



Clinical Study

Cognitive function, depression, anxiety and quality of life in Chinese patients with untreated unruptured intracranial aneurysms

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ABSTRACT

Detected unruptured intracranial aneurysms (UIA) are becoming more common with the increased utilization of CT angiography, MR angiography and digital subtraction angiography. A proportion of patients with UIA remain untreated. We investigated to assess cognitive function, depression, anxiety and quality of life (QoL) in Chinese patients with untreated UIA. Thirty one Chinese patients with untreated UIA and 25 healthy controls were identified and matched for variables including age, sex, and living area. Cognitive function was evaluated with the Montreal Cognitive Assessment (MoCA). Depression, anxiety and QoL were screened with the Self-Rating Depression Scale, Self-Rating Anxiety Scale, and Short Form-36, respectively. Non-parametric tests were used for comparisons between groups. No patient had cognitive dysfunction at 1 month or 1 year after detection of UIA. However, a significant decrease of overall MoCA subscores was found in 30 (97%) of 31 patients 5 years after UIA discovery, suggestive of mild cognitive impairment. A significant decrease in depression and anxiety was found in patients over time. QoL in patients was reduced most prominently in psychosocial function and social activities 1 year after detection of UIA, but these improved to within normal limits at the end of the follow-up period. For Chinese patients with untreated UIA, depression, anxiety and reduced QoL may be short-term complications. Mild cognitive impairment may be a long-term complication.

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1. Introduction

The worldwide prevalence of unruptured intracranial aneurysms (UIA) is around 2% [1]. The most severe risk for UIA is life-threatening bleeding, with the rupture incidence of UIA in the general adult population at least 1% per year [2]. Usually treatment (coiling or clipping) is an acceptable option for patients with cerebral aneurysms. However, the clinical goal in treating patients with UIA is to maximize the duration of high-quality life by optimally balancing the risks of aneurysm rupture with the risk of treatment-related adverse outcomes. Due to multiple different factors of UIA (including aneurysm location, vascular morphology and underlying systemic diseases), treatment-related risks exceed the risk of aneurysm rupture for some patients, and cerebral aneurysms in these patients undergo no further treatment [3]. In China, the detection rate of UIA greatly has increased with the

utilization of CT angiography (CTA), MR angiography (MRA) and digital subtraction angiography (DSA). According to the findings of the International Study of Unruptured Intracranial Aneurysms (ISUIA), small anterior circulation aneurysms (<7 mm) have a 0% risk of subarachnoid hemorrhage (SAH) within 5 years [4]. Many Chinese patients with small anterior circulation UIA, which can be treated by surgical clipping or endovascular coiling, chose conservative treatment and DSA follow-up after consideration of the treatment-related risk. In addition, a proportion of patients with UIA abandon further treatment due to their lower socioeconomic means and poor medical insurance.

For patients with ruptured intracranial aneurysms, cognitive impairment, psychological symptoms and reduced quality of life (QoL) are long-term complications [5–7], and are somewhat related to aneurysmal SAH [8] and cerebral hemodynamic changes [9]. Nevertheless, for patients with UIA, few studies on cognition, psychological function and QoL in post-diagnosis patients have been reported [10–13]. In regard to untreated UIA, psychosocial impairment and a decrease in overall QoL have been associated with harboring an identified but untreated UIA in two small cohort

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studies [14,15]. There may be differences between patients from Eastern and Western countries in regard to cerebrovascular diseases associated with psychological and cognitive impairment [16,17]. To our knowledge no study on cognitive function, psychological function and QoL in Asian patients with untreated UIA, with long-term follow-up data, has been published. We investigated the cognition, psychological function and QoL in Chinese patients with untreated UIA for 5 years. In order to evaluate if untreated UIA could be regarded as the main reason for the outcomes, we excluded various confounding factors as much as possible. Only otherwise healthy patients with untreated UIA were recruited to avoid potential confounding factors such as cerebral ischemic lesions, traumatic brain injury, other cerebrovascular diseases, or psychiatric disorders. The major aim of this study was to identify the effects of untreated UIA on cognitive function, psychological function and QoL, and to enhance our knowledge about the life of patients with untreated UIA.

2. Methods

2.1. Patient population

Screened patients and patients with suspected intracranial aneurysms underwent CTA or MRA in the Outpatient or Emergency Services of Tongji, Shanghai Changning and Changzheng Hospitals. If an UIA was detected on CTA or MRA, DSA was employed to confirm. Forty seven patients from these three clinical centers who were evaluated between 2004 and 2008 were eligible for this study. Inclusion criteria for adult patients with untreated UIA were the following: (i) UIA confirmed by DSA; (ii) of Chinese descent and aged between 18 and 60 years at the time of enrolment; (iii) chose no treatment for UIA after objectively being told the risk of aneurysm rupture and risk of surgical treatment; and (iv) Montreal Cognitive Assessment (MoCA) score >25 points at the time of enrolment (able to care for themselves in daily life). Exclusion criteria were as follows: (i) other cerebrovascular diseases such as arteriovenous malformation, (ii) history of SAH, (iii) severe systemic disease, (iv) taking psychotropic medicines, (v) aneurysm rupture during the follow-up period, and (vi) neurological conditions which might influence cognitive and psychological function during the follow-up period (such as traumatic brain injury, ischemic lesions, or epilepsy). The healthy control group consisted of subjects without systemic disease, mental disease or cerebrovascular disease, and were matched on variables including age, sex, and living area. Moreover, a previous published study [18] used normative data from the general Swedish population as the healthy control group. The validated data for Chinese normals were also used in this paper, as the data were relatively constant and all age brackets and ethnic backgrounds were included. This could be regarded as the standard data of the healthy Chinese population. Hence, Chinese normals were also applied as a control group in the present study.

The study was approved by the Ethics Committee of the Tongji Hospital, Tongji University, China. All the investigations were permitted by the participants and all signed informed consent.

2.2. Assessments

MoCA is a cognitive screening instrument designed to address some of the limitations of the Mini-Mental State Examination [19,20]. Cognitive function was measured by means of the validated Chinese version of MoCA, which involves items in visual space and execution, naming, memory, attention, language, abstraction, delayed recall and orientation [21]. In the Chinese version of MoCA, scores below 25 are considered abnormal

(sensitivity 100%, specificity 96%), and scores below 25 points but ≥ 14 points are considered to indicate mild cognitive impairment (MCI) (sensitivity 87.2%, specificity 83.6%) [22]. The Self-Rating Depression Scale (SDS) and the Self-Rating Anxiety Scale (SAS) were used to assess depression and anxiety. On the basis of 20 items, depression or anxiety are categorized into mild (scores 50–60), moderate (scores 61–70) and severe (scores >70) [23]. The QoL was evaluated using the Short Form-36 questionnaire (SF-36) [24], a valid and reliable QoL assessment in vascular disease [25]. The Chinese version of SF-36, which has a reasonable sensitivity and specificity [26], includes eight health related domains: physical functioning, physical role functioning, bodily pain, general health perception, vitality, social functioning, emotional role functioning and mental health. A higher SF-36 score indicates a better QoL.

2.3. Data collection

All patients eligible for the study were advised to have a follow-up DSA every year. Meanwhile, patients were asked to attend a face-to-face discussion with our doctor at 1 year and 5 years after detection of the untreated UIA. Patients who agreed to participate in this study were not explicitly told that the interview contained psychological and cognitive testing in an attempt to draw out more honest responses to the MoCA, SF-36, SDS and SAS items. All questionnaires were administered via face-to-face interview in our clinical rooms and were performed by the same examiner (S-H.S).

2.4. Data analysis

Data were analyzed with the Statistical Package for the Social Sciences version 17.0 (SPSS, Chicago IL, USA). Measurement data are presented as mean \pm standard deviation. A non-parametric test was used for comparisons as it is appropriate for small sample sizes and skewed distributions. The Wilcoxon matched-pairs signed-ranks test was used for two related samples tests. The Mann-Whitney U test was used for two independent samples tests. Numerical data are presented as percentages. The Chi-squared test was performed on numerical data. $p < 0.05$ was considered significant for all analyses.

3. Results

3.1. Patient characteristics

We selected 47 patients with untreated UIA for this long-term follow-up study. One refused to participate, two were lost to follow-up, six suffered aneurysm rupture during the follow-up period, and seven underwent surgical treatment for UIA during the follow-up period. Thus, the final study group comprised 31 patients (12 men and 19 women), with a median age of 48.1 ± 5.7 years (range 38–60). Three patients had multiple aneurysms, with one patient having aneurysms in the anterior communicating artery (AcomA) and posterior communicating artery (PcomA), one patient having aneurysms in the AcomA, PcomA and internal carotid artery, and one patient having aneurysms in the PcomA and posterior inferior cerebellar artery. Each of these aneurysms were counted in the subgroup analysis of aneurysm location and size. Based on initial DSA, the mean aneurysm size was 5.3 ± 2.5 mm (range 1–12.6), and it was 5.4 ± 2.6 mm (range 1.1–12.6) at the end of the 5 year follow-up period. No significant changes of aneurysmal morphology or other cerebrovascular morphology were found during the follow-up period.

The healthy controls consisted of 31 people matched for age, sex and living area. Six individuals were excluded in order to balance the baseline characteristics (smoking, hypertension,

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