L. KOKAINE [1,2,*], **M. RADZIŅA** [3], **M. LIEPA** [3], **A. GERIŅA-BĒRZIŅA** [4],
E. SĪVIŅA [4,5], **J. NIKOLAJEVA** [4], **A. GARDOVSKIS** [1,2], **J. GARDOVSKIS** [1,2], **E. MIKLAŠEVIČS** [5]

[1] Pauls Stradiņš Clinical University Hospital, Department of Surgery, Riga, Latvia
[2] Riga Stradiņš University, Department of Surgery, Riga, Latvia
[3] Pauls Stradiņš Clinical University Hospital, Institute of Radiology, Riga, Latvia
[4] Pauls Stradiņš Clinical University Hospital, Oncology Clinic, Riga, Latvia
[5] Riga Stradiņš University, Institute of Oncology, Riga, Latvia

* Correspondence: Email: linda.kokaine@rsu.lv

"WATCH AND WAIT" STRATEGY IN RECTAL CANCER PATIENTS WITH A COMPLETE CLINICAL RESPONSE AFTER NEOADJUVANT CHEMORADIATION THERAPY: A SINGLE-CENTER EXPERIENCE

Background. The non-operative management of rectal adenocarcinoma (RA) after neoadjuvant chemoradiation therapy (nCRT) has gained increasing attention. The "Watch and Wait" ("W&W") strategy allows one to avoid surgery-related reduction in the quality of life due to permanent pelvic organ dysfunction or irreversible stoma. Still, the oncological safety of this strategy is under evaluation. **Aim**. To share a single-center experience of the "W&W" strategy. **Materials and Methods**. The retrospective analysis of 125 patients who received nCRT in 2016—2021 was performed. Patients who met the European Society for Medical Oncology (ESMO, 2017) criteria of clinical complete response (cCR) and received non-operative management were analyzed. **Results**. Ten patients (8%) were re-staged after nCRT as cCR and followed the "W&W" strategy. Patients' characteristics: 7 female, 3 male; mean age 67.3 years. Tumor characteristics: pre-treatment N+ was present in 7 cases; G1 adenocarcinoma in a majority of cases; mean tumor distance from the anal verge — 5.85 cm; mean tumor circumference — 71%; mean tumor length — 3.87 cm. The mean follow-up time was 30 months. Local regrowth or/and distant metastases developed in 3 cases. The 2-year disease-free survival was 70%. **Conclusions**. Most of the patients following the "W&W" strategy have benefited. However, to reduce the number of relapses, it is necessary to perform a more careful selection of patients.

Keywords: "Watch and Wait" strategy, non-operative management, rectal cancer, clinical complete response, neoadjuvant therapy.

The incidence of rectal cancer in the European Union is 125,000 per year, i.e., 35% of the total colorectal cancer incidence, reflecting 15—25 cases/100 000 population per year, and is predicted to increase further in both genders [1]. According to the Latvian Cancer Registry data, the incidence of colorectal cancer in 2020 in Latvia was 34.6/100,000 (in 2020, 1.9 million inhabitants we-

L. Kokaine, M. Radziņa, M. Liepa, A. Geriņa-Bērziņa, E. Sīviņa, J. Nikolajeva, A. Gardovskis, J. Gardovskis, E. Miklaševičs

Fig. 1. Endoscopic appearance of cCR after nCRT — flattening of the mucosa in the previous tumor area (Case No. 2)

re registered in Latvia). In 2020, 1745 new cases of colorectal cancer were detected, 780 (44.7%) of them – rectal cancer. It is the third most common type of cancer in men and the second most common in women in Latvia.

The standard treatment of the locally advanced non-metastatic rectal adenocarcinoma (RA) is neoadjuvant chemoradiation therapy (nCRT) followed by the total mesorectal excision (TME), which provides satisfying oncological results. nCRT not only ensures a reduction of tumor volume and spread, thereby improving the radicality of surgical treatment and the future prognosis, but it has also been observed that in 10—40% of cases, a clinical complete response can be achieved [1, 2]. In the current rectal cancer treatment guidelines, the surgical treatment after nCRT is recommended as the golden standard. However, TME is a radical surgical procedure with a significant risk of perioperative morbidities, including bowel, sexual, and urinary dysfunction, and often results in the permanent stoma formation [3—5].

In 2004, the first long-term outcomes of a cohort of patients who achieved cCR after nCRT and were managed with a non-operative strategy were published that presented the results of a similar oncological safety if compared with the operative treatment group [6]. Since then, the "W&W" tactic has gained increasing attention. It provides an opportunity to apply organ-sparing strategies to a selected group of patients, thereby improving the quality of life.

In our center, the "W&W" tactic was initiated in 2017. Our study aimed to summarize and share the single-center experience.

Materials and Methods

Between 2016 and 2021, a total of 125 patients with RA received nCRT and were included in a retrospective study. The inclusion criteria were: RA localized up to 15 cm from the anal verge, cTanyN0M0 or cTanyN+M0 (according to the TNM Classification of Malignant Tumors, 8th Edition), and patients who received and finished neoadjuvant radiation and chemotherapy or radiotherapy alone. Patients with uncompleted nCRT or missing follow-up after nCRT were excluded. A long-course preoperative radiation therapy consisted of 1.8 Gy delivered in daily doses over a period of 28—29 days. The total radiation dose delivered by this regimen was 50.4—52.2 Gy. A short-course radiotherapy consisted of 5 Gy delivered in 5 days (overall 25 Gy). Starting from the first week of radiotherapy, the concomitant chemotherapy was given, mainly 5-fluorouracil-based (5-FU) agents or another depending on the indications. Patients were evaluated 6—12 weeks after the completion of nCRT by a multidisciplinary team (oncologist, surgeon, radiologist), using digital rectal examination (DRE), proctoscopy or colonoscopy, and pelvic magnetic resonance imaging (MRI) by the magnetic resonance tumor regression grade (mr-TRG) criteria, and the levels of CEA and CA 19-9 were evaluated.

Patients were re-staged as cCR if the findings met the ESMO criteria of cCR:

Minimal criteria

1. The absence of any irregularities or a palpable tumor on DRE.

2. No visible lesion on endoscopy except for a flat scar, telangiectasia, or whitening of the mucosa.

Additional criteria

3. The absence of any residual tumor in the primary site and draining lymph nodes on the imaging with MRI or the endorectal ultrasound (ERUS).

4. Negative biopsies from the scar.

5. An initially risen CEA level that returns to normal.

No biopsy of the tumor area was carried out if the DRE, proctoscopy, and radiological findings did not reveal signs of a tumor (Figs. 1, 2). It was done only when a near-complete response was suspected.

The "W&W" protocol was applied to selected patients: follow-up every 3 months for 2 years and 6 months for 3 years subsequently.

Statistical analysis. Local hospital databases were used for data collection and selection. The Kaplan — Meier method was used to estimate survival probabilities and their pointwise 95% confidence intervals. Statistical analysis was performed with EasyMedStat (version 3.21.5).

Results

Of 125 patients who received nCRT, 106 patients received radiation and chemotherapy, and 19 received radiation therapy alone (3 of them — the short course radiation therapy).

cCR was achieved in 10 patients (8%), and in these cases, the following "W&W" strategy was applied. The mean age at the moment of RA diagnosis was 67.3 (min 45, max 82); the gender distribution was 7 females and 3 males. Three patients had a concomitant cancer of another location. One patient had adenocarcinoma of the ascending colon detected at the same time as RA (radical surgery was performed). One patient had breast cancer and basal cell carcinoma detected at the same time as RA (sectoral excision of the breast cancer and the excision of the basalioma was performed followed by adjuvant radiation therapy and hormone therapy of the breast cancer). In one more patient, RA was detected in the course of hormone therapy of breast can-
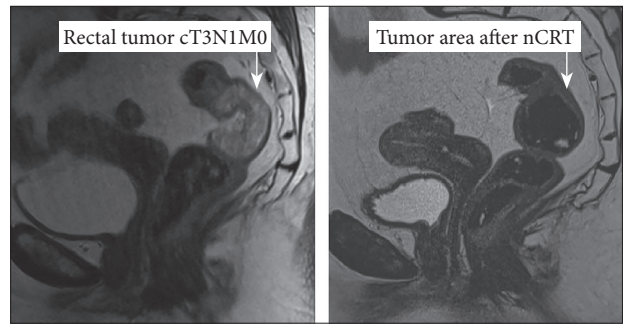
MRI scan before nCRT — rectal adenocarcinoma cT3N1M0

MRI scan 6 weeks after nCRT — mr-TRG1

Fig. 2. Pelvic MRI before and 6 weeks after nCRT with radiological remission of the tumor (Case No. 2)

cer that resulted in the complete clinical response. RA stage at the time of diagnosis: stage II in 2 patients, stage III in 8 patients. Lymph node positivity (N1 in all cases) was detected in 7 patients. Tumor characteristics are summarized in Table 1. Tumor morphology in the biopsy material before nCRT: G1 adenocarcinoma (AC) in 6 patients, G2 AC in 3 patients, and unknown in 1 patient. According to the endoscopy data, the infiltrative nature of the tumor was most often found (9 cases), and exophytic tumor was in 1 case. The mean distance of the tumor from the anal verge by MRI data was 5.85 cm (min 2.5 cm, max 10 cm). The mean size of the tumor was 3.87 cm (min 1.5 cm, max 5.1 cm). The mean tumor circumference was 71% (min 25%, max 100%). The minimal size of the regional lymph nodes was 0.3 cm and the maximal size was 0.7 cm.

Table 1. **Tumor characteristics**

Case	cTNM	TD	Endoscopic characteristics	DAV (cm)	TL (cm)	TC (%)	RLN (cm)
1	cT3N0M0	G2	Infiltrative	2.5	4.7	100	0.30
2	cT3N1M0	G1	Infiltrative	10	4.5	92	0.40
3	cT2N1M0	G1	Exophytic, mobile	10	1.5	25	0.70
4	cT2N1M0	Unknown	Infiltrative	9.4	2.3	44	0.36
5	cT3N0M0	G1	Infiltrative	2.7	2.5	72	None
6	cT3N1M0	G2	Infiltrative	2.5	4.5	100	0.55
7	cT2N1M0	G1	Infiltrative	5.5	5.1	100	0.33
8	cT4N0M0	G2	Infiltrative	3.2	5	69	0.51
9	cT3N1M0	G1	Infiltrative	6.3	4.6	53	0.56
10	cT2N1M0	G1	Infiltrative	6.4	4	50	0.50

Notes: TD — tumor differentiation, DAV — distance from the anal verge, TL — tumor length, TC — tumor circumference, RLN — regional lymph nodes.
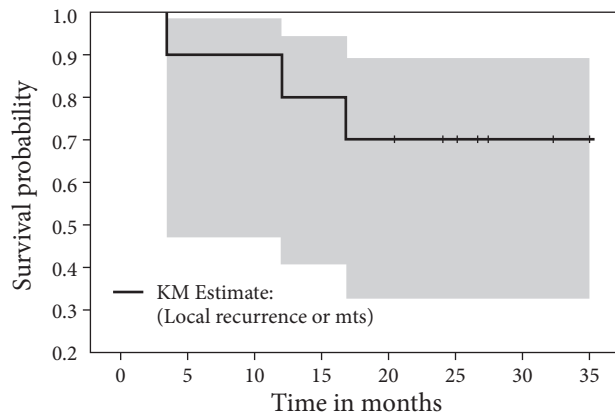
Fig. 3. DFS of clinical complete responders following the "W&W" strategy

The levels of CEA and CA 19-9 were evaluated before and after nCRT. Only one patient (case No.8) had elevated CA 19-9 (980 U/mL) while having a normal CEA level (2.65 ng/L). In this patient, no metastases were detected in the CT scan performed before nCRT, however, in the radiological examinations after nCRT, the pelvic MRI revealed complete cCR, but in the CT scan, liver metastases were detected (CEA remained elevated after nCRT — 419.59 U/mL). The treatment characteristics of the clinical complete responders are summarized in Table 2. Transanal biopsy after the completion of nCRT was performed in one patient.

The mean follow-up time was 30 months (min 20, max 60). cCR was detected in the patients who recei-

ved a long-course neoadjuvant radiation therapy with concomitant chemotherapy, except for one case when the patient received only radiation therapy.

At 12 months, the disease-free survival (DFS) was 80.0% (95% CI:40.9—94.6) and at 24 months, the DFS was 70.0% (95% CI: 32.9—89.2) (Fig. 3).

The results of the "W&W" follow-up are summarized in Table 3. One patient (Case No. 6) developed a local regrowth, but treatment was not initiated because the patient died of an unrelated cause. One patient developed distant metastases (Case No. 8) — a solitary metastasis in the liver 3 months after the completion of nCRT (it was treated with radiofrequency ablation) and 1.5 years later — metastases in the lungs (treated with ChT). One patient developed both local regrowth and distant metastases, and the local regrowth was detected twice (Case No. 1). After the first local regrowth, organ preservation surgery was performed. When a repeated local relapse developed, simultaneously with distant metastases in the liver, the palliative ChT was applied.

Discussion

The incidence of cCR in our study is 8%, which is a relatively low rate. However, it should be considered that the variability of this indicator is related to the selection criteria of the study group

Table 2. **Treatment characteristics of the clinical complete responders**

| Case | cTNM | RT | | ChT | Post-nCRT evaluation (weeks) | mr-TRG |
		RA (Gy)	PLN (Gy)			
1	cT3N0M0	50.4	45	5-FU inf	12	2
2	cT3N1M0	50.4	46.8	5-FU inf	6	2
3	cT2N1M0	50.4	46.8	•	8	1
4	cT2N1M0	50.4	46.8	5-FU inf	8	2
5	cT3N0M0	52.2	45	5-FU inf oxaliplatin (after the end of RT)	8	2
6	cT3N1M0	52.2	46.8	5-FU inf	9	2
7	cT2N1M0	50.4	45	Ribociclib, anastrozole (due to concomitant breast cancer)	9	1
8	cT4N0M0	50.4	45	5-FU inf	8	2
9	cT3N1M0	52.2	45	Tegafur	9	2
10	cT2N1M0	50.4	45	5-FU inf	10	2

Notes: RT — radiation therapy, ChT — chemotherapy, RA — rectal adenocarcinoma, PLN — pelvic lymph nodes, inf — infusional.

since our study did not include patients who continued their treatment or observation in another hospital, which would limit the collection of follow-up data. In addition, the complete pathological response was found in several patients after surgical treatment, which potentially could be classified in the "W&W" group. Also, when performing a post-therapy evaluation, there is a certain subjectivity, which also affects the cCR rate. The currently existing clinical and radiological evaluation methods in the case of cCR are not absolute, so in situations where there are doubts, a decision is made in favor of the radical surgical treatment.

Although it is known that a potentially better response to nCRT is expected in patients with a lower tumor stage (advanced T stage or lymph node positivity reduces the probability of cCR), however, in our study group, most patients had stage III and lymph node positivity before nCRT [7]. Similar characteristics of groups can be found in other studies, which suggests that the pre-treatment tumor stage will not always be the determining factor for the post-therapy treatment outcome [8, 9].

Apart from the degree of tumor invasion, there are several other tumor-characterizing clinical and morphological parameters that predict a possible worse response to nCRT, such as tumor size ≥ 3 cm, volume, tumor circumference > 60%, higher localization of the tumor above the anal verge, macroscopic ulceration, a lower degree of tumor differentiation, and a mucinous component [10—15].

In our study, it was observed that in two patients the tumor was localized in the proximal part of the rectum, in the other two in the middle part, and in the remaining 6 cases in the distal part. Patients with rectal cancer of any location are considered potential "W&W" candidates if cCR is achieved, however, patients with lower tumors can benefit the most from this situation, considering that distal tumors require a low anastomosis or abdominoperineal resection, which significantly affects the quality of life. Lower localized tumors not only have a higher chance of achieving a cCR, but if it occurs, the distal rectal segment is much easier to control during further active surveillance within "W&W" [7].

In our patients, the largest size of the tumor did not exceed 5.1 cm and in 7 cases out of 10 its size was ≥3 cm. The mean tumor circumference was 71%, and in 6 cases, it was >60%.

As seen, a diversity of clinical parameters can be observed in our study group, but it should be considered that the group consists of a small number of patients, therefore it is not possible to talk about statistically reliable tendencies. However, regarding the tumor differentiation grade, most patients were found to have well-differentiated AC and no patients were found to have poorly differentiated AC confirming the relationship between the lower tumor differentiation and the likelihood of achieving cCR.

CEA and CA 19-9 were evaluated in all patients before and after nCRT. In 9 of 10 cases, pre-treat-

Table 3. **The results of "W&W" follow-up**

Case	End of nCRT	LR	Mo. after nCRT	MTS	Mo. after nCRT	A/D	Follow-up (Mo. after nCRT)
1	12/2017	12/2018; 10/2020	12; 34	10/2020 (liver)	34	A	60
2	01/2020	No	—	No	—	A	36
3	09/2020	"	—	"	—	A	27
4	04/2020	"	—	"	—	A	32
5	10/2020	"	—	"	—	A	26
6	07/2020	12/2021	17	"	—	D	29
7	11/2020	No	—	"	—	A	25
8	10/2020	"	—	01/2021 (liver); 07/2022 (lungs)	3; 21	A	26
9	12/2020	"	—	No	—	A	24
10	04/2021	"	—	"	—	A	20

Notes: LR — local regrowth, Mo — months, MTS — metastases, A/D — alive /dead.

ment CEA and CA 19-9 were not elevated, which is one of the prognostic indicators of a positive response to nCRT and indicates a higher probability of achieving a cCR [2, 16].

In our hospital, all patients received standard nCRT, and there were no special treatment modalities that could affect the possibility of cCR. Although, several studies have investigated the usefulness of additional chemotherapy agents, e.g., oxaliplatin, EGFR and VEGFR inhibitors, in combination with fluoropyrimidines to improve the tumor response to nCRT [17—19].

In our study, post-treatment evaluation was performed 6—12 weeks after the completion of nCRT. The recommended interval between completion of nCRT to post-treatment evaluation and surgery is 6—8 weeks: it is a timeframe that promotes tissue response to radiation, provides recovery, and prevents the development of radiation-associated tissue fibrosis [2]. However, in practice, this recommended time interval may vary depending on recovery from the treatment, patient issues, and the availability of radiological examinations.

The tumor response to nCRT is time-dependent. Sometimes it takes months to reach a maximal regression. The challenge is to find an optimal timepoint when the tumor has the greatest regression, thereby increasing the patient's suitability for the "W&W" tactics, and the results of surgical treatment are not compromised, when surgery is unavoidable. Several studies have concluded that it is possible to achieve a higher rate of the complete pathological response when delaying surgery after nCRT [20].

In our study, the average follow-up time of the patients was 2.5 years (30 months). Over the first two years, patients undergoing non-operative management have the highest risk of local regrowth and distant metastases, therefore during this period, the most intensive follow-up plan is necessary. The risk of local regrowth in the published data is within 15%—30%, and the risk of distant metastases is within 4%—14% [21, 22]. This general trend is also observed in our group of patients.

Considering the existing risk of local relapse and distant metastases, the "W&W" strategy is still considered a strategy that can only be used in highly selective groups. However, it should be noted that even in such a case, there is some variability between the study centers that set dif-ferences in the results of the "W&W" strategy. The "W&W" strategy is attractive, both to clinicians and patients, considering that the individualized treatment approach is the current trend.

Undoubtedly, the "W&W" strategy has benefited a large proportion of patients with cCR, thus it is a valuable model of patient management that significantly improves the patient's quality of life. However, the results so far show that we do not fully understand which patients are the ones who will really benefit from the "W&W" strategy and which are the ones who are already destined to experience relapse.

Careful selection of patients for the application of non-operative tactics, which includes specific selection criteria, could improve the oncological results of the "W&W" strategy. A clear definition of predictive factors of tumor response or the creation of risk scales that include positive and negative prognostic factors would provide an opportunity to improve patient selection for the "W&W" strategy.

Several studies have attempted to find clinically useful parameters based on the molecular biology features of rectal cancer undergoing nCRT to predict a potential response to treatment. Unfortunately, in none of them, a parameter with clinical value, which would be applicable in daily practice, has been found [23].

It should also be considered that currently, there are no absolute radiological criteria for diagnosing cCR, as post-therapy changes are often difficult to differentiate from residual tumor remnants. If this "gray zone" remains in the post-therapy diagnostics, in case of doubt, a decision will always be made in favor of the oncologically safest option, namely, surgical treatment.

More careful analysis of relapse cases might give additional information about potential risk factors of regrowth. Unfortunately, such research in isolated centers is hampered by the small number of observed patients with cCR and the even smaller number of patients who experience relapse after diagnosis of cCR.

Most published studies are retrospective and start with a cohort of complete responders and not with a cohort of patients who start nCRT. Furthermore, the analyzed oncological results are often affected by the heterogeneity of the studied population — different patient age categories, comorbidities and

drug therapy, tumor stages, applied treatment regimens, post-therapy evaluation intervals, as well as different "W&W" monitoring protocols.

Nevertheless, the "W&W" strategy as an alternative to surgical treatment in the case of cCR, with the aim to avoid unnecessary surgery and preserve the rectum, is increasingly accepted, based on studies conducted in specialized cancer centers, therefore it should be part of the treatment discussion.

The "W&W" strategy is suitable for patients who are willing to take advantage of organ-sparing tactics, are well informed about the limitations of this strategy, are motivated to undergo strict surveillance, have good access to health care services, and are able to accept the uncertainty about the course of their illness.

The current study was limited by the small number of patients, single-center experience, and differences in patient characteristics and treatment strategies. Despite these limitations, this is the first study in Latvia that summarizes the results of the "W&W" strategy. Further larger prospective studies are needed.

Acknowledgements

Gratitude to the involved medical staff and patients.

Informed consent statement

The informed consent was obtained from all subjects involved in the study.

Conflicts of interest

The authors declare no conflict of interest.

REFERENCES

1. Glynne-Jones R, Wyrwicz L, Tiret E, et al. Rectal cancer: ESMO clinical practice guidelines. *Ann Oncol.* 2017;28 (Suppl. 4): iv22-iv40. https://doi.org/10.1093/annonc/mdx224
2. Wei IH, Garcia-Aguilar, J. Non-operative management of rectal cancer: Understanding tumor biology. *Minerva Chir.* 2018;73:601-618. https://doi.org/10.23736/S0026-4733.18.07743-X
3. Pienkowski EHA, Nordenvall C, Palmer G, et al. Prevalence of low anterior resection syndrome and impact on quality of life after rectal cancer surgery: population-based study. *BJS Open.* 2020, 4(5): 935-942. https://doi.org/10.1002/bjs5.50312
4. National Guideline Alliance (UK). Optimal management of low anterior resection syndrome. Colorectal cancer (update). Evidence review E2. NICE Guideline, No. 151. London: National Institute for Health and Care Excellence (NICE); 2020. ISBN-13: 978-1-4731-3657-1.
5. Paun BC, Cassie S, MacLean AR, et al. Postoperative complications following surgery for rectal cancer. *Ann Surg.* 2010;251:807-818. https://doi.org/10.1097/SLA.0b013e3181dae4ed
6. Habr-Gama A, Perez RO, Nadalin W, et al. Operative versus nonoperative treatment for stage 0 distal rectal cancer following chemoradiation therapy: long-term results. *Ann Surg.* 2004;240(4):711–717; discussion 717-718. https://doi.org/ 10.1097/01.sla.0000141194.27992.32
7. Huang CM, Huang CW, Ma CJ, et al. Predictive value of FOLFOX-based regimen, long interval, hemoglobin levels and clinical negative nodal status, and post chemoradiotherapy CEA levels for pathological complete response in patients with locally advanced rectal cancer afer neoadjuvant chemoradiotherapy. *J Oncol.* 2020:9437684. https://doi.org/ 10.1155/2020/9437684
8. Dossa F, Chesney TR, Acuna SA, Baxter NN. A watch-and-wait approach for locally advanced rectal cancer after a clinical complete response following neoadjuvant chemoradiation: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol.* 2017; 2(7):501-513. https://doi.org/10.1016/S2468-1253(17)30074-2
9. Renehan AG, Malcomson L, Emsley R, et al. Watch-and-wait approach versus surgical resection after chemoradiotherapy for patients with rectal cancer (the OnCoRe project): a propensity-score matched cohort analysis. *Lancet Oncol.* 2016;17(2):174-183. https://doi.org/10.1016/S1470-2045(15)00467-2
10. Das P, Skibber JM, Rodriguez-Bigas MA, et al. Predictors of tumor response and downstaging in patients who receive preoperative chemoradiation for rectal cancer. *Cancer.* 2007;109(9):1750-1755. https://doi.org/10.1002/cncr.22625
11. Bitterman DS, Salgado LR, Moore HG, et al. Predictors of complete response and disease recurrence following chemoradiation for rectal cancer. *Front Oncol.* 2015;5:286. https://doi.org/10.3389/fonc.2015.00286
12. Huang CM, Huang MY, Huang CW, et al. Machine learning for predicting pathological complete response in patients with locally advanced rectal cancer after neoadjuvant chemoradiotherapy. *Sci Rep.* 2020;10(1):12555. https://doi.org/10.1038/s41598-020-69345-9
12. Huang Q, Qin H, Xiao J, et al. Association of tumor differentiation and prognosis in patients with rectal cancer undergoing neoadjuvant chemoradiation therapy. *Gastroenterol Rep.* 2019;7(4):283-290. https://doi.org/10.1093/gastro/goy045

13. Choi E, Kim, JH, Kim OB, et al. Predictors of pathologic complete response after preoperative concurrent chemoradiotherapy of rectal cancer: A single center experience. *Radiat Oncol J*. 2016;34(2):106-112. https://doi.org/ 10.3857/ roj.2015.01585

14. Yu SK, Chand M, Tait DM, Brown G. Magnetic resonance imaging defined mucinous rectal carcinoma is an independent imaging biomarker for poor prognosis and poor response to preoperative chemoradiotherapy. *Eur J Cancer*. 2014;50(5):920-927. https://doi.org/10.1016/j.ejca.2013.12.007

15. Dayde D, Tanaka I, Jain R, et al. Predictive and prognostic molecular biomarkers for response to neoadjuvant chemoradiation in rectal cancer. *Int J Mol Sci*. 2017;18(3):573. https://doi.org/10.3390/ijms18030573

16. Kosinski L, Habr-Gama A, Ludwig K, Perez R. Shifting concepts in rectal cancer management: a review of contemporary primary rectal cancer treatment strategies. *CA Cancer J Clin*. 2012;62(3):173-202. https://doi.org/10.3322/ caac.21138

17. Beppu N, Yanagi H, Tomita N. A review of preoperative chemoradiotherapy for lower rectal cancer. *J Anus Rectum Colon*. 2017;1:65-73. https://doi.org/10.23922/jarc.2017-013

18. Clifford R, Govindarajah N, Parsons JL, et al. Systematic review of treatment intensification using novel agents for chemoradiotherapy in rectal cancer. *Br J Surg*. 2018;105:1553-1572. https://doi.org/10.1002/bjs.10993

19. Bernier L, Balyasnikova S, Tait D, Brown G. Watch and Wait as therapeutic strategy in rectal cancer. *Cur Colorectal Cancer Rep*. 2018;14(2):37-55. https://doi.org/10.1007/s11888-018-0398-5

20. Van der Valk MJM, Hiling DE, Bastiaannet E, et al. Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study. *Lancet*. 2018;391(10139):2537-2545. https://doi.org/10.1016/S0140-6736(18)31078-X

21. López-Campos F, Martín-Martín M, Fornell-Pérez R, et al. Watch and wait approach in rectal cancer: Current controversies and future directions. *World J Gastroenterol*. 2020;26(29):4218-4239. https://doi.org/10.3748/wjg.v26. i29.4218

22. Habr-Gama A, São Julião GP, Vailati BB, et al. Management of the complete clinical response. *Clin Colon Rectal Surg*. 2017;30(5):387-394. https://doi.org/10.1055/s-0037-1606116

Л. Кокайне [1,2], М. Радзина [3], М. Лієпа [3], А. Геріна-Берзина [4],
Е. Сивина [4,5], Ж. Ніколаєва [4], А. Гардовскіс [1,2], Ж. Гардовскіс [1,2], Е. Міклашевич [5]

[1] Клініка університету Паулса Страдиня, хірургічне відділення, Рига, Латвія
[2] Університет Паулса Страдиня, хірургічне відділення, Рига, Латвія
[3] Клініка університету Паулса Страдиня, Інститут радіології, Рига, Латвія
[4] Клініка університету Паулса Страдиня, онкологічна клініка, Рига, Латвія
[5] Клініка університету Паулса Страдиня, Інститут онкології, Рига, Латвія

ОЧІКУВАЛЬНА СТРАТЕГІЯ У ХВОРИХ НА РАК ПРЯМОЇ КИШКИ З ПОВНОЮ КЛІНІЧНОЮ ВІДПОВІДДЮ ПІСЛЯ НЕОАД'ЮВАНТНОЇ ХІМІОПРОМЕНЕВОЇ ТЕРАПІЇ: ДОСВІД ОДНОГО КЛІНІЧНОГО ЗАКЛАДУ

Стан питання. Консервативне ведення хворих на аденокарциному прямої кишки після неоад'ювантної хіміопроменевої терапії привертає все більшу увагу клініцистів. Очікувальна стратегія дозволяє уникнути зниження якості життя внаслідок спричинених хірургічним втручанням порушень функцій органів малого тазу або незворотної стоми. Разом з тим, онкологічна безпека такої стратегії потребує подальших досліджень. **Матеріали та методи**. Проведено ретроспективний аналіз 125 хворих, які одержували неоад'ювантну хіміопроменеву терапію в 2016—2021 рр. Проаналізовано клінічні дані хворих, які задовольняли критеріям повної клінічної відповіді за настановами Європейського товариства медичної онкології (ESMO, 2017) та були проліковані консервативними методами. **Результати**. 10 хворих (8%) (7 жінок, 3 чоловіки, середній вік 67,3 роки) після неоад'ювантної хіміопроменевої терапії було переглянуто щодо стадії захворювання та визначено повну клінічну відповідь з наступним застосуванням очікувальної стратегії у подальшому веденні цих хворих. До лікування 7 хворих були охарактеризовані як N+. У більшості випадків у хворих було діагностовано аденокарциному диференціювання G1; пухлина в середньому розташовувалась на відстані 5,85 см від краю анусу і займала в середньому 71% кола кишки; середня довжина пухлини була 3,87 см. Середній час подальшого спостережен-ня за хворими склав 30 місяців. Місцевий ріст пухлини та/або віддалені метастази визначено у трьох хворих. Дворічна виживаність без ознак хвороби склала 70%. **Висновки**. У більшості хворих очікувальна стратегія мала свої переваги. Однак для зменшення кількості рецидивів слід проводити більш ретельний відбір хворих, для яких буде застосовуватись такий підхід.

Ключові слова: очікувальна стратегія, консервативне ведення, рак прямої кишки, клінічна повна відповідь, неоад'ювантна терапія.