Prevalence and Risk Factors for Anxiety and Depression in Chinese Unruptured Intracranial Aneurysms Patients Treated by Endovascular Intervention

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Abstract

**Background**: Studies on anxiety and depression after treatment via endovascular intervention for unruptured intracranial aneurysm (UIA) patients are rare and controversial. We aimed to explore the prevalence of anxiety and depression among Chinese UIA patients treated by endovascular intervention and to identify which factors contribute to the development of these symptoms.

**Methods**: We performed a cross-sectional study of anxiety and depression in patients who underwent endovascular treatment for UIAs using the Hospital Anxiety and Depression Scale (HADS). The demographic, clinical and radiological data for all patients were retrospectively collected from the aneurysm database and medical records. Moreover, we utilized a large sample data and logistic regression analysis to investigate the risk factors for the anxiety and depression for these patients.

**Results**: Two hundred patients returned a completed questionnaire in this study. Of the 200 patients, 34 (17.0%) suffered from anxiety, and 31 (15.5%) suffered from depression after being discharged for 30.67±8.6 months. The multivariate analysis results indicated that treatment cost exceeding the annual household income was statistically significantly associated with anxiety (OR= 2.42, p= 0.03). Patients with shorter sleep time was statistically significantly associated with anxiety (OR= 1.51, p= 0.02) and depression (OR= 1.62, p= 0.007).

**Conclusion**: The prevalence of anxiety and depression in the UIA patients treated by endovascular intervention was 17.0% and 15.5% respectively. Treatment cost exceeding the annual household income was statistically significantly associated with anxiety. Patients with shorter sleep time was statistically significantly associated with anxiety and depression. Our findings provide valuable evidence for the clinical and psychological management of these patients.

**Background**

Unruptured intracranial aneurysm (UIA) is a common disease with a prevalence approximately 7% in Chinese adults aged 35 to 75 years[1]. In addition, advances in and the increasing availability of high-resolution imaging technologies have led to a higher rate of incidentally detected UIAs[1, 2]. Once aneurysm ruptured, its typically cause subarachnoid hemorrhage (SAH) and sequelae, resulting in significant morbidity and mortality[3, 4]. Anxiety and depression are common in aneurysm disease
and both are important determinants of quality of life in patients[5, 6]. The threat of rupture becomes most obvious cause on the preoperative anxiety and depression in patients with UIA[5, 7, 8]. However, studies on anxiety and depression after treatment via endovascular intervention for UIA patients are rare and controversial[5, 9, 10]. We aimed to explore the prevalence of anxiety and depression among Chinese UIA patients treated by endovascular intervention and to identify which factors contribute to the development of these symptoms.

Methods

Study Design and participants

A cross-sectional study was performed. We retrospectively reviewed the hospital database for all consecutive UIA patients who underwent endovascular treatment in the Department of Neurosurgery, Xuanwu Hospital of Capital Medical University, from January 1, 2015, to May 31, 2017. The inclusion criteria were as follows: (1) Patients diagnosed by digital subtraction angiography (DSA) and treated with endovascular intervention. (2) Patients aged 18 to 75 years. The exclusion criteria were as follows: (1) Patients with traumatic, mycotic, bacterial, dissecting or fusiform aneurysms. (2) Patients with a history of subarachnoid hemorrhage or cerebral hemorrhage due to aneurysms or other causes. (3) Patients that died during the follow-up period. (4) Patients with a history of treatment for intracranial aneurysms (including microsurgical or endovascular treatment). Ultimately, a total of 300 patients were included in this study.

Assessment Instrument

The Hospital Anxiety and Depression Scale (HADS) is a promising tool for identifying and quantifying depression and anxiety in physically ill patients[11, 12]. Therefore, the HADS was used to evaluate anxiety and depression in UIA patients. The HADS is composed of seven items related to anxiety symptoms and seven related to the depression symptoms, with 14 items in total[12, 13]. All of the 14 items are answered by patients using a four-point Likert scale. These scores were calculated based on the sum of the questions used to evaluate the anxiety and depression domains. In this study, scores ≥8 were considered positive for both the anxiety and depression domains. The content of the questionnaire is mainly composed of the HADS. In addition, it includes important items such as
average daily sleep time, educational level, ratio of treatment costs and annual household income and physical exercise level within the last month, etc. A combined online questionnaire will be sent to those patients willing to respond.

**Data Collection**

We conducted a telephone follow-up of the 300 patients who met the inclusion and exclusion criteria, 270 of which were successfully followed up, for a follow-up rate of 90.0%. We sent the combined online questionnaire to those 228 patients who are willing to respond. Eventually, 200 patients returned a completed questionnaire, accounting for 66.7% of all 300 UIA patients. The follow-up time of the 200 patients was distributed between 18 and 45 months, and the average follow-up time was 30.67±8.6 months. The demographic, clinical and radiological data for all patients were retrospectively collected from the aneurysm database and medical records. A good neurological outcome was defined as an mRS score of 2 or less. Radiological follow-up examinations included magnetic resonance angiography (MRA), computed tomography angiography (CTA) or DSA.

**Statistical Methods**

Categorical variables were compared between the 2 groups using the Pearson $\chi^2$ test, continuity correction, and Fisher’s exact 2-tailed test. Continuous variables were compared between groups using Student’s t test. Interval data are reported as the mean±standard deviation, and nominal data are expressed as absolute numbers and valid percentages. Data were tested for normal distribution by making P-P and Q-Q plots. A logistic regression analysis was used to identify the association of the described variables with the anxiety and depression of patients. Candidate variables with P values less than 0.20 in univariate analyses were considered in the logistic regression analysis. Statistical significance was defined as $p < 0.05$. Statistical analysis was performed using SPSS Statistics version 24.0 software (IBM Corp., Armonk, New York, USA).

**Results**

**Demographic, Clinical and Radiological Characteristics**

Two hundred patients returned a completed questionnaires in this study. The information regarding all patients were shown in Table 1 and Table 2. Of the 200 patients, 117 were female and 83 were
male; their mean age was 55.2±9.48 years (range 23–74 years). They had a total of 245 aneurysms (161 patients had one aneurysm, 34 had two, 4 had three, and one had four), and the majority of aneurysms occurred in the anterior circulation (81.5%) (Table 2). All patients included in the study had a good preoperative mRS score (mRS 0-2), and 160 (80%) patients undwented stenting or flow diversion (FD) rather than 40 patients (20%) underwent simple coiling. Based on the results of neurological or radiological examination, treatment-related complications occurred in 8 patients due to ischemia. No technical failures were observed in our cohort; one patient with severe postoperative ischemic complications had an mRS of 5 at discharge, and the other patients exhibited good postoperative neurological outcomes (mRS=0-2). All patients presented a good neurological outcome (mRS=0-2) at follow-up. In our study, radiological follow-up was available for 167 patients, with a mean radiological follow-up period of 30.76±8.43 months; 7 patients experienced recurrence and had not received further treatment at follow-up. A complete summary of the demographic, clinical and radiological characteristics is shown in Table 1 and Table 2.

**Prevalence and Risk Factors of Anxiety and Depression**

As shown in Table 2, of the 200 UIA patients, 34 (17.0%) suffered from anxiety, and 31 (15.5%) suffered from depression after being discharged for 30.67±8.6 months. Table 3 summarizes univariate analyses of determinants of anxiety and depression. The independent variables with a univariate analysis result of P values less than 0.20 were included in the logistic regression analysis. Therefore, anxiety-related variables including education level, hypertension, ischemic cerebrovascular disease history, location of aneurysm, sleep time and ratio of treatment costs to annual household income were included; depression-related variables including gender, sleep time, ratio of treatment costs to annual household income were included. Table 4 presents the explanatory variables that were statistically significantly associated with anxiety and depression. The multivariate analysis results indicated that a treatment cost exceeding the annual household income was statistically significantly associated with anxiety (OR= 2.42, p= 0.03). Patients with shorter sleep time was statistically significantly associated with anxiety (OR= 1.51, p= 0.02) and depression (OR= 1.62, p= 0.007).
Discussion
A pattern of significant psychological impairment was found to be associated with harboring an identified but untreated UIA\cite{5, 14, 15}. For example, Towgood K et al\cite{14} reported that 36\% of untreated UIA patients presented with a pattern of significant psychosocial impairment 6 months post-treatment. Su SH et al\cite{5} reported that 84\% patients were found to be have mild to severe anxiety at 1 year after discovering the UIA. In addition, even 5 years after detection of the UIA, 39\% patients were mildly to severely depressed and 32\% patients had mild to severe anxiety. When an aneurysm was detected, many patients presented with complex psychological changes due to the confusion of disease-related knowledge and sudden changes in the physical role and physical function. As a result, the anxiety or depression emerge.

Studies reported that patients with a longer post-treatment time typically showed a lower anxiety and depression level than those of post-treatment time shorter\cite{5, 9}. This phenomenon indicated that patients may still feel anxiety or depression for a short term after treatments, for fearing of bleeding or recurrence of the aneurysms, then gets better over time. Nevertheless, there are still a considerable number of UIA patients who underwent microsurgery or endovascular treatment suffered from anxiety or depression. For example, Li Y et al\cite{9} reported that 18.2\% (n=8) of the clipping group had anxiety and 27.3\% (n=12) had depression, 17.6\% (n=13) of the coiling group had anxiety and 24.3\% (n=18) had depression. Solheim et al\cite{10} reported that 26.9\% (n=7) of the open surgery group suffered from anxiety and 19.2\% (n=5) suffered from depression, 31.6\% (n=6) of the endovascular coiling group suffered from anxiety and 10.5\% (n=2) suffered from depression. Unfortunately, the results of these research are limited by many factors such as little sample size, different assessment instrument and the cooperation of patients. Therefore, such issues need further study.

Nowadays, endovascular treatment of UIAs was considered a first-line strategy because of its superiority to microsurgical clipping in terms of both morbidity and mortality\cite{16, 17}. However, as we mentioned above, studies on anxiety and depression of UIA patients treated by endovascular intervention are rare and controversial. In addition, the risk factors of anxiety and depression for these patients need to be identified. This large cross-sectional study that took place over an average
period of 30.67±8.6 months evaluated the anxiety and depression outcomes in UIA patients who underwent endovascular treatment. In our study, we found that 34 (17.0%) patients suffered from anxiety, and 31 (15.5%) suffered from depression, which means that many patients are still in a state of psychological impairment after an average recovery period of 30.67±8.6 months. The multivariate analysis results indicated that treatment cost exceeding the annual household income was statistically significantly associated with anxiety. Obviously, excessive financial burden tends to put patients in a state of anxiety. Therefore, corresponding policies and measures should be implemented to relieve the financial burden on these patients. Patients with shorter sleep time was statistically significantly associated with anxiety and depression. For these patients, we recommend that they should ensure adequate sleep and a healthy lifestyle.

The main limitation of this study was its retrospective design. The anxiety and depression of patients has not been assessed before treatment, so it is not possible to compare the anxiety and depression before and after treatment. It is necessary to conduct a prospective and multicenter study in the future.

Conclusion
In summary, the prevalence of anxiety and depression in the UIA patients treated by endovascular intervention was 17.0% and 15.5% respectively. A treatment cost exceeding the annual household income was statistically significantly associated with anxiety. Patients with shorter sleep time was statistically significantly associated with anxiety and depression. Our findings provide valuable evidence for the clinical and psychological management of these patients.

Declarations

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable requests.

**Authors’ contributions**

ZX and ZH designed questionnaires and study protocol, analysis of data, and write up of article. MY, Yj, LG, HC and HP analyzed data and contributed in write-up of the different sections of the manuscript. XS and WJ contributed in data analysis. All authors read and approved the final manuscript.

**Authors’ information**

Not applicable

**Ethics approval and consent to participate**

The ethic approval for this study was issued by the Institutional Review Board of the Xuanwu Hospital of Capital Medical University. The nature and purpose of this study was illustrated and full confidentiality guaranteed. A written informed consent was obtained from all participants. They were permitted to withdraw from the study at any time without negative consequences.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

**Abbreviations**

UIA: Unruptured intracranial aneurysm; HADS: Hospital Anxiety and Depression Scale; SAH: subarachnoid hemorrhage; DSA: digital subtraction angiography; MRA: magnetic resonance angiography; CTA: computed tomography angiography; mRS: modified Rankin Scale.

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Tables

Table 1. Demographic characteristics of UIAs patients.
| Characteristics                        | Value (n, %) |
|----------------------------------------|--------------|
| Age, years, mean±SD                    | 55.2±9.48    |
| Gender (Male)                          | 83 (41.5%)   |
| Hypertension                           | 108 (54.0%)  |
| Diabetes                               | 17 (8.5%)    |
| Heart disease                          | 25 (12.5%)   |
| ICVD history                           | 37 (18.5%)   |
| Smoking                                | 23 (11.5%)   |
| Physical exercise                      |              |
| 0 time a week                          | 6030.0%      |
| At least once a week                   | 140 (70.0%)  |
| Sleep time                             | 6.88±1.19    |
| Education level                        |              |
| ≤12                                    | 131 (65.5%)  |
| 12                                     | 69 (34.5%)   |
| Anxiety                                | 34 (17.0%)   |
| Depression                             | 31 (15.5%)   |
| Ratio$^3$                               |              |
| 0-100%                                 | 133 (66.5%)  |
| 100%                                   | 67 (33.5%)   |

$^1$ICVD represents “Ischemic cerebrovascular disease”, $^2$Ratio represents “Ratio of treatment cost and annual household income”

Table 2. Clinical and radiological characteristics of UIA patients.

| Characteristics                        | Value(n, %) |
|----------------------------------------|--------------|
| Diagnosis to treatment time            |              |
| 0-3 months                             | 158 (79.0%)  |
| 3 months                               | 42 (21.0 %)  |
| Preoperative mRS                        |              |
| 0                                      | 51 (25.5%)   |
| 1-2                                    | 149 (74.5%)  |
| Intervention materials                  |              |
| Simple coiling                         | 40 (20.0%)   |
| Stent or flow diversion                | 16080.0%     |
| Treatment-related complications         | 8 (4.0%)     |
| Follow-up time                          |              |
| ≤30 months                             | 101 (50.5%)  |
| 30 months                              | 99 (49.5%)   |
| Recurrence                              | 7/167 (4.19%)|
| Multiple aneurysms                      | 39 (19.5%)   |
| Remain untreated aneurysm               |              |
| Location                                |              |
| Anterior circulation                    | 16381.5%     |
| Posterior circulation                   | 32 (16.0%)   |
| Both                                   | 52.5%        |
Table 3. Univariate analysis of the anxiety and depression in UIA patients.

| Variables                              | Anxiety       | non-Anxiety  | P-value | Depression     | non-Depression |
|----------------------------------------|---------------|--------------|---------|----------------|----------------|
| Age, years, mean±SD                    | 54.9±8.88     | 55.25±9.62   | 0.86    | 55.26±9.40     | 55.19±9.40     |
| Gender (male)                          | 16 (47.1%)    | 67 (40.4%)   | 0.47    | 9 (29.0%)      | 74 (49.2%)     |
| Hypertension                           | 23 (67.6%)    | 85 (51.2%)   | **0.08**| 19 (61.3%)     | 89 (56.1%)     |
| Diabetes                               | 3 (8.8%)      | 14 (8.4%)    | 0.99    | 3 (9.7%)       | 14 (8.3%)      |
| Heart disease                          | 4 (11.8%)     | 21 (12.7%)   | 0.99    | 3 (9.7%)       | 22 (13.0%)     |
| 1ICVD history                          | 9 (26.5%)     | 28 (16.9%)   | **0.19**| 7 (22.6%)      | 30 (18.2%)     |
| Smoking                                | 5 (14.7%)     | 18 (10.8%)   | 0.73    | 3 (9.7%)       | 20 (11.8%)     |
| Physical exercise                      | 23 (67.6%)    | 117 (70.5%)  | 0.74    | 19 (61.3%)     | 121 (71.6%)    |
| Sleep time                             | 6.53±1.21     | 6.95±1.18    | **0.06**| 6.29±1.22      | 6.99±1.22      |
| Education level ≤ 12 years             | 26 (76.5%)    | 105 (63.3%)  | **0.14**| 22 (71.0%)     | 52 (31.4%)     |
| 2Ratio 100%                            | 17 (50.0%)    | 50 (30.1%)   | **0.03**| 14 (45.2%)     | 53 (31.4%)     |
| Diagnosis to treatment time ≤ 3 months | 27 (79.4%)    | 131 (78.9%)  | 0.99    | 25 (80.6%)     | 12 (71.0%)     |
| preoperative mRS=1 or 2                | 28 (82.4%)    | 121 (72.9%)  | 0.25    | 24 (77.4%)     | 12 (71.0%)     |
| Intervention materials (Stent or FD)   | 29 (85.3%)    | 131 (78.9%)  | 0.40    | 26 (83.9%)     | 12 (71.0%)     |
| Treatment-related complications        | 3 (8.8%)      | 5 (3.0%)     | 0.27    | 1 (3.2%)       | 7 (4.1%)       |
| Follow-up time                         | 31.50±7.82    | 30.49±8.77   | 0.54    | 30.06±8.06     | 30.78±8.12     |
| Recurrence                             | 2 (6.7%)      | 5 (3.6%)     | 0.81    | 2 (7.7%)       | 5 (3.5%)       |
| Multiple aneurysms                     | 7 (20.6%)     | 32 (19.3%)   | 0.99    | 8 (25.8%)      | 31 (19.2%)     |
| Remain untreated aneurysm              | 1 (2.9%)      | 9 (5.4%)     | 0.86    | 1 (3.2%)       | 9 (5.3%)       |
| Location                               | **0.04**      | 0.32         |         | 24 (77.4%)     | 13 (7.7%)      |
| Anterior circulation                   | 23 (67.6%)    | 140 (84.3%)  |         | 24 (77.4%)     | 13 (7.7%)      |
| Posterior circulation                  | 9 (26.5%)     | 23 (13.9%)   | 0.86    | 5 (16.1%)      | 27 (16.1%)     |
| Both                                   | 2 (5.9%)      | 3 (1.8%)     | 0.54    | 2 (6.5%)       | 3 (1.8%)       |

1ICVD represents “Ischemic cerebrovascular disease”, 2Ratio represents “Ratio of treatment cost to annual household income”
Table 4. Multivariable analysis of the anxiety and depression in UIA patients.

| Variables | OR (95%CI)       | P-value |
|-----------|------------------|---------|
| Anxiety   |                  |         |
| Hypertension | 1.99 (0.86–4.61)  | 0.11    |
| 1ICVD history | 2.03 (0.77–5.30)  | 0.15    |
| Education level | years≤12years  | 1.34 (0.54–3.35) | 0.53    |
| Ratio 100% | 2.42 (1.08–5.41)  | **0.03** |
| Sleep time | 1.51 (1.06–2.14)  | **0.02** |
| Location  |                  |         |
| Anterior circulation | 3.50 (0.43–28.49)  | 0.24   |
| Both      | 1.59 (0.17–14.55) | 0.68   |
| Depression|                  |         |
| Gender (male) | 0.66 (0.28–1.58)  | 0.35   |
| Sleep time | 1.62 (1.14–2.29)  | **0.007** |
| Ratio 100% | 1.80 (0.80–4.03)  | 0.15   |

1ICVD represents “Ischemic cerebrovascular disease”, 2Ratio represents “Ratio of treatment cost to annual household income”