Efficacy of Endoscopic Surveillance in the Detection of Local Recurrence After Radical Rectal Cancer Surgery is Limited: A Retrospective Study.

Michal Jankowski (✉ michaljankowski@post.pl)

Uniwersytet Mikolaja Kopernika Collegium Medicum https://orcid.org/0000-0001-9982-842X

Wojciech M. Wysocki

Andrzej Frycz Modrzewski Krakow University, Chair of Surgery; Department of General, Oncological and Health Sciences, 5th Military Clinical Hospital in Krakow, National Institute of Oncology, Maria Sklodowska-Curie Memorial, Scientific Editorial Office, Warszawa, Poland

Karol Tkaczyński

Oncology Center - Prof. Łukaszczyk Memorial Hospital, Bydgoszcz

Dorian Wiśniewski

Oncology Center - Prof. Łukaszczyk Memorial Hospital, Bydgoszcz

Manuela Las-Jankowska

Nicolaus Copernicus University in Toruń Ludwik Rydygier Collegium Medicum in Bydgoszcz: Uniwersytet Mikolaja Kopernika w Toruniu Collegium Medicum im Ludwika Rydygiera w Bydgoszczy, Oncology Center - Prof. Łukaszczyk Memorial Hospital, Bydgoszcz

Dariusz Bała

Nicolaus Copernicus University Faculty of Medicine: Uniwersytet Mikolaja Kopernika w Toruniu Collegium Medicum im Ludwika Rydygiera w Bydgoszczy; Oncology Center - Prof. Łukaszczyk Memorial Hospital, Bydgoszcz

Wojciech Zegarski

Nicolaus Copernicus University in Toruń Ludwik Rydygier Collegium Medicum in Bydgoszcz: Uniwersytet Mikolaja Kopernika w Toruniu Collegium Medicum im Ludwika Rydygiera w Bydgoszczy; Oncology Center - Prof. Łukaszczyk Memorial Hospital, Bydgoszcz

---

Research

Abstract

Background: Rectal cancer, one of most common neoplasms, is characterized by an overall survival rate exceeding 60%. Nonetheless, local recurrence (LR) following surgery for rectal cancer remains a formidable clinical problem. The aim of this study was to assess the value of postoperative endoscopic surveillance (PES) for the early detection of LR in rectal cancer after radical treatment.

Methods: We performed an anterior resection in 228 patients with stage I-III rectal cancer who had undergone surgery from 2001 to 2008 in the Oncology Center in Bydgoszcz, Poland. Of these patients, 169 had perioperative radiotherapy or radiochemotherapy. All patients underwent PES with imaging (abdominal ultrasound or computed tomography scan, pelvic magnetic resonance imaging) and endoscopic examinations. The ratios of sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and receiver operating characteristic curve were calculated to compare the diagnostic value of colonoscopy versus imaging techniques.

Results: During the 5-year follow-up, recurrences occurred in 49 (21%) patients; of these, 15 (6%) had LR, which was most often located outside the intestinal lumen (n = 10, 4%). Anastomotic LR occurred in 5 (2%) patients. The mean time to anastomotic LR was 30 months after initial surgery, similar to that of other locations (29 months). Both imaging and endoscopy were shown to be efficient techniques for the diagnosis of LR in anastomotic sites, and endoscopy did not provide any additional benefit in patients who were receiving radiation therapy.

Conclusions: The benefit of PES for the detection of LR after curative treatment of rectal cancer is limited. It remains a useful method, however, for the histopathological confirmation of suspected or confirmed recurrence.

Background

Colorectal cancer (CRC) is one of the most common malignancies worldwide. Its occurrence is associated with lifestyle and, according to global data, it is expected to increase to an estimated 2.2 million new cases per year in 2030 [1]. Most patients with CRC will undergo radical treatment for the disease; they represent the third largest group of long-term cancer survivors [2]. At least 30% of CRCs are located in the rectum [3].

In 2017, 5,617 Polish patients were diagnosed with cancer of the rectum and rectosigmoid junction [4]. Poland belongs to the group of countries with a medium risk of CRC, and the number of cases and cancer-related deaths is constantly increasing [1, 4].

Standard treatment of rectal cancer usually involves surgery, systemic therapies, and radiotherapy (RT). The 5-year survival rates of patients undergoing radical therapy can reach 60% or more in developed countries regardless of stage at diagnosis; the prognosis varies significantly, however, depending on the initial stage of the disease [5, 6]. The locoregional recurrence rate has decreased from about 30%-50−5%-10% as a result of precise qualification methods based on modern imaging, treatment that incorporates RT, and improved surgery with techniques such as total mesorectal excision (TME) [7−10].

Currently, most rectal cancer recurrence is systemic, not local. Nevertheless, local recurrence (LR) is still a major diagnostic and therapeutic problem in patients after radical treatment of rectal cancer, as its occurrence significantly reduces the patient's chances for long-lasting recovery.

Diagnostic and therapeutic possibilities depend largely on the localization of the LR. Although there is no universally accepted classification of LRs according to their location, 4 typical LR zones are frequently distinguished: central/axial (anastomotic site, perianal region, rest of the mesorectum tissue), lateral (lateral pelvic sidewall: iliac vessels, lateral pelvic lymph nodes, sidewall musculature), anterior (genitourinary region, pubic bone), and posterior (presacral zone) (Fig. 1).

Although radical resection is commonly accepted as the best option to effectively treat LR of rectal cancer, this treatment is feasible (with a curative intent) in only a minority of patients [11]. Oncological follow-up in patients after radical treatment aims to detect disease recurrence early and – theoretically – improve radical resection rates of non-advanced recurrence. However, the impact of intensive endoscopic and imaging surveillance on the improvement of survival in patients with rectal cancer has not yet been unequivocally proven [12–14]. Moreover, the methods used for recurrence surveillance are still under discussion and currently not enough data are available to support their efficacy [15].

In this study, we aimed to clarify the clinical value of endoscopic surveillance for the early detection of LR in rectal cancer after radical surgery.

Methods

Patient selection

Between 2001 and 2008, 228 patients with pathological TNM (pTNM) stages I-III of sporadic cancer of the rectum [16] underwent radical anterior resection with primary anastomosis. Patients were eligible for perioperative treatment according to the established principles described in Table 1. This retrospective study was approved by the Bioethical Committee at the Collegium Medicum Nicolaus Copernicus University.

Table 1
Framework for perioperative care of patients with rectal cancer

Type of treatment	Resectability status	pTNM classification (MRI or CT)	Tumor localization
Preoperative sRT[a]	Resectable	cT3 and/or N+	Middle or low rectum
Preoperative RT[b] or preoperative CRT[c]	Unresectable or probably not R0	cT3-4 and/or N+	
No RT	Resectable, contraindications	cT1-2, N0	
		cT3 and/or N+	High rectum
Postoperative RT[d] or postoperative CRT[e]	Not preoperative RT	pT3-4 and/or N+	
Postoperative CTx[f]		T4 and/or N+	

[a] Short-course radiotherapy (5 x 5 Gy) followed by immediate surgery (< 10 days from the first radiation fraction)

[b] 45−50 Gy in 28 fractions; a boost with a further 5.4 Gy

[c] 45−50 Gy in 28 fractions; a boost with a further 5.4 Gy combined with 2 cycles of 5-fluorouracil

[d] 45−54 Gy per fraction

[e] 1.8-2.0 Gy per fraction combined with 4−6 cycles of 5-fluorouracil

[f] 6 cycles of 5- fluorouracil

Abbreviations: CRT, chemoradiotherapy; CT, computed tomography; CTx, chemotherapy; MRI, magnetic resonance imaging; sRT, short-course radiotherapy; CT, computed tomography; pTNM, TNM classification; RT, radiotherapy

Treatment and follow-up

Patients with a tumor of the lower and middle part of the rectum underwent TME, whereas a partial mesorectal excision was performed for those with more proximal tumors (upper third of the rectum). All surgeries were performed with open surgical procedures. A protective stoma was not performed as standard procedure; rather, it was created only if an anastomotic leak was suspected following anastomosis (mostly ileostomy, infrequently colostomy). The overall 30-day perioperative mortality rate was 1.3% (3 patients).

A total of 169 patients (74%) received perioperative RT, of whom 149 (65%) had preoperative RT. One fourth of the total group did not receive irradiation because of various patient-related factors, including

previous RT for the pelvic region and lack of consent for RT. Short-course RT (sRT; 5 × 5 Gy) was the most common treatment approach, followed by immediate surgery (< 10 days from the first RT fraction). Ninety patients (39%) had stage III (ypTNM) disease at presentation. The characteristics of the patients who underwent surgery are presented in Table 2.

Table 2
Patient characteristics (n = 228)

Characteristic	N	%
Gender		
Female	105	46
Male	123	54
Age, years		
Median	61.3	
Range	33−90	
Distance from the anus, cm		
Median	8.9	
Range	3−15	
Stage (pTNM)		
I	48	21
II	85	37
III	91	40
pCR		
Yes	4	2
No	224	98
Perioperative treatment		
No	59	26
Preoperative RT	116	51
Preoperative CRT	33	14
Postoperative RT	20	9
Anastomotic leak requiring reoperation within 30 days of surgery		
Yes	16	7
No	212	93
Perioperative mortality 30 days after surgery		
Yes	3	1

Abbreviations: pCR, pathological complete response; others, see Table 1

Characteristic	N	%
No	225	91
Abbreviations: pCR, pathological complete response; others, see Table 1		

After treatment, all patients remained under surveillance according to the scheme described in Table 3. In the case of recurrence, patients were restaged in order to develop an appropriate treatment plan.

Table 3
Surveillance protocol after radical anterior resection for rectal cancer

Procedure	For years 1−2	For years 3−5
Physical examination, including the rectal	Every 3−4 months	Every 6 months
CEA	Every 3−4 months	Every 6 months
Chest X-ray	Every 12 months	
Abdominal ultrasound or CT of the abdominal cavity	Every 4 months	Every 6 months
CT or MRI of the pelvis	Up to 1−2 examinations during observation	
Gastrointestinal endoscopy (sigmoidoscopy, colonoscopy)	Every 12 months	
Abbreviations: CEA, carcinoembryonic antigen; others, see Table 1		

Statistical analysis

Statistical analysis was conducted by using the Statistica version 13.3 software package (TIBCO Software Inc., www.statistica.io). Qualitative and continuous variables are described with the usual descriptive statistics: numbers and percentages or medians with range (min-max).

The ratios of sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and receiver operating characteristic curve were calculated to compare the diagnostic value of colonoscopy versus imaging techniques. The significance level in the analyses was $P \leq 0.05$.

Results

The effectiveness of treatment

At 5-year follow-up, recurrences of any type were detected in 49 (21%) patients, 15 (6%) of whom had LR (Table 4). In the group of patients who had preoperative sRT, LR was detected in only 2 (2%) of them within 5 years of resection of rectal cancer. Distant metastases were confirmed in 41 (18%) patients, 8 of whom had distant metastases associated with LR. In total, LR affected 11 (6.5%) among patients treated with RT.

Table 4
Patient outcomes by radiotherapy type at 5-year follow-up

Treatment		n	LR	Distant metastases	Total relapses
Preoperative RT	5 x 5 Gy	116	2 (2%)	20 (17%)	21 (18%)
	CRT or RT 50.4 Gy	33	6 (18%)	10 (30%)	13 (39%)
	Total	**149**	**8 (5%)**	**30 (20%)**	**34 (23%)**
Postoperative RT		20	3 (15%)	3 (15%)	4 (20%)
No RT		59	4 (7%)	8 (14%)	12 (20%)
Total		**228**	**15 (7%)**	**41 (18%)**	**49 (21%)**
Abbreviations: LR, local recurrence; others, see Table 1					

LRs were most frequently found outside the intestinal lumen (n = 10, 4%): in the presacral region (n = 5), in the lateral zones of the pelvis (n = 4), and in the anterior region (n = 1). In this group of patients (n = 10), 4 (2%) had isolated LR. Among the 228 patients, 5 (2%) had LR in the anastomotic site, 4 of these LRs (1.7%) being isolated.

Detection of LR

In most cases, LR was not available for endoscopic examination (10 of 15; 67%). In these patients, the diagnosis of recurrence was made on the basis of imaging. After we analyzed the medical records, we found that endoscopic examination allowed for histopathological verification in 4 (of 5; 80%) patients with recurrence in the anastomosis. Only in 1 case was endoscopy the first examination to indicate the presence of LR; in the remaining 4 patients, endoscopy was performed after abnormal imaging results (imaging in these cases being the first indication of the presence of a recurrence). Time to diagnosis of recurrence from primary surgery did not differ between the intraluminal and non-intraluminal recurrence groups (30 months vs 29 months).

The use of imaging techniques and endoscopy in the analyzed material was of similar effectiveness in diagnosing LR, although the results of these methods were not completely consistent. The specificity of colonoscopy was satisfactory ($> 98\%$ in all groups); however, its sensitivity was much lower than that of imaging (46.7% for all recurrences and 80% for anastomotic recurrences).

The effectiveness of imaging modalities in detecting recurrent rectal cancer did not differ significantly between groups of patients who did or did not undergo RT. Our analysis showed that colonoscopy was a good method for diagnosing recurrent rectal cancer in the anastomosis (area under the receiver operating characteristic curve > 0.8); however, it did not provide advantages over other diagnostic methods for diagnosing LR in patients who did not receive RT ($P > 0.05$ for both types of recurrences; Table 5).

Table 5

Results of receiver operating characteristic analysis in determining the diagnostic power of colonoscopy versus imaging techniques

	All recurrences				Anastomotic recurrences			
	AUC	Sensitivity	Specificity	*P* value	AUC	Sensitivity	Specificity	*P* value
Whole group	0.7310	46.7%	99.5%	0.0066	0.8910	80.0%	98.2%	0.0002
PLR	0.7273	45.5%	100.0%	0.0228	0.9910	100.0%	98.2%	< 0.0001
NLR	0.7409	50.0%	98.2%	0.1383	0.8244	66.7%	98.2%	0.0525

Abbreviations: AUC, area under the receiver operating characteristic curve; NLR, negative likelihood ratio; PLR, positive likelihood ratio

Table 6

Endoscopic surveillance described in current recommendations after radical surgery of rectal cancer with total mesorectal excision (visualized by endoscopic ultrasound or magnetic resonance imaging with contrast)

	CS I	CS II-IV
ESMO Consensus Guidelines 2013	Colonoscopy must be carried out at year 1 and every 3−5 years thereafter, looking for metachronous adenomas and cancers	
ESMO Consensus Guidelines 2017	A completion colonoscopy within the first year if not done at the time of diagnostic workup (eg, if obstruction was present) History and colonoscopy with resection of colonic polyps every 5 years up to the age of 75 years	
PTO/PTChO 2015	Colonoscopy at year 1 and then every 5 years; rectosigmoidoscopy every 6 months for 2−5 years (in patients not undergoing radiotherapy or in the presence of T4 or N2 tumors)	
NCCN Consensus Guidelines 2020	Colonoscopy at the first year after surgery	Colonoscopy at year 1 after surgery; if no preoperative colonoscopy − in 3−6 months after surgery
	If advanced adenoma − repeat in 1 year; if no advanced adenoma − repeat in 3 years and then every 5 years	
	If no advanced adenoma − repeat in 3 years, then every 5 years	

Abbreviations: CS, clinical stage; ESMO, European Society for Medical Oncology; NCCN, National Comprehensive Care Network; PTO/PTChO, Polish Society of Oncology/Polish Society of Surgical Oncology

Discussion

Gastrointestinal endoscopy is used in the surveillance of patients after radical treatment of rectal cancer to identify and verify LR in order to increase the ultimate success rate. This method also enables clinicians to identify and remove metachronous tumors and precancerous lesions. Current guidelines recommend this examination as one of the foundations of surveillance. However, much of the evidence that forms the basis of these recommendations originates from outdated literature reported when patients were treated with various treatment regimens.

The vast majority of published studies on postoperative surveillance has included patients with 2 separate entities: colon cancer and rectal cancer [13–15]. Differences between these cancers include anatomical location (rectal cancer: retroperitoneal), diagnostic requirements (magnetic resonance imaging [MRI], transrectal ultrasound), and therapies used (RT), which in turn may affect the diagnostic and therapeutic processes of the LR. Recurrent tumors located up to 8 cm from the sphincters are usually available by digital rectal examination and, above all, they show earlier clinical symptoms (altered bowel habits, hematochezia, abdominal pain).

Currently, less than 10% of patients who undergo radical treatment experience LR [17–19], owing to the use of an appropriate surgical technique (TME), the radical nature of the procedures (R0, circumferential resection margins: negative), and the combined treatments based on the RT schedule delivering a biologically effective dose above 30 Gy [20, 21]. Several studies have shown that about half of LRs are isolated, with no distant metastatic lesions [22, 23].

The risk of LR is associated with the following factors (among others): more advanced disease stage (American Joint Committee on Cancer/TNM), more distal location of the tumor, and perioperative treatment used. Preoperative RT reduces LR by approximately 50%-70% and postoperative RT by approximately 30%-40% in all locations of the rectum [24, 25]. This effect may be enhanced by the use of concurrent computed tomography (CT) [26, 27]. Some studies reported a significant reduction in the risk of LR in anastomosis after anterior rectal resection after the use of preoperative 5 × 5 Gy sRT [25].

In patients with CRC, an estimated risk of the presence of synchronous neoplastic lesions is 2%-4% [28, 29]. Epidemiological data show that after radical treatment, patients with CRC have a 1.5- to 2-fold increased risk of developing metachronous lesions compared with that in a healthy population, as well as an increased risk (1%-2%) of developing a second primary CRC [30–32], especially in the first years after resection [29, 31]. The risk of developing metachronous adenoma after CRC resection can be estimated at less than 10% [33, 34], which is similar to that of developing adenomatous changes after polypectomy in the general population [35, 36].

Improvement of overall survival in patients under postoperative surveillance after resection was confirmed in studies in which carcinoembryonic antigen testing, imaging (such as CT or MRI), and clinical visits were regularly performed in addition to endoscopic examination [37]. Close monitoring of asymptomatic cancer patients allows for earlier detection of recurrence compared with a diagnosis based solely on the presence suspicious symptoms [38]. Nevertheless, the importance of extensive postoperative surveillance for

recurrence after rectal cancer resection remains controversial. More recent publications indicate that intensified surveillance after surgery does not improve treatment outcomes [39–41].

Endoscopic examination remains only part of a multidisciplinary approach. A few studies that have investigated the effects of intensified follow-up endoscopy have consistently showed that, despite more frequent detection of asymptomatic recurrences and thus more frequent qualification for radical treatment, there was no improvement in overall survival in groups subjected to frequent endoscopic examinations [42].

Earlier guidelines for post-rectal cancer surveillance included frequent endoscopic checkups of at least once every 6–12 months [43, 44]. The currently recommended schemas, based on current publications on surveillance after radical treatment of rectal cancer, advocate examinations at least 2–3 times over a 5-year follow-up period [45–47], that is, much less often than previously recommended (Table 6).

Our study has some limitations because of its single-center and retrospective nature. However, the fact that patients were analyzed in one center contributes to the standardization of therapeutic and diagnostic procedures. The percentage of LRs in our analysis, including those located directly in the anastomosis, remained low (6.5%, including 5 patients with anastomosis) and is similar to that reported by other studies [48–50]. The low recurrence rates are not conducive to reliable statistical analyses, although endoscopic examination is known to have a low sensitivity in detecting recurrences. Nonetheless, high specificity and the ability to sample biological material make endoscopy the preferred method for confirming the presence of recurrent lesions and verifying them histopathologically. Diagnosis of relapse is most often based on physical or imaging examinations (CT, MRI). Factors that increase the value of regular imaging tests as an alternative to endoscopy are the possibility of a simultaneous diagnosis of a lesion located outside the intestinal lumen and distant (systemic) lesions, as well as the diagnosis of possible consequences of radical treatment: postoperative fistulas, radiation-induced changes, and pelvic insufficiency fractures [51]. In addition, the invasiveness of endoscopic examinations should be taken into account, as they often result in poor patient tolerance associated with an increased risk of serious complications (including gastrointestinal perforation) [52]. Although small doses of radiation from X-rays that patients receive during imaging examinations (CT) have an impact on the body, the levels are too low to contraindicate even frequent examinations [41].

Our results do not confirm the advantage of endoscopic examinations in detecting recurrences in patients who are not receiving RT. This finding may have resulted from the small number of LRs detected (although a low rate of LR is the current standard). Given the results of other studies, however, a higher percentage of LRs and those located in the anastomosis can be suspected in this group of patients [25]. Although on the one hand, the use of RT reduces the number of local recurrences, on the other hand, it is recommended in more advanced tumors: in patients who are in general characterized as having a higher risk of LR, frequently located outside the bowel lumen. Thus, it remains debatable as to whether diagnostic indications for endoscopy in postoperative surveillance after rectal cancer treatment depend on the use of RT.

Conclusions

Endoscopy of the gastrointestinal tract in patients under multidisciplinary surveillance after radical treatment for rectal cancer remains a useful diagnostic test that allows for histopathological confirmation of LR. However, because most recurrences are located outside the intestinal lumen and because of the higher sensitivity of imaging examinations such as CT or MRI, the role of endoscopy seems to be limited. Both our own results and the updated recommendations of oncological associations confirm this hypothesis, also taking into account the risk of the presence of metachronous lesions, which are better diagnosed with modern imaging techniques. We conclude that imaging studies in the follow-up of patients with rectal cancer should play a leading role, whereas endoscopy – although necessary – should be regarded as an additional and supplementary modality limited mainly to the intraluminal inspection and verification of imaging-diagnosed lesions.

Abbreviations

CRC
colorectal cancer
CT
computed tomography
LR
local recurrence
MRI
magnetic resonance imaging
PES
postoperative endoscopic surveillance
RT
radiotherapy
sRT
short-course radiotherapy
TME
total mesorectal excision

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

Funding

Authors' contributions

MJ conceived the study. MJ, WMW, DB, and MLJ contributed to the design of the research. MJ, KT, DW, and DB were involved in data collection. MJ, WMW, MLJ, and DB analyzed the data. MJ and WZ coordinated the project. All authors read and approved the final manuscript.

Acknowledgements

References

1. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683-691.

2. Noone AM, Howlader N, Krapcho M, et al, eds. *SEER Cancer Statistics Review, 1975-2015*. Bethesda, MD: National Cancer Institute. Based on: November 2017 SEER data submission, posted to the SEER web site, April 2018. https://seer.cancer.gov/csr/1975_2015. (accessed Dec 10, 2020)

3. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005;55(2):74-108.

4. Krajowy rejestr nowotworow. http://onkologia.org.pl/raporty/#tabela_nowotwor. (accessed Dec 10, 2020)

5. Silberfein EJ, Kattepogu KM, Hu CY, Skibber JM, Rodriguez-Bigas MA, Feig B, et al. Long-term survival and recurrence outcomes following surgery for distal rectal cancer. Ann Surg Oncol. 2010;17(11):2863-9. 6. Joseph DA, Johnson CJ, White A, Wu M, Coleman MP. Rectal cancer survival in the United States by race and stage, 2001 to 2009: findings from the CONCORD-2 study. Cancer. 2017;123 Suppl 24(Suppl 24):5037-5058.

6. Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet. 1986;1(8496):1479-82.

7. Quirke P, Durdey P, Dixon MF, Williams NS.. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection: histopathological study of lateral tumour spread and surgical excision. Lancet. 1986;2(8514):996-9.

8. Swedish Rectal Cancer Trial; Cedermark B, Dahlberg M, Glimelius B, Påhlman L, Rutqvist LE, Wilking N. Improved survival with preoperative radiotherapy in resectable rectal cancer. N Engl J Med. 1997;336(14):980-7.

9. Akgun E, Ozkok S, Tekin M, Yoldas T, Caliskan C, Kose T, et al. The effects of chemoradiotherapy on recurrence and survival in locally advanced rectal cancers with curative total mesorectal excision: a prospective, nonrandomized study. World J Surg Oncol. 2017 Nov 22;15(1):205. 11. Westberg K, Palmer G, Hjern F, Johansson H, Holm T, Martling A. Management and prognosis of locally recurrent rectal cancer: a national population-based study. Eur J Surg Oncol. 2018;44(1):100-107.

10. Rodriguez-Moranta F, Salo J, Arcusa A, Boadas J, Piñol V, Bessa X, et al. Postoperative surveillance in patients with colorectal cancer who have undergone curative resection: a prospective, multicenter, randomized, controlled trial. J Clin Oncol. 2006;24(3):386-93.

11. Pfister DG, Benson AB III, Somerfield MR. Surveillance strategies after curative treatment of colorectal cancer. N Engl J Med. 2004;350(23):2375-82.

12. Jeffery M, Hickey BE, Hider PN, See AM. Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database Syst Rev. 2016; 11: CD002200 [update in Cochrane Database Syst Rev. 2019;11(11):CD002200.

13. Hassan C, Wysocki PT, Fuccio L, Seufferlein T, Dinis-Ribeiro M, Brandão C, et al. Endoscopic surveillance after surgical or endoscopic resection for colorectal cancer: European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Digestive Oncology (ESDO) Guideline. Endoscopy. 2019;51(3):266-277.

14. Greene FL, Page DL, Fleming ID, et al., eds. AJCC Cancer Staging Manual. 6th ed. Berlin, Germany: Springer-Verlag; 2002.

15. Yun JA, Huh JW, Kim HC, Park YA, Cho YB, Yun SH, et al. Local recurrence after curative resection for rectal carcinoma: the role of surgical resection. Medicine (Baltimore). 2016;95(27):e3942.

16. Van Gijn W, Marijnej CA, Nagtegaal ID, Kranenbarg EM, Putter H, Wiggers T, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12 year follow-up of the multicentre, randomized controlled TME trial. Lancet Oncol. 2011;12(6):575-82.

17. Zhao GH, Deng L, Ye DM, Wang WH, Yan Y, Yu T. Efficacy and safety of wait and see strategy versus radical surgery and local excision for rectal cancer with cCR response after neoadjuvant chemoradiotherapy: a meta-analysis. *World J Surg Oncol*. 2020;18(1):232. Published 2020 Aug 31. doi:10.1186/s12957-020-02003-6

18. Jin F, Luo H, Zhou J, Wu Y, Sun H, Liu H, et al. Dose-time fractionation schedules of preoperative radiotherapy and timing to surgery for rectal cancer. Ther Adv Med Oncol. 2020;12:1758835920907537.

19. 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.

20. Palmer G, Martling A, Cedermark B, Holm T. A population-based study on the management and outcome in patients with locally recurrent rectal cancer. Ann Surg Oncol. 2007;14(2):447-54.

21. Moore HG, Shoup M, Riedel E, Minsky BD, Alektiar KM, Ercolani M, et al. Colorectal cancer pelvic recurrences: determinants of resectability. Dis Colon Rectum. 2004; 47(10):1599-606.

22. Glimelius B, Groenberg H, Jarhult J, Wallgren A, Cavallin-Ståhl E.. A systematic overview of radiation therapy effects in rectal cancer. Acta Oncol. 2003;42(5-6):476-92.

23. Kusters M, Marijnen CA, van de Velde CJ, Rutten HJ, Lahaye MJ, Kim JH, et al. Patterns of local recurrence in rectal cancer: a study of the Dutch TME trial. Eur J Surg Oncol. 2010;36(5):470-6.

24. Braendengen M, Tveit KM, Berglund A, Birkemeyer E, Frykholm G, Påhlman L, et al. Randomized phase III study comparing preoperative radiotherapy with chemoradiotherapy in nonresectable rectal cancer. J Clin Oncol. 2008;26(22):3687-94.

25. Ciseł B, Pietrzak L, Michalski W, Wyrwicz L, Rutkowski A, Kosakowska E, et al.; Polish Colorectal Study Group. Long-course preoperative chemoradiation versus 5 × 5 Gy and consolidation chemotherapy for clinical T4 and fixed clinical T3 rectal cancer: long-term results of the randomized Polish II study. Ann Oncol. 2019;30(8):1298-1303.

26. Pinol V, Andreu M, Castells A, Payá A, Bessa X, Jover R. Synchronous colorectal neoplasms in patients with colorectal cancer: predisposing individual and familial factors. Dis Colon Rectum. 2004;47(7):1192-200.

27. Mulder SA, Kranse R, Damhuis RA, de Wilt JH, Ouwendijk RJ, Kuipers EJ, et al. Prevalence and prognosis of synchronous colorectal cancer: a Dutch population-based study. Cancer Epidemiol. 2011;35(5):442-7.

28. Green RJ, Metlay JP, Propert K, Catalano PJ, Macdonald JS, Mayer RJ, et al. Surveillance for second primary colorectal cancer after adjuvant chemotherapy: an analysis of Intergroup 0089. Ann Intern Med. 2002;136(4):261-9.

29. le Clercq CM, Winkens B, Bakker CM, Keulen ET, Beets GL, Masclee AA, et al. Metachronous colorectal cancers result from missed lesions and non-compliance with surveillance. Gastrointest Endosc. 2015;82(2):325-333.e2.

30. Liu L, Lemmens VE, De Hingh IH, de Vries E, Roukema JA, van Leerdam ME, et al. Second primary cancers in subsites of colon and rectum in patients with previous colorectal cancer. Dis Colon Rectum. 2013;56(2):158-68.

31. Lee SY, Kim BC, Han KS, Hong CW, Sohn DK, Park SC, et al. Incidence and risk factors of metachronous colorectal neoplasm after curative resection of colorectal cancer in Korean patients. J Dig Dis. 2014; 15(7):367-76.

32. Cubiella J, Gomez R, Sanchez E, Díez MS, Vega M.. Endoscopic follow-up of patients after curative surgery for colorectal cancer: results of a medical assistance protocol. Rev Esp Enferm Dig. 2003;95(4):278-81, 273-7. 33. Matsuda T, Fujii T, Sano Y, Kudo SE, Oda Y, Igarashi M, et al. Five-year incidence of advanced neoplasia after initial colonoscopy in Japan: a multicenter retrospective cohort study. Jpn J Clin Oncol. 2009; 39(7):435-42.

33. Yoshida N, Naito Y, Siah KT, Murakami T, Ogiso K, Hirose R, et al. High incidence of metachronous advanced adenoma and cancer after endoscopic resection of colon polyps ≥20 mm in size. Dig

Endosc. 2016; 28(2):194-202.

34. Chau I, Allen MJ, Cunningham D, Norman AR, Brown G, Ford HE, et al. The value of routine serum carcinoembryonic antigen measurement and computed tomography in the surveillance of patients after adjuvant chemotherapy for colorectal cancer. J Clin Oncol. 2004;22(8):1420-9.

35. Räsänen M, Carpelan-Holmström M, Mustonen H, Renkonen-Sinisalo L, Lepistö A.. Pattern of rectal cancer recurrence after curative surgery. Int J Colorectal Dis. 2015;30(6):775-85.

36. Snyder RA, Hu C, Cuddy A, Francescatti AB, Schumacher JR, Van Loon K, et al. Association between intensity of posttreatment surveillance testing and detection of recurrence in patients with colorectal cancer. JAMA. 2018;319(20):2104-2115.

37. Wille-Jørgensen P, Syk I, Smedh K, Laurberg S, Nielsen DT, Petersen SH et al. Effect of more vs less frequent follow-up testing on overall and colorectal cancer-specific mortality in patients with stage II or III colorectal cancer: the COLOFOL randomized clinical trial. JAMA. 2018;319(20):2095-2103.

38. Liu SL, Cheung WY. Role of surveillance imaging and endoscopy in colorectal cancer follow-up: quality over quantity? World J Gastroenterol. 2019;25(1):59-68.

39. Pita-Fernandez S, Alhayek-Ai M, Gonzalez-Martin C, López-Calviño B, Seoane-Pillado T, Pértega-Díaz S. Intensive follow-up strategies improve outcomes in nonmetastatic colorectal cancer patients after curative surgery: a systematic review and metaanalysis. Ann Oncol. 2015;26(4):644-656.

40. Rex DK, Kahi CJ, Levin B, Smith RA, Bond JH, Brooks D et al. Guidelines for colonoscopy surveillance after cancer resection: a consensus update by the American Cancer Society and US Multi-Society Task Force on Colorectal Cancer. CA Cancer J Clin. 2006;56(3):160-7

41. Jassem J, Duchnowska R, Kawecki A, Krajewski R, Krzakowski M, Mądry R et al. Post-treatment surveillance in most common solid malignancies in adults. Nowotwory Journal of Oncology. 2014;64(5):415-435.

42. Glynne-Jones R, Wyrwicz L, Tiret E, Brown G, Rödel C, Cervantes A 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.

43. Labianca R, Nordlinger B, Beretta GD, Mosconi S, Mandalà M, Cervantes A et al.; ESMO Guidelines Working Group. Early colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013; 24(suppl 6): vi64-72.

44. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Rectal cancer. Version 6.2020, June 25, 2020. http://www.nccn.org/professionals/physician_gls/PDF/rectal.pdf. (accessed Dec 10, 2020)

45. Rödel C, Liersch T, Becker H, Fietkau R, Hohenberger W, Hothorn T et al.; German Rectal Cancer Study Group. Preoperative chemoradiotherapy and postoperative chemotherapy with fluorouracil and oxaliplatin versus fluorouracil alone in locally advanced rectal cancer: initial results of the German CAO/ARO/AIO-04 randomised phase 3 trial. Lancet Oncol. 2012;13(7):679-87.

46. Erlandsson J, Holm T, Pettersson D, Berglund Å, Cedermark B, Radu C 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.

47. Jankowski M, Bała D, Las-Jankowska M, Wysocki WM, Nowikiewicz T, Zegarski W. Overall treatment outcome - analysis of long-term results of rectal cancer treatment on the basis of a new parameter. Arch Med Sci. 2020;16(4):825-833.

48. Jørgensen JB, Bondeven P, Iversen LH, Laurberg S, Pedersen BG. Pelvic insufficiency fractures frequently occur following preoperative chemo-radiotherapy for rectal cancer - a nationwide MRI study. Colorectal Dis. 2018;20(10):873-880.

49. ASGE Standards of Practice Committee, Fisher DA, Maple JT, Ben-Menachem T, Cash BD, Decker GA, Early DS et al. Complications of colonoscopy. Gastrointest Endosc. 2011;74(4):745-52.

Figures

Figure 1

Anatomical localization of a local recurrence of rectal cancer, showing patterns of rectal can-cer recurrence: (A) central (anastomotic site, perineal region, rest of mesorectum tissue), (B) lateral pelvic side

wall, (C) anterior (genitourinary region, pubic bone), (D) posterior/presacral zone.