Global Journal of Medical Research: F
Diseases
Volume 21 Issue 5 Version 1.0 Year 2021
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Urinary and Digestive Toxicities of 3D Conformal Radiotherapy of Localized Prostate Cancer at the Pointe a Pitre University Hospital in Guadeloupe

By Ibrahima Thiam, Kanta Ka, Boucar Ndong, El Hadj Amadou Sall, Ousseynou Sarr, Mahomed Yessoufou, Awa Sadikh Badiane & Papa Macoumba Gaye

National Hospital Universitary Center Dalal Jamm

Abstract- *Introduction:* At present, despite the advent of innovative methods such as IMRT, which improves therapeutic performance while reducing toxicity, RC3D is still widely used, especially in developing countries. The objective of this work was to evaluate the urinary and digestive toxicities of RC3D on prostate cancers located at the Pointe à Pitre University Hospital in Guadeloupe in order to position this technique in the therapeutic arsenal.

Materials and methods: We conducted a retrospective study of 29 patients with localized prostate cancer treated with RC3D. The endpoint was urinary and digestive toxicities.

Keywords: *toxicities, radiotherapy, cancer, prostate.*

GJMR-F Classification: *NLMC Code: WJ 752*

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Ibrahima Thiam [α], Kanta Ka [σ], Boucar Ndong [ρ], El Hadj Amadou Sall [ω], Ousseynou Sarr [¥], Mahomed Yessoufou [§], Awa Sadikh Badiane [χ] & Papa Macoumba Gaye [ν]

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Materials and methods: We conducted a retrospective study of 29 patients with localized prostate cancer treated with RC3D. The endpoint was urinary and digestive toxicities.

Results: Twenty-nine patients were enrolled. Their median age was 75 years. All patients were treated with RC3D +/- hormone therapy. Toxicities were assessed according to RTOG criteria. Acute toxicity was defined as all toxicities occurring during treatment and even 3 months after the end of treatment. Toxicities occurring beyond 3 months after treatment were considered late. Grade 1 acute bladder toxicity was found in 7 patients (24.14%), grade 2 in 1 patient (3.45%). Grade 1 acute rectal toxicity was found in 7 patients (24.14%). As for late bladder toxicity, it was found for grade 1 in 5 patients (17.24%), grade 2 in 3 patients (10.34%) and finally for grade 3 in 1 patient (3.45%). As for late rectal toxicity, grade 2 was found in 3 patients (10.34%) and grade 3 in 1 patient.

Conclusion: RC3D offers acceptable toxicities. However, for dose escalation with minimisation of toxicities, IMRT is better than 3D-CRT.

Keywords: toxicities, radiotherapy, cancer, prostate.

Author α ω χ: Radiotherapy Department of the Institut Joliot Curie, Dakar, Senegal. e-mails: ibathiam29@gmail.com, awasadikh@gmail.com, asall.jr@gmail.com
Corresponding Author σ: Radiotherapy Department, National Hospital Universitary Center Dalal Jamm, Guédiawaye, Senegal. e-mail: ka.kanta04@gmail.com
Author ¥ ν: Radiotherapy Department, National Hospital Universitary Center Dalal Jamm, Guédiawaye, Senegal. e-mail: weuzbidoc@gmail.com
Author ρ: Biophysics Laboratory, Cheikh Anta Diop University, Dakar, Senegal. e-mail: ndongboucar73@yahoo.fr
Author ρ: Nuclear Medicine Department of the National Hospital Universitary Center DalalJamm, Guédiawaye, Senegal.
Author ν: Cheikh Anta Diop University, Dakar, Senegal. e-mail: macoumba.gaye@gmail.com
Author §: Radiotherapy Department of the National Hospital Universitary Center Hassan II, Fez, Morocco. e-mail: akandeolatoundji@gmail.com

I. Introduction

Prostate cancer is the second most diagnosed cancer in men after lung cancer with 13.7% of cases [1]. Its incidence is high in Guadeloupe [2]. The treatment of prostate cancer is multidisciplinary, with radiotherapy and surgery as the main curative methods.

Radiotherapy is said to be conformal when the dose of ionising radiation used is delivered homogeneously to a precisely defined tumor volume while sparing healthy tissue and surrounding organs as much as possible. This is achieved through initial three-dimensional imaging for location and repositioning. The precise calculation of the dose to be delivered is achieved through computer-controlled multi-blade collimators.

Thanks to the progress made by conformal radiotherapy, the results obtained are becoming similar in terms of disease control to those of surgery, as shown by several comparative series. Radiotherapy has therefore become an essential technique in the treatment of prostate cancer despite its complications, notably urinary and digestive [3]. In this paper, we evaluate these complications that arise during the management of localised prostate cancer treated with 3D conformal radiotherapy.

II. Patients and Method

a) Patients

This was a descriptive, retrospective study that took place at the Radiotherapy Department of the Pointe à Pitre University Hospital in Guadeloupe, carried out over a period of one year (January 2015 to December 2015).

A total of 29 patients consulting for localized prostate cancer with a negative distant extension assessment were treated with 3D radiotherapy plus or minus hormone therapy. These patients had not received any previous specific treatment and their characteristics are summarised in Table I.

b) Method

Data were collected using archived medical records, from the Varian Aria software and Easily from the CHU Guadeloupe. A data collection form was drawn up for this purpose.

The data were entered and analysed on Epi info 7 on Microsoft Excel 2007. Histograms and other figures were produced with Microsoft Excel 2007.

III. Results

The median age of the patients was 75 years. The most common comorbidity was hypertension, which was found in 23 patients (79.31%). The diagnosis was made on the basis of urinary symptoms in 10 patients (34%). They were generally in good general condition. The median PSA level was 12 ng/ml with extremes of 3.05 and 79 ng/ml. Histological examination revealed adenocarcinoma in all patients. The Gleason score was heterogeneous with a score of 6 (3+3) in 6 patients (20, 69%), a score of 7 (3+4) in 12 patients (41, 38%) and another score of 7 (4+3) in 11 patients (37, 93%).

A loco-regional extension assessment by MRI was performed in 26 patients (89, 66%) and contraindicated in 3 patients. On imaging, we found T3a in 5 patients (19, 23%), T3b in 4 patients (15, 38%) and lymph node involvement in 1 patient (3, 8%). Thoracoabdomino-pelvic CT was performed in 9 patients (31.03%) and scintigraphy in 25 patients (86.21%).

The D'AMICO classification was established for all patients. It is a major criterion in the therapeutic decision.

Thus, 3 patients (10.34%) were classified as low risk, 12 patients (41.38%) as intermediate risk and 14 patients (48.28%) as high risk

Among the patients classified as intermediate risk, 7 were of favourable intermediate risk and 5 unfavourable intermediate.

All our patients had received 3D conformal radiotherapy for curative purposes. It was associated or not with hormone therapy. The time to treatment was defined as the time from the date of diagnosis to the start of radiotherapy.

The median time was 5.7 months (2.3-23) and the mean time was 6.4 months.

Pelvic irradiation was performed in 15 patients (51.72%). The median total dose delivered was 74 Gy, with a mean dose of 73.79 Gy and extremes of 70 Gy for the minimum and 76 Gy for the maximum.

In all our patients, conventional fractionation was used, i.e. 2 Gy per fraction, 5 days a week.

Hormone therapy was combined with radiotherapy in 17 patients (58.62%). All patients in the D'AMICO high-risk group had received long hormonal therapy and 3 patients in the intermediate-risk group had received short hormonal therapy.

The median follow-up after radiotherapy was 56 months (28-66 months). The median follow-up was 63 months (27.5-74.3 months).

Toxicities were assessed according to the RTOG criteria. Acute toxicity was defined as all toxicities occurring during treatment and up to 3 months after the end of treatment and all those occurring beyond 3 months were late. Thus, acute bladder toxicity was found in 7 patients (24.14%) with grade 1 acute toxicity and 1 patient (3.45%) with grade 2 acute toxicity. For acute rectal toxicity, all the patients had tolerated the treatment well in terms of digestion, with grade 1 symptoms in 7 patients (24.14%), then for late bladder toxicity grade 1, we found 5 patients (17.24%), 3 patients (10.34%) for grade 2 and 1 patient for grade 3, i.e. 3.45%. And finally, for late rectal toxicity grade 2, we found 3 patients (10.34%) and 1 patient grade 3.

IV. Discussion

The constant progress of irradiation techniques has mainly allowed an increase in the dose to the target volumes and a reduction of the dose to the organs at risk. Dearnaley et al. in a randomised study reported a reduction in GI toxicity in favour of 3DR compared to conventional radiotherapy with 56% grade 1 rectitis versus 37% and 12% versus 3% for grade 2 [4]. Koper et al, with the same comparison, found less intestinal toxicity, especially in the anus, in patients treated with RC3D [5].

Pelvic irradiation is a much debated topic with conflicting results from several retrospective studies, its toxicity remains quite acceptable [3].

Several randomised studies have shown that the risk of rectal toxicity was greater when a high dose of radiation (78-80 Gy) was delivered to the prostate compared to a standard dose (70 Gy) [6,7].

Regarding urinary toxicity, most randomised studies comparing a "standard" dose (70 Gy) with a high dose (78-80 Gy) did not find a significant increase in urinary toxicity, except for the French Gétug study 06 [6-9]. The lack of a clear conclusion regarding urinary toxicity may have several explanations. The main urinary manifestations seem to be of urethral rather than bladder origin. The urethra is consistently included in the high-dose volume treated and exceptionally delineated as such (10).

The median dose in our series was 74 Gy and 51.72% of patients had received pelvic irradiation.

The radiotherapy was well tolerated by the patients, no acute urinary or digestive toxicity of grade > 2 was noted in our series as in the study by Peeters et al [9]. Indeed, acute urinary toxicity grade 1 and 2 were respectively 24.14% and 3.45% and digestive toxicity was grade 1 in 10 patients (34.48%). These results are lower than those reported by Pollack, Beckendorf, Peeters and Elie Nasr which could be explained by the

small number of patients (8,9,11,12). Late toxicity was relatively lower than in the literature (Table 2-3).

Intensity-modulated conformal radiotherapy significantly reduces late grade 2 GI toxicity without impacting on urinary toxicity with dose escalation [13]. IMRT provides better coverage of the target volume with good sparing of organs at risk, particularly for the rectum according to the study by Pascal Fenoglietto et al [14]. Wang-Chesebro et al. demonstrated with pelvic IMRT a dose reduction in the bladder, V45 Gy (volume receiving 45 Gy) of 90%, 54% for the rectum V45 Gy and 54% of the small bowel V45 Gy compared to three-dimensional conformal radiotherapy [15].

V. Conclusion

Despite the good results obtained with RC3D, intensity modulated radiotherapy (IMRT and VMAT) with rigorous verification of the treatment position is the indicated technique for the treatment of prostate cancers. It allows dose escalation to target volumes with acceptable toxicity.

Table 1: Patient characteristics

Characteristics of patients	Headcount (percent)
Median age (years)	75 (54 - 83)
HTA	23 (79.31%)
Diabetes	12 (41.38%)
Heart disease	3 (10.34%)
CRI	1 (3.45%)
Systematic screening	19 (65.52%)
Urinary signs	10 (34.48%)
Performance status 0 1 2	 20 (69%) 8 (28%) 1 (3%)
TR abnormal	15 (51.72%)
Median PSA (ng/ml)	12 (3.05 - 79)
Gleason -6 (3 + 3) -7 (3 + 4) -7 (4 + 3)	 6 (20.69%) 12 (41.38%) 11 (37.93%)
Classification of D'AMICO -High risk -Low risk -Middle risk	 14 (48.28% 3 (10.34%) 12 (41.38%)

Table 2: Frequency of urinary toxicity in the literature

	Number of patients	Dose (Gy)	Acute urinary toxicity	Median follow-up (month)	Late urinary toxicity
Beckendorf et al (8)	306	70 vs 80	G1 44% vs 42% G2 31% vs 30% G3 5% vs 7%	57	G1 22% vs 27% G2 8% vs 16% G3 2% vs 1%
Pollack et al (11)	301	70 vs 80	G1 43% vs 42% G2 31% vs 23% G3 3% vs 5%	72	≥G2 10% vs 10%
Peeters et al (9)	669	68 vs 78	G1 40% vs 42% G2 13% vs 13%	36 84	≥G2 29% vs 30% ≥G2 41% vs 40%
Elie Nasr(12)	131	66-74	G1 31,3% G2 16,8% G3 2,3%	-	-
Notre étude	29	70-74	G1 24,14% G2 3,45%	56	G1 17,24% G2 10,34% G3 3,45%

Table 3: Frequency of digestive toxicity in the literature

	Number of patients	Dose (Gy)	Acute digestive toxicity	Median follow-up (month)	Toxicité digestive tardive
Beckendorf et al (8)	306	70 vs 80	G1 43% vs 37% G2 27% vs 28% G3 2% vs 2%	57	G1 23% vs 25% G2 12% vs 16% G3 2% vs 6%
Pollack et al (11)	301	70 vs 80	G1 43% vs 39% G2 38% vs 39% G3 2% vs 0%	72	≥G2 12% vs 26%
Peeters et al (9)	669	68 vs 78	G1 41% vs 47% G2 6% vs 4%	36 84	≥G2 23% vs 27% ≥G2 25% vs 35%
Elie Nasr(12)	131	66-74	G1 27,5% G2 9,1%	-	-
Notre étude	29	70-74	G1 24,14%	56	G2 10,34% G3 3,45%

Abbreviations

3D-CRT: 3D conformal radiotherapy

IMRT: intensity modulated conformal radiotherapy

VMAT: volumetric radiotherapy arc therapy

Conflicts of interest: none

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