Chirurgia (2025) 120: 131-141
No. 2, March - April

http://dx.doi.org/10.21614/chirurgia.3108

Comparison of Staging and Treatment of Rectal Cancer between Patients Younger and Older than 70 years – An International Multicenter Study

Jerzy Krzeszowiak[1], Ciprian Duta[2], Radosław Pach[3], Piotr Richter[3], Zbigniew Lorenc[4], Andrzej Rutkowski[5], Wojciech Zegarski[6], Mariusz Frączek[7], Łukasz Zyskowski[5], Maciej Gaciong[8], Bartosz Skonieczny[6], Wojciech Polkowski[9], Vlad Braicu[2], Michał Święch[4], Katarzyna Sędłak[9], Dorian Andrade[10], Florian Kuhn[10], Konrad Karcz[10], Michal Tenderenda[5], Andrzej Cichocki[5], Jarosław Kobiela[11], Piotr Spychalski[11], Kajetan Ochwat[12], Aneta Obcowska-Hamerska[7], Antoni Szczepanik[13]*

[1]Department of Medical Education, Jagiellonian University Medical College, Krakow, Poland
[2]2nd Surgical Clinic, Researching Future Chirurgie 2, Victor Babeș University of Medicine and Pharmacy, Timișoara, Romania
[3]First Department of Surgery, Jagiellonian University, Krakow, Poland
[4]Department of General, Colorectal and Multiple-Organ Surgery, Medical University of Silesia in Katowice, Katowice, Poland
[5]Department of Surgery of Gastrointestinal Cancers and Neuroendocrine Tumors, M. Skłodowska-Curie National Institute of Oncology, Warsaw, Poland
[6]Department of Surgical Oncology, Nicolaus Copernicus University in Torun, Collegium Medicum in Bydgoszcz, Bydgoszcz, Poland
[7]Department of General, Vascular and Oncological Surgery, Medical University of Warsaw, Warsaw, Poland
[8]Department of Gastroenterological Oncology, Maria Skłodowska-Curie National Institute of Oncology, Warsaw, Poland
[9]Department of Surgical Oncology, Medical University of Lublin, Lublin, Poland
[10]Department of General, Visceral, and Transplantation Surgery, Hospital of the LMU Munich, Ludwig-Maximilians-Universität (LMU), Munich, Germany
[11]Department of General, Endocrine and Transplant Surgery, Faculty of Medicine, Medical University of Gdansk, Gdansk, Poland
[12]Jagiellonian University Medical College, Krakow, Poland
[13]Third Department of Surgery, Jagiellonian University, Krakow, Poland

*Corresponding author:
Prof. Antoni Szczepanik, MD, PhD
Third Department of General Surgery
Jagiellonian University Medical College Krakow, Poland
E-mail: antoni.szczepanik@uj.edu.pl

Abbreviations:
AR: anterior resection;
APR: abdomino-perineal resection;
TEM: transanal endoscopic microsurgery;
SCRT: short-course radiotherapy;
CRT: chemoradiotherapy

Received: 16.01.2025
Accepted: 10.03.2025

Rezumat

Stadializarea și tratamentul cancerului rectal la pacienții sub și peste 70 de ani – un studiu comparativ, multicentric, internațional

Introducere: Cancerul colorectal rămâne una dintre principalele probleme de sănătate publică în medicina modernă, fiind printre cele mai frecvente neoplazii şi a doua cauză de deces prin cancer. În ciuda progreselor semnificative recente în metodele terapeutice şi a popularizării programelor de screening, parcursul terapeutic şi rezultatele variază încă semnificativ între pacienți. Scopul acestui studiu a fost de a observa diferențele referitoare la stadializare, conduită terapeutică şi supraviețuire, între pacienții cu vârsta <70 ani şi ≥70 ani diagnosticați cu cancer rectal.

Material şi metodă: Studiul constă într-o analiză retrospectivă a datelor colectate prospectiv din nouă centre situate în Polonia, România şi Germania. Au fost incluşi pacienți operați consecutiv pentru cancer rectal în perioada 2013–2019, care au fost împărțiți în două grupe: <70 ani şi ≥70 ani.

Rezultate: În total, au fost incluşi 2443 de pacienți, cu o vârstă mediană de 66 de ani şi o predominanță a sexului masculin (63,16%). Nu s-au identificat

diferențe semnificative între grupele de vârstă în ceea ce priveşte sexul, localizarea tumorii sau stadializarea acesteia. S-a observat un număr semnificativ mai mare de intervenții cu formare de stomă şi un număr mai mic de ganglioni limfatici recoltați la pacienții vârstnici. Nu s-au evidențiat diferențe semnificative privind rata rezecțiilor R0. Utilizarea radioterapiei preoperatorii a fost mai frecventă la pacienții mai tineri. Nu au fost identificate diferențe semnificative cu privire la rata de răspuns complet, însă supraviețuirea globală a fost semnificativ mai scăzută la pacienții vârstnici.
Concluzii: În ciuda unei stadializări similare, pacienții vârstnici şi cei tineri beneficiază de conduite terapeutice diferite, incluzând intervenții chirurgicale mai puțin radicale şi o utilizare limitată a radioterapiei. Supraviețuirea globală este mai redusă la pacienții vârstnici, indiferent de stadiul tumorii (I-IV).

Cuvinte cheie: cancer rectal, grupe de vârstă, radioterapie, chirurgie

Abstract

Introduction: Colorectal cancer remains one of the major issues in modern healthcare, being one of the most common neoplasms and the second leading cause of cancer-related deaths. Despite significant recent advances, treatment modalities and the popularization of screening programs, treatment course and outcomes still vary among patients. This study aimed to observe the differences in staging, course of treatment, and survival between patients <70 and ≥70 years old with rectal cancer.
Material and Methods: The study was a retrospective analysis of data collected prospectively in nine centers located in Poland, Romania, and Germany. Consecutive patients operated on for rectal cancer between 2013-2019 were included and divided into groups <70 and ≥70.
Results: A total of 2443 patients were included with a median age of 66 years and a predominance of male (63.16%). There were no significant differences in terms of sex, tumor localization or staging between the younger and the older group. A significantly higher number of procedures with stoma creation was observed and a lower number of lymph nodes yielded in older patients. There were no significant differences in the rate of R0 resections. The use of preoperative radiotherapy was also higher in the younger group. The rate of complete response did not differ significantly, and the overall survival was significantly lower in older patients.
Conclusions: Despite similar staging, older and younger patients receive different treatment course, including less radical surgery and less frequent use of radiotherapy. Overall survival is poorer in older patients in stages I-IV.

Keywords: rectal cancer, age groups, radiotherapy, surgery

Introduction

Colorectal cancer is one of the major concerns of present-day medicine. It is the third most common neoplasm worldwide, and the second leading cause of cancer-related deaths. When observing individuals ≥70 years old, a similar incidence is observed, making them the most prevalent age-related group of colorectal cancer occurrence (1,2). Rectal cancer is the most frequent location of colorectal cancer (3). In recent years, a general decrease in the prevalence of colorectal cancer has been observed. However, its incidence has increased significantly among the early-onset group (4-9).

Past advances in the treatment of rectal cancer have provided a wide range of modalities, tailored to the staging and condition of the patient (1,7,10-12). Optimal treatment not only enhances survival but also improves functional outcomes. However, significant discrepancies in the treatment of rectal cancer exist both between and within countries, resulting in guidelines not always being followed (13-15). One aspect of this disparity is that older patients are sometimes denied the best possible treatment options based solely on their chronological age, with no regard to their biological reserves (16-18). Several studies have indicated that older patients with rectal cancer less frequently receive radiotherapy, radical surgical treatment, or surgery itself, compared to younger patients with the same stage of disease (19-23). It has been proven that when older and younger patients (<80 and ≥80) receive similar treatment for rectal cancer, their long-term survival is comparable (16,20).

There is a general belief that colorectal cancer tends to have lower survival rates in older patients

(24). However, survival data for older patients with rectal cancer are, to a considerable extent, based on predictive models. Meanwhile, several studies indicate that patients with early-onset colorectal cancer are often diagnosed at more advanced stages of the disease (19,21), and may have poorer treatment outcomes (25).

The purpose of this study was to expand the knowledge of the differences in staging, survival, and treatment of rectal cancer between younger and older patients, based on actual patient data collected from multiple centers.

Material and Methods

The study was a retrospective analysis of prospectively collected clinical data. It was approved by the Bioethics Committee of Jagiellonian University in Krakow, Poland (number of approval: 1072. 6120.120.2021) and registered at ClinicalTrials.gov (registration number is: NCT04947020). The official acronym of the study is BARO-1 – which stands for the database for Analysis of Rectal cancer Oncological results.

Patients were enrolled from nine centers across three European countries (Poland, Romania, Germany), including both oncological and non-oncological centers. Oncological centers were defined as facilities with onsite access to both radiotherapy and chemotherapy.

Consecutive patients treated for primary rectal cancer between 2013 and 2019 at centers participating in the study were included. Information on patients' sex, age, tumor location and pathological staging, type of procedure, number of resected and positive lymph nodes, radicality of resection, use of different types of radiotherapy, and survival was gathered. Patients who did not have rectal cancer or had incomplete data on surgical treatment or radiotherapy were excluded from the study. In most analyses, patients were divided into two age groups based on a cutoff set at 70 years old.

Different types of the radiotherapy were defined as the following: preoperative short-course radiotherapy (SCRT) consisting of 5 x 5Gy fractions, preoperative chemo-radiotherapy (CRT) – 45-50 Gy in 25-28 fractions, or any postoperative radiotherapy. The TNM classification of rectal cancer was based on the pathological evaluation of surgical specimens, and staging was conducted according to UICC guidelines. Procedures involving stoma formation included abdomino-perineal resections (APR), Hartman procedures, and colostomies.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 29.0.2.0 (20). The distribution of analyzed variables was assessed using the Shapiro-Wilk test, which indicated abnormal distribution in all variables, necessitating the use of nonparametric tests. Chi2 test was used for the analysis of the nominal variables, and the U-Mann-Whitney test for quantitative variables. Overall survival and recurrence free survival was analyzed using Kaplan-Meier curves and the Cox regression model.

Results

A total of 2443 patients treated in nine centers in the three countries were included in the analysis. Of these, 1963 subjects were enrolled in Poland, 307 in Romania, and 163 in Germany. The median age of the included patients was 66 years (IQR 61-76). In the entire cohort and both age groups, there was a predominance of males (63.16%). Tumors in both age groups were most commonly located between 6-10 cm from the anal sphincter. Additionally, in both groups, most patients underwent surgery at stage pT2, pN0, and M0. There were no significant differences between the <70 and ≥70 age groups in terms of sex, tumor localization or staging (*Table 1*). However, when the N stage was analyzed dichotomously (N=0 or N>0), a significantly higher percentage of patients with N>0 was noted in the younger group (43.02% vs. 38.28%; p=0.026).

The most common type of surgical procedure performed was anterior resection (63.41%). When comparing the prevalence of procedures involving a stoma (APR, Hartman procedures and sigmoidostomies) versus those without (anterior resections (AR), transanal endoscopic microsurgery (TEM)), procedures involving a stoma were significantly more common in older patients (37.33% vs. 35.24%; p=0.001). In the group of patients with tumors located between 6-10 cm from the anal verge, there was also a significantly greater prevalence of procedures with a stoma in older patients (23.77% vs. 13.18%; p<0.001).

R0 resections were achieved in 81.87% of patients, without significant differences between the age groups. The younger group had a significantly higher median number of resected nodes (13 vs. 11; p<0.001). SCRT was used more often used in the older group, though not significantly, while CRT was significantly more common in the

Table 1. Group characteristics

		whole group	<70	≥70	p
Number of patients		2443	1567	876	
		100.00%	64.14%	35.86%	
Age	median	66	61	76	
	IQR 25-75	59-73	55-65	73-80	
Sex	female	900	559	341	0.110
		36.84%	35.67%	38.93%	
	male	1543	1008	535	
		63.16%	64.33%	61.07%	
Tumor localization					
	0-5 cm	731	489	242	0.121
		34.17%	35.36%	32.01%	
	6-10 cm	922	574	348	
		43.10%	41.50%	46.03%	
	>10 cm	486	320	166	
		22.72%	23.14%	21.96%	
pT	0	100	65	35	0.338
		4.28%	4.29%	4.25%	
	1	134	81	53	
		5.73%	5.35%	6.43%	
	2	574	372	202	
		24.54%	24.55%	24.51%	
	3	1296	839	457	
		55.41%	55.38%	55.46%	
	4	235	158	77	
		10.05%	10.43%	9.34%	
pN	0	1369	861	508	0.151
		58.65%	56.98%	61.73%	
	1	575	390	185	
		24.64%	25.81%	22.48%	
	2	390	260	130	
		16.71%	17.21%	15.80%	
pM	0	2038	1307	731	0.365
		85.96%	85.37%	87.02%	
	1	333	224	109	
		14.04%	14.63%	12.98%	

younger group. When analyzing preoperative radiotherapy (both SCRT and CRT), there was a significantly higher prevalence of radiotherapy use in the younger group. The use of postoperative chemoradiotherapy (PCRT) did not differ significantly between the age groups (*Table 2, Fig. 1*).

A subgroup from the whole study was identified that should receive preoperative radiotherapy based on guidelines, meaning they were classified as T≥3 or N>0 and M0 (1,26). This subgroup accounted for 56.12% of the whole cohort. The use of all forms of radiotherapy was higher in this subgroup than in the entire cohort. Similar to the whole group, the use of CRT was significantly higher in younger patients, while other forms showed no significant differences.

Within the T3/4N+M0 group, procedures involving stoma formation were significantly more common in older patients. The median of resected lymph nodes was significantly higher in younger patients. The percent of R0 resections and the number of positive lymph nodes did not differ significantly between the age groups (*Table 3, Fig. 2*).

The rate of complete response (T0 in pathological specimen) comprised 6.14% of patients who received preoperative SCRT or CRT. There was no significant difference in complete response between younger and older patients (6.43% vs. 5.60%; p=0.580). Similarly, the difference in near complete response rate (T1 in pathological specimen) between younger and older patients was not significant (4.29% vs. 4.31%; p=0.987).

When analyzing only patients who received preoperative CRT, the differences in complete response (<70 13.01% vs. ≥70 12.99%; p=0.996) or near complete response (3.27% vs. 2.49%; p=0.134) were also insignificant.

The median number of resected nodes was significantly lower in the group of patients with a complete response compared to those who received SCRT or CRT and did not achieve a complete response (10 vs. 13; p=0.003).

Table 2. The comparison of the treatment and its results between the age groups

		whole group	<70	≥70	p
Type of operation	APR	509	340	169	
		20.84%	21.70%	19.29%	
	AR	1549	1036	513	
		63.41%	66.11%	58.56%	
	Hartmann	237	114	123	
		9.70%	7.28%	14.04%	
	TEM	46	25	21	
		1.88%	1.60%	2.40%	
	Sigmoidostomies	67	32	35	
		2.74%	2.04%	4.00%	
Procedures with stoma		813	486	327	0.001
		33.76%	31.42%	37.98%	
R	0	2000	1302	698	0.368
		85.65%	86.23%	84.61%	
	1	119	70	49	
		5.10%	4.64%	5.94%	
	2	216	138	78	
		9.25%	9.14%	9.45%	
Lymph nodes resected	median	12	13	11	<0.001
	IQR 25-75	7-18	8-19	6-17	
Positive lymph nodes	median	0	0	0	0.027
	IQR 25-75	0-2	0-2	0-2	
SCRT	838	507	331	0.064	
	34.30%	32.35%	37.79%		
CRT	335	258	77	<0.001	
	13.71%	16.46%	8.79%		
SCRT or CRT	1173	765	408	0.02	
	48.01%	48.82%	46.58%		
PCRT	237	159	78	0.163	
	9.70%	10.15%	8.90%		

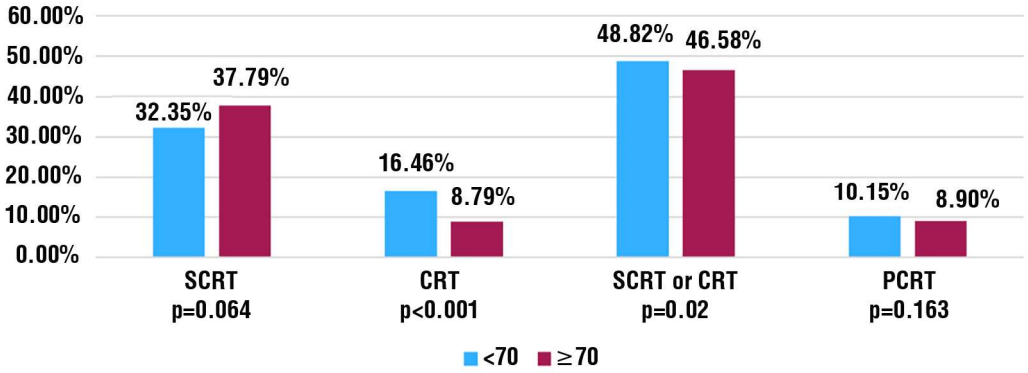

Figure 1. Comparison of the use of different forms of radiotherapy between groups <70 and ≥70.

Ninety-day mortality was significantly higher in the older group than in younger patients (6.51% vs. 2.54%; p<0.001). Survival rates were analyzed in 1, 2, 3, and 5-year periods. In each period, the percentage of patients who were alive was significantly higher in the younger group. Overall survival estimated using the Kaplan-Meier curve was significantly higher in the younger group (p<0.001) (*Fig. 3 A*). This difference persisted when calculated using Cox regression, adjusted for covariates such as sex and UICC stage (*Fig. 3 B*). Analyzing each UICC stages separately, overall survival was significantly higher in younger patients across all stages (1-4), except for UICC stage 0 (*Fig. 4*).

The overall survival in patients who received

Table 3. The comparison of the treatment of patients T3/4 or N+ and M0

		whole group	<70	≥70	p
number of patients		1371	894	477	
SCRT		515 37.56%	320 35.79%	195 40.88%	0.197
CRT		190 13.86%	146 16.33%	44 9.22%	<0.001
SCRT or CRT		705 51.42%	466 52.13%	239 50.10%	0.118
PCRT		166 12.11%	112 12.53%	54 11.32%	0.350
procedures with stoma		446 32.53%	268 29.98%	178 37.32%	0.006
R>0		89 6.49%	54 6.04%	35 7.34%	0.320
Number of resected lymph nodes	median IQR	13 8-19	14 9-19	12 7-19	0.005
Number of positive lymph nodes	median IQR	1 0-2	1 0-2	0 0-2	0.196

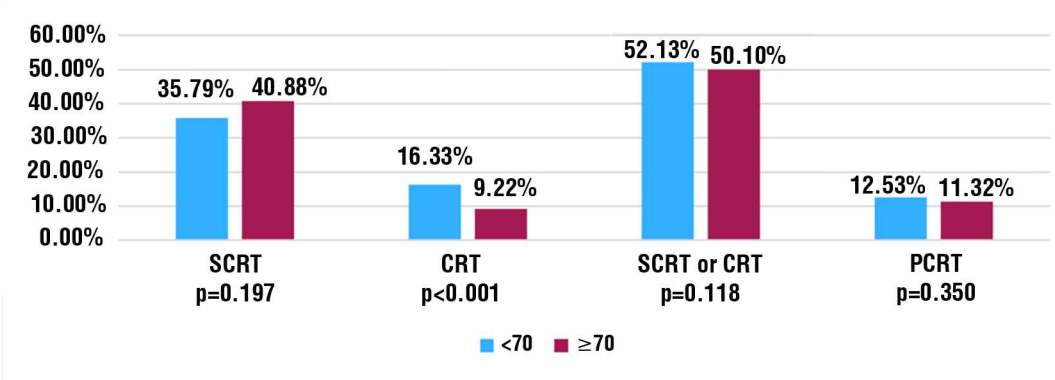

Figure 2. Comparison of the use of different forms of radiotherapy between patients <70 and ≥70 in the group T3/4 or N+ and M0.

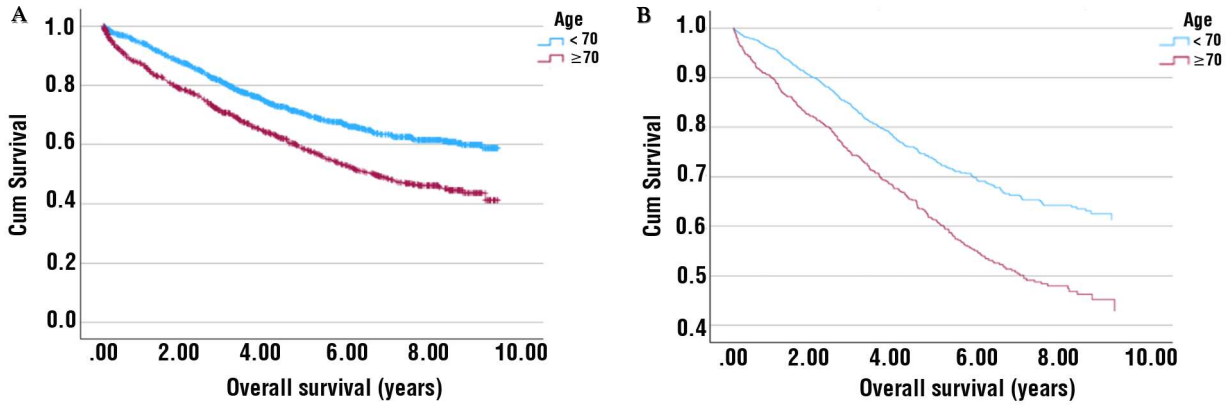

Figure 3. Overall survival analysis with comparison between age groups. **(A)** - Kaplan-Meier overall survival analysis; p<0.001; **(B)** - Cox regression – overall survival analysis with sex and UICC stage covariates; p<0.001.

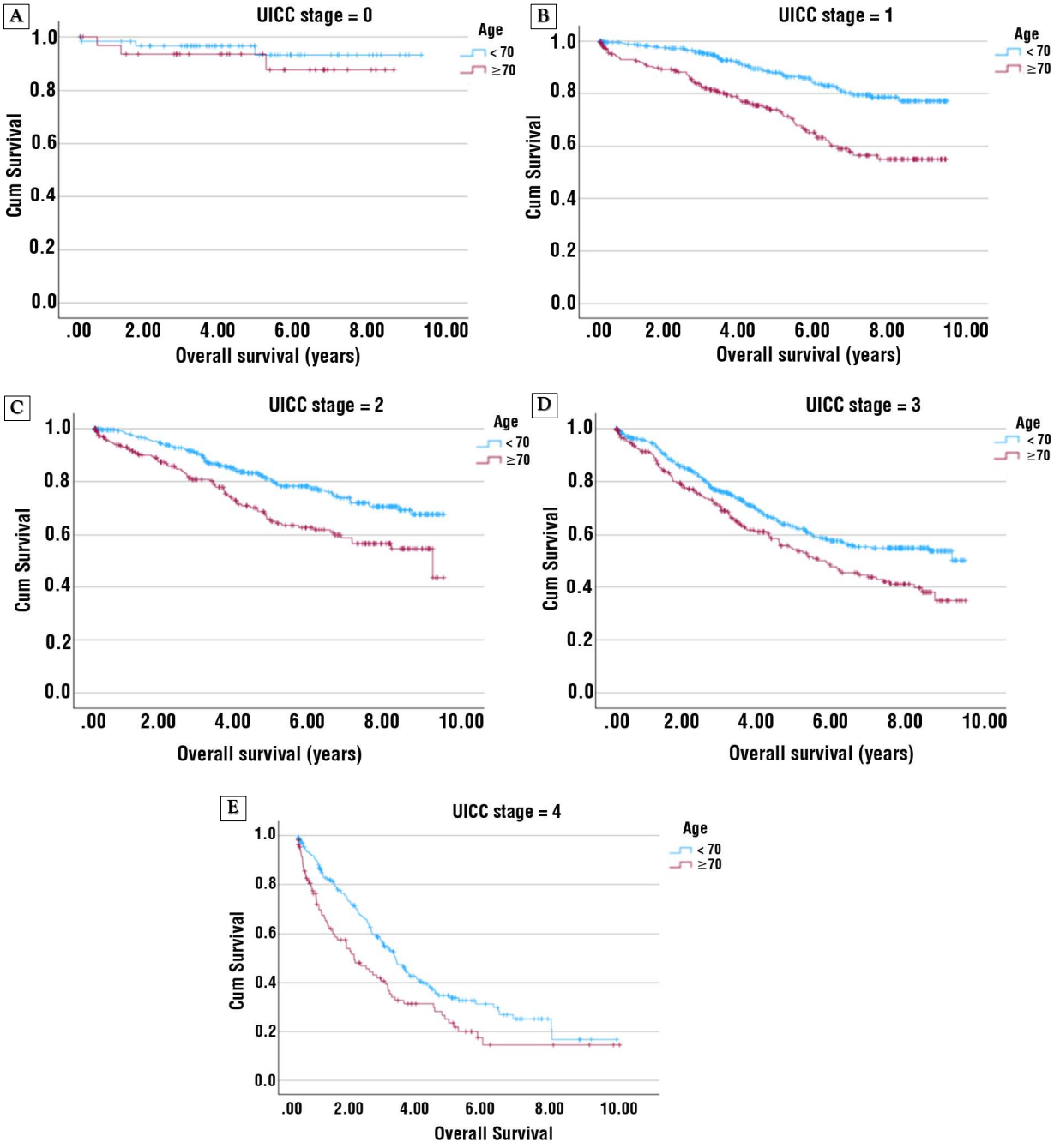

Figure 4. Overall survival in different UICC stages using Kaplan-Meier curve analysis. **(A)** - stage 0, p=0.448; **(B)** - stage 1, p<0.001; **(C)** – stage 2, p<0.001; **(D)** – stage 3, p=0.002 **(E)** – stage 4, p=0.003

SCRT or CRT was analyzed across all patients and within the subgroup T3/4 or N+ and M0. A significant difference in overall survival favoring the younger group was observed in both analyses. However, when specifically examining patients in whom R0 resection was achieved, there was no significant difference in overall survival between the age groups (*Fig. 5*).

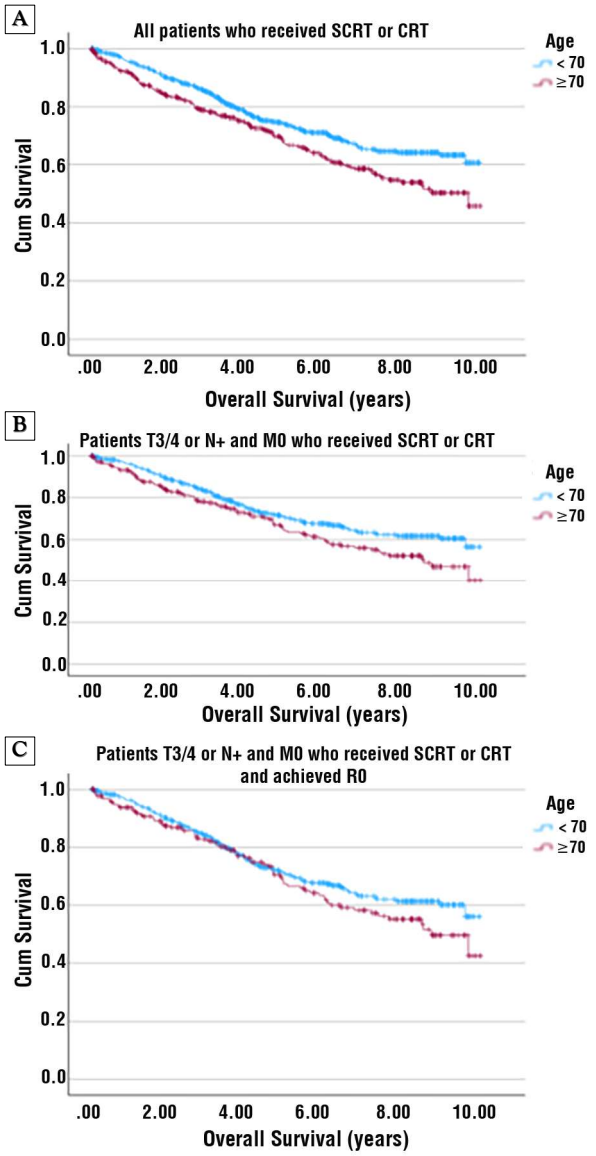

Figure 5. Kaplan-Meier analysis of overall survival between the age groups of patients who received SCRT or CRT. **(A)** – p=0.002; **(B)** – p=0.022; **(C)** – p=0.176.

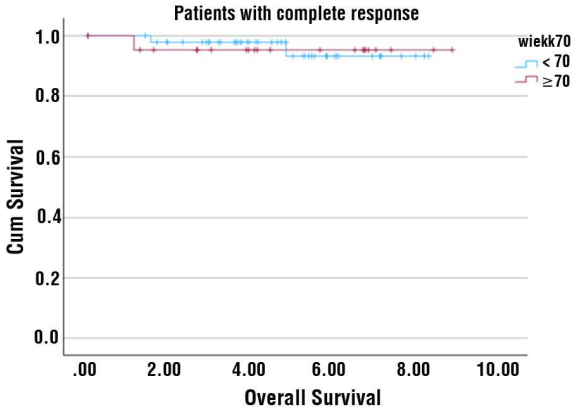

Figure 6. Comparison of the overall survival between patients <70 and ≥70 within the group of patients with a complete response to radiotherapy (n=69); p=0.924.

In patients who achieved a complete response to preoperative treatment (SCRT or CRT), 1-year survival rate was 97.14%. No significant difference in overall survival between younger and older patients was identified within this group (*Fig. 6*).

Discussion

An insight into the current literature reveals several discrepancies regarding the comparison between older and younger patients in terms of staging, treatment, and survival in rectal cancer. This study aimed to investigate these differences between patients <70 and ≥70 years of age.

No significant differences were observed in terms of sex, tumor staging, or localization between <70 and ≥70 groups. However, significant variations were observed in the course of treatment. Older patients presented with a higher prevalence of procedures involving stoma formation and a lower number of resected lymph nodes compared to the younger population. Furthermore, preoperative treatment strategies differed significantly between age groups, the use of SCRT or CRT was significantly higher in younger patients.

The subgroup of patients who, based on the guidelines should receive preoperative radiotherapy, encompassed 56.12% of the whole cohort. In these patients, the percentage treated with CRT and the number of resected lymph nodes were significantly higher in patients <70, while the number of procedures involving stoma creation was higher in patients ≥70.

There were no significant differences observed in the rates of complete response or near complete response rate between the age groups. Nevertheless, patients who achieved a complete response had a significantly lower number of lymph nodes yield compared to those who did not.

Overall survival was significantly lower in older patients. However, among patients T3/4N+M0 who received SCRT or CRT and achieved R0 resection or in patients who achieved a complete response, there were no significant differences in overall survival between age groups.

Previous studies have indicated that rectal cancer is often diagnosed at more advanced stages in younger patients (19,27–30). One possible explanation for this difference could be the widespread implementation and popularity of screening programs in older groups, which are not as common and easily-accessible among younger patients (7,31-34). In addition, awareness of colorectal cancer symptoms is supposed to be scarce among younger individuals, potentially leading to delayed diagnosis (35). However, the findings of the current study contradict the results of previous studies, showing no significant differences in staging between age groups. The cutoff between the age groups in present study was 70 years old, significantly higher than in reference studies that defined younger groups at ages 40 (29,30) or 50 (19,27,28) years.

Recent years have brought significant advancements in the treatment of rectal cancer, including the increased use of radiotherapy and the widespread implementation of multidisciplinary approach (36). Preoperative radiotherapy constitutes the gold standard for managing advanced cases of rectal cancer (26,37). The current study highlights a significantly lower use of SCRT or CRT in older patients, which is consistent with previous reports (21-23,38,39).

Several studies have revealed that a more conservative surgical approach was more common in older patients compared to younger individuals. Previous research has shown that older patients were less likely to be operated on with the intention to treat (20) (80 years cutoff point) or undergo major radical resections (16,23,40) (70-, 75- and 70-years cutoff point respectively) than their younger counterparts. However, the present study did not identify a significant difference in the radicality of resection between age groups. Older patients typically have a lower number of resected lymph nodes (41-43), which is supported by the results of the current study. Moreover, the median number of resected lymph nodes (11) in the group ≥70 in our study did not even reach the recommended benchmark of 12 nodes (44).

Numerous studies have demonstrated that neoadjuvant radiotherapy diminishes the nodes yield retrieved in surgical specimen (45-48). This finding could be potentially explained by the exposure to radiotherapy causing the immune processes and fibrosis, making nodes harder to identify during surgery. However, what is noteworthy in the current study is that the median of resected nodes was significantly lower in patients with a complete response to radiotherapy than in those who received SCRT or CRT and did not achieve it. Nevertheless, this observation aligns with findings from previous reports (49), similarly to the lack of differences in complete response rate between the age groups (50).

In the past there used to be a belief that younger patients with colorectal cancer have poorer prognosis (29). However, more recent research shows comparable survival outcomes between age groups (22,27,29,51,52). The results from our cohort show poorer survival in older groups in all stages. Nonetheless, it is important to note that previous studies focusing on younger patients used lower age cutoff points, which should be taken into consideration when interpreting these findings. Furthermore, younger and older groups may indeed present similar results, however, it was proven before that younger patients are diagnosed with worse staging, and older ones are often treated suboptimally. Additionally, in our cohort, overall survival among subgroup T3/4 or N+ and M0 who received SCRT or CRT and underwent R0 resection did not differ between younger and older patients. This may conclude that if patients receive optimal treatment at the same stage, they could have similar outcomes with no regard to their chronological age.

This research has several limitations. A major one is that staging relied solely on postoperative histopathological analysis without data on preoperative clinical assessment, which plays a crucial role in proper treatment tailoring (53,54). This limits the evaluation of the effect of radiotherapy. Moreover, poor reporting of recurrence events hindered a reliable analysis of recurrence-free survival, although overall survival was not affected due to the national, governmental registry data. Another limitation of the study was that only two age groups were compared, without a more comprehensive evaluation of age-related trends. Additionally, the study predominantly included centers located in Poland, where significant changes in oncological care organization were implemented during the study period, which could have affected the internal consistency of collected data (36).

Conclusions

The results of the study show that patients <70 and ≥70 in our cohort have similar staging at the time of diagnosis. Radiotherapy is used less frequently in older patients and the surgical treat-

ment is more conservative, including greater prevalence of procedures with stoma formation and lower number of resected lymph nodes. The overall survival is significantly higher in younger patients in all stages. However, within the group of patients with stage II or III, treated with SCRT or CRT who underwent radical surgery, the overall survival did not differ significantly. Further research, including an analysis of cTNM assessed before treatment initiation, should be conducted to obtain more conclusions.

Conflicts of Interest and Source of Funding

Authors report no personal, financial of substantive conflicts of interests. The study had no sources of funding.

References

1. Van De Velde CJH, Boelens PG, Borras JM, Coebergh JW, Cervantes A, Blomqvist L, et al. EURECCA colorectal: multidisciplinary management: European consensus conference colon & rectum. Eur J Cancer. 2014;50(1): 1.e1-1.e34.
2. Vercelli M, Capocaccia R, Quaglia A, Casella C, Puppo A, Coebergh JW. Relative survival in elderly European cancer patients: evidence for health care inequalities. The EUROCARE Working Group. Crit Rev Oncol Hematol. 2000; 35(3):161-79.
3. Hayne D, Brown RSD, Mccormack M, Quinn MJ, Payne HA, Babb P. Current trends in colorectal cancer: site, incidence, mortality and survival in England and Wales. Clin Oncol (R Coll Radiol). 2001;13(6):448-52.
4. Stoffel EM, Murphy CC. Epidemiology and Mechanisms of the Increasing Incidence of Colon and Rectal Cancers in Young Adults. Gastroenterology. 2020;158(2):341-353.
5. O'Connell LV, Zaborowski AM, Abdile A, Adamina M, Aigner F, D'Allens L, et al. Post-Operative Functional Outcomes in Early Age Onset Rectal Cancer. Front Oncol. 2022;12:868359.
6. Siegel RL, Fedewa SA, Anderson WF, Miller KD, Ma J, Rosenberg PS, et al. Colorectal Cancer Incidence Patterns in the United States, 1974-2013. J Natl Cancer Inst. 2017;109(8):djw322.
7. Keller DS, Berho M, Perez RO, Wexner SD, Chand M. The multidisciplinary management of rectal cancer. Nat Rev Gastroenterol Hepatol. 2020;17(7): 414-429.
8. Davis DM, Marcet JE, Frattini JC, Prather AD, Mateka JJL, Nfonsam VN. Is it time to lower the recommended screening age for colorectal cancer? J Am Coll Surg. 2011;213(3):352-61.
9. Meyer JE, Narang T, Schnoll-Sussman FH, Pochapin MB, Christos PJ, Sherr DL. Increasing incidence of rectal cancer in patients aged younger than 40 years: an analysis of the surveillance, epidemiology, and end results database. Cancer. 2010;116(18):4354-9.
10. Podda M, Sylla P, Baiocchi G, Adamina M, Agnoletti V, Agresta F, et al. Multidisciplinary management of elderly patients with rectal cancer: recommendations from the SICG (Italian Society of Geriatric Surgery), SIFIPAC (Italian Society of Surgical Pathophysiology), SICE (Italian Society of Endoscopic Surgery and new technologies), and the WSES (World Society of Emergency Surgery) International Consensus Project. World J Emerg Surg. 2021;16(1):35.
11. Feeney G, Sehgal R, Sheehan M, Hogan A, Regan M, Joyce M, et al. Neoadjuvant radiotherapy for rectal cancer management. World J Gastroenterol. 2019;25(33): 4850-4869.
12. Palmer G, Martling A, Cedermark B, Holm T. Preoperative tumour staging with multidisciplinary team assessment improves the outcome in locally advanced primary rectal cancer. Colorectal Dis. 2011;13(12):1361-9.
13. Breugom AJ, Bastiaannet E, Boelens PG, Van Eycken E, Iversen LH, Martling A, et al. Oncologic treatment strategies and relative survival of patients with stage I–III rectal cancer - A EURECCA international comparison between the Netherlands, Belgium, Denmark, Sweden, England, Ireland, Spain, and Lithuania. Eur J Surg Oncol. 2018;44(9):1338-1343.
14. Claassen YHM, Vermeer NCA, Iversen LH, van Eycken E, Guren MG, Mroczkowski P, et al. Treatment and survival of rectal cancer patients over the age of 80 years: A eurecca international comparison. Br J Cancer. 2018;119(4):517-522.
15. Gagliardi G, Pucciarelli S, Asteria CR, Infantino A, Romano G, Cola B, et al. A nationwide audit of the use of radiotherapy for rectal cancer in Italy. Tech Coloproctol. 2010;14(3):229-35.
16. Birch RJ, Taylor JC, Downing A, Spencer K, Finan PJ, Audisio RA, et al. Rectal cancer in old age –is it appropriately managed? Evidence from population-based analysis of routine data across the English national health service. Eur J Surg Oncol. 2019;45(7):1196-1204.
17. De Angelis R, Sant M, Coleman MP, Francisci S, Baili P, Pierannunzio D, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE - 5-a population-based study. Lancet Oncol. 2014;15(1):23-34.
18. Johnson M. Chemotherapy treatment decision making by professionals and older patients with cancer: A narrative review of the literature. Eur J Cancer Care (Engl). 2012;21(1):3-9.
19. Saraste D, Järţs J, Martling A. Population-based analysis of outcomes with early-age colorectal cancer. Br J Surg. 2020;107(3):301-309.
20. Høydahl Ø, Edna TH, Xanthoulis A, Lydersen S, Endreseth BH. The impact of age on rectal cancer treatment, complications and survival. BMC Cancer. 2022; 22(1):975.
21. Himbert C, Figueiredo JC, Shibata D, Ose J, Lin T, Huang LC, et al. Clinical characteristics and outcomes of colorectal cancer in the colocare study: differences by age of onset. Cancers (Basel). 2021;13(15):3817.
22. Zaborowski AM, Murphy B, Creavin B, Rogers AC, Kennelly R, Hanly A, et al. Clinicopathological features and oncological outcomes of patients with young-onset rectal cancer. Br J Surg. 2020;107(5):606-612.
23. Stornes T, Wibe A, Romundstad PR, Endreseth BH. Outcomes of rectal cancer treatment - Influence of age? Int J Colorectal Dis. 2014;29(7):825-34.
24. Araghi M, Arnold M, Rutherford MJ, Guren MG, Cabasag CJ, Bardot A, et al. Colon and rectal cancer survival in seven high-income countries 2010-2014: Variation by age and stage at diagnosis (the ICBP SURVMARK-2 project). Gut. 2021;70(1):114-126.
25. Zhang Y, Yan L, Wu Y, Xu M, Liu X, Guan G. Worse treatment response to neo-adjuvant chemoradiotherapy in young patients with locally advanced rectal cancer. BMC Cancer. 2020;20(1):854.
26. Glynne-Jones R, Wyrwicz L, Tiret E, Brown G, Rödel C, Cervantes A, et al. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2018;29(Suppl 4):iv263.
27. You YN, Dozois EJ, Boardman LA, Aakre J, Huebner M, Larson DW. Young-onset rectal cancer: Presentation, pattern of care and long-term oncologic outcomes compared to a matched older-onset cohort. Ann Surg Oncol. 2011;18(9):2469-76.
28. Fairley TL, Cardinez CJ, Martin J, Alley L, Friedman C, Edwards B, et al. Colorectal cancer in U.S. adults younger than 50 years of age, 1998-2001. Cancer. 2006;107(5 Suppl):1153-61.
29. O'Connell JB, Maggard MA, Liu JH, Etzioni DA, Ko CY. Are survival rates different for young and older patients with rectal cancer? Dis Colon Rectum. 2004;47(12):2064-9.
30. Endreseth BH, Romundstad P, Myrvold HE, Hestvik UE, Bjerkeset T, Wibe A. Rectal cancer in the young patient. Dis Colon Rectum. 2006;49(7):993-1001.
31. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA Cancer J Clin. 2021;71(1):7-33.
32. Murphy CC, Sandler RS, Sanoff HK, Yang YC, Lund JL, Baron JA. Decrease in Incidence of Colorectal Cancer Among Individuals 50 Years or Older After Recommendations for Population-based Screening. Clin Gastroenterol Hepatol. 2017;15(6):903-909.e6.
33. Atkin WS, Kralj-Hans I, Edwards R, Duff SW, Cuzick J, Atkin WS, et al. Once-only fl exible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. Lancet. 2010;375(9726):1624-33.
34. Segnan N, Armaroli P, Bonelli L, Risio M, Sciallero S, Zappa M, et al. Once-only sigmoidoscopy in colorectal cancer screening: Follow-up findings of the italian randomized controlled trial - SCORE. J Natl Cancer Inst. 2011;103(17):1310-22.
35. Yardley C, Glover C, Mersh A. Demographic factors associated with knowledge of colorectal cancer symptoms in a UK population-based survey. Ann R Coll Surg Engl. 2000;82(3):205-9.
36. Krzeszowiak J, Pach R, Richter P, Lorenc Z, Rutkowski A, Ochwat K, et al. The impact of oncological package implementation on the treatment of rectal cancer in years 2013-2019 in Poland – multicenter study. Pol Przegl Chir. 2024;96(3): 18-25.
37. Glynne-Jones R, Mathur P, Elton C, Train ML. The multidisciplinary management

of gastrointestinal cancer. Multimodal treatment of rectal cancer. Best Pract Res Clin Gastroenterol. 2007;21(6):1049-70.
38. Gefen R, Emile SH, Horesh N, Garoufalia Z, Wexner SD. Age-related variations in colon and rectal cancer: An analysis of the national cancer database. Surgery. 2023;174(6):1315-1322.
39. Guillerme F, Clavier JB, Nehme-Schuster H, Leroy V, Heitz D, Schumacher C, et al. Age impacts the pattern of care for elderly patients with rectal cancer. Int J Colorectal Dis. 2014;29(2):157-63.
40. Chang GJ, Skibber JM, Feig BW, Rodriguez-Bigas M. Are we undertreating rectal cancer in the elderly? An epidemiologic study. Ann Surg. 2007;246(2): 215-21.
41. Ha YH, Jeong SY, Lim SB, Choi HS, Hong YS, Chang HJ, et al. Influence of preoperative chemoradiotherapy on the number of lymph nodes retrieved in rectal cancer. Ann Surg. 2010;252(2):336-40.
42. Chou JF, Row D, Gonen M, Liu YH, Schrag D, Weiser MR. Clinical and pathologic factors that predict lymph node yield from surgical specimens in colorectal cancer: A population-based study. Cancer. 2010;116(11):2560-70.
43. Aan De Stegge WB, Van Leeuwen BL, Elferink MAG, De Bock GH. The Evaluation of more lymph nodes in colon cancer is associated with improved survival in patients of all ages. PLoS One. 2016;11(5):e0155608.
44. Fielding LP, Arsenault PA, Chapuisy PH, Gathright B, Hardcastlep P Hermanek JD, Jass JR, et al. Clinicopathological staging for colorectal cancer: An International Documentation System (IDS) and an International Comprehensive Anatomical Terminology (ICAT). J Gastroenterol Hepatol. 1991;6(4):325-44.
45. Ha YH, Jeong SY, Lim SB, Choi HS, Hong YS, Chang HJ, et al. Influence of preoperative chemoradiotherapy on the number of lymph nodes retrieved in rectal cancer. Ann Surg. 2010;252(2):336-40.
46. Wichmann MW, Gü Nther Meyer, Strauss T, Hornung HM, Lau-Werner U, Angele MK, et al. Effect of preoperative radiochemotherapy on lymph node retrieval after resection of rectal cancer. Arch Surg. 2002;137(2):206-10.
47. De La Fuente SG, Manson RJ, Ludwig KA, Mantyh CR. Neoadjuvant chemo-radiation for rectal cancer reduces lymph node harvest in proctectomy specimens. J Gastrointest Surg. 2009;13(2):269-74.
48. Damin DC, Rosito MA, Contu PC, Tarta C, Ferreira PR, Kliemann LM, et al. Lymph node retrieval after preoperative chemoradiotherapy for rectal cancer. J Gastrointest Surg. 2012;16(8):1573-80.
49. Narayanan S, Attwood K, Gabriel E, Nurkin S. Pathologic Complete Response Despite Nodal Yield Has Best Survival in Locally Advanced Rectal Cancer. J Surg Res. 2020:251:220-227.
50. Georgescu MT, Diaconu A, Iordan I, Georgescu FT, Bobirca F, Bobirca A, et al. Identification of Predictive Factors for Pathologic Complete Response in Rectal Cancer Patients Undergoing Neoadjuvant Treatment: A Retrospective Study. Chirurgia (Bucur). 2023;118(3):250-259.
51. Orsini RG, Verhoeven RHA, Lemmens VEPP, Van Steenbergen LN, De Hingh IHJT, Nieuwenhuijzen GAP, et al. Comparable survival for young rectal cancer patients, despite unfavourable morphology and more advanced-stage disease. Eur J Cancer. 2015;51(13):1675-82.
52. Ganapathi S, Kumar D, Katsoulas N, Melville D, Hodgson S, Finlayson C, et al. Colorectal cancer in the young: Trends, characteristics and outcome. Int J Colorectal Dis. 2011;26(7):927-34.
53. Smith N, Brown G. Preoperative staging of rectal cancer. Acta Oncol. 2008; 47(1):20-31.
54. Samee A, Selvasekar CR. Current trends in staging rectal cancer. World J Gastroenterol. 2011;17(7):828-34.