Quality of life outcomes over time in patients with unruptured intracranial aneurysms with and without preventive occlusion: a prospective cohort study

Algra, A.M.; Greving, J.P.; Wermer, M.J.H.; Walderveen, M.A.A. van; Schaaf, I.C. van der; Zwan, A. van der; ... ; Vergouwen, M.D.I.

RESEARCH ARTICLE

Quality of Life Outcomes Over Time in Patients With Unruptured Intracranial Aneurysms With and Without Preventive Occlusion

A Prospective Cohort Study

Annemijn M. Algra, MD, Jacoba P. Greving, PhD, Marieke J.H. Wermer, PhD, Marianne A.A. van Walderveen, PhD, Irene C. van der Schaaf, PhD, Albert van der Zwan, PhD, Johanna M.A. Visser-Meily, PhD, Gabriël J.E. Rinkel, FRCPE, and Mervyn D.I. Vergouwen, PhD

Correspondence
Dr. Algra
a.m.algra-3@umcutrecht.nl

Neurology® 2022;99:e1715-e1724. doi:10.1212/WNL.0000000000200831

Abstract

Background and Objectives

In counseling patients with an unruptured intracranial aneurysm (UIA), quality of life (QoL) outcomes are important for informed decision making. We evaluated QoL outcomes in patients with and without preventive aneurysm occlusion at multiple time points during the first year after UIA diagnosis and studied predictors of QoL outcomes.

Methods

We performed a prospective cohort study in patients aged ≥18 years with a newly diagnosed UIA in 2 tertiary referral centers in the Netherlands between 2017 and 2019. Patients were sent QoL questionnaires at 7 (aneurysm occlusion) or 5 (no occlusion) moments during the first year after diagnosis. We collected baseline data on patient and aneurysm characteristics, passive coping style (Utrecht Coping List), occlusion modality, and neurologic complications. We assessed health-related QoL (HRQoL) with the EuroQol 5 dimensions (EQ-5D), emotional functioning with the Hospital Anxiety and Depression Scale (HADS), and restrictions in daily activities with the Utrecht Scale for Evaluation of Rehabilitation–Participation (USER-P). We used a linear mixed-effects model to assess the course of QoL over time and to explore predictors of QoL outcomes.

Results

Of 153 eligible patients, 99 (65%) participated, of whom 30/99 (30%) underwent preventive occlusion. Patients undergoing occlusion reported higher baseline levels of passive coping, anxiety and depression, and restrictions than patients without occlusion. During recovery after occlusion, patients reported more restrictions compared with baseline (adjusted USER-P decrease 1 month post occlusion: −12.8 [95% CI −23.8 to −1.9]). HRQoL and emotional functioning gradually improved after occlusion (EQ-5D increase at 1 year: 8.6 [95% CI 0.1–17.0] and HADS decrease at 1 year: −5.4 [95% CI −9.4 to −1.5]). In patients without occlusion, the largest HRQoL improvement occurred directly after visiting the outpatient aneurysm clinic (EQ-5D increase: 9.2 [95% CI 5.5–12.8]). At 1 year, QoL outcomes were comparable in patients with and without occlusion. Factors associated with worse QoL outcomes were a passive coping style in all patients, complications in patients with occlusion, and higher rupture risks in patients without occlusion.

Discussion

After UIA diagnosis, QoL improves gradually after preventive occlusion and directly after counseling at the outpatient clinic in patients without occlusion, resulting in comparable 1-year QoL outcomes. A passive coping style is an important predictor of poor QoL outcomes in all patients with UIA.

MORE ONLINE

CME Course
NPub.org/cmelist

From the Department of Neurology and Neurosurgery (A.M.A., A.Z., G.J.E.R., M.D.I.V.), UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University; Julius Center for Health Sciences and Primary Care (J.P.G.), University Medical Center Utrecht, Utrecht University; Department of Neurology (M.J.H.W.), Leiden University Medical Center, Leiden University; Department of Radiology (M.A.A.W.), Leiden University Medical Center, Leiden University; Department of Radiology (I.C.S.), UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University; and Department of Rehabilitation (J.V.-M.), Physical Therapy Science and Sports, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, the Netherlands.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Glossary

EQ-5D = EuroQol 5 dimensions; **EQ-VAS** = EuroQol visual analog scale; **EVT** = endovascular treatment; **HADS** = Hospital Anxiety and Depression Scale; **HRQoL** = health-related QoL; **IQR** = interquartile range; **LUMC** = Leiden University Medical Center; **NST** = neurosurgical treatment; **QoL** = quality of life; **SAH** = subarachnoid hemorrhage; **UCL-P** = Utrecht Coping List; **UIA** = unruptured intracranial aneurysm; **UMCU** = University Medical Center Utrecht; **USER-P** = Utrecht Scale for Evaluation of Rehabilitation–Participation.

In management decisions on saccular unruptured intracranial aneurysms (UIAs), important factors that must be carefully balanced are risk of aneurysm rupture, risk of treatment complications, individual quality of life (QoL) aspects, and life expectancy.[1-4] In patients with an UIA, preventive aneurysm occlusion decreases the risk of aneurysmal subarachnoid hemorrhage (SAH), thereby reducing the number of life years with high QoL lost from SAH.[1,3,4] However, preventive aneurysm repair carries a risk of serious complications and patients who undergo preventive occlusion have to invest a certain amount of time in their recovery period during which they may have a reduced QoL and restrictions in their family, social, and worklife.[5,6] On the other hand, in patients without preventive occlusion, fear of aneurysm rupture can have a huge effect on QoL.[7,8] To enable patients to make informed choices about the risks and benefits of preventive occlusion, it is crucial to integrate QoL outcomes during counseling.[2,7] Previous studies have shown that a history of psychiatric disease and a passive coping style can negatively influence QoL in patients diagnosed with intracranial disease.[8-11] Most studies on QoL outcomes in patients with UIA so far have focused on QoL in patients who did not undergo aneurysm occlusion or only report on QoL changes after occlusion, with little data available on QoL preocclusion, QoL changes over time, or on predictors of QoL in these patients.[12,13] Therefore, we aimed to describe QoL outcomes in patients with UIA with and without preventive aneurysm occlusion at several time points during the first year after aneurysm diagnosis and to study which factors influence QoL outcomes.

Methods

Study Population

The study was conducted between January 2017 and October 2019 in 2 tertiary referral centers for aneurysm care in the Netherlands (University Medical Center Utrecht [UMCU] and Leiden University Medical Center [LUMC]). In both centers, standard clinical practice is to discuss UIA management options in a multidisciplinary team meeting directly after receiving the referral letter and imaging. Thereafter, the patient is invited to the outpatient aneurysm clinic for counseling with a physician experienced in aneurysm care. All adult patients aged ≥18 years with a newly detected UIA were eligible for our study. We excluded patients with a medical history of SAH or previously diagnosed UIA, patients with nonsaccular (fusiform or dissecting), mycotic, or flow-related aneurysms, and patients who were unable to complete questionnaires due to preexisting cognitive deficits, short life expectancy, or language barriers. Eligible patients were sent a letter about the purpose of the study and were contacted by phone before or directly after their initial visit to the outpatient clinic. Informed consent was obtained from all participants. Questionnaires were sent by email. If participants did not have an email address, questionnaires were sent by post. The study was approved by the Institutional Research Ethics Boards of the UMCU and the LUMC.

Data Collection

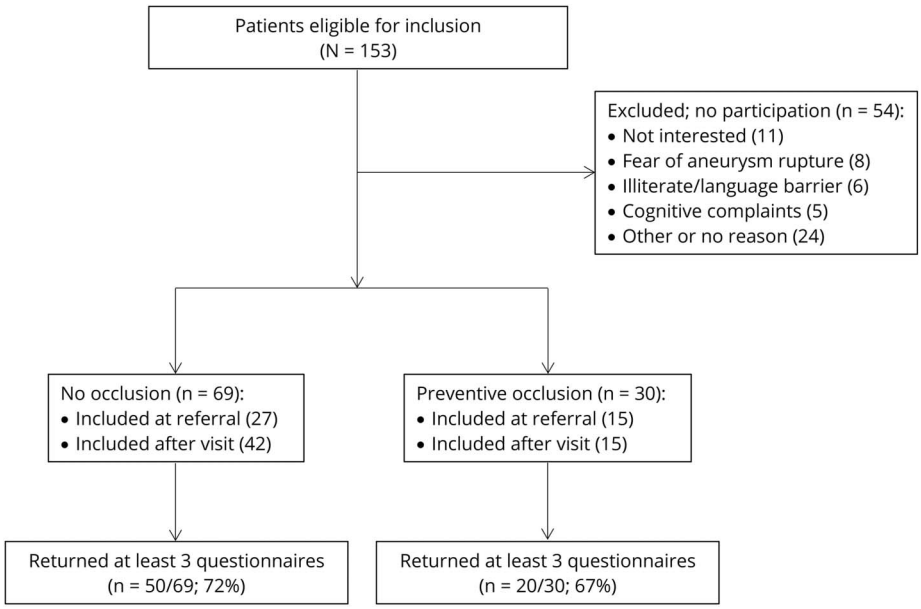
Patient and Aneurysm Characteristics

We recorded the following patient and aneurysm characteristics: age at aneurysm diagnosis, sex, medical and psychiatric history, reason of aneurysm detection, aneurysm multiplicity, size and location of the aneurysm, and rupture risk according to the PHASES score.[14] PHASES predicts the absolute 5-year risk of aneurysm rupture based on 6 patient and aneurysm characteristics: Population, Hypertension, Age, Size of aneurysm, Earlier SAH from another aneurysm, and Site of aneurysm. Scores range from 0 to 22 points, with associated risks ranging from 0.4% to 17.8%.[14] In case of preventive occlusion, we also collected data on occlusion modality, in-hospital neurologic complications, length of hospital stay, and discharge location. Patients were classified as having a psychiatric history if they were under psychological or psychiatric treatment or if the medical record reported the use of medication for depression, an anxiety disorder, or other psychiatric disorders. We assessed coping style at baseline with a subscale of the Utrecht Coping List (UCL-P).[15] The UCL-P consists of 7 items which can be scored on a 4-point scale ranging from 1 (seldom) to 4 (very often), resulting in a sum score between 7 (low) and 28 (high level of passive coping). High levels are considered unfavorable. We classified reason of aneurysm detection as incidental, symptomatic (symptoms of mass effect such as cranial nerve palsies, seizures, or ischemic event likely to be related to the aneurysm), or screening (familial or polycystic kidney disease). Occlusion modality was categorized into endovascular treatment (EVT, including coiling, balloon-assisted coiling, stent-assisted coiling, use of Woven-EndoBridge device, or use of flow-diverting stent) or neurosurgical treatment (NST; clipping only). We recorded all in-hospital neurologic complications resulting in clinical deterioration or death. Complications were scored as transient if clinical symptoms resolved within 30 days and were otherwise classified as persisting.

QoL Outcomes

Questionnaires were sent out at referral, after counseling at the outpatient clinic, and at 3 and 6 months and 1-year

Figure 1 Flowchart of Eligible Patients and Number of Questionnaires Sent Out and Returned



follow-up (eFigure 1, links.lww.com/WNL/C163). Patients who underwent preventive occlusion received additional questionnaires 2 and 4 weeks after treatment. We assessed QoL with 3 measures: health-related QoL (HRQoL), emotional functioning (levels of anxiety and depression), and restrictions in daily activities. HRQoL was measured with the EuroQol 5 dimensions (EQ-5D) questionnaire, emotional functioning with the Hospital Anxiety and Depression Scale (HADS), and restrictions in daily activities with the Utrecht Scale for Evaluation of Rehabilitation–Participation (USER-P).[16-18] The EQ-5D evaluates whether mild, moderate, or severe problems exist in one of the following domains: mobility, usual activities, pain or discomfort, self-care, and anxiety or depression. Taken together, the scores from all domains provide a descriptive EQ-5D health state that can be converted into a single overall HRQoL score ranging from 0 (worst) to 100 (best health). In addition, patients are asked to value their own HRQoL on a visual analog scale (EQ-VAS), also ranging from 0 (worst) to 100 (best imaginable health).[16] The HADS is a 14-item questionnaire, with scores ranging between 0 (low levels) and 42 (high levels of anxiety and depression).[17] The USER-P assesses participation in 11 activities, including vocational activities (work, study, and housekeeping), transport, leisure, and social activities. All items are scored between 0 (not possible at all) and 3 (no difficulty at all) or as not applicable. Sum scores can be converted to one overall score ranging from 0 (unfavorable) to 100 (favorable participation).[18]

Statistical Analysis

At baseline, we calculated median PHASES scores with interquartile ranges (IQRs) and mean UCL passive reaction patterns with SDs for patients with and without aneurysm occlusion. The cohorts were compared using the χ^2 or Student *t* test as appropriate. For patients with aneurysm occlusion, we also reported the rate of in-hospital neurologic complications. Based on the distribution of data, we calculated mean EQ-5D sum scores, EQ-VAS scores, HADS sum scores, and USER-P sum scores at baseline and during follow-up. We also calculated the proportion of patients with restrictions (scores ≤1) per individual USER-P activity at baseline and 1-year follow-up. We used a linear mixed-effects model with random intercept, random slope, and fixed time effects to assess the course of the EQ-5D, HADS, and USER-P sum scores over time in the cohorts with and without aneurysm occlusion and to explore predictors of QoL outcomes. We reported changes as mean differences with corresponding 95% CIs.

Results

Participants

In total, 153 patients who were referred with a newly diagnosed UIA met the inclusion criteria, of whom 99 (65%) participated (Figure 1). The most common reasons to decline participation were no interest (11 patients; 26%) and fear of aneurysm rupture (8 patients; 19%). Forty-two of the participants (42%) were included before their initial visit to the outpatient clinic and 57 participants (58%) directly after their initial clinic visit. During the study, 364/555 (66%) questionnaires were returned, of which 341 (94%) were complete. Three-quarters of the patients (70/99; 71%) returned at least 3 questionnaires. Return rates were comparable among patients with and without preventive aneurysm occlusion

Table 1 Baseline Characteristics for Included Patients

	Aneurysm occlusion	No aneurysm occlusion	*p* Value
Patient characteristics	n = 30	n = 69	
Women, n (%)	19 (63)	49 (71)	0.45
Mean age at diagnosis (SD)	57 (11)	63 (9)	0.01
Medical history, n (%)			
No comorbidity	3 (10)	5 (7)	0.64
TIA or stroke	6 (20)	16 (23)	0.73
Malignancy	1 (3)	7 (10)	0.25
Psychiatric history	4 (13)	5 (7)	0.33
Passive coping style			
Median UCL-P score (IQR)	5 (3–8)	3 (1–5)	0.03
Aneurysm characteristics	n = 30[a]	n = 89	
Aneurysm presentation, n (%)			
Incidental	24 (80)	63 (91)	0.05
Symptomatic	5 (17)	1 (1)	<0.01
Familial screening	1 (3)	5 (7)	0.92
Patients with ≥2 aneurysms, n (%)	3 (10)[b]	13 (19)	0.27
Median size of aneurysms in mm (IQR)	9 (6–12)	5 (4–7)	<0.01
Aneurysm location, n (%)			
Anterior cerebral arteries	9 (30)	17 (19)	0.61
Internal carotid artery	6 (20)	28 (31)	0.23
Posterior communicating artery	2 (7)	6 (7)	0.73
Other internal carotid artery	4 (13)	22 (25)	0.26
Middle cerebral artery	6 (20)	35 (39)	0.08
Posterior circulation	9 (30)	9 (10)	<0.01
Median PHASES score (IQR)	8 (6–9)	4 (3–5)	<0.01
Treatment characteristics	n = 29[a]	—	
Aneurysm occlusion modality, n (%)		—	—
NST	11 (38)		
EVT (any)	18 (62)		
Standard coil	6 (21)		
Advanced EVT	12 (41)		
In-hospital neurologic complication, n (%)	7 (24)	—	—
Transient complication	4 (14)		
Persisting complication	3 (10)		
Aneurysms occluded, n (%)	28 (97)	—	—
Days of hospitalization (range)	2 (2–10)	—	—
Transfer location, n (%)		—	—
Home	26 (90)		
Rehabilitation	3 (10)		

Abbreviations: EVT = endovascular treatment; IQR = interquartile range; NST = neurosurgical treatment; UCL-P = Utrecht Coping List–Passive.
[a] One patient was scheduled for EVT but did not undergo occlusion because of difficulties with the intubation procedure.
[b] Three patients in the aneurysm occlusion cohort had an additional aneurysm that was followed up.
Patients were classified as having a psychiatric history if they were under psychological or psychiatric treatment or if the medical record reported the use of medication for depression, an anxiety disorder, or other psychiatric disorders. Passive coping style was assessed at baseline with a subscale of the UCL-P. Sum scores range from 7 (low) to 28 points (high level of passive coping). The PHASES risk score assesses the absolute 5-year rupture rate.[14] Advanced EVT includes balloon-assisted coiling, stent-assisted coiling, the use of Woven-EndoBridge (WEB) devices, or the use of flow-diverting stents. Complications were scored as transient if clinical symptoms resolved within 30 days, and otherwise were considered persisting conservatively.

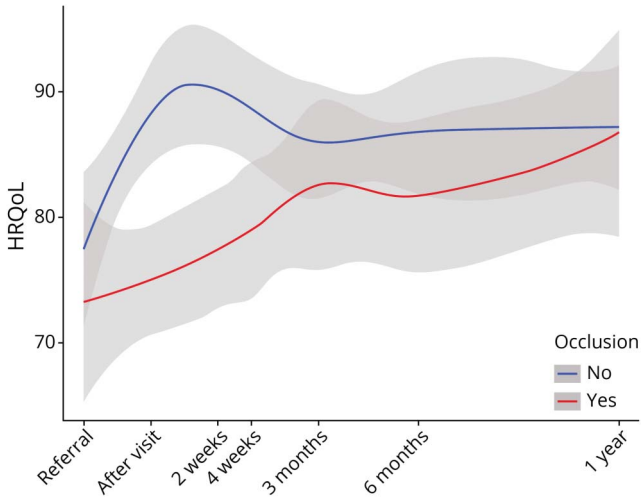
(Figure 1), but slightly lower among patients with treatment complications (4/7; 57%).

Patient and Aneurysm Characteristics at Baseline

Table 1 shows the baseline characteristics of the participating patients. Of the 99 participants, 30 underwent preventive aneurysm occlusion (11 [38%] underwent NST, and 18 [62%] EVT).

Patients with and without aneurysm occlusion did not differ in terms of sex or medical history, but patients with occlusion were younger than patients without occlusion (mean: 57 [SD 11] vs 63 years [SD 9]; $p < 0.01$) and had higher mean sum scores for passive coping style (occluded: median: 5/28 points [IQR 3–8] vs nonoccluded: 3/28 [IQR 1–5]; $p = 0.03$). In addition, compared with patients without occlusion, the aneurysms of patients with occlusion were more often symptomatic (5/30 [17%] vs 1/69 [1%]; $p < 0.01$), larger (9 mm [IQR 6–12] vs 5 mm [IQR 4–7]; $p < 0.01$), located in the posterior circulation (9/30 [30%] vs 9/69 [10%]; $p < 0.01$), and they had a higher 5-year rupture risk (median PHASES score: 8 points [IQR 6–9] vs 4 [IQR 3–5]; $p < 0.01$; Table 1). One patient was scheduled for EVT but did not undergo aneurysm occlusion because of difficulties with the intubation procedure. This patient only returned the questionnaires before treatment. Therefore, we left this patient in the preventive occlusion group for analyses of this time point. There were no crossovers in the nonocclusion group. Of the

Figure 2 HRQoL of Patients With UIA With and Without Preventive Aneurysm Occlusion Over Time



The graph illustrates the mean EQ-5D sum scores over time. The gray areas around the lines represent 95% CIs. HRQoL = health-related quality of life.

patients who underwent preventive occlusion, 4 patients (14%) had a transient neurologic complication and 3 patients (10%) a persisting neurologic complication. None of the patients with UIA had a SAH during follow-up.

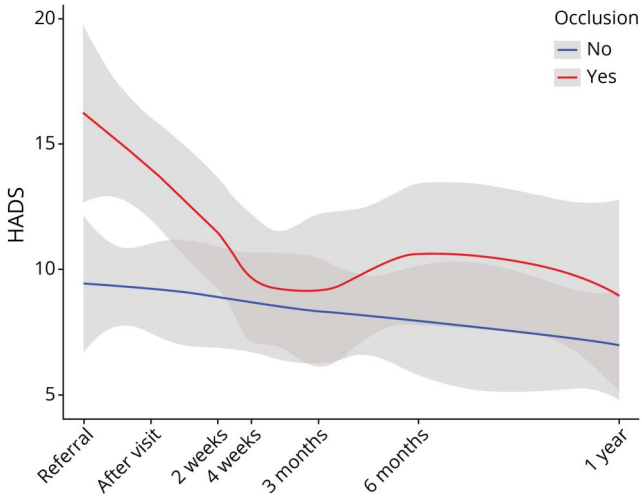
QoL Outcomes at Baseline

At baseline, HRQoL values were comparable for patients with (mean EQ-5D: 73.3; SD: 16.8) and without (77.4; SD: 17.7) preventive occlusion, as were EQ-VAS scores for both cohorts (Figure 2 and eTable 1, links.lww.com/WNL/C163) and HRQoL values according to treatment modality (eFigure 2 and eTable 2, links.lww.com/WNL/C163). In patients with aneurysm occlusion, baseline HADS sum scores were higher (mean: 15.7; SD: 7) than in patients without occlusion (9.4; SD: 6.8; Figure 3 and eTable 1, links.lww.com/WNL/C163). This was most pronounced among patients undergoing EVT (mean HADS: 19.4; SD: 9; eFigure 3 and eTable 2, links.lww.com/WNL/C163). USER-P sum scores were comparable for the cohort with aneurysm occlusion (mean USER-P sum score 78.4; SD: 15.6) and that without (86.5; SD: 15.5) (Figure 4 and eTable 1, links.lww.com/WNL/C163). Patients with aneurysm occlusion reported more restrictions at baseline than those with no aneurysm occlusion in the subdomains working life (9/12 [75%] vs 4/13 [31%]; risk difference: 44%; 95% CI 5%–69%), going out (9/14 [64%] vs 7/23 [30%]; risk difference: 34%; 95% CI 12%–58%), and activities outside home (11/14 [79%] vs 10/24 [42%]; risk difference: 37%; 95% CI 4%–59%; Figure 5 and eTable 3, links.lww.com/WNL/C163).

QoL Course Over Time

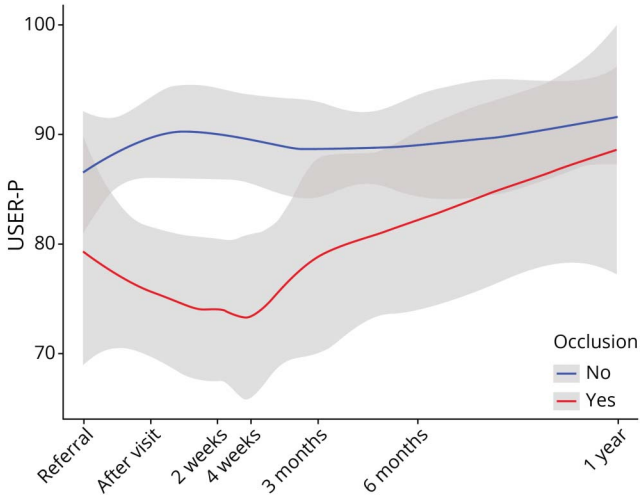
Unadjusted mean EQ-5D, HADS, and USER-P sum scores over time are given in eTable 1, links.lww.com/WNL/C163. The adjusted results from the mixed models on QoL changes over time are given in Table 2, Figures 2–4 (occlusion vs no occlusion) and eFigures 2–4, links.lww.com/WNL/C163 (according to aneurysm occlusion modality). In patients with preventive aneurysm occlusion, there was no HRQoL change after the initial visit to the outpatient clinic or during the recovery phase, but 1 year after UIA diagnosis, there was an improvement (mean adjusted EQ-5D sum score

Figure 3 Levels of Anxiety and Depression of Patients With UIA With and Without Preventive Aneurysm Occlusion Over Time



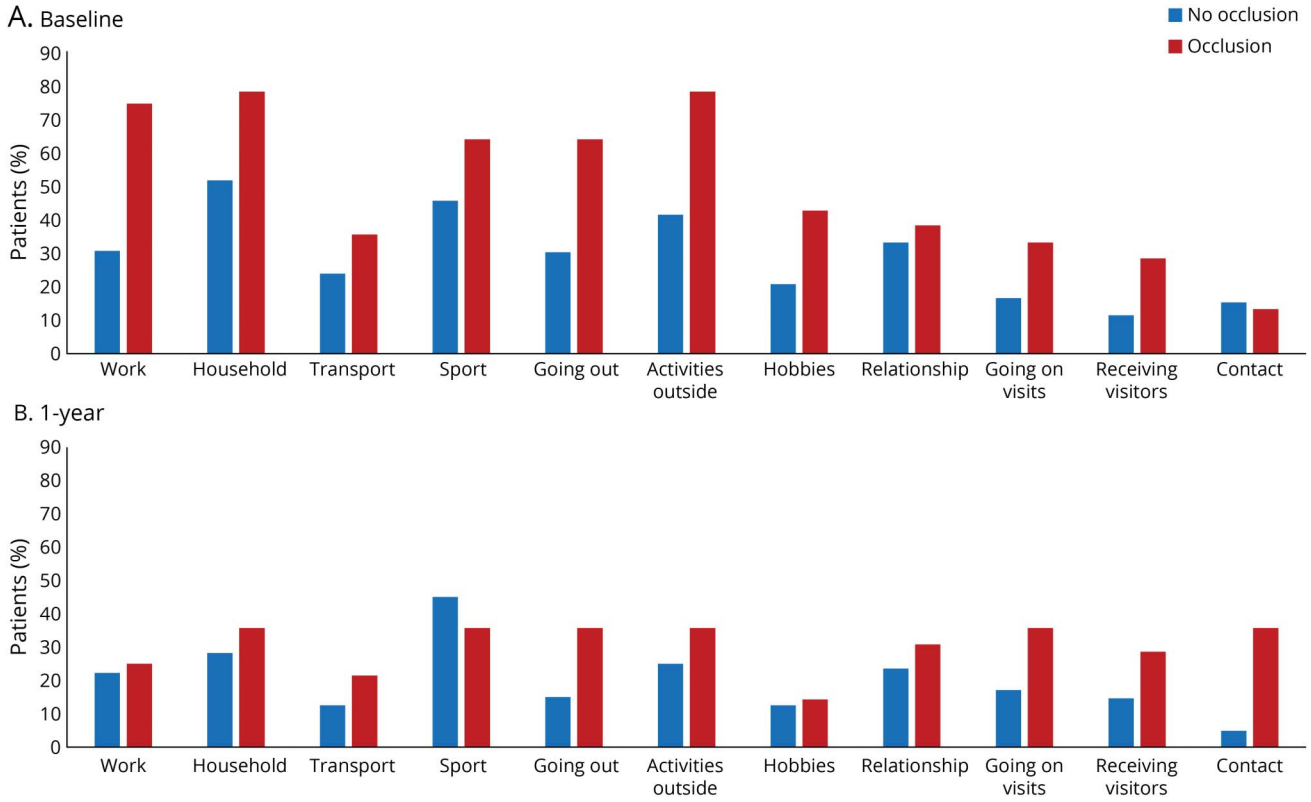
The graph illustrates the mean HADS sum scores over time. The gray areas around the lines represent 95% CIs. HADS = Hospital Anxiety and Depression Scale.

Figure 4 Levels of Restrictions in Participation of Patients With UIA With and Without Preventive Aneurysm Occlusion Over Time



The graph illustrates the mean USER-P sum scores over time. The gray areas around the lines represent 95% CIs. USER-P = Utrecht Scale for Evaluation of Rehabilitation–Participation.

Figure 5 Proportion of Patients With Restrictions for the Separate Daily Activities of the USER-P at Baseline (A) and 1-Year Follow-up (B)



USER-P = Utrecht Scale for Evaluation of Rehabilitation–Participation.

improvement at 1 year: 8.6; 95% CI 0.1–17.0; Figure 2 and Table 2), which was comparable for NST and EVT (eFigure 2, links.lww.com/WNL/C163). Compared with baseline, an improvement in HADS sum scores was seen at 1 month, 3 months, 6 months, and 1 year after occlusion (Figure 3, Table 2, and eFigure 3, links.lww.com/WNL/C163). During the recovery phase after aneurysm occlusion, more restrictions in daily activities were reported compared with baseline (mean USER-P sum score change at 1 month: −12.8; 95% CI −23.8 to −1.9; Figure 4 and Table 2), which was most pronounced among patients undergoing NST (eFigure 4, links.lww.com/WNL/C163). In patients without preventive aneurysm occlusion, the largest HRQoL improvement occurred directly after their initial visit to the outpatient clinic (EQ-5D sum score improvement: 9.2; 95% CI 5.5–12.8), with no changes in HADS or USER-P sum scores over time (Figures 2–4 and Table 2). For both cohorts, results for the separate EQ-5D subdomains mobility, self-care, usual activities, pain/discomfort, and anxiety/depression are given in eFigure 5, links.lww.com/WNL/C163. Results from the separate domains were comparable to the EQ-5D sum score patterns.

QoL Outcomes at 1-Year Follow-up

At 1-year follow-up, HRQoL did not differ between patients with (mean EQ-5D: 86.9; SD: 13.0 and EQ-VAS: 76.5; SD: 17.4) and without aneurysm occlusion (EQ-5D: 87.1; SD: 87.1 and EQ-VAS: 81.5; SD: 13.9; Figure 2 and eTable 1, links.lww.com/WNL/C163). Also, emotional functioning did no longer differ between the cohorts at 1 year (occluded: mean HADS: 8.9; SD: 5.9 vs nonoccluded: 7.0; SD: 6.6; Figure 3). Both patients with and without preventive aneurysm repair reported some restrictions in daily activities at 1 year, but no overall differences between the cohorts were seen (occluded: mean USER-P: 88.7; SD: 14.0 vs nonoccluded: 91.7; SD: 11.6; Figure 4). The baseline differences between patients with and without aneurysm occlusion in restrictions in working life, going out, and activities outside home were no longer seen (eTable 3, links.lww.com/WNL/C163), but patients with preventive occlusion did report more restrictions in contact with other people compared with patients without occlusion (2/41 [36%] vs 5/14 [5%]; risk difference: 31%; 95% CI 8%–57%; Figure 5 and eTable 3, links.lww.com/WNL/C163). We found no differences in HRQoL, emotional functioning, and restrictions in daily activities between patients with NST and EVT at 1 year (eFigures 2–4 and eTable 2, links.lww.com/WNL/C163).

Predictors of QoL Outcomes

After adjusting for covariates, higher levels of passive coping (specified per additional point on the UCL-P) negatively

Table 2 Results From Mixed-Model Analysis Assessing the Changes in QoL Outcomes of Patients With UIA With and Without Preventive Aneurysm Occlusion Over Time (Part A) and According to Predictors (Part B)

	HRQoL (EQ-5D) coefficient (95% CI)		Emotional functioning (HADS) coefficient (95% CI)		Restrictions in daily activities (USER-P) coefficient (95% CI)	
Variables	**Aneurysm occlusion**	**No aneurysm occlusion**	**Aneurysm occlusion**	**No aneurysm occlusion**	**Aneurysm occlusion**	**No aneurysm occlusion**
Changes over time						
Time point						
Before outpatient clinic visit	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
After outpatient clinic visit	−0.8 (−7.4 to 5.8)	9.2 (5.5 to 12.8)	−1.1 (−4.3 to 2.0)	−0.6 (−2.7 to 1.4)	−1.7 (−11.8 to 8.4)	0.3 (−4.4 to 5.1)
2 wks after occlusion	1.8 (−5.2 to 8.8)	—	−3.2 (−6.6 to 0.2)	—	−12.3 (−23.2 to −1.4)	—
4 wks after occlusion	0.7 (−6.6 to 8.1)	—	−4.9 (−8.4 to −1.5)	—	−12.8 (−23.8 to −1.9)	—
3 mo	7.3 (−0.1 to 14.7)	7.4 (3.1 to 11.6)	−6.2 (−9.5 to −2.9)	−1.2 (−3.4 to 0.9)	0.9 (−9.8 to 11.6)	−1.3 (−6.2 to 3.6)
6 mo	3.7 (−4.0 to 11.3)	6.9 (2.2 to 11.5)	−4.8 (−8.3 to −1.3)	0.7 (−1.6 to 3.0)	4.6 (−6.6 to 15.9)	−3.7 (−9.0 to 1.7)
1 y	8.6 (0.1 to 17.0)	6.9 (1.9 to 11.9)	−5.4 (−9.4 to −1.5)	−0.7 (−2.9 to 1.5)	7.4 (−5.4 to 20.2)	1.2 (−3.8 to 6.3)
Predictors[b]						
Female sex	2.1 (−6.5 to 10.7)	0.7 (−6.0 to 7.3)	1.2 (−3.2 to 5.6)	0.9 (−3.6 to 5.4)	0.3 (−19.0 to 19.5)	−6.8 (−16.7 to 3.1)
Age (continuous)	−0.2 (−0.6 to 0.2)	−0.1 (−0.4 to 0.3)	−0.1 (−0.3 to 0.1)	−0.1 (−0.3 to 0.1)	−0.00 (−0.9 to 0.9)	0.01 (−0.4 to 0.4)
Psychiatric history	15.7 (1.6 to 30.0)	3.0 (−7.8 to 13.8)	a	5.4 (−1.8 to 12.6)	a	−12.3 (−28.2 to 3.5)
Passive coping (per point increase in UCL-P)	−2.9 (−4.2 to −1.6)	−2.2 (−3.0 to −1.3)	1.4 (0.6 to 2.2)	1.5 (0.9 to 2.0)	−1.0 (−4.4 to 2.3)	−2.9 (−4.1 to −1.8)
Aneurysm size (continuous)	−0.4 (−1.7 to 0.9)	0.6 (−0.5 to 1.7)	−0.3 (−0.9 to 0.3)	−0.2 (−1.3 to 0.9)	−2.8 (−5.5 to −0.04)	−0.1 (−2.4 to 2.3)
Aneurysm rupture risk (per point increase in PHASES)	1.6 (−0.8 to 4.1)	−1.5 (−3.0 to 0.0)	0.3 (−1.1 to 1.7)	1.2 (0.1 to 2.3)	5.6 (−0.8 to 12.1)	−2.6 (−5.1 to −0.2)
Aneurysm occlusion modality						
NST	Ref.	—	Ref.	—	Ref.	—
EVT	1.2 (−6.9 to 9.4)	—	1.7 (−2.1 to 5.4)	—	−0.3 (−16.7 to 16.1)	—
In-hospital neurologic complication	−11.5 (−22.8 to −0.1)	—	4.6 (−1.6 to 10.7)	—	−17.9 (−45.2 to 9.3)	—

Abbreviations: UCL-P = Utrecht Coping List–Passive. PHASES = risk score assessing the absolute 5-year rupture rate; NST = neurosurgical treatment; EVT = endovascular treatment; EQ-5D = EuroQoL 5 dimensions; HRQoL = health-related quality of life; HADS = Hospital Anxiety and Depression Scale; USER-P=Utrecht Scale for Evaluation of Rehabilitation–Participation; Ref. = Reference.

[a] No patients with sum scores available.

[b] To estimate, for example, the HRQoL outcome for female sex at 1 year follow-up, you first add 8.6 to the reference value (the change in HRQoL over time) and subsequently add 2.1 (the influence of female sex). Patients were classified as having a psychiatric history if they were under psychological or psychiatric treatment or if the medical record reported the use of medication for depression, an anxiety disorder, or other psychiatric disorders. Passive coping style was accessed at baseline with a subscale of the UCL-P. Sum scores range from 7 (low) to 28 points (high level of passive coping). Complications were scored as transient if clinical symptoms resolved within 30 days, and otherwise were considered persisting.

influenced all QoL outcomes (HRQoL, emotional functioning, and participation in daily activities) in patients with and without aneurysm occlusion (Table 2).

A history of psychiatric disease was associated with a better HRQoL outcome in patients with preventive occlusion, but not in patients without aneurysm occlusion. Patients with in-hospital neurologic complications had a worse HRQoL outcome than patients without complications.

We found no differences according to aneurysm occlusion modality (Table 2 and eTable 2, links.lww.com/WNL/C163). In patients without preventive aneurysm occlusion, a higher absolute aneurysm rupture risk (specified per additional point on the PHASES score) was associated with worse outcomes in emotional functioning and more restrictions in daily activities.

Discussion

In this prospective cohort study, we found several differences between patients with and without preventive aneurysm occlusion at baseline and in their QoL trajectories over time but showed that QoL outcomes were comparable 1 year after UIA diagnosis. Initially, patients with aneurysm occlusion reported more restrictions during their recovery phase, but their HRQoL and emotional functioning gradually improved over time. In patients without aneurysm occlusion, the largest improvement in HRQoL occurred directly after the initial visit to the outpatient aneurysm clinic. Factors associated with worse QoL outcomes were a passive coping style in all patients, in-hospital complications in patients with preventive occlusion, and higher rupture risks in patients without occlusion.

Several previous studies reported on QoL aspects in patients with UIA, but most had a cross-sectional design and did not assess QoL outcomes at multiple standardized time points during follow-up.[12,13] We found 3 studies comparing patients with UIA with and without preventive aneurysm occlusion.[19-21] One study assessed QoL 6 months after preventive occlusion or study enrollment and reported a decrease in QoL in patients without preventive occlusion compared with patients with occlusion.[19] Two cross-sectional studies reported no differences in QoL outcomes between patients with and without preventive occlusion but found that overall QoL outcomes in patients with UIA were reduced compared with reference populations. In contrast, the QoL outcomes in patients with and without preventive aneurysm occlusion of our study are comparable to EQ-5D measurements and HADS values from general populations in the literature 1 year after UIA diagnosis.[22,23] The longer time between diagnosis and QoL assessment may have resulted in fewer fully recovered patients participating in previous studies.[20,21]

The baseline differences in emotional functioning and restrictions we found between patients with and without occlusion could, at least partly, be explained by confounding by indication. Larger aneurysms with a higher risk of rupture are more likely to be occluded preventively, which may introduce more fear of rupture and restrictions in daily activities in patients with preventive occlusion than in patients without. These differences in QoL measures may even be present before the formal treatment decision has been made, depending on what the referring physician has already discussed with the patient at the time of UIA diagnosis. Some physicians may have hinted toward the need for preventive occlusion. Alternatively, the higher levels of passive coping and reduced emotional functioning at baseline in patients with preventive aneurysm occlusion may also reflect differences in individual coping style and other psychological characteristics or personality traits. These factors can influence the process and outcome of decision making in that sense that patients with more fear of rupture and more perceived restriction in daily life activities may be more inclined to opt for preventive occlusion. These baseline differences in individual coping style and other psychological characteristics or personality traits may then introduce QoL differences at baseline and over time.[8,9,24]

Four previous studies assessed QoL outcomes in patients with UIA with preventive aneurysm occlusion with measurements before occlusion and at 3 months and 1 year after occlusion.[25-28] The results from these studies are in line with our finding that QoL improved between 3 months and 1 year post-occlusion, with an initial decrease in QoL in the short term. However, in contrast with our study, QoL outcomes in previous studies did not fully return to preocclusion levels at 1-year follow-up, and in 1 study, it took up to 3 years for QoL outcomes to normalize postclipping.[27] One explanation for this discrepancy may be that preventive aneurysm care, including options for aneurysm occlusion and treatment risks, has changed substantially since the previous studies were performed.[5]

We found that a substantial proportion of patients with preventive occlusion reported restrictions in daily activities, including working life, prior to occlusion. One previous study compared employment status preocclusion and postocclusion and found that a considerable proportion of patients with UIA had a suboptimal employment status before occlusion.[28] This could indicate that a reduced working capability following aneurysm repair is not solely attributable to the aneurysm occlusion itself, but may also be influenced by baseline patient and aneurysm characteristics and what a physician discusses with the patient.[12,21] Some physicians may advise patients with UIA to take it easy during the recovery phase after occlusion.

None of the previous studies in patients with UIA compared QoL outcomes before and after the initial visit to an outpatient aneurysm clinic. One previous study in patients with abdominal aortic aneurysms described that patients experience the conservative nature of surveillance as reassuring.[29] A similar mechanism may apply for intracranial aneurysms. Both relief that no invasive treatment is needed and reassurance

that the aneurysm has a low rupture risk are likely to play a role in a positive counseling effect.

Our study has some limitations. First, our study population is relatively small and may represent a selected group, as not all eligible patients with UIA participated in our study. Some patients declined the invitation to participate because of fear for aneurysm rupture or a reduced QoL. This may have biased QoL measurements at baseline and over time and could, at least partly, explain why we found no differences in QoL outcomes between patients with UIA and the general Dutch population at 1-year follow-up.[19,20] Second, not all respondents returned all scheduled questionnaires, resulting in variation in group size and distribution during follow-up. However, because we sent out questionnaires at many time points, we had detailed and prospective tracking data for most patients and could account for missing data by using robust linear mixed-effects models.

The main strength of our study is that it was a prospective cohort study that assessed HRQoL, emotional functioning, and restrictions in daily activities simultaneously at several standardized moments during follow-up in both patients with UIA with and without preventive aneurysm occlusion. In addition, we report QoL outcomes before and after the initial visit to an outpatient aneurysm clinic. This enabled us not only to relate the QoL outcomes over time to differences that exist between patients with UIA with and without preventive occlusion but also to systematically compare QoL outcomes at several time points and to identify factors that influence QoL outcomes.

After UIA diagnosis, QoL improves gradually after preventive occlusion and directly after counseling at an outpatient aneurysm clinic in case of no occlusion. QoL outcomes were eventually comparable in patients with and without preventive aneurysm occlusion at 1-year follow-up. Factors associated with worse QoL outcomes were a passive coping style in all patients, complications in patients with preventive occlusion, and higher rupture risks in patients without occlusion. The differences we found in the trajectories of QoL recovery between patients with and without preventive aneurysm occlusion, and the associated amount of time spent with a reduced QoL, should be part of shared decision making in UIA management. This can be realized by adding QoL data to patient information cards or videos or by using tools that assess the needs and preferences of patients during counseling, such as the time trade-off method to assess how many QALYs a patient is willing to invest in different treatment options.[7,30] During counseling, patients can be informed that although QoL trajectories differ in the first year between patients undergoing preventive occlusion and patients without preventive aneurysm occlusion, at the end of this year, QoL is on group level similar for these 2 groups. In addition, it is important to identify patients with an unfavorable coping style early following aneurysm diagnosis. By introducing a short intake questionnaire at the outpatient aneurysm clinic, the process of shared decision making, patient guidance, and education following diagnosis may be further improved.[30,31] Future studies should assess, ideally in a randomized setting, whether such new counseling approaches can improve QoL outcomes.[32]

Study Funding

This study was funded by a personal grant from the Dutch Heart Foundation (AMA; Dr. Dekker Grant 2016T023).

Disclosure

This study was funded by a personal grant from the Dutch Heart Foundation (AMA; Dr. Dekker Grant 2016T023); M.D.I. Vergouwen was supported by a Clinical Established Investigator grant from the Dutch Heart Foundation (2018T076). Go to Neurology.org/N for full disclosures.

Publication History

Received by *Neurology* September 5, 2021. Accepted in final form April 22, 2022.

Appendix Authors

Name	Location	Contribution
Annemijn M. Algra, MD	Department of Neurology and Neurosurgery, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; and analysis or interpretation of data
Jacoba P. Greving, PhD	Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; and analysis or interpretation of data
Marieke J.H. Wermer, PhD, Professor	Department of Neurology, Leiden University Medical Center, Leiden University, Leiden, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content, and analysis or interpretation of data
Marianne A.A. van Walderveen, PhD	Department of Radiology, Leiden University Medical Center, Leiden University, Leiden, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content, and analysis or interpretation of data
Irene C. van der Schaaf, PhD	Department of Radiology, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content
Albert van der Zwan, PhD, Professor	Department of Neurology and Neurosurgery, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content, and analysis or interpretation of data
Johanna M.A. Visser-Meily, PhD, Professor	Department of Rehabilitation, physical therapy science and sports, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; and analysis or interpretation of data

Continued

Appendix *(continued)*

Name	Location	Contribution
Gabriël J.E. Rinkel, FRCPE, Professor	Department of Neurology and Neurosurgery, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; and analysis or interpretation of data
Mervyn D.I. Vergouwen, PhD	Department of Neurology and Neurosurgery, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; and analysis or interpretation of data

References

1. Etminan N, Rinkel GJ. Unruptured intracranial aneurysms: development, rupture and preventive management. *Nat Rev Neurol.* 2016;12(12):699-713.
2. Etminan N, Brown RD Jr, Beseoglu K, et al. The unruptured intracranial aneurysm treatment score: a multidisciplinary consensus. *Neurology.* 2015;85(10):881-889.
3. Brown RD Jr., Broderick JP. Unruptured intracranial aneurysms: epidemiology, natural history, management options, and familial screening. *Lancet Neurol.* 2014; 13(4):393-404.
4. Greving JP, Rinkel GJE, Buskens E, Algra A. Cost-effectiveness of preventive treatment of intracranial aneurysms: new data and uncertainties. *Neurology.* 2009;73(4): 258-265.
5. Algra AM, Lindgren A, Vergouwen MDI, et al. Procedural clinical complications, case-fatality risks, and risk factors in endovascular and neurosurgical treatment of unruptured intracranial aneurysms: a systematic review and meta-analysis. *JAMA Neurol.* 2019;76(3):282-293.
6. Backes D, Rinkel GJE, van der Schaaf IC, et al. Recovery to preinterventional functioning, return-to-work, and life satisfaction after treatment of unruptured aneurysms. *Stroke.* 2015;46(6):1607-1612.
7. Yoshimoto Y, Tanaka Y. Risk perception of unruptured intracranial aneurysms. *Acta Neurochir (Wien).* 2013;155(11):2029-2036.
8. Wenz H, Wenz R, Maros ME, Groden C, Schmieder K, Fontana J. The neglected need for psychological intervention in patients suffering from incidentally discovered intracranial aneurysms. *Clin Neurol Neurosurg.* 2016;143:65-70.
9. Fontana J, Wenz R, Groden C, Schmieder K, Wenz H. The preinterventional psychiatric history as a major predictor for a reduced quality of life after treatment of unruptured intracranial aneurysms. *World Neurosurg.* 2015;84(5):1215-1222.
10. 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. *Ther Adv Neurol Disord.* 2019;12:1756286419833492.
11. Visser MM, Heijenbrok-Kal MH, Spijker AV, Oostra KM, Busschbach JJ, Ribbers GM. Coping, problem solving, depression, and health-related quality of life in patients receiving outpatient stroke rehabilitation. *Arch Phys Med Rehabil.* 2015;96(8): 1492-1498.
12. Towgood K, Ogden JA, Mee E. Neurological, neuropsychological, and psychosocial outcome following treatment of unruptured intracranial aneurysms: a review and commentary. *J Int Neuropsychol Soc.* 2004;10(1):114-134.
13. Bonares MJ, de Oliveira Manoel AL, Macdonald RL, Schweizer TA. Behavioral profile of unruptured intracranial aneurysms: a systematic review. *Ann Clin Transl Neurol.* 2014;1(3):220-232.
14. Greving JP, Wermer MJH, Brown RD Jr, et al. Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies. *Lancet Neurol.* 2014;13(1):59-66.
15. Schreurs PJG, Van de Willige G, Brosschot JF, Tellengen B, Graus GMH. *Handleiding Utrechtse Coping Lijst UCL (Herziene Versie) [Manual Utrecht Coping List UCL (Revised Version)].* Swets & Zeitlinger; 1993.
16. Brooks R. EuroQol: the current state of play. *Health Policy.* 1996;37(1):53-72.
17. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1983;67(6):361-370.
18. Post MWM, Van der Zee CH, Hennink J, Schafrat CG, Visser-Meily JMA, Van Berlekom SB. Validity of the Utrecht scale for evaluation of rehabilitation-participation. *Disabil Rehabil.* 2012;34(6):478-485.
19. Towgood K, Ogden JA, Mee E. Psychosocial effects of harboring an untreated unruptured intracranial aneurysm. *Neurosurgery.* 2005;57(5):858-856; discussion 858-866.
20. Buijs JE, Greebe P, Rinkel GJE. Quality of life, anxiety, and depression in patients with an unruptured intracranial aneurysm with or without aneurysm occlusion. *Neurosurgery.* 2012;70(4):868-872.
21. 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.
22. Janssen MF, Szende A, Cabases J, Ramos-Goni JM, Vilagut G, Konig HH. Population norms for the EQ-5D-3L: a cross-country analysis of population surveys for 20 countries. *Eur J Health Econ.* 2019;20(2):205-216.
23. Spinhoven P, Ormel J, Sloekers PP, Kempen GI, Speckens AE, Van Hemert AM. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychol Med.* 1997;27(2):363-370.
24. Lemos M, Roman-Calderon JP, Calle G, Gomez-Hoyos JF, Jimenez CM. Personality and anxiety are related to health-related quality of life in unruptured intracranial aneurysm patients selected for non-intervention: a cross sectional study. *PLoS One.* 2020;15(3):e0229795.
25. Raaymakers TW. Functional outcome and quality of life after angiography and operation for unruptured intracranial aneurysms. On behalf of the MARS Study Group. *J Neurol Neurosurg Psychiatry.* 2000;68(5):571-576.
26. Brilstra EH, Rinkel GJE, van der Graaf Y, et al. Quality of life after treatment of unruptured intracranial aneurysms by neurosurgical clipping or by embolisation with coils. A prospective, observational study. *Cerebrovasc Dis.* 2004;17(1):44-52.
27. 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 Psychiatry.* 2007;78(5):497-500.
28. Haug T, Sorteberg A, Sorteberg W, Lindegaard KF, Lundar T, Finset A. Surgical repair of unruptured and ruptured middle cerebral artery aneurysms: impact on cognitive functioning and health-related quality of life. *Neurosurgery.* 2009;64(3):412-420; discussion 421-422.
29. Tomee SM, Gebhardt WA, de Vries JPP, Hamelinck VC, Hamming JF, Lindeman JH. Patients' perceptions of conservative treatment for a small abdominal aortic aneurysm. *Patient Prefer Adherence.* 2018;12:119-128.
30. Keij SM, van Duijn-Bakker N, Stiggelbout AM, Pieterse AH. What makes a patient ready for Shared Decision Making? A qualitative study. *Patient Educ Couns.* 2021; 104(3):571-577.
31. Mellema JJ, O'Connor CM, Overbeek CL, Hageman MG, Ring D. The effect of feedback regarding coping strategies and illness behavior on hand surgery patient satisfaction and communication: a randomized controlled trial. *Hand.* 2015;10(3): 503-511.
32. Ten Have IA, van den Bekerom MP, van Deurzen DF, Hageman MG. Role of decision aids in orthopaedic surgery. *World J Orthop.* 2015;6(11):864-866.