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Prostate radiotherapy

3-D conformal radiotherapy of localized prostate cancer: A subgroup analysis of rectoscopic findings prior to radiotherapy and acute/late rectal side effects

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Abstract

***Background and purpose*: To identify endoscopic pathological findings prior to radiotherapy and a possible correlation with acute or chronic rectal side effects after three-dimensional conformal radiotherapy (3D-CRT) for prostate cancer.**

***Patients and methods*: Between 03/99 and 07/02, a total of 298 patients, who consented in a voluntary rectoscopy prior to radiotherapy were included into the analysis. Patients were treated with a total dose of either 70 or 74 Gy. Pathological rectoscopic findings like hemorrhoids, polyps or diverticula were documented. Acute and late rectal side effects were scored using the EORTC/RTOG score.**

***Results*: The most frequent pathological endosopic findings were hemorrhoids (35%), polyps (24%) and diverticula (13%). Rectal toxicity was mostly low to moderate. Grade 0/1 cumulative acute and late rectal side effects were 82 and 84%, grade 2 were 18 and 17%, respectively. We could not identify any correlation between preexisting pathological findings and rectal side effects by statistical analysis.**

***Conclusions*: There is no evidence that prostate cancer patients presenting with endoscopic verified pathological findings in the rectal mucosa at diagnosis are at an increased risk to develop rectal side effects when treated with 3D-CRT of the prostatic region.**

Keywords: Conformal radiotherapy; Prostate cancer; Rectal toxicity; Endoscopy

One limiting factor in 3D conformal radiotherapy for localized prostate cancer is the incidence of gastrointestinal side effects. According to the published series radiogen-induced proctitis occurs in a frequency between 5 and 20% [2,19,20,23,28]. Gastrointestinal side effects are considered to be related to the total dose applied and to the rectal volume irradiated with a certain dose [5,6,9,11,14,15,19,22–24,26]. The knowledge of other factors, beside this dose-volume effect, influencing rectal toxicity is therefore of great importance.

Pathologic changes of the rectal mucosa such as hemorrhoids, polyps and diverticula show an increasing prevalence with age [1,7,12,13]. Is there any evidence that prostate cancer patients presenting with pathological findings in the rectal mucosa at diagnosis are at an increased risk to develop rectal side effects when treated with 3D-CRT of the prostatic region?

Endoscopy is considered to give the best estimation of rectal mucosal damage which is not directly correlated to clinically evident proctitis. However, endoscopic signs of mucosal damage from radiotherapy of prostate cancer are described in a consistent way or correlated with gastrointestinal side effects only in a limited number of studies [18,28,29]. Therefore in our prospective multicenter phase II study a rectoscopy prior to irradiation and 12 and 24 months after radiotherapy was included. Aim of this evaluation was to analyze the correlation between acute and late gastrointestinal side effects and endoscopic findings prior to radiotherapy.

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Material and methods

Patients

Four hundred and eighty six patients with primary localized prostate cancer have been enrolled in the German–Austrian multicenter trial for primary 3D-CRT of localized prostate cancer from 03/1999 to 07/2002. The data of 298/486 (61%) patients accepting a voluntary rectoscopy prior to irradiation are available. Patients with stage T1 through T3, Nx/N0, and M0 histologically verified prostate cancer were eligible. According to the study protocol they were divided into three risk groups derived from tumor differentiation, pretreatment PSA-values and T-stage. A neo-adjuvant hormonal therapy was given in the intermediate and high risk group.

Endoscopy

Prior the start of radiation each patient had an endoscopic examination of the rectosigmoidal area up to 30–40 cm from the anal verge. A saline enema (Clysmol^{R}, 125 ml) was given 1 h before examination. The examination was done by internal specialists for gastroenterology in the different participating centers using a flexible endoscope. To enable a systematic description of rectoscopic findings, the documentation of each examination was performed using a descriptive graduation for endoscopic findings based on the terminology of the World Organization for Digestive Endoscopy (OMED) [4] and also according to the protocol published in detail by our group elsewhere [29]. Beside teleangiectasia, congested mucosa or ulceration—changes of the rectal mucosa expected primarily after radiotherapy—also additional findings like haemorrhoidal nodes, polyps, diverticula, increased number of vessels or papillae were documented. In some patients (patients with large or a high number of polyps), the internal specialist decided to perform an additional colonoscopy.

Radiotherapy

The CTV was defined based on series of CT and MRI slices and included the prostate in the low risk group and the prostate and the seminal vesicles, in the intermediate and high risk group. Treatment planning was performed so that more than 95% of the PTV received the prescribed dose. The low- and intermediate-risk group were treated up to a total dose of 70 Gy (2 Gy per fraction), the high-risk group to a dose of 74 Gy (2 Gy per fraction). A rectal balloon catheter was placed before each treatment for internal immobilisation and to reduce dose to the dorsal rectal wall [27]. All patients were treated with a four-field-box-technique with individualized blocks derived from beam's-eye-view.

Clinical

Acute rectal side effects were documented by use of the EORTC/RTOG score [3] before, during (first third/second third/third third of radiation) and 6 weeks after radiotherapy. Late rectal side effects were documented every 3 months in the first year, and every 6 months in the second and third year after radiotherapy and afterwards once a year using again EORTC/RTOG score [3].

Table 1
Rectoscopic findings prior to radiotherapy ($n=298$)

Haemorrhoidal nodes	104 (35%)
Polyps	70 (24%)
Diverticula	39 (13%)
Increased number of vessels	23 (8%)
Congested mucosa	16 (5%)
Papillae	6 (2%)
Teleangiectasia	3 (1%)
Patients with pathological findings	180 (60%)

Statistics

Statistical analyses were performed using SPSS 11.5 for windows. Maximum acute/late and actuarial late rectal side effects using Kaplan–Meier were evaluated. Correlations between maximum and actuarial side effects and pathological rectoscopic findings were performed using chi square test and Kaplan–Meier log-rank test, respectively. A value of $P<0.05$ (two sided test) was considered significant.

Results

Patients

The median age at time of radiotherapy was 70 years (52–84 years). The distribution of all 298 patients concerning T-stage was T1 (28%), T2 (56%) and T3 (16%). 74% were treated up to a dose of 70 Gy and 26% received 74 Gy.

Endoscopy

Rectoscopy prior to radiotherapy was performed in all 298 patients. The most frequent pathological findings were haemorrhoidal nodes, polyps and diverticula

(35/24/13%). Table 1 shows the findings in detail.

Clinical

The data of the maximum cumulative acute rectal toxicity which was mostly low to moderate are available for all 298 patients. Grade 2 GI side effects were found in only 18%. Concerning late rectal side effects the data are available for 274/298 (92%) patients with a median follow-up of 14,5 months (6–42 months). Grade 2 late rectal side effects were found in 45/274 (17%)—43 patients with rectal bleeding and 2 patients with grade 2 rectal toxicity had diarrhea and excessive rectal mucus (Table 2). Tables 3 and 4 show the distribution of maximum cumulative rectal side effects (acute/late) in correlation with the most frequent

Table 2
Distribution of maximum cumulative acute/late rectal side effects (EORTC/RTOG Score)

Rectal side effects	Acute	Chronic
Score 0	155 (52%)	199 (73%)
Score 1	90 (30%)	30 (11%)
Score 2	53 (18%)	45 (17%)
All patients	298 (100%)	274 (100%)