International Journal of Radiation Oncology biology • physics

www.redjournal.org

Clinical Investigation: Gynecologic Cancer

Predictors of Grade 3 or Higher Late Bowel Toxicity in Patients Undergoing Pelvic Radiation for Cervical Cancer: Results From a Prospective Study

Supriya Chopra, MD,* Tapas Dora, MD,* Anand.N. Chinnachamy, MD,† Biji Thomas, BSc,* Sadhna Kannan, MSc,‡ Reena Engineer, DNB,† Umesh Mahantshetty, MD,† Reena Phurailatpam, DRP,* Siji N. Paul, DRP,* and Shyam Kishore Shrivastava, MD†

**Department of Radiation Oncology, Advanced Centre for Treatment Research and Education in Cancer (ACTREC), Tata Memorial Centre, Kharghar, Navi Mumbai, Maharashtra, India; †Department of Radiation Oncology, Tata Memorial Hospital, Tata Memorial Centre, Parel, Mumbai, Maharashtra, India; and ‡Epidemiology and Clinical Trials Unit, Advanced Centre for Treatment Research and Education in Cancer (ACTREC), Tata Memorial Centre, Kharghar, Navi Mumbai, Maharashtra, India*

Received Jul 23, 2013, and in revised form Sep 19, 2013. Accepted for publication Nov 8, 2013.

Summary

This study investigated the correlation between bowel dose volume parameters and grade 3 or higher late toxicity in women undergoing postoperative radiation for cervical cancer. The volume of the small and large bowel receiving 15 Gy (V15) was identified as an independent predictive factor. Restricting small bowel and large bowel volume to less than 275 cc and 250 cc, respectively, can reduce the incidence of severe late

Purpose: The present study investigates relationship between dose−volume parameters and severe bowel toxicity after postoperative radiation treatment (PORT) for cervical cancer.
Methods and Materials: From June 2010 to December 2012, a total of 71 patients undergoing PORT were included. Small bowel (SB) and large bowel (LB) loops were contoured 2 cm above the target volume. The volume of SB and LB that received 15 Gy, 30 Gy, and 40 Gy was calculated (V15 SB, V15 LB, V30 SB, V30 LB, V40 SB, V 40 LB). On follow-up, bowel toxicity was scored using Common Terminology Criteria for Adverse Events (CTCAE), version 3.0. A reciever operating characteristic (ROC) curve identified volume thresholds that predicted for grade 3 or higher toxicity with highest specificity. All data was dichotomized across these identified cut-off values. Univariate and multivariate analysis was performed using SPSS, version 15.
Results: The median patient age was 47 years (range, 35-65 years). Of the 71 patients, 46 received image-guided intensity modulated radiation therapy, and 25 received conformal radiation (50 Gy in 25 fractions for 5 weeks). Overall, 63 of 71 patients received concurrent chemotherapy. On a median follow-up of 18 months (range, 8-29 months), grade 2 or higher bowel toxicity was seen in 22 of 71 patients (30.9%) and grade 3 or higher bowel toxicity was seen in 9 patients (12.6%). On univariate analysis, V15 SB <275 cc ($P=.01$), V30 SB <190 cc ($P=.02$), V40 SB <150 cc ($P=.01$), and V15 LB <250 cc ($P=.03$), and V40 LB <90 cc ($P=.04$) predicted for absence of grade 3 or higher toxicity. No other patient- or treatment-related factors were statistically significant. On multivariate analysis, only V15 SB ($P=.002$) and V15 LB ($P=.03$) were statistically significant.

Reprint requests to: Supriya Chopra, MD, DNB, Associate Professor, Radiation Oncology, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai, India 410210. Tel: 912227405113, 912224177147.; E-mail: schopra@actrec.gov.in

Conflict of interest: none.

Acknowledgments—The authors acknowledge the Department of Atomic Energy Clinical Trials Centre (DAE-CTC) for research funding. T.D. and B.T. receive salary support through DAECTC research funding.

Int J Radiation Oncol Biol Phys, Vol. 88, No. 3, pp. 630−635, 2014
0360-3016/$ - see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ijrobp.2013.11.214

bowel toxicity to less than 5%.

Conclusions: V 15 Gy SB and LB are independent predictors of late grade 3 or higher toxicity. Restricting V15 SB and V15 LB to <275 cc and <250 cc can reduce grade 3 or higher toxicity to less than 5%. © 2014 Elsevier Inc.

Introduction

Adjuvant pelvic radiation with or without chemotherapy is recommended in patients with intermediate or high risk factors after a Wertheim operation. Postoperative radiation therapy (PORT) reduces the rate of both local (13.9% vs 20.7%) and distant (2.9% vs 8.6%) recurrence (1). Even higher benefit is observed in patients with high risk factors (1, 2). Surgical extirpation of the uterus results in adhesions of bowel loop and altered microvasculature increasing vulnerability of bowel to the adverse effects of PORT. These changes may severely impair intestinal function if stricture formation occurs (3), thereby leading to serious gastrointestinal (GI) sequelae (4-6). A retrospective study reported a 16.4% incidence of late grade 2 to 4 bowel toxicity among patients treated with PORT and brachytherapy. A pelvic dose of >54 Gy and age >60 years were identified as risk factors for late bowel toxicity (7). Platinum-based chemoradiation (8-12) further adds to toxicity. Clinically meaningful data can also be derived from PORT studies for rectal cancer. Long-term follow-up of the Uppasla trial reported a 6% incidence of obstruction after surgery alone and 11% after postoperative radiation (13). An overview undertaken by Kavanagh et al reported incidence of late small bowel (SB) perforation of the order of 2% to 9% with 50 Gy of pelvic radiation therapy (14). However, the risk may be increased in patients undergoing PORT with brachytherapy and chemotherapy.

Intensity modulated radiation therapy (IMRT) minimizes the volumes of irradiated SB (14, 15). A statistically significant correlation has been demonstrated between volume of irradiated bowel and severe acute toxicity (16, 17). Although there are recent studies (18) that correlate acute toxicity with irradiated bowel volume, there is a paucity of data regarding correlation of bowel dose–volume histogram (DVH) parameters with late toxicity. In the era of increasing use of conformal or IMRT, it will be worthwhile to evaluate correlation of bowel parameters with late bowel toxicity and develop DVH recommendations for minimizing bowel toxicity.

Methods and Materials

From January 2010 to December 2012, all patients undergoing adjuvant or salvage pelvic chemoradiation were included. All patients signed informed consent forms and were treated within the context of institutional review board-approved clinical trials. A uniform methodology for simulation and target delineation was followed (19-21).

Simulation

All patients emptied the bladder and then consumed 500 mL of water. Imaging was done after 30 minutes. Patients were positioned supine with arms above the head. Three radio-opaque fiducial markers were placed at laser intersection points on the lower abdomen, and a radio-opaque marker was placed at the vaginal introitus while obtaining the scan. A contrast-enhanced computed tomography (CECT) scan was obtained from the diaphragm to the mid-thigh at an interslice thickness of 3 mm. The image data sets were transferred to Oncentra treatment planning system (version 4.1).

Target delineation

Wherever present, gross residual disease was contoured. In patients with no gross residual disease, the vaginal apex was identified with the help of silver markers placed before simulation. The vaginal apex or residual gross tumor volume was expanded anteriorly by 1.5 cm, superiorly by 1 cm, posteriorly until the mesorectal fascia, and laterally until the pelvic muscles. In patients with no residual disease, one-half of the vagina was included, and in patients with gross residual disease, a caudal margin of 2 to 2.5 cm was used to generate the clinical target volume (CTV). An additional 1-cm margin (7 mm posteriorly) was used to generate a planning target volume (PTV) for the primary. Nodal delineation was done using standard guidelines (22). In addition, lymphoceles and gross lymph nodes were included in the nodal CTV. Nodal CTV was expanded by 5 mm to generate a nodal PTV. A Boolean operation was used to perform the union of nodal and primary PTV to generate the final PTV. All organs at risk (OARs) except the bowel were delineated using standard guidelines (23). Bowel delineation included contouring individual bowel loops for the small as well as the large bowel (LB). The bowel was delineated up to 2 cm above the PTV.

Radiation planning

All patients underwent conformal or image-guided intensity-modulated radiation therapy (IG-IMRT) planning. Those undergoing conformal radiation received treatment with a 4-field, multileaf collimeter shaped box field technique, and IG-IMRT treatment was executed using tomotherapy. During plan approval, all care was taken to cover 95% of the target with 95% of the prescription dose. Care was also taken to reduce the bowel dose through beam weighting during conformal planning. During IMRT planning, dose constraints were used to restrict the volume of SB receiving 15 and 40 Gy (V15/V40 SB) to <190 cc and <100 cc, respectively. All patients received 50 Gy in 25 fractions for 5 weeks with or without weekly cisplatin (40 mg/m^2). This was followed by brachytherapy. For the purpose of the present study, for each patient the absolute volume of SB and LB and that receiving 15 Gy (V15), 30 Gy (V30), and 40 Gy (V40) was recorded. All patients were treated with a full bladder regimen. For those undergoing conformal treatment, once weekly electronic portal or cone beam imaging was performed to ensure bony match. Patients undergoing IG-IMRT with tomotherapy underwent a daily pretreatment megavoltage CT (MVCT) scan.

Download English Version:

https://daneshyari.com/en/article/8220201

Download Persian Version:

https://daneshyari.com/article/8220201

Daneshyari.com