Cancer Association of South Africa (CANSA)

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Fact Sheet
on
Rectal Bleeding Following Radiation Therapy for Prostate Cancer

Introduction

According to **Takemoto, et al.,** (2012) chronic rectal bleeding is one of the most common complications of radiation therapy for prostate cancer.

[Picture Credit: Radiation Prostate Cancer]

This view is shared by various oncologists and researchers.

The aetiology of radiation proctitis is considered to be chronic mucosal ischemia caused by tissue fibrosis and obliterative endarteritis. The injured rectal wall can bleed easily, occasionally leading to a chronic ischaemic state and causing episodes of severe rectal bleeding.

Takemoto, S., Shibamoto, Y., Ayakawa, S., Nagain, A., Hayashi, A., Ogino, H., Baba, F., Yanagi, T., Sugie, C., Kataoka, H. & Mimura, M. 2012.

Background:

Radiation proctitis after intensity-modulated radiation therapy (IMRT) differs from that seen after pelvic irradiation in that this adverse event is a result of high-dose radiation to a very small area in the rectum. We evaluated the results of treatment for hemorrhagic proctitis after IMRT for prostate cancer.

Methods:

Between November 2004 and February 2010, 403 patients with prostate cancer were treated with IMRT at 2 institutions. Among these patients, 64 patients who developed late rectal bleeding were evaluated. Forty patients had received IMRT using a linear accelerator and 24 by tomotherapy. Their median age was 72 years. Each patient was assessed clinically and/or endoscopically. Depending on the severity, steroid suppositories or enemas were administered up to twice daily and Argon plasma coagulation (APC) was performed up to 3 times. Response to treatment was evaluated using the Rectal Bleeding Score (RBS), which is the sum of Frequency Score (graded from 1 to 3 by frequency of bleeding) and Amount Score (graded from 1 to 3 by amount of bleeding). Stoppage of bleeding over 3 months was scored as RBS 1.

Results:

The median follow-up period for treatment of rectal bleeding was 35 months (range, 12–69 months). Grade of bleeding was 1 in 31 patients, 2 in 26, and 3 in 7. Nineteen of 45 patients (42%) observed without treatment showed improvement and bleeding stopped in 17 (38%), although mean RBS did not change significantly.

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Eighteen of 29 patients (62%) treated with steroid suppositories or enemas showed improvement (mean RBS, from 4.1 ± 1.0 to 3.0 ± 1.8, $p = 0.003$) and bleeding stopped in 9 (31%). One patient treated with steroid enema 0.5-2 times a day for 12 months developed septic shock and died of multiple organ failure. All 12 patients treated with APC showed improvement (mean RBS, 4.7 ± 1.2 to 2.3 ± 1.4, $p < 0.001$) and bleeding stopped in 5 (42%).

Conclusions:

After adequate periods of observation, steroid suppositories/enemas are expected to be effective. However, short duration of administration with appropriate dosage should be appropriate. Even when patients have no response to pharmacotherapy, APC is effective.

Lint, D.C., Chen, K.S., Boit, R.M., Beriwal, S. & Smith, R.P. 2019.

Purpose: There is limited long-term data on outcome and side effects of Cs-131 prostate brachytherapy and minimal patient-reported data on rectal bleeding with any isotope. We aimed to describe the incidence, prevalence, and predictors of late patient-reported rectal bleeding after Cs-131 brachytherapy.

Methods and materials: We reviewed a prospectively collected database of 620 men treated with Cs-131 prostate brachytherapy. Of 620 patients, 390 (62.9%) received brachytherapy as monotherapy; the remainder received combination therapy with external beam radiation therapy (EBRT). Patients were administered Expanded Prostate Cancer Index Composite questionnaires preoperatively and postoperatively at each follow-up visit. The primary outcome was late rectal bleeding, defined as rectal bleeding reported at the 6-month follow-up or later. Clinically significant rectal bleeding was defined as occurring more than "rarely," and clinically significant bother from rectal bleeding was defined as considering bleeding more than a "very small problem." Univariate and multivariate Cox regression were performed to identify factors predictive for rectal bleeding.

Results: With a median follow-up time of 48 months, the cumulative incidence of clinically significant late rectal bleeding was 12.4%, with 15.2% reporting clinically significant bother from bleeding. At the time of last follow-up, the prevalence of clinically significant rectal bleeding and bother were 4.0% and 4.7%, respectively. On univariate analysis, acute clinically significant rectal bleeding, defined as occurring within the first 6 months (P = .001) and combination therapy with EBRT (P = .001) predicted for clinically significant late rectal bleeding. On multivariate analysis, both EBRT (P = .001; hazard ratio, 2.50; 95% confidence interval, 1.58-3.94) and acute rectal bleeding (P < .001; hazard ratio, 3.11; 95% confidence interval, 1.75-5.53) remained significant predictors for late rectal bleeding.

Conclusions: Prostate brachytherapy with Cs-131 is well tolerated in the long term. Although the incidence of clinically significant patient-reported late rectal bleeding was 12.4%, the prevalence at last follow-up was only 4.0%, suggesting that this problem tends to resolve.

Risk Factors for Rectal Bleeding Following Radiation Therapy for Prostate Cancer

Various researchers list risk factors for rectal bleeding following radiation therapy for prostate cancer. Brennan, Nicholson, & Kelly (2017), also list several possible risk factors for rectal bleeding following radiation therapy for prostate cancer have been identified. They list the following risk factors:

- Adjuvant external beam radiation therapy, brachytherapy of both
- Antiplatelet (AP) or anticoagulant (AC) medications
- Hypertension
- Hypercholesterolaemia
- Diabetes mellitus
- Ischaemic heart disease (IHD)

- Peripheral vascular disease (PVD)
- History of stroke

Brennan, V.S., Nicholson, J. & Kelly, P.J. 2017.

Purpose/Objective(s)

Rectal bleeding is a common late side effect following prostate radiotherapy that can significantly impair quality of life. Additional investigations and treatments are also burdensome on healthcare resources. We examined potential risk factors and treatment characteristics of a group of patients who experienced late rectal bleeding following prostate radiotherapy. We hypothesize that a predictive model could be generated to predict a patient's subsequent risk of bleeding incorporating these potential risk factors.

Materials/Methods

We identified 80 patients with rectal bleeding who underwent prostate radiotherapy between 2011 and 2016. We included those treated definitively or adjuvantly with external beam radiotherapy (EBRT), brachytherapy or both. Severity was graded according to the RTOG /EORTC Late Radiation Morbidity Scoring System. We retrospectively evaluated patient records from their baseline and follow-up visits and recorded use of antiplatelet(AP) or anticoagulant(AC) medications. We also recorded the presence of the following vascular risk factors: hypertension, hypercholesterolaemia, diabetes mellitus or ischaemic heart disease (IHD), peripheral vascular disease (PVD) or a history of stroke. The EBRT plans were evaluated with reference to D_{2cc}, V_{65Gy} and PTV volume(cc). For statistical purposes patients were divided into 2 groups; Group A containing patients with grades 1-2 rectal bleeding and Group B containing grades 3-4. Groups were compared for statistical significance using Chi-squared tests and Mann-Whitney U tests.

Results

42 patients (52.5%) were on AP/AC medication. There were 57 patients with Grades 1-2 rectal bleeding and 23 with Grades 3-4. Proportionally more patients in Group B were on AP/AC medication compared with Group A (65.2% versus 47.4%), however this was not statistically significant (p=0.15). There was a high prevalence of cardiovascular risk factors in both groups. 22 patients had ≥3 cardiovascular risk factors representing 24.6% of Group A and 34.8% of Group B, but this was not statistically significant (p=0.35). There were no statistically significant differences in rectal doses D_{2cc}, V_{65Gy}or PTV volume between the groups.

Conclusion

The majority of patients experiencing late rectal bleeding were on AP/AC agents. The highest prevalence of AP/AC use was in those with ≥grade 3 bleeding. Patients with more vascular risk factors had numerically higher rates of high grade rectal bleeding. We did not identify any significant difference between the groups in terms of radiation dose to the rectum. We hypothesize that use of AP/AC agents and cardiovascular comorbidity are risk factors for late rectal bleeding following prostate radiotherapy. This requires prospective validation.

The type and severity of side effects one may have with external beam radiation for prostate cancer may depend on the dose and on the amount of healthy tissue that is exposed to the radiation. Most side effects are temporary, can be controlled and generally improve over time once treatment has ended.

Newer technologies, such as intensity-modulated radiation therapy (IMRT) or proton beam, deliver the highest dose of radiation to the target while sparing surrounding healthy tissue. This helps minimize side effects of external beam radiation treatment.

Potential side effects of external beam radiation therapy for prostate cancer may include:

- Frequent urination
- Difficult or painful urination
- Blood in the urine

- Urinary leakage
- Abdominal cramping
- Diarrhoea
- Painful bowel movements
- Rectal bleeding
- Rectal leaking
- Fatigue
- Sexual dysfunction, including diminished erectile function or decrease in the volume of semen
- Skin reactions (similar to a sunburn)
- Secondary cancers in the region of the radiation

Most of the side effects are mild and tolerable. Some side effects may develop months to years later. Serious late side effects are uncommon. Ask your doctor about potential side effects, both short- and long-term, that may occur during and after your treatment.

Reducing the Risk of Rectal Bleeding After Radiotherapy for Prostate Cancer
There are means whereby the risk of rectal bleeding after radiotherapy for prostate cancer can be reduced.

Serrano, N.A., Kalman, N.S. & Anscher, M.S. 2017.
"Dose escalation is now the standard of care for the treatment of prostate cancer with radiation therapy. However, the rectum tends to be the dose-limiting structure when treating prostate cancer, given its close proximity. Early and late toxicities can occur when the rectum receives large doses of radiation therapy. New technologies allow for prevention of these toxicities. In this review, we examine the evidence that supports various dose constraints employed to prevent these rectal injuries from occurring. We also examine the use of intensity-modulated radiation therapy and how this compares to older radiation therapy techniques that allow for further sparing of the rectum during a radiation therapy course. We then review the literature on endorectal balloons and the effects of their daily use throughout a radiation therapy course. Tissue spacers are now being investigated in greater detail; these devices are injected into the rectoprostatic fascia to physically increase the distance between the prostate and the anterior rectal wall. Last, we review the use of systemic drugs, specifically statin medications and antihypertensives, as well as their impact on rectal toxicity."

Prostate Cancer Foundation. No Date.
"Solid waste that is excreted from the body moves slowly down the intestines, and, under normal circumstances, the resultant stool exits through the rectum and then the anus. Damage to the rectum can result in bowel problems, including rectal bleeding, diarrhea, or urgency.
"Radiation therapy is targeted to the prostate, but the rectum sits right behind the prostate. With modern radiation therapy (IMRT or IGRT), it is very rare to have moderate or severe bowel problems. During radiation therapy you may experience softer stools and, rarely, diarrhea (less than 10% of men report this side effect). These symptoms typically resolve within a few weeks of completing radiation therapy. With modern radiation, only 2% to 3% of men will have bothersome rectal bleeding that continues months or years after treatment. Be sure to discuss with your doctor the types of radiation therapy that are appropriate for you, as older forms of radiation therapy (called 3D conformal) can increase rectal side effects significantly.
"Overall, it is more common with radiation therapy to have slightly lower rates of overall bowel function compared with surgery. This is temporary and largely resolves by 6 to 12 months post-treatment.

"As of 2016, select centers have begun to use an approved device called SpaceOAR, a gel that is injected between the prostate and the rectum in men for whom there is major concern of rectal irritation. It has been shown to further reduce the chance of rectal side effects in some men."

Grading of Late Rectal Bleeding Following Radiotherapy for Prostate Cancer
According to Phan, et al., (200(0 late rectal bleeding following radiotherapy for prostate cancer is graded as follows:

Grade	Description	Criteria
Grade 1	Mild and self-limiting	Minimal, infrequent bleeding or clear mucous discharge, rectal discomfort not requiring analgesics, loose stools not requiring medications.
Grade 2	Managed conservatively, lifestyle (performance status) not affected	Intermittent rectal bleeding not requiring regular use of pads, erythema of rectal lining on proctoscopy, diarrhoea requiring medications.
Grade 3	Severe, alters patient lifestyle	Rectal bleeding requiring regular use of pads and minor surgical intervention, rectal pain requiring narcotics, rectal ulceration
Grade 4	Life-threatening and disabling	Bowel obstruction, fistula formation, bleeding requiring hospitalisation, surgical intervention required

Phan, J., Swanson, D.A., Levy, L.B., Kudchadker, R.J., Bruno, T.L. & Frank, S.J. 2009.

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The **South African National Clinical Trials Register** provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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