



O'Cathail, S.M. , Gilbert, D.C., Sebag-Montefiore, D. and Muirhead, R. (2020) Challenges and consequences of COVID-19 in the management of anorectal cancer: coming together through social distancing. *Clinical Oncology*, 32(7), pp. 413-416. (doi: [10.1016/j.clon.2020.04.009](https://doi.org/10.1016/j.clon.2020.04.009))

The material cannot be used for any other purpose without further permission of the publisher and is for private use only.

There may be differences between this version and the published version. You are advised to consult the publisher's version if you wish to cite from it.

<http://eprints.gla.ac.uk/215617/>

Deposited on 11 May 2020

Enlighten – Research publications by members of the University of
Glasgow

<http://eprints.gla.ac.uk>

Challenges and consequences of COVID-19 in the management of anorectal cancer: Coming together through social distancing

Sean M. O’Cathail^{1,2}, Duncan C Gilbert³, David Sebag-Montefiore⁴,
& Rebecca Muirhead^{5*}

Affiliations:

¹ Institute of Cancer Sciences, University of Glasgow, Glasgow, UK.

² Beatson West of Scotland Cancer Centre, Glasgow, UK

³ Sussex Cancer Centre, Brighton and Sussex University Hospitals NHS Trust, Brighton, UK.

⁴ University of Leeds and Leeds Cancer Centre, Faculty of Medicine & Health, University of Leeds, United Kingdom.

⁵ Oxford University NHS Foundation Trust, Oxford, UK

Summary:

Lower Gastrointestinal Cancer Treatment During the COVID-19 Pandemic

Keywords:

rectal cancer; COVID-19; treatment; hypofractionated; radiotherapy; chemoradiation

*Correspondence to: Dr Rebecca Muirhead

Churchill Hospital

Old Road

Oxford

OX3 7LE

Email: Rebecca.muirhead@oncology.ox.ac.uk

Tel: +44 (0) 7989445591

SARS-CoV-2 (COVID19) requires little introduction. COVID19 has already had, and will progressively have, profound consequences on our practise during the pandemic and beyond. As oncologists, we pride ourselves that our practice is evidence-based. However, we are increasingly making decisions with limited or an absence of high-quality evidence. We aim to discuss how the pandemic is currently affecting our patients, multidisciplinary working, treatment choices and consider longer term consequences of COVID19.

Our patients are vulnerable. The impact of the comorbidity of cancer on mortality is based on preliminary, emerging data [1,2,3,4]. However colorectal cancer is a disease of age and unequivocally, COVID 19 carries a high case fatality for older patients (8% and 14.8% China, 12.8% and 20.2% Italy) for patients over the age of 70 and 80 respectively [1]. Previous data from pandemic influenza, and early modelling work from Imperial College suggest that the cancer and chemotherapy immunosuppression are risk factors for death [5,6]. Lei et al reported increased surgical risks, with a 21% operative mortality of 34 patients who acquired COVID following elective surgery for a range of conditions [7]. Minimising hospital visits is crucial, with some studies indicating over 40% of COVID positive patients contracted it in hospital and reporting a higher incidence in those attending a cancer centre than the general population [8,9].

Implications of COVID-19 on our Multidisciplinary Team

MDT working faces numerous challenges as the availability of different components of care are likely to change simultaneously. Web-based meetings require technological solutions to facilitate multidisciplinary review of imaging and pathology. The differences between video-conferencing and face-to-face discussion require adjustment where the perception and ascertainment of peer support may be diminished. The weekly meeting also allows different specialties to update the status of their department. Allowing the team to contemporaneously balance strategies for patient care on the functionality of different departments.

The workforce will decline due to the increasing impact of infection, self-isolating, childcare responsibilities and redeployment. The latter is particularly affecting nurse specialists and palliative care.

Perhaps the biggest impact will be on surgical practice. Procedures requiring high dependency, intensive care input or significant inpatient stay will be increasingly deferred. National guidance suggests limiting radiological and endoscopic investigations to emergencies only, confirming even investigations of suspected cancer may not be possible during the pandemic [10,11,12].

Suggestions for management

In these unprecedented times we must work together to come up with the best clinical decisions that we consider to be in the best interest of the patient. The Royal College of Radiologists online forum has offered a platform for clinicians around the country to share experience and local strategies (<https://www.rcr.ac.uk/network/colorectal-chemotherapy-light-covid-19-0>).

General Principles

- Manage expectations of patients by offering clear explanations of what is and isn't possible. Decide amongst the MDT who will speak to patients and what will be said to avoid duplication.
- Work in teams so if a team member becomes unwell it is relatively easy for others to pick up their work. Alternating days in the hospital may avoid all team-members falling unwell at once.
- Develop a method for keeping track of patients where decisions have been influenced by Covid19 for future audit, and outstanding investigations and treatments that will be performed when "normal" service resumes.
- Follow up should be performed where possible by phone. New patient telephone consultations may be appropriate for some patients.
- Working within a cancer alliance may allow distribution of services, particularly surgery, in different hospitals that may have more capacity.

Rectal Cancer

A European expert panel have recently published evidence-based, consensus guidance for use during the pandemic on the management of rectal cancer using the framework of the ESMO guidelines [13]. Below we describe our perspective in a UK context. Radiotherapy for localised rectal cancer fulfils priority 3 under recently published NICE guidance [14].

Early and intermediate rectal cancer.

Consensus guidance suggests TME continue to be standard of care for early rectal cancer and TME alone or SCRT/CRT if good quality mesorectal excision cannot be assured. Despite the NICE guidelines suggesting radiotherapy should not be given to T1/2N0 patients [15], we are fortunate to have Level I evidence that hypofractionation with 25Gy in 5# and delay is an oncologically sound approach [16]. Due to diminishing surgical capacity, we suggest that this will result in an increased use of this strategy allowing surgery to be performed at a time when there is available capacity. In addition, a multicentre UK cohort study using SCRT and local excision in early stage cancer, demonstrated a pCR rate of 32% [17]. If imaging is limited, a single MRI at 2-3 months, will guide further management.

Locally advanced rectal cancer

In non-margin threatening disease, consensus guidance strongly suggests the use of SCRT instead of long course radiotherapy (LCRT) with a delay to surgery for 4-8 weeks following SCRT in keeping with Stockholm III [15]. A longer delay can be considered in responding patients.

In disease threatening or involving the margin or pelvic side wall disease, the consensus guidance suggests three options: LCRT, SCRT and delay or SCRT with a period of neo-adjuvant chemotherapy similar to the Polish trial [18]. Although LCRT is the most established treatment in this group, there is no level 1 evidence LCRT is superior to SCRT in reducing local recurrences and is not an 'under treatment'. Should a patient acquire COVID during LCRT, there is the risk of the infection itself but also the risk of compromised radiotherapy treatment due to treatment gaps. As such, LCRT should only be considered as an option for young fit patients without comorbidities with appropriate consent and isolation advice. We acknowledge the right decision for each patient will depend on the patient and their risk factors, the tumour

and the situation in the department at the time. Post treatment imaging will depend on availability; however, imaging can identify patients in whom a further delay can be safely considered. Surgery should proceed if appropriate as and when it is safely possible.

Adjuvant Chemotherapy

Adjuvant chemotherapy in rectal cancer should be limited, as it is in many other countries routinely, due to the evidence suggesting no or limited benefit [19]. “Adjuvant” chemotherapy following metastatectomy is not advised.

Metastatic disease

NCCN guidelines suggest similar measures to those already brought in nationwide [20]. Palliative chemotherapy should be given to those with large disease burden, rapid progression or those showing systemic symptoms of malignancy. Level 1 evidence suggests that breaks in treatment do not affect outcome, so 3 months of palliative chemotherapy can be followed by a break [21]. NHS England now allow treatment breaks of biological agents. Metastasis directed therapy in oligometastatic disease could be delayed in those with metachronous disease and a long disease-free interval. For those where benefit of immediately treatment of oligometastatic disease outweighs risk, SABR may be preferable as it does not require inpatient stay or anaesthetic support.

All patients currently on chemotherapy require conversations about the altered risk / benefit ratios and advice regarding isolating.

Anal Cancer

The majority of anal cancers are cured by definitive CRT and it a priority 1 radiotherapy treatment per NICE guidance [17]. The risk-benefit ratio favours treatment for anal cancer, therefore it is appropriate to offer current standard of care. Clinical trial recruitment will be limited by resource, but for those still able to offer it, all three arms of PLATO remain open [22]. Two thirds randomised into ACT4 will receive one week less treatment. In elderly patients or those with poor performance status a less intensive treatment schedule should

be considered. There is published data for 30Gy in 15# concurrent with chemotherapy [23, 24]. Further hypofractionation using of 30Gy in 10 fractions concurrent with chemotherapy may also be considered although we lack prospective data on this regimen.

Beyond COVID-19.

Despite the challenges of COVID19, there is a real opportunity to learn from the novel and amended approaches treatments being used. Although undoubtedly of interest to service providers, it is vital we understand the impact on patients, particularly cancer outcomes and toxicities, as a central focus of induced to changes in anorectal treatments beyond COVID19.

The CTRad COVID RT initiative is working with radiotherapy centres across the UK to capture the impact of COVID19 on radiotherapy outcomes. In rectal cancer, the aim is to capture alterations in the treatment pathway, chosen regimen and treatment compliance to assess the impact of the decisions on outcome. We also support the UK national coronavirus cancer monitoring project [29].

This represents a once in a generation challenge. Professionally, we must ensure we are collectively discussing management widely, as hospital pressures and the knowledge base evolves over coming weeks and months; understand we are all finding our footing in a constantly shifting terrain and there are few known wrong, or right, answers. Beyond our professional responsibility, we have to acknowledge we are all trying our best, support our colleagues, friends and families. If ever there was a time to come together, this is it.

References

- [1] Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.4683>.
- [2] Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *Int J Infect Dis* 2020. <https://doi.org/10.1016>
- [3] Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. *BMJ* 2020;368. <https://doi.org/10.1136/bmj.m1198>./j.ijid.2020.03.017.
- [4] Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020; published online Feb 14. [http://dx.doi.org/10.1016/S1470-2045\(20\)30096-6](http://dx.doi.org/10.1016/S1470-2045(20)30096-6).
- [5] Cooksley CD, Avritscher EBC, Bekele BN, Rolston KV, Geraci JM, Elting LS. Epidemiology and outcomes of serious influenza-related infections in the cancer population. *Cancer* 2005;104:618–28. <https://doi.org/10.1002/cncr.21203>.
- [6] Williams M, Calvez KL, Mi E, Chen J, Dadhania S, Pakzad-Shahabi L. Estimating the Risks from COVID-19 Infection in Adult Chemotherapy Patients. *MedRxiv* 2020:2020.03.18.20038067. <https://doi.org/10.1101/2020.03.18.20038067>.
- [7] Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-10 infection. *EClinicalMedicine* 000 (2020) 100331
- [8] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. *JAMA* 2020;323:1061–9. <https://doi.org/10.1001/jama.2020.1585>.
- [9] 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. <https://doi.org/10.1001/jamaoncol.2020.0980>.
- [10] CT Colonography activity and Covid-19: British Society of Gastrointestinal and Abdominal Radiology guidance, March 2020. <https://www.bsgar.org/society/covid-19-and-bsgar-updates-1/covid-19-and-bsgar-update-archive/>. Accessed 30 March 2020.
- [11] COVID-19 and BSGAR Update ARCHIVE | BSGAR n.d. <https://www.bsgar.org/society/covid-19-and-bsgar-updates-1/covid-19-and-bsgar-update-archive/> (accessed March 29, 2020).
- [12] GI Endoscopy Activity and COVID-19: Next steps. *Br Soc Gastroenterol* 2020. <https://www.bsg.org.uk/covid-19-advice/gi-endoscopy-activity-and-covid-19-next-steps/> (accessed March 29, 2020).
- [13] Marijnen CAM, Peters FP, Rodel C, et al. International expert consensus statement regarding radiotherapy treatment options for rectal cancer during the COVID19 pandemic. In press. DOI: <https://doi.org/10.1016/j.radonc.2020.03.039>
- [14] NICE guideline [NG162]. COVID-19 rapid guideline: delivery of radiotherapy, March 2020. <https://www.nice.org.uk/guidance/NG162>. Accessed 30 March 2020.

- [15] NICE guideline [NG151]. Colorectal Cancer, January 2020.
<https://www.nice.org.uk/guidance/ng151/chapter/Recommendations#management-of-local-disease>. Accessed 5 April 2020.
- [16] 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;18:336–46.
[https://doi.org/10.1016/S1470-2045\(17\)30086-4](https://doi.org/10.1016/S1470-2045(17)30086-4).
- [17] Smart CJ, Korsgen S, Hill J, et al. Multicentre study of short-course radiotherapy and transanal endoscopic microsurgery for early rectal cancer. *Br J Surg* 2016;103:1069-75
- [18] Bujko K, Wyrwicz L, Rutkowski A, et al. Long-course oxaliplatin-based preoperative chemoradiation versus 5 x 5 Gy and consolidation chemotherapy for cT4 or fixed cT3 rectal cancer: results of a randomized phase III study. *Annals of Oncol* 2016;27:834-842
- [19] Carvalho C, Glynne-Jones R. Challenges behind proving efficacy of adjuvant chemotherapy after preoperative chemoradiation for rectal cancer. *Lancet Oncol* 2017;18:e354–63.
[https://doi.org/10.1016/S1470-2045\(17\)30346-7](https://doi.org/10.1016/S1470-2045(17)30346-7).
- [20] NCCN. Principles for Management of Colorectal Cancer Patients During the COVID-19 Pandemic. April 2020. <https://www.nccn.org/covid-19/pdf/Colorectal%20COVID-19.pdf>. Accessed 15 April 2020.
- [21] Adams RA, Meade AM, Seymour MT et al. Intermittent versus continuous oxaliplatin and fluoropyrimidine combination chemotherapy for first-line treatment of advanced colorectal cancer: results of the randomised phase 3 MRC COIN trial. *Lancet Oncol*. 2011 Jul;12(7):642-53
- [22] Sebag-Montefiore D, Adams R, Bell S. et al. The development of an umbrella trial (PLATO) to address radiation therapy dose questions in the locoregional management of squamous cell carcinoma of the anus. *Int J Radiat Oncol Biol Phys* 2016;96(2);E164-E165
- [23] Hatfield P, Cooper R, Sebag-Montefiore D. Involved-field, low-dose chemoradiotherapy for early-stage anal carcinoma. *Int J Radiation Oncol Biol Phys* 2008;70(2):419-424
- [24] Charnley N, Choudhury A, Chesser P, et al. Effective treatment of anal cancer in the elderly with low-dose chemoradiotherapy. *Br J Cancer* 2005;92(7):1221-1225
- [29] UK Coronavirus cancer monitoring project, March 2020.
<https://ukcoronaviruscancermonitoring.com/>. Accessed 30 March 2020