Surgical Oncology 23 (2014) 211–221

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

Review

Short-course preoperative radiotherapy with immediate surgery versus long-course chemoradiation with delayed surgery in the treatment of rectal cancer: A systematic review and meta-analysis

Zhi-Rui Zhou [a, b], Shi-Xin Liu [c, *], Tian-Song Zhang [d], Ling-Xiao Chen [e], Jun Xia [f], Zhi-De Hu [g], Bo Li [h]

[a] Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai 200032, PR China
[b] Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, PR China
[c] Department of Radiation Oncology, Tumor Hospital of Jilin Province, No. 1018, Huguang Road, 130012 Changchun, PR China
[d] Internal Medicine of Traditional Chinese Medicine Department, Jing'an District Central Hospital of Shanghai, No. 259, Xikang Road, 200040 Shanghai, PR China
[e] Department of Orthopaedics, Tianjin Medical University General Hospital, 154 Anshan Road, Heping District, Tianjin, PR China
[f] Systematic Review Solutions Ltd, Nottingham NG72TU, UK
[g] Department of Laboratory Medicine, General Hospital of Ji'nan Military Command Region, 250031 Ji'nan, PR China
[h] Department of Digestive System, Xiyuan Hospital, China Academy of Traditional Chinese Medicine, Xiyuan No.1, 100091 Beijing, PR China

ARTICLE INFO

Article history:
Accepted 17 October 2014

Keywords:
Rectal cancer
Preoperative radiotherapy
Chemoradiotherapy
Meta-analysis

ABSTRACT

Background: Long-course chemoradiotherapy (LCRT) with delayed surgery or short-course radiotherapy (SCRT) with immediate surgery is probably the most frequent regimen in the treatment of rectal cancer. Debate is still going on whether SCRT or LCRT is more effective. So we performed this meta-analysis to evaluate the safety and efficacy of SCRT with immediate surgery versus LCRT with delayed surgery for the management of rectal cancer.

Methods: Literature were searched from PubMed, Embase, Web of science, Cochrane Library up to May, 2014. Quality of the randomized controlled trials (RCTs) was evaluated according to the Cochrane's risk of bias tool of RCT. RevMan 5.3 was used for statistical analysis. Pooled risk ratio (RR) and 95% confidence interval (CI) were calculated. Subgroup analysis and sensitivity analysis were employed to explore heterogeneity.

Results: 16 trials were included in the qualitative systematic review. 12 trials were included in meta-analyses. 4 of them were RCTs; other 8 were non-RCTs. Meta-analysis demonstrated that there were no significant differences in overall survival (OS), disease free survival (DFS), local recurrence rate (LRR), distant metastasis rate (DMR), sphincter preservation rate, R0 resection rate and late toxicity. Compared with SCRT, LCRT obviously increased pCR rate [RR = 0.15, 95%CI (0.08, 0.28), $P = 0.003$], while LCRT obviously increased the grade 3–4 acute toxicity [RR = 0.13, 95%CI (0.06, 0.28), $P < 0.00001$].

Conclusions: SCRT with immediate surgery is as effective as LCRT with delayed surgery for treatment of rectal cancer in terms of OS, DFS, LRR, DMR, Sphincter preservation rate, R0 resection rate and late toxicity. Though LCRT increased pCR rate, LCRT also increased acute toxicity compared with SCRT. SCRT is a better choice in centers with a long waiting list or lack of medical resources.

Contents

* Corresponding author. Tel.: +86 431 85879121; fax: +86 431 85871228.
E-mail address: liushixin1964@126.com (S.-X. Liu).

http://dx.doi.org/10.1016/j.suronc.2014.10.003
0960-7404/

Introduction

Several randomized controlled trials have demonstrated preoperative radiotherapy or chemoradiotherapy, as compared with postoperative chemoradiotherapy, improved local control and was associated with reduced toxicity and better compliance of radiotherapy [1–3]. In the preoperative treatment of resectable rectal cancer patients, long-course chemoradiotherapy (45–50 Gy in 25 fractions) with delayed surgery or short-course radiotherapy (25 Gy in 5 fractions) with immediate surgery are probably the most frequent regimens [1,4–6].

The Swedish Rectal Cancer Trial indicated that short-course preoperative radiotherapy (SCRT) reduced the risk of local recurrence rate (LRR) by half compared with surgery alone. In this trial, improved overall survival was also found [4]. The Dutch Rectal Cancer Trial demonstrated that short-course preoperative radiotherapy maintains its benefit when combined with the best surgical practice—total mesorectal excision (TME) [6]. The MRC (Medical Research Council) CR07 rectal trial, which compared short-course preoperative radiotherapy with selective postoperative chemoradiotherapy, provided further support for the short course regimen [2]. Long-course preoperative chemoradiotherapy (LCRT) of 50.4 Gy in 6 weeks and 5 days with concurrent chemotherapy has been widely practiced in the last 15 years. This regimen's superiority, in terms of local control, was demonstrated in the German rectal cancer trial, when compared with postoperative chemoradiotherapy [1,7].

Similar long-term overall survival, local control and late toxicity have been reported for both these regimens in several RCTs and controlled trials [8–13]. The benefit of the short-course schedule is a lower rate of acute radiation toxicity than with long-course chemoradiation [8,11,14]. In addition, short-course irradiation is less expensive and more convenient, especially in centers with a long waiting list or lack of medical resources [8]. On the other hand, long-course chemoradiation might be better than the short-course irradiation schedule at increasing pathologic complete response (pCR) and R0 resection rate [8,9,12], because the tumor bulk might be reduced before surgery. However, Debate is still going on whether SCRT or LCRT is more effective neoadjuvant modality to improve outcomes for rectal cancer [15–19]. So we performed this systematic review and meta-analysis to systematically analyze the safety and efficacy of SCRT with immediate surgery versus LCRT with delayed surgery as a modality for the management of rectal cancer.

Methods

Inclusion criteria

According to the PICOS principles, we define inclusion criteria: (1) Participants (P): All the patients that were diagnosed as rectal cancer using pathology and cytology were included in systematic review. Metastatic rectal cancer patients were excluded. The nationality was not limited, and all the patients did not have serious cardiopulmonary diseases and other severe basic diseases. (2) Interventions (I) and comparisons (C): Comparing the efficacy and safety of short-course radiotherapy with immediate surgery +/− adjuvant chemotherapy vs. long-course radiotherapy or chemoradiotherapy with delayed surgery +/− adjuvant chemotherapy in management of rectal cancer. Short course is not more than one week, and long course should be more than 4 weeks at least. Total dose of short-course was at least more than 20 Gy, and long-course was more than 45 Gy. (3) Outcomes (O): The following outcomes were evaluated: sphincter preservation rate, R0 resection rate, downstaging (T stage decreased), pCR rate, local recurrence rate (LRR), distant metastasis rate (DMR), disease free survival rate (DFS), overall survival rate (OS), grade 1–4 acute toxicity, grade 3–4 acute toxicity, grade 1–4 late toxicity, grade 3–4 late toxicity. (4) Study design (S): RCTs or non-randomized concurrent controlled trials or retrospectively controlled trials.