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REVIEW

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Radiotherapy management of rectal cancer in the backdrop of the COVID pandemic

Shirley Lewis[1] | Kaustav Talapatra[2]

[1]Department of Radiotherapy and Oncology, Kasturba Medical College, Manipal, Manipal Academy of Higher Education, Manipal, India

[2]Department of Radiation Oncology, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India

Correspondence
Kaustav Talapatra, Department of Radiation Oncology, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India.
Email: kaustee@gmail.com

Abstract

Background: COVID-19 outbreak was declared as a pandemic by the World Health Organization in March 2020. Over the last 3 months, the pandemic has challenged the diagnosis and treatment of all cancer, including rectal cancer. Constraints in resources call for a change in the treatment strategy without compromising efficacy.

Recent Findings: Delivery of shorter treatment schedules for radiotherapy offers advantages like short overall treatment time, improved throughput on the machine, improved compliance and reduced risk of transmission of COVID 19. Other strategies include delaying surgery, reducing the intensity of chemotherapy and adoption of organ preservation approach.

Conclusion: The curative treatment of rectal cancer should not be hindered during the COVID pandemic, and modifications in the multi-modality treatment will help achieve quality care.

KEYWORDS

COVID 19, radiotherapy, rectal cancer

1 | INTRODUCTION

COVID 19 pandemic is arguably the most extensive global healthcare emergency of this millennium.[1,2] It has rapidly spread across the countries with over 34 205 913 cases and 1 019 605 deaths. Various hospitals have been paralyzed by the enormous needs of COVID 19 patients.[3,4] The transmission of COVID in India is increasing with 6 312 584 cases and 98 708 deaths. However, with easing out of public restrictions, more patients will likely be affected. Cancer care during these difficult times is challenging and may lose its priority.[5,6] Various aspects of care are put on a back burner.[7] There is a danger of high mortality both from COVID and inadequately treated cancer.[8-10]

There are constraints on resources (particularly supplies and operating room) and hospital staff, which may make delivery of current standard approaches for the treatment of cancer difficult.[11] Demands on hospital infrastructure and staff lead to rationing of patient care services. The functioning of operating rooms is affected by short staffing of anesthesia personnel, risk of aerosol generation during surgery and inability to provide adequate postoperative care in intensive care units. The disinfection protocols in the operating room, or linear accelerator suite, impact the number treated per day with reduced staff. There is a shortage or low-quality personal protective equipment for these specialized services. Many frontline medical workers are getting infected, which causes reorganization of other healthcare professionals. Saving most lives receives maximum priority.[12] Thus, changes like shorter treatment times and telemedicine patient consults are favored. The pandemic has already transformed significant aspects of cancer care, and experts predict the changes in oncology treatment wrought upon by the epidemic may not be short-lived.[5]

2 | DISCUSSION

Radiation plays a vital role in the multi-modality treatment of rectal cancer.[13,14] Rectal cancer patients with intermediate and high-risk factors on preoperative MRI and neoadjuvant radiotherapy are required for down-staging the disease before surgery.[15] During the COVID pandemic, radiation use for rectal cancer has been classified as medium priority. To maintain continuity of care without compromising outcomes, changes to optimize practice or delivery of multi-modality treatment are needed. "Less is more" is the newfound mantra, and the RADS framework by Zaorksy et al is very appropriate for all settings.[16,17] The major changes proposed are shortening chemoradiation from 5 weeks to 1 week, delaying surgery from 4-6 weeks to 12 weeks, less intensive chemotherapy and organ preservation approach. These may yield the least chance of side effects while maintaining excellent outcomes and avoid the risk of contracting COVID 19 infection. In this paper, we shall review the evidence for these approaches and their applicability during the COVID pandemic.

2.1 | Adoption of shorter fractionation schedules

There has been a resurgence of short-course radiotherapy (SCRT) in recent years. SCRT is shown to be safe, effective and allows treatment in a short time, thereby reducing patient visits.[18] Despite similar outcomes to long course RT (LCRT), the adoption of SCRT in routine practice is low with concerns for increased late toxicity and poor down-staging in case of locally advanced cases.[19] The Swedish rectal cancer study reported late gastrointestinal effects.[20] However, the portals used for radiotherapy in this study were more extensive than currently used, which spare significant dose spillage to the bowel. During the pandemic, SCRT has various advantages, which make it the preferred treatment schedule. Shorter visits due to the fractionation facilitate physical distancing measures, avoids treatment breaks due to travel restrictions, make it possible to treat more patients with a therapeutic approach on the radiotherapy machine, reduce the chances of contracting the infection (both for patient and physicians) and avoids the need of concurrent chemotherapy (risk of immunosuppression). The role of SCRT in operable rectal cancer and locally advanced/advanced rectal cancer has been proven in randomized control trials. Both the polish trial by Bujko et al and the Australian Trans-Tasman Radiation Oncology Group (TROG) trial compared SCRT with immediate surgery and LCRT with surgery at 4 to 6 weeks in resectable rectal cancer (most in the intermediate-risk group as per ESMO risk stratification). They showed equivalent local recurrence rates, disease-free survival (DFS), overall survival (OS), acute and late toxicity.[21,22] Down-staging and pathological complete response (pCR) rates were low in SCRT arms; however, no difference was seen in patients requiring APR in distal cancers (<5 cm).[22,23]

Similarly, in locally advanced and advanced cancers, SCRT with integrated consolidation chemotherapy in waiting period to surgery has the advantage of better down-staging, improved compliance and reduced risk of distant metastases, and studies exploring this approach have shown excellent results. Bujko et al compared SCRT and consolidation chemotherapy (3 cycles FOLFOX 4) with oxaliplatin-based LCRT in 515 cT4 or fixed T3 rectal cancer patients.[24] The R0 resection rates (primary endpoint), pCR rates, local recurrence and distant metastases were similar in both arms at a median follow-up of 35 months. The OS was higher in SCRT arm (73% vs 65%), and the acute preoperative toxicity was lower in SCRT arm. The updated results of this trial, with a median follow-up of 8 years, show similar 8-year OS of 49% in both arms with no difference in late grade 3+ toxicity between the arms (11% vs 9%).[25] The major drawbacks of this trial are that MRI was not used for staging (with a possibility of under staging), nonstandard oxaliplatin-based concurrent chemotherapy in the control arm and was not designed based on survival endpoints. These factors are being addressed in the RAPIDO trial, comparing SCRT followed by chemotherapy with LCRT ± adjuvant chemotherapy in locally advanced rectal cancer with DFS as the primary endpoint.[26] The early results show compliance of over 80% with SCRT + chemotherapy (6 cycles of CAPOX) at the expense of higher grade 3+ toxicity.[27] The results of RAPIDO in abstract form was presented at ASCO 2020 by Hospers et al, which showed low 3-year disease-related treatment failure (23.7% vs 30.4%; $P = .02$), distant metastasis (19.8% vs 26.6% $P = .004$) and high pathological completed response (27.7% vs 13.8%; $P < .001$) with SCRT and chemotherapy.[28] The locoregional failure rates (8.7% vs 6.0%; $P = .10$) and quality of life were similar between the two arms. The full manuscript of the RAPIDO trial and results of the STELLAR trial are awaited.[29] During the COVID pandemic, while the patient awaits surgery after SCRT, consolidation chemotherapy may be added and, to reduce toxicity, dose reductions may be considered.

SCRT is a cost-effective treatment strategy, compared to LCRT, based on an economic modeling study by Raldow et al.[30] They showed that SCRT was associated with an incremental cost-effectiveness ratio of $133 495 per quality-adjusted life-year. SCRT plus chemotherapy is also a cost-effective approach, as demonstrated by Wang et al.[31] Although cost-effectiveness is not proven in LMIC, it is logical that 1 week of radiotherapy would reduce the financial burden in terms of stay and reduce exposure to COVID in the hospital setting.

Based on these studies, the adoption of shorter fractionation schedules is strongly recommended by the international expert panel and ESMO.[32,33] This change is being adopted in major cancer centers, including the United States and Europe, during the pandemic.[34,35] Rosenblatt et al (IAEA trial with 55% patients from India) and Chakrabarti et al show the feasibility and improved compliance of SCRT in the low middle-income country (LMIC).[36,37] This change in practice in a resource-constrained setting would benefit the patient greatly during the prolonged pandemic times and beyond.

2.2 | Delayed surgery

The usual practice is to consider surgery within 3 to 7 days or 4 weeks of SCRT and 6 weeks of LCRT. A delay after radiation has benefits in

COVID scenario where scheduling of surgery may be difficult due to resource and staff constraints.[38] The delay will help in down-staging, particularly in cases of distal cancers (< 5 cm from the anal verge), as shown in the Stockholm trial. The Stockholm trial compared SCRT with immediate surgery vs SCRT with delay and found no difference in the local recurrence rates, recurrence-free survival and OS between the two arms.[39] The pCR rates were 11.8% and fewer postoperative morbidity in the delayed group.[40] In a real-world scenario, the United Kingdom population-based study, in a cohort of 3469 patients, showed no difference in postoperative outcomes with delayed surgery.[41] In a meta-analysis by Huang et al, there was no difference in OS in LCRT with late surgery, SCRT with immediate surgery and SCRT with delayed surgery.[42] However, the authors also conclude that larger studies are required to come to a more convincing conclusion. In patients who have completed chemoradiation, and awaiting surgery, postponing surgery to 11 weeks can be considered based on GRECCAR 6 trial.[43] There was no difference in 3-year OS, or DFS, however, the complications were higher at 11 weeks vs 6 weeks.[44] Higher postoperative complications seen in GRECCAR trial have not been seen in RAPIDO trial, or trials using total neoadjuvant approach.[27,45]

The response to radiation could be used to tailor the type of surgery (local excision in place of TME) during the pandemic with ongoing triage and rationing of cancer surgeries. GRECCAR 2 trial is a multicentric randomized trial, which compared local excision with TME in 148 down-staged (residual <2 cm) bulky low rectal cancer (good responders to LCRT in T2-T3 disease).[46] Completion of TME was performed in local excision group if pathological stage revealed T2/T3. At a median follow-up of 60 months, there was no difference in local recurrence rates, DFS, OS, distant metastases or cancer-specific mortality. A total of 35% in local excision required TME for completion.[47]

2.3 | Postoperative radiotherapy

Few patients who are in early stage, and get operated upfront, may be upstaged after surgery and may need adjuvant chemoradiotherapy. As per ESMO guidelines, adjuvant radiotherapy is indicated in pT4, margin positivity, N2, especially with low tumors and poor-quality surgery.[15] Postoperative radiotherapy has shown in randomized trials and meta-analyses to reduce local recurrence rates significantly.[48] The decision to treat should be carefully weighed and may be deferred in low-risk cases. In case of high risk, LCRT is to be favored.

2.4 | Less intensive chemotherapy

Chemotherapy has the risk of myelosuppression, and early reports from China and Italy suggest higher complications from COVID, in patients, after chemotherapy.[10,49] Thus, changes in the regimens of chemotherapy to minimize myelosuppression should be considered. Intensive regimens can be substituted with lesser ones, and oral drugs may replace intravenous, where feasible, to reduce hospital visits.[50] Avoidance of severe grade 3-4 reactions necessitating emergency room visits can be tried with upfront dose reductions up to 25% and optimal use of growth factors to prevent neutropenia.

The role of chemotherapy in rectal cancer after neoadjuvant chemoradiation in the adjuvant setting is controversial and has not shown survival benefit.[15] The evidence for adjuvant chemotherapy is primarily extrapolated from colon cancer, and the prospective trials are flawed due to low patient numbers. There is a small disease-free survival benefit, especially in nonresponders after neoadjuvant chemoradiation and node-positive patients with no overall survival benefit.[51] There is wide variation in the use of adjuvant chemotherapy worldwide with oncologists from the United States recommending it, and those from Europe negating it. While deciding adjuvant chemotherapy, risk vs benefit should be assessed based on the patient's comorbidities and impact of the pandemic, and the same to be communicated with the patient. For low-risk patients, omitting adjuvant chemotherapy may be considered. In high-risk patients, requiring doublet chemotherapy, initiation of oxaliplatin may be delayed or omitted as it adds very little to single-agent 5FU/Capecitabine.[50] The use of oral capecitabine is to be preferred as it is proven to be equivalent to 5FU and should replace intravenous 5FU. Dosing of capecitabine may be reduced (fixed dosing 1500 mg twice daily 5 days a week or 7 days on and 7 days off) to reduce the risk of severe mucositis and diarrhea.

Following neoadjuvant SCRT, in cases where there is a delay to surgery due to pandemic, chemotherapy may be considered. Studies exploring the total neoadjuvant treatment (TNT) approach have shown significant response rates and are safely tolerated.[52] Although the TNT approach generally uses LCRT, the use of SCRT has demonstrated promising results.[24,53] These regimens involve the use of doublet chemotherapy, which is FOLFOX based. In addition to the modifications suggested, skipping the bolus 5FU and delaying each cycle by 2 to 3 weeks may help balance toxicity with benefit. The use of telemedicine consults to inform blood reports performed at local should be encouraged to avoid hospital visits.

2.5 | Organ preservation approach

Organ preservation approach may be considered in patients with a complete response after neoadjuvant radiotherapy.[54] Studies have shown that wait and watch after complete response has similar outcomes compared to those undergoing surgery. The international wait and watch database of 1009 patients from 15 countries showed that the local regrowth rate is 25% with over 80% occurring within 2 years.[55] The regrowths are limited to bowel wall in 97% and amenable for salvage with a 5-year OS of 85%. Salvage surgery is feasible in 83% of cases with regrowth.[56] Nonoperative management (NOM) may reduce the risk of post-surgery complications and ICU admissions during the COVID pandemic. Although SCRT is criticized for poor down-staging, SCRT with delay or chemotherapy may result in complete responders. Koeter et al evaluated the radiological response rates in 47 elderly patients with comorbidities, treated with SCRT and

TABLE 1 Modification in practice of rectal cancer

S. No.	Treatment modality	Modification strategy
1.	Radiotherapy	• Intermediate risk: SCRT where needed • Locally advanced: SCRT followed by chemotherapy • Avoid post-operative radiotherapy. Indicated only in select T4, margin positive and N2 disease • Wait and watch approach where feasible
2.	Surgery	Delay in surgery following radiation: • 4 to 6 weeks after SCRT • ≥12 weeks after LCRT or SCRT with chemotherapy
3.	Chemotherapy	• Avoid adjuvant chemotherapy • Oral capecitabine-based chemotherapy in high-risk cases • Omit addition of oxaliplatin • Total neoadjuvant approach • Avoid bolus 5FU

Abbreviations: LCRT, long-course radiotherapy; SCRT, short-course radiotherapy.

delayed surgery (14 weeks).[57] A majority had locally advanced (T3/T4: 84.5%) and advanced disease with MRF involvement in over 50%. Radiological down-staging was achieved in 73% with 12% showing a complete response. 82% underwent surgery with a pCR of 9%, and local recurrence rates were 8% at a median follow-up of 30 months. Bujko et al showed 20% complete clinical response after SCRT and delay.[58] In complete responders, nonoperative management may be proposed, especially in frail, unfit elderly patients who are at high risk during COVID. This approach needs diligent monitoring with imaging and follow-up assessments, especially in LMIC's, where patients are often lost to follow-up. It can be considered in educated and well-informed patients who will adhere to follow-up assessments.

3 | APPLICATIONS TO CLINICAL PRACTICE

The modifications discussed are backed by evidence to ensure curative treatment of rectal cancer during the COVID crisis. Table 1 summarizes the approaches. This is particularly applicable for LMIC like India where the existing challenges of access to cancer care, economic burden, are further compounded by the pandemic. Both patient- and healthcare-related factors contribute to delays in treatment in these times.[59] Experts believe 50 to 60% of surgeries have been postponed in the first 12 weeks of the pandemic.[60] Patients are hesitant to come to hospital due to COVID restrictions and are likely to present in late stage. Adoption of these changes enables continuity of care while adhering to the new norms of physical distancing with short and few patient visits.

4 | CONCLUSION

The curative treatment of rectal cancer should not be hindered during the COVID pandemic and is a priority. Modifications in the multimodality treatment will help achieve quality care. These include transition to SCRT in appropriately selected patients, optimally delay in surgery, less intensive chemotherapy and making room for a wait and watch strategy where feasible.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ETHICAL STATEMENT

Not applicable.

AUTHOR CONTRIBUTIONS

Shirley Lewis: Conceptualization; methodology; supervision; validation; writing-original draft; writing-review and editing. **Kaustav Talapatra:** Conceptualization; methodology; supervision; validation; visualization; writing-original draft; writing-review and editing.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

ORCID

Shirley Lewis https://orcid.org/0000-0001-5306-1649

REFERENCES

1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. *Acta Biomed*. 2020;91(1):157-160.
2. Gates B. Responding to Covid-19—a once-in-a-century pandemic? *N Engl J Med*. 2020;382(18):1677-1679.
3. Willan J, King AJ, Jeffery K, Bienz N. Challenges for NHS hospitals during covid-19 epidemic. *BMJ*. 2020.368 m1117https://doi.org/10.1136/bmj.m1117.
4. Spinelli A, Pellino G. COVID-19 pandemic: perspectives on an unfolding crisis. *Br J Surg*. 2020;107:785-787.
5. Ueda M, Martins R, Hendrie PC, et al. Managing cancer care during the COVID-19 pandemic: agility and collaboration toward a common goal. *J Natl Compr Canc Netw*. 2020;18(4):1-4.
6. Spicer J, Chamberlain C, Papa S. Provision of cancer care during the COVID-19 pandemic. *Nat Rev Clin Oncol*. 2020;17:329–331.
7. Dave M, Seoudi N, Coulthard P. Urgent dental care for patients during the COVID-19 pandemic. *Lancet*. 2020;395(10232):1257.
8. Yu J, Ouyang W, Chua MLK, Xie C. SARS-CoV-2 transmission in patients with cancer at a Tertiary Care Hospital in Wuhan, China. *JAMA Oncol*. 2020;6:1108-1110.
9. Zhang L, Zhu F, Xie L, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol*. 2020;31(7):894-901.
10. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol*. 2020;21(3):335-337.
11. van de Haar J, Hoes LR, Coles CE, et al. Caring for patients with cancer in the COVID-19 era. *Nat Med*. 2020;26(5):665-671.
12. Emanuel EJ, Persad G, Upshur R, et al. Fair allocation of scarce medical resources in the time of Covid-19. *N Engl J Med*. 2020;382(21):2049-2055.

13. Häfner MF, Debus J. Radiotherapy for colorectal cancer: current standards and future perspectives. *Visc Med*. 2016;32(3):172-177.
14. Pramateftakis M-G, Kanellos D, Tekkis PP, Touroutoglou N, Kanellos I. Rectal cancer: multimodal treatment approach. *Int J Surg Oncol*. 2012;2012:279341.
15. Glynne-Jones R, Wyrwicz L, Tiret E, et al. Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2017;28(suppl_4):iv22-iv40.
16. Achard V, Tsoutsou P, Zilli T. Radiotherapy in the time of the coronavirus pandemic: when less is better. *Int J Radiat Oncol Biol Phys*. 2020.107(3):600-601.
17. Zaorsky NG, Yu JB, McBride SM, et al. Prostate cancer radiotherapy recommendations in response to COVID-19. *Adv Radiat Oncol*. 2020;5:26-32.
18. Kane C, Glynne-Jones R. Should we favour the use of 5x5 preoperative radiation in rectal cancer. *Cancer Treat Rev*. 2019;81:101908.
19. Adam M, Turner M, Moore H, Mantyh C, Migaly J, eds. *Use of Neoadjuvant Short-Course Radiotherapy for Rectal Adenocarcinoma in the United States: Insights into Patterns of Practice and Outcomes. Diseases of the Colon & Rectum*. Philadelphia, PA: Lippincott Williams & Wilkins Two Commerce SQ; 2018.
20. Birgisson H, Påhlman L, Gunnarsson U, Glimelius B. Adverse effects of preoperative radiation therapy for rectal cancer: long-term follow-up of the Swedish rectal cancer trial. *J Clin Oncol*. 2005;23(34):8697-8705.
21. Bujko K, Nowacki MP, Nasierowska-Guttmejer A, Michalski W, Bebenek M, Kryj M. Long-term results of a randomized trial comparing preoperative short-course radiotherapy with preoperative conventionally fractionated chemoradiation for rectal cancer. *Br J Surg*. 2006;93(10):1215-1223.
22. Ngan SY, Burmeister B, Fisher RJ, et al. Randomized trial of short-course radiotherapy versus long-course chemoradiation comparing rates of local recurrence in patients with T3 rectal cancer: trans-Tasman radiation oncology group trial 01.04. *J Clin Oncol*. 2012;30(31):3827-3833.
23. Bujko K, Nowacki MP, Nasierowska-Guttmejer A, et al. Sphincter preservation following preoperative radiotherapy for rectal cancer: report of a randomised trial comparing short-term radiotherapy vs. conventionally fractionated radiochemotherapy. *Radiot Oncol*. 2004;72(1):15-24.
24. Bujko K, Wyrwicz L, Rutkowski A, et al. Long-course oxaliplatin-based preoperative chemoradiation versus 5 × 5 Gy and consolidation chemotherapy for cT4 or fixed cT3 rectal cancer: results of a randomized phase III study. *Ann Oncol*. 2016;27(5):834-842.
25. Ciseł B, Pietrzak L, Michalski W, et al. 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. Nilsson PJ, van Etten B, Hospers GA, et al. Short-course radiotherapy followed by neo-adjuvant chemotherapy in locally advanced rectal cancer - the RAPIDO trial. *BMC Cancer*. 2013;13:279.
27. van der Valk MJM, Marijnen CAM, van Etten B, et al. Compliance and tolerability of short-course radiotherapy followed by preoperative chemotherapy and surgery for high-risk rectal cancer - results of the international randomized RAPIDO-trial. *Radiother Oncol*. 2020;147:75-83.
28. Hospers G, Bahadoer RR, Dijkstra EA, et al. Short-course radiotherapy followed by chemotherapy before TME in locally advanced rectal cancer: the randomized RAPIDO trial. *J Clin Oncol*. 2020;38(15_suppl):4006.
29. Jin J, Liu S, Zhu Y, et al. The updated results for the phase 3 study of 5× 5 Gy followed by chemotherapy in locally advanced rectal cancer (STELLAR trial). *Int J Radiat Oncol Biol Phys*. 2017;99(2):E157.
30. Raldow AC, Chen AB, Russell M, et al. Cost-effectiveness of short-course radiation therapy vs long-course chemoradiation for locally advanced rectal cancer. *JAMA Netw Open*. 2019;2(4):e192249.
31. Wang S, Wen F, Zhang P, Wang X, Li Q. Cost-effectiveness analysis of long-course oxaliplatin and bolus of fluorouracil based preoperative chemoradiotherapy vs. 5x5Gy radiation plus FOLFOX4 for locally advanced resectable rectal cancer. *Radiat Oncol*. 2019;14(1):113.
32. Tchelebi LT, Haustermans K, Scorsetti M, et al. Recommendations for the use of radiation therapy in managing patients with gastrointestinal malignancies in the era of COVID-19. *Radiother Oncol*. 2020;148:194-200.
33. Marijnen CAM, Peters FP, Rödel C, et al. International expert consensus statement regarding radiotherapy treatment options for rectal cancer during the COVID 19 pandemic. *Radiother Oncol*. 2020;148:213-215.
34. Romesser PB, Wu AJ, Cercek A, et al. Management of locally advanced rectal cancer during the COVID-19 pandemic: a necessary paradigm change at Memorial Sloan Kettering Cancer Center. *Adv Radiat Oncol*. 2020;5:687-689.
35. De Felice F, Petrucciani N. Treatment approach in locally advanced rectal cancer during coronavirus (COVID-19) pandemic: long course or short course? *Colorectal Dis*. 2020;22(6):642-643.
36. Rosenblatt E, Jones G, Engineer R, et al. Short-course radiation for locally advanced rectal cancer: an IAEA randomized trial. *Int J Radiat Oncol Biol Phys*. 2019;105(1):S107.
37. Chakrabarti D, Rajan S, Akhtar N, et al. Long-course chemoradiation in carcinoma rectum; is it really worth it? Perspectives from a developing nation. *Ann Oncol*. 2019;30(Supplement_4):IV5.
38. Skowron KB, Hurst RD, Umanskiy K, Hyman NH, Shogan BD. Caring for patients with rectal cancer during the COVID-19 pandemic. *J Gastrointest Surg*. 2020;24(7):1698-1703.
39. Erlandsson J, Holm T, Pettersson D, et al. Optimal fractionation of preoperative radiotherapy and timing to surgery for rectal cancer (Stockholm III): a multicentre, randomised, non-blinded, phase 3, non-inferiority trial. *Lancet Oncol*. 2017;18(3):336-346.
40. Pettersson D, Lörinc E, Holm T, et al. Tumour regression in the randomized Stockholm III trial of radiotherapy regimens for rectal cancer. *Br J Surg*. 2015;102(8):972-978. discussion 8.
41. Levick B, Gilbert A, Spencer K, et al. Time to surgery following short-course radiotherapy in rectal cancer and its impact on postoperative outcomes. A population-based study across the English National Health Service, 2009-2014. *Clin Oncol*. 2020;32(2):e46-e52.
42. Huang YJ, Tai C, Kang YN, Wei PL. Early versus delayed surgery after short-course radiotherapy for rectal cancer: a network meta-analysis of randomized controlled trials. *Asian J Surg*. 2020.43(8):810-818.
43. Lefevre JH, Mineur L, Kotti S, et al. Effect of interval (7 or 11 weeks) between neoadjuvant radiochemotherapy and surgery on complete pathologic response in rectal cancer: a multicenter, randomized, controlled trial (GRECCAR-6). *J Clin Oncol*. 2016;34(31):3773-3780.
44. Lefèvre JH, Mineur L, Cachanado M, et al. Does a longer waiting period after neoadjuvant radio-chemotherapy improve the oncological prognosis of rectal cancer? three years' follow-up results of the Greccar-6 randomized multicenter trial. *Ann Surg*. 2019;270(5):747-754.
45. Garcia-Aguilar J, Chow OS, Smith DD, et al. Effect of adding mFOLFOX6 after neoadjuvant chemoradiation in locally advanced rectal cancer: a multicentre, phase 2 trial. *Lancet Oncol*. 2015;16(8):957-966.
46. Rullier E, Rouanet P, Tuech JJ, et al. Organ preservation for rectal cancer (GRECCAR 2): a prospective, randomised, open-label, multicentre, phase 3 trial. *Lancet*. 2017;390(10093):469-479.
47. Rullier E, Vendrely V, Asselineau J, et al. Organ preservation with chemoradiotherapy plus local excision for rectal cancer: 5-year results of the GRECCAR 2 randomised trial. *Lancet Gastroenterol Hepatol*. 2020;5(5):465-474.
48. Group CCC. Adjuvant radiotherapy for rectal cancer: a systematic overview of 8507 patients from 22 randomised trials. *Lancet*. 2001;358(9290):1291-1304.

49. Lambertini M, Toss A, Passaro A, et al. Cancer care during the spread of coronavirus disease 2019 (COVID-19) in Italy: young oncologists' perspective. *ESMO Open*. 2020;5(2):e000759.
50. Marshall JL, Yarden RI, Weinberg BA. Colorectal cancer care in the age of coronavirus: strategies to reduce risk and maintain benefit. *Colorectal Cancer*. 2020;9(1):CRC17.
51. Hong YS, Kim SY, Lee J-S, et al. Oxaliplatin-based adjuvant chemotherapy for rectal cancer after preoperative chemoradiotherapy (ADORE): long-term results of an open-label, multicentre, phase 2, randomised controlled. *J Clin Oncol*. 2019;37(33):3111-3123.
52. Cercek A, Roxburgh CS, Strombom P, et al. Adoption of total neoadjuvant therapy for locally advanced rectal cancer. *JAMA Oncol*. 2018;4(6):e180071.
53. Jia AY, Narang A, Safar B, et al. Sequential short-course radiation therapy and chemotherapy in the neoadjuvant treatment of rectal adenocarcinoma. *Radiat Oncol*. 2019;14(1):1-6.
54. Bernier L, Balyasnikova S, Tait D, Brown G. Watch-and-wait as a therapeutic strategy in rectal cancer. *Curr Colorectal Cancer Rep*. 2018;14(2):37-55.
55. van der Valk MJM, Hilling 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.
56. Kong JC, Guerra GR, Warrier SK, Ramsay RG, Outcome HAG. Salvage surgery following "watch and wait" for rectal cancer after neoadjuvant therapy: a systematic review. *Dis Colon Rectum*. 2017;60(3):335-345.
57. Koëter T, van Elderen S, van Tilborg G, et al. MRI response rate after short-course radiotherapy on rectal cancer in the elderly comorbid patient: results from a retrospective cohort study. *Radiat Oncol*. 2020;15(1):1-7.
58. Bujko K, Pietrzak L, Partycki M, et al. The feasibility of short-course radiotherapy in a watch-and-wait policy for rectal cancer. *Acta Oncol*. 2017;56(9):1152-1154.
59. Kumar D, Dey T. Treatment delays in oncology patients during COVID-19 pandemic: a perspective. *J Glob Health*. 2020;10(1):010367.
60. Sharma DC. Lockdown poses new challenges for cancer care in India. *Lancet Oncol*. 2020;21(7):884.

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