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ARTICLE

Predictive Value of the Estimation of Physiologic Ability and Surgical Stress for Postoperative Recurrent Laryngeal Nerve Injury in Patients With Type 2 Diabetes Mellitus Complicated by Thyroid Cancer: A Retrospective Cohort Study

Jiameng Guo[1,2,*], Ning Xiao[3], Jiawen Zhang[4]

[1]Department of Nursing, School of Medicine, Hunan Normal University, Changsha, Hunan, China
[2]Department of Nursing, Xinzheng Huaxin Minsheng Hospital, Xinzheng, Henan, China
[3]Department of Nursing, Changsha Dongxiesheng Hospital, Changsha, Hunan, China
[4]Department of Endocrinology, The Fourth Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, China
*Correspondence: 15333826279@163.com (Jiameng Guo)

Abstract

Aims/Background In the postoperative management of patients with type 2 diabetes mellitus (T2DM) and thyroid cancer, recurrent laryngeal nerve (RLN) injury is a significant complication. Due to existing metabolic abnormalities, surgical stress may further impair the recovery of physiological functions in these patients. This study aimed to investigate the predictive value of the Estimation of Physiologic Ability and Surgical Stress (E-PASS) system for postoperative RLN injury in patients with T2DM complicated by thyroid cancer.

Methods A retrospective analysis was conducted on 210 patients with T2DM complicated by thyroid cancer who were admitted to Xinzheng Huaxin Minsheng Hospital from January 2021 to December 2023. Clinical data were collected from the electronic medical record system. Patients were divided into the injury group (n = 60) and the non-injury group (n = 150) based on the occurrence of postoperative RLN injury. Univariate and multivariate logistic regression analyses were performed to identify factors associated with RLN injury. The predictive value of E-PASS for postoperative RLN injury was evaluated using receiver operating characteristic (ROC) curve analysis.

Results Univariate and multivariate logistic regression analyses revealed that preoperative risk score (PRS), surgical stress score (SSS), and comprehensive risk score (CRS) were independent risk factors for RLN injury in patients with T2DM and thyroid cancer ($p < 0.05$). ROC curve analysis indicated that the area under the curve (AUC) for E-PASS was 0.866, with a standard error of 0.026 (95% CI: 0.814–0.917). The optimal cutoff value was 0.70, yielding a sensitivity of 91.54% and a specificity of 62.55%.

Conclusion The comprehensive risk assessment provided by E-PASS demonstrates good predictive value for RLN injury in patients with T2DM complicated by thyroid cancer. Integrating PRS, SSS, and CRS can enhance risk assessment and guide early intervention to promote postoperative recovery.

Key words: type 2 diabetes mellitus; thyroid cancer; recurrent laryngeal nerve injuries

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Introduction

Recurrent laryngeal nerve (RLN) injury is a common complication of thyroid surgery, especially in thyroid cancer procedures, and significantly impacts the quality of life of patients (Chen et al, 2022). During thyroid surgery, the anatomical

position of the RLN is complex and delicate, making it highly susceptible to surgical trauma. In patients with type 2 diabetes mellitus (T2DM) and thyroid cancer, diabetes-related vascular lesions may cause insufficient blood supply to the RLN, impairing nerve nutrition and metabolism and thus increasing the risk of nerve injury. Additionally, diabetic patients have relatively impaired wound healing capabilities and may experience delayed postoperative recovery. Consequently, once RLN injury occurs, the recovery process may be slower and more complex. Therefore, for such patients, comprehensive preoperative assessment and risk prediction are particularly critical. The risk of RLN injury in patients with T2DM complicated by thyroid cancer may be further increased due to the vascular and neurological complications associated with diabetes. Therefore, identifying effective methods to predict the risk of postoperative RLN injury in these patients is crucial for optimizing surgical strategies and enhancing perioperative safety (Wolff et al, 2025).

Physiological ability refers to an individual's capacity to perform normal activities and maintain functional stability across multiple systems, such as cardiovascular, respiratory, and nervous systems (Bulut et al, 2024). The surgical stress score reflects the degree of surgical burden on the patient's body, encompassing factors such as the magnitude of surgery, operative duration, and intraoperative blood loss. Both physiologic status and surgical stress are closely associated with the risk of RLN injury (Chen et al, 2021).

The Estimation of Physiologic Ability and Surgical Stress (E-PASS) scoring system is primarily employed to evaluate a patient's baseline physiological state and response to surgical stress. E-PASS enables physicians to gain a comprehensive understanding of a patient's physical condition, estimate surgical risk, and predict postoperative outcomes (Dai et al, 2022; Kato et al, 2024). However, studies evaluating the predictive value of physiologic ability and surgical stress on postoperative RLN injury in T2DM patients with thyroid cancer are currently limited.

This study aimed to investigate the predictive potential of E-PASS in assessing the risk of postoperative RLN injury through a retrospective analysis. The findings will provide a scientific foundation for clinical decision-making, assisting physicians in more accurately assessing preoperative risks, developing rational surgical plans, and formulating effective postoperative recovery strategies. Ultimately, this may reduce the incidence of RLN injury and improve the postoperative quality of life for patients.

Methods

Research Objects

A total of 210 patients with T2DM complicated by thyroid cancer, admitted to Xinzheng Huaxin Minsheng Hospital between January 2021 and December 2023, were retrospectively selected. The patient selection process is shown in Fig. 1. The inclusion criteria were as follows: (1) All patients met the clinical diagnostic criteria for T2DM complicated by thyroid cancer (Baloch and LiVolsi, 2005; Harreiter and Roden, 2023). (2) Preoperative electronic laryngoscopy showed normal vocal cord function. (3) Patients had no preoperative hoarseness or vocal cord paralysis. The

exclusion criteria were as follows: (1) Patients with other concurrent malignant tumors. (2) Patients with a history of mental disorders. (3) Patients with cardiac, hepatic, pulmonary, or renal dysfunction. (4) Patients who withdrew from follow-up prematurely.

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Medical Ethics Committee of Xinzheng Huaxin Minsheng Hospital (Approval No. 2024HS012). Informed consent was obtained from all patients.

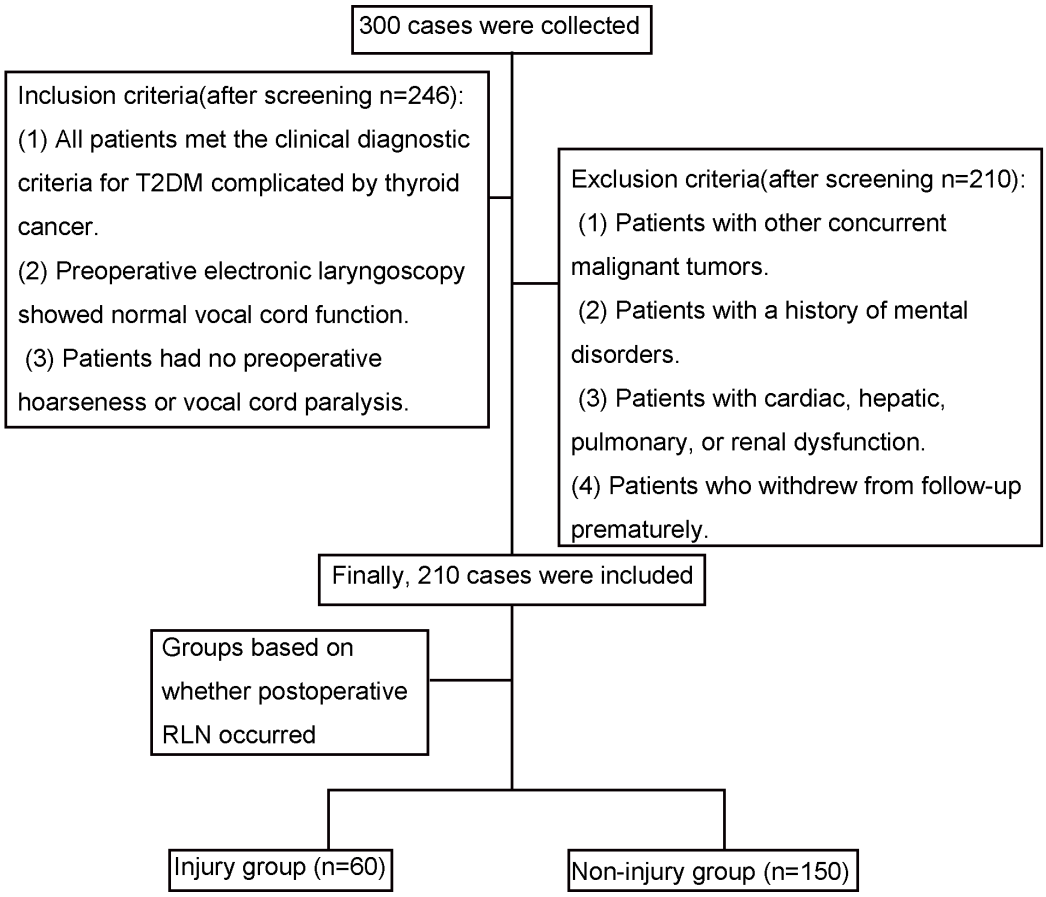

Fig. 1. Flowchart of patient inclusion and analysis. T2DM, type 2 diabetes mellitus; RLN, recurrent laryngeal nerve.

Research Methods

General patient data were collected through the electronic medical record system of the hospital. Patients were categorized into the injury group (n = 60) and the non-injury group (n = 150) based on whether postoperative recurrent laryngeal nerve (RLN) injury occurred. Diagnostic criteria for RLN injury (Hydman et al, 2009): Following total thyroidectomy for thyroid cancer, patients exhibiting hoarseness, loss of voice, or respiratory difficulty within one week were evaluated by electronic laryngoscopy. RLN was diagnosed if vocal cord movement impairment was confirmed. Temporary RLN injuries were defined as symptom resolution within

three months postoperatively. If symptoms persisted without significant improvement for more than three months and continued for up to six months postoperatively, the injury was considered permanent.

Preoperative risk score (PRS), surgical stress score (SSS), and comprehensive risk score (CRS) were calculated using the E-PASS system. The scoring equations (Haga et al, 2001) were as follows:

$$PRS = -0.0686 + 0.00345 \times X1 + 0.323 \times X2 + 0.205 \times X3 + 0.153 \times X4 + 0.148 \times X5 + 0.0666 \times X6$$

$$SSS = -0.342 + 0.0139 \times X1 + 0.0392 \times X2 + 0.352 \times X3$$

$$CRS = -0.328 + 0.936 \times PRS + 0.976 \times SSS$$

Risk indicators for the preoperative risk score (PRS) included: (1) X1: Age. (2) X2: Presence of severe heart disease, defined as New York Heart Association class III or IV, or arrhythmia requiring supportive treatment (yes = 1; no = 0). (3) X3: Presence of severe lung disease, defined as vital capacity (VC) <60% and/or percentage of forced expiratory volume in 1 second (FEV1%) <50% (yes = 1; no = 0). (4) X4: Presence of diabetes based on WHO diagnostic criteria (yes = 1; no = 0). (5) X5: Performance status index, graded 0 to 4 according to Japanese Cancer Therapy Society standards. (6) X6: American Society of Anesthesiologists (ASA) classification, graded from 1 to 5.

Risk indicators for surgical stress score (SSS) included: (1) X1: Blood loss-to-body weight ratio (mL/kg). Blood loss (mL) was estimated as: Blood loss (mL) = (Postoperative gauze weight (g) – Preoperative gauze weight (g)) + Suction bucket fluid (g) – Flushing fluid weight (g) (Lin et al, 2024). (2) X2: Operation time (minutes). (3) X3: Incision type (0 = minimally invasive similar to laparoscopically; 1 = thoracotomy).

Surgeon screening and standardization: To ensure technical consistency, only case data from senior surgeons with ≥10 years of clinical experience and an annual operation volume of more than 200 procedures were included. Standardized operating specifications were formulated, including steps for RLN exposure, anatomical landmark identification, and standardized instrument usage. All participating doctors underwent a preoperative standardized assessment and a three-month special training program focusing on RLN identification and protection strategies using a simulated surgery platform. Practical sessions were supplemented with video review to ensure operational consistency. Intraoperative nerve monitoring systems were employed to provide real-time feedback on RLN electrical signals, with data transmitted to an independent analysis system to minimize observer bias.

Statistical Analysis

The collected experimental data were analyzed using SPSS version 27.0 (International Business Machines Corporation, Armonk, NY, USA). The Shapiro-Wilk test was used to assess data normality. For data following a normal distribution, results were expressed as mean ± standard deviation ($\bar{X} \pm S$), and comparisons were made using independent samples *t*-tests. For skewed variables, data were described using median and interquartile range (IQR), and analyzed with non-parametric tests, specifically the Mann-Whitney U test. Categorical variables were presented as

Table 1. Univariate analysis of factors associated with postoperative RLN injury in patients with T2DM complicated with thyroid cancer.

Baseline data	Injury group (n = 60)	Non-injury group (n = 150)	t/χ^2 value	p-value
Age (years)	54.97 ± 10.64	55.16 ± 9.97	0.122	0.903
Gender			0.048	0.827
Male	31	75		
Female	29	75		
Smoking status			0.875	0.350
Yes	21	63		
No	39	87		
Alcohol consumption			0.231	0.631
Yes	16	45		
No	44	105		
BMI (kg/m^2)	21.66 ± 1.21	21.55 ± 1.16	0.613	0.540
Maximum tumor diameter (cm)	2.13 ± 1.02	2.24 ± 0.97	0.732	0.465
Tumor location*			4.084	0.043
Left	20	73		
Right	40	77		
Pathological type			0.023	0.989
Papillary thyroid carcinoma	40	100		
Follicular carcinoma	10	26		
Medullary carcinoma	10	24		
Clinical stage			0.034	0.983
Stage I	10	25		
Stage II	9	24		
Stage III	41	101		
Intraoperative nerve monitoring*			4.295	0.038
Yes	19	71		
No	41	79		
Number of surgeries			0.119	0.730
First-time	15	41		
Multiple	45	109		
E-PASS scores				
PRS*	0.31 ± 0.11	0.29 ± 0.01	2.212	0.028
SSS**	0.50 ± 0.10	0.31 ± 0.10	12.438	<0.001
CRS**	0.46 ± 0.13	0.28 ± 0.06	13.724	<0.001
Anesthesia method			0.193	0.664
General + cervical plexus block	28	65		
General only	32	85		
Operation time (minutes)	100.58 ± 15.64	99.87 ± 15.91	0.294	0.769
Intraoperative blood loss (mL)	30.54 ± 11.54	30.82 ± 11.26	0.162	0.872
Lymph node dissection			1.680	0.195
Yes	24	46		
No	36	104		

Note: BMI, body mass index; PRS, preoperative risk score; E-PASS, the Estimation of Physiologic Ability and Surgical Stress; SSS, surgical stress score; CRS, comprehensive risk score. *$p < 0.05$, **$p < 0.01$.

counts and analyzed with chi-square or Fisher's exact tests, where appropriate. Collinearity was assessed via linear regression diagnostics. Univariate and multivariate logistic regression analyses were conducted to identify factors associated with postoperative RLN injury in patients with T2DM complicated by thyroid cancer. The predictive value of the E-PASS for postoperative RLN injury was evaluated using receiver operating characteristic (ROC) curves. Missing data were excluded from the analysis. A p-value < 0.05 was considered statistically significant.

Results

Univariate Analysis of Factors Influencing RLN Injury in Patients With T2DM Complicated by Thyroid Cancer

There were no statistically significant differences in age, gender, smoking status, alcohol consumption, body mass index (BMI), maximum tumor diameter, pathological type, clinical stage, number of surgeries, operation time, intraoperative blood loss, lymph node dissection, or anesthesia method between the RLN injury and non-injury groups ($p > 0.05$). However, statistically significant differences were observed in tumor location, use of intraoperative nerve monitoring, PRS, SSS, and CRS ($p < 0.05$), as shown in Table 1.

Multifactorial Logistic Regression Analysis of Influencing Factors

Tumor location, intraoperative nerve monitoring, PRS, SSS, and CRS were included as independent variables, with postoperative RLN injury as the dependent variable (injury = 1, non-injury = 0). The results of multivariate logistic regression analysis indicated that PRS, SSS, and CRS were independent influencing factors of RLN injury in patients with T2DM complicated by thyroid cancer ($p < 0.05$), as shown in Table 2.

Receiver Operating Characteristic (ROC) Curve Analysis

ROC curve analysis demonstrated that the area under the curve (AUC) for E-PASS in predicting postoperative RLN injury was 0.866, with a standard error of 0.026 (95% CI: 0.814–0.917). The optimal cutoff value was determined to be 0.70, corresponding to a sensitivity of 91.54% and a specificity of 62.55%, as shown in Table 3 and Fig. 2.

Discussion

This study aimed to evaluate the predictive value of physiological capacity and the E-PASS system in predicting the risk of postoperative RLN injury in T2DM patients with thyroid cancer. Through retrospective analysis of 210 patients, the study found that CRS has significant predictive value for postoperative RLN injury in this patient population.

Initially, the baseline characteristics of patients were described and compared. The results showed significant differences in tumor location, intraoperative nerve monitoring, PRS, SSS and CRS between the RLN injury and non-injury group. Previous findings by Kasap et al (2022) have shown that E-PASS correlates with

Table 2. Multifactorial logistic regression analysis of factors associated with RLN injury.

Variable	β coefficient	SE	Wald value	OR	95% CI	p-value	Tolerance	VIF
Tumor location	–1.571	1.667	0.889	0.208	0.008–5.451	0.346	0.996	1.004
Intraoperative nerve monitoring	–1.860	1.596	1.357	0.156	0.007–3.557	0.244	0.969	1.032
PRS*	0.264	0.122	4.686	1.303	1.025–1.655	0.030	0.387	2.585
SSS*	0.543	0.246	4.859	1.721	1.062–2.790	0.028	0.384	2.606
CRS**	0.141	0.049	8.221	1.152	1.046–1.269	0.004	0.430	2.327
Constant	–9.300	1.347	7.650	<0.001	-	-	-	-

Note: VIF, variance inflation factor. *$p < 0.05$, **$p < 0.01$.

Table 3. Receiver operating characteristic (ROC) curve analysis of E-PASS components for predicting RLN injury.

Variable	AUC	SE	95% CI	p-value	Youden index	Sensitivity (%)	Specificity (%)
PRS**	0.634	0.044	0.547–0.721	0.002	0.27	33.33	94.21
SSS**	0.857	0.028	0.803–0.911	<0.001	0.53	60.00	92.71
CRS**	0.832	0.031	0.770–0.893	<0.001	0.49	53.33	95.33
Joint indicator (E-PASS)**	0.866	0.026	0.814–0.917	<0.001	0.54	91.54	62.55

Note: E-PASS, Estimation of Physiologic Ability and Surgical Stress; AUC, area under the curve. **$p < 0.01$.

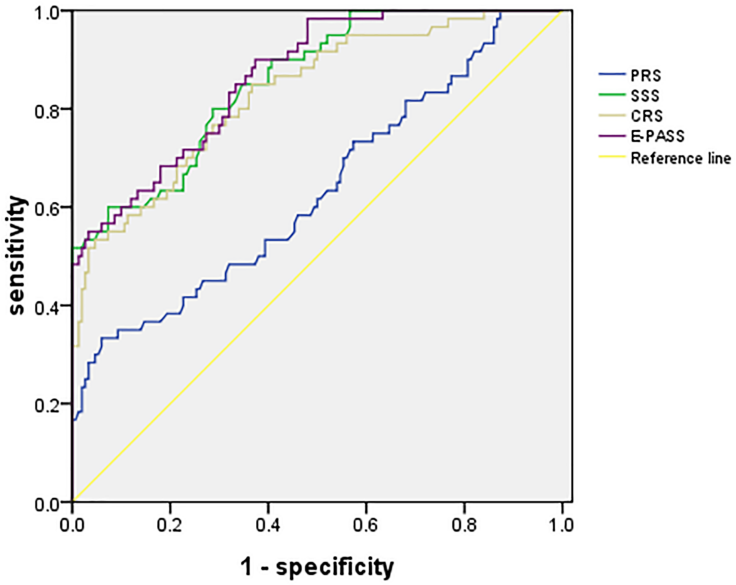

Fig. 2. Receiver operating characteristic (ROC) curve analysis of predictive scores. The ROC curve shows that CRS has the largest AUC, indicating the highest predictive value for postoperative RLN injury among the evaluated scores.

the severity of postoperative complications and can effectively predict postoperative risks. These findings are consistent with the current study, suggesting that these parameters are closely related to the occurrence of postoperative RLN injury. Multivariate logistic regression analysis was subsequently used to identify independent predictors of postoperative RLN injury in patients with T2DM and thyroid cancer. The analysis confirmed that PRS, SSS, and CRS, individually and in combination as E-PASS, were independent risk factors of postoperative RLN injury. Tumor location emerged as a critical determinant of RLN injury risk, particularly when tumors are located close to or involve the recurrent laryngeal nerve, significantly increasing the risk of nerve injury during surgery. Consequently, precise preoperative assessment of tumor location is crucial to mitigate this risk.

Additionally, intraoperative nerve monitoring was shown to be an effective tool for real-time assessment of the RLN function, assisting surgeons in avoiding nerve injury during surgery (Shi et al, 2022). The present study demonstrated that patients who underwent intraoperative nerve monitoring exhibited a significantly reduced incidence of postoperative RLN injury, underscoring its importance as a protective measure. Furthermore, the PRS is derived from the evaluation of patients' preoperative physiological conditions, reflecting their overall health status before surgery (Kayra et al, 2024). A higher PRS indicates an increased surgical risk, including the risk of postoperative RLN injury. The findings of this study support this view, showing that PRS is an independent influencing factor for postoperative RLN injury.

The surgical stress score (SSS) represents the level of physiological stress experienced by patients during surgery. Elevated surgical stress is associated with a higher probability of complications during postoperative recovery (Murakami et al, 2020), including RLN injury. This study observed a close relationship between

SSS and the risk of postoperative RLN injury, highlighting the importance of controlling surgical stress to help prevent such complications.

The comprehensive risk score (CRS) integrates PRS and SSS, reflecting the overall perioperative risk faced by patients during surgery (Norimatsu et al, 2022). The results of this study demonstrated that CRS exhibited the highest predictive value for RLN injury in T2DM patients with thyroid cancer, with high sensitivity and specificity. This suggests that a combined assessment of preoperative physiological condition and intraoperative stress allows for a more accurate prediction of postoperative RLN injury.

Previous studies (Efanov et al, 2021; Norimatsu et al, 2022) have shown the clinical utility of the E-PASS scoring system in various surgical contexts. However, its application in thyroid cancer is still insufficient. This study applied the E-PASS scoring system to patients with type 2 diabetes and thyroid cancer to evaluate its predictive value for postoperative RLN injury. By comprehensively assessing the patient's physiological ability and surgical stress level, E-PASS provides a valuable tool for risk stratification. This application not only broadens the scope of E-PASS, but also provides a new perspective and scientific rationale for optimizing perioperative management in this high-risk patient group.

Moreover, previous research by Morishima et al (2025) showed that E-PASS holds value in the assessment of perioperative complications in neck surgeries. The ROC analysis in this study further confirmed the predictive accuracy of E-PASS for RLN injury, with an area under the curve (AUC) of 0.866. This value exceeded that of individual components, PRS (AUC = 0.634), SSS (AUC = 0.857), and CRS (AUC = 0.832), indicating that E-PASS has superior overall predictive performance. Further analysis showed that setting the E-PASS cutoff value at 0.70 yielded a sensitivity of 91.54%, indicating that 91.54% of patients who experienced RLN injury were correctly identified. At the same time, the specificity was 62.55%, indicating that 62.55% of patients without RLN injury were accurately classified as negative. This balance of high sensitivity and moderate specificity makes E-PASS a highly practical and clinically applicable tool for perioperative risk assessment in thyroid cancer patients with T2DM.

The results of this study have important implications for clinical practice. Firstly, by evaluating a patient's CRS using the E-PASS, clinicians can more effectively identify individuals at high risk for postoperative RLN injury. This is crucial for developing personalized surgical plans and tailoring postoperative recovery strategies. Secondly, for patients with high CRS, greater caution should be exercised when selecting a surgical approach. Surgeons should also employ more refined surgical techniques during the procedure to minimize the risk of RLN injury. Additionally, postoperative monitoring and follow-up for these patients should be intensified to enable early detection and management of potential complications. In addition to the surgical procedures, the findings also suggest that for T2DM patients with thyroid cancer, the prevention of postoperative RLN injury should incorporate assessments of overall physiological status and surgical stress levels. Therefore, during the preoperative preparation phase, clinicians should conduct a comprehensive assessment of the patient's physiological condition and optimize glycemic control and

overall health status. This may help reduce intraoperative stress responses, thereby lowering the risk of postoperative RLN injury (Stanciu et al, 2022; Stanciu et al, 2023). Furthermore, the results of this study highlight the significant role of intraoperative nerve monitoring in preventing RLN injury. For T2DM patients with thyroid cancer, especially those with tumors located adjacent to the RLN, intraoperative nerve monitoring should be incorporated as a routine component of the surgical procedure. This enables real-time monitoring of RLN functional integrity and allows for timely intraoperative adjustments to minimize the risk of RLN injury.

While this study has made significant progress, several limitations should be acknowledged. Firstly, the study design was retrospective, which may introduce inherent biases in data collection and analysis. Secondly, the relatively small sample size may limit the generalizability and reliability of the findings. Therefore, future research should focus on larger-scale, prospective studies to further validate the predictive value of E-PASS for postoperative RLN injury in T2DM patients with thyroid cancer. Additionally, this study primarily focuses on the application of E-PASS in predicting postoperative RLN injury and does not explore other potential complications or prognostic indicators. Hence, future studies could explore the application value of E-PASS in predicting additional postoperative complications or in assessing patient outcomes.

Conclusion

In conclusion, this study conducted a retrospective analysis of clinical data from 210 T2DM patients with thyroid cancer and found that CRS has significant predictive value for postoperative RLN injury. These findings have important implications for clinical practice, suggesting that clinicians should comprehensively assess patients' physiological conditions and surgical stress levels preoperatively. Personalized surgical plans and postoperative recovery strategies should be developed based on CRS to minimize the risk of postoperative RLN injury. Future research should further validate these findings and explore the broader application of E-PASS in predicting other postoperative complications and assessing patient outcomes.

Key Points

- This study investigated the predictive value of E-PASS for RLN injury in T2DM patients with thyroid cancer.
- Univariate and multivariate logistic regression analyses were used to identify E-PASS as a factor affecting RLN injury in patients with T2DM and thyroid cancer.
- ROC analysis identified that the area under the curve for E-PASS was 0.866, with an optimal cutoff value of 0.70.
- The E-PASS comprehensive risk assessment demonstrates good predictive value for RLN injury in patients with T2DM and thyroid cancer and is useful for risk assessment and early clinical intervention.

Availability of Data and Materials

The data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

JMG and NX conceived and designed the study. JMG and JWZ performed experiments and acquired data. JMG and JWZ analyzed and interpreted the data. JMG drafted the initial manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Medical Ethics Committee of Xinzheng Huaxin Minsheng Hospital (Approval No. 2024HS012). The principle of informed consent was followed throughout the experiment, and information about the study was provided to patients or their families, and consent was obtained.

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Conflict of Interest

The authors declare no conflict of interest.

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