# Evaluation of Glasgow Microenvironment Score in Colorectal Carcinoma and Its Association with Prognostic Markers

**Adil Aziz Khan, Sana Ahuja, Mukul Singh, Sufian Zaheer**

Department of Pathology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

Received May 29, 2025; Accepted February 26, 2026.

**Key words:** Colorectal carcinoma – Glasgow Microenvironment Score – Prognostic markers – Tumour microenvironment

**Abstract:** Colorectal carcinoma (CRC) ranks among the most prevalent cancers worldwide, contributing significantly to cancer-related mortality. Despite advancements in understanding CRC's pathophysiology, traditional staging systems like tumour, node, and metastasis (TNM) lack comprehensive prognostic indicators, particularly regarding tumour microenvironment and host-related factors. The Glasgow Microenvironment Score (GMS) integrates inflammatory cell infiltration and stromal percentage, offering a potentially more comprehensive prognostic tool. This study aims to evaluate GMS in CRC and its correlation with established clinicopathological prognostic markers and pathological tumour, node, and metastasis (pTNM) staging. A retrospective study involving 68 CRC patients who underwent curative surgery between January 2022 and March 2024. Haematoxylin and eosin-stained sections were assessed for inflammatory infiltration (Klintrup-Mäkinen score) and tumour stromal percentage, forming the GMS. Statistical analyses evaluated associations between GMS and clinicopathological markers, including lymphovascular invasion (LVI), perineural invasion (PNI), nodal status, and histological grading. The study found significant correlations between GMS and poor prognostic markers. High GMS was associated with increased LVI, PNI, and nodal involvement. GMS showed significant associations with LVI ($p<0.0003$), PNI ($p<0.026$), and nodal involvement ($p<0.002$). GMS serves as a robust prognostic indicator in CRC, correlating with key pathological features that influence patient outcomes. This scoring system could enhance traditional prognostic models, aiding in better stratification of CRC patients for therapeutic interventions.

**Mailing Address:** Dr. Sufian Zaheer, Department of Pathology, Vardhman Mahavir Medical College and Safdarjung Hospital, Ansari Nagar, 110029 New Delhi, India; Phone: +91 965 059 48 18; e-mail: sufianzaheer@gmail.com

https://doi.org/10.14712/23362936.2026.2

Prague Medical Report / Vol. 127 (2026) No. 1, p. 15–20

## Introduction

Colorectal carcinoma (CRC) is one of the most prevalent cancers globally, ranking third in terms of frequency and being the third and fourth leading cause of cancer-related deaths in women and men, respectively (Siegel et al., 2014). The gut microbiota plays a crucial role in maintaining health, and disruptions in this balance, known as dysbiosis, can contribute to cancer development through chronic inflammation.

CRC has a high rate of morbidity and mortality unless detected early. Multiple clinicopathological parameters influence its progression and prognosis, including histological grade, stage, lymphovascular invasion (LVI), perineural invasion (PNI), and nodal metastasis. These elements are critical in assessing tumour biology and its aggressiveness (Poornakala and Prema, 2019).

Although there has been significant progress in understanding the pathophysiological mechanisms behind colorectal cancer (CRC), the tumour, node, and metastasis (TNM) staging system, which forms the foundation of clinical management, does not fully capture the factors influencing prognosis. One limitation of the TNM system is that it does not consider host-related factors, such as systemic inflammation or the local inflammatory response to the tumour (Dolan et al., 2017). A scoring method known as the Glasgow Microenvironment Score (GMS) was developed to address this. GMS evaluates the tumour microenvironment using haematoxylin and eosin (H and E)-stained slides, combining the assessment of inflammatory cell infiltration at the tumour's invasive margin (Klintrup-Mäkinen [KM] grade) with the tumour stromal percentage (TSP), which measures the amount of connective tissue in the tumour (Park et al., 2014, 2015; Nayak et al., 2018; Poornakala and Prema, 2019). A higher TSP is linked to a worse prognosis, including decreased overall survival (Freeman et al., 2013). The presence of peritumoral lymphocytes possesses anti-tumour activity and has also shown increased survival following immunotherapy (Roxburgh and McMillan, 2012). By combining these two critical parameters, the GMS provides enhanced prognostic value. The present study aims to evaluate the GMS score, followed by its association with known poor prognostic clinic-

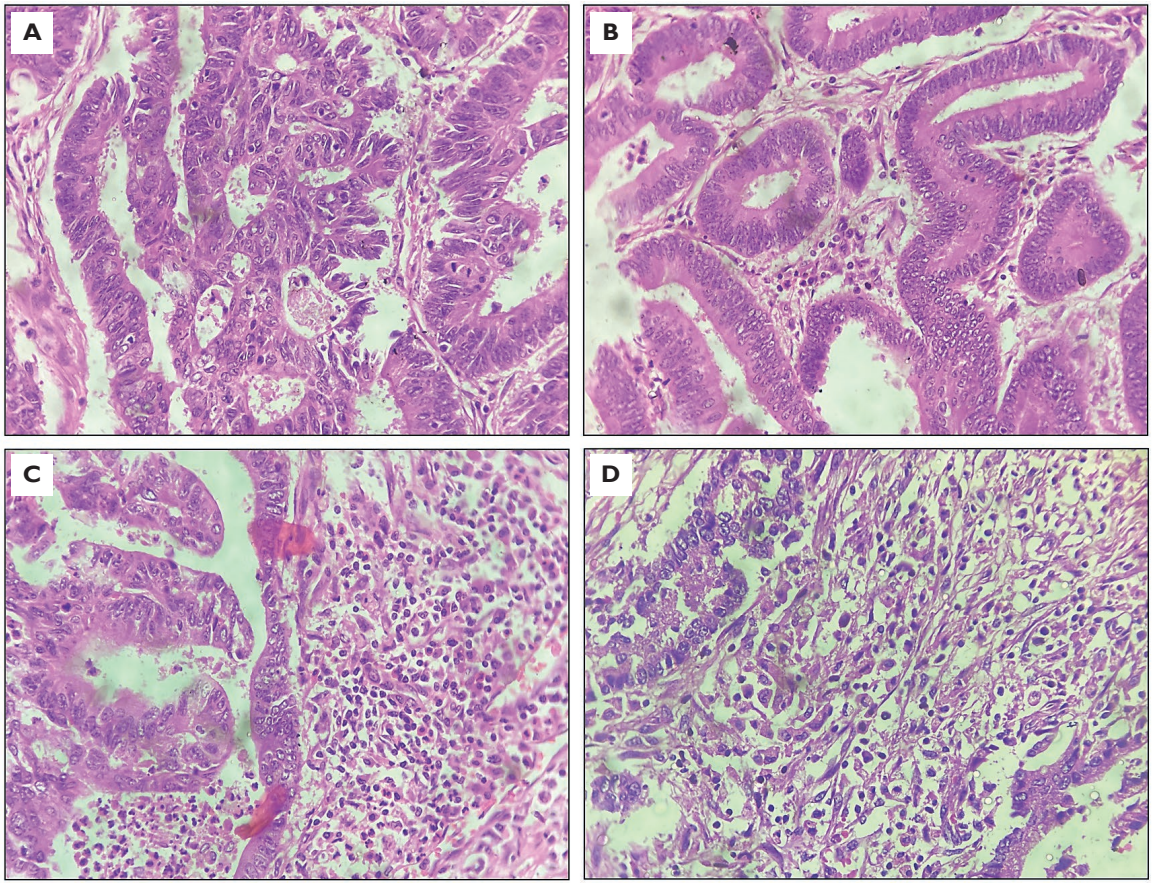


*Figure 1: KM (Klintrup-Mäkinen) inflammation score. (A) KM score 0 showing no increase in lymphocytes. (B) KM score 1 shows only mild increase in lymphocytes. (C) KM score 2 shows band-like infiltrate of lymphocytes. (D) KM score 3 shows prominent lymphocytic infiltration along with tumour nest destruction (400×).*

pathological markers and pathological tumour, node, and metastasis (pTNM) staging.

## Material and Methods

This was a retrospective study which included a total of 68 patients who underwent curative surgery for colorectal cancer between January 2022 to March 2024 in a tertiary care hospital. All the patients who received neo-adjuvant chemotherapy were excluded from the study. H and E-stained sections from the tumour were examined, and the scanner (4X lens) invasive tumour front or hot spot was identified. Lymphocytes surrounding the tumour cells were identified in the hot spot region and the invasive front of the tumour cells at the scanner (4X). The lymphocytes were counted as per the KM inflammation score at five high-power field. The score is assigned as follows: 0 = no increase in lymphocytes; 1 = only mild increase in lymphocytes; 2 = band-like infiltrate at invasive margin along with destruction of tumour nests; 3 = prominent destruction of tumour islands by inflammatory cells (Klintrup et al., 2005). Based on the above scoring, patients were graded as low (score 0/1) and high (2/3) (Figure 1). Using the same hot spot region stroma percentage is assessed in comparison to the tumour islands at 10× magnification. Stroma > 50% is considered to be high, and a stroma < 50% is classified as low, as done in previous studies (Figure 2). The GMS was calculated by combining these two parameters (Table 1).

The histological sections from the tumour were also assessed for lymphovascular invasion (LVI), perineural invasion (PNI), nodal involvement, extranodal extensions, serosal involvement, extent of tumour in the bowel wall and subsequently the pTNM staging.

**Table 1: GMS classification**

| GMS score | KM score | Tumour stroma (%) |
|---|---|---|
| 0 | high (2 or 3) | – |
| 1 | low (0 or 1) | low (<50%) |
| 2 | low (0 or 1) | high (>50%) |

GMS – Glasgow Microenvironment Score; KM – Klintrup-Mäkinen

### Statistical analysis

The presentation of the categorical variables was done in the form of numbers and percentages (%). On the other hand, the quantitative data were presented as the means ± SD (standard deviation) and as median with 25$^{th}$ and 75$^{th}$ percentiles (interquartile range). The following statistical tests were applied to the results.

The association of the variables, which were qualitative in nature, were analysed using the chi-square test. If any cell had an expected value of less than 5, then Fisher's exact test was used.

The data entry was done in the Microsoft EXCEL spreadsheet, and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, v. 25.0.

For statistical significance, a p-value of less than 0.05 was considered statistically significant.

## Result

The study population consisted of 68 individuals, comprising 38 males (55.88%) and 30 females (44.12%). Regarding the T-stage classification, 28 cases (41.18%) were T2, 26 cases (38.24%) were T3, 8 cases (11.76%) were T4, and 6 cases (8.82%) were T1. Nodal involvement was observed in 28 cases (41.18%), whereas node-negative cases were 40 (58.82%). The metastatic evaluation was not available due to the retrospective design.

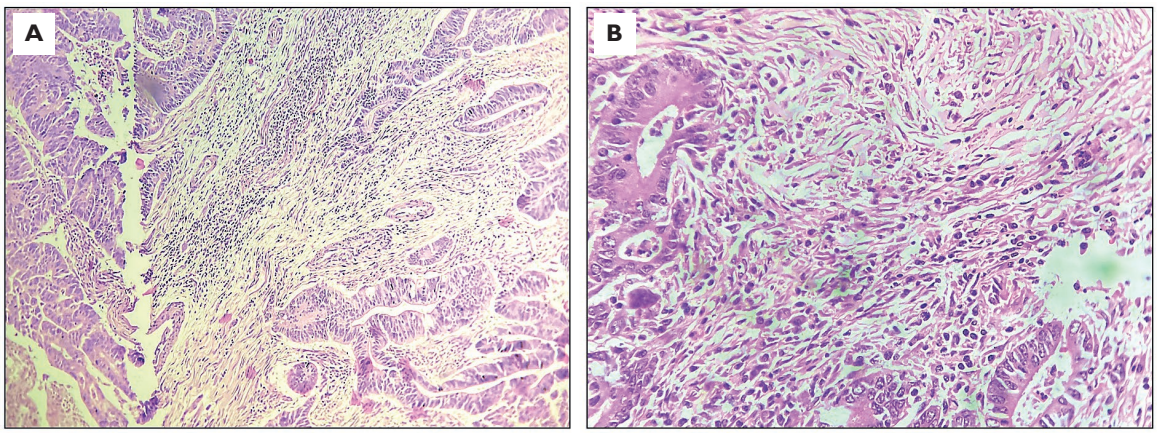


*Figure 2: Assessment of stromal percentage. (A) <50% desmoplastic stroma. (B) >50% desmoplastic stroma (100×, 200×).*

Prague Medical Report / Vol. 127 (2026) No. 1, p. 15–20

**Table 2: Patient characteristics distribution**

| Patient characteristics | | N (%) | Mean ± SD | Median (25th–75th percentile) | Range |
|---|---|---|---|---|---|
| Gender | Female | 30 (44.12%) | – | – | – |
| | Male | 38 (55.88%) | | | |
| T-stage | T1 | 6 (8.82%) | – | – | – |
| | T2 | 28 (41.18%) | | | |
| | T3 | 26 (38.23%) | | | |
| | T4 | 8 (11.76%) | | | |
| Nodal status | Negative | 40 (58.82%) | – | – | – |
| | Positive | 28 (41.18%) | | | |
| LVI | Negative | 40 (58.82%) | – | – | – |
| | Positive | 28 (41.18%) | | | |
| PNI | Negative | 50 (73.53%) | – | – | – |
| | Positive | 18 (26.47%) | | | |
| KM score | 0 | 10 (14.70%) | – | – | – |
| | 1 | 30 (44.11%) | | | |
| | 2 | 24 (35.29%) | | | |
| | 3 | 4 (05.88%) | | | |
| Tumour stroma ratio | Low | 36 (52.94%) | – | – | – |
| | High | 32 (47.05%) | | | |
| ENE | Negative | 52 (76.47%) | – | – | – |
| | Positive | 16 (23.53%) | | | |
| GMS score | 0 | 28 (41.18%) | – | – | – |
| | 1 | 10 (14.70%) | | | |
| | 2 | 30 (44.11%) | | | |
| Histological grade | Well differentiated | 22 (32.35%) | – | – | – |
| | Moderately differentiated | 26 (38.24%) | | | |
| | Poorly differentiated | 20 (29.41%) | | | |
| Age (years) | | – | 46.09 ± 13.3 | 45.5 (39.25–53.5) | 15–75 |

SD – standard deviation; LVI – lymphovascular invasion; PNI – perineural invasion; KM – Klintrup-Mäkinen; ENE – extranodal extension; GMS – Glasgow Microenvironment Score

For pathological characteristics, LVI was negative in 40 cases (58.82%) and positive in 28 cases (41.18%). PNI was negative in 50 cases (73.53%) and positive in 18 cases (26.47%). KM scoring was performed as 0 in 10 cases (14.7%), 1 in 30 cases (44.11%), 2 in 24 cases (35.29%), and 3 in 4 cases (5.88%). High stroma was identified in 32 cases (47.06%), whereas low stroma was observed in 36 cases (52.94%). Extranodal extension (ENE) was absent in 52 cases (76.47%) and present in 16 cases (23.53%).

GMS system showed 30 cases (44.11%) had a score of 2, 10 cases (14.70%) had a score of 1, and 28 cases (41.18%) had a score of 0. Histological grading revealed that 26 cases (38.24%) were moderately differentiated, 22 cases (32.35%) were well differentiated, and 20 cases (29.41%) were poorly differentiated.

The mean age of the study subjects was 46.09 ± 13.3 years, with a median age of 45.5 years (interquartile range 39.25–53.5). Detailed information is provided in Table 2.

Statistical significance of GMS was also done for the clinic-pathological parameters, in which we observed nodal involvement, LVI, PNI, ENE, and histological grading to be statistically significant ($p<0.002$, $<0.0003$, $<0.026$, $<0.045$, $<0.0001$, respectively). A significantly higher number of patients with GMS 0 had an absence of LVI (100%), absence of PNI (100%), absence of ENE (100%), absence of nodal involvement (78.57%), and well-differentiated histological grade (71.42%) (Table 3).

**Table 3: Association of patient characteristics with combined score**

| Patient characteristics | | 0 (n=28) | 1 (n=10) | 2 (n=30) | Total | p-value |
|---|---|---|---|---|---|---|
| Gender | Female | 16 (57.14%) | 2 (20.00%) | 12 (40.00%) | 30 (44.12%) | 0.1760* |
| | Male | 12 (42.85%) | 8 (80.00%) | 18 (60.00%) | 38 (55.88%) | |
| Nodal status | Positive | 22 (78.57%) | 2 (20.00%) | 4 (13.33%) | 28 (41.18%) | 0.0020* |
| | Negative | 6 (21.42%) | 8 (80.00%) | 26 (86.66%) | 40 (58.82%) | |
| T-stage | Low stage (T1–T2) | 16 (57.14%) | 4 (40.00%) | 14 (46.66%) | 34 (50.00%) | 0.6340* |
| | High stage (T3–T4) | 12 (42.85%) | 6 (60.00%) | 16 (53.33%) | 34 (50.00%) | |
| LVI | Negative | 28 (100%) | 4 (40.00%) | 8 (26.66%) | 40 (58.82%) | 0.0003* |
| | Positive | 0 (0%) | 6 (60.00%) | 22 (73.33%) | 28 (41.18%) | |
| PNI | Negative | 28 (100%) | 6 (60.00%) | 16 (53.33%) | 50 (73.53%) | 0.0260* |
| | Positive | 0 (0%) | 4 (40.00%) | 14 (46.66%) | 18 (26.47%) | |
| ENE | Negative | 28 (100%) | 6 (60.00%) | 18 (60.00%) | 52 (76.47%) | 0.0450* |
| | Positive | 0 (0%) | 4 (40.00%) | 12 (40.00%) | 16 (23.53%) | |
| Histological grade | Well differentiated | 20 (71.42%) | 0 (0.00%) | 2 (06.66%) | 22 (32.35%) | <0.0001* |
| | Moderately differentiated | 6 (21.42%) | 6 (60.00%) | 14 (46.66%) | 26 (38.24%) | |
| | Poorly differentiated | 2 (07.14) | 4 (40.00%) | 14 (46.66%) | 20 (29.41%) | |
| Age (years) | | 55.45 ± 11.33 | 44.95 ± 9.72 | 25.75 ± 8.85 | 46.09 ± 13.33 | <0.0001** |

*Fischer exact test; **One-way ANOVA; LVI – lymphovascular invasion; PNI – perineural invasion; ENE – extranodal extension

## Discussion

The prognostic outcome in CRC depends on several factors, including the size of tumour, nodal status, LVI, PNI, histological grade, and molecular subtypes. The presence of peritumoral lymphocytes and tumour stroma ratio have been studied individually in the recent past. Both parameters, to some extent, showed their utility in determining prognosis and overall survival. Huijbers et al. (2013) in a trial observed that high stroma in CRC is a stage-independent marker. In their VICTOR trial, they found decreased survival in patients having higher stroma percentages. Interestingly, these patients did not show any benefit from 5-fluorouracil-based adjuvant chemotherapy.

The GMS provides a combined assessment of these parameters and can be used as an independent prognostic marker once validated in a larger cohort. Jakubowska et al. (2017) in their study observed that a weak or absent inflammatory cell infiltrate at the invasive front of the tumour is significantly associated with shorter disease-free survival.

Ahuja et al. (2023) also studied the utility of GMS in CRC patients, and they concluded that a lower GMS is a better prognostic marker. In the present study, we found 78.57% of the patients with low GMS had negative nodes, and a statistically significant association was observed with lymphovascular invasion. The observations were in line with Ahuja et al. (2023), who also found a positive correlation between LVI and GMS.

Out of 68 patients low tumour stroma ratio (TSR) was seen in 52.94% whereas high KM was seen in 53% of the cases. Ahuja et al. (2023) reported 54.05% of cases with low stroma and 45.95% of patients with high KM. Another study was conducted by Richards et al. (2012) in CRC patients to assess the peritumoral inflammatory infiltrate response on patient outcome. They observed that 48% of patients with low-grade inflammatory infiltrate showed poor survival when compared with the high-grade inflammatory infiltrate patients.

In our study, we also observed a statistically significant association of GMS with PNI and nodal involvement. The findings were concordant with Ahuja et al. (2023), in which they exhibited a positive correlation with PNI and lymph node metastasis (p=0.01, p=0.003). Alexander et al. (2021) studied the interaction of adjuvant therapy and GMS in their study, and they observed a significant interaction between chemotherapy type (p=0.01) and GMS. They also observed that disease-free survival was strengthened in patients receiving FOLFOX with a 5-year disease free survival (DFS) for GMS 0, 1 and 2 of 88, 62 and 54%, respectively.

GMS assessment is a simple, cost-effective method that can be incorporated into routine histopathological reporting. The role of tumour microenvironment has

been established in many solid tumours, however, combining different tumour microenvironment parameters further increases the efficacy when compared to individual entities. Our observations emphasize that GMS can be used as another prognostic tool while evaluating colorectal carcinoma patients. One of the limitations in our study was the lack of follow-up of our patients and their association with survival outcomes.

## References


Ahuja, M., Dwarak, A., Mallya, V., Mandal, S., Tomar, R., Khurana, N., Lal, P., Singh, K. (2023) Utility of Glasgow Microenvironment Score as a prognostic tool in colorectal carcinoma. *J. Cancer Res. Ther*. **19**, S172–S176.

Alexander, P. G., Roseweir, A. K., Pennel, K. A., van Wyk, H. C., Powell, A. G., McMillan, D. C., Horgan, P. G., Kelly, C., Hay, J., Sansom, O., Harkin, A., Roxburgh, C. S. D., Graham, J., Church, D. N., Tomlinson, I., Saunders, M., Iveson, T. J., Edwards, J., Park, J. H. (2021) The Glasgow Microenvironment Score associates with prognosis and adjuvant chemotherapy response in colorectal cancer. *Br. J. Cancer* **124**, 786–796.

Dolan, R. D., Lim, J., McSorley, S. T., Horgan, P. G., McMillan, D. C. (2017) The role of the systemic inflammatory response in predicting outcomes in patients with operable cancer: Systematic review and meta-analysis. *Sci. Rep*. **7**, 16717.

Freeman, M. R., Li, Q., Chung, L. W. (2013) Can stroma reaction predict cancer lethality? *Clin. Cancer Res*. **19**, 4905–4907.

Huijbers, A., Tollenaar, R. A., Pelt, G. W., Zeestraten, E. C., Dutton, S., McConkey, C. C., Domingo, E., Smit, V. T., Midgley, R., Warren, B. F., Johnstone, E. C., Kerr, D. J., Mesker, W. E. (2013) The proportion of tumor-stroma as a strong prognosticator for stage II and III colon cancer patients: Validation in the VICTOR trial. *Ann. Oncol*. **24**, 179–185.

Jakubowska, K., Kisielewski, W., Kańczuga-Koda, L., Koda, M., Famulski, W. (2017) Diagnostic value of inflammatory cell infiltrates, tumor stroma percentage and disease – Free survival in patients with colorectal cancer. *Oncol. Lett*. **14**, 3869–3877.

Klintrup, K., Mäkinen, J. M., Kauppila, S., Väre, P. O., Melkko, J., Tuominen, H., Tuppurainen, K., Mäkelä, J., Karttunen, T. J., Mäkinen, M. J. (2005) Inflammation and prognosis in colorectal cancer. *Eur. J. Cancer* **41**, 2645–2654.

Nayak, S. S., Roy, P., Arora, N., Arun, I., Roy, M. K., Banerjee, S., Mallick, I., Mallath, M. K. (2018) Prevalence estimation of microsatellite instability in colorectal cancers using tissue microarray-based methods – A tertiary care center experience. *Indian J. Pathol. Microbiol*. **61**, 520–525.

Park, J. H., Richards, C. H., McMillan, D. C., Horgan, P. G., Roxburgh, C. S. (2014) The relationship between tumour stroma percentage, the tumour microenvironment and survival in patients with primary operable colorectal cancer. *Ann. Oncol*. **25**, 644–651.

Park, J. H., McMillan, D. C., Powell, A. G., Richards, C. H., Horgan, P. G., Edwards, J., Roxburgh, C. S. (2015) Evaluation of a tumor microenvironment-based prognostic score in primary operable colorectal cancer. *Clin. Cancer Res*. **21**, 882–888.

Poornakala, S., Prema, N. S. (2019) A study of morphological prognostic factors in colorectal cancer and survival analysis. *Indian J. Pathol. Microbiol*. **62**, 36–42.

Richards, C. H., Flegg, K. M., Roxburgh, C. S. D., Going, J. J., Mohammed, Z., Horgan, P. G., McMillan, D. C. (2012) The relationships between cellular components of the peritumoral inflammatory response, clinicopathological characteristics and survival in patients with primary operable colorectal cancer. *Br. J. Cancer* **106**, 2010–2015.

Roxburgh, C. S., McMillan, D. C. (2012) The role of the *in situ* local inflammatory response in predicting recurrence and survival in patients with primary operable colorectal cancer. *Cancer Treat. Rev*. **38**, 451–466.

Siegel, R., Desantis, C., Jemal, A. (2014) Colorectal cancer statistics, 2014. *CA Cancer J. Clin*. **64**, 104–117.