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Techniques, Dosimetric Constraints, and Tumor Control of Anal Canal Squamous Cell Carcinoma Treated with Concurrent Chemoradiotherapy

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Abstract **Original Research Article**

Introduction: Anal squamous cell carcinoma is a rare tumor whose incidence is increasing. Concomitant chemoradiotherapy [CCT] constitutes the standard treatment with tumor control rates exceeding 70%. This study aims to describe the epidemiological, clinical, therapeutic, and dosimetric characteristics associated with tumor control in patients treated with concomitant chemoradiotherapy [CCT]. ***Methods:*** Descriptive and analytical retrospective study involving 56 patients with anal canal squamous cell carcinoma, treated with RCC between January 2016 and December 2025 at the Oncology-Radiotherapy Department of CHU MOHAMMED VI in MARRAKECH. The epidemiological, clinical, therapeutic, dosimetric, and evolutionary characteristics were collected and analyzed. ***Results:*** The median age was 57 years, with a clear male predominance [sex ratio 6/1] and tobacco intoxication in 64.29% of patients. Stage T3 was found in 67.86% of the patients. All patients received an RCC, primarily performed using 3D conformational radiotherapy, with a median dose of 54 Gy. The dosimetric constraints for the bladder [V50, V60] and peritoneum [V15, V45] were frequently exceeded, while those for the femoral heads were respected thanks to the electron boost. A complete remission was achieved in 42.55% of the patients with a mortality rate of 31.91%. ***Conclusión:*** The RCC ensures satisfactory tumor control but at the cost of toxicity related to the dosimetric limits of 3D conformational radiotherapy. The transition to IMRT/VMAT and the development of predictive biomarkers represent prospects for the management of this tumor.

Keywords: Anal canal, squamous cell carcinoma, concomitant chemoradiotherapy, conformational radiotherapy, Marrakech, Morocco.

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INTRODUCTION

Anal canal cancer is rare, accounting for 2.5% of digestive cancers and 6% of anorectal cancers [1]. The incidence of these cancers is increasing, with factors including infection by the human papillomavirus [HPV] and the human immunodeficiency virus [HIV], immunosuppression, smoking, and multiple sexual partners [2,3].

Squamous cell carcinoma is by far the most common histological type among tumors in this location, accounting for more than 80 to 90% of cases, far ahead of adenocarcinoma, melanoma, or neuroendocrine tumors [1].

Since the abandonment of radical surgery from the 1980s onward, concomitant chemoradiotherapy, combining external irradiation [most often conformational with intensity modulation] with chemotherapy using 5FU [or capecitabine] and mitomycin or cisplatin, has become the standard treatment for squamous cell carcinomas of the anal canal, achieving tumor control rates in more than 70% of cases. The evolution of irradiation techniques, from three-dimensional conformal radiotherapy [3D-CRT] to intensity-modulated radiotherapy [IMRT], has allowed for better preservation of adjacent at-risk organs [bladder, small intestine, femoral heads, external genital organs] while maintaining, or even improving, tumor control. A multidisciplinary approach, involving radiation oncologists, medical oncologists, surgeons, radiologists, and pathologists, remains essential given the rarity of this pathology and the need for precise evaluation before treatment [4].

Data regarding anal canal squamous cell carcinoma remain rare and fragmented, limited to small monocentric series. In this context, the experience of the Oncology-Radiotherapy department at CHU Mohammed VI in Marrakech, which serves a large population in southern Morocco, constitutes a valuable source of information to better characterize this pathology and its management modalities. In this study, we aim to determine the clinical, histological, and dosimetric factors influencing the tolerance and effectiveness of the treatment.

MATERIALS AND METHODS

This is a descriptive and analytical retrospective study, involving 56 patients followed over a 10-year period, from January 2016 to December 2025, at the Oncology-Radiotherapy Department of CHU MOHAMMED VI in Marrakech. We included all patients with histologically diagnosed squamous cell carcinoma treated with RCC. Patients with anal-rectal adenocarcinoma, anal melanoma, or neuroendocrine tumors, as well as incomplete records, were excluded from the analysis. The parameters studied included epidemiological characteristics [age, sex, smoking history, HIV serology], clinical parameters [average consultation delay, revealing sign, TNM classification], therapeutic modalities [radiotherapy technique and dose, concomitant chemotherapy protocol], dosimetric parameters from DV histograms for organs at risk [bladder, peritoneal sac, femoral heads], as well as the evolution.

Results: We collected data on 56 patients, representing 1.6% of digestive cancers during the study period.

I- Epidemiological characteristics: [Table I]
The average age was 57 years [range: 36–82 years], with a clear male predominance [sex ratio: 6/1]. Tobacco intoxication was found in 36 patients [64.29%], and 3 patients [5.35%] were seropositive.

II- Clinical characteristics: [Table II]
The average consultation delay was 12 months [1–36 months]. Rectal bleeding was the main symptom [64.29%]. At diagnosis, 67.86% of patients were classified as T3, with lymph node involvement in 16 patients.

III-Therapeutic modalities: [Table III]
All patients received concomitant radio-chemotherapy. Radiotherapy was based on a 3D conformational technique in the majority of cases. The median total dose delivered was 54 Gy [extremes: 45–59.4 Gy], with a conventional fractionation of 1.8 to 2 Gy per session over an average spread of 6 weeks. The pelvic and inguinal lymph node areas were prophylactically irradiated in the majority of patients.

IV- Dosimetric Parameters: [Table IV]: From a dosimetric perspective, the analysis of dose-volume histograms [DVH] showed tumor coverage with a conformity and homogeneity index of 0.1, but limited sparing of organs at risk due to the three-dimensional technique. At the bladder level, the volume receiving at least 50 Gy [V50] averaged 72%, while the V60 reached 48%. Regarding the peritoneal sac, the volume receiving 15 Gy [V15] was high, with an average of 1120cc, and the average V45 was 380cc, frequently exceeding the recommended constraints. On the other hand, the constraints for the femoral heads were generally respected thanks to the use of electron boost. The toxicities were mainly marked by grade 3 radiodermatitis in 30.36%, followed by grade 2 diarrhea in 44.64%.

V-Evolution: [Table V]: The evolution was marked by complete remission in 29 patients, or 51.79%, 15 patients died, 7 patients had tumor progression, and 5 patients had partial remission.

Table I: Epidemiological characteristics:

Age group	**Number of individuals(n]**	**Percentage [%]**
Under 40 years	06	10,71
40-49 years	09	16,07
50-59 years	15	26,79
60-69 years	16	28,57
≥ 70 years	10	17,86
Total	56	100
Sex		
Male	48	85,71
Female	08	14,29
Total	56	100
smoking		
Active smokers	36	64,29
Non smokers	20	35,71
Total	56	100
HIV Serology		
HIV positive	03	5,36
HIV négative	53	94,64
Total	56	100

Table II: The clinical characteristics

Consultation period	Number of individuals [n]	Percentage [%]
≤ 3 months	10	17,86
4-6 months	12	21,43
7-12 months	16	28,57
13-24 months	12	21,43
> 24 months	6	10,71
Total	56	100
Revealing sign		
Rectal bleeding	36	64,29
Anal/pelvic pain	20	35,71
Anal swelling	14	25,00
Anal pruritus	10	17,86
Rectal syndrome	8	14,29
Incontinence anale	5	8,93
Abscess	4	7,14
TNM Classification		
T1	5	8,93
T2	11	19,64
T3	38	67,86
T4	02	3,57
Total	56	100
N0	40	71,43
N+	16	28,57
Total	56	100

Table III: Therapeutic characteristics

Modalities	[n]	Percentage [%]
Concurrent chemoradiotherapy	56	100
Radiotherapy techniques		
3D Conformal	54	96,43
IMRT/VMAT	02	3,57
Classic fractionation [1,8-2 Gy/fraction]	**56**	**100**
Prophylactic pelvic and inguinal lymph node irradiation	**56**	**100**

Table IV: The dosimetric characteristics

Organs at risk / Parameter	Average value
Bladder – V50 [%]	72
Bladder – V60 [%]	48
Peritoneal sac – V15 [cc]	1120
Peritoneal sac – V45 [cc]	380
Femoral heads	Constraints respected [boost by electrons]

Table V: Evolution

Évolution	n [%]
Complete remission	20 [42,55]
Partial remission	5 [10,64]
Tumor progression	7 [14,89]
Death	15 [31,91]

DISCUSSION

The frequency of anal canal cancers among all digestive cancers in our series [1.6%] is in agreement with the literature data, thus confirming the rarity of this tumor location [1,2]. Contrary to classical epidemiological data that report a female predominance, our series highlights a clear male predominance: sex ratio 6:1 [2,3]. This discrepancy could be explained by the particularities of the local sociocultural context and the different distribution of risk factors, particularly smoking, found in nearly two-thirds of our patients.

In our series, the main symptom was rectal bleeding, a nonspecific clinical sign, which explains the prolonged average diagnostic delay we observed,

contrasting with the data in the literature [4]. This diagnostic delay likely contributes to the predominance of T3 stages [67.86%] and the frequency of lymph node involvement [28.57%] observed in our cohort, the latter remaining within the 30 to 40% range reported in the literature [2].

If RCC remains the therapeutic standard with reported complete response rates of 60 to 90% in major randomized trials that established 5FU-mitomycin C [7,8], our results show efficacy at the cost of toxicities, with a 51.79% complete remission rate, which can be attributed on one hand to a more advanced stage at the time of diagnosis in our series and, on the other hand, to the irradiation technique used. Indeed, the majority of our patients were treated with 3D conformal radiotherapy, a less precise technique than intensity-modulated radiotherapy [IMRT], which has demonstrated its ability to significantly reduce the doses delivered to the bladder, small intestine, and genitourinary-perineal organs while allowing for full doses to be delivered in shorter timeframes, with a reduction in toxicity compared to conventional techniques.

This technical limitation is directly reflected in our dosimetric data, where the recommended constraints for the peritoneal sac [V15 and V45] and for the bladder [V50 and V60] were frequently exceeded, exposing patients to an increased risk of acute digestive and urinary toxicity, which could compromise therapeutic adherence and, consequently, final tumor control. The use of electron boost, however, allowed for compliance with constraints to the femoral heads, illustrating the possible technical adaptation efforts even in the absence of IMRT.

The prognostic factors classically identified in major randomized trials [EORTC 22861, RTOG 98-11, ACT I] are male sex, lymph node involvement, particularly inguinal, tumor size greater than 5 cm, and skin ulceration. Our series accumulates several of these unfavorable factors, particularly the male predominance and the frequency of T3 stages, which could partly explain the observed mortality rate [31.91%] within the treated cohort.

These findings advocate for an improvement in early screening, particularly through increased awareness of the non-specific nature of rectorrhagia, for enhanced support in smoking cessation, as well as for a gradual transition to modern irradiation techniques [IMRT/VMAT] allowing for better sparing of at-risk organs. The development of predictive biomarkers, such as the expression of p16 as a surrogate marker for HPV infection, as well as the evaluation of therapeutic de-escalation strategies for HPV-positive tumors, represent promising prospects for personalized management of this pathology.

Limits:

This study presents several limitations that must be taken into account in the interpretation of the results. Its retrospective and monocentric nature exposes it to selection bias and limits the generalizability of the results to other contexts. The unavailability of IMRT during most of the study period does not allow for a direct comparison of the efficacy and tolerance of the two irradiation techniques within the same cohort. Moreover, the HPV status was not systematically investigated, which did not allow for the evaluation of its prognostic impact. Finally, the sample size, although significant for a rare pathology, remains insufficient for a robust multivariate analysis of prognostic factors.

CONCLUSION

Concomitant radio-chemotherapy ensures satisfactory tumor control but at the cost of notable toxicity in 3D radiotherapy. The optimization of techniques, particularly IMRT, would improve the sparing of at-risk organs and tolerance. New approaches, including immunotherapy and therapeutic de-escalation for HPV-positive tumors, are under evaluation and will enable personalized care to improve patient survival and quality of life.

Contribution of the study:

This study provides detailed dosimetric data, rarely available in African series, illustrating the concrete limitations of 3D conformal radiotherapy. it highlights an atypical epidemiological profile [male predominance] in a Moroccan context. Finally, she highlights a transition toward IMRT/VMAT.

Conflicts of interest: The authors declare no conflicts of interest.

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