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RESEARCH ARTICLE

Ryan tumor regression scoring in rectal cancers operated after neoadjuvant therapy; single-center experience

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ABSTRACT

Aim: This study aimed to evaluate pathological response rates using the Ryan tumor regression grading system in rectal cancer patients who underwent surgery after neoadjuvant therapy and to investigate the relationship between response levels and clinicopathological parameters.

Materials and Methods: In this retrospective single-center study, 58 patients diagnosed with rectal cancer between January 2020 and December 2025 and treated with neoadjuvant therapy followed by surgery were included. Patients who did not receive neoadjuvant therapy were excluded. Demographic, clinical, and pathological data were recorded. Tumor response was graded according to the Ryan tumor regression system, and associations with clinicopathological variables were analyzed statistically.

Results: Ryan score distribution was 10.3% (n=6) for Score 0, 20.7% (n=12) for Score 1, 25.9% (n=15) for Score 2, and 43.1% (n=25) for Score 3. Residual tumor size increased significantly as pathological response decreased ($p<0.001$). No statistically significant associations were found between Ryan score and age, gender, total or metastatic lymph node count, T stage, lymphovascular invasion, perineural invasion, or tumor localization.

Conclusion: The Ryan tumor regression score is a practical and reliable method for evaluating treatment response in rectal cancer after neoadjuvant therapy. In this series, residual tumor size was significantly associated with treatment response, whereas other clinicopathological parameters were not.

Keywords: rectal cancer, neoadjuvant therapy, Ryan tumor regression score

INTRODUCTION

Rectal cancer constitutes a significant proportion of colorectal cancers and requires a multidisciplinary treatment approach, particularly in patients with locally advanced disease. In recent years, preoperative neoadjuvant chemoradiotherapy (CRT) has been adopted as the standard treatment protocol for

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locally advanced rectal cancer (1). The primary aims of neoadjuvant therapy are to reduce tumor size, increase the rate of surgical resectability, enhance the likelihood of sphincter-preserving surgery, and decrease the risk of local recurrence (2).

The histopathological evaluation of tumor response following neoadjuvant therapy is of great importance for both prognostic prediction and planning adjuvant treatment. For this purpose, several tumor regression grading systems have been developed. Among these, the Ryan tumor regression grading system (Tumor Regression Grade, TRG) has become the standard system recommended by the American Joint Committee on Cancer (AJCC) and the College of American Pathologists (CAP) (3,4). Numerous studies have shown that patients with low Ryan score (0–1) have lower local recurrence rates and significantly longer disease-free and overall survival (5-7).

In the present study, we aimed to evaluate the pathological response rates according to the Ryan tumor regression grading system in rectal cancer cases operated after neoadjuvant therapy and to investigate the relationship between response levels and clinical and pathological parameters.

MATERIALS AND METHODS

Patients diagnosed with rectal cancer between January 2020 and December 2025 were retrospectively reviewed in our study. Patients who did not receive neoadjuvant therapy were excluded from the study. Ethical approval was obtained from the Abant Izzet Baysal University Clinical Research Ethics Committee (2026/26).

Patient characteristics including gender, age, clinical tumor stage before neoadjuvant therapy, and tumor location in the rectum (upper, middle, lower) were recorded. Postoperative pathological parameters such as total number of excised lymph nodes, number of metastatic lymph nodes, tumor size, lymphovascular invasion, and perineural invasion were determined.

In the histopathological evaluation of the patients, the Ryan tumor regression grading system was used to assess the response to neoadjuvant therapy. Treatment response was classified as follows: Score 0 (no viable cancer cells, only fibrosis; complete response), Score 1 (single or small groups of cancer cells; near-complete response), Score 2 (residual cancer with evident tumor regression but more than single cells or rare small groups; partial response), and Score 3 (extensive residual cancer with no evident tumor regression; poor or no response) (Figure 1) (3,4). The tumor treatment response was evaluated using the Ryan score in accordance with the protocols of the College of American Pathologists. Acellular mucin pools observed in specimens following neoadjuvant therapy were interpreted as indicative of complete tumor regression and were excluded from pT staging and from the assessment of lymph node positivity.

In cases demonstrating limited treatment response, the largest measurable dimension of the tumor was recorded as the tumor size. In cases with a more pronounced treatment response, characterized by prominent central regression and a scattered distribution of residual tumor cell clusters, the greatest dimension of the largest residual tumor focus was recorded as the tumor size.

Statistical analysis of the data was performed using IBM SPSS (Statistical Package for the Social Sciences) for Windows, Version 20.0. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Data with normal distribution were expressed as mean ± standard deviation, while non-normally distributed data were expressed as median (minimum–maximum). For comparisons between two groups, Student's t-test was used for normally distributed variables, and for comparisons among three or more groups, one-way analysis of variance (ANOVA) was applied. For non-normally distributed data, the Kruskal–Wallis test was used for multiple group comparisons. Categorical variables were compared using the chi-square test and were expressed as number (n) and percentage (%). Relationships between variables were evaluated using Pearson correlation analysis, and Spearman rank correlation analysis was used when the assumption of normal distribution was not met. A p-value of <0.05 was considered statistically significant.

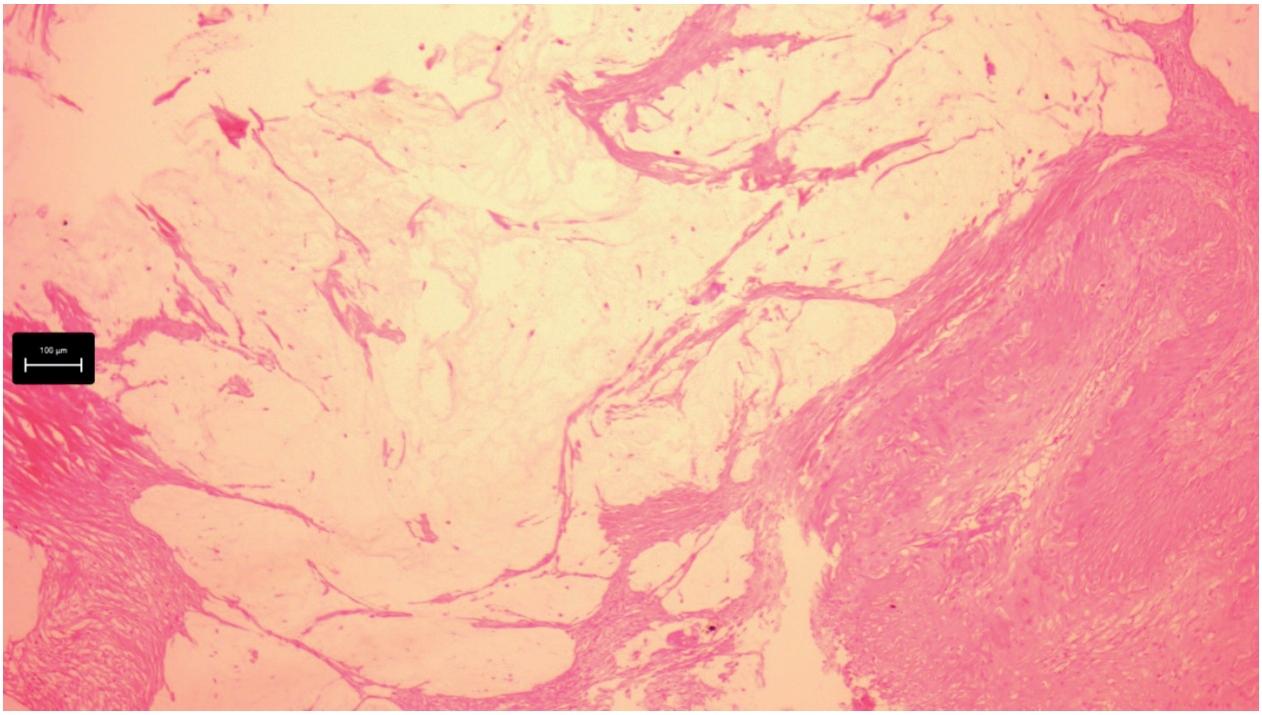

Figure 1. Ryan score 0 , full response with extensive hyalinization and mucin pools hematoxylin eosin x50.

RESULTS

A total of 58 patients were included in the study. Of these, 41 (71%) were male and 17 (29%) were female. No statistically significant difference was found between gender distribution and Ryan score groups (p=0.897). When gender distribution was evaluated according to Ryan score groups, there were 4 males and 2 females in the Score 0 group, 8 males and 4 females in the Score 1 group, 10 males and 5 females in the Score 2 group, and 19 males and 6 females in the Score 3 group.

The mean ages according to Ryan score groups were 64.3±11.6 years for Score 0, 67.5±10.7 years for Score 1, 63.7±10.9 years for Score 2, and 63.1±10.1 years for Score 3. No statistically significant difference was observed between the groups in terms of age (p=0.689).

The distribution of pathological response to neoadjuvant therapy was as follows: 10.3% (n=6) in Score 0, 20.7% (n=12) in Score 1, 25.9% (n=15) in Score 2, and 43.1% (n=25) in Score 3.

The distribution of residual tumor size according to Ryan score was as follows: 0 mm in Score 0, 7.5±3.6 mm in Score 1, 22.1±11.2 mm in Score 2, and 30.4±22.8 mm in Score 3. As the pathological response decreased, residual tumor size increased significantly, and this finding was statistically significant (p<0.001).

The mean total number of retrieved lymph nodes was 6.7±3.0 in Score 0, 10.6±6.3 in Score 1, 7.9±5.4 in Score 2, and 11.0±6.2 in Score 3. No statistically significant difference was found between the groups (p=0.228). Similarly, no statistically significant difference was found between Ryan score groups in terms of the number of metastatic lymph nodes (p=0.442).

Regarding T stage distribution, 5.2% of patients were T1, 32.8% were T2, 44.8% were T3, and 17.2% were T4. When T stage distribution was evaluated according to Ryan score groups, there were 0 T1, 2 T2, 3 T3, and 1 T4 patients in the Score 0 group; 0 T1, 5 T2, 6 T3, and 1 T4 patients in the Score 1 group; 1 T1, 4 T2, 6 T3, and 4 T4 patients in the Score 2 group; and 2 T1, 8 T2, 11 T3, and 4 T4 patients in the Score 3 group. No statistically

Table 1. Distribution of patients' demographic and clinical characteristics according to RYAN score

	Score 0 (n=6)	Score 1 (n=12)	Score 2 (n=15)	Score 3 (n=25)	P value
Age(years)	64.3 ± 11.6	67.5 ± 10.7	63.7 ± 10.9	63.1 ± 10.1	0.689
Gender (male/female)	4 / 2	8 / 4	10 / 5	19 / 6	0.897
Tumor size (mm)	0	7.5 ± 3.6	22.1 ± 11.2	30.4 ± 22.8	<0.001
Total lymph node count	6.7 ± 3.0	10.6 ± 6.3	7.9 ± 5.4	11.0 ± 6.2	0.228
Metastatic lymph node	0	0	0	0.24 ± 0.83	0.442
T Stage (T1/T2/T3/T4)	0 / 2 / 3 / 1	0 / 5 / 6 / 1	1 / 4 / 6 / 4	2 / 8 / 11 / 4	0.947
Lymphovascular invasion (n, %)	1 (%16.7)	0	0	1 (%4.0)	0.247
Perineural invasion (n, %)	0	1 (%8.3)	1 (%6.7)	1 (%4.0)	0.692
Tumor localization (Lower/Middle/Upper)	2 / 2 / 2	4 / 4 / 4	5 / 5 / 5	9 / 10 / 6	0.659

significant relationship was found between T stage and Ryan score (p=0.947).

Lymphovascular invasion was detected in 3.4% (n=2) of patients, one in the Score 0 group and one in the Score 3 group. No statistically significant relationship was found between lymphovascular invasion and Ryan score (p=0.247).

Perineural invasion was detected in 5.2% (n=3) of patients, with one patient in each of the Score 1, Score 2, and Score 3 groups. No statistically significant relationship was found between perineural invasion and Ryan score (p=0.692).

In terms of tumor localization, 34.5% of patients had tumors located in the lower rectum, 36.2% in the middle rectum, and 29.3% in the upper rectum. No statistically significant relationship was found between tumor localization and Ryan score (p=0.659) (Table 1).

DISCUSSION

In the present work, the relationship between the Ryan tumor regression score and clinical and pathological parameters was evaluated in patients with rectal cancer who underwent surgery after neoadjuvant chemoradiotherapy. The findings demonstrated a statistically significant association, particularly between tumor size and the Ryan score, while no significant associations were observed with other clinicopathological parameters.

The evaluation of pathological response after neoadjuvant therapy is considered an important prognostic indicator in rectal cancer. In the current literature, the Ryan tumor regression grading system has been shown to be a standardized and reliable method, with lower score (0–1) associated with better disease-free and overall survival (8,9). In our study, approximately 30% of patients had Ryan score between 0 and 1, supporting the notion that tumor regression is a direct indicator of treatment efficacy.

A significant relationship was observed between tumor size and the Ryan score. As the pathological response decreased, tumor size increased. Similarly, previous studies have reported that patients who respond well to neoadjuvant therapy show a marked reduction in tumor size, which is associated with improved prognosis (10-12). In the present study, tumor size was approximately 30 mm in 43% of patients, suggesting that tumor size is not only a morphological parameter but also an indicator of treatment response. On the other hand, no significant relationship was found between the Ryan score and age, gender, total number of lymph nodes, or number of metastatic lymph nodes. The literature presents conflicting results regarding the relationship between these parameters and tumor regression. While some studies have reported an association between lymph node involvement and pathological response, others have found no significant relationship (13,14). This discrepancy may be explained by the heterogeneous nature of tumor biology.

It is noteworthy that no significant relationship was found between T stage and the Ryan score. Although lower response rates are generally expected in tumors with advanced T stage, the response to neoadjuvant therapy may not be explained solely by anatomical staging. Recent studies emphasize that molecular characteristics and microscopic features of the tumor play a significant role in treatment response (15,16). A major challenge is that advanced T stage is often associated with a poorer response to neoadjuvant therapy and a more advanced clinical presentation. In such cases, surgeons may face more complex procedures, and patients may have a worse prognosis.

No significant relationship was found between the Ryan score and prognostic factors such as lymphovascular invasion and perineural invasion. The most likely explanation for this finding is the low incidence of these parameters and the limited sample size in our study. Larger series have demonstrated significant associations between these factors and poor prognosis (17,18). Similarly, no significant relationship was observed between tumor localization and pathological response. The literature indicates that tumors located in different segments of the rectum do not show significant differences in response to neoadjuvant therapy (19). This finding supports the notion that tumor location alone has a limited role in determining treatment response.

In the present study, a significant positive correlation was also identified between the Ryan score and tumor size in both Pearson and Spearman analyses, indicating that the results are statistically robust and consistent. Likewise, previous studies have reported significant correlations between tumor regression grade and tumor size (8,10,20).

This work has some limitations. First, its retrospective, single-center design limits the generalizability of the findings. Additionally, the relatively small sample size reduced the statistical power of some subgroup analyses. However, the homogeneity of the patient population and the use of standardized pathological evaluation are important strengths of the study.

In conclusion, a significant relationship was found between the Ryan tumor regression score and tumor size in patients with rectal cancer who underwent surgery after neoadjuvant therapy. The Ryan score is a practical and reliable method for evaluating treatment response and may be useful in prognostic assessment. These findings should be confirmed by larger, prospective studies.

Ethical approval

This study has been approved by the Bolu Abant Izzet Baysal University Non-Interventional Clinical Research Ethics Committee (approval date 20/01/2026, number 2026/26). Written informed consent was obtained from the participants.

Author contribution

Concept: SPO, BO; Design: SPO, BO; Data Collection or Processing: SPO, BO; Analysis or Interpretation: SPO, BO; Literature Search: SPO, BO; Writing: SPO, BO. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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