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Factors Affecting Long-Term Outcomes and Quality of Life of Patients with Pituitary Adenoma After Endoscopic Endonasal Transsphenoidal Surgery (EETS) Using the SF-36 Questionnaire (Indonesian Version)

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Abstract

Objective. To evaluate the quality of life (QoL) of patients with pituitary adenoma following Endoscopic Endonasal Transsphenoidal Surgery (EETS) and identify factors influencing long-term outcomes.

Methodology. A cross-sectional study was conducted at the National Brain Center Hospital, Indonesia. Secondary data were obtained from medical records and the pituitary registry, while primary data were collected through patient interviews using the validated Indonesian version of the SF-36 questionnaire. Statistical analyses included univariate, bivariate, and multivariate linear regression with the backward method to identify independent predictors of QoL.

Results. Among 90 patients (45 males, 45 females), visual disturbances (85.6%) and hormonal deficiencies (93.3%) were common. Most had macroadenomas (95.6%) and received combined EETS and medical therapy (62.2%). Physical component scores (PCS) exceeded mental component scores (MCS). The highest domain scores were in physical functioning and role-emotional functioning; vitality and mental health had the lowest scores. Gender was significantly associated with four QoL domains, and hormonal deficiency affected the role-emotional domain. Multivariate analysis identified gender and hormonal deficiency as predictors of MCS (R^2 = 74%); no factors significantly influenced PCS.

Conclusion. Postoperative QoL after EETS is generally good in physical aspects but suboptimal in mental health. Gender and hormonal deficiency affect mental QoL, highlighting the need for holistic, long-term care strategies.

Key words: pituitary adenoma, quality of life, EETS, SF-36, hormonal deficiency

INTRODUCTION

Pituitary adenoma is a benign tumor of the pituitary gland that can cause a wide range of symptoms due to mass effect and hormonal dysregulation. It accounts for approximately 12.2% of all central nervous system tumors, with a global prevalence ranging between 75.7 and 115.6 per 100,000 population.[1–3] A meta-analysis reported a prevalence of 16.7%, with 14.4% based on autopsy studies and 22.5% from radiological findings.[4] A landmark study in Iceland also reported a prevalence of 115 per 100,000 population.[2,4] In Indonesia, national data on the prevalence and incidence of pituitary adenomas remain scarce. However, the National Cancer Control Committee estimates an annual incidence of 1 to 2 cases per 100,000 people for functional pituitary tumors.[5] At Cipto Mangunkusumo Hospital, pituitary adenomas accounted for 13.9% of all brain tumor cases.[6] A similar study at Kariadi Hospital in Semarang identified 26 cases of pituitary adenomas from January 2020 to December 2022, with 80.8% of patients undergoing

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Endoscopic Endonasal Transsphenoidal Surgery (EETS).[7] Additionally, data from the National Brain Center Hospital (RSPON) recorded 132 cases of pituitary adenoma (58.14%) out of 227 suprasellar tumors from January 2020 to June 2023.

EETS has become the primary surgical approach for treating pituitary adenomas, offering a minimally invasive route with reduced risk of complications, shorter recovery time, direct access to the sella turcica and minimal postoperative pain and infection risk. Although EETS is effective in reducing mass effect and improving symptoms, adjuvant therapy such as medical treatment and hormonal evaluation is often still required. Unfortunately, in many low- and middle-income countries, including the Philippines and Indonesia, medical therapy remains expensive and difficult to access.[8–11] Medications like dopamine agonists, somatostatin analogs, and Cushing-specific therapies are costly and often not covered by health insurance. Treatment for acromegaly costs approximately €9,200–32,807, while treatment for Cushing's disease costs €26,269–34,992. Even for non-functioning pituitary adenomas (NFPAs), which incur lower annual treatment costs (~€3,040) compared to functioning adenomas, the financial burden remains substantial, particularly for patients with hormone deficiencies.[12,13]

While treatment success is typically assessed through hormonal assays and imaging results, quality of life (QoL) is a crucial yet often neglected outcome.[14] Studies show that patients with functioning pituitary adenomas experience worse preoperative QoL, particularly in the social domain, while non-functioning tumors cause symptoms like headaches and visual disturbances.[15] Patients with uncontrolled disease report significantly lower QoL scores on both physical and mental components.[15] Tools such as the QoL-AGHDA and QLS-H confirm decreased QoL in these populations. Though EETS generally improves emotional and mental aspects of QoL postoperatively, physical recovery, such as vitality, physical function and performance of roles, may take longer and depend on tumor size and surgical extent.[6,15] The Indonesian version of the SF-36 has been validated and shown to be reliable for assessing health-related quality of life in Indonesian populations. Salim et al., reported acceptable validity and reliability of the Indonesian SF-36 in patients with permanent pacemakers, with good internal consistency and test-retest reliability. Arovah and Heesch also demonstrated that the Indonesian SF-36 had adequate reliability and construct validity among middle-aged and older Indonesian adults, supporting its use as a generic instrument for evaluating physical and mental components of quality of life in Indonesian settings.[16,17]

Long-term monitoring of QoL is vital for evaluating treatment success holistically. However, this is often hindered by high costs and limited availability of hormonal testing, especially in resource-constrained settings. Prices for diagnostic agents like corticorelin and synacthen have surged, and the costs of essential medications such as insulin and hydrocortisone have risen dramatically over the past decade, further limiting access to care.[18]

Even after surgery, many patients continue to experience reduced QoL due to hormonal imbalances, postoperative complications, chronic fatigue, limited physical activity, or long-term psychosocial effects. Although EETS improves clinical outcomes, these lingering issues highlight the need for better post-treatment support.[19–21]

In Indonesia, there is a lack of research specifically examining QoL among patients with pituitary adenomas after EETS. Therefore, this study aims to: (1) describe the quality of life profile including Physical Component Summary (PCS) and Mental Component Summary (MCS) scores across eight SF-36 domains of pituitary adenoma patients who underwent EETS at the National Brain Center Hospital (RSPON); (2) identify demographic and clinical variables (gender, age, tumor size, hormonal deficiency, visual impairment, therapy type, comorbidity, employment status and postoperative duration) that are significantly associated with each SF-36 domain through bivariate analysis; and (3) determine independent predictors of PCS and MCS using multivariate linear regression analysis. As the first study of its kind in Indonesia, the findings are expected to contribute comprehensive epidemiological data and support the development of more effective and holistic strategies for improving long-term outcomes and well-being in this patient population.

METHODOLOGY

Study design

This study employed a cross-sectional design and was conducted at the pituitary clinic of the National Brain Center Hospital Prof. Dr. dr. Mahar Mardjono, which implements a one-gate multidisciplinary system. The medical team that patients encounter consists of neurosurgeons, internists, neurologists and ENT specialists. The baseline data used in this study were secondary data obtained from the hospital's pituitary clinic registry, while quality-of-life data were collected as primary data through interviews using the validated Indonesian version of the SF-36 quality-of-life questionnaire.

Population and samples

The study population consisted of all adult patients with pituitary adenoma treated at the National Brain Center Hospital Prof. Dr. dr. Mahar Mardjono. The accessible population included adult patients diagnosed with pituitary adenoma who had undergone endoscopic endonasal transsphenoidal surgery (EETS) at the same hospital between January 2020 and December 2024 in Jakarta. The study subjects were all adult patients with pituitary adenomas at the hospital who met the inclusion criteria and did not meet any exclusion criteria.

The inclusion criteria were: (1) patients with a confirmed diagnosis of pituitary adenoma who had undergone EETS between January 2020 and December 2024, (2) aged over 18 years (adults), and (3) able to communicate and be interviewed to complete the data required for the study. The exclusion criteria were: (1) patients who could not be contacted or were lost to follow-up, (2) patients with cognitive impairments (e.g., intellectual disability or dementia) that prevented them from being interviewed about their quality of life, (3) patients with psychiatric diagnoses that could introduce bias in the quality-of-life assessment, (4) patients who could not speak Indonesian fluently, and (5) patients who declined to participate in the study.

Sample size was determined through a power analysis for multiple linear regression. With a significance level of $\alpha = 0.05$, a statistical power of 80% ($1-\beta = 0.80$), and a minimum expected coefficient of determination (R^2) of 0.16 based on prior literature, the minimum required sample size was calculated to be 87 subjects. This calculation accounted for eight independent variables included in the regression model. A total of 90 subjects were enrolled, exceeding the minimum requirement.

Study instrument

The instrument used in this study consisted of two main sources of data. First, secondary data were obtained through the Pituitary Clinic Registry of the National Brain Center Hospital Prof. Dr. dr. Mahar Mardjono, which contained complete information on patient demographic characteristics, laboratory examination results, and medical imaging such as MRI or CT scans that had been systematically documented. Second, to assess patients' quality of life, the validated Indonesian version of the SF-36 questionnaire was used. This questionnaire was administered to each subject who met the inclusion criteria and had signed informed consent. The interviewers, consisting of the principal investigator and trained research assistants, were responsible for guiding respondents through the questionnaire. Each questionnaire was assigned a subject identification number to ensure data confidentiality and facilitate the analysis process.

Data collection

Data were collected from two main sources. Secondary data were obtained from the pituitary clinic registry at the National Brain Center Hospital Prof. Dr. dr. Mahar Mardjono, which included patients' demographic information, hormonal laboratory results (FT4, TSHs, cortisol, prolactin), MRI imaging and visual field test results. Primary data were collected through interviews using the validated Indonesian version of the SF-36 questionnaire. The interviews were conducted by the researcher or research assistants with patients who met the inclusion criteria and provided informed consent.

Each patient was assigned a subject identification number and interviewed via video call, which included confirmation of registry data and complete administration of the SF-36 questionnaire. SF-36 scores were then calculated for eight domains: physical functioning, role limitations due to physical problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems and mental health. These domains were grouped into two major components: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). All domain scores were converted to a 0–100 scale, with higher scores indicating better quality of life.

Data analysis

Data analysis was performed using SPSS Statistics version 24.0. Univariate analysis was conducted to describe the distribution and frequency of all demographic and clinical variables, as well as SF-36 domain scores. Data normality was assessed using the Kolmogorov-Smirnov test. Since the SF-36 domain scores were not normally distributed ($p < 0.05$), nonparametric tests were applied for bivariate analysis: the Mann-Whitney U test for comparisons between two independent groups (e.g., gender, hormonal deficiency, therapy type, comorbidity, visual impairment, employment status) and the Kruskal-Wallis test for variables with more than two categories (e.g., age group, postoperative duration, complaint duration). Variables yielding $p < 0.250$ in bivariate analysis were entered into multivariate analysis. Multivariate analysis was conducted using multiple linear regression with the backward elimination method to identify independent predictors of PCS and MCS scores. Potential confounders, including age group, comorbidity status, and hormonal deficiency, were included in the initial multivariate model and controlled for throughout the backward elimination process. Statistical significance was defined as $p < 0.05$. Missing data were handled by excluding subjects with incomplete SF-36 questionnaire responses or missing registry variables. The final dataset comprised 90 subjects with complete information on all study variables.

RESULTS

The study involved 90 patients with a mean age of 48.11 years (SD ±12.74). Most participants were aged 40 to 60 years (57.8%), followed by those under 40 years (24.4%) and over 61 years (17.8%). The gender distribution was equal, with 45 men (50%) and 45 women (50%). More than half of the participants were employed (58.9%), while the rest were unemployed (41.1%). Hormonal deficiency was present in 84 patients (93.3%), and absent in 6 (6.7%). The majority of tumors were macroadenomas (93.3%), with only 4 cases (4.4%) classified as microadenomas. Regarding treatment, 34 patients (37.8%) underwent endoscopic endonasal transsphenoidal surgery (EETS) alone, while 56 (62.2%) received EETS combined with medical therapy. Comorbidities were found in 29 patients (32.2%), while 61 (67.8%) had no comorbid conditions. Postoperative

duration varied, with 24.4% having undergone surgery within the last year, 33.3% between 1–3 years, and 42.3% more than 3 years prior (Table 1).

Based on the SF-36 questionnaire, the median physical function score was 100 (IQR 85–100), and the role physical domain also had a high median of 100 (75–100), indicating minimal physical limitations in most patients after surgery. The bodily pain domain had a median score of 78 (55–99), indicating moderate levels of perceived pain. General health was rated with a median score of 77 (54–83), and vitality had a slightly lower median of 70 (60–75). Social functioning showed a strong median of 88 (50–100), reflecting relatively preserved social interactions. The role emotional domain achieved a full score of 100 (100–100), suggesting no emotional role limitations in most patients. Mental health had a median score of 72 (56–85), indicating generally good mental well-being. The composite scores were also high, with the Physical Component Summary (PCS) at 84 (73–98) and the Mental Component Summary (MCS) at 83 (72–96). Overall, these results suggest that patients experienced a relatively good quality of life following EETS (Table 2).

Figure 1 shows a radar chart illustrating the distribution of quality-of-life domains based on SF-36 scores among patients following EETS. The chart demonstrates that the highest scores were observed in physical function, role physical, and role emotional, indicating minimal limitations in these areas. Domains such as mental health, social functioning, and bodily pain appear slightly lower, suggesting moderate well-being and some discomfort. Vitality and general health are positioned closer to the center of the chart, indicating these aspects were relatively more affected. Overall, the radar chart reflects the data in Table 2, indicating that patients experienced generally good quality of life after surgery, with variations across specific health domains.

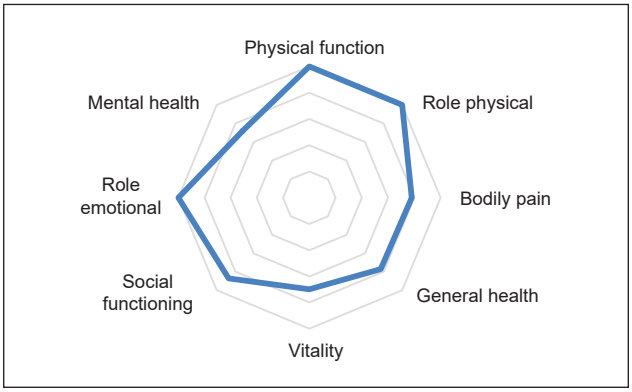

Figure 1. Radar Chart of Quality of Life Domains (SF-36) in Pituitary Adenoma Patients Following EETS (N = 90). Each axis represents one of the eight SF-36 domains on a scale of 0–100, where higher scores indicate better quality of life. The chart illustrates that physical functioning, role physical, and role emotional domains achieved the highest median scores, while vitality and mental health domains were relatively lower, reflecting greater impairment in energy and psychological well-being post-surgery.

Table 1. Characteristics of the study

Characteristic	N = 90
Age (years), median (SB)	48.11 (12.74)
Age category, n (%)	
<40 years	22 (24.4)
40-60 years	52 (57.8)
>61 years	16 (17.8)
Gender, n (%)	
Male	45 (50)
Female	45 (50)
Post operative time range, n (%)	
<1 year	22 (24.4)
1-3 year	30 (33.3)
>3 year	38 (42.3)
Complaint duration, n (%)	
≤1 year	43 (47.8)
>1 years	47 (52.2)
Visual impairment, n (%)	
No	13 (14.4)
Yes	77 (85.6)
Hormone deficiency, n (%)	
No	6 (6.7)
Yes	84 (93.3)
Tumor size	
Microadenoma	4 (4.4)
Macroadenoma	86 (93.3)
Therapy	
EETS only	34 (37.8)
EETS + medicine	56 (62.2)
Comorbid, n (%)	
No	61 (67.8)
Yes	29 (32.2)
Paying Job, n (%)	
Jobless	37 (41.1)
Have Job	53 (58.9)

Table 2. Quality of life status of recipients after undergoing EETS

SF-36	Median (RIK)
Physical function	100 (85-100)
Role physical	100 (75-100)
Bodily pain	78 (55-99)
General health	77 (54-83)
Vitality	70 (60-75)
Social functioning	88 (50-100)
Role emotional	100 (100-100)
Mental health	72 (56-85)
PCS	84 (73-98)
MCS	83 (72-96)

Data were presented as median (interquartile range) for continuous variables and number (%) for categorical variables

Table 3 presents the bivariate analysis of SF-36 domain scores, indicating that gender was the only variable significantly associated with multiple aspects of quality of life. Male patients had significantly higher scores than female patients in the domains of role limitations due to physical problems ($p = 0.042$), vitality ($p = 0.049$), role limitations due to emotional problems ($p = 0.036$), mental health ($p = 0.007$), and the Mental Component Summary (MCS) score ($p = 0.005$). In contrast, other variables, including age, duration of illness, tumor size, visual field impairment, hormonal

Table 3. Bivariate analysis of subject characteristic associated with SF-36 quality of life domain

Variable	Physical function	Role physical	Bodily pain	General health	Vitality	Social functioning	Role emotional	Mental health	PCS	MCS
	Median (IQR)									
Age (years)										
<40	100 (90–100)	100 (94–100)	68 (45–100)	79 (53–83)	70 (60–75)	94 (47–100)	100 (100–100)	78 (55–88)	87 (70–95)	87 (62–89)
40–60	98 (80–100)	100 (75–100)	78 (58–100)	75 (63–83)	68 (60–75)	87 (55–100)	100 (100–100)	76 (56–84)	86 (74–94)	85 (68–89)
≥61	98 (63–100)	100 (56–100)	60 (38–95)	42 (73–82)	70 (58–79)	50 (38–100)	100 (100–100)	66 (54–82)	77 (53–94)	68 (63–89)
p-value	0.713	0.701	0.298	0.314	0.923	0.722	0.580	0.635	0.407	0.494
Gender										
Male	100 (93–100)	100 (100–100)	80 (59–100)	79 (67–83)	70 (65–80)	100 (58–100)	100 (100–100)	84 (60–88)	86 (74–95)	86 (69–90)
Female	95 (85–100)	100 (75–100)	70 (50–95)	75 (48–83)	65 (58–73)	63 (44–100)	100 (67–100)	68 (52–82)	83 (67–90)	73 (58–87)
p-value	0.069	**0.042***	0.201	0.542	**0.049***	0.093	**0.036***	**0.007***	0.102	**0.005***
Complaint duration (years)										
≤1	100 (90–100)	100 (75–100)	70 (55–100)	75 (54–83)	70 (60–75)	88 (50–100)	100 (100–100)	72 (60–84)	84 (72–95)	76 (67–89)
>1	95 (83–95)	100 (75–100)	78 (50–100)	79 (65–83)	70 (60–75)	88 (50–100)	100 (100–100)	76 (56–88)	86 (69–84)	84 (66–88)
p-value	0.382	0.818	0.952	0.606	0.780	0.912	0.521	0.762	0.877	0.903
Tumor size										
Microadenoma	95 (86–100)	100 (63–100)	85 (44–98)	83 (46–90)	68 (61–74)	56 (31–81)	100 (100–100)	62 (47–80)	90 (60–97)	73 (61–83)
Macroadenoma	100 (85–100)	100 (75–100)	74 (55–100)	75 (54–83)	70 (60–75)	88 (50–100)	100 (100–100)	74 (59–88)	84 (71–95)	84 (56–89)
p-value	1.000	0.887	0.872	0.336	0.932	0.317	0.551	0.289	0.489	0.443
Visual field impairment										
No	90 (53–100)	100 (38–100)	80 (56–100)	83 (50–83)	70 (60–78)	88 (56–100)	100 (83–100)	76 (56–90)	86 (51–92)	75 (64–89)
Yes	100 (90–100)	100 (75–100)	70 (55–100)	75 (58–83)	70 (60–75)	88 (50–100)	100 (100–100)	72 (58–84)	84 (72–95)	84 (67–89)
p-value	0.062	0.146	0.489	0.418	0.986	0.962	0.569	0.756	0.483	0.982
Hormonal deficiency										
No	100 (90–100)	88 (56–100)	75 (62–100)	60 (31–83)	65 (46–76)	56 (44–100)	83 (50–100)	52 (6–78)	76 (52–96)	84 (46–87)
Yes	88 (61–100)	100 (75–100)	77.5 (55–100)	77 (63–83)	70 (60–75)	88 (50–100)	100 (100–100)	74 (60–88)	84 (72–94)	84 (67–89)
p-value	0.231	0.342	0.685	0.468	0.418	0.377	**0.041***	0.050	0.523	0.122
Medical therapy										
EETS only	100 (81–100)	100 (75–100)	80 (60–100)	79 (54–83)	70 (60–75)	94 (50–100)	100 (100–100)	68 (55–84)	87 (60–93)	84 (67–89)
EETS + medication	97.5 (89–100)	100 (75–100)	70 (45–100)	75 (56–83)	65 (60–79)	88 (50–100)	100 (100–100)	74 (60–88)	84 (73–95)	82 (66–89)
p-value	0.903	0.470	0.252	0.571	0.814	0.444	0.940	0.336	0.603	0.809
Comorbidity										
No	100 (85–100)	100 (75–100)	70 (56–100)	75 (51–83)	65 (60–75)	88 (50–100)	100 (100–100)	72 (56–84)	84 (68–93)	83 (66–89)
Yes	100 (88–100)	100 (100–100)	80 (45–100)	79 (71–83)	70 (63–78)	88 (50–100)	100 (100–100)	76 (58–88)	85 (71–95)	86 (67–90)
p-value	0.671	0.115	0.923	0.242	0.309	0.986	0.238	0.633	0.422	0.457

*p <0.05 (statistically significant); [a] Kruskal-Wallis test; Mann-Whitney U test for all other variables. IQR = interquartile range.

deficiency, receipt of medical therapy and comorbidity status, did not show statistically significant associations with most quality-of-life domains (p >0.05).

Although hormonal deficiency was not significantly associated with most domains, it showed a statistically significant association with the emotional role domain (p = 0.041) and a borderline association with the mental health domain (p = 0.050). Meanwhile, none of the assessed variables were significantly associated with physical function, bodily pain, general health, social functioning, or the Physical Component Summary (PCS). Due to the limited number of variables meeting the p <0.250 criterion, multivariate analysis was not performed for most domains.

Table 4 presents the results of the multivariate linear regression analysis examining factors associated with each SF-36 quality-of-life domain. The analysis identified gender as a significant predictor across several domains. Specifically, male gender was significantly associated with higher scores in the role physical (β = 12.2; p = 0.032), vitality (β = 5.58; p = 0.045), emotional role (β = 11.8; p = 0.025),

Table 4. Multivariate analysis of subject characteristic associated with SF-36 quality of life domain

Domain	Significant predictors	β coefficient	*p*-value
Physical functioning	Visual impairment	-13.122	0.083
Role physical	Visual impairment	-14.885	0.101
Role emotional	Hormone deficiency	-17.857	0.123
Mental health	Gender	-9.067	**0.008**
	Hormone deficiency	-13.810	**0.043**
Mental Component Summary (MCS)	Hormone deficiency	-12.204	0.083

mental health (β = 10.6; p = 0.006), and mental component summary (MCS) domains (β = 8.24; p = 0.004).

In addition to gender, hormonal deficiency was a significant predictor in the emotional role domain, with patients with hormonal deficiency having higher scores (β = 10.5; p = 0.038) than those without.

These results indicate that male patients and those with hormonal deficiency tended to report better mental and emotional quality of life following EETS, as reflected by higher scores in the relevant SF-36 domains. No other variables showed statistically significant associations in the multivariate models for the remaining domains.

DISCUSSION

This study used the Indonesian version of the SF-36 questionnaire to assess the quality of life of patients following endoscopic endonasal transsphenoidal surgery (EETS). The Kolmogorov-Smirnov normality test indicated that the data were not normally distributed (p <0.05); therefore, bivariate analysis was conducted using the Mann-Whitney test to examine associations between quality-of-life domains and various clinical variables.

The analysis showed that in the domain of physical role limitations, only the variable gender was significantly associated (p = 0.042), with male subjects having a higher median score than females. This suggests that women are more likely to experience physical limitations in daily activities. Nevertheless, the overall median score was 100, indicating a potential ceiling effect. Previous studies by Johnson et al., and Vega-Beyhart et al., support the finding that EETS effectively improves motor function and reduces tumor mass effect, allowing patients to perform daily activities optimally.[6,22] In the domain of physical functioning, no variables showed statistically significant associations. However, gender, visual field impairment and hormonal deficiency had p-values <0.250 and were included in multivariate analysis. The median score was 100, indicating that most patients did not report significant physical limitations. In the domain of bodily pain, the median score was 78. No significant variables were identified; however, postoperative pain may be related to hormonal dysfunction such as TSH or ACTH deficiency. Previous studies, such as Uveilus et al., and Kołtowska-Häggström et al., have reported that hypothyroidism and cortisol deficiency may lead to muscle and joint pain, further exacerbating pain perception. Additionally, nerve damage and vitamin D deficiency after surgery may also contribute to pain.[23,24] In the domain of general health, the median score of 77 reflected patients' positive perception of their health status after surgery, although no variable showed a statistically significant association. Capatina et al., reported that improved hormonal function and reduced tumor-related symptoms contributed to a better perception of general health following treatment.[25] In the domain of vitality, only gender was significantly associated (p = 0.049), with males having a higher median score. This suggests that women experience fatigue more often. Kołtowska-Häggström et al., stated that hormonal imbalances can influence energy levels and overall vitality.[24] In the domain of social functioning, no variables were significantly associated, although high median scores indicated that patients did not experience significant social limitations. Nevertheless, Molitch noted that some patients may still experience social difficulties due to psychological burden or disease-related stigma.[26] In the domain of emotional role limitations, significant associations were found with gender (p = 0.036) and hormonal deficiency (p=0.041). Female patients and those without hormonal deficiency had lower scores. This suggests that emotional responses may be influenced by hormonal fluctuations, as discussed by Johnson et al.[6] In the mental health domain, gender (p = 0.007) and duration of symptoms (p = 0.021) were significantly associated. Male patients had higher scores than females, indicating better mental well-being. Findings from Banskota and Adamson and Zhang et al., are in line with these results, suggesting that pituitary hormonal imbalance may lead to depression, anxiety and sleep disturbances, negatively impacting mental health.[27,28]

In the multivariate analysis, linear regression was conducted for variables with p <0.250 from the bivariate analysis. In the physical functioning and physical role limitation domains, only visual field impairment remained in the final model, though it was not statistically significant. In the emotional role limitation domain, hormonal deficiency was the final variable retained, with a regression coefficient of B = –17.857 (p = 0.123). In the mental health domain, both gender (B = –9.067; p = 0.008) and hormonal deficiency (B = –13.810; p = 0.043) were statistically significant, underscoring the importance of gender and hormonal status in determining mental quality of life.

In the physical component summary (PCS), no variables were significantly associated, although the highest

median scores were observed in patients aged <40 years. This is consistent with findings by Vega-Beyhart et al., who reported that younger patients tended to have better physical recovery postoperatively.[22] Conversely, in the mental component summary (MCS), both gender and hormonal deficiency were significantly associated. Male subjects had a higher median score (86) than female subjects (73). Hormonal deficiency also had a near-significant *p*-value ($p = 0.050$), and in the final model, it was the only remaining variable ($p = 0.083$; B = –12.204). Hormonal imbalance after surgery may affect mood, cognition and self-perception, as described by Kołtowska-Häggström et al.,[24] Overall, EETS is a safe and effective procedure in improving the quality of life for patients with pituitary adenoma. However, psychosocial factors, hormonal disturbances, and access to postoperative hormone therapy remain major challenges. Vega-Beyhart et al., and Salim et al., noted that financial constraints and lack of healthcare infrastructure can negatively affect long-term monitoring and treatment.[22,29] Both MCS and PCS are important indicators for evaluating patient quality of life. They are closely interrelated, with physical improvement supporting psychological well-being and vice versa. Capatina et al., emphasized that comprehensive management of both physical and mental aspects can provide the best outcomes for patients with pituitary adenoma.[25]

The present study was limited to demographic and clinical variables available through the institutional pituitary registry and did not assess financial or social determinants of postoperative QoL, which constitute recognized domains of unmet need in this patient population. Socioeconomic factors, including insurance status, income level and access to primary care, have been shown to significantly influence postoperative follow-up, medication adherence and long-term clinical outcomes following EETS for pituitary adenomas.[29,30] In resource-constrained settings such as Indonesia, the financial burden of long-term hormonal replacement therapy, including cortisol, thyroid hormone and gonadotropin preparations, is particularly pronounced, as coverage under the national health insurance scheme (JKN) remains incomplete for many endocrine conditions.[13,16] This concern is further supported by the broader evidence on financial toxicity in patients with endocrine and oncological conditions in low- and middle-income countries, which has been associated with catastrophic health expenditure, reduced treatment adherence, and progressive deterioration of psychosocial well-being.[31] Future prospective studies should incorporate validated instruments for financial toxicity and social support alongside the SF-36 to provide a more comprehensive characterization of QoL determinants in Indonesian pituitary adenoma patients undergoing long-term postoperative surveillance.

A salient finding of the present study is the more pronounced impairment of the mental component of QoL relative to the physical component in the postoperative period — a pattern that is consistent with emerging evidence in the pituitary adenoma literature. A 2024 systematic review by Castle-Kirszbaum and Goldschlager, encompassing studies of non-functioning pituitary adenomas using validated QoL instruments, demonstrated that patients exhibit significantly worse QoL than healthy controls across both mental and physical domains, with the mechanisms of impairment identified as multifactorial, including hypopituitarism, sleep dysfunction, pain, illness-related stigma, and treatment-related anxiety.[32] Multiple pathophysiological and psychosocial mechanisms may account for the disproportionate mental QoL burden observed in the present cohort. First, postoperative hypopituitarism, which affected 93.3% of study participants, leads to deficiencies of cortisol, thyroid hormone, and gonadotropins, all of which exert significant neuromodulatory effects on mood regulation, cognitive function and stress resilience. The attainment of biochemical equilibrium through hormonal replacement is a gradual process, often spanning several months, during which patients remain in a state of endocrine vulnerability that disproportionately affects psychological well-being.[22] Second, the chronic illness trajectory associated with pituitary adenoma, characterized by prolonged diagnostic delay, recurrent outpatient visits and indefinite pharmacological dependency, has been associated with heightened psychological distress, health anxiety and disease-related stigma that persist beyond the resolution of physical symptoms.[25,26] Third, long-term prospective data from Joustra et al., using multi-dimensional HRQoL assessment over a median follow-up of 8.5 years, demonstrated that psychological and social HRQoL domains exhibited the most sustained impairment and the slowest trajectory of recovery following EETS, corroborating the notion that mental health recovery is a more protracted process than physical restoration after pituitary surgery.[33] Collectively, these mechanisms underscore the need for structured, longitudinal psychosocial support as an integral component of postoperative care in patients with pituitary adenomas.

Based on these findings, several evidence-informed clinical and health policy strategies are proposed to improve postoperative QoL in these patients within the Indonesian healthcare context. First, routine psychological screening using validated instruments, such as the Hospital Anxiety and Depression Scale (HADS), should be systematically incorporated into the standard postoperative follow-up protocol.[34] Given that gender and hormonal deficiency were identified as independent predictors of reduced mental QoL in the present study, female patients and those with confirmed hypopituitarism represent high-priority subgroups for early psychological assessment and intervention. Second, implementation of multidisciplinary, psychosocially-oriented rehabilitation programs encompassing structured patient education regarding hormonal replacement regimens, peer support networks, and liaison with mental health specialists should be considered as standard postoperative care at pituitary centers. The systematic review by Castle-Kirszbaum and Goldschlager identified targeted management of disease-related anxiety

and hypopituitarism as evidence-based pathways to optimize QoL outcomes in pituitary adenoma patients.[32] Third, individualized monitoring of adequacy of hormonal replacement, with periodic biochemical reassessment during the early postoperative period, is warranted given the established association between hormonal deficiency and both emotional role limitations and mental QoL impairment, as demonstrated in this study. Fourth, at the health systems level, low socioeconomic status and inadequate insurance coverage have been identified as significant predictors of postoperative follow-up non-adherence and adverse clinical outcomes in pituitary adenoma patients.[29] Accordingly, advocacy for expanded insurance reimbursement of essential postoperative endocrine therapies under the national JKN scheme, as well as the development of a national, multicenter pituitary adenoma registry, would represent meaningful steps toward equitable and comprehensive long-term care. Collectively, these strategies reflect the imperative for a patient-centered, multidisciplinary approach that integrates biomedical, psychological and socioeconomic dimensions into the long-term postoperative management of patients with pituitary adenoma following EETS.

Several studies have explored the effects of pituitary tumors on patients' quality of life. For example, a study by Gil et al., reported that 74% of patients experienced improvement across all domains of quality of life after endoscopic endonasal transsphenoidal surgery (EETS), with emotional domains showing significantly greater improvements compared to preoperative status.[35] Another study by Karabatsou et al., using the SF-36 questionnaire in 54 patients, demonstrated improvement in all domains, except for the general health score, which showed only modest gains.[36] A Japanese study comparing patients' SF-36 scores before and at 1 and 6 months after EETS found that physical scores declined in the short term but improved thereafter, while mental scores showed continuous improvement postoperatively.[37]

CONCLUSION

The overall quality of life of patients after undergoing EETS surgery in this study was generally good, with higher scores observed in the physical component compared to the mental component. Assessment using the SF-36 instrument revealed that the physical functioning and emotional role limitations domains had the highest scores, indicating stable physical capabilities and emotional resilience. Conversely, lower scores were observed in the domains of vitality and mental health, reflecting reduced energy levels and psychological well-being among some patients. Despite these variations, both the physical and mental components remained within an acceptable range, suggesting a generally favorable postoperative quality of life.

Several factors were identified as influencing quality of life across the SF-36 domains. Gender was significantly associated with physical role limitations, vitality, emotional functioning, and mental health, while hormonal deficiency was linked to emotional functioning. Further multivariate analysis confirmed that both gender and hormonal deficiency had a significant impact on the mental health domain, with gender also influencing the overall Mental Component Summary (MCS) score. These findings highlight the importance of considering biological and psychosocial factors in the holistic management of patients with pituitary adenoma post-surgery.

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All authors certified fulfillment of ICMJE authorship criteria.

CRediT Author Statement
NRZ: Conceptualization, Investigation, Data curation, Formal analysis, Validation, Writing – original draft, Writing – review and editing, Visualization. **TJET**: Conceptualization, Methodology, Validation, Supervision, Project administration, Writing – review and editing. **RP:** Methodology, Validation, Supervision, Writing – review and editing. **MA:** Supervision, Validation, Writing – review and editing, Project administration. **B, AGR,**: Validation, Writing – review and editing. **ERW**: Methodology, Validation, Supervision, Writing – review and editing. All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Data Availability Statement
All data generated and analyzed during this study are included in this published article and its supplementary materials. No additional datasets were generated beyond the data extracted from the included published studies.

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