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Chemoradiotherapy versus radiotherapy alone in the management of early-stage anal squamous cell carcinoma: A comparative analysis of the French cohort FFCD-ANABASE

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ABSTRACT

Introduction: Early-stage anal squamous cell carcinomas (ASCC) are usually treated with chemoradiotherapy (CRT), with good outcomes. Radiotherapy (RT) alone might be sufficient while reducing toxicity.
Methods: Patients included in the French prospective FFCD-ANABASE and treated for T1–2N0 ASCC between 2015/01 and 2020/04 were divided into CRT and RT groups. Clinical outcomes and toxicity were reported. Propensity score matching was conducted for 105 pairs of patients.
Results: 440 patients were analyzed: 261 (59.3 %) in the CRT group and 179 (40.7 %) in the RT group. The median follow-up was 35.7 months. Patients receiving CRT were younger, had better Performance Status (PS) and larger tumors. No statistical difference was observed for 3-year Disease-free survival (85.3 % vs 83 %, $p = 0.28$), Overall survival (89.6 % vs 94.8 %, $p = 0.69$) and Colostomy-free survival (84.5 % vs 87.2 %, $p = 0.84$) between CRT and RT groups, respectively. Propensity score-matched analysis confirmed these findings. Treatment interruptions were significantly more frequent in the CRT group (36.3 % vs 21.9 %, $p = 0.0013$), resulting in an Overall Treatment Time (OTT) extended by 7 days. Grade 3 CTCAE v4.0 toxicities were more prevalent in the CRT group (46 % vs 19 %, $p < 0.001$).
Conclusion: Adding chemotherapy to radiotherapy did not significantly improve outcomes for T1–2N0 ASCC in our study, but increased toxicity and OTT.

1. Introduction

ASCC accounts for 2.5 % of gastrointestinal malignant tumors [1] and has seen a rising incidence in recent years [2].

Several trials have established concurrent chemoradiotherapy (CRT) with 5-Fluorouracil (5FU) and Mitomycin (MMC) as the gold standard of treatment compared to radiation alone (RT) [3-5].

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However, these studies mainly included advanced stages: T1–2N0 tumors were excluded in the UKCCCR [3] and RTOG 98–11 trials [4], and the EORTCG trial did not include T1N0 tumors [5]. In studies that did include early-stage tumors, outcomes were favorable compared to more advanced tumors, with a 3-year Disease Free Survival (DFS) around 80 % [6]. Our prior analysis of the entire FFCD-ANABASE cohort revealed a significant difference in 3-year DFS between early-stage (T1–2N0) and locally advanced tumors (T3–4 or N+): 84.3 % 95 %CI [80.6;88.2] vs 64.6 % 95 %CI [60.0;69.0], respectively ($p < 0.001$) [7]. This suggests early-stage tumors might be overtreated with CRT. Indeed, CRT is usually associated with increased toxicity (compared to RT alone), especially in the acute phase, as shown by the UKCCCR trial (48 % vs 38.6 %, $p = 0.03$) [3]. The additional toxicity from chemotherapy can possibly result in treatment interruption in 40 to 60 % of patient [8], thus allowing tumor repopulation, which could increase the risk of relapse [9].

Therefore, the use of concomitant chemotherapy remains a matter of debate for T1–2N0 tumors. The 2024 international NCCN guidelines v1.24 recommend treating all non-metastatic anal carcinoma with CRT [10]. French guidelines list exclusive RT as a treatment option for tumors less than 3 cm N0 [11].

The objective of this study was to assess the clinical outcomes and toxicity of CRT compared to RT for patients with T1–2N0 ASCC included in the FFCD-ANABASE cohort.

2. Materials and methods

2.1. Study design

ANABASE is a French prospective observational cohort conducted by the Fédération Francophone de Cancérologie Digestive (FFCD), including patients treated for ASCC across 60 centers [7]. Our study specifically focused on the subgroup with T1–2N0 ASCC. The primary endpoint was 3-year disease-free survival (DFS). Secondary endpoints were overall survival (OS), colostomy-free survival (CFS), and toxicity.

2.2. Population and parameters collected

Among patients included in the FFCD-ANABASE cohort, all patients with T1–2N0 ASCC were analyzed in this study. Patients and tumors characteristics, treatment details, outcomes, and Grade 3 toxicity or higher according to the National Cancer Institute – Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 4.0 were collected.

2.3. Statistical analyses

Baseline characteristic comparisons between the CRT and RT group were conducted. The Wilcoxon rank sum test was utilized to compare quantitative variables. The Chi-Square test or Fisher's exact test were assessed to compare qualitative variables.

DFS was defined as the time between treatment initiation and the date of first relapse (local, regional or metastatic) or death (any cause). OS was the time between treatment initiation and death due to any cause. CFS was the time between treatment initiation and first colostomy or death (due to any cause). Patients without any event were censored from the date of the last follow-up. Survival endpoints were analyzed using the Kaplan-Meier method to present rates and event time distributions with a 95 % confidence interval (95 % CI) for each group. The two groups were compared using Logrank tests, and Cox models were used for univariate and multivariate analyses. SAS software 9.4 (SAS Institute, Cary, NC) was used.

Additionally, survival rate analyses were performed among patients with tumors smaller than 3 cm and 4 cm.

2.4. Propensity score

We employed the propensity score method to limit bias stemming from potential unbalanced confounders between the groups. The score was generated from an unconditional multivariate logistic regression, estimating the probability of receiving concomitant chemotherapy based on patient and tumor characteristics. The model's performance and fit were evaluated using the area under the curve (AUC) and the Hosmer-Lemeshow test, respectively. We first matched a patient in the CRT group with a patient in the RT group based on the propensity score with a standard of 0.1. Subsequently, we applied in a univariate Cox model the inverse probability of treatment weighting (IPTW) method using the propensity score. The propensity score, derived from a multivariate logistic regression analysis, was performed to estimate the probability of receiving concomitant chemotherapy based on age <65 years, PS status and tumor size. The AUC for the multivariate logistic model was 0.75, and the p-value of the Hosmer-Lemeshow test was 0.5, showing good performance and fit of the model. The matching algorithm resulted in 105 matched pairs.

3. Results

3.1. Patient and tumor characteristics

Among 1015 patients treated for ASCC from 01/2015 to 04/2020 in the FFCD-ANABASE cohort, 440 patients had T1–2N0 ASCC. Patients were divided into two groups according to treatment: 261 patients in the CRT group and 179 in the RT group. Co-infection by Human Papillomavirus, tested in 272 available biopsies, was positive in 95 % of cases. Baseline staging was determined using CT scan for 237 patients (53.9 %), MRI for 305 patients (69.3 %), endoscopic ultrasound for 145 patients (33 %), and PET-CT for 305 patients (69.3 %). Patients in the CRT group were found to be younger ($p = 0.01$), had a better performance status (PS) ($p = 0.01$), and a larger median tumor size ($p < 0.001$). Among 318 patients with T2 tumors, 235 (73.9 %) received CRT and 83 (26.1 %) RT alone ($p < 0.001$). Among 226 patients with a tumor size of 3 cm or less, 100 patients were treated with CRT and 126 patients with RT ($p < 0.0001$). Among 340 patients with a tumor size of 4 cm or less, 187 patients were treated with CRT and 153 patients with RT ($p = 0.01$) (Table 1).

3.2. Radiotherapy

Details about radiotherapy are available in Table 2. There was no significant difference in the techniques used between both groups ($p = 0.616$). The median dose delivered to the primary tumor was significantly higher in the CRT group ($p < 0.001$). Irradiation of inguinal nodes was more frequent in the CRT group, with significant difference ($p = 0.0004$). Median overall treatment time (OTT) was 50 days in the CRT group and 43 days in the RT group. Treatment interruptions exceeding 3 days were significantly more frequent in the CRT group ($n = 94$; 36.3 %) compared to the RT group ($n = 39$; 21.9 %) ($p = 0.0013$). Treatment breaks were planned for 71 patients : 47 (66.2 %) in the CRT group and 24 (33.8 %) in the RT group, without significant difference ($p = 0.2474$).

3.3. Chemotherapy

Chemotherapy was based on 5FU-Mitomycin C for 63 % of patients and Capecitabin-Mitomycin C for 27 %; Capecitabin alone for

Table 1
Patient and tumor characteristics in CRT and RT groups.

		CRT group N (%)	RT group N(%)	All N (%)	p value
Number of patients (N)		261	179	440	
Sex	Male	59 (22.6)	41 (22.9)	100 (22.7)	0.9413
	Female	202 (77.4)	138 (77.1)	340 (77.3)	
Age (years)	Median	64	66	65	**0.0079**
	Q1-Q3	57–70	57–76	57–73	
	Min - Max	35–92	41–94	35–94	
PS status	n	251	177	428	**0.0125**
	0	197 (78.5)	130 (73.4)	327 (76.4)	
	1	53 (21.1)	39 (22.0)	92 (21.5)	
	2	1 (0.4)	8 (4.5)	9 (2.1)	
	3	0 (0.0)	0 (0.0)	0 (0.0)	
Human Immunodeficiency virus status	n	259	176	435	0.4121
	Positive	20 (7.7)	15 (8.5)	35 (8.0)	
	Negative	97 (37.5)	55 (31.3)	152 (34.9)	
	Unknown	142 (54.8)	106 (60.2)	248 (57.0)	
Smoking status	n	228	163	391	0.2296
	Yes	126 (55.3)	100 (61.3)	226 (57.8)	
	No	102 (44.7)	63 (38.7)	165 (42.2)	
Tumor location	n	255	175	430	0.3469
	Anal margin	33 (12.9)	29 (16.6)	62 (14.4)	
	Anal canal	203 (79.6)	139 (79.4)	342 (79.5)	
	Lower rectum	18 (7.1)	7 (4.0)	25 (5.8)	
	Other	1 (0.4)	0 (0.0)	1 (0.2)	
Tumor Initial staging	T1N0M0	26 (10.0)	96 (53.6)	122 (27.7)	**< 0.001**
	T2N0M0	235 (90.0)	83 (46.4)	318 (72.3)	
Tumor size (cm)	n	253	176	429	**< 0.001**
	Mean (SD)	3.09 (0.94)	2.31 (1.09)	2.77 (1.07)	
	Median	3.00	2.00	2.70	
	Q1-Q3	2.50 – 4.00	1.50–3.00	2.00–3.50	
	Min-Max	0.70–5.00	0.20–5.00	0.20–5.00	

Table 2
Radiotherapy characteristics for the chemoradiotherapy (CRT) and radiotherapy (RT) group (IMRT: intensity-modulated radiation therapy; Gy: Gray).

		CRT group N(%)	RT group N(%)	All	p value
Number of patients (N)		261	179	440	
Radiation technique	n	257	176	433	0.6160
	3D	49 (19.1)	34 (19.3)	83 (19.2)	
	Static IMRT	47 (18.3)	24 (13.6)	71 (16.4)	
	Rotational IMRT	132 (51.4)	95 (54.0)	227 (52.4)	
	Tomotherapy	29 (11.3)	23 (13.1)	52 (12.0)	
Dose to the primary tumor (Gy)	n	258	179	437	**< 0.001**
	Median	60.00	56.00	59.40	
	Q1; Q3	50.40–64.80	45.00–61.00	45.00–63.00	
Pelvic prophylactic dose (Gy)	n	156	108	264	**0.001**
	Median	45.00	45.00	45.00	
	Q1; Q3	45 - 46	45 - 45	45 - 45	
Irradiation of inguinal nodes	n	249	174	423	**0.0004**
	No	55 (22.1)	66 (37.9)	121 (28.6)	
	Yes	194 (77.9)	108 (62.1)	302 (71.4)	
Treatment interruption	n	259	178	437	**0.0013**
	No	165 (63.7)	139 (78.1)	304 (69.6)	
	Yes	94 (36.3)	39 (21.9)	133 (30.4)	
Brachytherapy boost	n	256	178	434	**<0.001**
	No	213 (83.2)	115 (64.6)	328 (75.6)	
	Yes	43 (16.8)	63 (35.4)	4.4)	

5.8 % and 5FU-Cisplatin for 0.8 %. 3.4 % of patients in the CRT group received another chemotherapy protocol.

3.4. Disease-free survival

Median follow-up was 35.7 months (95 %CI [34.7;36.4]). 3-year DFS was 83.0 % in the RT group and 85.3 % in the CRT group (HR = 1.32 95 %CI [0.8;2.19]), without significant difference (p = 0.28) (Fig. 1). In the univariate analysis, poorer DFS was associated with male gender (HR = 2.42 95 %CI [1.45;4.03], p = 0.001), PS≥ 1 (HR = 2.7 95 %CI [1.61;4.55], p < 0.001) and tumor size ≥ 3 cm (HR = 2.04 95 %CI [1.20 ;3.45], p = 0.008). No association was found due to initial TNM staging (HR = 1.10 95 %CI [0.64;1.91], p = 0.726), HIV infection (HR = 1.59 95 %CI [0.71;3.58], p = 0.259) or treatment interruption during radiotherapy (HR = 1.34 95 %CI [0.8;2.25], p = 0.267). Multivariate analysis confirmed poorer DFS was associated with male gender (HR = 2.21 95 %CI [1.31;4.3,73], p = 0.003); PS ≥ 1 (HR = 2,44 95 %CI [1,42; 4,00], p = 001) and tumor size ≥ 3 cm (HR = 2,04 95 %CI [1,19;3,45], p = 0.009). No significant difference in DFS was observed for patients with tumor size < 3 cm (HR = 1.91 95 %CI [0.78;4.64], p = 0.1472) between RT and CRT groups. For patients with tumor size < 4 cm, DFS was statistically different between both groups (HR = 2.03 95 %CI [1.07;3.88]; p = 0.031). (Supplementary Figure 1).

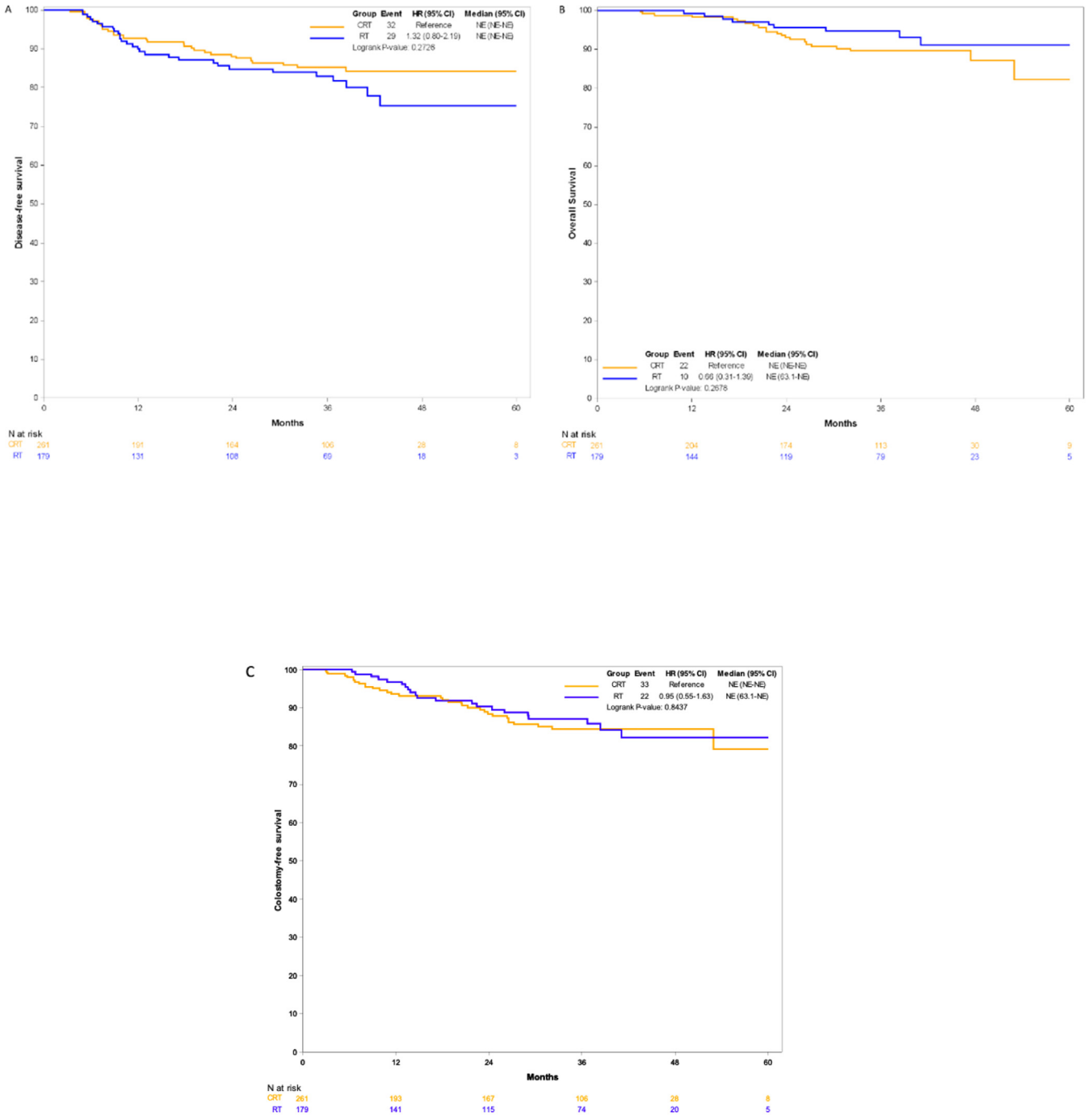

Fig. 1. (A) Disease free survival (DFS), (B) Overall survival (OS) and (C) Colostomy-free survival (CFS) rates for treated for T1–2N0M0 ASCC with CRT or RT alone. CI : confidence interval ; CRT : chemoradiotherapy group ; HR : Hazard ratio ; N : number ; NE : number of events ; RT : radiotherapy group.

3.5. Overall survival

3-year OS was 94.8 % in the RT group and 89.6 % in the CRT group (HR 0.66 95 %CI [0.31;1.39]), without any significant difference (p = 0.27). (Fig. 1). Among the 32 deceased patients, 22 were treated with CRT and 10 with RT alone. The most common cause of death was cancer progression: 13 patients (59.1 %) in the CRT group and 6 patients in the RT group (60 %). One death in the CRT group was related to treatment toxicity and other cause: the patient died from infection and post-operative embolism. Multivariate analysis showed poorer OS for male gender (HR = 2.40 95 %CI [1.18;4.9], p = 0.016), PS ≥ 1 (HR = 2.94 95 %CI [1.45;5.88], p = 0.006) and tumor size ≥ 3 cm (HR = 3.85 95 %CI [1.63;9.09], p = 0.002). No significant difference in OS was observed for patients with tumor size <3 cm (HR = 0.78 95 %CI [0.2;3.13], p = 0.728) or <4 cm (HR = 1.06 95 %CI [0.38;2.92], p = 0.914) between CRT and RT groups (Supplementary Figure 1).

3.6. Colostomy-free survival

3-year colostomy-free survival (CFS) was 87.2 % in the RT group and 84.5 % in the CRT group (HR 0.95 95 %CI [0.55;1.63]), without any significant difference (p = 0.84). Multivariate analysis shown a poorer CFS associated with male gender (HR = 2.19 95 %CI [1.26;3.78], p = 0.005), PS ≥ 1 (HR = 2.17 95 %CI [1.25;3.708], p = 0.006) and tumor size ≥ 3 cm (HR = 2.08

Table 3
Combined toxicity (from radiotherapy and chemotherapy) grade 3 or more according CTCAE v4.0 for CRT and RT group (CRT = chemoradiotherapy; RT = radiotherapy).

	CRT group N(%)	RT group N(%)	p value
Number of patients (N)	261	179	
At least one toxicity grade 3 or more CTCAE v4.0	120 (46.0)	34 (19.0)	**<0.001**
Dermatitis	86 (33.0)	27 (15.1)	**<0.001**
Gastro-intestinal	38 (14.6)	9 (5.0)	**0.0015**
Urinary disorders	5 (1.9)	1 (0.6)	0.23

95 %CI [1.19;3.70], p = 0.01). No significant difference was observed in CFS for patients with tumor size <3 cm (HR = 1.48 95 %CI [0.59;3.72], p = 0.4) or <4 cm (HR = 1.44 95 %CI [0.74;2,79], p = 0.286) between RT and CRT groups (Supplementary Figure 1).

3.7. Pattern of relapse

Twenty-three patients relapsed (9.1 %) in the CRT group, including 13 (56.5 %) local relapses. In the RT group, 25 patients (13.9 %) relapsed: the majority of which were local (40 %, N = 10) or regional (40 %, N = 10). Distribution of local, regional or metastatic relapses was statistically different between both groups (p = 0.0419). Relapse data are available in Supplementary Table 1.

3.8. Propensity score

Among the 105 matched patients, no statistical difference was found in terms of age, PS status; initial tumor staging and tumor size. Data are available in Supplementary Table 2.

No statistical difference was found in DFS (HR = 1.44 95 %CI [0.69;2.99], p = 0.329), OS (HR = 0.70 95 %CI [0.26;1.89], p = 0.484) and CFS (HR = 1.05 95 %CI [0.48;2.26], p = 0.908) (Fig. 2). Results of multivariate Cox models for both match-weighted and IPTW analyses show non-statistically significant differences in survival for patients treated with CRT vs. RT.

3.9. Toxicity

During radiotherapy, Grade 3 or more toxicity was more prevalent in the CRT group compared to the RT group: 46.0 % vs 19.0 %, respectively (p < 0.001). Within the CRT group, hematologic toxicity G3+ appeared in 20 patients (7.7 %). Thrombocytopenia was the most frequent disorder (4.2 %; n = 11) followed by leukopenia (2.3 %; n = 6) and anemia (1.5 %; n = 1). In the CRT group, one patient died due to sepsis and post-operative embolism, another presented a stroke during treatment, and a third presented cytolytic hepatitis attributed to Capecitabin. Data about treatment toxicity can be found in Table 3.

4. Discussion

We confirm good prognostic outcomes for T1–2N0 ASCC, with a 3-year DFS higher than 80 % and 3-year OS above 90 % in both groups. These results are in line with the literature [12,13]. In contrast to the U.S database where 7.5 % of patients were treated by RT alone [14], the proportion of patients between CRT and RT groups was well balanced in our cohort. RT alone appears to be more prevalent treatment option in Europe or France.

We focused on recently treated patients, limiting heterogeneity linked to treatment evolution. Chemotherapy mainly consisted of 5-FU or Capecitabin and Mitomycin, consistent with current practices since the gold standard of Mitomycin was established [4]. Less than 20 % of the population underwent 3D radiotherapy, consistent with European guidelines [15] recommending IMRT.

Contrary to data from U.S databases, the median dose delivered to the primary tumor was more important in the CRT group [16]. Median dose to the primary tumor was about 60 Gy with a pelvic prophylactic median dose of 45 Gy, consistent with French guidelines suggesting tumor dose must be about 45–54 Gy for T1 and 54–65 Gy T2, respectively; and 45 Gy for pelvic prophylactic irradiation [17]. This is higher than NCCN guidelines which recommend delivery of 50.4 Gy to the tumor [10] in accordance with to RTOG 05–29 trial [18]. Surprinsingly, local relapses were more frequent in the CRT group. This raises the question of radioresistance, supported by a Danish study suggesting relapses occur within high-dose volumes [19]. In our study, 70 % of the population underwent inguinal irradiation, more frequently so in the CRT group. This could at least in part explain several relapses in the RT group, considering a retrospective study showed a risk of inguindal recurrence of 12 % for inguinal recurrence in T1–2 tumors without inguinal prophylactic irradiation [20]. With the idea of customizing treatment according to tumor stage, the UK PLATO platform (PersonaLising rAdioTherapy dOse for anal cancer) and ACT4 trial will study efficacy and toxicity of delivering only 41.4 Gy compared to 50.4 Gy in association with chemotherapy for T1–2N0 tumors (less than 4 cm) [21]. The U.S DECREASE phase III will study if lower dose radiotherapy in T1–2N0 (less than 4 cm) tumors can maintain a 2-year disease control of 85 % or higher while improving anorectal health-related quality of life; with results expected in 2025 [22]. Our analysis found a statistical difference in DFS for patients with tumor size< 4 cm; whereas DFS was not statistically different for tumor size< 3 cm. This result could suggest therapeutic de-escalation and the omission of chemotherapy should be considered above all for tumors <3 cm.

Propensity score matching addressed differences in patient characteristics between both groups. It has already been used in U.S. databases with discordant results: the MEDICARE database, with 299 patients (200 by CRT and 99 by RT), didn't present significant difference in OS or DFS [23]. Using the American National Cancer Database (NCDB), Miller et al. reported a 4-year OS improved from 75.7 % to 84 % (p = 0.023) for 287 pairs of patients treated by RT or CRT respectively, for stage I ASCC [24].

The benefit of concurrent chemotherapy remains controversial in the literature. Also using the FFCD-ANABASE cohort, Bacci et al. reported on 99 cases of T1N0 ASCC, including 17 (17.2 %) receiving CT either after local excision (n = 4, 4.9 %) or with RT (n = 13, 15.9 %): no difference in Recurrence-free Survival was observed (HR 2.31; 95 % CI 0.70–7.70; p = 0.17) [25]. A French study on 69 patients with T1N0 tumors < 1 cm showed a 5-year OS of 100 %; with 62 patients (89.9 %) treated with RT [26]. This suggests RT alone is enough for tumors < 1 cm. A French multicenter retrospective study involving 167 patients treated for T1–2 ASCC between 1975 and 2001 reported that CRT improved OS and 5-year PFS in multivariate analysis [27]. In our study, tumor size > 3 cm was also statistically associated with poorer DFS and OS. In 2011, a Swiss retrospective study of 146 patients with T1-T2N0 tumors found that loco-regional control (LRC) and cancer-specific survival (CSS) seemed to improve for patients receiving CRT, despite a non-

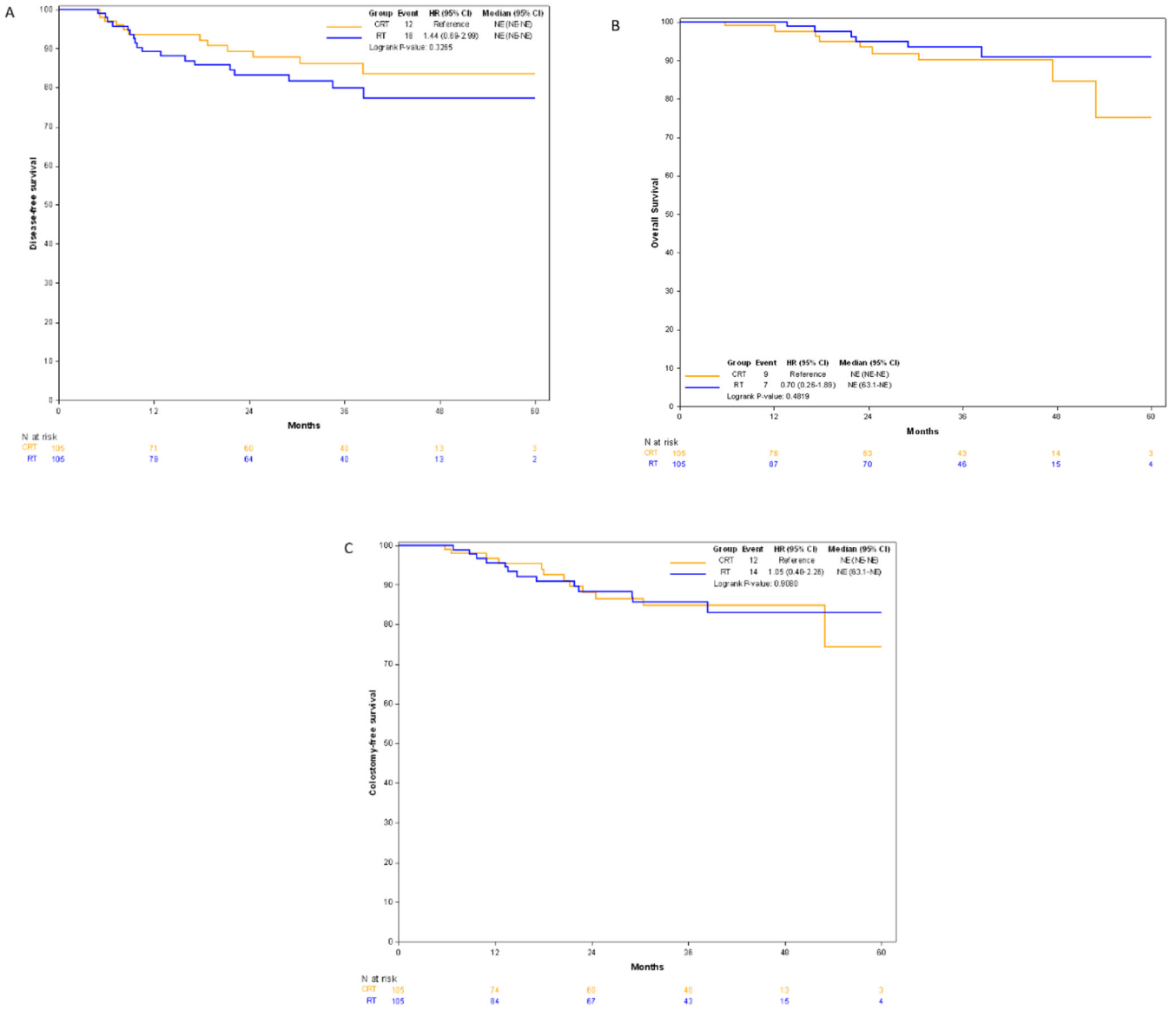

Fig. 2. (A) Disease-free survival, (B) Overall survival (OS) and (C) Colostomy-free survival (CFS) rates for 105 matched patients in each CRT and RT group.

significant difference: the 5-year LRC rate was 75.5 % ± 6.0 % in the CRT group vs 86.8 % ± 4.1 % in the RT group (p = 0.155); and 5-year CSS rate was 88.5 % ± 4.5 % in the CRT group vs. 94.9 % ± 2.9 % in the RT group (p = 0.161) [28]. In a European study involving 122 patients with T1–2N0 ASCC, CRT (used in 70 patients) improved local control, without significantly increasing G3+ acute and late toxicity [29]. Huffman et al. published data from the NCDB on 2959 patients treated for cT1N0M0 ASCC: CRT improved OS (65 % in the RT group vs 86 % in th CRT group, respectively) [30]. Less than 10 % of patients were treated with RT alone; they were older and had a poorer PS status. This may partially explain the difference in OS, suggesting that RT alone might be reserved for vulnerable patients with poor life expectancy, unable to receive chemotherapy. Data also from the NCDB about 4564 patients treated for T1–2N0MO ACSS showed an improved 5-year OS for the CRT group (86.6 %) compared to the RT group (79.1 %) (p = 0.001). In subgroup analyses, this was significant only for T2N0 tumors (84.7 % vs 72.8 %, p < 0.0001) [16].

We reported a median prolongation of OTT of 7 days in the CRT group, which could in part be related with treatment toxicity. Several studies reported an increased risk of relapse with prolonged OTT [31,32], inducing tumoral repopulation. Extended OTT could potentially mask the benefits of chemotherapy.

We must keep in mind the significant difference in tumor size and stage between both groups in our study. The CRT group consists mostly of T2 tumors (90.0 %), whereas the RT group is more balanced (83 patients with T2 tumors, 46.4 %).

Limitations of our study include its rather small population size compared to other studies using databases, even though we included patients from 60 centers, which may result in a lack of statistical power. Among the 440 patients, 63 did not undergo PET-CT or CT for baseline staging. Some patients might have had unknown nodal invasion at diagnosis, which would have benefited more from CRT. One-hundred and thirty-five patients (30.7 %) didn't undergo MRI, which could have led to inaccurate tumor staging. Despite all, this national study provides a clearer vision of management of early-stage ASCC in terms of both chemotherapy and radiotherapy; to choose the treatment with the best risk-benefit ratio for this population with high-rates survival for which late toxicities remain a major issue after cancer cure.

5. Conclusion

Treatment with radiotherapy alone or concomitant chemoradiotherapy both resulted in high rates survival for early-stage node negative anal cancers, without a significant difference in our study. The addition of chemotherapy increased overall treatment time, which is known to be a major determinant for disease local control. Toxicity was higher with concomitant chemoradiotherapy. Further studies on treatment personalization and de-escalation, including considerations of dose and volumes will provide additional insights into optimal treatment strategies forT1–2N0 anal cancers.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dld.2024.06.022.

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