Analysis of definitive chemo-radiation outcomes in anal cancer: insights from a tertiary cancer center in the MENA Region

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Introduction and Background:

Outcomes of chemo-radiation (CRT) for anal cancer in Middle East and North Africa (MENA) are scarce. We aim to report treatment outcomes for anal cancer treated at tertiary cancer center, with a particular focus on patients managed with non-oncological surgery prior definitive CRT.

Anal cancer is a rare malignancy of the gastrointestinal (GI) tract, comprising approximately 1-2% of all GI cancers. The predominant type is squamous cell carcinoma (SCC), with a higher incidence observed in individuals aged 55-64 years. (1)
The incidence of anal carcinoma in Middle East and North Africa (MENA) remains lower than other regions in the world (2).

In Jordan, anal cancer constitutes 0.2% of all newly diagnosed malignancies, as per the national cancer registry 2016 (3), which is lower than the global incidence of 0.5%, according to Surveillance, Epidemiology, and End Results (SEER) data (4).

Anal cancer treatment has evolved significantly over the past three decades. Organ-preserving chemoradiation therapy (CRT) has been established as a standard of care for locally advanced disease instead of abdominoperineal resection (5). This approach is formed of concurrent 5-fluorouracil (5-FU) or capecitabine and mitomycin C (MMC) with definitive radiation therapy. Chemoradiation offers a high level of disease control and successfully preserves the anal sphincter.

Materials and Methods

We conducted a retrospective review of patients diagnosed with locally advanced anal carcinoma, who underwent definitive CRT in the King Hussein Cancer Center, from January 2007 till January 2020. Patient demographics and disease characteristics were extracted, and a univariate chi-squared test was employed to assess the impact of chemotherapy type, HPV status, and pre-treatment non-oncological surgery on outcomes, including complete remission (CR), disease-free survival (DFS), and overall survival (OS). Kaplan–Meier tests were employed to analyze the obtained survival data.

Assessment of response involved digital rectal examination, endoscopy, and pelvic MRI. Complete remission (CR) was characterized by the clinical and radiographic evidence confirming the complete disappearance of the tumor.

Results

Patient Characteristics:

Characteristics		Number (N)	Percentage (%)
Age (years)	≥50	24	80 %
	<50	6	20 %
Gender	Male	15	50 %
	Female	15	50 %
Smoking	Yes	18	60 %
	No	12	40 %
Stage	I	2	6.7 %
	II	13	43.3 %
	III	15	50 %
Chemotherapy	5 FU/Xeloda + MMC	23	76.7 %
	5 FU/Xeloda + Cisplatin	7	23.3 %
HPV	Positive	21	70 %
	Negative	4	13.3 %
	N/A	5	16.7 %
Radiotherapy Technique	3D	9	30 %
	IMRT	21	70 %
Non-oncologic resection	Yes	10	33.3 %
	No	20	66.7 %

Characterstics vs Treatment outcomes:

Characteristics		pCR	*p* value	DFS	*p* value	OS	*p* value
Age (years)	≥50	79.2 %	0.34	75.0%	0.73	76.5 %	0.79
	<50	83.3 %		66.7%		83.3 %	
Gender	Male	86.7 %	0.54	80.0 %	0.38	85.7 %	0.33
	Female	73.3 %		66.7 %		70.6 %	
Smoking	Yes	73.7 %	0.43	68.0 %	0.66	77.4 %	0.067
	No	90.9 %		81.8 %		78.8 %	
Stage	I	100 %	0.83	100 %	0.26	100 %	0.76
	II	84.6%		84.6%		76.2%	
	III	73.3%		59.3%		77.1%	
Chemotherapy	5 FU/Xeloda + MMC	73.9%	0.3	69.0%	0.38	71.6%	0.14
	5 FU/Xeloda + Cisplatin	100.0%		85.7%		100.0%	
HPV	Positive	95.0%	0.006	85.0%	0.02	89.6%	0.001
	Negative	25.0%		25.0%		25.0%	
Radiotherapy Technique	3D	66.7 %	0.08	66.7 %	0.57	75.0 %	0.83
	IMRT	85.7 %		75.6 %		79.8 %	
Non- oncologic resection	Yes	90.0%	0.51	90.0%	0.15	89.9%	0.32
	No	75.0%		64.2%		73.6%	

24 (80%) patients attained CR following definitive CRT. The overall 5-year OS for the entire group was 78%. Notably, 20 out of 21 HPV-positive patients achieved CR, versus 1 out of 4 HPV-negative patients, p=0.006 3 out of 4 HPV negative patients experienced disease recurrence, compared to 3 out of 21 patients in the HPV-positive group, p= 0.03. There was no statistical significant difference in patients outcomes as regard type of chemotherapy, radiation technique and non-oncologic resection prior to CRT.

To the best of our knowledge, this is the first report on anal cancer from the MENA region. We reported a 5-years OS of 78%, which aligns with survival rates reported in the literature.

In a systematic review, that tested the correlation between HPV status and treatment response, They found patients with HPV-positive status exhibited superior disease-free survival and overall survival compared to those with HPV-negative disease. This difference is attributed, at least in part, to the more favorable response to CRT in HPV-positive cases. (6) Similarly, another study conducted in Japan, revealed a more favorable response in patients with HPV-positive anal cancer. (7) Our data from the MENA region further adds to the existing pool of literature that HPV associated anal cancer is indeed more responsive to treatment.

We observed no statistical difference in outcomes based on the type of chemotherapy. A randomized controlled trial by Ajani et al, compared recurrence rates between MMC-5FU and cisplatin5FU, the recurrence rate with MMC was 25% and 33% in the cisplatin group, but the difference between the groups was not statistically significant. This data is consistent with results obtained in our study.

A study by O'Brien and colleagues compared patients with hemorrhoidal SCC to those with non-hemorrhoidal SCC. They reported a higher proportion of stage I/II in the hemorrhoidal SCC arm, but no significant difference in OS between the two groups (8). These findings aligned with our data, indicating that hemorrhoidal surgery did not impact the oncological outcomes of the underlying anal SCC.

Conclusions

This is the first report on anal cancer from the MENA region. Our findings clearly showed that HPV positive patients showed significantly higher CR, DFS and OS than HPV-negative patients. Furthermore, non-oncological resection before CRT did not impact oncological outcomes.

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Further information

You can read the full paper published in:
https://www.frontiersin.org/journals/oncology/articles/10.3389/fonc.2023.1333558/full
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