


The Influencing Factors of Frailty and Quality of Life in Elderly Patients After Spinal Surgery

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Background: To study the related factors of frailty and quality of life in elderly patients after spinal surgery.

Methods: The anxiety, depression, frailty, and quality of life of all patients were assessed by the Anxiety screening scale (GAD-7), Depression screening scale (PHQ-9), Frailty screening scale (FRAIL), and European five-dimensional health scale (EQ-5D-5L) 1 day before surgery (DAY-0). A numeric rating scale (NRS) was used to evaluate patients' pain during activities on the 1st day (POD-1), 3rd day (POD-3), and 30th day (POD-30) after operation. FRAIL scale and EQ-5D-5L were used to evaluate patients' frailty and quality of life on POD-30 and 90th day (POD-90) after the operation.

Results: There were significant differences in age, body mass index (BMI), preoperative serum albumin level (ALB), and NRS score on POD-1 between the two groups ($P < 0.05$). Age and PHQ-9 score were positively correlated with EQ-5D-5L score ($P < 0.05$, $r_{\text{Age}} = 0.245$, $r_{\text{PHQ-9}} = 0.217$), and preoperative ALB level was negatively correlated with EQ-5D-5L score ($P < 0.05$, $r_{\text{ALB}} = -0.274$).

Conclusion: The older the age, the larger the BMI and the higher the NRS score on the first day after surgery, the more prone to frailty in elderly patients after spinal surgery; The older age and the lower the preoperative ALB level, the worse the quality of life in elderly patients after spinal surgery.

Keywords: elderly patients, spinal surgery, frailty, quality of life

Introduction

Compared with the young, the organs and physiological functions of the elderly have different degrees of decline, and the decline of the neuromuscular system has caused a series of spinal diseases.¹ Most patients with spinal diseases often present with chronic pain and tend to have inappropriate pain perception, such as kinesiophobia, hypervigilance, and pain catastrophizing, which can lead to poor treatment results and seriously affect the quality of life. It is the main cause of increased disability rates, increased medical expenses, and decreased quality of life.^{2,3} Studies have shown that neuropathic pain and walking distance can be improved by surgery, so some patients with severe conditions need surgery.⁴ Surgical traumatic stress and pain can cause frailty in elderly patients (prevalence rate 4.0%~59.1%), increase the incidence of adverse health events, and thus affect the quality of early postoperative rehabilitation.⁵ Therefore, early diagnosis, intervention, and guidance for frailty are extremely important.

Frailty is a multi-dimensional and multi-system clinical syndrome, which is mainly an age-related non-specific state with decreased anti-stress ability due to decreased reserve capacity of physiological function. Clinically, frailty can be manifested as fatigue, slow walking speed, and weight loss.⁶ The occurrence of frailty is not caused by a single factor. Advanced age, female, ethnic minorities, smoking, multiple diseases, chronic diseases, obesity or malnutrition, depression, and other factors can cause frailty.^{7,8} However, there are few studies on the occurrence of frailty after spinal surgery

in the elderly and analysis of its related risk factors, to intervene in related risk factors and improve the quality of life of patients after surgery.

This study intends to follow up with elderly patients undergoing spinal surgery, evaluate the anxiety, depression, frailty, pain, and quality of life of the patients with relevant scales, collect the perioperative data of the patients, such as medical records, surgical anesthesia-related data, postoperative acute pain, etc., and find out the related risk factors of frailty and analyze its impact on quality of life. Then, the improvement of quality of life before and after spinal surgery was compared to find out the factors affecting the quality of life of patients after surgery, to accelerate the early recovery of patients through the intervention of related risk factors.

Materials and Methods

Patients and Groups

Elderly patients undergoing spinal joint surgery in the First Affiliated Hospital of Guangxi Medical University from October 2020 to October 2022 were selected and divided into the non-frailty group and frailty group according to whether frailty occurred on POD-30.

Inclusion criteria: age greater than or equal to 65 years; elective spinal surgery; No frailty occurred before surgery; ASA grade I~III; language communication barrier-free, with a certain language understanding, and reading ability; patients or family members agreed to participate in the follow-up and signed informed consent.

Exclusion criteria: emergency surgery; preoperative patients with severe disturbance of consciousness, mental illness, such as coma patients, schizophrenia, severe dementia, personality cognitive disorder, etc.; Severe loss of hearing or vision; patients and their families refused follow-up. To ensure the authenticity of the data, the investigator did not participate in the anesthesia and perioperative management of the patients, and the investigator blinded the anesthesia and perioperative management.

Research Program

After approval by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (ethics number: 2019PHB258-01) and obtaining the written consent of the selected patients, we included 102 patients with elective surgery. This study was conducted according to the Declaration of Helsinki. All participants were informed of the purpose of the experiment. Patients who met the criteria were followed up, signed the informed consent of anesthesia, and invited patients to participate in and complete the project questionnaire (FRAIL, GAD-7, PHQ-9, EQ-5D-5L scale) to assess the patient's frailty, anxiety, depression, and quality of life at DAY-0. A postoperative questionnaire survey (NRS) was conducted on POD-1, POD-3, and POD-30 after surgery to evaluate the pain of patients during activity. The postoperative questionnaire survey (FRAIL, EQ-5D-5L scale) was conducted on POD-30 and POD-90 to evaluate the level of frailty and quality of life of patients. All patients were investigated by face-to-face questionnaire during hospitalization and followed up by telephone after discharge. All patients were followed up 90 days after surgery. Follow-up was conducted by a researcher who was not involved in anesthesia and perioperative treatment. Researchers were unaware of anesthesia and perioperative treatment.

Assessment Scale and Data Collection

The main data of this study are five scale scores, namely FRAIL, GAD-7, PHQ-9, EQ-5D-5L, and NRS scale scores. Through the hospital's electronic medical record system (HIS) and preoperative visits, the patient's general information (gender, age, BMI, and ethnicity), preoperative associated diseases (hypertension, diabetes, coronary heart disease, anxiety or depression), laboratory results (Hb and ALB) and intraoperative conditions (surgical site, surgical grade, ASA grade, anesthesia method, surgery time, anesthesia time, recovery time and bleeding loss) were collected. This study aimed to analyze the independent risk factors of frailty and the difference in postoperative quality of life between the two groups.

Statistical

All data were analyzed using IBM SPSS 25.0 software. Measurement data conforming to normal distribution or approximate normal distribution were expressed as mean \pm standard deviation ($\bar{x} \pm s$). Two-sample *t*-test was used for inter-group comparison. The measurement data that did not conform to the normal distribution were expressed as median (P25, P75), and the non-parametric test was used for comparison between groups. Counting data were represented by the number of cases (%). The chi-square test and Fisher exact test were used for comparison between groups. Logistic regression analysis was used for multivariate analysis. Spearman rank correlation analysis and multiple linear regression analysis were used to analyze the correlation between the scores of the scales and repeated measures ANOVA was used to analyze the scales at different time points. $P < 0.05$ was considered statistically significant.

Result

Data Information

According to the inclusion and exclusion criteria, a total of 113 elderly patients participated in this study, of which 2 died, 9 were lost to follow-up, 102 patients completed the 30th-day postoperative follow-up, and 1 was lost on the 90th day after surgery. A total of 101 patients completed all follow-up. The effective date of all patients was included in the statistical analysis.

Incidence of Postoperative Frailty

The incidence of frailty on POD-30 was 35.3% (36/102), and the incidence of frailty on POD-90 was 11.9% (12/101) (Table 1, Figure 1).

Univariate analysis of general data, surgical anesthesia of the two groups

The results showed that there were no statistically significant differences in gender, ethnicity, preoperative-associated diseases (hypertension, diabetes, coronary heart disease, anxiety, or depression), preoperative Hb, and factors related to surgical anesthesia (surgical site, ASA classification, surgical classification, anesthesia method, surgery time, anesthesia time, recovery time and bleeding loss) between the two groups ($P > 0.05$). There were significant differences in age, BMI, and preoperative ALB between the two groups ($P < 0.05$) (Table 2).

Univariate Analysis of Postoperative Pain of the Two Groups

Applying the Mann–Whitney *U*-test for analysis, our results showed that the NRS scores of the frailty group were higher than those of the non-frailty group on the 1st, 3rd, and 30th days after surgery, but the difference in NRS scores only on POD-1 was statistically significant between the two groups ($P < 0.05$), and the difference in NRS score between the 3rd day and the 30th day after surgery was not statistically significant ($P > 0.05$) (Table 3).

Analysis of Multiple Risk Factors for Frailty

The results of the above univariate analysis showed that age, BMI, preoperative ALB, and NRS score on POD-1 might be the influencing factors of postoperative frailty. All the above 4 factors were included in Logistic multivariate regression analysis. Our results showed that preoperative ALB did not independently predict the occurrence of postoperative frailty ($P > 0.05$). Age, BMI and NRS score on POD-1 were independent risk factors for postoperative frailty ($P < 0.05$). In other words, with all other factors remained constant, for every 1-year increase in age, the risk of postoperative frailty increased 1.161 times (95% CI:

Table 1 Incidence of Frailty at Different Time Points (n, %)

	POD-30	POD-90
Non-frailty group[cases (%)]	66(64.7)	89(88.1)
Frailty group[cases (%)]	36(35.3)	12(11.9)

Abbreviations: POD-30, the 30th day after operation; POD-90, the 90th day after operation.

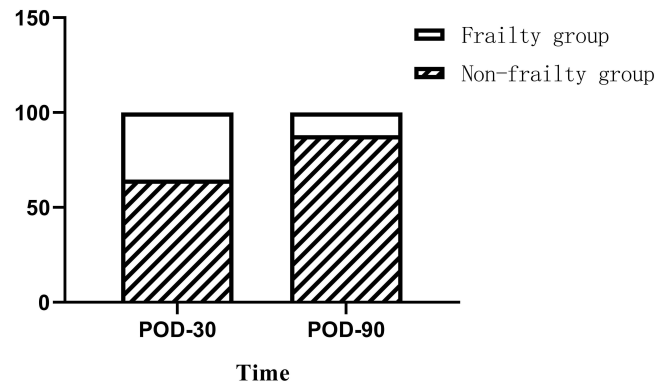


Figure 1 Incidence of frailty at different time points. The chi-square test and Fisher's exact test were used to compare the incidence of frailty between groups. **Abbreviations:** POD-30, the 30th day after operation; POD-90, the 90th day after operation.

1.043~1.293); for every 1-unit increase in BMI, the risk of postoperative frailty increased 1.197 times (95% CI: 1.034~1.387); and for every 1-unit increase in NRS on POD-1, the risk of postoperative frailty increased 1.607 times (95% CI: 1.205~2.143), that is, the older the patient, the higher the BMI, and the higher the NRS score on POD-1, the greater the risk of postoperative frailty (Table 4, Figure 2).

Table 2 Preoperative Analysis of Related Factors in the Two Groups of Patients ($\bar{x} \pm s, \%$)

Index	Non-Frailty Group (n=66)	Frailty Group (n=36)	P-value
Age (years)	69.55±4.11	71.42±5.07	0.046
Gender [cases (%)]			
Male	29(43.9)	15(41.5)	0.825
Female	37(56.1)	21(56.9)	
BMI (kg/m ²)	22.8±2.90	24.42±3.73	0.028
Ethnicity [cases (%)]			
Han nationality	45(68.2)	23(63.9)	0.660
Ethnic minorities	21(31.8)	13(36.1)	
Hypertension [cases (%)]			
YES	26(39.4)	13(36.1)	0.744
NO	40(60.6)	23(63.9)	
Diabetes[cases (%)]			
YES	7(10.6)	4(11.1)	1.000
NO	59(89.4)	32(88.9)	
Coronary heart disease[cases (%)]			
YES	4(6.1)	6(16.7)	0.160
NO	62(93.9)	30(83.3)	
Anxiety[cases (%)]			
YES	17(25.8)	6(16.7)	0.294
NO	49(74.2)	30(83.3)	
Depression[cases (%)]			
YES	8(12.1)	6(16.7)	0.524
NO	58(87.9)	30(83.3)	
Preoperative Hb (g/L)	126.86±17.73	130.16±16.78	0.362
Preoperative ALB (g/L)	42.2(39.9, 43.2) ^a	40.7(38.0, 41.9) ^a	0.023

Notes: ^aData described as median (P25, P75); Except for the preoperative ALB level, which was expressed as the median (P25, P75), and the chi-square test was applied for between-group comparisons, all other data were expressed as the mean ± standard deviation, and the two-sample t-test was applied for comparison between groups. P<0.05 indicated that the difference was statistically significant.

Abbreviations: BMI, body mass index; ALB, serum albumin level.

Table 3 Comparison of NRS Scores Between the Two Groups at Different Times M (P25, P75)

	NRS Score		
	POD-1	POD-3	POD-30
Non-frailty group	(2,4)*	(2,3)	(0,2)
Frailty group	(2,25,6)	(2,3)	(0,3)
Z	-2.846	-1.291	-1.232
P	0.004	0.197	0.218

Notes: Applying the Mann–Whitney U-test for analysis. Compared with the frail group at the same time point, *P < 0.05.

Abbreviations: POD-1, the 1st day after operation; POD-3, the 3rd day after operation; POD-30, the 30th day after operation; NRS, Numeric rating scale.

Table 4 Multivariate Logistic Regression Analysis of Frailty (n=102)

Independent variable	β	SE	Wald χ^2	P	OR	95% CI
Constant	-12.878	5.453	5.577	0.018	<0.001	
Age	0.149	0.055	7.427	0.006	1.161	1.043~1.293
BMI	0.180	0.075	5.772	0.016	1.197	1.034~1.387
Preoperative ALB	-0.102	0.067	2.297	0.130	0.903	0.792~1.030
NRS on POD-1	0.474	0.147	10.422	0.001	1.607	1.205~2.143

Note: P<0.05 was considered statistically significant.

Abbreviations: BMI, body mass index; ALB, serum albumin level; NRS, Numeric rating scale; POD-1, the 1st day after operation.

Comparison of Postoperative Quality of Life Between Patients with Frailty and Patients Without Frailty

We first recorded the FRAIL and EQ-5D-5L scores of all patients on DAY-1 as a reference for non-surgical status. The FRAIL and EQ-5D-5L scales were also used on the 30th and 90th days after surgery to evaluate the postoperative frailty and quality of life of patients. The results showed that there was no statistical significance in EQ-5D-5L scores between the two groups on DAY-1 (P>0.05), the EQ-5D-5L scores of the frailty group on the 30th day and the 90th day after

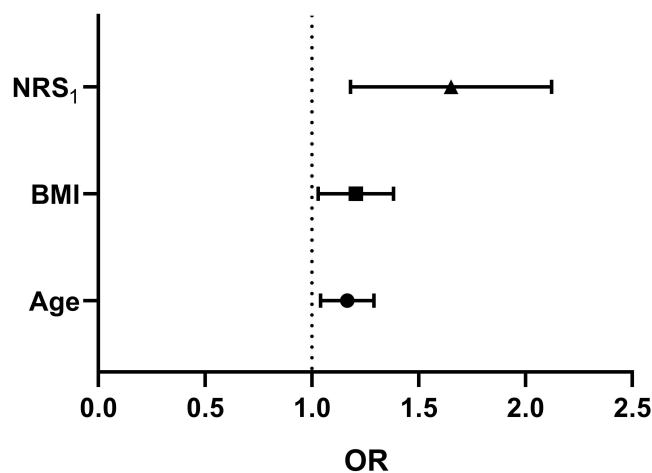


Figure 2 Frailty-related risk factors analysis. Logistic multivariate regression analysis was applied to analyze the risk factors associated with frailty, and the results showed that Age, BMI, and NRS₁ were independent risk factors for postoperative frailty (P<0.05).

Abbreviations: BMI, body mass index; NRS, Numeric rating scale; NRS₁, the NRS score on the first day after surgery.

Table 5 Comparison of EQ-5D-5L Scores Between the Two Groups at Different Times ($\bar{x} \pm s$)

	EQ-5D-5L		
	DAY-0	POD-30	POD-90
Non-frailty group	9.89±3.43*	6.95±2.69 ^{a*}	5.94±1.75 ^{ab*}
Frailty group	11.11±3.98	11.61±4.37	9.28±4.60 ^{ab}

Notes: $F_{\text{time}} = 21.100$, $P_{\text{time}} < 0.001$; $F_{\text{group}} = 43.382$, $P_{\text{group}} < 0.001$; $F_{\text{group} \times \text{time}} = 6.943$, $P_{\text{group} \times \text{time}} = 0.001$; Compared with DAY-0 in the same group, ^a $P < 0.05$; Compared with POD-30 in the same group, ^b $P < 0.05$; Compared with the frail group at the same time point, * $P < 0.05$.

Abbreviations: DAY-0, 1 day before surgery; POD-30, the 30th day after operation; POD-90, the 90th day after operation; EQ-5D-5L, European five-dimensional health scale.

surgery were higher than those of the non-frailty group ($P < 0.05$) (Table 5, Figure 3). That is, patients with postoperative frailty had worse quality of life than patients without postoperative frailty.

The results showed that compared with DAY-1, the EQ-5D-5L scores of the two groups decreased on the 30th day and the 90th day after surgery, and the EQ-5D-5L score on POD-90 was lower than that on POD-30 ($P < 0.05$) (Table 5, Figure 3). Our results indicate that the quality of life of patients in both groups gradually improved with the prolongation of postoperative time, and the postoperative quality of life in the non-frailty group was always better than that in the frailty group.

Age and Preoperative ALB Were Independent Risk Factors for Postoperative Quality of Life

Correlation analysis of EQ-5D-5L scores on POD-30 showed that age and PHQ-9 scores were positively correlated with EQ-5D-5L scores ($P < 0.05$, $r_{\text{age}} = 0.245$, $r_{\text{PHQ-9}} = 0.217$). ALB levels were negatively correlated with EQ-5D-5L scores ($P < 0.05$, $r_{\text{Preoperative ALB}} = -0.274$) (Table 6). Age, PHQ-9 score, and preoperative ALB were included in the linear regression model, and the results showed that age and preoperative ALB were independent risk factors affecting postoperative quality of life ($P < 0.05$) (Table 7), that is, the older the patient, the lower the preoperative ALB level, the higher the score of EQ-5D-5L, the worse the quality of life.

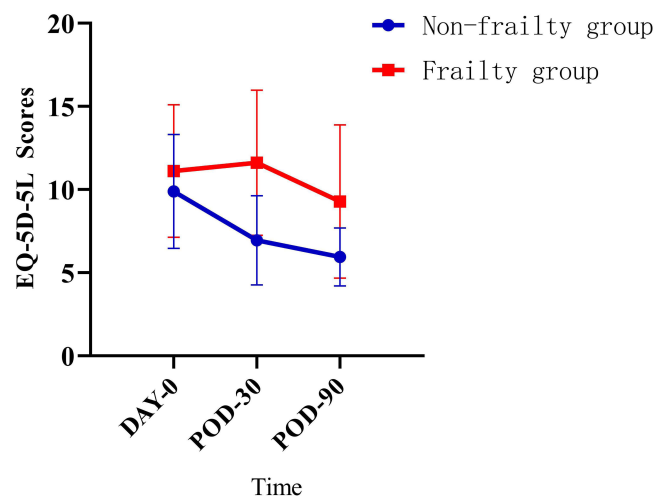


Figure 3 Comparison of EQ-5D-5L scores between the two groups at different time points. Repeated-measures ANOVA was applied to compare the differences in EQ-5D-5L scores between the two groups of patients at different time points.

Abbreviations: DAY-0, 1 day before surgery; POD-30, the 30th day after operation; POD-90, the 90th day after operation; EQ-5D-5L, European five-dimensional health scale.

Table 6 Correlation Analysis of EQ-5D-5L Scores 30 Days After Surgery (n=102)

Variable	r	P
Age	0.245*	0.013
Gender	-0.017	0.863
BMI	0.145	0.147
Ethnicity	-0.065	0.513
Hypertension	-0.026	0.793
Diabetes	0.118	0.236
Coronary heart disease	0.073	0.465
Preoperative GAD-7 score	0.126	0.208
Preoperative PHQ-9 score	0.217*	0.028
Preoperative Hb	0.065	0.518
Preoperative ALB	-0.274**	0.006
ASA classification	0.063	0.526
Surgical classification	-0.057	0.570
Anesthesia method	-0.075	0.451
Surgery time	0.038	0.707
Anesthesia time	0.031	0.756
Recovery time	0.047	0.641
Bleeding loss	0.079	0.432
NRS score on POD-1	0.142	0.154
NRS score on POD-3	0.016	0.871
NRS score on POD-30	0.063	0.532

Notes: *At 0.05 level (two-tailed), the correlation was significant; **At 0.01 level (two-tailed), the correlation was significant. P<0.05 was considered statistically significant.

Abbreviations: EQ-5D-5L, European five-dimensional health scale; BMI, body mass index; GAD-7, Anxiety screening scale; PHQ-9, Depression screening scale; ALB, serum albumin level; NRS, Numeric rating scale; POD-1, the 1st day after operation; POD-3, the 3rd day after operation; POD-30, the 30th day after operation.

Table 7 Multiple Linear Regression of EQ-5D-5L at 30 Days After Surgery (n=102)

Variable	Standard Error	P
(constant)	7.098	0.561
Age	0.084	0.011
Preoperative PHQ-9 score	0.118	0.323
Preoperative ALB	0.099	0.007

Note: P<0.05 was considered statistically significant.

Abbreviations: EQ-5D-5L, European five-dimensional health scale; PHQ-9, Depression screening scale; ALB, serum albumin level.

Discussion

The incidence of frailty is higher in the elderly, and it is often higher after external stimuli such as surgical trauma, pain, inflammation, and oxidative stress, which can be manifested as a decline or change in the physiological functions of multiple systems.^{9,10} In this study, the incidence of frailty in elderly patients on POD-30 was 35.3%. In a 2022 prospective cohort study of the long-term effects of frailty on elderly patients after emergency surgical surgery, 82 patients over 70 years of age were followed up to 18 months after surgery, and the prevalence of postoperative frailty in elderly patients was 14.6% to 29.6%.¹¹ Studies have also reported a prevalence of frailty ranging from 4.0% to 59.1%.⁵

The results of this study are consistent. In this study, it was found that age could independently predict the occurrence of postoperative frailty in elderly patients undergoing spinal surgery. There are also many studies at home and abroad that reported that age is one of the independent risk factors for frailty.^{12,13} Some Chinese scholars analyzed the risk factors of frailty in 3836 cases of geriatric internal medicine patients and found that aging is the risk factor of frailty.⁸ Our research also confirms this. Frailty itself is an age-related clinical syndrome with a variety of clinical causes and intricate molecular mechanisms. It may be related to age-related systemic immune cell aging, mitochondrial structural dysfunction, loss of telomere structure, increased generation of oxygen free radicals, and poor self-repair ability of deoxyribonucleotides. However, the theoretical mechanism needs to be further confirmed.^{14,15}

Bennett et al conducted a cross-sectional descriptive study on frailty and related factors in 216 breast cancer patients and found that compared with patients without frailty, the risk of frailty increased by 1.12 times for every 1 unit increase in BMI (95% CI:1.04~1.19).¹⁶ Many domestic and foreign research results show that obesity and a higher BMI index are more likely to lead to frailty.^{17,18} In this study, BMI was also found to be an independent risk factor for frailty after spinal surgery in older patients. Patients undergoing spinal surgery often need to carry out postoperative rehabilitation exercises. When the patient's BMI level is high and the muscle content is reduced, exercise endurance is reduced during the rehabilitation process, and accidents such as falls are prone to occur, leading to frailty. However, some scholars have reported that low BMI is a risk factor for frailty,⁸ and a study on the relationship between nutritional status and functional risk factors among elderly people in the community found that BMI cannot independently predict the occurrence of frailty.¹⁹ Therefore, our research results can only indicate that BMI can independently predict the occurrence of frailty in elderly patients with spinal surgery. There is still some controversy, and we need to further study and confirm the correlation between BMI and frailty.

Compared with general surgery, patients undergoing spinal surgery often have different degrees of pain before surgery due to intervertebral disc compression of the spinal cord, spinal stenosis, and other reasons, and the degree of pain is often more serious. This acute strong stress source can lead to the imbalance of internal environmental homeostasis and autonomic nervous disorder in elderly patients, leading to postoperative frailty. Studies have found that pain plays an important role in the occurrence of frailty.^{20,21} This study also found that the degree of pain on POD-1 was a risk factor for postoperative frailty. Frailty may be a risk factor for pain regulation acting on the descending inhibitory pathway, and the two may share some molecular mechanisms such as inflammation and neuroinflammation, which strengthen the interaction between the two.²²

This study compared the quality of life of all patients at POD-1, POD-30, and POD-90, and the results showed that the quality of life of elderly patients after spinal surgery was significantly improved over time, but the quality of life of patients with frailty improved more slowly and the improvement effect was weaker than that of the non-frailty group. Chotai et al followed up on the quality of life of 448 elderly patients over 70 years old after lumbar surgery for 1 year and found that even though the quality of life of patients with frailty after surgery was improved compared with that before surgery, the quality of life of patients with frailty after surgery was worse than that of non-frail patients.²³ For further study, we analyzed the related factors of quality of life in elderly patients at POD-30 and found that age and preoperative ALB could independently predict the quality of life of patients after surgery. With the increase of age, the function of various organs in the elderly also decreases, and the endurance and grip strength decrease, which leads to the poor quality of life after surgery. A study of functional outcomes and mortality after hip fracture in elderly patients found that low ALB levels were an independent risk factor for postoperative death, impaired hip function recovery, and impaired ability to perform activities of daily living after surgery.²⁴ The main role of ALB is to maintain the colloid osmotic pressure of the blood. After surgery, the body is in a high metabolic state in response to acute stress, which can lead to a negative nitrogen balance. The lower the preoperative ALB level, the more serious the negative nitrogen balance, which can lead to postoperative wound tissue edema and infection, affect wound healing, and further affect early postoperative rehabilitation.

This study is a prospective cohort study of elderly patients over 65 years old. There are few reports on the influencing factors of frailty and quality of life after spinal surgery. This study has certain innovations. As a clinician, early intervention of related risk factors after spinal surgery in elderly patients can avoid the occurrence of postoperative frailty and promote early postoperative recovery of patients. However, there are some limitations in this study. This study only followed the elderly patients on POD-30 and POD-90 and did not follow up to 6 months, 1 year, and 2 years after the operation, which could only evaluate the short-term prognosis of the elderly patients. At the same time, the sample size included in this study is small, and

the reliability and sensitivity of the risk factors for predicting the occurrence of frailty and postoperative quality of life changes are small. It is still necessary to further expand the number of cases for follow-up and analysis.

Conclusion

The older the age, the larger the BMI and the higher the NRS score on the first day after surgery, the more prone to frailty in elderly patients after spinal surgery. The older age and the lower the preoperative ALB level, the worse the quality of life in elderly patients after spinal surgery. The quality of life of elderly patients after spinal surgery improved significantly compared to the preoperative period, but the quality of life of patients with frailty improved more slowly than those without frailty after surgery.

Abbreviations

DAY-0, 1 day before surgery; POD-1, the 1st day after operation; POD-3, the 3rd day after operation; POD-30, the 30th day after operation; POD-90, the 90th day after operation; BMI, body mass index; ALB, serum albumin level; NRS, Numeric rating scale; NRS₁, the NRS score on the first day after surgery; EQ-5D-5L, European five-dimensional health scale; GAD-7, Anxiety screening scale; PHQ-9, Depression screening scale; FRAIL, Frailty screening scale.

Data Sharing Statement

The datasets generated and analyzed during the current study are not publicly available due to limitations of ethical approval involving the patient data and anonymity but are available from the corresponding author upon reasonable request.

Ethics Approval and Informed Consent

After approval by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (ethics number: 2019PHB258-01) and obtaining the written consent of the selected patients. This study was conducted according to the Declaration of Helsinki. All participants were informed of the purpose of the experiment.

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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