

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: <http://www.elsevier.com/locate/rpor>

Original research article

Gender-related significance of time interval between radiotherapy and surgery in hypofractionated preoperative radiotherapy for rectal cancer patients' survival



Anna Gasinska^{a,*}, Zbigniew Darasz^b, Agnieszka Adamczyk^a,
Jan Skolyszewski^c

^a Department of Applied Radiobiology, Maria Skłodowska – Curie Memorial Cancer Centre and Institute of Oncology, Cracow Branch, Poland

^b Department of Surgery, Maria Skłodowska – Curie Memorial Cancer Centre and Institute of Oncology, Cracow Branch, Poland

^c Department of Radiation Oncology, Maria Skłodowska – Curie Memorial Cancer Centre and Institute of Oncology, Cracow Branch, Poland

ARTICLE INFO

Article history:

Received 17 June 2015

Received in revised form

30 October 2015

Accepted 21 January 2016

Available online 20 February 2016

Keywords:

Rectal cancer

Break in the treatment

Preoperative radiotherapy

Patients' survival

Overall treatment time

ABSTRACT

Aim and background: An optimal break between radiotherapy (RT) and surgery in short-course of RT (SCRT) for locally advanced rectal cancer is not clearly established.

The aim of the study was to investigate the influence of the break in the preoperative SCRT and overall treatment time (OTT) for locally advanced rectal cancer patients (whole group and male/female subgroups) on patients overall survival (OS), recurrence-free survival (RFS), metastasis-free survival (MFS).

Materials and methods: 131 patients were treated with SCRT (5 Gy/5 days), followed by surgery 3–53 days later. Break was calculated as the time interval between the end of irradiation to surgery and OTT as time interval from the beginning of RT to surgery.

Results: Mean break was 21.5 (range 3–53.0) days and mean OTT was 26.5 (range 7–58.0) days. In univariate analysis, a break longer than 15 days and OTT >23 days were negative prognostic factors for OS for all patients, and particularly for the male patients' subgroup. RFS was non-significantly higher ($P=0.066$) for patients treated with a break ≤ 15 days and OTT ≤ 23 days ($P=0.099$), irrespectively of patients' sex. Patients treated with a break longer than 15 days and OTT >23 days had non-significantly lower level of MFS than those treated with a shorter break ($P=0.269$) and OTT ≤ 23 days ($P=0.498$).

Conclusion: In SCRT, a break in the treatment longer than 15 days, especially in the male patients subgroup, should be avoided, because it negatively affects patients' survival.

© 2016 Greater Poland Cancer Centre. Published by Elsevier Sp. z o.o. All rights reserved.

* Corresponding author at: Department of Applied Radiobiology, Maria Skłodowska – Curie Memorial Cancer Centre and Institute of Oncology, Cracow Branch, Garncarska 11, 31-115 Cracow, Poland. Tel.: +48 126348251; fax: +48 124226680.

E-mail address: z5gasins@cyf-kr.edu.pl (A. Gasinska).

<http://dx.doi.org/10.1016/j.rpor.2016.01.004>

1507-1367/© 2016 Greater Poland Cancer Centre. Published by Elsevier Sp. z o.o. All rights reserved.

1. Background

Currently, there is no consensus on the definition of early rectal cancer, and the optimal treatment for non-advanced rectal cancer remains a topic of debate.¹ Two modalities of preoperative radiotherapy (RT) have been used in treating localized (T2-4 and NO M0, locally resectable) rectal carcinoma: either short course RT (SCRT) with 5 × 5 Gy followed by immediate surgery or long course radio-chemotherapy with 50.4 Gy in 25–28 fractions with surgery after a 4–8 weeks' break.² The Stockholm III study addressed the question of the optimum interval between RT and surgery and compared the complication rate after SCRT and surgery given in one of the three schedules: SCRT with 25 Gy in 5-Gy fractions followed by surgery within 1 week, SCRT with 25 Gy in 5-Gy fractions followed by surgery 4–8 weeks later, or longer-course RT (25 × 2-Gy fractions) followed by surgery 4–8 weeks later. The study showed that SCRT and immediate surgery tended to be associated with more postoperative complications than the other schedules, and the authors suggest that surgery may be performed either within 5 days after the initiation of SCRT or 4 weeks afterwards.³

In radiotherapy, it is obvious that overall treatment time (OTT), that is the time interval from the beginning of RT to surgery is an important factor influencing the efficacy of RT.⁴ Therefore, in treatment comprising SCRT, OTT might have an influence on patients' survival, as the accelerated repopulation of tumor clonogenic cells surviving irradiation is considered to be the reason for reduced local control when treatment time is prolonged without dose compensation.⁵

In our earlier study,⁶ we suggested that in rectal cancer treated with SCRT and delayed surgery (longer than 15 days after RT), correlation between pretreatment Ki-67, Ku70, and BCL-2 proteins expression and pTNM (at surgery) might indicate tumor progression during the break.

2. Aim

The aim of the study was to check how break in the treatment and OTT may influence patient's survival. The results may provide the answer to the question whether in SCRT longer breaks in the treatment can be used.

3. Materials and methods

3.1. Patients

One-hundred and thirty-one patients with rectal carcinoma who underwent preoperative radiation between November 2003 and January 2006 were included in the study. Patients were qualified either for SCRT (5 Gy/5 days) and surgery about 1 week after RT or for SCRT and a 4-week interval before surgery. Because the interval between RT and surgery appeared to be longer than planned, a mean break in the treatment lasted from 3 to 53 days. Inclusion and exclusion criteria and detailed information on irradiation and surgery were given earlier.⁷ Postoperative chemotherapy (CMT; fluorouracil and levamisole) was given to 39 (29.8%) patients (29 males and

10 females). Tumors were classified according to the World Health Organization classification of intestinal carcinoma⁸ and staged according to the AJCC TNM 2002 classification.⁹ The protocol was approved by the local Ethical Committee of the Regional Medical Chamber in Cracow and each patient had given their written consent.

3.2. BED calculations

3.2.1. Defining parameters chosen

Biologically effective dose for tumor and early reactive tissues (BED₁₀) were calculated according the following formula¹⁰:

$$\text{BED}_{10} = nd(1 + d/\alpha/\beta) \quad (1)$$

where for $\alpha/\beta = 10$ Gy, d is the dose fraction and $n \times d$ is the total dose. For the calculation of biologically effective doses for late reacting tissues (BED₃), in the BED formula for $\alpha/\beta = 3$ Gy was used.

The normalized total dose (NTD), i.e. the dose given in standard fractionation using the dose per fraction of 2 Gy, which has the same effect (survival fraction) as the dose given with nonstandard dose per fraction (d), was calculated from the following equation:

$$\text{NTD} = D(\alpha/\beta + d)/(\alpha/\beta + 2),$$

where D denotes total physical dose given with a fraction size of d Gy.

3.3. Statistical methods

Statistical analysis was performed with STATISTICA vs.9. For determination of mean values for variables and standard errors of means (SE), descriptive statistics were used. Inter-group differences in the mean values were tested with one-way ANOVA test or Student's *t*-test. Associations between investigated categorical parameters and clinicopathological variables were evaluated by Pearson's Chi² test. Differences were considered significant at *P* value of <0.05. The survival function was estimated using the Kaplan-Meier method.¹¹ The difference in survival rates between groups was assessed by the log-rank test. Break between RT and surgery was calculated as the interval between the last day of RT to surgery. Survival was measured from surgery to death or last follow-up. In univariate analysis, 15 days for break between RT and surgery, and median OTT of 23 days were the first significant time-points in log-rank test, and therefore were used as cut-off points.

4. Results

A total of 131 patients were included in the study. Mean break in the treatment was 21.5 (range 3–53.0) days and mean OTT was 26.5 (range 7–58.0) days. There were 87 males and 44 females with a mean age for the entire group of 61.2 (range 30–82) years (Table 1). At the time of recruitment, no statistical differences between the two groups were found for prognostic factors such as age, tumor stage or histological grade, interval between RT and surgery, and type of surgery,

Download English Version:

<https://daneshyari.com/en/article/1855527>

Download Persian Version:

<https://daneshyari.com/article/1855527>

[Daneshyari.com](https://daneshyari.com)