Prognostic and Predictive Significance of Microsatellite Status in Patients with Colorectal Cancer in Stage II and Stage III Disease: Single-Centre Experience

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SUMMARY

Background: *Colorectal cancer (CRC) is one of the leading causes of cancer-related morbidity and mortality worldwide. Microsatellite instability (MSI) is a crucial biomarker with prognostic and predictive value, influencing treatment decisions in CRC.*

Methods: *This retrospective study investigated the impact of the MSI status on clinical outcomes in 184 CRC patients treated at the Oncology Institute of Vojvodina between 2018 and 2023. The MSI status was determined using the immunohistochemical analysis of mismatch repair proteins.*

Results: *Among the cohort, 75% of tumors were microsatellite-stable (MSS), 4.3% exhibited low MSI (MSI-L), and 20.6% displayed high MSI (MSI-H). MSI-H tumors were significantly associated with right-sided CRC, mucinous differentiation, and female gender ($p<0.05$). The survival analyses revealed that the MSI-H patients with stage II disease had significantly better disease-free survival (DFS) and overall survival (OS) than the MSS counterparts ($p=0.024$ and $p=0.006$, respectively). Conversely, the MSI-H status in stage II patients receiving adjuvant therapy was linked to shorter DFS ($p=0.000$), highlighting the limited benefit from 5-fluorouracil-based regimens. In stage III CRC, the MSI status did not significantly affect DFS or OS.*

Conclusion: *These findings underscore the dual role of MSI as a favorable prognostic marker in early-stage CRC and a predictor of the reduced benefit from adjuvant chemotherapy in stage II disease. This study emphasizes the need for individualized treatment strategies based on the MSI status and supports the potential integration of immunotherapy in the adjuvant setting for MSI-H CRC.*

Keywords: *colorectal cancer; microsatellite instability; adjuvant chemotherapy; stage II; stage III*

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INTRODUCTION

Colorectal cancer (CRC) is the third most common malignancy worldwide and the second leading cause of cancer-related deaths (1). According to the data from 2021, approximately 4,500 new cases of colorectal cancer are registered annually in Serbia, placing it among the countries with the highest incidence of this cancer in Europe (2). Although colorectal cancer is considered a disease that affects the older population, the concerning trend of the rising incidence among younger patients under 50 years of age highlights the need to redefine the approaches to prevention, diagnosis, and treatment (3).

Modern oncology is based on the principles of individualized and personalized treatment, enabling therapy to be tailored to each patient based on the specific characteristics of their tumor. A key element of this approach is the use of prognostic and predictive factors. One of the most important biomarkers in the context of colorectal cancer is microsatellite instability (MSI) (4). Testing for MSI is currently recommended for most patients after a CRC diagnosis, both for the screening of hereditary syndromes and for its prognostic and therapeutic implications.

MSI refers to genetic instability arising from defects in DNA repair mechanisms. Numerous studies have focused on evaluating MSI as a prognostic marker, especially in early-stage colorectal cancer, as well as on assessing its predictive role in treatments based on 5-fluorouracil (5-FU). It is well established that MSI-High (MSI-H) is associated with favorable prognostic outcomes and the lack of benefit from 5-FU-based treatment in low-risk stage II CRC (5). Current guidelines therefore do not recommend adjuvant chemotherapy for these patients (6). Although the data on the predictive value of the MSI status for adjuvant chemotherapy remain controversial, it is known that the MSI status has predictive significance in terms of the absence of the benefits from 5-FU-based adjuvant therapy in stage II patients. On the other hand, the benefits from the adjuvant treatment with fluoropyrimidines combined with oxaliplatin-based regimens (CAPOX/FOLFOX) for stage III patients regarding the MSI status are still debatable.

The aim of this study is to examine the impact of the MSI status on the effectiveness of adjuvant therapy in patients with stage II and III colorectal cancer. Understanding this relationship is crucial for improving the treatment strategies and achieving better outcomes for patients.

MATERIALS AND METHODS

This observational (retrospective) study included a total of 184 patients who underwent surgery for colorectal cancer from January 2018 to June 2023. All the patients included in the study had histopathologically verified colorectal cancer. The pathohistological parameters that were analyzed included the tumor type, grade of differentiation, presence of lymphovascular and peri-

neural invasion, number of examined and affected lymph nodes, resection margins, clinical course of the disease presented using disease-free survival (DFS), overall survival (OS), as well as the microsatellite status.

The microsatellite status determination was performed at the Oncology Institute of Vojvodina. Formalin-Fixed Paraffin-Embedded (FFPE) tissue samples were sectioned at 4 μm onto Superfrost glass slides and stained according to the manufacturer's protocols using the Ventana Benchmark GX system (Ventana Medical Systems, Tucson, USA). Four immunohistochemical antibodies were used to assess the microsatellite instability (MSI) status, in line with the revised Bethesda Guidelines.

The immunohistochemical analysis was performed using antibodies against PMS2 (ready-to-use, Dako), MLH1 (ready-to-use, Dako), MSH2 (ready-to-use, Dako), and MSH6 (ready-to-use, Dako). The intact or positive expression was defined as nuclear reactivity/staining within tumor cells, while the loss of expression was defined as a lack of nuclear staining in tumor cells with internal positive controls (lymphocytes, stromal cells, non-neoplastic mucosa). Tumors were considered MSI if there was a loss of nuclear expression of one or more analyzed proteins. MSI-L tumors exhibited a loss of expression in one MMR protein, while MSI-H tumors showed a loss in two or more analyzed proteins.

The data were collected from the electronic database of the Institute. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee.

The patients were grouped based on the stage of disease and the microsatellite status into two categories: microsatellite-stable tumors (MSS, including MSI-L) and microsatellite-unstable tumors (MSI). The correlation of the microsatellite status was analyzed in regards to pathohistological features, disease stage, and clinical course depending on the application of adjuvant chemotherapy in stage III disease. Additionally, the impact of the microsatellite status on disease-free survival and overall survival was examined.

Statistical analysis

Continuous variables were analyzed using the Student's t-test or one-way ANOVA. For contingency variables, the chi-squared test or Fisher's exact two-tailed test was applied when the expected counts were below five. Continuous data are presented as a mean ± standard deviation (X±SD), while categorical data are shown as the number of cases with their corresponding percentages. The Kaplan-Meier method was used to estimate the overall and disease-free survival distributions, and the differences were assessed using the Log-rank test. A P-value of less than 0.05 was deemed statistically significant for all analyses. All statistical evaluations were conducted with the licensed Sigma Plot 14.0 software.

RESULTS

Study Population

The clinicopathological characteristics of the CRC patients included in this study are summarized in Table 1. The study included 184 patients, with a median age of 62 years (range: 29–71 years). The cohort comprised 56.5% males and 43.5% females. Most patients had a tumor stage of T3/4 (83.3%), with 12.1% being lymph node positive and 3.3% having metastatic disease. The majority (69.9%) were at TNM stage II. Of the total CRC patients, 104 had left-sided including the rectum and 78 had CRC right-sided CRC. Regarding the postoperative treatment, 54.1% received adjuvant therapy.

Table 1. The clinicopathological characteristics of colorectal cancer (CRC) patients.

Clinicopathological Parameteres	Number of Patients (%)
Age median	
<62	87 (47.3%)
≥62	97 (52.7%)
Gender	
Male	104 (56.5%)
Female	80 (43.5%)
Pathological T-stage	
T1	5 (2.7%)
T2	28 (15.2%)
T3	117 (63.6%)
T4	34 (18.5%)
Pathological N-stage	
N0	159 (86.4%)
N1	11 (6.0%)
N2	14 (7.6%)
Metastatic disease	
Yes	7 (3.8%)
No	177 (96.2%)
TNM Stage	
TNM I	29 (15.7%)
TNM II	128 (69.6%)
TNM III	20 (10.9%)
TNM IV	7 (3.8%)
Localization	
left-sided CRC	105 (57.0%)
right-sided CRC	79 (43.0%)
Mucinous Component of The Tumor	
No	133 (72.3%)
Yes	51 (27.7%)
Gradus	
G1	17 (9.2%)
G2	147 (79.9%)
G3	20 (10.9%)
LVI	
Positive	67 (36.4%)
negative	117 (63.6%)
PNI	
positive	59 (32.0%)
negative	125 (68.0%)

Clinicopathological Parameteres	Number of Patients (%)
Tumor budding	
Low	96 (52,2%)
Intermediate	27 (15.1%)
High	61 (32.7%)
Adjuvant treatment	
Yes	100 (54.1%)
No	84 (45.9%)

The association between MSI Status and Clinicopathological Features

Table 2. The relationship between the MSI status and clinical-pathological factors.

Clinicopathological Parameteres	MSI type			*p*
	MSS (%)	MSI-L (%)	MSI-H (%)	
Age median	60.188±10.179	51.750±14.280	57.553±14.949	0.079
Gender				
Male	83/104 (79.8)	7/104 (6.7)	14/104 (13.5)	**0.007**
Female	55/80 (68.8)	1/80 (1.3)	24/80 (30.0)	
Pathological T-stage				
T1/T2	27/33 (81.8)	2/33 (6.0)	4/33 (12.2)	0.463
T3/T4	111/151 (72.9)	6/151 (4.6)	34/151 (22.5)	
Pathological N-stage				
N0	121/159 (76.1)	7/159 (4.4)	31/159 (19.5)	0.959
N1/N2	17/25 (68.0)	1/25 (4.0)	7/25 (28.0)	
Metastatic disease				
Yes	7/7 (100.0)	0/7 (0.0)	0/7 (0.0)	0.364
No	131/177 (74.0)	8/177 (4.5)	38/177 (21.5)	
TNM Stage				
TNM I	24/29 (82.8)	1/29 (3.4)	4/29 (13.8)	0.654
TNM II	94/128 (73.4)	6/128 (4.7)	28/128 (21.9)	
TNM III	13/20 (65.0)	1/20 (5.0)	6/20 (30.0)	
TNM IV	7/7 (100.0)	0/7 (0.0)	0/7 (0.0)	
Localization				
left-sided CRC	96/105 (91.4)	3/105 (2.8)	6/105 (5.8)	**0.000**
right-sided CRC	41/79 (51.9)	5/79 (7.6)	38/79 (40.5)	
Mucosal Component of The Tumor				
No	106/133 (79.7)	6/133 (4.5)	21/133 (15.8)	**0.031**
Yes	32/51 (62.7)	2/51 (3.9)	17/51 (33.3)	
Gradus				
G1	13/17 (76.5)	1/17 (5.9)	3/17 (17,6)	0.148
G2	114/147 (77.5)	6/147 (4.1)	27/147 (18.4)	
G3	11/20 (55.0)	1/20 (5.0)	8/20 (40.0)	
LVI				
Positive	54/67 (80.6)	2/67 (3.0)	11/67 (16.4)	0.327
negative	84/117 (71.8)	6/117 (5.1)	27/117 (23.1)	
PNI				
positive	44/59 (74.5)	3/59 (5.1)	12/59 (20.4)	0.976
negative	94/125 (75.2)	5/125 (4.0)	26/125 (20.8)	
Tumor budding				
Low	82/96 (85.4)	4/96 (4.2)	10/96 (10.4)	0.149
Intermediate	15/27 (55.6)	2/27 (7.4)	10/27 (37.0)	
High	41/61 (67.2)	2/61 (3.3)	18/61 (29.5)	
Adjuvant treatment				
Yes	87/100 (87.0)	4/100 (4.0)	9/100 (9.0)	**0.000**
No	51/84 (60.7)	4/84 (4.8)	29/84 (34.5)	

Among the 184 selected CRC patients with the determined microsatellite instability (MSI) status, 138 patients (75%) were MSS, while 8 patients (4.3%) had low MSI (MSI-L), and 38 patients (20.6%) had high MSI (MSI-H). Table 2 displays the clinical and histopathological features of the patients and tumors associated with the MSI status.

The identified MSI-H status in the analyzed cohort was significantly linked to the female gender ($p=0.007$), right-sided CRC ($p=0.000$), mucosal component of the tumors ($p=0.031$), and absence of adjuvant treatment ($p=0.000$). The remaining analyzed clinicopathological parameters did not show a statistically significant association with the MSI status ($p>0.05$ in all tests).

The impact of the microsatellite instability (MSI) status on the relapse of disease and death outcome

Among all the CRC patients, 168 (91.3%) remained alive throughout the follow-up period, while there were 16 cases (8.7%) where death outcomes were recorded. Additionally, 38 patients (30.6%) experienced a confirmed recurrence of the disease. The MSI status concerning the disease's outcome and relapse is displayed in Table 3. The obtained results demonstrated that the MSI status was not significantly associated with the frequency of local recurrences and metastasis ($p=0.764$). The death outcomes were mostly detected in MSS patients (10.9% vs. 0% for MSI-L and 2.6% for MSI-H), although the observed distribution was not statistically significant ($p=0.188$).

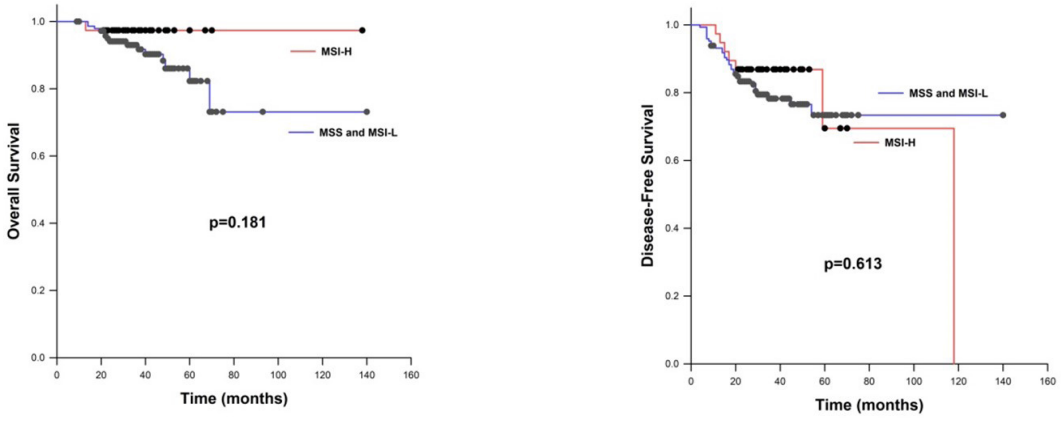
The overall survival and disease-free survival rates in relation to MSI status

In this study, the median follow-up period after surgery was 35.5 (range: 9.0–140.0) months. The median survival without the recurrence of the disease was 32 (range 4.0-140.0) months. To estimate the differences in the overall and disease-free survival among the CRC patients according to the MSI status, the Log-rank tests were used. The obtained results demonstrated that there were no significant difference in OS and DFS among the group of patients with MSI-H versus the MSS and MSI-L patients group ($p=0.181$ and $p=0.613$, respectively) (Figure 1).

The prognostic and predictive implications of the microsatellite instability (MSI) status were further analyzed in patients with colorectal cancer (CRC) in relation to the TNM stage and the use of adjuvant therapy. To evaluate the combined impact of the MSI and TNM stage on overall survival (OS) and disease-free survival (DFS), we established four categories: MSS, MSI-L/TNM II; MSI-H/TNM II; MSS, MSI-L/TNM III; and MSI-H/TNM III. The combined survival analysis showed that the MSS and MSI-L/TNM III group had the shortest OS (51.245 ± 5.748 months) and DFS (42.194 ± 7.729 months (Figure 2). Additionally, we observed that the MSI-H/TNM II group had significantly better overall survival and disease-free survival compared to the MSS and MSI-L/TNM III, and MSI-H/TNM III groups (OS: $p=0.006$; DFS: $p=0.024$) (Figure 2).

Table 3. The association between the MSI status and the outcomes and relapse of the disease.

MSI Status	Relapse of Disease		*p*	Death Outcome		*p*
	YES n (%)	NO n (%)		YES n (%)	NO n (%)	
MSS	30/138 (21.7)	108/138 (78.3)		15/138 (10.9)	123/138 (89.1)	
MSI-L	1/8 (12.5)	7/8 (87.5)	0.764	0/8 (0.0)	8/8 (100.0)	0.188
MSI-H	7/38 (18.4)	31/38 (81.6)		1/138 (2.6)	37/38 (97.4)	



(A) (B)

Figure 1. The Kaplan-Meier survival curves for overall (A) and disease-free survival (B), stratified by the MSI status.

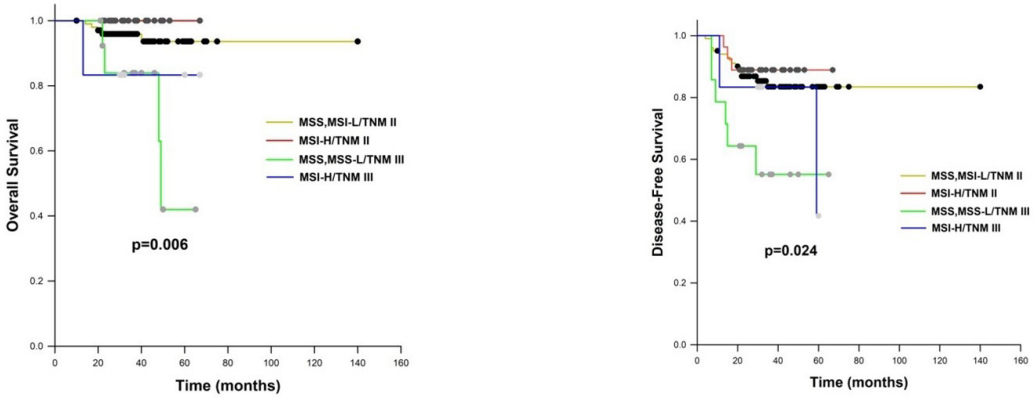


Figure 2. The Kaplan-Meier survival curves representing overall survival (A) and disease-free survival (B), grouped according to the MSI status and TNM stage.

The combined prognostic effect of the microsatellite instability (MSI) status and adjuvant therapy was assessed by comparing overall survival (OS) and disease-free survival (DFS) among four groups of patients: MSS, MSI-L with adjuvant therapy (MSS,MSI-L/adj+), MSI-H with adjuvant therapy (MSI-H/adj+), MSI-H with no adjuvant therapy (MSI-H/adj-) and MSS with no adjuvant therapy (MSS,MSI-L/adj-). The log-rank test revealed that MSI-H patients who received adjuvant therapy had the shortest DFS, with a mean of 59.832 ± 2.632 months (p = 0.006), compared to the other three groups. However, no significant difference in OS was observed among these four categories of CRC patients (p = 0.277) (Figure 3).

Among the patients in stage TNM II who received adjuvant treatment we noted that the patients with a MSI-H status had significantly shorter DFS than patients with MSS and MSI-L (14.000±1.000 vs. 61.604±2.446 months, p=0.000), while these differences were not observed regarding overall survival (p=0.800) (Figure 4). In patients with stage TNM III who received adjuvant therapy, we did not observe significant differences in OS and DFS among the groups regarding the MSI status (OS: p=0.920; DFS: p=0.998).

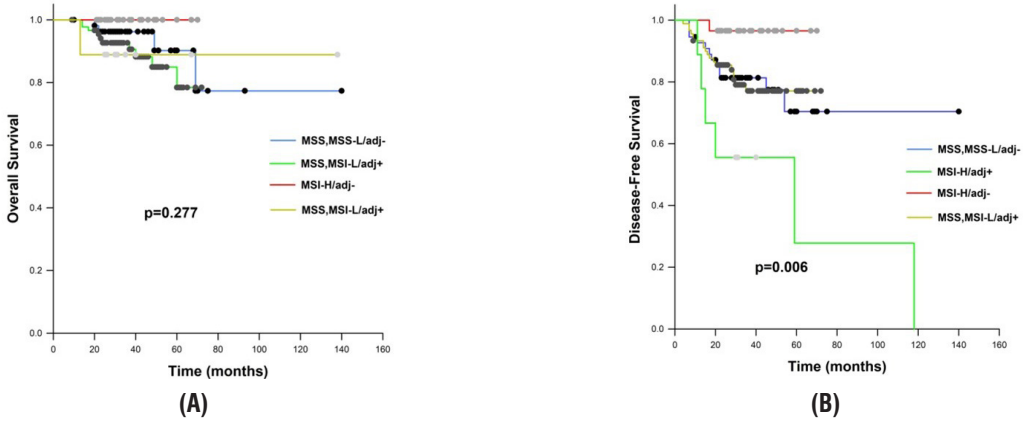


Figure 3. The Kaplan-Meier survival curves representing overall survival (A) and disease-free survival (B), grouped by the MSI status and adjuvant therapy application.

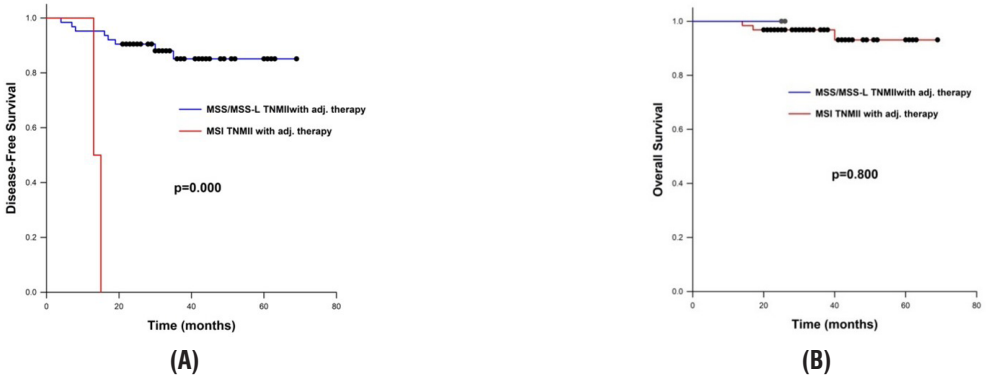


Figure 4. The Kaplan-Meier survival curves for overall (A) and disease-free survival (B) of the patients in the TNM II stage who received adjuvant therapy, stratified by the MSI status.

DISCUSSION

Colorectal cancer develops as a result of complex genetic and epigenetic changes, significantly influenced by external factors. Understanding tumor biology, including microsatellite instability (MSI) is key to personalized treatment, as it allows a better prediction of therapy responses. MSI is present in approximately 15% of all colorectal cancer cases, and its prevalence is higher in the earlier stages of the disease (stage I–II: 15–20%, stage III: 10–15%, stage IV: about 5%) (7-9). In our sample, 20% of the patients exhibited a MSI-H status, specifically 21.2% in stage II and 30% in stage III. The MSI-H status was statistically more frequently detected in females, likely due to the higher incidence of right-sided colorectal cancer in women compared to men (10,11). Right-sided colon cancers more often exhibit microsatellite instability compared to left-sided ones (12), which was also the case in our sample ($p = 0.000$). Furthermore, colorectal cancers are more likely to express a MSI-H status if they display mucinous differentiation (13), which was also shown in our study ($p = 0.031$).

The presence of MSI has multiple implications for the treatment of colorectal cancer patients. In stage II, where the disease is localized, MSI-positive tumors have a better prognosis and a lower risk of metastasis compared to MSS tumors in terms of relapse-free survival, disease-free survival, and overall survival. Therefore, adjuvant therapy is not always necessary (14). In our study, MSS colorectal cancers, regardless of disease stage, more frequently developed relapses and death outcomes, though without statistical significance. Regarding stage II and the prognostic value of the MSI status, our study showed that patients with the MSI-H/TNM stage II disease had statistically significantly better overall survival and disease-free survival compared to the other patient groups (OS: $p = 0.006$; DFS: $p = 0.024$).

In stage III, where the disease involves regional lymph nodes, the MSI status becomes potentially important for predicting therapy responses. Some studies implicate that the mandatory application of adjuvant chemotherapy for MSI-positive tumors in stage III is not recommended unless there are additional risk factors (15). Our results indicate that among the four observed groups (MSS/MSI-L vs. MSI-H, with vs. without adjuvant therapy), the MSI-H group that received adjuvant therapy exhibited statistically significantly shorter DFS ($p = 0.006$) compared to other groups, but not OS ($p = 0.277$). A further analysis of the MSI status and adjuvant therapy regarding the TNM stage noted that DFS was significantly shorter in the MSI patients in II stage of the disease. A significant difference in DFS and OS regarding III stage was not observed. These facts confirm that MSI-H is a predictor of poor responses to adjuvant chemotherapy in II stage of the disease, possibly due to the resistance to the drug 5FU.

A meta-analysis by Tomasello et al. (16) showed that overall survival in MSI-H colorectal cancers in stage III was statistically significantly higher when the patients received any form of adjuvant chemotherapy compared to those who did not (HR 0.42, 95% CI 0.26–0.66; $P < 0.01$). The study concluded that the MSI status is an important predictive factor for radically resected colorectal cancers with positive lymph nodes. Regarding the MSI status as a predictive factor for adjuvant therapy in stage II disease, Koenig et al. (17) indicated in their meta-analysis that patients with an MSS status benefitted from adjuvant chemotherapy (multivariate HR 0.52, $p < 0.001$), unlike the MSI patients who did not ($p = 0.61$). A meta-analysis by Guetz et al. examined both the stage II and III disease, considering the benefit of adjuvant therapy based on the MSI status (18). Their results suggested that adjuvant therapy did not improve survival in the MSI-H group, indicating that these patients should not receive adjuvant therapy unless other poor prognostic factors are present, such as perforation, pT4 stage, or lymphovascular or perineural invasion.

The study also has its limitations. First, it is retrospective and conducted in a single healthcare institution, limiting its generalizability. Second, this study did not evaluate if stage III patients that were MSI-H and who received adjuvant treatment had unfavorable prognostic factors such as perforation, pT4 stage, and lymphovascular or perineural invasion had different outcomes compared to the same group of patients that were MSI-L/MSS. Also, the analysis did not include the patients with metastatic colorectal cancer, for whom MSI plays a critical role in treatment decisions, given the proven superiority of immunotherapy as a first-line treatment compared to chemotherapy alone for the MSI-H patients (19).

CONCLUSION

Based on the results of this study, it can be concluded that microsatellite instability is an important prognostic and predictive marker in colorectal cancer. Ongoing studies are investigating the efficacy of adjuvant immunotherapy in patients with MSI-H colorectal cancer, with the hope of replacing chemotherapy in the adjuvant regimen for this patient group, especially those at high risk of disease relapse. Further research is needed to better define the predictive value of the MSI status in the context of adjuvant chemotherapy, particularly in stage III disease, to develop new therapeutic strategies for patients with deficient MMR systems. In the future, integrating new molecular biomarkers into clinical practice could significantly improve the treatment selection and reduce the risk of recurrence in colorectal cancer management.

REFERENCES

1. Morgan E, Arnold M, Gini A, et al. Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCANGut 2023;72:338-44.
2. International Agency for Research on Cancer. GLOBOCAN 2021: Serbia Fact Sheet [Internet]. Global Cancer Observatory; 2021 [cited 2024 Dec 5]. Available from: https://gco.iarc.who.int/
3. Zhao J, Xu L Sunet J al. Global trends in incidence, death, burden and risk factors of early-onset cancer from 1990 to 2019.BMJ Oncology 2023;2:e000049.
4. Battaglin F, Naseem M, Lenz H, Salem M. Microsatellite instability in Colorectal Cancer: Overview of its Clinical significance an Novel Perspectives.Clin Adv Hematol Oncol.2018 November;16(11):735-45
5. Sinicrope FA, Foster NR, Thibodeau SN, Marsoni S, Monges G, Labianca R et al. DNA mismatch repair status and colon cancer recurrence and survival in clinical trials of 5-fluorouracil-based adjuvant therapy. J Natl Cancer Inst. 2011;103(11):863-75.
6. Benson AB, Venook AP, Adam M, Chang G, Chen YJ, Ciombor KK, et al. Colon Cancer, Version 3.2024, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2024;22(2):e240029.
7. Argilés G, Tabernero J, Labianca R, Hochhauser D, Salazar R, Iveson T et al. ESMO Guidelines Committee.Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020;31(10):1291-05.
8. Kawakami H, Zaanan A, Sinicrope FA. Microsatellite instability testing and its role in the management of colorectal cancer. Curr Treat Options Oncol. 2015;16(7):30.
9. Puccini, A.; Berger, M.D.; Zhang, W.; Lenz, H.J. What We Know About Stage II and III Colon Cancer: It's Still Not Enough. Target Oncol. 2017;12(3):265–75.
10. Kim SE, Paik HY, Yoon H, Lee JE, Kim N, Sung MK. Sex- and gender-specific disparities in colorectal cancer risk. World J Gastroenterol. 2015;21(17):5167-75.
11. Choi Y, Kim N. Sex Difference of Colon Adenoma Pathway and Colorectal Carcinogenesis. World J Mens Health. 2024;42(2):256-82.
12. Acar T, Acar N, Kamer E, Cengiz F, Tekindal MA, Bağ H et al. Do tumor localization, microsatellite instability and mismatch repair deficiency have an impact on the prognosis of colorectal cancer? Niger J Clin Pract. 2021;24(12):1814-23.
13. Huang A, Yang Y, Shi JY, Li YK, Xu JX, Cheng Y, Gu J. Mucinous adenocarcinoma: A unique clinicopathological subtype in colorectal cancer. World J Gastrointest Surg. 2021;13(12):1567-83.
14. Taieb J, Karoui M, Basile D. How I treat stage II colon cancer patients. ESMO Open. 2021;6(4):100184.
15. Shaib WL, Zakka KM, Jiang R, Yan M, Alese OB, Akce M et al. Survival outcome of adjuvant chemotherapy in deficient mismatch repair stage III colon cancer. Cancer. 2020;126(18):4136-47.
16. Tomasello G, Ghidini M, Galassi B, Grossi F, Luciani A, Petrelli F. Survival benefit with adjuvant chemotherapy in stage III microsatellite-high/deficient mismatch repair colon cancer: a systematic review and meta-analysis. Sci Rep. 2022;12(1):1055.
17. Koenig JL, Toesca DAS, Harris JP, Tsai CJ, Haraldsdottir S, Lin AY, et al. Microsatellite Instability and Adjuvant Chemotherapy in Stage II Colon Cancer. Am J Clin Oncol. 2019;42(7):573-80.
18. Des Guetz G, Schischmanoff O, Nicolas P, Perret GY, Morere JF, Uzzan B. Does microsatellite instability predict the efficacy of adjuvant chemotherapy in colorectal cancer? A systematic review with meta-analysis. Eur J Cancer. 2009;45(10):1890-6.
19. Diaz LA Jr, Shiu KK, Kim TW, Jensen BV, Jensen LH, Punt C et al. KEYNOTE-177 Investigators. Pembrolizumab versus chemotherapy for microsatellite instability-high or mismatch repair-deficient metastatic colorectal cancer (KEYNOTE-177): final analysis of a randomised, open-label, phase 3 study. Lancet Oncol. 2022;23(5):659-70.