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## Research Article

# Late Side Effects after Radiation Therapy in Patients with Prostate Cancer: 2D vs 3D vs IMRT

Antonio Augusto Claudio Pereira<sup>1\*</sup>, Danielle Horing Grubert<sup>1</sup>, Gabriela Guimarães Ferreira<sup>1</sup>, José Octavio Haggi Rodrigues Ferreira<sup>2</sup>, Denise Lessa Aleixo<sup>1</sup> and Ana Regina Casaroto Moreschi<sup>3</sup>

<sup>1</sup>Department of Medicine, University Center of Maringá, Maringá, Paraná, Brazil

<sup>2</sup>Department of Medicine, State University of Maringá, Maringá, Paraná, Brazil

<sup>3</sup>Dentistry School, Federal University of Amazonas, Manaus, Brazil

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### ABSTRACT

**Introduction:** Prostate adenocarcinoma (PAC) ranks sixth among the most common malignancies in the world. Acute and chronic toxicities from radiotherapy depend on both the radiation dose and the radiotherapy technique (RT), such as two-dimensional radiotherapy (2D-RT), three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT). The aims of this study were to identify the secondary effects of radiotherapy on patients with PAC and to correlate these effects with the use of 2D-RT, 3D-RCT, or IMRT and with the use of other treatments, such as radical prostatectomy (RP) and hormonal therapy (HT).

**Methods:** We selected 68 patients and collected data, such as age, type of health insurance, T and N staging, and RT used, from their medical records. Through a semi-structured instrument, the patients were interviewed about late side effects resulting from the RT treatment.

**Results:** Most patients underwent 2D-RT (50%), and the urinary tract was the most affected system. A late effect of incontinence was related to the RP and RT treatments ( $P < 0.05$ ). Patients who underwent RP were more likely to develop incontinence and leakage with coughing/sneezing ( $P < 0.01$ ). However, the prevalence of secondary effects was not associated with a specific type of RT. Although bowel and sexual changes did not show a relationship with a specific type of RT, sexual dysfunction had an association with bowel alterations ( $P < 0.05$ ).

**Conclusions:** The use of both RP and RT increased the risk of effects on bladder function. These results can contribute to the development of new research to improve RT, facilitating access to less harmful techniques, and even mitigating undesirable effects.

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### Introduction

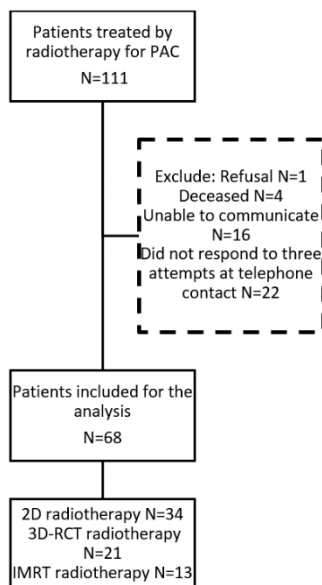
Prostate adenocarcinoma (PAC) is the second-most common malignancy that affects men around the world, after lung cancer. In Brazil, there is a high incidence among men with an estimated 68,220 new cases of prostate cancer diagnosed in 2019 [1]. The progression of PAC is usually slow and asymptomatic, with initial detection of the tumour being possible through digital rectal exams or by the

measurement of serum prostate specific antigen (PSA) [1, 2]. Several therapeutic modalities are used for the treatment of PAC, including radiotherapy, chemotherapy, hormone therapy and surgical removal of the tumour [1, 3]. Each year, these techniques are improved, and factors such as age, tumour stage, degree of histological differentiation, PSA levels, physical state and socioeconomic characteristics of the patient are determinants for the decision as to which is the most appropriate therapeutic plan for each case [3]. Radiotherapy is the preferred treatment for localized PAC and has undergone significant

\*Correspondence to: Antonio Augusto Claudio Pereira, Department of Medicine, University Center of Maringá, Guedner Avenue, 1610, 87050-390, Maringá, Paraná, Brazil; Tel: +5544991768269; E-mail: antonio-augusto\_@hotmail.com

improvements over the last 20 years [4, 5]. Radiotherapy can be used alone or in combination with other therapeutic modalities [6]. The radiation promotes cell damage, culminating in the death of neoplastic cells but also the death of non-tumour cells [6]. The radiation delivery systems have increasingly attempted to concentrate the dose of radiation only on the target volume and to reach its maximum away from the adjacent organ systems, thus minimizing the damage to non-neoplastic cells and reducing the toxicity of the treatment [2, 7].

Among the irradiation techniques, two-dimensional radiotherapy or conventional radiotherapy (2D-RT), three-dimensional conformal radiotherapy (3D-CRT) and intensity modulated radiotherapy (IMRT) have been widely used in the treatment of PAC [2]. In general, these techniques exhibit the advantages of being painless, non-invasive, and without anaesthetic risks, and these techniques can be applied to elderly patients and those with surgical contraindications [7]. On the other hand, the effects of late toxicity secondary to radiotherapy may manifest months to years after the end of the treatment, significantly affecting the patient's quality of life [8]. It is known that the greater the selectivity of the technique, the safer the dose of irradiation, which minimizes the damage to the adjacent structures, such as the rectum, bladder and femoral heads [2, 5, 9, 10]. In this context, the present study aimed to identify the secondary effects of radiotherapy on patients with PAC and to correlate these effects with the three common radiotherapy techniques, namely, 2D-RT, 3D-CRT and IMRT, and with other treatments, such as radical prostatectomy (RP) and hormonal therapy (HT).



**Figure 1:** Flowchart of patient selection with exclusion criteria. PAC, prostate adenocarcinoma; 2D, conventional radiation therapy; 3D-CRT, 3-dimensional conformal radiation therapy; IMRT, intensity modulated radiation therapy.

## Methods

### I Patient Selection and Eligibility

This study was approved by the Research Ethics Committee of the Health Area of the UniCesumar (Process n°3.076.444) and complied with Resolution n° 166/12 of the National Health Council and the main

ethical principles of the Declaration of Helsinki. This is a cross-sectional descriptive study that included PAC patients treated at an oncology and radiotherapy institute in southern Brazil who underwent radiotherapy during the year 2016. For inclusion criteria of the study, we considered those older than 18 years, with a primary diagnosis of PAC, who had been treated for at least 91 days (National Cancer Institute, NCI; Cancer Therapy Evaluation Program, CTEP) and up to 24 months with curative radiotherapy using 2D, 3D-CRT or IMRT, according to the treatment protocols used and/or authorized by the service in question. The exclusion criteria included patients undergoing chemotherapy or other adjuvant treatments, patients with another type of cancer, and patients with M1 staging indicative of metastases. Initially, 111 patients were selected, and information, such as age, type of health insurance, T and N staging, and the radiotherapy technique used (purpose and dose), was taken from their medical records. The final sample consisted of 68 individuals (Figure 1).

### II Assessment of the Side Effects

Telephone interviews were conducted by the researchers between October and December 2017, in which eligible patients were questioned regarding the late effects of radiation therapy. Individuals who refused to give recorded consent or were unable to meet the research needs, as well as individuals who did not answer the phone call, even after three attempts at different times, were not considered for the study.

For the interviews, a semi-structured instrument was used, which was developed by the authors themselves based on the pertinent literature and the validated questionnaire Expanded Prostate Cancer Index Composite (EPIC) [8, 11-17]. The questionnaire was composed of objective questions related to the main side effects experienced by the patient, based on the literature, and related to the radiotherapy treatment of PAC. Among the issues raised were those related to gastrointestinal, urinary, sexual and dermatological symptoms. The patients were questioned about all of these effects, one by one, and asked to express their perception of the symptom at the time of the interview, so that it was possible to relate these late symptoms to the radiation techniques used. The interviewees were also questioned about their perception of symptom changes before and after the radiotherapy.

### III Statistical Analysis

The association between the late effects and treatment type was verified by univariate analysis chi-square tests, considering  $P$  values  $< 0.25$  and  $0.05$ . The late effects with  $P < 0.25$  were considered, since they may indicate that other treatments, used together, may influence the occurrence of these late effects. The association strength between the variables was determined by the contingency coefficients. Then, the late effect estimation according to treatment was determined by a multivariate model with a 5% significance level.

## Results

### I General Features

During the study period, 68 patients treated with radiotherapy for non-metastatic PAC were identified. The characteristics of the patients are listed in (Table 1).

**Table 1:** Patient characteristics.

Factors	No. (%)	No. (%)		
		2D-RT	3D-CRT	IMRT
Median age (years)		71 (56-85)	73* (55-85)	72 (57-80)
Median RT dose	66 – 68 Gy	10 (15)	0	7 (33)
	72 – 74 Gy	39 (57)	34 (100)	23 (14)
	76 – 78 Gy	19 (28)	0	11 (53)
T Stage	T1 / T2	57 (84)	31 (91)	17 (81)
	T3 / T4	5 (7)	1 (3)	3 (14)
	-	6 (9)	2 (6)	1 (5)
N Stage	N0	30 (44)	13 (38)	11 (52)
	N1	3 (4)	2 (6)	1 (5)
	NX	29 (43)	17 (50)	8 (38)
	-	6 (9)	2 (6)	1 (5)
Gleason score	2 – 6	21 (31)	12 (35)	4 (19)
	7 – 10	47 (69)	22 (65)	17 (81)
Treatment	RP	15 (22)	3 (20)	7 (47)
	HT	46 (68)	26 (57)	14 (30)

2D-RT, conventional radiotherapy; 3D-CRT, conformal radiotherapy; IMRT, intensity-modulate radiotherapy; RT, radiotherapy; RP, radical prostatectomy; HT, hormonal therapy; -, not informed.

Regarding the RT modality employed, the majority of patients underwent 2D-RT (34 patients, 50%), followed by 3D-CRT (21 patients, 31%) and IMRT (13 patients, 19%). The age at diagnosis of PAC ranged from 55 to 85 years, with an average age of 72 years, and had a significant association with 3D-CRT ( $P = 0.009$ ) (Table 7). Furthermore, the majority of patients also underwent hormonal therapy (46 patients, 68%), and more than half of these patients underwent 2D-RT (26 patients, 57%), whereas 15 patients (22%) underwent radical prostatectomy (RP) before RT, and the majority of them underwent 3D-CRT (7 patients, 47%).

The prescribed dose varied according to the RT method used. Lower doses were applied to patients after RP. All patients who underwent 2D-RT (34 patients) received a standard dose of 72 Gy, while for 3D-CRT and IMRT, most patients received doses between 76 and 78 Gy, and there was a significant difference between these techniques ( $P < 0.02$ ) (Table 7). According to the contingency coefficient (value close to 1), there was a strong association between 2D-RT and the RT total dose.

## II Bowel Function

The bowel function results are shown in (Table 2). Overall, regardless of the radiographic technique used, the majority of patients (66%) did not report persistent intestinal function alterations after RT. Although 34% of the patients (23 patients) reported they had a bowel disorder, only 10% (7 patients) reported more than three bowel movements a day. Compared to before RT, 28% had more frequent bowel movements, and the majority of these patients underwent 2D-RT (12 patients, 35%). Only three patients reported daily episodes of diarrhoea. None of the patients who underwent IMRT reported haematochezia, while 10% of the patients who underwent 2D-RT and 3D-CRT complained of weekly episodes. Faecal urgency was reported by 25% of the patients (17 patients), and the majority of these patients underwent 2D-RT (10 patients). Approximately 90% of the patients did not experience faecal incontinence or rectal pain.

## III Bladder Function

The bladder function results are shown in Table 3. Although 60 patients (88%) did not complain of persistent dysuria, it was reported by eight (12%) of the interviewees; five (8%) and three (4%) patients reported occasional and frequent dysuria, respectively, without a predilection for the RT technique. Similarly, 66 patients (97%) did not observe haematuria, and only one patient who underwent IMRT reported frequent bleeding with urine, and another who underwent 2D-RT reported occasional haematuria.

On the other hand, 69% of the patients (47 patients) complained about nocturia. Nocturia of 2 to 3 times or more was reported by 53% of patients (38 patients), and the majority of these patients underwent 2D-RT (18 patients), followed by 3D-CRT (12 patients) and IMRT (8 patients). Furthermore, 31% of all patients (21 patients) reported incontinence to be a problem after RT, of which eight underwent 2D-RT, five 3D-CRT and eight IMRT. However, among these patients, nine patients were prostatectomized before RT and then referred to 2D-RT (2 patients), 3D-CRT (3 patients) or IMRT (4 patients). Urine leakage with coughing or sneezing occurred in 10% of patients (7 patients), and three patients underwent 2D-RT, two patients 3D-CRT and two patients IMRT. The use of protective devices (e.g., diapers) was reported by only five patients (7%). The late effects of incontinence and leakage with coughing/sneezing were significantly associated with RP ( $P < 0.01$ ), in addition to the relationship between incontinence and RT ( $P < 0.05$ ). According to  $P < 0.25$ , late effect haematuria may be related to the combination of RT and HT treatment and the need to wear protection for incontinence related to RP (Table 3).

In addition, RP treatment increased the chances of developing the late effects incontinence ( $P = 0.02$ , OR = 5.95) and leakage with coughing/sneezing ( $P = 0.001$ , OR = 12.97) (Table 5). Considering  $P < 0.25$ , IMRT was the most likely RT method to cause these late effects (incontinence,  $P = 0.15$ , OR = 3.2; leakage with coughing/sneezing,  $P = 0.23$ , OR = 2.8). On the other hand, according to the contingency coefficient (value of 0.3), there was only a slight association between

IMRT and incontinence and leakage with coughing/sneezing. Despite the  $P < 0.05$ , 2D-RT only increased the chances of developing

incontinence and leakage with coughing/sneezing by 0.13 and 0.11, respectively.

**Table 2:** Alteration of bowel function according to the radiotherapy technique.

Category	No. (%)	No. (%)		
		2D-RT	3D-CRT	IMRT
Bowel function frequency				
<3/week	6 (9)	3 (9)	3 (14)	0
1/day	37 (54)	14 (41)	13 (62)	10 (77)
2-3/day	18 (27)	12 (35)	4 (19)	2 (15)
4-5/day	5 (7)	4 (12)	1 (5)	0
>5/day	2 (3)	1 (3)	0	1 (8)
Bowel function compared to before RT				
Same	45 (66)	21 (62)	16 (52)	8 (61)
More frequent	19 (28)	12 (35)	3 (10)	4 (31)
Less frequent	4 (6)	1 (3)	2 (6)	1 (8)
Diarrhoea				
Never	64 (94)	32 (94)	21 (100)	11 (84)
1/week	1 (1)	0	0	1 (8)
Daily	3 (5)	2 (6)	0	1 (8)
Haematochezia (last 6 months)				
Never	61 (90)	30 (88)	18 (85)	13 (100)
1/week	3 (5)	2 (6)	1 (5)	0
Daily	4 (5)	2 (6)	2 (10)	0
Faecal urgency				
Yes	17 (25)	10 (29)	5 (24)	2 (15)
No	51 (75)	24 (71)	16 (76)	11 (85)
Faecal incontinence				
Yes	9 (13)	6 (18)	2 (6)	1 (8)
No	59 (87)	28 (82)	19 (94)	12 (92)
Rectal pain				
Yes	2 (3)	1 (3)	1 (5)	0
No	66 (97)	33 (97)	20 (95)	13 (20)

2D-RT, conventional radiotherapy; 3D-CRT, conformal radiotherapy; IMRT, intensity-modulate radiotherapy; RT, radiotherapy.

#### IV Sexual Function

The sexual function results are shown in (Table 4). After RT, sexual potency was decreased in almost half of the patients (47%), and most of these patients (29 patients, 43%) reported a significant, persistent impact on sexual function. Of these, 16 patients (47%) underwent 2D-RT, followed by 3D-CRT (7 patients) and IMRT (6 patients). Thus, full erections were achieved in only 35% after RT. Partial or no erections were reported by 17 patients who underwent 2D-RT, eight 3D-CRT and seven IMRT. Discrete erections were reported by three patients with one representative of each technique. It is noteworthy that 20 of the patients who reported sexual dysfunction had used hormonal therapy. Furthermore, sexual dysfunction showed a significant association with bowel dysfunction ( $P < 0.05$ ) (Table 6).

#### Discussion

In our study, most patients with PAC underwent 2D-RT, and bladder function was the most affected system after the treatments. A late effect of incontinence was related to the combination of RP and RT treatment. Patients who underwent RP were more likely to develop incontinence and leakage with coughing/sneezing. However, the prevalence of the

secondary effects of radiotherapy was not associated with a specific type of RT, despite the slight association between the IMRT and late urinary effects. Although bowel and sexual changes did not show a relationship with a specific RT method and other treatments, sexual dysfunction had an association with bowel alterations.

Acute and chronic toxicities are related to the treatment protocol for PAC, the RT method and the radiation dose [18]. Among the available RT methods, 2D-RT has the lowest selectivity with a wide field of treatment, delivering radiation to healthy organs and, consequently, leading to higher acute and late toxicity [7]. 3D-CRT emits multiple rays of uniform intensity with the aid of computed tomography to delimit the anatomical structures and better concentrate the radiation dose over the tumour target [2, 5, 7]. Developed to reduce acute and late side effects, IMRT allows the delivery of radiation to the target area contour from multiple angular and modulated intensity radiation rays, offering greater radiation in areas of interest but with minimal exposure to adjacent tissues [2, 5, 19, 20]. Thus, patients should be treated with the three-dimensional techniques instead of the conventional 2D-RT modality, especially at sites with high toxicity to neighboring tissues, such as the head and neck, prostate and skull tumours [19].

**Table 3:** Alteration of bladder function according to the radiotherapy technique.

Category	No. (%)	No. (%)		
		2D-RT	3D-CRT	IMRT
Dysuria present				
Never	60 (88)	31 (91)	18 (86)	11 (85)
Occasional	5 (8)	2 (6)	1 (5)	2 (15)
Frequent	3 (4)	1 (3)	2 (9)	0
Haematuria present				
Never	66 (97)	33 (97)	21 (100)	12 (92)
Occasional	1 (1.5)	1 (3)	0	0
Frequent	1 (1.5)	0	0	1 (8)
Nocturia present				
None	21 (31)	12 (35)	6 (29)	3 (23)
Once	9 (13)	4 (12)	3 (14)	2 (15)
2-3 times	17 (25)	10 (29)	4 (19)	3 (23)
>3 times	21 (31)	8 (24)	8 (38)	5 (38)
Incontinence present				
Yes	21 (31)	8 (24)	5 (24)	8 (62)
No	45 (66)	26 (76)	16 (76)	5 (38)
Leakage with cough/sneeze	7 (10)	3 (43)	2 (28.5)	2 (28.5)
Wears protection for incontinence				
Yes	5 (7)	1 (3)	2 (9)	2 (15)
No	63 (93)	33 (97)	19 (91)	11 (85)

2D-RT, conventional radiotherapy; 3D-CRT, conformal radiotherapy; IMRT, intensity-modulate radiotherapy; RT, radiotherapy.

**Table 4:** Alteration of sexual function according to the radiotherapy technique.

Category	No. (%)	No. (%)		
		2D-RT	3D-CRT	IMRT
RT impact on sexual function				
None	35 (51)	16 (47)	13 (62)	6 (46)
Discrete	3 (4)	1 (3)	1 (5)	1 (8)
Significant	29 (43)	16 (47)	7 (33)	6 (46)
Not informed	1 (2)	1 (3)	0	0
Erection status after RT				
Full erections	35 (51)	16 (47)	13 (62)	6 (46)
Partial/No erections	32 (47)	17 (50)	8 (38)	7 (54)
Not informed	1 (2)	1 (3)	0	0

2D-RT, conventional radiotherapy; 3D-CRT, conformal radiotherapy; IMRT, intensity-modulate radiotherapy; RT, radiotherapy.

A dose of ionizing radiation equal to or greater than 78 Gy has greater local disease control. Conventional 2D-RT with a usual dose of 72 Gy does not allow for the safe delivery of high doses, which weakens its indications for the treatment of PAC [2]. All patients in this study who underwent 2D-RT received a standard dose of 72 Gy, while for both 3D-CRT and IMRT, most cases received doses between 76 and 78 Gy, with a strong association between 2D-RT and the RT total dose. On the other hand, it has been noted that a high dose between 74 and 81 Gy can decrease treatment failures but does not affect PAC mortality [5]. Even at lower RT doses, a reduction in the late effects, mainly to the genitourinary system, is difficult, since the bladder and prostate urethra areas are within the treatment volume [5].

Gastrointestinal and genitourinary changes are considered to be the main late effects after RT, significantly affecting the quality of life of patients with PAC [10]. These effects mainly involve the bladder and intestinal motility, with diarrhea, sometimes accompanied by bleeding [13, 16].

However, in this study, we did not observe a significant relationship between gastrointestinal changes and the method of RT. Overall, regardless of the radiographic technique used, the majority of patients (66%) in this study did not report changes in persistent intestinal function after RT. Among the other effects included in the survey, a minority of patients reported an increase in the number of daily bowel movements, occasional haematochezia, and faecal urgency. Regarding the genitourinary function, most patients in this study did not report significant changes. Among the reported complaints, the most relevant complaint was urinary incontinence (n: 21, 31%), in addition to dysuria, haematuria, and nocturia. However, some other factors may contribute to the urinary incontinence outcome, including patient age and RP history [5]. As observed in our study, patients who underwent RP were more likely to develop incontinence and leakage with coughing/sneezing.

Studies have shown lower genitourinary and gastrointestinal toxicity in patients undergoing IMRT compared to 2D-RT [2, 19]. It has been

previously observed that there was a significant difference between IMRT (11%) and 3D-CRT (28%) in the combined incidence of acute and late effects on the genitourinary (GU) and gastrointestinal (GI) systems, confirming the superiority of IMRT in regard to lower acute and late toxicity [19]. On the other hand, a superiority of IMRT over 3D-CRT with reduced gastrointestinal toxicity and rectal bleeding has been noticed, but IMRT had higher acute and late genitourinary toxicity [10]. It was observed there was a significant reduction in radiation proctitis and bleeding in a group undergoing 3D-CRT compared to 2D-RT [5]. We observed a significant relationship between IMRT and late effects incontinence and leakage with coughing/sneezing, but with only a slight association (contingency coefficient of 0.3). As late toxicity may be intensified in patients undergoing RP before RT, we emphasize that the patients with genitourinary toxicity underwent RP before IMRT, which may explain this association observed in our study [2].

**Table 5:** Association between late effect and treatment type.

Late effects	Treatment (P Value)		
	RT	RP	HT
Alteration of bowel function			
Diarrhoea			
Haematochezia			
Faecal urgency			
Faecal incontinence			
Rectal pain			
Dysuria			
Haematuria		0.07 <sup>#</sup>	0.19 <sup>#</sup>
Nocturia			
Incontinence	0.04 <sup>*</sup>	0.01 <sup>*</sup>	
Leakage with cough/sneeze	0.06 <sup>#</sup>	0.003 <sup>*</sup>	
Wears protection for incontinence		0.12 <sup>#</sup>	
Reduction of erection capacity			

RT, radiotherapy; RP, radical prostatectomy; HT, hormonal therapy. \*, p<0.05 (Chi-square test); #, p<0.25 (Chi-square test). P values were shown only for cases in which significant differences were seen.

**Table 6:** Association between sexual and bowel functions.

Sexual function	No.	No. (%)		P Value
		Bowel dysfunction		
Sexual dysfunction	Yes	32	16 (70)	0.026 <sup>*</sup>
	No	35	7 (30)	
Decreased erection capacity	Yes	32	16 (70)	0.016 <sup>*</sup>
	No	35	7 (30)	
Significant Discreet	Significant	29	14 (82)	0.046 <sup>*</sup>
	Discreet	3	3 (18)	

\*, p<0.05 (Chi-square test).

Even at high doses, IMRT reduces the amount of radiation delivered to the structures adjacent to the target and is considered to be the technique with the fewest late side effects [19]. Studies have shown a reduction in the radiation delivered by IMRT to the rectum, bladder, femoral heads, and penile bulb, resulting in a reduction in complications from 14% to

5% compared to other RT methods [2, 5, 20]. Patients undergoing IMRT at doses above 80 Gy had a lower risk of treatment failure, metastasis, and reduced mortality, in addition to the absence of toxic genitourinary or gastrointestinal effects [2, 20]. In addition, RT abandonment is lower for patients using IMRT compared to 2D-RT [2, 20]. Diarrhea, rectal bleeding, and rectal ulceration were found to be the most severe gastrointestinal symptoms. In the same study, the authors reported that 80% of patients had only one genitourinary event, such as an obstruction, haematuria or irritated symptoms [21].

**Table 7:** Association between variables and radiotherapy technique.

Category	RT (P Value)		
	2D-RT	3D-CRT	IMRT
Age	0.18 <sup>#</sup>	0.009 <sup>*</sup>	
RT dose	2.7e-09 <sup>*</sup>	0.00005 <sup>*</sup>	0.015 <sup>*</sup>
Gleason score			
RP	0.19 <sup>#</sup>		0.13 <sup>#</sup>
HT			
Bowel function frequency			
Diarrhoea			
Haematochezia			
Faecal urgency			
Rectal pain			
Dysuria			
Haematuria			
Nocturia			
Incontinence			0.03 <sup>*</sup>
Leakage with cough/sneeze	0.24 <sup>#</sup>		0.054 <sup>#</sup>
Wears protection for incontinence			
Decreased erection capacity			

RT, radiotherapy; 2D-RT, conventional radiotherapy; 3D-CRT, conformal radiotherapy; IMRT, intensity-modulate radiotherapy; RP, radical prostatectomy; HT, hormonal therapy. \*, p<0.05 (Chi-square test); #, p<0.25 (Chi-square test). P values were shown only for cases in which significant differences were seen.

Regarding sexual function, studies have shown a lower incidence of alterations in patients undergoing RT alone compared to those with associated RP treatment [2]. In our study, sexual potency was decreased in almost half of the patients (47%) after RT, with the majority of those affected undergoing 2D-RT. It is noteworthy that 20 of the patients who reported sexual alterations also used hormone therapy that can potentiate RP-like sexual dysfunction. The penile bulb is the main structure affected by radiation, and the toxic effects in this tissue are greater with an increased dose to the target organ and the RT method used in the treatment [13]. However, erectile dysfunction is also associated with multiple ageing-related variables, such as hypertension, diabetes mellitus, hypercholesterolemia, smoking, and even psychological factors [13]. Studies that compare sexual function pre-treatment with the RT dose used, as well as the technique, are still lacking. Techniques using magnetic resonance imaging are now superior and provide greater safety in sexually active patients [13]. The three-dimensional modalities allow for the adoption of higher radiation doses, increasing the likelihood of

therapeutic success without increasing the patient's exposure to adverse effects, thus justifying their preference for patients with PAC indicated for RT. Clinical practice shows us that the acute side effects are lower with IMRT; however, as seen in this study, there was no significant correlation of late toxic symptoms with the type of RT applied.

Although the Brazilian state is expanding investments in oncology, there is still a delay in initiating therapy in prostate cancer patients. Implicated in this problem are the low number of available services (154 nationwide)-it is estimated there is a deficit of 225 RT services and devices-the lack of modernization of techniques, and the high cost of equipment and taxes. The lack of specialized training and the limited remuneration of professionals are also barriers for the accessibility of better modalities and completeness in treatment [22, 23]. Despite being widely used in developed countries, the three-dimensional techniques are not in the list of health procedures established by the National Supplementary Health Agency (ANS) and offered by the Unified Health System (SUS) [19, 20, 22]. There are still no substantial data to encourage the implementation of the IMRT technique as the first line for SUS patients, mainly due to its high cost. However, the benefits of this technique in reducing acute and late side effects is proven, and it is recommended by the Brazilian Society of Radiotherapy, with undeniable curative superiority.

## Conclusion

In summary, the results of this study show that the covariates RP and RT are factors that increase the risk of a patient with PAC to experience the late effects of urinary incontinence and leakage with coughing/sneezing after treatment. These findings were related to the use of IMRT, but it was also the group with the largest number of cases who underwent RP, which might explain this result. Thus, IMRT alone does not increase the incidence of urinary symptoms. The other secondary effects were not significantly associated with the type of RT.

## Conflicts of Interest

None.

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