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Watch and wait policy after preoperative radiotherapy for rectal cancer; management of residual lesions that appear clinically benign

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Abstract

Background: During an ongoing phase II observational study on watch and wait policy in rectal cancer, a substantial number of patients presented residual lesion after radiotherapy with a clinical benign appearance. This article aims to discuss the clinical significance of such findings.

Materials and methods: Main entry criteria were age ≥70 years and small tumour (≤5 cm and ≤60% of circumferential involvement) located in the low rectum. Patients received chemoradiation (50 Gy, 2 Gy per fraction concomitantly with a 5-Fu bolus and leucovorin) or 5 × 5 Gy if considered unfit for chemotherapy. Patients with clinical complete response (cCR) were observed. Those with persistent tumours underwent transanal endoscopic microsurgery [TEM] if the baseline tumour was ≤3 cm and cN0 or total mesorectal excision.

Results: The watch and wait procedure was used in 11 out of the total 35 patients (31%) with a cCR; 17 patients (49%) with residual tumours that appeared clinically malignant were referred for TEM or abdominal surgery. In the remaining seven (20%), the residual tumour clinically appeared benign. Of these, there were two invasive cancers, four high-grade dysplasias and one low-grade dysplasia. The five patients with dysplasia, underwent local lesion resection without recurrence within a median of 11 months follow-up.

Conclusions: The majority of lesions that appeared clinically benign after radio(chemo)therapy were also benign on pathological examination. Thus, local excision of such lesions should be considered.

Keywords: Organ preservation; Rectal cancer; Preoperative radiotherapy

Introduction

The watch and wait policy for patients with clinical complete response (cCR) after preoperative radiotherapy[1–6] or undertaking full-thickness local excision in those with radiosensitive tumours,[7–10] enables organ preservation in rectal cancer. Indeed, favourable local control and survival have been reported after such procedures. Moreover, such approaches make it possible to avoid severe postoperative complications and permanent stoma. In addition, it is expected that anorectal, urinary and sexual functions are improved after the organ preserving procedures when compared to total mesorectal excision. Such procedures are however considered still experimental because evidence is still scant on their safety.

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In a population-based study, postoperative mortality, as measured at 6 months after total mesorectal excision, was 16% for patients aged ≥75 years compared with 4% for younger patients.[11] Thus for elderly patients, organ sparing procedures may lead to a survival benefit by avoiding the risk of postoperative deaths.[12] These procedures are thereby expected to be the most beneficial for elderly patients.[12]

We have launched a phase II observational study that evaluates efficacy of organ sparing procedures after preoperative radiotherapy in elderly patients by either using the watch and wait policy in patients with cCR or through local excision for those with residual tumours (ClinicalTrials.gov NCT01863862). The main rationale of our trial was to avoid postoperative deaths associated with abdominal surgery. The decision to incorporate local excision in the study design was based on our previous trial, where preoperative radiotherapy and full-thickness local excision for a small lesion led to favourable outcomes for elderly patients.[7] We unexpectedly noticed that a substantial proportion of patients, 8–10 weeks after radiotherapy, presented with residual lesions with a clinical benign appearance. Because such observations have not yet been published, the primary aim of this article is to highlight this issue.

Materials and methods

Study design

The main entry criteria were age ≥70 years and small tumour size (Fig. 1). Cut-off points that differentiate between a high or a low chance for a pathological complete response seems to be about a 5 cm of maximum tumour diameter and about a 60% of circumferential bowel wall involvement.[13–15] These cut-off points were therefore accepted as entry criteria. Only patients with a pathologically proven adenocarcinoma located either in the low rectum (accessible to digital rectal examination) or in the anal canal were eligible. According to current guidelines,[16] we have adopted preoperative radiotherapy and local excision using transanal endoscopic microsurgery (TEM) in elderly patients with small tumours as a routine procedure assuming that they are at surgical risk when total mesorectal excision is being performed. Therefore patients were assigned at baseline into two groups; candidates for TEM or for total mesorectal excision. Indications for preoperative radiotherapy and TEM included; ≤cT3a tumour without nodal disease and tumour size ≤3 cm. Indications for preoperative radiotherapy and total mesorectal excision included; bulky cT2 tumour requiring abdominoperineal resection, cT3, cT4 or cN+. The experimental part of the study concerned only patients who achieved cCR (Fig. 1). Patients with persistent tumours undertook our routine surgical procedure according to the pre-treatment assignment. The trial received ethical committee approval at our institution.

Statistics

The study hypothesis assumed that local recurrence occurs in not more than 25% of patients with cCR after

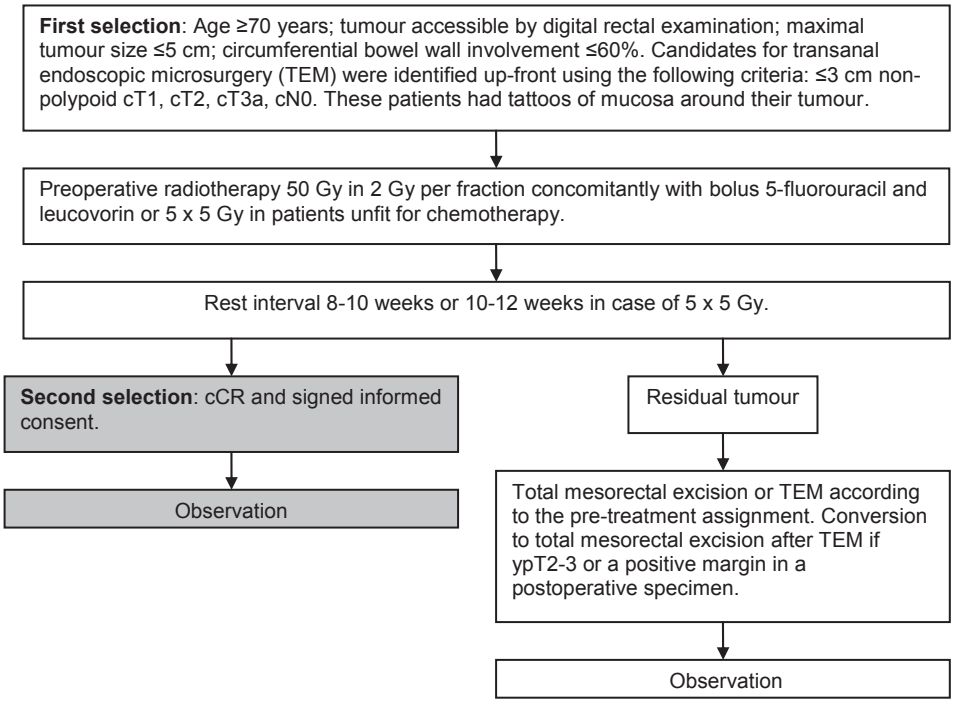

Figure 1. The trial profile. Patients on the experimental part of the trial were only those with clinical complete response (cCR) after radiotherapy – marked with grey. The patients with residual tumour received routine treatments according to our protocols.