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ABOUT COVER

Editorial Board Member of *World Journal of Gastroenterology*, Nikolaos Papadopoulos, MD, PhD, Director, 2nd Department of Internal Medicine, 401 General Army Hospital of Athens, Athens 11525, Attica, Greece. nipapmed@gmail.com

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Enhancing prognostic accuracy in predicting rectal neuroendocrine neoplasms

Renin Peter AA Raj, Abdulqadir J Nashwan

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Renin Peter AA Raj, Department of Medicine, Aston Medical School, Birmingham B4 7ET, United Kingdom

Abdulqadir J Nashwan, Department of Nursing & Midwifery Research, Hamad Medical Corporation, Doha 3050, Qatar

Corresponding author: Abdulqadir J Nashwan, MSc, PhD, Research Scientist, Department of Nursing & Midwifery Research, Hamad Medical Corporation, Rayyan Road, Doha 3050, Qatar. anashwan@hamad.qa

Abstract

The recently published retrospective study introduces the GATIS score, a new predictive model for rectal neuroendocrine neoplasms. By analyzing data from a large Chinese multicenter cohort, the study shows that the GATIS score, incorporating tumor grade, T stage, tumor size, age, and prognostic nutritional index, demonstrates superior predictive power for overall survival and progression-free survival compared to traditional World Health Organization grade and tumor, nodes and metastases staging systems. This editorial aims to discuss the importance of the GATIS score, its potential impact on clinical practice, and the strengths and limitations of the study. Finally, it explores the significance, methodology, and clinical implications of these findings.

Key Words: Rectal neuroendocrine neoplasm; Nomogram; Random forest; Prognosis; Overall survival; Progression-free survival

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Core Tip: The GATIS score, developed from a 12-year study of 1408 patients with rectal neuroendocrine neoplasms (R-NENs) across 17 major Chinese centers, predicts overall survival and progression-free survival more accurately than World Health Organization grade and tumor-node-metastasis staging. This score offers improved personalized patient management and treatment planning. However, the study includes limitations such as short follow-up durations and exclusion of molecular and genetic factors. Addressing these in future research could further enhance treatment strategies for R-NENs.

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INTRODUCTION

Neuroendocrine neoplasms (NENs) are a diverse group of cancers originating from neuroendocrine cells. According to the 2022 World Health Organization (WHO) classification of endocrine and neuroendocrine tumors (NETs), NENs are classified into three groups: Well-differentiated NETs, poorly differentiated neuroendocrine carcinomas (commonly referred to as NECs), and mixed neuroendocrine-non-NENs. NETs are generally graded as G1, G2, and G3 based on their proliferation index, while NECs are, by definition, high-grade neoplasms[1].

Although NETs have a low incidence, they have a relatively high prevalence[2]. In a nationwide retrospective multicenter study conducted in China (2001-2010), an analysis of 2010 gastroenteropancreatic NEN cases found that rectal NENs (R-NENs) accounted for 29.6% of the total. The incidence of R-NENs increased over the study period, with the data also showing that metastatic involvement at diagnosis was observed in 8.7% of grade 1 (G1), 16.9% of grade 2 (G2), and 17.7% of grade 3 (G3) NEN patients, indicating a correlation between higher tumor grades and disease progression[3]. Survival rates vary by stage and tumor grade. The overall prognosis of R-NENs is favorable, with a 5-year survival rate as high as 90%[4].

Most rectal NETs are discovered incidentally during endoscopic evaluations for colorectal cancer screening, appearing as small lesions typically less than 12 mm in diameter and slightly elevated from the mucosa. Treatment plan depends on the size and severity of the R-NETs. Treatment for rectal NETs can range from endoscopic or local excision to radical rectal resection and lymph node dissection, depending on the size and severity of the R-NETs[5].

PROMISE OF THE GATIS SCORE IN RECTAL NENS PROGNOSTICATION

Zeng *et al*[4] and colleagues conducted a retrospective study aiming to develop and test a novel prognostic score for patients with R-NENs. Their objective was to create a tool that could more accurately predict overall survival (OS) and progression-free survival (PFS) than existing methods.

The study involved 1408 patients with R-NENs treated at 17 major referral medical centers across China from January 2010 to December 2021. The researchers utilized a combination of random forest and Cox proportional hazard models to identify significant prognostic factors. These factors included tumor grade, T stage, tumor size, age, and a prognostic nutritional index (PNI). The resulting GATIS score was then validated through decision curve analysis and time-dependent receiver operating characteristic (referred to as ROC) curves.

The GATIS score demonstrated superior predictive accuracy compared to the WHO classification and tumor-node-metastasis (TNM) staging systems, with C-indexes of 0.915 for OS and 0.908 for PFS in the training set. Decision curve analysis showed a higher net benefit for the GATIS score in predicting patient outcomes. Time-dependent ROC curves confirmed the enhanced predictive power of the GATIS score over different time intervals. The study provides a comparative analysis showing that the GATIS score outperforms traditional WHO grading and TNM staging systems, offering a more individualized approach to patient management.

One of the primary strengths of this study is its large sample size, encompassing 1408 patients from 17 Large-scale referral medical centers in China with data collected over a span of 12 years. This extensive data set enhances the reliability of the findings which along with its wide geographical representation increases the generalizability of the findings.

While previous studies have explored nomogram models for R-NENs, they often have small sample sizes and overlook preoperative hematologic factors[4]. This study addresses these limitations by utilizing a large sample size and identifying the PNI as a significant predictor of patient outcomes. The PNI, a nutrition-related indicator, has been confirmed to be inversely correlated with patient prognosis in various tumors. The study finds that individuals with an elevated preoperative PNI, indicating adequate nutritional status, exhibit a reduced risk of mortality[4]. As a marker of nutritional and immunological status, its integration into the GATIS score highlights the importance of preoperative nutritional status in the prognosis of R-NENs, which could inform preoperative care strategies to improve patient outcomes.

However, the study is not without limitations. Despite the comprehensive data collection, the authors acknowledge that the study's median follow-up duration of 34 months is relatively short. Longer follow-up periods are essential to validate the long-term applicability of the GATIS score. As molecular and genetic testing becomes more integral to cancer prognosis, the authors recognize the exclusion of these factors as a limitation of the GATIS score. Future versions of the model could improve predictive accuracy further by incorporating genomic data.

Although the study provides significant insights based on a Chinese cohort, the applicability of the GATIS score to populations outside of China requires further validation. Differences in culture, genetics, and healthcare systems could influence the model's accuracy in other contexts. Conducting similar studies in different geographic and demographic settings will help validate the GATIS score's applicability globally and identify any necessary adjustments for different populations.

The study reported 44 patient deaths (3.7%) during the follow-up period but lacked a comprehensive analysis of their impact on OS and PFS calculations. While the deaths were acknowledged, the study moved quickly to presenting the results of the predictive models without detailing how these events were factored into the survival analysis. To enhance the model's robustness, a more detailed examination of mortality data, including reasons for death and their timing relative to diagnosis and treatment is recommended. Additionally, discussing how the deaths were handled in the statistical analysis (*e.g.*, censoring methods) would provide clarity.

Another unexplored area includes the exclusion criteria of the study, which did not consider patients with metastases at diagnosis, those undergoing neoadjuvant therapy, and those with incomplete data. However, it did not explore how the excluded populations might differ from the included cohort. Discussing the characteristics of the excluded patients and the potential impact on the generalizability of the findings would strengthen the study. Including a sensitivity analysis to show how different exclusion criteria might affect the results could also be beneficial.

CONCLUSION

The retrospective study on the GATIS score for predicting the prognosis of R-NENs provides valuable insights and a robust predictive model. By incorporating a range of clinical and pathological factors, it offers a more accurate prediction of patient outcomes than existing WHO grading and TNM staging systems. However, addressing the identified gaps, including a more detailed analysis of deaths during the study duration, exploring the impact of exclusion criteria, incorporating molecular and genetic data, extending the follow-up duration, and validating the model in different geographical contexts, would enhance the study's comprehensiveness and applicability. Future research should aim to integrate these elements to provide a more holistic and precise prognostic tool for R-NENs.

FOOTNOTES

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Country of origin: Qatar

ORCID number: Abdulqadir J Nashwan 0000-0003-4845-4119.

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