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EVALUATION OF THE EFFICACY AND TOXICITY OF NEO-ADJUVANT SHORT COURSE RADIATION THERAPY CONCURRENTLY WITH CONTINUOUS INFUSION 5-FLUOROURACIL IN THE MANAGEMENT OF LOCALLY ADVANCED RECTAL CANCER PATIENTS

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Purpose: *To assess the safety and efficacy of neo-adjuvant short-course radiation therapy (SCRT) concurrently with continuous infusion of 5-fluorouracil (5-FU) in the treatment of locally advanced rectal cancer.* ***Method and material:*** *Patients with cT3-4 or any T with N+ rectal cancer diagnosed by magnetic resonance imaging (MRI) and proved pathologically as adenocarcinoma were eligible to be enrolled in our study. Patients received continuous infusion of 5-FU with dose escalation from 100mg/m2/day up to 200mg/m2/day through 5 days concurrently with a SCRT (5 Gy x 5 fractions), followed by 2 months of neo-adjuvant mFOLFOX, radical surgery with total mesorectal excision (TME) was done for patients with complete clinical (cCR), partial response (PR) or stationary disease (SD) and was follow by 4 months of adjuvant mFOLFOX.* ***Results:*** *Twenty patients were included in the study. All patients completed a SCRT concurrently with 5-FU and the 5-FU dose was safely escalated to 200 mg/m2/d with no dose-limiting toxicity (DLT). Four patients (20%) out of 20 patients showed cCR, 14 patients (7o%) had PR, and 2 patients (10%) had disease progression (PD). Four patients (26.7) out of 15 patients had complete pathological response (pCR), and 11 patients (73.3%) had PR. The most common grade III and IV toxicities according to common terminology criteria of adverse events version 5.0 (CTCAE) were diarrhea and abdominal pain. The most common grade I and II toxicities were non-hematological toxicity mainly gastrointestinal.*

Keywords: *5-fluorouracil; total mesorectal excision; dose-limiting toxicity; complete pathological response; common terminology criteria of adverse events version 5.0*

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer after breast and lung cancer and the second most common cause of cancer-related mortality worldwide as estimated by Global Cancer Observatory 2020 (GLOBOCAN 2020). New cases of cancer rectum estimated by GLOBOCAN 2020 were 732,210 with 339,022 cancer deaths.[1] In Egypt, rectal cancer became the 18th most commonly recorded tumor in the year 2020, according to GLOBOCAN, with 1512 new cases and 807 cancer mortality.[2]

The standard approach for treating locally advanced rectal cancer patients is 5 to 6 weeks of neo-adjuvant chemo-radiation (CCRTH) then surgery after 6 to 8 weeks (delayed surgery) followed by adjuvant chemotherapy.[3] The neo-adjuvant approach aimed at downstage tumors, possible sphincter preservation, less acute toxicity owing to a lesser dose of irradiation to the small bowel, and irradiation

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of well-oxygenated tissues with greater efficacy.[4]

SCRT has been tested using 3D conformal/ intensity modulated radiation therapy (IMRT) resulting in greater normal tissue sparing, lower dose to critical organs, and fewer long-term complications.[5] The Swedish Rectal Cancer Trial randomized patients with clinically resectable rectal cancer to neo-adjuvant SCRT followed by surgery versus surgery alone resulted in better local control as well as a longer overall survival (OS) in the radiotherapy arm.[6]

Also, the Dutch Colorectal Cancer Group Study and the Medical Research Council CR07 trial, both demonstrated better local control, disease-free survival (DFS), and OS with the addition of TME to neo-adjuvant short-course radiation.[7&8] However, there was less pCR, sphincteric preservation, and more positive circumferential resection margin (CRM) occurs in SCRT as compared to long course chemo-radiation owing to the short interval between radiotherapy and surgery and lack of concurrent chemotherapy in short course protocol.[9] In this regard, several trials tested the possibility of increase the interval between radiotherapy and surgery by more than 7 weeks (delayed surgery) and reported about a 10% increase in pCR in the group with delayed surgery.[10-12] Also, the addition of neo-adjuvant chemotherapy to radiotherapy and delayed surgery was associated with higher local control and lower rates of systemic relapse and that was comparable to the conventional long course chemo-radiotherapy, but with less toxicity.[13]

Due to the concerns about increasing toxicity, only a few trials are conducted testing the addition of concurrent chemotherapy to short-course radiation in the pre-operative setting and consolidative chemotherapy followed by delayed surgery with appropriate results and acceptable complications rate.[14]

PATIENTS AND METHODS

Patients

This prospective interventional study aimed at evaluation of the efficacy and toxicity of neo-adjuvant SCRT concurrently with continuous infusion of 5FU in the management of locally advanced rectal cancer patients.

Patients with locally advanced rectal cancer treated at the Clinical Oncology Department, Assiut University Hospital from October 2020 to October 2021 were included in the study.

The protocol of the study was approved by the ethics committee of Assiut University before data collection with IRB number 17200481.

Patients eligible for the study were required to have pathologically confirmed cancer rectum (adenocarcinoma) with an age between 20-80 and a performance status 0-1 based on the Eastern Cooperative Oncology Group scale (ECOG). Patients were staged according to American Joint Committee on cancer 8th edition[15] and included only patients with clinical T3\4 or any T with node-positive disease by MRI (locally advanced patients).

Methods

The initial workup of patients was total colonoscopy to exclude the presence of synchronous lesions of the colon and rectum and for the biopsy. Pre-operative pelvic MRI with contrast was done to assess the depth of tumor penetration, the presence of local lymph nodes metastases and liver metastasis, and predict CRM before surgery, in addition to a computerized tomography of the chest (CT) to exclude lung metastases.

Concurrent chemo-radiotherapy (CCRTH)
Short-course RT

The patient had a CT simulation for radiation planning in either a prone or a supine position with a full bladder and empty rectum for both planning and daily treatment, with the use of a total radiation dose of 2500 cGy with a fraction size of 500 cGy, in 5 consecutive days using linear Elekta synergy with Monaco planning system.

The gross tumor volume (GTV) included the primary tumor and any involved pelvic lymph nodes based on imaging studies. The clinical target volume (CTV) covered the GTV with a minimum of 1.5–2 cm margin superiorly and inferiorly and should include the entire rectum, mesorectum, and presacral space. A 1–2 cm margin around areas of gross tumor

invasion into adjacent organs was added. Also, the right and left internal iliac and obturator lymph nodes for T3 tumors and right and left external iliac lymph nodes for T4 tumors were simulated. Anteriorly, a 1–1.5 cm margin was added into the bladder to account for changes in bladder and rectal filling changes. A 5-mm expansion was added to the clinical target volume for the final planning target volume (PTV).

A 3D treatment plan was generated with ≥6 MV photons, with planning goals including ≥95% of the PTV receiving ≥95% and ≤107% of the prescribed dose.

The constraints on the organs at risk was scaled from the Radiation Therapy Oncology Group (RTOG) 0822 rectal cancer protocol and included volumetric and maximum dose constraints on the small bowel, bladder, and femoral heads as shown in (figure 1).

Dose-escalated concurrent 5-FU

The starting dose of 5-FU was 100 mg/m2/d over 24 hrs, and if the patient tolerate this dose clinically on the day1, dose escalation of 5-FU was considered. So, the patient received 5-FU with the dose of 150mg/m2/day on the day 2, and 200mg/m2/day on the days3, 4, and 5.

mFOLFOX: was given 2 weeks after CCRTH for a total of 4 cycles (2 months), with each cycle every 14 days. The oxaliplatin was 85 mg/m2 IV over 2 hrs, and the leucovorin was 400 mg/m2 IV concurrently with the oxaliplatin followed by 5-FU as 400 mg/m2 IV bolus then a continuous infusion over 46 hrs at a dose of 2400 mg/m2.

Assessment of toxicities

Toxicity assessment was done by using National Cancer Institute CTCAE version 5.0.

DLT is defined as any of the following occurring during chemo-radiation or within 21 days from the completion of chemo-radiation:

- Grade 3 non-hematologic toxicity, preventing treatment for >3 days
- Grade 4 non-hematologic toxicity
- Grade 4 febrile neutropenia
- Grade 4 thrombocytopenia or neutropenia toxicity lasting >7 days
- Elevation of ALT or AST >10 x upper limit of normal for >7 days.

Restaging/Assessing treatment response: was done by chest CT, and pelvic abdominal MRI within 14 days before surgery and based on the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) criteria. If the patient developed progressive or metastatic disease, he/she shifted to second line chemotherapy.

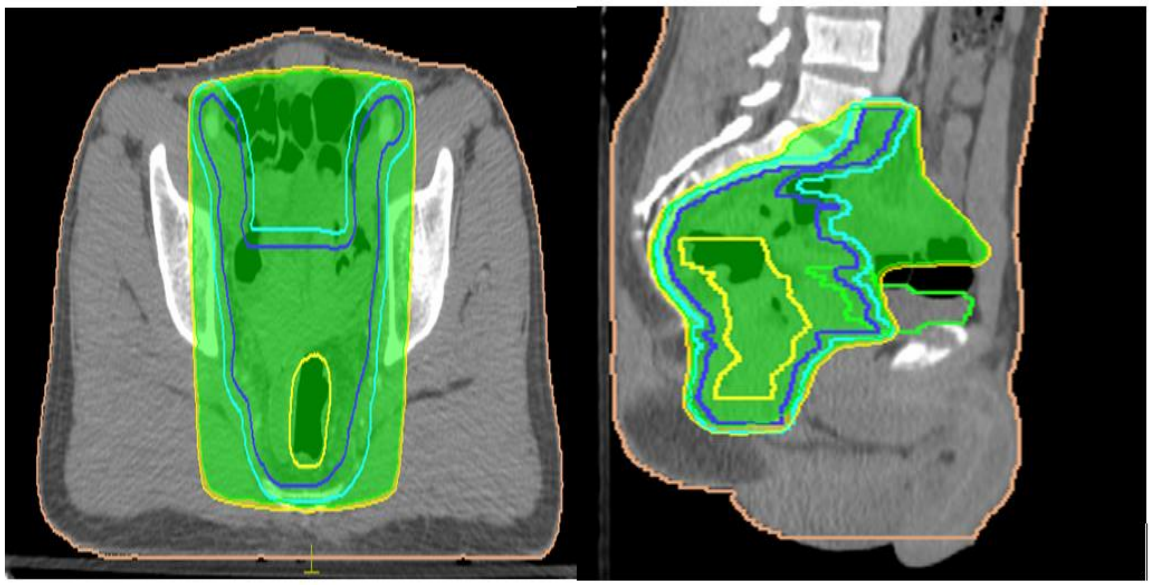

Fig. 1: Example of a 3D treatment plan of a patient in the study group.

Surgery: The treating surgeon assessed the distal margin of the tumor by digital rectal examination (DRE) and endoscopy for complete clinical response lesions then remove the primary tumor with adequate circumferential and distal margins and treat the draining lymph nodes by TME with the possibility of sphincteric preservation without compromising the oncological outcome. The surgery was considered 2-4 weeks after the end of neo-adjuvant therapy.

Adjuvant: mFOLFOX6: to complete 6 months of chemotherapy for patients who have complete resection of rectal cancer. Chemotherapy began between 2 and 4 weeks after surgery.

Follow-up of the patients: CT chest and abdomen every 6-12 months and pelvic MRI every 3-6 months after the surgery and adjuvant chemotherapy.

RESULTS AND DISCUSSION

Results

Patient demographics

A total number of 20 patients were included with 10 males (50%) and 10 females (50%) patients, and the mean age at the time of diagnosis was 49.05 years (SD ± 12.137) as shown in (table 1).

The 5 -FU was safely escalated from 100 mg/m2 on day 1 to 150 mg/m2 on day 2, and 200 mg/m2 on day 3, 4, and 5 with no DLT.

Regards the site of the tumor, 9 patients (45%) had middle rectum (5-10cm from anal verge) disease, the lower (<5cm from anal verge) and upper rectum (>10cm from anal verge) were presented in 6 patients (30%) and 5 patients (25%) respectively.

Clinical TNM staging was as follows: 4 patients (20%) with cT2, 13 patients (65%) with cT3, and 3 patients (15%) with cT4. Regarding the nodal status, 3 patients were with N0 (15%) and 17 patients with N+ (85%).

Table 1: Demographic and clinical data in the study group.

Item	Number of the patients "n=20"
1- Age "years":	49.05±12.137
2- Sex:	
- Male	10(50%)
- Female	10(50%)
3- Site:	
- Lower (<5cm from anal verge)	6(30%)
- Middle (5-10cm from anal verge)	9(45%)
- Upper (>10cm from anal verge)	5(25%)
4- Clinical T:	
- T2	4(20%)
- T3	13(65%)
- T4	3(15%)
5- Clinical N:	
- N0	3(15%)
- N+	17(85%)

Toxicity assessment

Adverse events were in the study group as assessed by CTCAE version 5.0 as shown in (table 2).

The most common grade Ⅲ and Ⅳ toxicities were diarrhea (10%) and abdominal pain (5%) with no grade Ⅲ and Ⅳ hematological or investigational toxicities. The most common grade Ⅰ and Ⅱ toxicities included diarrhea (25%), abdominal pain (20%), and anaemia (10%).

Regarding grade Ⅰ and Ⅱ hematological toxicity, only 2 patients (10%) developed anaemia and 1 patient (5%) developed neutropenia with no patients developing febrile neutropenia or thrombocytopenia.

Regarding non-hematological toxicities, 4 patients (20%) complained of grade Ⅰ, Ⅱ abdominal pain versus 1 patient (5%) with grade III, Ⅳ, and the pain was related to acute appendicitis developed 1 week after the end of radiotherapy. Diarrhea was the commonest side effect as 5 patients (25%) developed grade Ⅰ and Ⅱ, and 2 patients (10%) developed grade Ⅲ and Ⅳ.

Grade Ⅰ, Ⅱ mucositis and constipation occurred in 3 patients (15%) and 1 patient (5%) respectively with no grade III, IV mucositis, and constipation.

There was no hepato-biliary toxicity with only one patient (5%) with one attack of acute infection and one patient (5%) with one attack of acute renal injury which improved with medical treatment.

Efficacy of the treatment

Four out of the 20 patients (20%) had a clinical complete response with 2 patients having middle rectal tumors and 2 patients having lower rectal tumors who underwent radical surgery with sphincteric preservation. 14 patients (70%) out of 20 patients had significant tumor regression on MRI, but 3 of them died before undergoing surgery, one of them with acute appendicitis, one with pulmonary embolism and one without any apparent cause with their age range between 65 and 75. Two patients (10%) out of 20 patients developed progressive disease, and surgery could not be done and proceed to second-line chemotherapy as shown in (table 3).

Table 2: Adverse events in the study group assessed by CTCAE.

1- **Hematological toxicity:**	Grade Ⅰ-Ⅱ n=20 "%"	Grade III-Ⅳ n=20 "%"
- **Anaemia:**	2(10%)	Zero
- **Neutropenia:**	1(5%)	Zero
- **Febrile neutropenia :**	Zero	Zero
- **Thrombocytopenia:**	Zero	Zero
2- Non-hematological toxicity:	Grade Ⅰ-Ⅱ n=20 "%"	Grade III-Ⅳ n=20 "%"
A) Gastrointestinal:		
- **Abdominal pain:**	4(20%)	1(5%)
- **Mucositis:**	3(15%)	Zero
- **Diarrhea:**	5(25%)	2(10%)
- **Constipation:**	1(5%)	Zero
B) Hepato-biliary (Investigation):		
ALT/AST/total bilirubin	Zero	Zero
C) Infection :	1(5%)	Zero
D) Acute renal injury:	1(5%)	Zero

Table 3: The response to pre-operative treatment in the study group.

Response N (%)	Complete response n (%)	Partial response n (%)	Stable disease n (%)	Disease progression n (%)
Clinical response (20 patients)	4 (20%)	14 (70%)	0 (0%)	2 (10%)*
Pathological response (15 patients)	4 (26.7%)	11 (73.3)	0 (0%)	0 (0%)

*2 patients progressed clinically and not underwent surgery, 3 patients died before doing surgery with good clinical response.

Out of the 15 patients who had radical surgery, 4 patients (26.7%) had pCR with R0 resection, 11 patients (73.3%) had a pathological PR with R0 resection with only one patient with positive margin despite down-staging due to fibrosis, and no patient with stationary disease as shown in (table 3).

Discussion

Short-course RTH is an accepted alternative to long-course chemo-radiation for the neo-adjuvant treatment of locally advanced rectal cancer.[16]

We proposed that 5-FU can be given safely concurrently with short-course RTH, the role of prolonging the interval between short course and the surgery with excellent rates of down-staging, and the outcome of the surgery.[17]

To date, the use of short-course RTH concurrently with chemotherapy as radio-sensitizers has been tested in few trials owing to the theoretical concern for unacceptable toxicity of adding chemotherapy to short course RTH.[18&19]

There were 14 patients in Emma et al trial who completed the short-course RTH concurrently with 5-FU with 3 dose levels including 100 mg/m2/d, 150mg/m2/d, and 200 mg/m2/d with no DLT. Unlike our study, the most common grade III and IV toxicities were decreased neutrophil count (21.4%) and decreased lymphocyte count (21.4%), but in both studies, the most common grade I and II toxicities were diarrhea.[20]

Regarding the clinical response, there were 21.4% (3 patients out of 14) with complete clinical response, and 63.4% (9 patients out of 14) with clinical partial response which proved pathologically in Emma et al trial which was comparable with the response in our study group. Unfortunately in our study we have 2 patients out of 20 patients with progressive disease who could not undergo surgery and shifted to second-line chemotherapy, but there was no disease progression in Emma et al trial.[21]

In the KROG-10-01 trial, 73 patients received 25 Gy in 5 fractions over 5 consecutive days by tomotherapy concurrently with chemotherapy including intravenous bolus injection of 5fu (400 mg/m2/day) and leucovorin (20 mg/m2/day) and then delayed surgery was performed. [22] Unfortunately, this study had severe (grade III, IV) toxicities in 27 (38%) patients from CCRTh until 3 months after surgery which was not the condition in our study. This can be explained by the radiotherapy technique machine, giving chemotherapy as a bolus which was associated with higher rates of toxicity, or using double tolerated dose in the previous mentioned trial.[21]

Regarding the timing of surgery, the role of delayed surgery was tested in several trials and raised the concept of prolong the interval between neo-adjuvant treatment and surgery gives the chance of better response, and higher pCR with less surgical morbidity which underpins the hypothesis of total neo-adjuvant therapy.[22& 23]

This delay between short course RTH and surgery can be covered by chemotherapy that

was traditionally given postoperatively. The consolidation pre-operative chemotherapy was tolerable and resulted in pCR around 21% and 31%[18&24]

Conclusion

Short course radiation therapy can be safely given concurrently with continuous infusion 5-FU with the dose of 200mg/m2/day in patients with locally advanced cancer rectum without DLT and with high efficiency. We recommend conduct a randomized control trial between standard of care and the use of chemotherapy concurrently with SCRT.

REFERENCES

1. H. Sung, J. Ferlay, R. L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, and F. Bray, "Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries", ***CA,*** 71(3), 209-249 (2021).
2. A. H. Ibrahim and E. Shash, "General Oncology Care in Egypt", ***in Cancer in the Arab World,*** edited by Humaid O. Al-Shamsi, Ibrahim H. Abu-Gheida, Faryal Iqbal, and Aydah Al-Awadhi (Springer Singapore, Singapore), 41-61 (2022).
3. T. W. Bauer and F. R. Spitz, "Adjuvant and neoadjuvant chemoradiation therapy for primary colorectal cancer", ***J Surg Oncol,*** 7 (3), 175-181 (1998).
4. J. F. Bosset, L. Collette, G. Calais, L. Mineur, P. Maingon, L. Radosevic-Jelic, A. Daban, E. Bardet, A. Beny, and J. C. Ollier, "Chemotherapy with preoperative radiotherapy in rectal cancer", ***NEJM*** 355 (11), 1114-1123 (2006).
5. T. S. Hong and H. Mamon, "Short-course versus standard chemoradiation in T3 rectal cancer", ***J Oncol,*** 16(5), 717-721 (2011).
6. B. Cedermark, M. Dahlberg, B. Glimelius, L. Påhlman, L. E. Rutqvist, and N. Wilking, "Improved survival with preoperative radiotherapy in resectable rectal cancer", ***NEJM,*** 336(14), 980-987 (1997).
7. E. Kapiteijn, C. A. Marijnen, I. D. Nagtegaal, H. Putter, W. H. Steup, T. Wiggers, H. J. Rutten, L. Pahlman, B. Glimelius, J. H. van Krieken, J. W. Leer, and C. J. van de Velde, "Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer", ***NEJM,*** 345(9), 638-646 (2001).
8. D. Sebag-Montefiore, R. J. Stephens, R. Steele, J. Monson, R. Grieve, S. Khanna, P. Quirke, J. Couture, C. de Metz, A. S. Myint, E. Bessell, G. Griffiths, L. C. Thompson, and M. Parmar, "Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial", ***Lancet (London, England)***, 373(9666), 811-820 (2009).
9. A. M. Wolthuis, F. Penninckx, K. Haustermans, G. De Hertogh, S. Fieuws, E. Van Cutsem, and A. D'Hoore, "Impact of interval between neoadjuvant chemoradiotherapy and TME for locally advanced rectal cancer on pathologic response and oncologic outcome", **Ann Surg Oncol,** 19(9), 2833-2841 (2012).
10. Y. Cheng, Q. Qin, X. Huang, P. Lan, L. Wang, X. Gao, and T. Ma, "Effect of interval between preoperative radiotherapy and surgery on clinical outcome and radiation proctitis in rectal cancer from FOWARC trial", ***Cancer Med,*** 9(3), 912-919 (2020).
11. G. Macchia, M. A. Gambacorta, C. Masciocchi, G. Chiloiro, G. Mantello, M. di Benedetto, M. Lupattelli, E. Palazzari, L. Belgioia, A. Bacigalupo, A. Sainato, S. Montrone, L. Turri, A. Caroli, A. De Paoli, F. Matrone, C. Capirci, G. Montesi, R. M. Niespolo, M. F. Osti, L. Caravatta, A. Galardi, D. Genovesi, M. E. Rosetto, C. Boso, P. Sciacero, L. Giaccherini, S. Parisi, A. Fontana, F. R. Filippone, V. Picardi, A. G. Morganti, and V. Valentini, "Time to surgery and pathologic complete response after neoadjuvant chemoradiation in rectal cancer: A population study on 2094 patients", ***CTRO,*** 4, 8-14 (2017).
12. J. Erlandsson, E. Lörinc, M. Ahlberg, D. Pettersson, T. Holm, B. Glimelius, and A. Martling, "Tumour regression after radiotherapy for rectal cancer - Results

from the randomised Stockholm III trial", ***Radiotherapy and oncology : ESTRO,*** 135, 178-186 (2019).
13. F. Papaccio, S. Roselló, M. Huerta, V. Gambardella, N. Tarazona, T. Fleitas, D. Roda, and A. Cervantes, "Neoadjuvant Chemotherapy in Locally Advanced Rectal Cancer", ***J Cancer,*** 12 (12), 3611 (2020).
14. E. Fields, B. Kaplan, J. Karlin, J. Myers, N. Mukhopadhyay, X. Deng, H. Sankala, S. Grossman, and K. Matin, "Phase 1 Study of Neoadjuvant Short-Course Radiotherapy Concurrent with Infusional 5-Fluorouracil for the Treatment of Locally Advanced Rectal Cancer", ***Adv Radiat Oncol,*** 4(4), 605-612 (2019).
15. M. R. Weiser, "AJCC 8th Edition: Colorectal Cancer", ***Ann Surg Oncol,*** 25 (6), 1454-1455 (2018).
16. C. Chen, P. Sun, J. Rong, H. Weng, Q. Dai, and S. Ye, "Short Course Radiation in the Treatment of Localized Rectal cancer: A Systematic Review and Meta-Analysis", ***Sci Rep,*** 5(1), 10953 (2015).
17. V. M. Meyer, R. R. Meuzelaar, Y. Schoenaker, J. de Groot, E. de Boer, O. Reerink, W. tot N. Cappel, G. L. Beets, and H. L. van Westreenen, "Delayed Surgery after Neoadjuvant Treatment for Rectal Cancer Does Not Lead to Impaired Quality of Life, Worry for Cancer, or Regret", in ***J Cancer,*** 13(4), 742 (2021).
18. M. Aghili, S. Sotoudeh, R. Ghalehtaki, M. Babaei, B. Farazmand, M. Fazeli, A. Keshvari, P. Haddad, and F. Farhan, "Preoperative short course radiotherapy with concurrent and consolidation chemotherapies followed by delayed surgery in locally advanced rectal cancer: preliminary results", ***Radiat Oncol,*** 36(1), 17-24 (2018).
19. J. H. Lee, J. G. Kim, S. T. Oh, M. A. Lee, H. G. Chun, D. Y. Kim, T. H. Kim, *et al.*, "Two-week course of preoperative chemoradiotherapy followed by delayed surgery for rectal cancer: a phase II multi-institutional clinical trial (KROG 11-02) ", ***Radiother and Oncolo: ESTRO,*** 110(1), 150-154 (2014).
20. E. C. Fields, B. J. Kaplan, J. Karlin, J. L. Myers, N. Mukhopadhyay, X. Deng, H. Sankala, S. R. Grossman, and K. Matin, "Phase 1 Study of Neoadjuvant Short-Course Radiation Therapy Concurrent With Infusional 5-Fluorouracil for the Treatment of Locally Advanced Rectal Cancer", ***Adv Radiat Oncol,*** 4 (4), 605-612 (2019).
21. S. G. Yeo, J. H. Oh, D. Y. Kim, J. Y. Baek, S. Y. Kim, J. W. Park, M. J. Kim, H. J. Chang, T. H. Kim, J. H. Lee, H. S. Jang, J. G. Kim, M. A. Lee, and T. K. Nam, "Preoperative short-course concurrent chemoradiation therapy followed by delayed surgery for locally advanced rectal cancer: a phase 2 multicenter study (KROG 10-01) ", ***Int J Radiat Oncol Biol Phys,*** 86(1), 34-39 (2013).
22. S. Maliske, J. Chau, T. Ginader, J. Byrn, S. Bhatia, A. Bellizzi, D. J. Berg, and V. Monga, "Timing of surgery following neoadjuvant chemoradiation in rectal cancer: a retrospective analysis from an academic medical center", ***J Gastrointest Oncol,*** 10(4), 597-604 (2019).
23. R. R. Bahadoer, E. A. Dijkstra, B. van Etten, C. A. M. Marijnen, H. Putter, *et al.*, "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", ***The Lancet,*** 22(1), 29-42 (2021).
24. M. J. Chung, D. W. Kim, W. K. Chung, S. H. Lee, S. Jeong, J. K. Hwang, and C. S. Jeong, "Preoperative short- vs. long-course chemoradiotherapy with delayed surgery for locally advanced rectal cancer", ***Oncotarget,*** 8(36),60479-60486 (2016).

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تقيم الفاعلية و السمية للعلاج الاشعاعى و الكيمائى المصغر ما قبل الجراحة فى علاج اورام المستقيم المتقدمة موضعيا

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الهدف من الرسالة: تقيم الفاعلية و السمية للعلاج الاشعاعى المصغر و الكيمائى فلورويراسيل بجرعة تصل الى ٢٠٠مجم/م٢/يوم لمدة ٥ ايام ما قبل الجراحة فى علاج اورام المستقيم المتقدمة موضعيا.

المرضى و الوسائل: أجريت هذة الرسالة على ٢٠ مريض أورام مستقيم متقدمة موضعيا بقسم علاج الأورام والطب النووى– كلية الطب– جامعة أسيوط فى الفترة من أكتوبر ٢٠٢٠ الى أكتوبر ٢٠٢١ حيث تلقى جميع المرضى العلاج الأشعاعى الكصغر بجرعة ٥٠٠ جراى لمدة خمس أيام مع العلاج الكيمائى المحفز ٥ فلورويراسيل بجرعة تصل الى ٢٠٠مجم/م٢/يوم على مدار ٢٤ ساعة بدا من أول يوم للجلسات و تم حساب السمية والفاعلية حسب المقاييس العالمية.

النتائج: كان عدد المرضى فى البحث ٢٠ مريض و متوسط أعمارهم ٤٩ عام. كان اكثر الأعراض الجانبية من الدرجة الأولى و الثانية هم الأسهال و الأنيميا بالدم و كان أكثر الأعراض الجانبية من الدرجة الثالثة و الرابعة هم الأسهال و ألام بالبطن. قد حقق ٤ مرضى أستجابة أكلينيكة كاملة و ١٤ مريض حققوا أستجابة جزئية و ٢ مرضى عانوا من زيادة فى حجم الورم .

التوصيات: وجد أن العلاج الكيمائى المحفز للعلاج الأشعاعى المصغر ذو فاعلية فى علاج حالات أورام المستقيم المتقدمة موضعيا دون الزيادة فى الأعراض الجانبية المصاحبة للعلاج.