ORIGINAL RESEARCH PAPER
Volume-8 | Issue-11 | November - 2019 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

OUTCOME OF CHEMORADIATION THERAPY FOR MUSCLE INVASIVE BLADDER CANCER

Oncology

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ABSTRACT

Aim: To study treatment outcome in carcinoma urinary bladder patients who underwent chemoradiation.

Methods: A single institutional study of patients of muscle invasive bladder carcinoma treated with transurethral resection of bladder tumour (TURBT) followed by chemoradiation from January 2014-january 2019 where retrospectively evaluated for response after treatment.

Results: A total of 24 patients were treated from 2014-2019. Age group of 46-84years, mean age 65year. 20 patients were males and 4 female patients. All 24 patients underwent TURBT and radiation therapy. Radical radiation was changed to palliative radiation in 2 patients (due to deteriorating general condition and progressive disease). Rest of 21 patients received concurrent chemoradiation with average dose of 60-66 Gy in 33 fractions, 2Gy per dose fraction. Of this 24 patients, 3 patients expired during the course of treatment, (1patient had seizure disorder and developed aspiration pneumonia,1 due to cardiac arrest and renal failure due volume over load, other patient had sudden cardiac arrest). Complete response was seen in 9 patients, 3 patients had residual disease, 5 patients had progressive disease and 4patients were lost to follow up. Grade 1-3 toxicities were seen during treatment and no grade 4 acute or late toxicity was encountered.

Conclusion: Most of the patients referred to radiation were elderly patients with multiple comorbidities with poor performance status. Our results demonstrate that radiation dose above 60Gy is associated with improved bladder preserved overall survival rates. Overall, concurrent chemoradiation in muscle invasive bladder cancer has demonstrated reasonable efficacy.

KEYWORDS

INTRODUCTION:

Bladder cancer incidence accounts for 3% of all malignancy of all sites, of which Muscle-invasive bladder cancer (MIBC) constitutes about 30% of newly diagnosed bladder cancers, with about 70% being non-invasive. About 15% of non-invasive bladder cancer cases progress to invasive cancer after transurethral resection of bladder tumour (TURBT) [1,2].

Radical cystectomy has been a curative treatment option for MIBC. However, mortality and morbidity rates after surgery cannot be ignored [3]. For many patients who are unfit for surgery due to elderly age, poor medical condition, comorbidities or patient refusal, radiotherapy (RT) is a good alternative therapeutic option. Surgery produces a 5-year local control rate of about 50% and overall survival (OS) rates of 20% to 40% [4,5,6,7,8]. More recently, bladder-preserving therapy including maximal TURBT followed by radiation therapy with or without concurrent chemotherapy in selected patients has become widely used.

Bladder-preserving therapy has several benefits compared to radical surgery. Patients with bladder-preserving therapy can have a better quality of life with intact bladder function. In several recent studies, survival outcomes after bladder-preserving therapy are reportedly comparable to those seen in radical cystectomy series [9,10,11,12].

The present study is designed to retrospectively examine treatment outcomes after bladder-preserving therapy with transurethral resection of bladder followed by radiation or chemoradiation therapy in patients treated at our institution.

MATERIALS AND METHODS

The clinical and pathological case record of patients with histologically proven carcinoma bladder with features of muscle invasion treated at Department of Radiotherapy Father Muller Medical College between 2014 to 2019 were reviewed retrospectively. 24 patients have undergone TURBT and concurrent chemo-radiotherapy at department of radiation oncology, Father Muller Medical College Mangalore. Patients were staged retrospectively according to AJCC classification 2017.The histological grading was according to the World Health Organization classification. Total external beam radiation dose was 60- 66Gy in 30-33Gy per fraction, 5 fractions per week over 6 weeks along with weekly Injection Cisplatin/carboplatin/ combination with gemcitabine and carboplatin concurrently with radiation. Follow up included physical examination, ultrasound abdomen and cystoscopy 3months from the date of treatment completion and then every 6 months thereafter for 2years and annually thereafter. Further investigations were performed when appropriate.

RESULTS

Clinico-pathological characteristics

Median age (range), years	65(46-84)
sex	
Men	20
women	4
ECOG performance scale	
1	15
2	9
Cystoscopy findings	
Unifocal growth	18
Multifocal growth	6
Hydronephrosis	
Present	5
Absent	19
Histology	
TCC	22
Squamous	2
Adenocarcinoma	0
Primary tumour stage, cT	
T2	12
T3	6
T4a	6
Nodal stage, cN	
N0	15
N1	6
N2	3
N3	0

All the patients underwent radiation therapy, 91% received it with radical intent and 9% with palliative intent. 21 patients (87%) received concurrent chemotherapy; 16 of these patients were given weekly carboplatin, whereas 2 patients received weekly cisplatin, 3 patients gemcitabine +carboplatin. 10 patients (40%) completed the planned course of 5-6 cycles of weekly chemotherapy. 79 percent were prescribed >60Gy RT dose and 80% showed complete compliance to RT.

Complete response was seen in 9 patients(37%), 3 patients(12%) had residual disease, 5 patients had progressive disease20%, 4 patients

were lost to follow up(16%). Grade 1-3 toxicities were during treatment. No grade 4 acute or late toxicities were seen.

Treatment and outcome characteristics

Radiotherapy intent	
Radical	22
palliative	2
Radiotherapy dose to primary site	
<60	5
>60	19
Technique	
3DRT	15
IMRT	9
Radiotherapy compliance	
Completed course	19
Defaulted	5
Concurrent chemotherapy	21
cisplatin	2
carboplatin	16
Gemcitabine and carboplatin	3
No chemotherapy	3
Status at last follow up	
Disease free	9
Alive with disease	3
Died of disease/other cause	7
Lost to follow up	4

DISCUSSION

The aim of any oncological intervention is to achieve cure with organ preservation and minimal normal tissue side effects. This directly correlates with quality of life. The most favourable therapeutic strategy to combat muscle invasive bladder cancer is yet to be clearly defined

Munro et all in his study on 458 patients demonstrate that survival comparing RT (37.4% alive at 5 years) with surgery (36.5% alive at 5 years). Initial deaths after surgery were significantly in excess of those after RT, and this correlated with a significant 3-month surgical mortality of 8.3%, vs. 1.65% for RT. Thereafter, the rate of death after primary surgery declined in comparison with RT, until at 5 years the proportion of patients remaining alive remained similar for both treatments and treatment outcomes after 10 years of follow-up between RT (21.6% alive) and surgery (24.1% alive) were almost similar, and the survival curves remain convergent[9].

Kotwal et al. analysed 169 patients and showed the treatment outcomes after radical RT in the form of EBRT or radical cystectomy. About a half of patients were in stage T3 or worse disease in radical RT group and the 5-year OS and disease-specific survival (DSS) was 34.6% and 56.8%, respectively.

RT has a conclusive role in improving bladder preservation therapies with a good impact on quality of life and offering patients a choice of treatment. Early tumor stage, absence of hydronephrosis, and a complete response are the most important factors predicting bladder preservation rate and survival

CONCLUSION

Most of our patient were elderly with multiple comorbidities. Our results demonstrate that radiation dose above 60Gy is associated with improved bladder preserved overall survival rates. Certainly, our study being retrospective in nature, limited number of patients, it has inherent flaws to deduce a definite conclusion. Overall, concurrent chemoradiation in muscle invasive bladder cancer has demonstrated reasonable efficacy.

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