

Postoperative Symptoms and Quality of Life in Pituitary Macroadenomas Patients



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ABSTRACT

BACKGROUND: Patients with pituitary macroadenoma commonly experience symptoms such as headache, visual disturbance, and olfactory dysfunction due to tumor effects. Even after undergoing surgery for tumor removal, patients continue to experience these symptoms and have difficulty resuming their general activities, decreasing their quality of life (QOL). Although some studies have focused on QOL in pituitary macroadenoma, few studies have examined the relationship between postoperative symptoms and patient QOL in the period after surgery. This study aimed to identify the relationships between postoperative symptoms and QOL among pituitary macroadenoma patients. **METHODS:** This study used a descriptive cross-sectional design to identify relationships between postoperative symptoms and QOL in pituitary macroadenoma patients. Medical records of 62 patients with pituitary macroadenomas who had undergone surgery were retrieved and reviewed 3 months after surgery; at that time, all participants completed a self-report survey addressing their current symptoms and QOL. The researchers then evaluated patient QOL and 3 common symptoms—headache, objectively measured visual disturbance, and olfactory dysfunction—using correlation analysis and multiple linear regression. **RESULTS:** Three months after surgery, patients still experienced headache and lack of olfactory function. Headache showed a strong negative correlation with physical ($r = -0.501, P < .001, R^2 = 36\%$) and mental ($r = -0.448, P < .001, R^2 = 26\%$) QOL. Headache was a significant factor influencing QOL. **CONCLUSION:** Study findings show that continuous assessment and intervention for headache are essential for improving QOL in pituitary macroadenoma patients after surgery. Nurses should prioritize assessment and management of postoperative headache in long-term care for such patients. The study findings support development of a clinical guideline for managing headache in such patients and thus improving their QOL.

Keywords: headache, olfaction disorders, pituitary neoplasms, quality of life, visual disorders

Pituitary adenoma is the third most common brain neoplasm, accounting for approximately 15% of all primary brain tumors, and approximately 40% of pituitary adenomas are reportedly endocrine inactive.^{1,2} Among the various types of pituitary

adenomas, nonfunctioning pituitary macroadenoma (adenoma exceeding 1 cm in diameter) is one of the most common, and the increased tumor size can produce neurological symptoms. The symptoms reported are headache, visual defect, olfactory dysfunction, and various hypopituitarism symptoms such as weakness, vomiting, and infertility.³⁻⁷ As common neurologic symptoms, headache and visual defect occur in approximately 40% to 70% of nonfunctioning pituitary adenoma cases, and most macroadenoma patients exhibit hormone deficiencies resulting from compression of the pituitary adenoma. In addition, transsphenoidal surgery involves varying degrees of destruction of the nasal structure, and thus some olfactory symptoms may occur postoperatively.⁸⁻¹¹ In the clinical setting, patients frequently complain about various postoperative symptoms and physiological effects.¹²

On a long-term basis, these symptoms and conditions are risk factors for decreased quality of life (QOL) in patients with pituitary macroadenoma.^{13,14} One longitudinal study reported that pituitary macroadenoma patients had lower physical QOL before and 1 month after surgery and that their physical QOL slowly improved to a level comparable with that of the general population at 6 months postsurgery.⁷ A systematic review reported

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that headache severity, visual defect, pain, sleep disorder, and hypopituitarism had negative impacts on QOL in pituitary macroadenoma patients.¹⁴ Although transsphenoidal surgery is effective for removal of pituitary macroadenomas, patients can still experience these symptoms well after surgery. Consequently, nurses and other practitioners need to assess patients for possible adverse effects of surgical treatment that could pose a risk for decreasing QOL. Magnetic resonance imaging (MRI), ophthalmologic monitoring, and hormone tests are routinely included in postoperative follow-up care,⁸ but these are inadequate to detect all the symptoms that patients may experience. Thus, symptoms can go undetected and unmanaged, detracting from QOL.

Despite the postoperative symptoms commonly experienced by nonfunctioning pituitary macroadenoma patients, relatively few nursing studies of their QOL^{15,16} and its relationship to symptoms have been published. Thus, it is crucial to measure patients' postoperative symptoms, evaluate their QOL, and understand the relationships between symptoms and QOL to provide effective clinical nursing intervention. The aim of this study was to identify relationships between postoperative symptoms of headache, visual disturbance, and olfactory dysfunction and QOL in nonfunctioning pituitary macroadenoma patients who underwent transsphenoidal surgery.

Methods

This cross-sectional study used convenience sampling to measure the postoperative QOL of pituitary adenoma patients and its contributing factors. This study was approved by the institutional review board (approval no. 2013-0494). Patients were recruited from the database of Yonsei Hospital in Korea. The target population was determined according to G-power using multiple linear regression analysis (effect size, 0.25; G-power (1- β), 0.87; α = .05). A total of 62 patients was included in this study as they met the following criteria: (1) older than 20 years, (2) diagnosed with macroadenoma (greater than 1 cm in longest diameter) based on MRI with definite optic compression and its relevant symptoms, (3) not indicated for medical treatment (endocrine-inactive pituitary adenoma), (4) no history of recurrence, and (5) underwent transsphenoidal surgery at Y Hospital. Data collection for the results of the Humphrey test and Korean Version of Sniffin' Sticks (KVSS) was mainly performed by review of medical records. The Korean versions of the Short-Form Health Survey (SF-36) and Headache Impact Test-6 (HIT-6) were completed by all patients. Patients included in this study underwent transsphenoidal surgery from June 2013 until February 2014. Patients' symptoms and QOL were measured at 3 months postoperative. Written consent was obtained from all participants. To

Headache was the strongest predictor of both physical and mental quality of life.

address potential sources of bias, data collection and analysis were carefully performed by the researchers.

The SF-36 was used to measure the QOL of the patients, and this was devised by Ware et al in 1993 as a patient-reported survey comprising 36 items.¹⁷⁻²⁰ This was translated into Korean and validated by Koh²¹ et al in 1997. The SF-36 consists of 8 domains that measure either physical health or mental health. Each scale is directly transformed into a 100-point scale on the assumption that each question carries equal weight. The lower is the score, the greater is the disability. The reliability of SF-36 during development is represented as a Cronbach α of .94; in this study, the Cronbach α was .79. To quantitate the visual symptoms, patients' visual field defect was evaluated by the Humphrey test 3 months after surgery. The mean deviation (MD) of 120 eye fields from 60 patients was analyzed, excluding 2 patients who did not take the Humphrey test 3 months after surgery. Mean deviation is an indicator of overall visual field change, measured automatically by the Humphrey test, and can be simply quantified as the amount visible compared with a normal field of view. The normal value of MD is within 0 to -2 dB. Thus, the MD of the average person is closer to 0, and a more negative value indicates a larger visual field disturbance. To detect and quantitate postoperative olfaction, the KVSS test was performed. The test was devised by Kobal²² et al in 1996, and its Korean version was modified to include scents familiar to Koreans.²³ When the total score was equal to or lower than 30, hyposmia was diagnosed. A total of 53 patients completed KVSS as a test of their olfactory function 3 months postoperatively; 9 of the 62 patients did not complete the KVSS. The HIT-6 was used for evaluation of postoperative headache.²⁴ This measure reflects the complexity of headache through 6 domains that evaluate pain, social functioning, role functioning, cognitive functioning, psychological distress, and vitality. Each item has a score ranging from 6 to 13, and the total score ranges from 36 to 78. Total scores are divided into 4 categories: little- to no-impact headache (36-49), moderate-impact headache (50-55), substantial-impact headache (56-59), and severe-impact headache (60-78).

The patients' general characteristic was analyzed with a descriptive statistical method. The correlations

of patient QOL and postoperative symptoms were analyzed by Pearson correlation analysis in which $P < .05$ was considered significant. Multiple linear regression was used to analyze the effects of multiple independent variables on the dependent variable (QOL). To account for missing data for visual disturbance and olfactory dysfunction, maximum likelihood estimation was performed. All statistical analyses were completed using SPSS software (version 24.0; SPSS).

Results

The 62 participants consisted of 29 men (46.8%) and 33 women (53.2%) with a mean age of 49.8 years. Total resection was achieved in 49 patients (79.0%), and 13 patients (21.0%) underwent intended subtotal resection with a plan for further adjuvant treatment. At 3 months after surgery, 38 patients (61.3%) needed hormone replacement therapy because of postoperative hypothyroidism and hypocortisolism.

Postoperative QOL was assessed using the SF-36 3 months after surgery. The patients' total physical health summary score was 64.40 ± 22.12 , and their

total mental health summary score was 66.81 ± 18.97 (Table 1). The highest physical health–related score was 78.15 ± 19.92 in the physical functioning domain. The social role functioning domain showed the highest score of 77.22 ± 20.06 among all mental health–related domains. Detailed analysis of the 8 domains revealed that patients with a college education showed a higher score in vitality compared with the others, and this difference showed statistical significance on Scheffé post hoc comparison analysis ($F = 4.933$, $P < .010$).

Postoperative visual field was assessed using the Humphrey test. Improved visual fields showed an MD of -2.17 ± 3.26 , which means their visual field defects were almost perfectly restored. Patients whose visual fields worsened or did not change compared with the preoperative state showed an MD of -4.33 ± 5.14 , which was much lower than that of improved visual fields. With evaluation of postoperative olfaction, the KVSS test revealed a score of 32.29 ± 4.36 ; however, it ranged from 21 to 41, and there were 6 patients (11.3%) experiencing postoperative anosmia at 3 months after surgery. Both the Humphrey test and the KVSS test were

TABLE 1. Characteristics of Participants and Quality of Life (N = 62)

Characteristics	Categories	n	Physical Health, ^a Mean (SD)	Mental Health, ^a Mean (SD)
Sex	Male	29	66.91 (21.79)	66.45 (20.29)
	Female	33	62.20 (22.50)	67.13 (18.05)
Age, y	20–40	19	64.08 (22.54)	63.71 (17.80)
	41–60	24	68.10 (19.29)	67.99 (19.09)
	>60	19	60.06 (25.22)	66.81 (18.97)
Marital status	Married	48	64.14 (22.99)	68.51 (18.88)
	Not married	14	65.31 (19.59)	60.99 (18.81)
Religion	Christian	22	66.40 (22.30)	66.47 (17.44)
	Buddhist	13	59.52 (24.35)	67.42 (21.35)
	Catholic	3	79.79 (7.24)	84.96 (11.50)
	Others	24	63.31 (21.91)	64.53 (19.46)
Employment	Yes	14	67.81 (20.46)	68.33 (19.02)
	No	22	56.09 (24.35)	63.11 (18.88)
Economic burden	High	26	70.88 (25.54)	69.86 (16.55)
	Moderate	44	61.80 (19.52)	71.92 (19.63)
	Low	18	64.64 (23.02)	64.45 (18.96)
Other disease	None	30	67.88 (18.28)	68.74 (18.36)
	Diabetes	3	61.25 (30.34)	63.75 (22.75)
	Hypertension	8	52.81 (25.60)	64.51 (21.21)
	Others	21	64.33 (25.10)	65.37 (19.71)
Hormone deficiency	Yes	24	60.01 (21.35)	63.57 (18.50)
	No	38	67.19 (22.42)	68.86 (19.22)
Operation	Total resection	49	64.30 (21.78)	67.82 (19.10)
	Subtotal resection	13	64.80 (24.27)	62.81 (18.73)

^aPhysical and mental health data were collected using the Short-Form Health Survey.

analyzed by physicians in an outpatient setting. For headaches, the HIT-6 showed a score of 43.81 ± 7.24 , indicating that patients still experienced headache at 3 months postoperative.

Correlation analysis revealed a strong negative correlation between physical health–related QOL and headache ($r = -0.501, P < .001$). In addition, mental health–related QOL showed a strong negative correlation with headache ($r = -0.448, P < .001$). Multiple linear regression analysis was performed for headache, visual disturbance, olfactory dysfunction, and QOL (Table 2). The model was statistically significant ($F = 8.02, P < .001; R^2 = 0.36$). The most influential factor for physical health–related QOL was headache ($\beta = -0.59$). For analysis of mental health–related QOL, the linear multiple regression model showed statistical significance ($F = 5.54, P < .001; R^2 = 0.26$). The most influential factor for mental health–related QOL was also headache ($\beta = -0.52$).

Discussion

This study identified the relationships between common postoperative symptoms and QOL among pituitary macroadenoma patients. Among headache, visual disturbance, and olfactory dysfunction, headache was the strongest predictor of both physical and mental QOL in these patients.

To be specific, the HIT-6 showed a score of 43.81 ± 7.24 , suggesting that patients still experience significant headache after surgery in an outpatient setting. In addition, the correlation analysis revealed that

postoperative headache was negatively correlated with physical health–related QOL ($r = -0.501, P < .001$) and mental health–related QOL ($r = -0.448, P < .001$). In other words, headache at 3 months postoperative could affect patient QOL. Similar to our study, an observational study also reported that headache was inversely related to the physical ($r = -0.473, P = .01$) and mental ($r = -0.547, P = .005$) dimensions of QOL.²⁵ On the basis of these findings, neuroscience clinical nurses should recognize that pituitary macroadenoma patients can still experience headache for a considerable period after surgery. In addition, depending on how much variable pituitary tissue is present, pituitary function can be restored after surgery; the postoperative recovery time needed for restoration of function can vary from 1 to 6 months. Clinical symptoms have been reported to normalize within 3 months after surgery.^{26,27} It is necessary to quantify the severity of a patient's headache with careful consideration of various factors such as intracranial pressure, tumor size, pituitary hormone status, family history of headache, and patient susceptibility as well as appropriate use of pain scale tools.^{28–30} Intranasal packing was applied to our study patients until the day after surgery, and the high pressure exerted by this packing may have indirectly or directly affected patients' headache. As various conditions exacerbate headache symptoms, a checklist that can assess comprehensive factors with associations in the case of headaches is needed for proper nursing intervention.

Regarding visual disturbance, the Humphrey test showed an MD of -2.17 ± 3.26 on the improved

TABLE 2. Multiple Regression Analysis of Quality of Life and Patient Symptoms (N = 62)

Quality of Life	B	SE	β	t	P
Physical health–related quality of life					
(Constant)	177.98	23.64		7.53	.000
Improved visual field	0.91	0.97	0.15	0.94	.353
Visual field defect	-0.17	0.62	-0.04	-0.27	.788
Olfactory	-1.17	0.58	-0.23	-2.03	.048 ^a
Headache	-1.70	0.33	-0.59	-5.14	.000 ^b
$R^2 = 0.41, \text{adj. } R^2 = 0.36, F = 8.02, P < .001$					
Mental health–related quality of life					
(Constant)	155.11	21.96		6.88	.000
Improved visual field	0.34	0.89	0.06	0.38	.706
Visual field defect	0.20	0.58	0.06	0.34	.736
Olfactory	-0.72	0.54	-0.16	-1.35	.182
Headache	-1.33	0.31	-0.52	-4.30	.000 ^b
$R^2 = 0.32, \text{adj. } R^2 = 0.26, F = 5.54, P < .001$					

Abbreviations: adj., adjusted; SE, standard error.

^a $P < .05$.

^b $P < .001$.

visual fields and an MD of -4.33 ± 5.14 on the others. In a previous study, the study reported an average MD of -6.06 ± 8.14 , specifically -5.69 ± 7.55 for improved visual field and -9.39 ± 10.67 for worsened visual field.³¹ In a previous study, there was a significant negative correlation between tumor volume and tumor removal, with an MD ($r = -0.069$, $P < .001$), meaning that surgical tumor removal could dramatically help pituitary macroadenoma.³² This reveals that immediate recovery of visual field defects produces high patient satisfaction. In our study, however, there was no significant relationship between visual disturbance and QOL; this is because our study design only collected data from patients around 3 months after surgery, not immediately after surgery. At this point, patients' already-improved visual functions might not be a significant factor influencing their QOL. Future studies will be very important to further evaluate a correlation between visual symptoms and QOL in a continuous manner with consideration of preoperative status.^{25,33}

The KVSS test revealed a score of 32.29 ± 4.36 in our study. As hyposmia is defined as a score of less than 30 on KVSS, the mean KVSS score indicates that postoperative olfaction was normal in our study at 3 months after surgery. However, as it ranged from 21 to 41, and there were 6 patients (11.3%) who showed a score of less than 30, hyposmia was present even 3 months after surgery. A prospective cohort study reported that olfactory dysfunction was higher at 1 week and 1 month after surgery compared with before surgery ($P < .001$).¹⁰ These findings indicate that olfactory function was significantly decreased even at 4 months after surgery. Particularly, longer duration of surgery, tumor partial removal, and lower education level were risk factors influencing olfactory dysfunction after surgery. Thus, olfactory function assessment as a postoperative follow-up test is recommended in an outpatient setting, and clinical nurses should monitor patient olfactory function carefully even at 3 months postoperative.

Even after treatment in our study, pituitary macroadenoma patients still experienced a decreased QOL. In a previous study, an analysis of the QOL of patients with nonfunctional pituitary tumors using SF-36 showed similar results with each level of each QOL domain.³⁴ In addition, in 1 case-control study, a comparison of all SF-36 results from 125 controls, with adjustment for age, showed that patients with nonfunctioning pituitary macroadenoma had significantly impaired general health perception, role limitation, and social functioning among QOL domains.³⁵ This result shows that pituitary macroadenoma patients need ample time for full recovery, and the time required for full recovery and return to normal life varies according to

individual and treatment-related factors. Therefore, health providers should identify patients' common symptoms and QOL and be aware of the factors decreasing QOL, in turn providing earlier patient-based interventions to more effectively improve their QOL. Despite the lower QOL and higher symptoms at 3 months after surgery, health providers often do not fully evaluate these common symptoms but only assess MRI and hormone levels in the outpatient setting. To manage this issue, providers should continuously assess barriers influencing their postoperative symptoms and suggest proper pharmacological and nonpharmacological interventions to prevent exacerbation of symptoms and decrease of QOL.

One limitation of this study is its lack of comparison of patients' preoperative and postoperative status, and thus no conclusions can be drawn regarding causal relationships. Because headache etiology is multifactorial in nature and because pituitary adenoma is incidentally discovered in many cases, there is a possibility that many factors could influence patient headache. Thus, the numerous mechanisms underlying headache in pituitary adenoma patients need to be more fully understood, and genetic predisposition for primary headache also needs to be assessed. In future research, various headache-related factors should be considered, and the presurgery and postsurgery headache patterns of patients should be compared. In addition, this study focused on pituitary macroadenomas and did not address functioning pituitary adenomas such as acromegaly, prolactinoma, and Cushing disease. To increase the generalizability of research findings, other types of pituitary adenomas should be assessed, and multiple centers should be involved in the research. For example, future studies could focus on Cushing disease and acromegaly, which typically present with various endocrine-related symptoms. Furthermore, research designs allowing continuous comparison of symptoms during different postoperative periods should be used to enhance understanding of proper postoperative nursing care for pituitary adenoma patients. More in-depth research is needed to identify risk factors for reduced QOL in postoperative pituitary adenoma patients to screen for individuals at a high risk.

Conclusions

We contributed to the understanding of the main symptoms affecting postoperative QOL in pituitary tumor patients and provided essential findings that can be used to develop effective nursing interventions. Even 3 months after transsphenoidal surgery for pituitary adenomas, patients showed a significantly decreased QOL and postoperative symptoms of visual disturbance, olfactory dysfunction, and headache symptoms. Notably, headache was the strongest contributing

factor for decreased QOL. This result contributes to the identification of factors that affect QOL, and it demonstrates that nurses need to provide continuous monitoring and proactive management during the postoperative period in the neuroscience practical field. Finally, as pituitary adenoma patients need distinguished postoperative care from those with other brain tumors, detailed analysis of the patients' QOL and its related symptoms will be helpful for neuroscience nursing management.

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