Original Article

Analysis of perioperative negative emotion risk factors in patients with pituitary adenoma and its impact on prognosis: a retrospective study

Guiping Yang, Sen Shen, Jiajia Zhang, Yan Gu

Department of Neurosurgery, Affiliated Hospital of Nantong University, Nantong, China

Contributions: (I) Conception and design: G Yang; (II) Administrative support: Y Gu, J Zhang; (III) Provision of study materials or patients: S Shen, (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Yan Gu. Department of Neurosurgery, Affiliated Hospital of Nantong University, No. 20, Xisi Road, Nantong 226000, China. Email: Guyan202112@163.com; Jiajia Zhang. Department of Neurosurgery, Affiliated Hospital of Nantong University, No. 20, Xisi Road, Nantong 226000, China. Email: zhangjiajiantdx@163.com.

Background: Pituitary adenoma (PA) is the third most common tumor in craniocerebral surgery. Most patients will experience varying degrees of negative emotions before and after surgery, which may affect the prognosis of surgery. This study analyzed the perioperative negative emotional risk factors of patients with different characteristics of PA and their impact on prognosis, so as to provide a reference for improving the prognosis of patients with PA.

Methods: A total of 234 patients who underwent PA surgery in the Affiliated Hospital of Nantong University from January 2017 to January 2022 were selected as the observation population. The general characteristics of the subjects were collated using a general information questionnaire designed by the researchers. The negative emotions of the patients were evaluated using a Self-rating Anxiety Scale (SAS) and a Self-rating Depression Scale (SDS). The prognosis of patients was determined by assessing the hypophyseal hormone levels. Multiple regression analysis and logistic regression were used to analyze the risk factors of perioperative negative emotions and the effects of negative emotions on patient prognosis.

Results: Multiple regression analysis showed that with and without children, education, income, PA type, PA size, and surgical approach were independent factors influencing negative emotions in patients after PA surgery ($P<0.05$). Logistic regression analysis showed that negative emotion was an independent prognostic factor ($P<0.05$).

Conclusions: There are many factors that affect the anxiety and depression of patients after PA surgery. The family members and medical staff of the patients should take effective measures to relieve the anxiety and depression of the patients so as to improve the prognosis of patients according to the influencing factors.

Keywords: Pituitary adenoma (PA); perioperative period; anxiety; depression; prognosis

Submitted Jun 09, 2022. Accepted for publication Jul 15, 2022.
doi: 10.21037/gs-22-387
View this article at: https://dx.doi.org/10.21037/gs-22-387

Introduction

Pituitary adenoma (PA) is a tumor derived from the endocrine cells of the anterior pituitary. It is the most common tumor in the sellar region and the third most common tumor in craniocerebral surgery. The incidence of PA in the general population is 16.7% (1). PA can be divided according to size into microadenomas (diameter <10 mm), macroadenomas (10 mm ≤ diameter <40 mm), and giant adenomas (diameter ≥40 mm). The World Health Organization (WHO) updated the classification

of PA in 2017 to include the following: growth hormone-secreting (GH) adenoma, prolactin-secreting (PRL) adenoma, thyroid stimulating hormone-secreting (TSH) adenoma, adrenocorticotropic hormone secreting (ACTH) adenoma, null cell adenoma, multi-hormonal adenoma, non-functioning pituitary adenoma (NFPA), and follicle stimulating hormone-secreting/luteinizing hormone (FSH/LH) adenoma (2). While most PAs are benign tumors, its associated incidence and mortality rates exert a significant effect on the labor force (3). About 0.1–0.2% of PAs are invasive, and the degree of malignancy is often directly related to patient prognosis (4). Interestingly, the incidence rate of PA varies greatly in different regions. An epidemiological study in Sweden from 2001 to 2011 showed that the total standardized incidence rate (SIR) of PA was 3.9/100,000, with an of 3.3/100,000 and 4.7/100,000 in males and females, respectively. The study also found that male SIR increased with age, while female SIR peaked at the age of 25–34 years (5). Another retrospective study conducted in Latin America found that the overall annual SIR of PA was 7.39/100,000, with women accounting for 73% of cases and the average age at diagnosis was 46.4 years (3).

The clinical manifestations of PA are complex. Depending on the degree of hypophysis, hormone levels, and tumor size, PA can show different clinical symptoms or no obvious symptoms at all (6). When PA patients present with endocrine disorder caused by massive hormone secretion or obvious compression symptoms caused by tumor enlargement, clinical treatment involving medication, surgery, and/or radiotherapy is required. A large number of studies have suggested that PA patients can develop physiological, psychological, and social symptoms related to treatment (7-10). Compared with the general population, patients with PA have significantly increased neurotic personality traits related to anxiety (11). Anxiety and depression are two common mental health problems, which have a great impact on patients' social roles and quality of life (12). While surgical resection remains the primary form of management for PA patients (13), the traumatic nature of the procedure, as well as the type of PA and complexity of symptoms, inevitably leads to a range of complications during and after the operation (14). Ownsworth *et al.* found that a third of PA patients have significant anxiety and depression (15), and most patients will have different degrees of negative emotions before and after surgery. Negative emotions refer to the lasting and significant changes in a patient's mood and emotions, such as depression and anxiety. It is believed that these negative emotions will further aggravate physical symptoms, including sleeping disorders, loss of appetite, decreased sexual desire, social withdrawal, and reduced activity, which can affect the success and prognosis of the surgery (16). However, the causes and influencing factors of perioperative negative emotions in patients with PA have not been fully elucidated. This current study analyzed the perioperative negative emotional risk factors of patients with different characteristics of PA and their impact on prognosis, so as to provide a reference basis for improving the prognosis of patients with PA. We present the following article in accordance with the SURGE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-22-387/rc).

Methods

Research participants

A total of 250 patients who underwent PA surgery in the Affiliated Hospital of Nantong University from January 2017 to January 2022 were considered for participation in this study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Affiliated Hospital of Nantong University (No. 2021-K084-01). Informed consent was obtained from all patients.

The following inclusion criteria were applied: (I) patients aged ≥18 years old; (II) conscious patients who can cooperate and complete the questionnaire; (III) patients who are able to read, write, and communicate effectively; and (IV) patients who agreed to participate in this study and provided signed informed consent.

The following exclusion criteria were applied: (I) patients with a history of any other malignant tumor; (II) mental patients and patients with other diseases affecting observation; and (III) patients with severe disability, major surgery, acute infection, acute heart failure, severe cerebrovascular sequelae, or any other acute and critical disease (*Figure 1*).

Finally, according to the inclusion and exclusion criteria, 234 cases of PA were enrolled in this study.

The general rule of multiple linear regression requires that the ratio of the number of items to the sample size be 1:5 to 1:10. Therefore, the sample size of the research object in this study was 200 cases. Considering that the subjects of this study are discharged patients, 250 questionnaires were

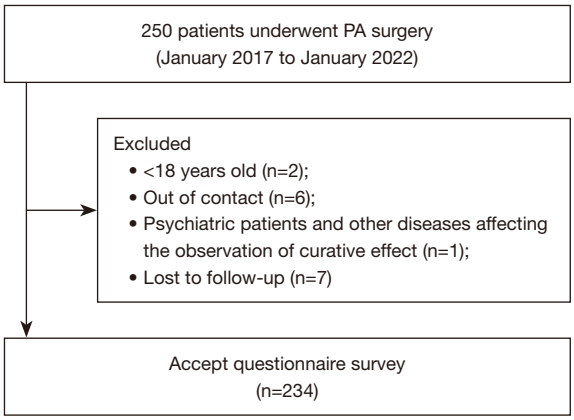

Figure 1 Study flowchart. PA, pituitary adenoma.

planned for distribution.

All patients were given face-to-face questionnaires one week after the operation, and again at three months after the operation. Pituitary magnetic resonance imaging (MRI) plain scans plus enhancement were performed and patient hormone levels were measured.

General information questionnaire

The general information questionnaire included demographic data (such as gender, age, marital status, fertility status, education level, occupation, and income) and clinical data (such as PA type, PA size, clinical symptoms, surgical approach, etc.).

Negative emotion assessment

The Self-rating Anxiety Scale (SAS) (17) was used to reflect the presence of anxiety and the degree of anxiety. It includes 20 items, and each item is scored from 1–4. The scores of each item were added to obtain the rough score, which was then multiply by 1.25 to obtain the standard score. A SAS score >50 was used as the evaluation standard, and a score of 50–59 was considered mild anxiety, a score of 60–69 was considered moderate anxiety, and scores 70 and above were considered severe anxiety. The SAS has good reliability and validity, with the coefficients of Cronbach's α above 0.75.

The Self-rating Depression Scale (SDS) (18) was used to reflect the presence of depression and the degree of depression. It consists of 20 items. A SDS score >52 was used as the evaluation standard. Patients with a SDS score ≥53 were considered to have depression, and scores from 53–62 were considered mild depression, scores from 63–72 were considered moderate depression, and scores >72 were considered severe depression. The SDS has good reliability and validity, with the coefficients of Cronbach's α above 0.75.

Prognostic evaluation

Prognosis was evaluated based on the patient's hypophyseal hormone levels (19). Growth hormone, insulin-like growth factor-1 (IGF-1), thyroid function [free triiodothyronine (T3), free thyroxine (T4), thyroid-stimulating hormone (TSH), adrenal axis function (adrenocorticotropic hormone (ACTH), cortisol], prolactin, follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone, estrogen; The samples were detected in fasting venous blood taken in the morning after fasting for more than 8 hours overnight. If the levels of serum hormone decreased to normal and the symptoms disappeared, the patient was considered to be cured. If the level of serum hormone decreased to normal levels or more than half of the original hormone levels, and the symptoms improved, the patient was considered to be improved. If the serum hormone levels did not decrease or decreased by less than half, and the symptoms did not improve, the patient was considered to not have improved.

Tumor recurrence was defined as: (I) presence of symptoms and signs such as amenorrhea, lactation, visual impairment, and visual field aggravation after the operation; and (II) the average hormone levels measured several times in the 3 months after the operation were higher than that in the 3 months before the operation.

The last follow-up occurred in January 2022.

Statistical analysis

The results of each scale were input into the computer for score conversion and statistical analyses were performed using the SPSS 23.0 software (IBM Corp., Armonk, NY, USA). The measurement data are expressed as means and standard deviation, and the counting data are expressed as frequency and percentage. *T*-tests, analysis of variance, and chi square tests were used for inter-group statistical analyses. The influencing factors of anxiety and depression were analyzed using multiple linear regression, and the influence of negative emotion on prognosis was analyzed by logistic regression. A P value <0.05 was considered statistically significant.

Results

Baseline data

The baseline characteristics of the patient are shown in

Table 1. A total of 234 postoperative patients with PA, with an average age of 44.77±11.56 years (range, 18–79 years), were enrolled in this study, including 97 (41.5%) males and 137 (58.5%) females. There were 86 cases of PRL adenoma (36.8%), 23 cases of ATCH adenoma (9.8%), 21 patients with GH adenoma (9.0%), 5 patients with FSH/LH adenoma (2.1%), 3 with TSH adenoma (1.3%), and 96 with NFPA (41.0%). In terms of tumor size, 57 patients had microadenoma (24.4%), 162 had macroadenoma (69.2%), and 15 presented with giant adenoma (6.4%). A total of 187 patients underwent surgery with the transsphenoidal approach (79.9%), 40 patients had a craniotomy (17.1%), and 7 patients underwent surgery with a gamma knife (3.0%).

Perioperative negative emotions in patients with PA

There were significant differences in the SAS scores and the SDS scores between PA patients with and without children, education level, income, PA type, PA size, and surgical approach (P<0.05; *Tables 1*,*2*).

Analysis of the influencing factors of postoperative negative emotional status of patients

The results of multiple regression analysis showed that fertility, education, income, PA type, PA size, and surgical approach were independent influencing factors of anxiety in PA patients (P<0.05), while fertility, education, income, PA type, PA size, and surgical approach were independent influencing factors of depression in PA patients (P<0.05; *Tables 3*,*4*).

Prognosis of PA patients

Among the 234 postoperative patients with PA, 163 cases were cured, 46 cases were effective, and 25 cases recurred. The questionnaire score showed that there was a significant

Table 1 Perioperative SAS scores in patients with PA

Item	N (%)	SAS, mean ± SD	t/F	P
Gender			0.738	0.461
Male	97 (41.5)	56.28±4.52		
Female	137 (58.5)	55.80±5.07		
Age (years)			1.692	0.186
<40	76 (32.5)	55.74±4.66		
40–60	140 (59.8)	55.89±4.92		
>60	18 (7.7)	58.00±4.86		
With or without children			14.978	0.000
With children	157 (67.1)	53.62±3.47		
Without children	77 (32.9)	60.84±3.45		
Degree of education			11.020	0.000
Junior high school and below	129 (55.1)	57.02±4.36		
Technical secondary school or high school	74 (31.6)	55.58±4.49		
College degree or above	31 (13.2)	52.74±6.05		
Occupation			0.679	0.566
Mental	70 (29.9)	55.97±4.37		
Physical strength	93 (39.7)	56.04±4.74		
Unemployed	21 (9.0)	57.24±5.89		
Retired	50 (21.4)	55.44±5.25		

Table 1 (*continued*)

Table 1 (*continued*)

Item	N (%)	SAS, mean ± SD	t/F	P
Monthly household income (yuan)			37.871	0.000
<3,000	77 (32.9)	61.32±2.86		
3,000–6,000	131 (56.0)	54.48±2.12		
>6,000	26 (11.1)	47.88±1.73		
Address			1.850	1.160
Countryside	89 (38.0)	55.62±4.74		
Town	59 (25.2)	55.42±4.71		
City	86 (36.8)	56.79±5.00		
Tumor type			4.560	0.001
PRL	86 (36.8)	55.38±4.54		
ACTH	23 (9.8)	60.26±5.07		
GH	21 (9.0)	55.76±5.42		
FSH/LH	5 (2.1)	54.8±3.11		
TSH	3 (1.3)	52.67±3.21		
NFPA	96 (41.0)	55.75±4.6		
Tumor size			6.702	0.000
Microadenoma	57 (24.4)	51.3±4.43		
Macroadenoma	162 (69.2)	57.12±3.61		
Giant adenoma	15 (6.4)	61.80±4.72		
Type of operation			7.520	0.000
Transsphenoidal approach	187 (79.9)	55.17±4.56		
Craniotomy	40 (17.1)	59.85±3.9		
Gamma knife	7 (3.0)	56.14±7.01		

SAS, Self-rating Anxiety Scale; PA, pituitary adenoma; PRL, prolactin-secreting adenoma; ACTH, adrenocorticotropic hormone secreting adenoma; GH, growth hormone-secreting adenoma; FSH/LH, follicle stimulating hormone-secreting/luteinizing hormone; TSH, thyroid stimulating hormone-secreting adenoma; NFPA, non-functioning pituitary adenoma.

Table 2 Perioperative SDS scores in patients with PA

Item	N (%)	SDS, mean ± SD	t/F	P
Gender			0.751	0.453
Male	97 (41.5)	60.12±4.44		
Female	137 (58.5)	59.64±4.97		
Age (year)			1.620	0.200
<40	76 (32.5)	59.67±4.59		
40–60	140 (59.8)	59.69±4.83		
>60	18 (7.7)	61.78±4.65		

Table 2 (*continued*)

Table 2 (*continued*)

Item	N (%)	SDS, mean ± SD	t/F	P
Fertility or not			14.765	0.000
Have children	157 (67.1)	57.54±3.49		
No children	77 (32.9)	64.56±3.27		
Degree of education			9.882	0.000
Junior high school and below	129 (55.1)	60.78±4.26		
Technical secondary school or high school	74 (31.6)	59.5±4.46		
College degree or above	31 (13.2)	56.77±5.98		
Occupation			0.946	0.419
Mental	70 (29.9)	59.77±4.32		
Physical strength	93 (39.7)	59.88±4.61		
Unemployed	21 (9.0)	61.33±5.78		
Retired	50 (21.4)	59.26±5.12		
Monthly household income (yuan)			38.674	0.000
<3,000	77 (32.9)	65.12±2.59		
3,000–6,000	131 (56.0)	58.31±2.16		
>6,000	26 (11.1)	52.00±1.94		
Address			1.896	1.153
Countryside	89 (38.0)	59.48±4.59		
Town	59 (25.2)	59.25±4.67		
City	86 (36.8)	60.63±4.92		
Tumor type			4.619	0.000
PRL	86 (36.8)	59.24±4.4		
ACTH	23 (9.8)	64.04±4.78		
GH	21 (9.0)	59.57±5.36		
FSH/LH	5 (2.1)	58.4±3.21		
TSH	3 (1.3)	56.67±3.21		
NFPA	96 (41.0)	59.61±4.58		
Tumor size			6.293	0.000
Microadenoma	57 (24.4)	55.30±4.41		
Macroadenoma	162 (69.2)	60.89±3.54		
Giant adenoma	15 (6.4)	65.87±4.27		
Type of operation			9.827	0.000
Transsphenoidal approach	187 (79.9)	58.99±4.48		
Craniotomy	40 (17.1)	63.83±3.64		
Gamma knife	7 (3.0)	60.00±6.43		

SDS, Self-rating Depression Scale; PA, pituitary adenoma; PRL, prolactin-secreting adenoma; ACTH, adrenocorticotropic hormone secreting adenoma; GH, growth hormone-secreting adenoma; FSH/LH, follicle stimulating hormone-secreting/luteinizing hormone; TSH, thyroid stimulating hormone-secreting adenoma; NFPA, non-functioning pituitary adenoma.

Table 3 Multiple linear regression analysis of SAS

Related factor	β	SE	β'	t	P
With or without children	–3.869	0.336	–0.376	–11.517	0.000
Degree of education	–0.165	0.214	–0.024	–2.772	0.041
Monthly household income	–3.793	0.281	–0.491	–3.499	0.013
Tumor type	–0.139	0.050	–0.065	–2.773	0.046
Tumor size	2.204	0.327	0.239	6.741	0.000
Type of operation	1.110	0.252	0.112	2.398	0.009

SAS, Self-rating Anxiety Scale.

Table 4 Multiple linear regression analysis of SDS

Related factor	β	SE	β'	t	P
With or without children	–3.645	0.325	–0.361	–11.206	0.000
Degree of education	0.064	0.208	0.010	2.307	0.009
Monthly household income	–3.767	0.272	–0.498	–3.845	0.003
Tumor type	–0.131	0.048	–0.063	–2.705	0.007
Tumor size	2.325	0.317	0.257	7.342	0.000
Type of operation	1.235	0.244	0.127	2.053	0.012

SDS, Self-rating Depression Scale.

Table 5 Correlation between prognosis and negative emotion in pituitary adenoma patients

Prognosis	Cure (n=163)	Effective (n=46)	Recurrence (n=25)	χ^2	P
SAS				14.000	0.001
≤50	61	4	7		
>50	102	42	18		
SDS				7.798	0.020
≤50	46	4	5		
>50	117	42	20		

SAS, Self-rating Anxiety Scale; SDS, Self-rating Depression Scale.

difference in the prognosis of PA patients with anxiety and depression (P<0.05; *Table 5*).

Logistic regression analysis showed that the SAS [odds ratio (OR) =1.324, 95% confidence interval (CI): 0.279–6.287, P=0.002] and SDS (OR =2.504, 95% CI: 1.418–7.458, P=0.003) were independent factors affecting the prognosis of patients (*Table 6*).

Discussion

Tumor is a major stressor which directly affects an individual's subjective emotional state. Adverse life events are related to the occurrence of individual negative emotions, and PA is a serious adverse experience that can stimulate the release of negative emotions. Research has shown that

Table 6 Multivariate logistic regression analysis of prognosis in pituitary adenoma patients

Factor	β	S.E.	Wald	P	OR	95% CI
SAS	1.735	0.256	10.035	0.002	1.324	0.279–6.287
SDS	0.847	0.282	9.046	0.003	2.504	1.418–7.458
Constant	−7.346	0.953	15.538	0.000	–	–

SAS, Self-rating Anxiety Scale; SDS, Self-rating Depression Scale; OR, odds ratio; CI, confidence interval.

PA patients have clinical specific symptom burden, such as fatigue, lactation, menstrual disorder, infertility, male sexual dysfunction, vision problems, appearance changes, anxiety, and depression, all of which can lead to physical and psychological problems at the time of admission (20-24). Furthermore, the uncertainty of diagnosis, operation, and prognosis can lead to the accumulation of negative emotions of anxiety and depression, which can affect the overall quality of life and patient outcomes (7). Patients with PA experience significant anxiety and depression, which can have serious impacts on social function and quality of life. A study has shown that more than half of all patients will show anxiety and depression before brain surgery. In addition, the number of patients with depression after surgery is relatively large, especially in the first 1–3 months after surgery (25).

While most PAs are benign tumors, most patients will experience symptoms of anxiety and depression. This current study demonstrated that the severity of anxiety and depression in patients who have yet to bear children was greater than that in patients who have already bore children. PA will have varying degrees of impact on the fertility of patients of childbearing age. Female patients may experience amenorrhea and menstrual disorders, while male patients may experience impotence and sexual dysfunction (26). Fertile patients who have not yet bore children may experience mental and psychological pressures, which will exert varying degrees of impact on their daily life, social interactions, and marriage (27). Therefore, it is necessary to provide relevant knowledge and psychological comfort to patients who have not yet bore any offspring but who wish to do so in the future. Their family members should be encouraged to provide emotional support so as to alleviate their anxiety and depression. The results also showed that the higher the economic income and educational background of PA patients, the less depression they experience. A study has shown that patients with higher education have more knowledge about diagnosis and treatment (28), and can therefore discuss their condition, treatment methods, and rehabilitation with doctors. Patients with higher education also tend to have higher treatment compliance, as they are better informed about the disease. Higher economic income is an economic guarantee for better treatment. Patients with lower economic income lack strong economic support, and are prone to anxiety and depression.

This investigation revealed that the type (ACTH tumor) and size of the PA affected the degree of anxiety and depression in patients, and this was similar to the results of related studies (21,23,29). Clinically, microadenomas can only have endocrine manifestations, with visual impairment not being obvious and slow growth of the tumor. Patients often seek medical diagnosis when they present with headaches, visual impairment, visual field defects, and hypophysis (30). With the growth of the tumor, long-term compression of the optic nerve and pituitary tissue will lead to irreversible damage. The greater the PA, the more severe the clinical symptoms. Raappana *et al.* (21) showed that patients with ACTH tumors and GH tumors had the worst quality of life, while NFMA adenomas and PRL tumors were less damaging to the quality of life. Tanemura *et al.* (23) confirmed that pituitary macroadenoma can affect the physical and psychological well-being of patients. Herein, the multivariate analysis showed that patients with ACTH tumors experienced the worst anxiety and depression compared to patients with other types of PAs, but this result may come from the sample deviation. Among the patients included in this study, GH tumor patients are mostly in the period of symptom control, and the small sample size of ACTH tumor is related to other factors. At present, there is a lack of individualized nursing and health education to address the physical and psychological injuries of PA patients.

Similar to the result of the study of Heald *et al.* (31), patients with transfrontal craniotomy experienced worse anxiety and depression status compared to patients with transsphenoidal surgery. Patients with transfrontal craniotomy mostly have giant adenomas or recurrence, and such patients have severe visual field defects. Visual defects, hypopituitarism, and large PAs are associated with

more severe clinical symptoms, which in turn affects the patient's psychology and emotions. Therefore, medical staff should pay more attention and guidance to patients undergoing transfrontal surgery. When determining the surgical approach, doctors should consider the patient's psychological and physical rehabilitation, and quality of life.

In this study cohort, the recurrence rate of postoperative patients was 10.68%, which is similar to previous reports (32,33). A study of Arnold *et al.* has shown that there are many complications after PA, and the recurrence rate is high (34). The total recurrence rate of PA within 5 years is 7–35%, and the recurrence rate of simple operation is 45–57%. Patients are often readmitted to the hospital due to complications, tumor remnants, or recurrence. Readmission will have a great impact on the patient's psychology, potentially affecting the doctor-patient relationship, the nurse-patient relationship, as well as treatment compliance. In general, readmission is not conducive to the treatment and rehabilitation of the patient. A study has also found that the trust in the hospital, medical staff, medical technology, and equipment is also an element that affects the emotion and prognosis of patients with PA (24). Therefore, effective discharge education and follow-up after surgery is crucial, as well as continued community care. Clinicians need to understand the risk factors that affect the negative emotions of patients with PA. From admission through to follow-up, medical staff should explore the inner feelings of patients and adjust and control factors such as prevention and treatment of complications, psychological changes, etc. Successful postoperative management can improve the prognosis of patients.

There were some limitations to this study. First, the subjects were all from one city, and the presence of regional bias cannot be excluded. Second, the study was limited to one hospital and the results may not be representative of the general population. Further multicentered experimental research should be performed to verify these results.

Conclusions

This study demonstrated that there are many factors that affect the anxiety and depression of patients after PA operation. Family members should be encouraged to provide companionship and support to elevate the patient's sense of well-being. Medical staff should pay attention to the attitude and psychological status of patients with recurrent PA, identify the negative cognition and emotions of such patients as soon as possible, and provide early psychological guidance and emotional support so as to improve the negative emotions and prognosis of these patients.

Acknowledgments

Funding: The study was supported by Guiding Project of Nantong Basic Research and Livelihood Science and Technology Plan in 2021 (No. jcz21046).

Footnote

Reporting Checklist: The authors have completed the SURGE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-22-387/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-22-387/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-22-387/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Affiliated Hospital of Nantong University (No. 2021-K084-01). Informed consent was obtained from all patients.

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(English Language Editor: J. Teoh)

Cite this article as: Yang G, Shen S, Zhang J, Gu Y. Analysis of perioperative negative emotion risk factors in patients with pituitary adenoma and its impact on prognosis: a retrospective study. Gland Surg 2022;11(7):1240-1250. doi: 10.21037/gs-22-387