Early outcome of management of Bladder Carcinoma in Octogenarian at Tertiary care hospital

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ABSTRACT

Introduction: Urothelial bladder cancer is a cancer of environment and age. Its incidence increases with age, peaking in the 80's. Unlike other malignancies in which cancer tends to be aggressive in young individuals, the probability of developing muscle invasive bladder cancer increases with age. The standard treatment for non-metastatic muscle invasive bladder cancer (MIBC) is radical cystectomy. However, there is controversy regarding the outcome of radical cystectomy in elderly patients, especially more than 80 years of age.

Methods: This is a retrospective study of collected data. All patients more than 80 years of age with bladder carcinoma were included in the study. Patients with good functional status were offered radical cystectomy (RC). Patients not fit for surgery or refusing surgery were managed with TURBT and chemotherapy.

Results: Out of 23 patients, 13 patients underwent RC with ileal conduit (IC) and 10 patients who refused surgery were managed with TURBT and chemotherapy. Patients who had undergone RC for MIBC survived more than two years while those managed with TURBT succumbed within two years (P value < 0.05).

Conclusions: RC is a safe, feasible and effective treatment option for the carefully selected octogenarian. Age is just a number and should not be an absolute contraindication for RC in patients with non-metastatic muscle invasive bladder cancer.

Key Words: Cystectomy, Octogenarian, Urothelial.

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INTRODUCTION

With gradual increase in life expectancy, the octogenarian population is also on the rise in Nepal. In 2019, the life expectancy of Nepalese at 80 years of age was 5.75 years and the population aged more than 80 years was approximately 216.87 thousand.[1] Urothelial bladder cancer is a cancer of environment and age and its incidence increases with age peaking in the 80's. Unlike other malignancies in which the cancer tends to be aggressive in young individuals, the probability of developing a muscle invasive bladder cancer increases with age.[1,2] The treatment of bladder cancer in the octogenarian population is gaining importance.[3]

The standard treatment for non-metastatic muscle invasive bladder cancer is radical cystectomy. There is controversy regarding the outcome of radical cystectomy in elderly patients, especially in patients over 80 years of age.[4] With improvement in anesthetic techniques, the physiological insult of operation is lowered, hence better outcomes of a surgical procedure are expected even in advanced chronological age. Comorbidity assessed with Charlson Index was associated with decreased cancer-specific survival.[5] Multiple studies have shown that chronological age per se is not a contraindication for radical cystectomy and it can be performed safely in carefully selected elderly populations.[6-9]

There is lack of research regarding the outcome of bladder carcinoma among our population. Hence, this study is conducted with an aim to determine the outcome of management of bladder carcinoma in octogenarian population in a tertiary care hospital in Kathmandu, Nepal.

METHODS

This is a retrospective observational study of collected data among octogenarian with bladder carcinoma. They were managed either by radical cystectomy with ileal conduit (RC + IC) or TURBT and chemotherapy for muscle invasive non-metastatic bladder cancer (MIBC) at a 750 bedded tertiary care center, Shree Birendra Hospital (SBH) affiliated to NAIHS (Nepalese Army Institute of Health Sciences), Kathmandu. The study was conducted for a period of three years from Jan 2017 to Jan 2020 after taking approval from the ethical committee and IRC, NAIHS reference number is 487. Twenty three patients over the age of 80 years were included in the study among which 10 underwent TURBT and chemotherapy (Group A) while 13 patients underwent RC + IC (Group B). Metastatic workup was done in all patients preoperatively with contrast-enhanced CT of chest, abdomen, and pelvis. Those patients who gave consent for RC were admitted one week before the operation date. Incentive spirometry, counseling, adequate hydration, antibiotics, nutritional support (TPN or Albumin) were started according to protocol and patient's need. All patients underwent open RC and pelvic lymphadenectomy with urinary diversion (Ileal-conduit) under Epidural and general anesthesia. The enhanced recovery protocol (ERAS) for urological surgeries was followed postoperatively. Patients were started on clear fluids 12 hours postoperatively, bedside ambulation started on the first postoperative day, drains were removed on postoperative day 4 - 5, soft diet started on day 3 and the ureteric catheter was removed on day 7. We compared tumor pathological characteristics and oncologic results in both groups. None of the patients received neo-adjuvant radiotherapy and / or chemotherapy. Data on patient demographics, operation time, intraoperative blood loss, postoperative complications, stage of the disease, mortality and survival outcome were collected and analyzed. Statistical analysis was performed by using the IBM SPSS ver. 24.0. The $\chi 2$ or Fisher's exact test were used for qualitative variables. The required significance level was set at a p-value less than 0.05.

RESULTS

A total of 23 patients over the age of 80 years with bladder carcinoma were managed during the period of study period in the study hospital. Among them 10 patients underwent conservative (TURBT + Chemotherapy) while 13 patients had undergone radical cystectomy (RC) and adjuvant chemotherapy. The mean age was 87.04 ± 3.1 years (81 – 88 years) in group A, and 83.04 ± 5.1 years (81 – 85 years) in group B. Among 10 patients who underwent conservative therapy, eight were males while two were females and among 13 patients who underwent RC, 12 were males and one female. There was however no significantly difference between gender (P value = 0.141) (Table 1).

Among those patients who underwent RC, it was performed as per the standard practice guidelines with removal of the bladder, distal ureters, seminal vesicles and prostate in men and uterus, anterior vagina and urethra in women. Pelvic lymphadenectomy as shown in Figure 1 was performed in all the patients. An ileal conduit was the urinary diversion of choice in all patients as shown in Figure 2.

Table 1. Demographic profile of the patients with bladder carcinoma

S No	Particulars	Group A (TURBT + Chemo therapy)	Group B RC + Chemo therapy	P value
1.	Total no. of patients	10	13	
2.	Mean age	87.04 ± 3.1	83.04 ± 5.1	
3.	Gender			
	Male	08 (80%)	12 (92.3%)	0.141
	Female	02 (20%)	01(7.2%)	

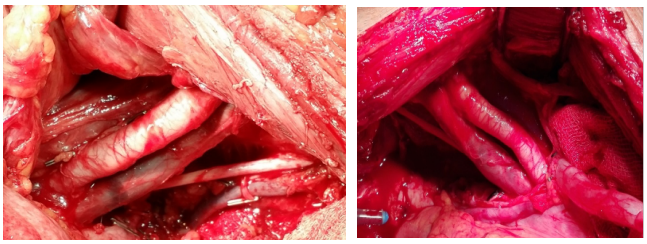

Figure 1. Bilateral Pelvic Lymphadenectomy in patients who underwent Radical Cystectomy (RC).

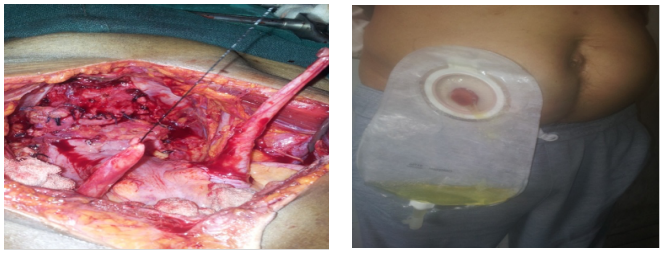

Figure 2. Intraoperative and postoperative figure showing functional Ileal-Conduit among patient who underwent Radical cystectomy (RC).

Indication for cystectomy included any muscle-invading cancer not deemed suitable for segmental resection. Histopathological staging of patient who underwent conservative and surgical procedure is shown in Table 2. Urothelial carcinoma was present in seven (70%) & 10 (76.9%) in patients managed conservatively and surgically respectively, while non-urothelial carcinoma were present in three (30%) and three (23.07%) respectively as shown in Table 2.

Follow-up of the patients ranged from four months to two years. Among patients who underwent conservative management (TURBT + Chemotherapy), six cases of mortality were recorded within two years due to disease progression leading to chronic kidney disease (CKD), urosepsis, chest and cardiac complication secondary to obstructive uropathy. One patient failed to follow up while three patients are still in follow-up.

Table 2. Histopathological staging of the patients with bladder Ca

S. No	Particulars	Group A (TURBT + Chemo therapy)	Group B RC + Chemo therapy	P value
1.	Pathologic stage			
	P T1	-	-	
	pT2	03 (30%)	08 (61.5%)	0.411
	pT3	06 (60%)	05(38.46%)	
	pT4	01 (10%)	-	
2.	Grade			
	I			
	II	06 (60%)	07(53.8%)	0.371
	III	04 (40%)	06 (46.15%)	
3.	Histological Type			
	Urothelial ca	07 (70%)	10 (76.9%%)	0.611
	Non - urothelial ca	03 (30%)	03 (23.07%)	

Table 3. Comparison of overall survival among patients

S. No	Particu-lars	Group A TURBT + Chemother-apy	Group B RC + IC	P value
1.	Mortality within two years	6 (60%)	3 (30.76%)	0.018
2.	Survival more than two years	4 (40%)	10 (69.23%)	

In those patient who underwent surgical procedure (RC + IC), only three patients expired within two years of surgery of which two were due to unrelated causes and one due to disease progression. This was found to be statistically significant (P value = 0.018). One patient failed to follow-up, two patients were started on adjuvant chemotherapy due to nodal metastases and are doing well 12 months and six months after surgery respectively. The other four patients on follow-up are doing well even after two years.

DISCUSSION

Bladder cancer is the tenth most common cancer in both sexes with 430,000 new cases diagnosed in the year 2012 worldwide. It is seventh most common cancer overall and second most common cancer

of genitourinary tract in males. In Nepal, it is fourth most common cancer in males. It is three times more common in males than females worldwide with 80% cases occurring in between 50 to 80 years age group.[4,5] Urinary bladder cancer is commonly seen in males than in females (M: F = 3:1).[5-8] Furthermore, studies done in India revealed higher M: F ratio 8.6:1 which shows male preponderance.[9] Hence similar to other part of the world, in Nepal too, incidence of carcinoma bladder is higher in males than in females. Our study showed similar finding with male predominance of 4.7:1. A similar proportion of incidence has been reported in other studies conducted in Nepal as well. A study conducted in Kathmandu by Joshi HN et al[10] showed the incidence of urinary bladder carcinoma is four-fold higher in the male population and painless hematuria is the most common initial presenting symptom in the Nepalese population. The reason for higher incidence in males could be attributed to environmental conditions, dietary exposure, anatomical differences, urinary habits and hormonal factors whereas, less incidence of bladder cancer in females could be due to less exposure of females to individual carcinogen and less smoking.[10]

Ninety-five percent of bladder tumors are epithelial and the rest are mesenchymal (Non- urothelial). Urothelial tumors account for approximately 90% cases of primary urinary bladder tumors. Our study however showed 70% of cases with epithelial carcinoma. Similar findings were seen in few other studies with a percentage of epithelial carcinoma up to 80%.[11,12] Non- epithelial carcinoma is further sub-classified into urothelial carcinoma in situ, papillary urothelial carcinoma, high grade and low grade, papillary urothelial neoplasm of low malignant potential (PUNLMP), urothelial papilloma and inverted urothelial papilloma.[10-14] Our study showed a similar percentage of more than 50% with high grade tumor among patient who underwent RC. RC with IC or with orthotropic neo-bladder reconstruction has been considered as a standard treatment modality for bladder carcinoma.[12-18] However, out of 23 patients with muscle-invasive disease, only 13 (55.52%) underwent RC. Similar result was seen in the study conducted in Kathmandu, Nepal which showed that only 50% of patient opted for surgery while remaining patient deferred surgery and opted conservative therapy.[10] This could be due to reluctance to undergo major surgery, low acceptance for urinary stoma / conduit, visit to different centers for further treatment, failure to follow after neo-adjuvant chemotherapy. Awareness about treatment and support group, discussion with cancer survivors will help to motivate patients in the future.

The treatment goal in any cancer surgery is to cure the primary neoplasm and preserve quality of life. Though RC with IC has been considered as a challenging procedure that carries a significant risk of short and long-term complications it has been considered superior over conservative management with chemotherapy alone.[16-20] Conservative or alternative strategies often result in progressive, uncontrolled pelvic cancer associated with bleeding, pain disability, obstruction and repeated bladder manipulations.[18] Our study showed similar findings with increased incidence of disease progression leading to chronic kidney disease (CKD), urosepsis, chest and cardiac complication secondary to obstructive uropathy leading to mortality in more than 60% of patient who opted for conservative therapy. Similar findings were noted in studies among patients who opted for conservative therapy in patient with bladder carcinoma.[15-18] Most authors therefore consider that cystectomy is justified in elderly patients whose life expectancy is more than two years.[19,20] The only critical factor for the success of treatment for muscle-invasive carcinoma urinary bladder in the elderly is patient selection.[20]

Our study also showed the better survival rate among patient who underwent RC with IC. The percentage of two year survival among these patients ranged up to 69.23% compared to 40% in patient who underwent conservative therapy alone. Similar findings were noted in a study conducted by Game X et al[21] which showed increased survival rate among patient who underwent surgical management among patient with bladder carcinoma.

RC has been the treatment of choice for the management of Muscle Invasive Bladder carcinoma (MIBC) in most of the Western and developed countries.[7-11] RC and IC can be performed in individuals 80 years of age or older. The survival rates of RC for MIBC are greater when compared with bladder conservation surgery such as transurethral resection of bladder tumors, radiotherapy and chemotherapy. Postoperatively, the majority of patients yield acceptable functional status. The main limitation of our study is that it is a retrospective study subjected to recall and selection bias, and multiple confounding factors might have affected the outcome. Data from this study can be utilized to plan further studies on the same topic in the future.

CONCLUSIONS

With the increasing number of invasive bladder cancer diagnosed among octogenarian's population, age alone should not exclude them from a curative procedure. The treatment goal in any cancer surgery is to cure the primary neoplasm and preserve quality of life. Our study showed that with careful patient selection, RC is a safe, feasible and effective treatment option among octogenarian population with bladder carcinoma.

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