e-ISSN 2083–4640
ISSN 1507–1367

RESEARCH PAPER

Reports of Practical Oncology and Radiotherapy
2025, Volume 30, Number 1, pages: 54–61
DOI: 10.5603/rpor.104387
Submitted: 05.07.2024
Accepted: 07.01.2025

Results of radical treatment of locally advanced rectal cancer in geriatric and non-geriatric patients

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ABSTRACT

Background: It is estimated that 60% of new rectal cancer cases will be diagnosed in patients ≥ 65 years old. The geriatric patient is heterogeneous and underrepresented in clinical trials, and oncologic therapies are often tailored with little evidence. We describe a cohort of patients diagnosed with locally advanced rectal cancer in geriatric and non-geriatric patients.

Materials and methods: Retrospective and descriptive analysis of 137 patients, 44 (32.1%) ≥ 75 years old and 93 (67.9%) ≤ 75 years old, with diagnosis of locally advanced rectal cancer. All patients received neoadjuvant chemoradiotherapy (nCRT), followed by total mesorectal excision (TME) and adjuvant chemotherapy.

Results: Mean age was 79.5 for ≥ 75 years and 62.7 for ≤ 75 years, tumor location was: upper rectum (16.1% and 11.3%), middle rectum (60.2% and 47.7%) and lower rectum (23.7% and 41%), using the Eastern Cooperative Oncology Group (ECOG) 0: 74.1% and 81.8%, ECOG 1: 25.9% and 18.2%. Pathological complete response was 21.5% and 22.7%, partial response, 57% and 59% and no response, 21.5% and 18.3%, respectively. Tumor shrinkage in both groups after neoadjuvant treatment was 34.5% and 35.46%. Local recurrence was 2.2% and 3.2% and distance recurrence, 11.3% and 8.6%, respectively.

Conclusion: The study shows similar outcomes in both groups following radical treatment, with similar rates of pathological complete response. However, it has notable limitations, including a small sample size and the absence of a comprehensive geriatric assessment. To enhance these findings, future research should involve larger patient cohorts with comparative analysis and clinical trials specifically focused on the geriatric population.

Keywords: rectal cancer; geriatrics; complete pathologic response; radiotherapy; chemotherapy; neoadjuvant therapy

Rep Pract Oncol Radiother 2025;30(1):54–61

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Introduction

Colorectal cancer (CCR) is the second most common tumor diagnosed worldwide in women and the third in men, according to data from the World Health Organization (WHO) [1]. In Spain, according to data from the Red Española de Registro de Cáncer (REDECAN) [2], the estimated prevalence for the year 2023 was 42.721 cases, of which 14.256 were new cases of rectal cancer and of these 8.651 (60%) were diagnosed in patients over 65 years of age, which makes rectal cancer a disease linked to the aging of the population.

Multiple theories have been described that could explain the etiopathogenesis of cancer in the elderly patient: prolonged exposure to carcinogens (carcinogenesis), decreased hepatic and renal function (altered metabolism) that imply less metabolization and excretion of potentially carcinogenic products, alteration of the immune system (decreased number of T lymphocytes) and exposure to free radicals that favor the development of mutations [3]. However, chronological age does not reflect the functional reserve of each patient, geriatric patients are very heterogeneous from frail patients to fit patients and current clinical guidelines do not contemplate the special management of this group of patients, which is today a challenge in oncological consultations and leads to different therapeutic strategies with very heterogeneous results [4]. Geriatric patients usually have more comorbidities, as well as a higher probability of complications and therefore a worse prognosis [5].

The EURECCA study is an international study that evaluated the treatment and survival of patients with rectal cancer in patients >80 years of age. The study found a very heterogeneous treatment in each participating center, mainly in the use of neoadjuvant radiotherapy in locally advanced stages, in up to 7.9% of patients **[6]**. These data are coincident with those described by Thiels et al. **[7],** they analyzed patients with a mean age of 80 years and a diagnosis of rectal cancer who underwent surgery: 30% received neoadjuvant therapy and 33.8% adjuvant therapy. This tendency to avoid chemotherapy and/or radiotherapy in this group of patients is due to comorbidity and frailty, accepting high recurrence rates as long as an acceptable functional status and quality of life are maintained. This opens the debate on the optimal management of this group of patients where questions arise such as watch and wait strategies, local excision, radiotherapy scheme: short course vs. long course, timing of surgery and the benefit of adjuvant chemotherapy [8–10]. Geriatricians propose comprehensive geriatric assessment (CGA) as a tool to classify elderly cancer patients in order to adapt oncologic treatments [11, 12].

In view of the lack of evidence in this setting, a descriptive retrospective study of a group of patients with locally advanced rectal cancer (LARC) undergoing radical treatment is performed, making a sub-analysis of geriatric patients.

Materials and methods

Patients

This retrospective analysis included 137 patients with a histologically confirmed diagnosis of locally advanced rectal adenocarcinoma who received neoadjuvant chemoradiotherapy (nCRT) between January 2016 and March 2020. Tumor staging was conducted following the American Joint Committee on Cancer (AJCC) 8th edition Cancer Staging guidelines. Data for all patients were collected retrospectively from digitized medical records, covering diagnosis, treatment, and follow-up through January 2023.

Treatment

Radiotherapy

All patients received external beam radiotherapy with a 3D conformal technique, targeting the pelvic lymph node chains (external, internal iliac, presacral, and obturator) and mesorectum, delivering a dose of 45 Gy with a tumor boost of up to 50.4 Gy across 28 fractions, using a 5 mm PTV margin. Treatment was administered with 3D conformal radiotherapy (RT3D-C) on a linear accelerator (Elekta Synergy) with 6 MV photons and daily cone-beam CT (CBCT).

Chemotherapy

Patients received oral capecitabine (825 mg/m^2) twice daily during radiotherapy days as a radiosensitizer.

Surgery

8–10 weeks after completion of nCRT, the patients underwent total mesorectal excision (TME), after evaluation with pelvic magnetic resonance imaging (MRI) and by a surgeon specialized in colorectal pathology with more than 10 years of experience, who decided, according to the tumor location and radiological clinical response, on the type of surgery: ultra-low anterior resection (ULAR), low anterior resection (LAR) or abdominoperineal amputation (APA).

Performance status

The functional capacity of all patients was assessed using the Eastern Cooperative Oncology Group (ECOG) scale.

Follow-up

Follow-up of all treated patients was performed as described in clinical guidelines [13–15] with the following tests: computed axial tomography (CT), blood analysis with tumor markers: carcinoembryonic antigen (CEA), pelvic MRI and colonoscopy.

Toxicity

The assessment of adverse effects was performed according to the criteria of the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Statistic

The statistical operations were performed using SPSS version 22.0 for Windows (IBM Corp., Armonk, NY). Descriptive statistics summarize the patient characteristics, tumor response, acute toxicity, recurrence and mortality. Absolute and relative frequencies to express qualitative variables and the confidence interval of the percentage are also included to depict the dispersion of the results.

Results

Patient characteristics

A total of 137 patients with diagnosis of LARC, III stage (AJCC) underwent radical nCRT treatment. Patients were divided in two groups: one consisting of 44 patients ≥ 75 years old, with a mean age of 79.5 years (75–88) of whom 22 (50%) were men and 22 (50%) were women. Another group was constituted by 93 patients, ≤ 75 years old, with a mean age of 62.7 years old (range 40–74) including 49 (52.6%) men and 44 (47.4%) women (Tab. 1).

After ECOG assessment, 35 patients (81.8%) were ECOG 0 and 9 (18.2%) were ECOG 1, within the geriatric group. In the other cohort 69 patients (74.1%) were ECOG 0 and 24 patients (25.9%) ECOG 1.

All patients were diagnosed with adenocarcinoma. Among the geriatric group, 5 (11.3%) had high-grade tumors (G3), 26 (59.1%) had moderate-grade tumors (G2), and 13 (29.6%) had low-grade tumors (G1). In the non-geriatric group, 10 (10.8%) were G3, 68 (73.1%) were G2, and 15 (16.1%) were G1.

All patients completed the nCRT treatment. The tumor location of the geriatric patients was as follows: 5 (11.3%) upper rectum, 21 (47.7%) middle rectum and 18 (41%) lower rectum. The distribution in the other cohort was 15 patients (16.1%) upper rectum, 56 (60.2%) middle rectum and 22 (23.7%) lower rectum.

All patients, following the completion of nCRT, underwent TME performed by specialized sur-

Table 1. Characteristics of patients

Characteristic	≤ 75 years old	≥ 75 years old
Patients	93	44
Sex		
Male	49 (52.6%)	22 (50%)
Female	44 (47.4%)	22 (50%)
ECOG		
0	69 (74.1%)	35 (81.8%)
1	24 (25.9%)	9 (18.2%)
Histologic grade		
Low grade (G1)	15 (16.1%)	13 (29.6%)
Moderate grade (G2)	68 (73.1%)	26 (29.1%)
High grade (G3)	3 (3.2%)	5 (11.3%)
Unknown	7 (7.6%)	0 (0%)
Microsatellite instability	3 (3.2%)	0 (0%)
Tumor location		
Upper rectum	15 (16.1%)	5 (11.3%)
Medium medio	56 (60.2%)	21 (47.7%)
Lower rectum	22 (23.7%)	18 (41%)
Tumoral size (cm)	5.47 (0.9-15)	5.48 (2.2-9.8)
Carcinoembryonic antigen (CEA)	4.42 (2.6-10)	4.85 (0.8-23.8)

ECOG — Eastern Cooperative Oncology Group

Table 2. Treatment details

Characteristic	≤ 75 years old	≥ 75 years old
Chemotherapy (capecitabine)	93	44
Radiotherapy	93	44
Surgery type		
Ultra-low anterior resection (ULAR)	35 (37.6%)	12 (27.2%)
Low anterior resection (LAR)	33 (35.4%)	14 (31.8%)
Abdominoperineal amputation (APA)	25 (27%)	18 (41%)

geons in the Colorectal Unit. In the geriatric cohort, 12 patients (27.2%) underwent ULAR, 14 (31.8%) underwent LAR, and 18 (41%) underwent APA. In the non-geriatric cohort, 35 patients (37.6%) underwent ULAR, 33 (35.4%) underwent LAR, and 25 (27%) underwent APA (Tab. 2).

Toxicity

Acceptable tolerance to treatment was obtained in the geriatric cohort, with G3 skin toxicity in 2 (4.5%) patients and gastrointestinal toxicity in 2 (4.5%) patients. No patient had genitourinary toxicity ≥ G3. The other cohort presented similar toxicity, with G3 skin toxicity in 6 patients (6.4%), G3 gastrointestinal toxicity in 3 patients (3.2%) and no genitourinary toxicity in any case (Tab. 3).

Tumor response

In the geriatric cohort 10 (22.7%) patients obtained a complete pathologic response (cPR), 26 (59%) partial pathologic response (pPR) and 8 (18.3%) no response. In this group of patients the mean tumor size was 5.48cm (range 2.2–9.8 cm) and after neoadjuvant treatment a reduction of 34.5% to 3.54 cm (range 0.12–8cm) was obtained. In the non-geriatric cohort, 20 patients (21.5%) had complete pathological response, 53 (57%) patients had partial pathological response and 20 patients (21.5%) had no change after neoadjuvant treatment. The mean tumor size was 5.47 cm (range 0.9–15 cm) with a 35.4% reduction after neoadjuvant treatment to 3.53 cm (Tab. 4).

Local recurrence

In the geriatric group, 1 patient (2.2%) experienced local progression. In the other group, 3 patients (3.2%) had locoregional progression that necessitated surgical salvage. In both groups surgical salvage was performed (Tab. 4).

Table 3. Treatment toxicity

Toxicity (CTCAE) v. 5.0)*	≤ 75 years old	≥ 75 years old
Skin		
G1	68 (73.1%)	33 (75%)
G2	19 (20,5%)	9 (20,5%)
G3	6 (6.4%)	2 (4.5%)
Gastrointestinal		
G1	48 (51.6%)	27 (61.3%)
G2	42 (45.2%)	15 (34.2%)
G3	3 (3.2%)	2 (4.5%)
Genitourinary		
G1	13 (13,9%)	5 (11.3)
G2	8 (8.6%)	2 (4.5%)
G3	0 (0%)	0 (0%)

CTCAE — Common Terminology Criteria for Adverse Events

Table 4. Pathological response and recurrence

Characteristic	≤ 75 years old	≥ 75 years old
Pathological complete response (pCR)	20 (21.5%)	10 (22.7%)
Pathological partial response (pPR)	53 (57%)	26 (59%)
No response	20 (21.5%)	8 (18.3%)
Local recurrence	1 (2,2%)	3 (3.2%)
Distance recurrence	8 (8.6%)	5 (11.3%)

Recurrence at distance

Among the geriatric patients, 5 (11.3%) developed metastatic progression. In the non-geriatric cohort, 8 patients (8.6%) experienced metastases. Both groups were treated with chemotherapy (Tab. 4).

Mortality

Of the 44 geriatric patients, 6 (13.6%) died of disease-related causes and 5 (11.3%) from other causes. In the other group, 8 (8.6%) died from disease progression, 2 (2.1%) from new neoplasms (pancreas and lung) and 2 (2.1%) from other non-oncologic causes.

Discussion

The treatment of rectal cancer is stage-dependent. According to the AJCC, LARC is treated with

nCRT, followed by surgery (TME), and then adjuvant chemotherapy. This treatment regimen typically spans approximately 8 months [16]. This is the protocol followed by our patients.

The surgical mortality rate of patients undergoing TME, according to American Society of Anesthesiologists (ASA) type III and IV can reach 45.4% [17, 18]. However, this rate is not stratified by age, leading to a lack of data specific to geriatric patients. This gap has prompted oncological societies to establish guidelines to identify vulnerable geriatric patients at higher risk for complications from oncological treatments. The International Society of Geriatric Oncology (ISGO) recommends a comprehensive assessment of geriatric patients, considering factors such as functionality, comorbidities, fall risk, depression, cognitive status, and nutrition, to guide treatment decisions [19]. In our cohort of geriatric patients, neither frailty screening nor a comprehensive geriatric assessment (CGA) was conducted. Treatment was based on the clinical expertise of the specialists involved, resulting in a non-cancer mortality rate of 11.3%. The installation of an oncogeriatric unit and consequently CGA began in 2021 after data collection was completed.

Current evidence supports that patients ≥ 75 years old can safely tolerate nCRT, the standard scheme involves oral capecitabine or continuous infusion of 5-fluoruracil (indicated in case of renal failure) [20, 21] concomitantly with radiotherapy [22]. This scheme was used in both groups with similar results in terms of tolerance. However, new schemes, such as total neoadjuvant therapy (TNT) including induction chemotherapy with FOLFOX or CAPEOX for 12–16 weeks prior to nCRT, allow adjuvant chemotherapy to be avoided [16]. A multi-institutional phase III study assessed adding mFOLFOX for 2, 4 or 6 cycles achieving a pathologic complete response rate of 25%, 30% and 38%, respectively, compared to 18% without mFOLFOX. These pathologic response rates have been achieved at the expense of greater neutropenia and lymphopenia than with conventional schemes [23]. This approach with intensive chemotherapy must be tailored to the patient's context, and in the case of the geriatric cohort it appears that the toxicity associated with intensive chemotherapy is not the best option. In our cohort all patients were treated with a combination of oral capecitabine, presenting low rate of chemotherapy related toxicity and the pathological response in both cohorts was similar and comparable to that described in the literature.

Radiotherapy is used to reduce the probability of local recurrence, with a toxicity profile which highlights fecal incontinence that directly impacts the quality of life of patients, as well as sexual dysfunction, vaginal fibrosis and urinary incontinence [24]. Based on the attempt to reduce this radiotherapy-induced toxicity, the PROSPECT trial (NCT01515787) is comparing neoadjuvant chemotherapy with FOLFOX versus nCRT, using pCR as the primary endpoint, with the idea of avoiding radiotherapy in the treatment scheme. On the other hand, radiotherapy has demonstrated its role in the neoadjuvant scheme and there is another scheme: short course radiotherapy (SCRT) with acceptable pCR rates according to the results of Stockholm III [25] and RAPIDO Trial [26]. We don't include patients with short course radiotherapy. In our patients treated with long course (LCRT) there was little toxicity, highlighting G3 at the skin level and gastrointestinal G2 which resolved within a few weeks without differences in both groups, so we believe that radiotherapy treatment provides a clear benefit and for the moment there is no evidence to avoid it.

Another approach that is increasingly used is "watch and wait", a recent systematic review demonstrated a high clinical complete response after neoadjuvant chemotherapy and a 3-year survival of 93.5%. In patients who required salvage surgery, 93% were R0 margins [27]. The detection of relapses was early, all due to the intensive follow-up program including continuous MRI with validated criteria, such as the mrTRG described by Brown et al [28]. This latter approach is suitable for geriatric patients who are not candidates for aggressive therapies but are candidates for chemotherapy, and should also be closely monitored for possible relapse. Our patients had a pCR of 22.7% in the geriatric cohort and 21.5% in the non-geriatric cohort, with a tumor shrinkage of 34.5% and 35.4%, respectively, and according to Dattani et al. [27], would be candidates for a "watch and wait" protocol. The relapse rate is 31%, subsidiary of surgical salvage. According to the data described by Habr-Gama et al. [29], a salvage therapy in this scenario is possible in ≥ 90%

of cases, with 94% local control and 78% organ preservation [29]. Therefore, this protocol should be followed in specialized centers with a multidisciplinary team with clear inclusion and follow-up criteria. However, despite the growing interest in the "watch and wait" strategy, surgery continues to be the cornerstone of treatment with TME. In geriatric patients, greater complications have been described at the ostomy level, leading to hydroelectrolyte imbalances, paralytic ileus, urinary dysfunctions, infections, and other disorders, leading to prolonged hospitalizations that are associated with higher mortality, have a negative impact on recovery and cause the loss of functional capacity [30–32]. Despite advances in robotic surgery, laparoscopic and transanal surgery, it is therefore essential to identify those patients who can achieve a pCR with conservative therapy [33], in case of partial response this could be treated with local excision [33].

In the adjuvant setting, radiotherapy (RT) is considered for patients with risk factors, provided it was not previously administered in the neoadjuvant setting. Chemotherapy, on the other hand, is included in the treatment plan when TNT is not used, except in the presence of risk factors. In elderly patients, treatment is tailored according to the results presented by Sargent et al. [34] and Tournigand et al. [35], which demonstrated that chemotherapy with 5-FU alone, without oxaliplatin, improves survival in patients aged ≥ 70 years without increasing toxicity. However, additional studies are needed to establish the optimal chemotherapy regimen for this patient population.

Tumor grade is a significant prognostic factor, though it was not analyzed in this study. However, it is known that factors such as histological variation, mitotic figures, glandular architecture, and nuclear polarity can be evaluated to develop a more comprehensive index for predicting the course of the disease in all patients with this tumor type [17].

This study has several limitations, including a small sample size in both groups, unbalanced groups, the absence of a comparative analysis, and no CGA in the geriatric cohort. Nonetheless, it appears that the geriatric group, in general, demonstrates similar tolerance to oncological treatment and comparable effectiveness to the broader population.

Future perspectives are oriented towards radiomic models that can predict pCRT after nCRT, as described by Shin et al. [36], where they emphasize the importance of radiomics, which provides information through the quantitative extraction of information from the images. This has led to the development of predictive models, using pre- and post-nCRT MRI based on T2-weighted-imaging or multiparametric sequences; however, validated studies that help standardize this practice are lacking. More information is currently provided by the use of Diffusion-weighted imaging (DWI) and the calculation of the apparent diffusion coefficient (ADC) to evaluate residual tumor after RT and its distinction from actinic fibrosis [37], becoming a factor that can predict response in this group of patients. Linking this concept with that of adaptive radiotherapy (ART) in linear accelerators with resonance (MR-LINAC) can help to make treatment adaptations with dose intensification at points where there may be tumor viability, according to what was published by Ingle et al. [38]. Another object of study corresponds to circulating tumor cells and, more specifically, ctDNA obtained through liquid biopsy with studies reporting high levels/persistence of ctDNA after cCRT as a clear predictor of poor response [39]. In geriatric patients clinical trials are currently being evaluated highlighting the impact of CGA (NCT05851235, NCT01321658), the combination of radiotherapy with new drugs (NCT02992886) and even comparisons of radiotherapy schemes (NACRE, NCT02551237) with the intention of obtaining comparable cure rates in this population with a low toxicity rate.

Conclusion

Rectal cancer is a complex disease that requires a multidisciplinary approach in locally advanced stages, especially in geriatric patients. In the cohort analyzed, both geriatric and non-geriatric patients presented a pCR similar to those described in the literature without treatment de-intensification; therefore, geriatric patients despite greater comorbidities respond equally to radical treatment of rectal cancer. Randomized clinical studies with this patient profile are necessary to optimally approach oncologic treatment with curative intent without negative impact on their quality of life.

Ethical permission

Ethical approval was not necessary for the preparation of this article.

Conflicts of interest

Authors declare no conflicts of interest.

Funding

None declared.

References

1. World Health Organization GLOBOCAN database. https://gco.iarc.fr/today/home (08.03.2021).
2. Estimaciones De La Incidencia Del Cáncer En España, 2023. https://redecan.org/storage/documents/02d62122-9adb-4d35-b6d0-551435dbe4ae.pdf.
3. Capítulo 74. Cáncer. Neoplasias Más Frecuentes. María Victoria Farré Mercadé Raquel Benavent Boladeras (SEGG).
4. Babaei M, Jansen L, Balavarca Y, et al. Neoadjuvant Therapy in Rectal Cancer Patients With Clinical Stage II to III Across European Countries: Variations and Outcomes. Clin Colorectal Cancer. 2018; 17(1): e129–e142, doi: 10.1016/j.clcc.2017.09.002, indexed in Pubmed: 29074354.
5. Shahir MA, Lemmens VE, van de Poll-Franse LV, et al. Elderly patients with rectal cancer have a higher risk of treatment-related complications and a poorer prognosis than younger patients: a population-based study. Eur J Cancer. 2006; 42(17): 3015–3021, doi: 10.1016/j.ejca.2005.10.032, indexed in Pubmed: 16797967.
6. Claassen YHM, Vermeer NCA, Iversen LH, 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, doi: 10.1038/s41416-018-0215-6, indexed in Pubmed: 30057408.
7. Thiels CA, Bergquist JR, Meyers AJ, et al. Is Chemotherapy or Radiation Therapy in Addition to Surgery Beneficial for Locally Advanced Rectal Cancer in the Elderly? A National Cancer Data Base (NCDB) Study. World J Surg. 2016; 40(2): 447–455, doi: 10.1007/s00268-015-3319-7, indexed in Pubmed: 26566779.
8. Chadi SA, Malcomson L, Ensor J, et al. Factors affecting local regrowth after watch and wait for patients with a clinical complete response following chemoradiotherapy in rectal cancer (InterCoRe consortium): an individual participant data meta-analysis. Lancet Gastroenterol Hepatol. 2018; 3(12): 825–836, doi: 10.1016/S2468-1253(18)30301-7, indexed in Pubmed: 30318451.
9. Smith FM, Ahad A, Perez RO, et al. Local Excision Techniques for Rectal Cancer After Neoadjuvant Chemoradiotherapy: What Are We Doing? Dis Colon Rectum. 2017; 60(2): 228–239, doi: 10.1097/DCR.0000000000000749, indexed in Pubmed: 28059920.
10. Monsellato I, Alongi F, Bertocchi E, et al. Standard (8 weeks) vs long (12 weeks) timing to minimally-invasive surgery after NeoAdjuvant Chemoradiotherapy for rectal cancer: a multicenter randomized controlled parallel group trial (TiMiSNAR). BMC Cancer. 2019; 19(1): 1215, doi: 10.1186/s12885-019-6271-3, indexed in Pubmed: 31842784.
11. Myint AS, Gérard JP. Role of radiotherapy in the treatment of rectal cancer in older patients. Eur J Surg Oncol. 2020; 46(3): 349–357, doi: 10.1016/j.ejso.2019.12.017, indexed in Pubmed: 31926607.
12. Mohile SG, Dale W, Somerfield MR, et al. Practical Assessment and Management of Vulnerabilities in Older Patients Receiving Chemotherapy: ASCO Guideline for Geriatric Oncology. J Clin Oncol. 2018; 36(22): 2326–2347, doi: 10.1200/JCO.2018.78.8687, indexed in Pubmed: 29782209.
13. Benson AIB, Venook AP, Al-Hawary MM, et al. NCCN Guidelines Insights: Rectal Cancer, Version 6.2020. J Natl Compr Canc Netw. 2020; 18(7): 806–815, doi: 10.6004/jnccn.2020.0032, indexed in Pubmed: 32634771.
14. Capdevila J, Gómez MaA, Guillot M, et al. SEOM-GEMCAD-TTD clinical guidelines for localized rectal cancer (2021). Clin Transl Oncol. 2022; 24(4): 646–657, doi: 10.1007/s12094-022-02816-9, indexed in Pubmed: 35303269.
15. Glynne-Jones R, Wyrwicz L, Tiret E, et al. ESMO Guidelines Committee. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2017; 28(suppl_4): iv22–iv40, doi: 10.1093/annonc/mdx224, indexed in Pubmed: 28881920.
16. Sheikh AR, Yameen H, Hartshorn K. Treatment of Rectal Cancer in Older Adults. Curr Oncol Rep. 2018; 20(12): 102, doi: 10.1007/s11912-018-0746-2, indexed in Pubmed: 30456634.
17. Pares S. Nuevo sistema de puntuación con valor pronóstico de mortalidad en la peritonitis del colon izquierdo . http//www.sccirugia.org/actachir/comunicacions/scocolon.htm.
18. Almeraya J, Blas M, Pichardo M, et al. Resultados a largo plazo en el manejo quirúrgico del cáncer de recto: supervivencia a 5 años. Cir Gen. 2014; 36(4): 225–231.
19. Personalized treatment of elderly patients with rectal cancer. A position paper by the SIOG- surgical task force, ESSO, ESCP and OSTRiCh Consortium collaborative group | SIOG. http://www.siog.org/node/495.
20. Margalit DN, Mamon HJ, Ancukiewicz M, et al. Tolerability of combined modality therapy for rectal cancer in elderly patients aged 75 years and older. Int J Radiat Oncol Biol Phys. 2011; 81(5): e735–e741, doi: 10.1016/j.ijrobp.2010.12.056, indexed in Pubmed: 21377289.
21. Tougeron D, Roullet B, Paillot B, et al. Safety and outcome of chemoradiotherapy in elderly patients with rectal cancer: results from two French tertiary centres. Dig Liver Dis. 2012; 44(4): 350–354, doi: 10.1016/j.dld.2011.10.017, indexed in Pubmed: 22119617.
22. Gérard JP, Azria D, Gourgou-Bourgade S, et al. Clinical outcome of the ACCORD 12/0405 PRODIGE 2 randomized trial in rectal cancer. J Clin Oncol. 2012; 30(36): 4558–4565, doi: 10.1200/JCO.2012.42.8771, indexed in Pubmed: 23109696.
23. Garcia-Aguilar J, Chow OS, Smith DD, et al. Timing of Rectal Cancer Response to Chemoradiation Consortium. Effect of adding mFOLFOX6 after neoadjuvant chemoradiation in locally advanced rectal cancer: a multicentre, phase 2 trial. Lancet Oncol. 2015; 16(8): 957–966, doi: 10.1016/S1470-2045(15)00004-2, indexed in Pubmed: 26187751.
24. Wiltink LM, Marijnen CAM, Meershoek-Klein Kranenbarg E, et al. A comprehensive longitudinal overview of health-related quality of life and symptoms after treatment for

rectal cancer in the TME trial. Acta Oncol. 2016; 55(4): 502–508, doi: 10.3109/0284186X.2015.1088171, indexed in Pubmed: 26406287.
25. Erlandsson J, Holm T, Pettersson D, et al. Optimal fractionation of preoperative radiotherapy and timing to surgery for rectal cancer (Stockholm III): a multicentre, randomised, non-blinded, phase 3, non-inferiority trial. Lancet Oncol. 2017; 18(3): 336–346, doi: 10.1016/S1470-2045(17)30086-4, indexed in Pubmed: 28190762.
26. Bahadoer RR, Dijkstra EA, van Etten B, et al. RAPIDO collaborative investigators. Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial. Lancet Oncol. 2021; 22(1): 29–42, doi: 10.1016/S1470-2045(20)30555-6, indexed in Pubmed: 33301740.
27. Dattani M, Heald RJ, Goussous G, et al. Oncological and Survival Outcomes in Watch and Wait Patients With a Clinical Complete Response After Neoadjuvant Chemoradiotherapy for Rectal Cancer: A Systematic Review and Pooled Analysis. Ann Surg. 2018; 268(6): 955–967, doi: 10.1097/SLA.0000000000002761, indexed in Pubmed: 29746338.
28. Battersby NJ, How P, Moran B, et al. MERCURY II Study Group. Prospective Validation of a Low Rectal Cancer Magnetic Resonance Imaging Staging System and Development of a Local Recurrence Risk Stratification Model: The MERCURY II Study. Ann Surg. 2016; 263(4): 751–760, doi: 10.1097/SLA.0000000000001193, indexed in Pubmed: 25822672.
29. Habr-Gama A, Gama-Rodrigues J, São Julião GP, et al. Local recurrence after complete clinical response and watch and wait in rectal cancer after neoadjuvant chemoradiation: impact of salvage therapy on local disease control. Int J Radiat Oncol Biol Phys. 2014; 88(4): 822–828, doi: 10.1016/j.ijrobp.2013.12.012, indexed in Pubmed: 24495589.
30. Yeo HL, O'Mahoney PRA, Lachs M, et al. Surgical oncology outcomes in the aging US population. J Surg Res. 2016; 205(1): 11–18, doi: 10.1016/j.jss.2016.04.038, indexed in Pubmed: 27620993.
31. Aquina CT, Mohile SG, Tejani MA, et al. The impact of age on complications, survival, and cause of death following colon cancer surgery. Br J Cancer. 2017; 116(3): 389–397, doi: 10.1038/bjc.2016.421, indexed in Pubmed: 28056465.
32. Couwenberg AM, de Beer FSA, Intven MPW, et al. The impact of postoperative complications on health-related quality of life in older patients with rectal cancer; a prospective cohort study. J Geriatr Oncol. 2018; 9(2): 102–109, doi: 10.1016/j.jgo.2017.09.005, indexed in Pubmed: 29032962.
33. Kosinski L, Habr-Gama A, Ludwig K, et al. Shifting concepts in rectal cancer management. CA Cancer J Clin. 2012; 62(3): 173–202, doi: 10.3322/caac.21138.
34. Sargent DJ, Goldberg RM, Jacobson SD, et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. N Engl J Med. 2001; 345(15): 1091–1097, doi: 10.1056/NEJMoa010957, indexed in Pubmed: 11596588.
35. Tournigand C, André T, Bonnetain F, et al. Adjuvant therapy with fluorouracil and oxaliplatin in stage II and elderly patients (between ages 70 and 75 years) with colon cancer: subgroup analyses of the Multicenter International Study of Oxaliplatin, Fluorouracil, and Leucovorin in the Adjuvant Treatment of Colon Cancer trial. J Clin Oncol. 2012; 30(27): 3353–3360, doi: 10.1200/JCO.2012.42.5645, indexed in Pubmed: 22915656.
36. Shin J, Seo N, Baek SE, et al. MRI Radiomics Model Predicts Pathologic Complete Response of Rectal Cancer Following Chemoradiotherapy. Radiology. 2022; 303(2): 351–358, doi: 10.1148/radiol.211986, indexed in Pubmed: 35133200.
37. Schurink NW, Lambregts DMJ, Beets-Tan RGH. Diffusion-weighted imaging in rectal cancer: current applications and future perspectives. Br J Radiol. 2019; 92(1096): 20180655, doi: 10.1259/bjr.20180655, indexed in Pubmed: 30433814.
38. Ingle M, Blackledge M, White I, et al. Quantitative analysis of diffusion weighted imaging in rectal cancer during radiotherapy using a magnetic resonance imaging integrated linear accelerator. Phys Imaging Radiat Oncol. 2022; 23: 32–37, doi: 10.1016/j.phro.2022.06.003, indexed in Pubmed: 35756883.
39. Nikolic A, Krivokapic Z. Nucleic acid-based markers of response to neoadjuvant chemoradiotherapy in locally advanced rectal cancer. Surg Oncol. 2022; 41: 101743, doi: 10.1016/j.suronc.2022.101743, indexed in Pubmed: 35358913.