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RESEARCH ARTICLE
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CLINICAL OUTCOME AND TOLERANCE OF RADICAL CHEMORADIATION FOR ANAL CANAL CARCINOMA

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ABSTRACT

Background: Anal canal carcinoma is an uncommon malignancy and concurrent chemoradiation is the standard of care curative treatment in locally advanced anal canal carcinoma. Concurrent chemoradiation have resulted in good outcomes in terms of overall survival, disease free survival. With this study we wanted to assess the clinical outcome of patients with Anal canal carcinoma treated with radical chemoradiation at our centre.

Materials & Methods: This was a retrospective study which included all anal canal carcinoma patients who underwent radical chemoradiation from January 2013 to June 2021 at our centre. Demographic, treatment, toxicity and follow up details were carefully recorded from case records and RT charts.

Results: A total of 18 patients were analysed and the median age of patient population was 59 years. Patients were predominantly males (72%), most common T stage was T3 (72%) and were mostly node positive (67%). Conformal radiotherapy technique was used in all patients. RT dose ranged from 50 Gy to 59.4 Gy, commonest schedule used was 54 Gy in 30 fractions (44%). 17 (94%) patients had acute Grade 3 dermatitis, but Grade 3 or more hematological (2,11%) and

gastrointestinal toxicities (1,5%) were less. Out of the 18 patients only one patient could not complete the planned course of RT. Disease free survival at 1 year, 2 years and 3 years were 82.6%, 67.6% and 56.3% respectively. Overall survival at 1 year, 2 years and 3 years were 88.1%, 80.1% and 70.1% respectively.

Conclusion: Our study have shown that Concurrent chemoradiation for Anal canal carcinoma have good outcomes in terms of DFS and OS, with significant incidence of acute Grade 3 dermatitis, with minimal incidence of Grade 3 or more hematological and gastrointestinal toxicity. RT treatment breaks were seen in less proportion of patients and almost all patients completed the planned course of RT.

INTRODUCTION

Anal canal carcinoma is an uncommon malignancy with an annual incidence of around 5000 cases in India. (1) In locoregionally advanced Squamous cell carcinoma of the anal canal (SCCA) the standard of care curative treatment approach is concurrent chemoradiation. Concurrent chemoradiation have resulted in better progression free survival (PFS), Colostomy free survival (CFS) and locoregional control in locoregionally confined SCCA. (2–6) Concurrent chemoradiation can result in severe acute toxicity in significant proportion of patients. (7) Conformal radiotherapy techniques like IMRT can reduce the incidence severe adverse events. (8–12) Compared to 3DCRT technique RTOG 0529 study have shown reduction in acute gastrointestinal, hematological and dermatological toxicity with IMRT technique. (13) From India only few studies have reported the tolerance and treatment outcome for Anal canal carcinoma. Hence with this study we wanted to assess the tolerance and clinical outcome of chemoradiation for Anal canal carcinoma patients

MATERIALS & METHODS

This was a retrospective study which included all anal canal carcinoma patients who underwent radical chemoradiation from January 2013 to June 2021 at our centre. Demographic, treatment, toxicity and follow up details were carefully recorded from case records and RT charts.

Operational definition

Disease free survival (DFS): Date of end of treatment to date of disease recurrence.
Overall survival (OS): Date of diagnosis to date of death /date of last follow up.

STATISTICAL ANALYSIS

Descriptive statistics like mean, median, frequencies and percentages were used. Survival outcome like Disease free survival (DFS) & Overall survival (OS) were analysed using Kaplan Meir method.

RESULTS

Total of 18 patient details were analysed. Median age was 59 years. Age ranged from 47years to 71 years. Clinicodemographic details of the patients are given in Table 1

Various treatment details including radiotherapy dosage (RT) schedules, Concurrent chemotherapy schedules, RT technique, treatment break and acute Grade III/IV toxicities are shown in Table 2.

Disease free survival (DFS) at 1 year, 2 years and 3 years were 82.6%, 67.6% and 56.3% respectively. Kaplan Meier curve of DFS is shown in Figure 1.

Overall survival at 1 year, 2 years and 3 years were 88.1%, 80.1% and 70.1% respectively. Kaplan Meier curve of Overal survival (OS) is shown in Figure 2.

DISCUSSION

In our study there were 18 patients with Anal canal carcinoma. Median age of the patients in our study was 59 years. It was similar to study by Kim et al. (14). In another study the median age of patients were slightly higher than that in ours.(15) In our study majority were males(72%). But in similar studies a female preponderance was noticed.(14,15) In our study 17 (94%) patients had Squamous cell carcinoma as histology, but one patient had small cell carcinoma histology. In

majority of studies the histology was only Squamous cell carcinoma. In our study there 3(17%) patients had HIV infection and this proportion was lower compared to a similar study.(16) We staged our patients as per AJCC 8th edition. Majority patients had T3 (72%) as tumor stage . In our study 12 (67%) patients were node positive. But a similar study had a higher proportion of T2 stage patients and node negative patients.(15) The radiotherapy technique most commonly employed was Volumetric modulated Arc therapy (VMAT). Study by Poissel et al have shown better treatment compliance and outcome with VMAT for anal canal carcinoma.(17) Different RT dosage schedules were used in our study and the common schedules being 54Gy in 30 fractions (44%) & 59.4 Gy in 33 fractions (28%) . Median dose was 59.4 Gy in a similar study with a range 57.4 Gy to 63.6 Gy. (18) Capecitabine & Mitomycin combination chemotherapy was the concurrent chemotherapy regimen in 12 patients (67%), 5 FU & Mitomycin combination in 4 patients (22%). One patient who had small cell carcinoma histology received Cisplatin & Etoposide combination chemotherapy as concurrent regimen. Another patient who had synchronous Carcinoma Oropharynx primary received Capecitabine & Cisplatin combination as concurrent chemotherapy. Studies have shown similar efficacy and good tolerance with Capecitabine & Mitomycin combination as concurrent chemotherapy for anal canal carcinoma.(19) Interruption in chemotherapy was observed in 7 patients (39%). Treatment break during radiotherapy was observed in 3 patients (17%) and maximum duration of break was 10 days. Grade 3 or above toxicity were observed in 17 patients. All these 17 patients had Grade 3 dermatitis. One each patient had Grade 4 hematological, Grade 3 hematological and Grade 3 diarrhoea as toxicity. In contrast to our study the Grade 3 or more toxicities were lesser in a similar study.(17) 17 patients completed the planned course of RT. One patient defaulted after 10 fractions of RT and another patient did not complete the last two fractions of the planned course of RT due to toxicity.

Survival outcome in our study were assessed in terms of Disease free survival (DFS) & Overall survival (OS). Median follow up period in our study was 45 months. Median follow up period was different in similar studies.(13,15)DFS in our study at 1year, 2 years and 3 years were 82.6%, 67.6% and 56.3% respectively. OS of our patients at 1year, 2 years and 3 years were 88.1%, 80.1% and 70.1% respectively. 4 year OS, PFS were better in a study which included 127 patients.(13) 2 year DFS was better in another study with larger number of patients.(19) Another study with larger number of patients and longer follow up period showed a better DFS & OS. (15)

CONCLUSION

Concurrent chemoradiation is the standard of care treatment for locoregionally confined anal canal carcinoma. In view of rarity of disease there are no much studies from India looking into the toxicity profile and treatment outcome and with our retrospective study we wanted to assess that. Grade 3 dermatitis was seen for almost all patients, but Grade 3 or more hematological and gastrointestinal toxicity were minimal. RT treatment breaks were seen in only small proportion of patients and almost all patients completed the planned course of RT treatment and hence concurrent chemoradiation can be considered as well tolerated. Survival outcomes in terms of DFS & OS were not in accordance with available literature and was slightly lesser compared to some of the published studies. The propable reason for that could be lesser number of patients, being a single institution experience in an uncommon malignancy.

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Ethics approval and consent
Study was commenced after obtainining Institutional Ethics committee (Ethics Committee of Malabar Cancer Centre, Kerala, India). Consent to participate was deemed not applicable as this was a retrospective study using data with no violation of patient privacy.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions
VNV, APS, GKE were involved in the conception and design of the study, and in the analysis and interpretation of the results. AJ and NY were involved in data collection. VNV, APS, GKE and AM were involved in the preparation of the draft of the manuscript. APN and JJ confirmed the authenticity of all the raw data. All authors have read and approved the final manuscript.

Patient consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Tables

Table1 shows Clinicodemographic details

Variable	Frequencies
Gender	Male : 13 (72%) Female : 5 (28%)
Comorbidities	Yes : 4 (22%) No : 14 (78%)
HIV infection	Yes : 3(17%) No : 15(83%)
T stage distribution	T2 : 2 (11%) T3 : 13 (72%) T4 : 3 (17%)
N stage distribution	N0 : 6 (33%) N1 : 12 (67%)

Table 2 shows treatment details

Variable	Frequencies
RT Dosage schedules	54 Gy in 30 fractions: 8 (44%) 59.4 Gy in 33 fractions: 5 (28%) 53.2 Gy in 28 fractions : 2 (11%) 50.4Gy in 28 fractions: 2 (11%) 50 Gy in 25 fractions :1(6%)
Concurrent chemotherapy schedules	Capecitabine &Mitomycin: 12 (66%) 5 FU &Mitomycin : 4 (22%) Cisplatin &Capecitabine : 1 (6%) Cisplatin &Etoposide : 1(6%)
RT technique	3DCRT : 3(17%) VMAT : 15(83%)
Treatment break	Yes : 3(17%) No : 15 (83%)
Grade III/IV toxicity	Grade III Dermatitis : 17(94%) Grade III hematological : 1(6%) Grade IV hematological : 1 (6%) Grade III diarrhea : 1 (6%)

Figures

Figure 1 shows Kaplan Meier Curve of Disease free survival (DFS)

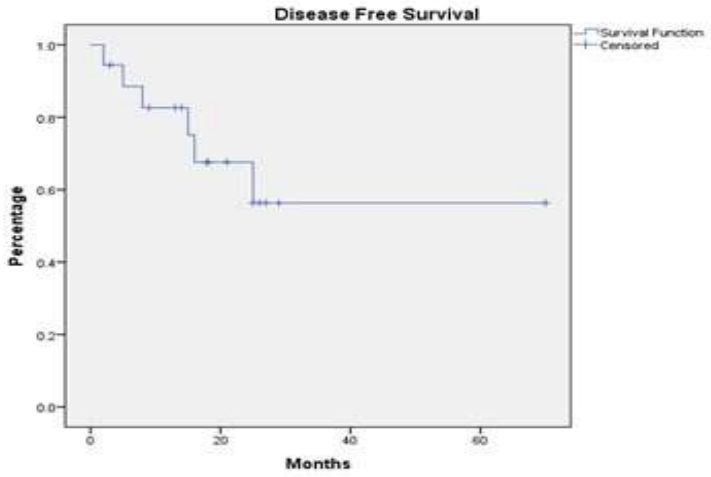

Figure 2 shows Kaplan Meier Curve of Overall Survival (OS)