing factors on patients' quality of life.

Funding

Not applicable.

Ethical approval

The study was conducted according to the International Declaration of Helsinki and was approved by the local ethics committee (number KEK 2019–02415).

CRediT authorship contribution statement

Francis J. Kissling: Writing – original draft, Methodology, Formal analysis, Data curation. **Johannes Goldberg:** Writing – review & editing. **Andreas Raabe:** Writing – review & editing, Supervision. **David Bervini:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We thank Mrs Nicole Söll for collecting and monitoring the data of 15D QoL questionnaires.

References

1. Vlak MH, Algra A, Brandenburg R, Rinkel GJ. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. *Lancet Neurol*. 2011;10(7):626–636. https://doi.org/10.1016/s1474-4422(11)70109-0.
2. Hop JW, Rinkel GlJ, Algra A, Van Gijn J. Case-fatality rates and functional outcome after subarachnoid hemorrhage: a systematic review. *Stroke; a journal of cerebral circulation*. 1997;28(3):660–664.
3. Mackey J, Khoury JC, Alwell K, et al. Stable incidence but declining case-fatality rates of subarachnoid hemorrhage in a population. *Neurology*. 2016;87(21):2192–2197.
4. Alshekhlee A, Mehta S, Edgell RC, et al. Hospital mortality and complications of electively clipped or coiled unruptured intracranial aneurysm. *Stroke; a journal of cerebral circulation*. 2010;41(7):1471–1476.
5. Bekelis K, Gottlieb DJ, Su Y, et al. Comparison of clipping and coiling in elderly patients with unruptured cerebral aneurysms. *J Neurosurg*. 2017;126(3):811–818.
6. Burns JD, Brown RD. Treatment of unruptured intracranial aneurysms: surgery, coiling, or nothing? *Curr Neurol Neurosci Rep*. 2009;9(1):6–12.
7. Campi A, Ramzi N, Molyneux AJ, et al. Retreatment of ruptured cerebral aneurysms in patients randomized by coiling or clipping in the International Subarachnoid Aneurysm Trial (ISAT). *Stroke; a journal of cerebral circulation*. 2007;38(5):1538–1544.
8. Darsaut TE, Findlay JM, Magro E, et al. Surgical clipping or endovascular coiling for unruptured intracranial aneurysms: a pragmatic randomised trial. *J Neurol Neurosurg Psychiatr*. 2017;88(8):663–668.
9. Investigators* C. Rates of delayed rebleeding from intracranial aneurysms are low after surgical and endovascular treatment. *Stroke; a journal of cerebral circulation*. 2006;37(6):1437–1442.
10. Kotowski M, Naggara O, Darsaut TE, et al. Safety and occlusion rates of surgical treatment of unruptured intracranial aneurysms: a systematic review and meta-analysis of the literature from 1990 to 2011. *J Neurol Neurosurg Psychiatr*. 2013;84(1):42–48.
11. Wiebers DO. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet*. 2003;362(9378):103–110. https://doi.org/10.1016/s0140-6736(03)13860-3.
12. King JT, Kassam AB, Yonas H, Horowitz MB, Roberts MS. Mental health, anxiety, and depression in patients with cerebral aneurysms. *J Neurosurg*. 2005;103(4):636–641.
13. Yoshimoto Y, Tanaka Y. Risk perception of unruptured intracranial aneurysms. *Acta Neurochir*. 2013;155(11):2029–2036.
14. Buijs JE, Greebe P, Rinkel GJ. Quality of life, anxiety, and depression in patients with an unruptured intracranial aneurysm with or without aneurysm occlusion. *Neurosurgery*. 2012;70(4):868–872.
15. Dammann P, Wittek P, Darkwah Oppong M, et al. Relative health-related quality of life after treatment of unruptured intracranial aneurysms: long-term outcomes and influencing factors. *Therapeutic advances in neurological disorders*. 2019;12,1756286419833492.
16. Li Y, Dai W, Zhang J. Anxiety, depression and quality of life in patients with a treated or untreated unruptured intracranial aneurysm. *J Clin Neurosci*. 2017;45:223–226.
17. Pala A, Pawlikowski A, Brand C, et al. Quality of life after treatment of unruptured intracranial aneurysms. *World neurosurgery*. 2019;121:e54–e59.
18. Raaymakers TW. Functional outcome and quality of life after angiography and operation for unruptured intracranial aneurysms. *J Neurol Neurosurg Psychiatr*. 2000;68(5):571–576.
19. Yamashiro S, Nishi T, Koga K, et al. Postoperative quality of life of patients treated for asymptomatic unruptured intracranial aneurysms. *J Neurosurg*. 2007;107(6):1086–1091.
20. Brilstra EH, Rinkel GJ, van der Graaf Y, et al. Quality of life after treatment of unruptured intracranial aneurysms by neurosurgical clipping or by embolisation with coils. *Cerebrovasc Dis*. 2004;17(1):44–52.
21. Yamashiro S, Nishi T, Koga K, et al. Improvement of quality of life in patients surgically treated for asymptomatic unruptured intracranial aneurysms. *J Neurol Neurosurg Psychiatr*. 2007;78(5):497–500.

22. Sintonen H. The 15D instrument of health-related quality of life: properties and applications. *Ann Med*. 2001;33(5):328–336.
23. Alanne S, Roine RP, Räsänen P, Vainiola T, Sintonen H. Estimating the minimum important change in the 15D scores. *Qual Life Res*. 2015;24(3):599–606.
24. Solheim O, Eloqayli H, Muller T, Unsgaard G. Quality of life after treatment for incidental, unruptured intracranial aneurysms. *Acta Neurochir*. 2006;148(8):821–830.