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Analysis of factors influencing the psychological status and cognitive function of postoperative head and neck tumor patients

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The aim was to analyze the factors influencing the psychological status and cognitive function in postoperative head and neck tumor (HNT) patients. 170 patients, including 90 benign HNT (BHNT) patients and 80 malignant HNT (MHNT) patients, were included in this study. Psychological status was evaluated using the distress thermometer. Cognitive function was evaluated using the Multiple Ability Self-Reported Questionnaire. The psychological status and cognitive function were both statistically significantly better in BHNT patients than in MHNT patients ($P < 0.001$ and $P < 0.001$, respectively). MHNT patients in the moderate and severe appearance defect groups had a higher incidence of psychological distress than those in the no facial appearance defect group ($P = 0.006$ and $P = 0.011$, respectively). Both BHNT and MHNT patients in the group under the age of 60 had a higher incidence of psychological distress than those in the group over the age of 60 ($P = 0.017$ and $P = 0.017$, respectively). Educational level of both BHNT and MHNT patients was negatively correlated with the extent of cognitive impairment ($P = 0.012$ and $P = 0.004$, respectively). The influence of postoperative time on the psychological condition varied in different groups. Postoperative time of both BHNT and MHNT patients was negatively correlated with the extent of cognitive impairment ($P = 0.027$ and $P < 0.001$, respectively).

Keywords Head and neck tumor, Psychological status, Cognitive function

Compared with other types of tumors, head and neck tumor (HNT) has a direct negative effect on appearance. Although reconstructive procedures can neutralize such negative effects to a certain extent, postoperative HNT patients are still likely to suffer from psychological distress and cognitive dysfunction.

Psychological distress refers to an unpleasant experience caused by multiple factors, such as social, mental, physical, etc., which will influence the recovery process and quality of life of a patient[1]. Hassel et al. found that patients diagnosed with HNT will experience different degrees of psychological stress, including depression, anxiety, paranoia, etc[2]. In addition, due to the particularity of the location of HNT, the appearance and function of postoperative HNT patients may be influenced to different degrees.

Postoperative cognitive dysfunction refers to the cognitive and behavioral impairment of patients after general anesthesia and surgical procedures[3–5]. It is a stable and reversible long-term cognitive impairment that has a dramatic impact on a patient[6]. Such long-term cognitive impairment may even progress to irreversible cognitive impairment. The basis for the cognitive impairment of postoperative HNT patients is complex. Studies have proved that the relationship between tumors and inflammation is complicated[7,8]. At the same time, chronic inflammation and metabolism-related factors play a vital role in the occurrence and development of mild cognitive impairment[9]. It was reported that peripheral surgery might lead to a transient inflammatory response in adults[10–12]. It was also confirmed that the elevated level of markers of acute inflammatory response may be associated with postoperative cognitive impairment[13,14].

Considering the complexity of the mental effects of HNT on a patient, clinical treatment should not be limited to physical therapy. Mental status and recovery should also be emphasized. Therefore, the aim of this study was to analyze the factors influencing the psychological status and cognitive function in postoperative HNT patients.

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Materials and methods

Patient selection

This cross-sectional study analyzed the psychological status and cognitive function of postoperative HNT patients. The study complied with the Declaration of Helsinki. The study was approved by the institutional review board of China Medical University. Informed consent was obtained from all of the patients who participated in this study.

The following patients were included: (1) postoperative patients diagnosed with primary benign HNT (BHNT) (squamous cell papilloma of head and neck; pleomorphic adenoma, adenolymphoma, or basal cell adenoma of salivary gland; or ameloblastoma of mandible) or malignant HNT (MHNT) (squamous cell carcinoma of head and neck; mucoepidermoid carcinoma, adenoid cystic carcinoma, or acinic cell carcinoma of salivary gland); (2) adult patients; (3) patients not experiencing recurrence or metastasis; (4) patients without a history of psychiatric diseases or systematic diseases.

The following patients were excluded: (1) not primary BHNT or MHNT; (2) pediatric patients; (3) patients experiencing recurrence or metastasis; (4) patients with a history of psychiatric diseases or systematic diseases.

Outcome evaluation

Information on sex, age, education level, per capita family income, length of stay, appearance defect, operation time, and postoperative time was collected postoperatively. Appearance defect was evaluated by asking the patients to compare their postoperative appearance with their appearance before the disease occurred. The results were classified into three levels based on the extent of disfigurement: no (no disfigurement), moderate (minor disfigurement), and severe (major disfigurement).

Psychological status was evaluated using the distress thermometer (DT). Patients were instructed to mark the number that best matches the level of distress they have experienced in the last week[15]. The results ranged from 0 to 10, with higher scores indicating greater psychological distress. According to the National Comprehensive Cancer Network, a score of 4 or greater was defined as the positive symptom of DT.

Cognitive function was evaluated using the Multiple Ability Self-Reported Questionnaire (MASQ). The results ranged from 1 to 5, with higher scores indicating greater cognitive impairment[16].

Statistical analysis

The data were analyzed using SPSS 27.0 (IBM Corporation, Armonk, New York). $P<0.05$ was considered statistically significant. Continuous data between the BHNT group and the MHNT group was compared using the 2-sample independent t-test.

Factors influencing the psychological status of BHNT patients and MHNT patients were analyzed separately. The bivariate analysis was performed using the Chi-square test to analyze the relationship between patient information and the positive symptom of DT. Statistically significant factors in the bivariate analysis were included in the binary logistic regression model for the multivariate analysis. In order not to overlook any possible factors, the P-value of the multivariate analysis was adjusted to 0.20.

Factors influencing the cognitive function of BHNT patients and MHNT patients were also analyzed separately. The bivariate analysis was performed using the Spearman correlation test to analyze the relationship between patient information and the MASQ score. Statistically significant factors in the bivariate analysis were included in the stepwise regression model for the multivariate analysis. In order not to overlook any possible factors, the P-value of the multivariate analysis was adjusted to 0.20.

Results

Patient information was summarized in Table 1. 170 patients, including 90 BHNT patients and 80 MHNT patients, were included in this study. 35 (38.9%) out of 90 BHNT patients were DT-positive, while 46 (57.5%) out of 80 MHNT patients were DT-positive. The comparison of the DT scores and the MASQ scores between BHNT patients and MHNT patients was summarized in Table 2. The average DT scores of BHNT patients and MHNT patients were 2.51 ± 1.83 and 3.68 ± 2.05, respectively ($P<0.001$). The average MASQ scores of BHNT patients and MHNT patients were 57.84 ± 14.24 and 71.74 ± 12.44, respectively ($P<0.001$).

Psychological status

BHNT patients

The results of the bivariate analysis were shown in Table 3. The results of age, education level, appearance defect, and postoperative time were statistically significant, indicating that these factors were associated with the positive symptom of DT.

The results of the multivariate analysis were shown in Table 4. In order not to overlook any possible factors, the P-value was adjusted to 0.20. Therefore, age, education level, facial appearance defect, postoperative time, and per capita family income were included in the binary logistic regression model.

The results showed that age and postoperative time were independent factors influencing the positive symptom of DT. Patients in the group under the age of 60 had a higher incidence of the positive symptom of DT than those in the group over the age of 60 ($P=0.017$). The influence of postoperative time on the psychological condition was analyzed by comparing the incidence of positive symptom of DT of the 3-month postoperative group, the 6-month postoperative group, and the 9-month postoperative group with that of the 1-month postoperative group, respectively. All three groups showed improvements compared with the 1-month postoperative group. However, the difference between the 3-month postoperative group and the 1-month postoperative group was not statistically significant ($P=0.221$). The difference between the 6-month postoperative group and the

	BHNT ($n=90$)		MHNT ($n=80$)	
	n	%	n	%
Sex				
Male	35	38.9	47	58.7
Female	55	61.1	33	41.3
Age				
Under the age of 60	43	47.8	26	32.5
Over the age of 60	47	52.2	54	67.5
Educational level				
Junior high school or below	21	23.3	29	36.3
Senior high school	25	27.8	27	33.7
College or above	44	48.9	24	30.0
Per capita family income				
less than 150 USD	23	25.6	24	30.0
150 to 450 USD	35	38.9	31	38.7
more than 450 USD	32	35.5	25	31.3
Length of stay				
less than 7 days	50	55.6	12	15.0
7 to 14 days	22	24.4	21	26.2
more than 14 days	18	20.0	47	58.8
Appearance defect				
No	60	66.7	11	13.8
Moderate	16	17.8	27	33.7
Severe	14	15.5	42	52.5
Operation time				
less than 3 h	46	51.1	17	21.2
3 to 4 h	23	25.6	21	26.3
more than 4 h	21	23.3	42	52.5
Postoperative time				
1 month	20	22.2	20	25.0
3 months	25	27.8	20	25.0
6 months	25	27.8	20	25.0
9 months	20	22.2	20	25.0

Table 1. The patient information.

	BHNT	MHNT	*P*
DT (mean ± SD)	2.51 ± 1.83	3.68 ± 2.05	< 0.001
MASQ (mean ± SD)	57.84 ± 14.24	71.74 ± 12.44	< 0.001

Table 2. The comparison of the DT scores and the MASQ scores between BHNT patients and MHNT patients.

1-month postoperative group and the difference between the 9-month postoperative group and the 1-month postoperative group were statistically significant ($P=0.026$ and $P=0.011$, respectively).

MHNT patients

The results of the bivariate analysis were shown in Table 5. The results of sex, age, length of stay, appearance defect, and postoperative time were statistically significant, indicating that these factors were associated with the positive symptom of DT.

The results of the multivariate analysis were shown in Table 6. In order not to overlook any possible factors, the P-value was adjusted to 0.20. Therefore, sex, age, length of stay, appearance defect, postoperative time, and educational level were included in the binary logistic regression model.

The results showed that age, appearance defect, and postoperative time were independent factors influencing the positive symptom of DT. Patients in the group under the age of 60 had a higher incidence of the positive symptom of DT than those in the group over the age of 60 ($P=0.017$). Patients in the moderate and severe appearance defect groups had a higher incidence of the positive symptom of DT than those in the no facial appearance defect group ($P=0.006$ and $P=0.011$, respectively). The influence of postoperative time on the

	DT-positive ($n=35$)	DT-negative ($n=55$)	*P*
Sex			
Male	16	19	0.289
Female	19	36	
Age			
Under the age of 60	23	20	0.007
Over the age of 60	12	35	
Educational level			
Junior high school or below	12	9	0.025
Senior high school	12	13	
College or above	11	33	
Per capita family income			
less than 150 USD	12	11	0.193
150 to 450 USD	14	21	
more than 450 USD	9	23	
Length of stay			
less than 7 days	17	33	0.222
7 to 14 days	12	10	
more than 14 days	6	12	
Appearance defect			
No	18	42	0.036
Moderate	8	8	
Severe	9	5	
Operation time			
less than 3 h	17	29	0.869
3 to 4 h	10	13	
more than 4 h	8	13	
Postoperative time			
1 month	13	7	0.016
3 months	11	14	
6 months	7	18	
9 months	4	16	

Table 3. The results of the bivariate analysis of psychological status of BHNT patients.

	OR (95%CI)	*P*
Age		
Under the age of 60	1.000	
Over the age of 60	0.320 (0.125–0.815)	0.017
Postoperative time		
1 month	1.000	
3 months	0.456 (0.130–1.605)	0.221
6 months	0.225 (0.060–0.834)	0.026
9 months	0.147 (0.034–0.644)	0.011

Table 4. The results of the multivariate analysis of psychological status of BHNT patients.

psychological condition was analyzed by comparing the incidence of positive symptom of DT of the 3-month postoperative group, the 6-month postoperative group, and the 9-month postoperative group with that of the 1-month postoperative group, respectively. All three groups showed improvements compared with the 1-month postoperative group. However, the difference between the 3-month postoperative group and the 1-month postoperative group was not statistically significant ($P=0.527$). The difference between the 6-month postoperative group and the 1-month postoperative group was at the critical value ($P=0.050$). The difference between the 9-month postoperative group and the 1-month postoperative group was statistically significant ($P=0.004$).

	DT-positive ($n=46$)	DT-negative ($n=34$)	*P*
Sex			
Male	22	25	0.021
Female	24	9	
Age			
Under the age of 60	20	6	0.015
Over the age of 60	26	28	
Educational level			
Junior high school or below	16	13	0.168
Senior high school	22	10	
College or above	8	11	
Per capita family income			
less than 150 USD	17	7	0.287
150 to 450 USD	16	15	
more than 450 USD	13	12	
Length of stay			
less than 7 days	3	9	0.044
7 to 14 days	14	7	
more than 14 days	29	18	
Appearance defect			
No	2	9	0.012
Moderate	19	8	
Severe	25	17	
Operation time			
less than 3 h	8	9	0.412
3 to 4 h	11	10	
more than 4 h	27	15	
Postoperative time			
1 month	16	4	0.027
3 months	13	7	
6 months	10	10	
9 months	7	13	

Table 5. The results of the bivariate analysis of psychological status of MHNT patients.

	OR (95%CI)	*P*
Age		
Under the age of 60	1.000	
Over the age of 60	0.223 (0.065–0.762)	0.017
Appearance defect		
No	1.000	
Moderate	18.531 (2.329-147.457)	0.006
Severe	14.072 (1.844-107.411)	0.011
Postoperative time		
1 month	1.000	
3 months	0.600 (0.123–2.921)	0.527
6 months	0.210 (0.044–0.997)	0.050
9 months	0.099 (0.021–0.473)	0.004

Table 6. The results of the multivariate analysis of psychological status of MHNT patients.

Cognitive function

BHNT patients

The results of the bivariate analysis were shown in Table 7. The results of educational level and postoperative time were statistically significant, indicating that these factors were associated with the MASQ score.

	r	*P*
Sex	-0.169	0.111
Age	0.017	0.876
Educational level	-0.253	0.016
Per capita family income	-0.104	0.327
Length of stay	0.150	0.159
Appearance defect	0.141	0.185
Operation time	0.114	0.283
Postoperative time	-0.261	0.013

Table 7. The results of the bivariate analysis of cognitive function of BHNT patients.

	b	Standard error	β	t	*P*
(Constant)	75.654	4.910		15.407	< 0.001
Educational level	-4.542	1.766	-0.260	-2.572	0.012
Postoperative time	-3.026	1.341	-0.228	-2.256	0.027

Table 8. The results of the multivariate analysis of cognitive function of BHNT patients.

	r	*P*
Sex	0.476	0.081
Age	0.170	0.131
Educational level	-0.267	0.017
Per capita family income	-0.174	0.122
Length of stay	-0.022	0.847
Appearance defect	-0.128	0.257
Operation time	0.009	0.935
Postoperative time	-0.370	0.001

Table 9. The results of the bivariate analysis of cognitive function of MHNT patients.

	b	Standard error	β	t	*P*
(Constant)	80.571	5.913		13.625	< 0.001
Postoperative time	-4.31	1.084	-0.390	-3.978	< 0.001
Educational level	-4.701	1.587	-0.291	-2.962	0.004
Age	6.422	2.589	0.243	2.481	0.015

Table 10. The results of the multivariate analysis of cognitive function of MHNT patients.

The results of the multivariate analysis were shown in Table 8. In order not to overlook any possible factors, the P-value was adjusted to 0.20. Therefore, educational level, postoperative time, sex, length of stay, and appearance defect were included in the stepwise regression model.

The results showed that educational level and postoperative time were independent factors influencing the MASQ score. Educational level was negatively correlated with the extent of cognitive impairment ($P = 0.012$). The lower the educational level was, the more severe the cognitive impairment was. Postoperative time was also negatively correlated with cognitive impairment ($P = 0.027$). The shorter the postoperative time was, the more severe the cognitive impairment was.

MHNT patients

The results of the bivariate analysis were shown in Table 9. The results of educational level and postoperative time were statistically significant, indicating that these factors were associated with the MASQ score.

The results of the multivariate analysis were shown in Table 10. In order not to overlook any possible factors, the P-value was adjusted to 0.20. Therefore, educational level, postoperative time, sex, age, and per capita family income were included in the stepwise regression model.

The results showed that age, educational level, and postoperative time were independent factors influencing the MASQ score. Age was positively correlated with cognitive impairment ($P = 0.015$). The patients in the

group over the age of 60 had more serious cognitive impairment than patients in the group under the age of 60. Educational level was negatively correlated with cognitive impairment ($P=0.004$). The lower the educational level was, the more severe the cognitive impairment was. Postoperative time was also negatively correlated with cognitive impairment ($P<0.001$). The shorter the postoperative time was, the more severe the cognitive impairment was.

Discussion

Apart from the negative effects on function and appearance, the psychological status and cognitive function of postoperative HNT patients will also be influenced. Therefore, it is essential to assess these parameters and investigate the factors influencing them.

The study at the stage of selecting factors for multivariate analysis is still exploratory. In order to ensure that potentially important factors were not overlooked in the early stages, a P-value threshold of 0.2 was set to allow for the inclusion of factors that might not meet the traditional threshold for statistical significance but still had a potential impact on the outcome. Although this helped reduce the risk of type II errors (false negatives) by reducing the chances of missing factors that could be important, this may also increase the risk of type I errors (false positives).

The psychological status and cognitive function were both statistically significantly better in BHNT patients than in MHNT patients ($P<0.001$ and $P<0.001$, respectively) (Table 2). In this study, the rates of psychological distress in patients with BHNT and MHNT were 38.9% and 57.5%, respectively. The results of MHNT in this study were much higher than the results of other studies analyzing other types of malignancies conducted by Zabora et al. (35.1%) and Carlson et al. (37.8%)[17,18]. This may be due to the fact that MHNT patients are more likely to suffer from aesthetic, functional, and mental damage due to the specificity of the tumor site and the higher risks of disfigurement.

Appearance defect was a statistically significant factor influencing the psychological status of MHNT patients ($P=0.006$ and $P=0.011$, respectively) (Table 6). Patients in the moderate and severe appearance defect groups had a higher incidence of psychological distress than those in the no facial appearance defect group. This may be due to the fact that MHNT patients are more likely to have soft or hard tissue defects due to radical surgical resection. They may feel ashamed and, therefore, are less willing to communicate or socialize. Moreover, soft or hard tissue defects and surgical complications may lead to functional disorders, such as reduced mastication efficiency, dysphagia, dysarthria, facial paralysis, shoulder motor dysfunction, etc., in the surgical field. These negative impacts can dramatically decline the quality of life and psychological status.

Age was a statistically significant factor influencing the psychological status of patients of both BHNT and MHNT patients ($P=0.017$ and $P=0.017$, respectively) (Tables 4 and 6, respectively). Patients in the group under the age of 60 had a higher incidence of psychological distress than those in the group over the age of 60. This conclusion was consistent with the results of the studies conducted by Chambers et al.[19]. Multiple reasons may contribute to this result. On the one hand, this may be due to the incompatibility between the "life development stage" and the severity of the disease. On the other hand, the fact that patients under 60 years of age also need to face work problems, participate in communication and social activities, and face the problem of children's education, which makes their lives more stressful.

Educational level was a statistically significant factor influencing the cognitive function of both BHNT and MHNT patients ($P=0.012$ and $P=0.004$, respectively) (Tables 8 and 10, respectively). It was negatively correlated with the extent of cognitive impairment. The lower the educational level was, the more severe the cognitive impairment was. This conclusion was consistent with the results of studies conducted by Ardila and Moreno[20]. In the bivariate analysis of the correlation between educational level and the MASQ scores of BHNT patients, the results were statistically significant in different groups. In the multivariate analysis, educational level became a relatively large risk factor in the cognitive impairment of BHNT patients. The educational level was negatively correlated with cognitive impairment.

The influence of postoperative time on the psychological condition was analyzed by comparing the incidence of psychological distress of the 3-month postoperative group, the 6-month postoperative group, and the 9-month postoperative group with that of the 1-month postoperative group, respectively. All three groups showed psychological improvement compared with the 1-month postoperative group. However, psychological improvement of the 3-month postoperative group compared with the 1-month postoperative group was not statistically significant in both BHNT patients and MHNT patients ($P=0.221$ and $P=0.527$, respectively) (Tables 4 and 6, respectively). Psychological improvement of the 6-month postoperative group compared with the 1-month postoperative group was statistically significant in BHNT patients, while it was at the critical value in MHNT patients ($P=0.026$ and $P=0.050$, respectively) (Tables 4 and 6, respectively). Psychological improvement of the 9-month postoperative group compared with the 1-month postoperative group was statistically significant in both BHNT patients and MHNT patients ($P=0.011$ and $P=0.004$, respectively) (Tables 4 and 6, respectively). This indicate that psychological distress is likely to weaken as time goes by. The longer the postoperative time is, the less severe the psychological distress may be.

Postoperative time was also a statistically significant factor influencing the cognitive function of both BHNT and MHNT patients ($P=0.027$ and $P<0.001$, respectively) (Tables 8 and 10, respectively). It was negatively correlated with the extent of cognitive impairment. The lower the educational level was, the more severe the cognitive impairment was. Brown CH et al. reported that most of the cognitive functions of cardiac surgery patients returned to normal at one year postoperatively[21]. Von Ah et al. reported that cognitive impairment may last for up to 20 years or even longer after breast cancer treatment[22]. Therefore, the length of time required for cognitive function recovery varied in different fields. Further investigation is still required.

Currently, there are relatively more studies analyzing the psychological condition of postoperative systemic tumor patients and the factors influencing cognitive function in patients with brain tumors and chronic diseases,

while there are relatively fewer studies analyzing HNT patients. In addition, previous studies analyzing factors influencing the psychological status and cognitive function have focused on malignant tumors, while few studies have reported these aspects on benign tumors. As a result, this study, for the first time, analyzed the factors influencing the psychological status and cognitive function of postoperative BHNT and MHNT patients, which confirmed both aspects might be influenced by a combination of factors.

Potential programs aimed to prevent or alleviate the postoperative psychological distress or cognitive impairment should be designed. Based on the risk factors analyzed in this study, professionals or clinicians can assess the probability of such postoperative negative effects by collecting demographic data preoperatively. According to our study, attention should be paid to the following patients who possess certain risk factors: (1) MHNT patients; (2) young patients; (3) patients who are likely to have postoperative appearance defects; (4) less educated patients. Such risk factors may contribute to postoperative psychological distress and postoperative impairment. Therefore, individualized interventions should be customized according to the specific needs of these patients to improve their quality of life and sense of well-being. Moreover, based on the results of this study, it is also important to assure the patients that such negative feelings will weaken steadily and significantly as time goes by.

Limitations.

Firstly, this cross-sectional study recorded data at a single point each time. Although it was useful for examining associations between factors, it did not permit the identification of cause-and-effect relationships. Therefore, the results should be interpreted as correlational rather than causal. Moreover, although the sample size of 170 patients may be sufficient for detecting statistically significant effects within the studied participants, considering that this was a single-center study, the sample size may not reflect the wider population, potentially impacting the generalization of the conclusions. Future longitudinal studies with larger and more diverse samples would be helpful in confirming the reliability and validity of the conclusion.

Secondly, surgical factors, such as the types of surgery, the extent of tissue removal, anesthesia time, etc., which may impact patients' recovery process and subsequent state of mind, were not analyzed separately. Without controlling these confounding factors, the results of the study may not be completely accurate. This may also impact the reliability and validity of the conclusion.

Thirdly, the lack of objective measurement tools in this field may impact the accuracy of outcome assessment. Compared with objective assessment conducted by professionals, patient-reported assessment is inherently subjective. Participants may not always have accurate self-perceptions and, therefore, may report in a biased manner. The subjective nature of self-reports can also lead to inconsistency when multiple assessments are conducted among different participants or over time. Self-reported assessment also lack the specificity that professional evaluations provide. This can lead to higher risks of inaccuracy with less reliability and validity.

Conclusion

The psychological status and cognitive function were both statistically significantly better in BHNT patients than in MHNT patients ($P<0.001$ and $P<0.001$, respectively). MHNT patients in the moderate and severe appearance defect groups had a higher incidence of psychological distress than those in the no facial appearance defect group ($P=0.006$ and $P=0.011$, respectively). Both BHNT and MHNT patients in the group under the age of 60 had a higher incidence of psychological distress than those in the group over the age of 60 ($P=0.017$ and $P=0.017$, respectively). Educational level of both BHNT and MHNT patients was negatively correlated with the extent of cognitive impairment ($P=0.012$ and $P=0.004$, respectively). Psychological improvement of the 6-month postoperative group compared with the 1-month postoperative group was statistically significant in BHNT patients, while it was at the critical value in MHNT patients ($P=0.026$ and $P=0.050$, respectively). Psychological improvement of the 9-month postoperative group compared with the 1-month postoperative group was statistically significant in both BHNT patients and MHNT patients ($P=0.011$ and $P=0.004$, respectively). Postoperative time of both BHNT and MHNT patients was negatively correlated with the extent of cognitive impairment ($P=0.027$ and $P<0.001$, respectively).

Data availability

The data that support the finding of this study is available from the corresponding author upon reasonable requests.

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Declarations

Competing interests
The authors declare no competing interests.

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