12.
Rectal cancer

Background

Rectal cancer is less common than colon cancer but presents difficult treatment decisions because, while it is frequently curable, treatment may involve radical surgery including the need for a colostomy, which can have a profound effect on a survivor's quality of life.

Equally, recurrent rectal cancers produce distressing symptoms and are difficult to treat and frequently require re-irradiation for symptom control, exenterative surgery or both.

The aim of radiotherapy in rectal cancers is to allow radical treatment to take place for more advanced cancers or to reduce the risk of relapse for early stage cancers (neoadjuvant therapy). In recurrent or incurable disease, radiotherapy can reduce the disease burden and help control symptoms.

Neoadjuvant therapy

Operable tumours

Preoperative radiotherapy is preferred to postoperative treatment as the preoperative technique is more effective and less toxic (Level 1a).[1–3]

For operable rectal cancers, as defined by preoperative pelvic magnetic resonance (MR) scan and staging chest, and abdomen and pelvis computed tomography (CT) scans, preoperative short-course rectal radiotherapy (SCRT) has been evaluated in several prospective randomised controlled trials (RCTs). The Dutch total mesorectal excision (TME) versus SCRT (25 Gray [Gy] in five fractions) + TME trial demonstrated a reduction in local recurrence rate, though with a longer median follow-up of 6.1 years the benefit appears to decrease (10.9% versus 5.6%; 49% relative reduction in risk).[4,5] The overall survival was same in both groups (Level 1b).[3] The MRC-07 trial demonstrated the advantage of SCRT (25 Gy in five fractions) for operable rectal cancer over selective postoperative (chemo-) radiation, in terms of reducing the relative risk of local recurrence after a median follow-up of four years by 61% (HR 0.39, CI 0.27–0.58). This translates to an absolute reduction in risk of local relapse of 6.2% at three years. There is also an absolute improvement in disease free survival of 6% at three years with no effect on overall survival (Level 1b).[3,6]

SCRT, however, increases long-term toxicity, with poorer functional outcomes especially in terms of continence (Level 1b).[3,7] The benefit seems to be mainly for cancers in the mid-rectum and 'intermediate-risk' cancers as defined in the National Institute of Health and Care Excellence (NICE) guidance (Level 1b).[3,8]

Recommendation

Short course preoperative radiotherapy:

25 Gy in 5 daily fractions (Grade A)

Followed by definitive surgery within a week

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.[3]

Inoperable tumours

For inoperable cancers, cancers which involve or threaten the circumferential margin or for cancers deemed to be at high risk of relapse (NICE guidance), down-staging treatment is recommended.[8] If not otherwise contraindicated, concurrent chemotherapy is recommended to improve response rates.

Doses of >30 Gy improve the response rate and long-course chemo-radiotherapy (LCCRT) has been shown to improve response rate and the likelihood of a R0 resection compared to long-course radiotherapy alone (Level 1a), though the sphincter preservation rate and long-term outcomes appear to be similar.[1,3,9,10] A dose of 45–50.4 Gy in 1.8 Gy per fraction with concurrent chemotherapy is commonly used in the UK, though there is little good quality RCT research underpinning this.

Fluorouracil (5-FU)-based chemotherapy has been used in all major trials since the 1980s and more recently, capecitabine has been shown to have similar efficacy in several phase 2 studies (Level 2b); it has replaced infusional 5-FU as the drug of choice for LCCRT to the rectum.[3,11,12] The UK ARISTOTLE trial (EUDRACT No. 2008-005782-59) is currently investigating the effect of the addition of intravenous (IV) irinotecan to capecitabine on local control rates in advanced rectal cancers.[13] Some authors have reported a 'boost' of 5.4 Gy in three fractions to the gross tumour volume plus margin following 45 Gy in 25 fractions to a larger volume.[12] The efficacy and toxicity of this remains unknown (Level 2b).[3]

Retrospective series from Sweden and the UK, looking at patients with locally advanced unresectable rectal cancer who are unfit for standard LCCRT, treated with 25 Gy in five fractions, have reported significant tumour regression, with 60–80% of patients going on to have delayed surgery (Level 2c).[3,14,15]

Recommendations

For downstaging LCCRT:

45 Gy in 25 daily fractions with concurrent chemotherapy (Grade A)
Optional boost of 5.4 Gy in 3 (Grade C) fractions to smaller volume
50.4 Gy in 28 daily fractions with concurrent chemotherapy (Grade A)

For patients not fit for chemotherapy:

45 Gy in 25 daily fractions (Grade A) with or without boost
50.4 Gy in 28 daily fractions (Grade A)

For elderly patients or those with significant co-morbidities:

25 Gy in 5 daily fractions (Grade B)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.[3]

Brachytherapy

Low-energy contact brachytherapy (Papillion technique) and high-dose rate (HDR) brachytherapy have both been used, generally in combination with external beam radiotherapy (EBRT), for the treatment of rectal cancers. The aim of treatment has been either palliative or as part of neoadjuvant treatment to improve response. In patients unfit for surgery, these techniques can be used to improve local control.

Apart from one RCT (Level 1b), most of the evidence for the Papillion technique comes from case series and retrospective analyses.[3,16] Similarly, there is only one published RCT evaluating a neoadjuvant 10 Gy in two fractions HDR brachytherapy boost (endoluminal) along with 50.4 Gy in 28 fractions of EBRT (Level 1b).[3,17] This trial showed no improvement in pathological complete response (pCR) or long-term survival despite a better R0 resection rate for T3 tumours treated with HDR brachytherapy boost along with standard chemoradiotherapy.[17] There is increasing experience in the UK and worldwide of the use of the Papillon technique, usually in combination with EBRT, for the radical treatment of patients not suitable for surgery or those who refuse a stoma.[18–22] It is also used for the palliative treatment of patients with a recurrence or metastases not suitable for surgery.

Contact radiotherapy is also offered to patients with a resected pT1 malignant polyp in combination with EBRT, though there is no randomised trial evidence comparing this approach with radical surgery. It may be most appropriate for elderly, frail patients who cannot undergo radical resection.

Dose recommendations are derived from published trials and current consensus among UK centres offering brachytherapy.

Recommendations

Postoperative:

pT1 or pT2 with R1 resection if patient refuses further surgery
60 Gy in 2 weekly fractions followed by EBRT (Grade B)

Radical treatment (unfit patients or those who refuse surgery):

cT1 (<3 centimetres [cm]) 110 Gy in 4 fractions over 6 weeks (30 Gy every 2 weeks x 3 and final boost 20 Gy) (Grade D)

High-risk tumours not fit for surgery cT1, cT2, cT3a, (>3 cm)

45 Gy in 25 fractions or 50.4 Gy in 28 fractions over 5–5.5 weeks with concurrent chemotherapy (Grade D)
or 25 Gy in 5 daily fractions in 1 week in patients not fit for chemotherapy (Grade D)

followed by:

contact radiotherapy boost 90 Gy in 3 fractions over 4 weeks to responders (regression to <3 cm) and consider final boost 20 Gy (total 110 Gy in 4 fractions over 6 weeks) (Grade D)
HDR brachytherapy 12 Gy in 2 fractions (Grade D)
Consider salvage surgery if no response after external beam chemoradiotherapy (EBCRT)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.[3]

Palliative treatment

There are no good-quality trials evaluating different dose fractionation schedules for palliative treatment. An appropriate regime should be chosen after considering the patient's likely prognosis, disease burden, symptoms and performance status.

Recommendations

30 Gy in 10 daily fractions (Level D)
20–25 Gy in 5 daily fractions (Level D)
HDR brachytherapy 10 Gy at 1 cm single dose (Level D)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.[3]

Re-irradiation

Following previous SCRT or LCCRT, some patients will experience a local or regional relapse. Such patients should be discussed in specialist multidisciplinary team meetings (MDTMs) with the relevant expertise in treating recurrent rectal cancer.

Where possible, recurrences after neoadjuvant radiotherapy should be treated with surgery or systemic therapy, avoiding further radiation. However, if surgery is not feasible with clear margins or holds excess risks, re-irradiation should be considered for limited volumes, including the use of stereotactic body radiotherapy (SABR) techniques. This may yield good symptomatic relief as a palliative treatment and long-term control is possible.

When curative resection is to be considered but re-irradiation is required to achieve this, currently, hyperfractionated chemoradiotherapy should be preferred to limit late toxic (Grade D).[3]

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