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CLINICAL AND ONCOLOGICAL OUTCOME OF SALVAGE CYSTECTOMY AFTER RADIOTHERAPY FAILURE IN BLADDER CANCER

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ABSTRACT

Objectives: To analyze the clinical and oncological outcomes of Salvage Cystectomy after radiotherapy failure in bladder cancer.

Methodology: A retrospective study was conducted over a 12-year period (January 2005 to December 2017) at the Uro-oncology department of the Shaukat Khanum Memorial Cancer Hospital and Research Center, involving 21 patients who underwent salvage cystectomy. The patients were monitored through cystourethroscopy and imaging (CT/MRI) after receiving chemo-radiotherapy for bladder cancer. Those with histologically confirmed recurrence of malignancy were eligible for salvage cystectomy, excluding metastatic and non-resectable cases. Survival was calculated using the Kaplan-Meier method, and complications were divided into early and late categories.

Results: Of the 21 patients, 86% were male. The median age was 60 years (range, 45-73 years). The median follow-up duration from time of cystectomy was 43 months (range, 5-103 months). The three and five years disease free survival rates were 60% and 47%, respectively, while the calculated three and five years overall survival rates were 58% and 43%, respectively. RC with ileal conduit was performed in all patients. Tumor under staging was noted in 57 % of cases. Distant metastasis was reported in 12 patients (two patients had both local and distant recurrence). Of the 16 cases with complications, early complications (within a month) and delayed complications (after a month) were 9(43%) and 7(33%) respectively.

Conclusion: Salvage cystectomy remains a viable option with acceptable morbidity in bladder-sparing treatment failure for muscle-invasive bladder cancer.

Keywords: Salvage cystectomy; Combined modality therapy; Chemoradiotherapy; Radical cystectomy; Transurethral; Resection; Bladder Tumor; Overall survival; Disease-free survival

INTRODUCTION

Bladder cancer is the 11th most common malignancy in both sexes and the 7th most common malignancy in males worldwide.¹ Muscle-invasive bladder cancer (MIBC) has a very aggressive behavior and poor prognosis. If not treated up to 15 % of patients will survive only for two years.² For many decades, radical cystectomy (RC) has been the gold standard for MIBC. In many centers for T2-T4 bladder cancer, the treatment of choice is RC with urinary diversion due to its acceptable rate of complications and low mortality.^{3,4} Several studies have reported favorable results for RC, while others have shown that these procedures can compromise the quality of life.^{5,6} Bladder preservation treatment has gained interest to maintain the quality of life. Combined modality treatment (CMT) is considered an effective alternative to RC that includes transurethral resection of bladder tumor (TURBT), radiotherapy

and chemotherapy.⁷ Patients with local urinary bladder tumor recurrence after radiotherapy are considered for salvage cystectomy. Salvage cystectomy can be technically challenging due to post-radiotherapy changes.⁸ The desmoplastic reaction surrounding the tissues makes it difficult to distinguish the anatomical surgical planes. Also, tissue ischemia due to radiotherapy can result in vulnerable intestinal tissue with a higher risk of anastomotic site leak and stenosis, prolonged ileus, and delayed wound healing.

METHODOLOGY

After Institutional Review Board approval from the hospital committee, 21 patients were analyzed retrospectively who had undergone salvage cystectomy between January 2005 and December 2017 in Shaukat Khanam Memorial Hospital and Research Center. Patients in our set-up who had been treated with

chemoradiotherapy were followed up with radiological imaging and cystoscopic examination. Initial imaging and cystoscopy were performed three months after the treatment completion and continued at regular intervals. Patients with tumor recurrence on cystoscopy underwent TURBT. Those with histologically proven malignancy were considered for salvage cystectomy.

Patients included in the study were staged clinically prior to the salvage cystectomy (cT) and pathologically post procedure (pT). Organ-confined tumors included T1 and T2, while locally advanced tumors included T3 and T4. Patients with pelvic or abdominal wall involvement (cT4b), lymphatic or visceral metastasis were excluded from the study. Complication rates were defined as the percentage of patients with complications (some patients had more than one complication). Complications reported within 30 days of surgery were called early and others were referred to as delayed. Oncological survival was calculated using the Kaplan-Meier technique.

RESULTS

Most of the 21 patients (86%) were male, with a median age of 60 years (ranging from 45 to 73 years). Out of the 21 patients, 12 passed away due to bladder cancer progression after undergoing salvage cystectomy. Patients hailed from various provinces and a country including Khyber Pakhtunkhwa (7), Punjab (10), Balochistan (1), Sindh (1), and Afghanistan (1), while three deaths were caused by non-cancer factors. One patient was lost to follow-up after 4 years. Six patients were alive and free of disease. RC with ileal conduit was performed in all patients. The three and five years disease free survival (DFS) rates were 60% and 47% respectively (figure 1) while the calculated three and five years overall survivals (OS) rate were 58% and 43 %, respectively (figure 2). Comparison between clinically and pathological

staging's are presented in Table 1. Under staging was reported in 12 (57%) patients. Resection margins were negative in all cases. In 12 patients distant metastasis were diagnosed after salvage cystectomy (while 2 patients were found to have both distant and local disease recurrence within the true pelvis). Median follow-up duration from time of cystectomy was 43 months (range 5 to 103). No patient was found with pathological involvement of lymph node. Of the 16 total complications, early complications (within one month) and delayed complications (after a month) were 9(43%) and 7(33%) respectively. Some patients had more than 1 complication. Early complications included ileus(defined as failure of commencement of oral clear liquids by 6th postoperative day) (2), wound infection (3), deep venous thrombosis (DVT) (2), pulmonary embolism (PE) (1) and

pneumonia (1). Reported delayed complications included uretero-ileal stricture (4), incisional hernia (1), stomal retraction (1) and stomal stenosis(1) (Table 2).

DISCUSSION

In patients with muscle invasive bladder cancer, the main aim of treatment is to provide long term survival with a good quality of life. Although radical cystectomy has shown a clear advantage over other treatments to extend survival but is also associated with significant morbidity and effect on quality of life. Chemo radiotherapy is not the treatment of choice for MIBC but is now being supported by emerging data.²

The reason for a growing interest in bladder preserving chemo-RT (combined chemo

Table 1: Clinical and pathological staging

cT	pT					
	pT0	pTa/T1	pT2	pT3	pT4a	pT4b
T2	9	3	2	4	-	-
T3	12	-	2	5	5	-

Table 2: Early and delayed complications of salvage cystectomy

	Complications	No of Patients
Early (9)	Uretero-ileal anastomotic leak	-
	Abdominal wall dehiscence	-
	Wound infection	3
	Deep venous thrombosis	2
	Pneumonia	1
	Pulmonary embolism	1
	Bleeding	-
	Ileus	2
Delayed (7)	Incisional hernia	1
	Uretero-ileal stenosis	4
	Stomal retraction	1
	Stomal stenosis	1
	Para stomal hernia	-
	Para stomal skin excoriation	-

and radiotherapy) has been because of is the benefit of retaining the native urinary bladder with maintenance of quality of life along with a comparable survival.^{9,10}

At our institution non metastatic muscle invasive bladder cancer patients were counseled about radical surgery and chemo-RT. Treatment modality depended upon the patient choice. Post chemo-RT failure patients with resectable disease were offered salvage cystectomy. MRI and CT are useful investigations test to assess adjacent organs involvement and gross lymphatic metastases. However, in post radiotherapy patients it is difficult to differentiate between tumor infiltration and radiation fibrosis.¹¹ Due to post radiotherapy desmoplastic reaction and anatomical plans obliteration, it is difficult to determine the exact clinical staging and result in substantial under-staging.¹² We noted under staging in almost 57% of our study.

In our study DFS and OS are very close to each other. The overall survival probability in our study is slightly higher than that reported by Netherlands Cancer institute (3- and 5-year survival probability was 46% and 33 % respectively).¹³ Other long term studies with large number of patients have reported better results with 10-year disease free survival rate of 48%¹⁴ and 44%.¹⁵ Three patients our study died of non bladder cancer causes. One patient was diagnosed with a second primary colorectal tumor during follow up and died of that cancer as it was irresectable.

The early and delayed complications in our study were 43% and 23% respectively. All patients with wound infections needed no surgical intervention and were treated with culture and sensitivity based antibiotics. Patient with pulmonary embolism and DVT were treated with anti-coagulants. Four patients with urteroileal anastomotic strictures, were initially treated with PCN (per cutaneous nephrostomy tube) to relieve the obstructed

pelvi calyceal system. Thereafter one of them underwent exploration with re anastomosis and other was treated with balloon dilatation. Intervention was not feasible in two patients and continued with indwelling PCN tubes on permanent bases. Stomal dilatation and stoma refashioning were performed in patients with stomal stenosis and retracted stoma respectively. Patient with incisional hernia had no distressing symptom and was managed conservatively.

Multiple studies have reported complications with different management approaches, hence one should be careful during comparison. Early (within 30 days) complication rate of 33% after salvage cystectomy was reported by two studies Nieuwenhuijzen¹³ et al and Bochner et al¹⁶. At median follow up of 57 months Wammack et al reported 1.14 complications per patient.¹⁷ Some studies have reported the complication rate that occurred within and after 90 days. The initial 90-day complication rates reported by two different studies were 77%¹⁸ and 69%.¹⁴ Our reported study size is small with all the patients having undergone a urinary diversion with an ileal conduit. This precludes assessment of any complications associated with a neo bladder formation post salvage cystectomy.

CONCLUSION

Tumor under staging remains a significant disadvantage during workup and planning for a salvage cystectomy. Till newer modalities are available to treat chemo radiotherapy failure in MIBC patients, salvage cystectomy remains a viable option with acceptable morbidity.

REFERENCES

1. Ferlay J, Colombet M, Soerjomataram I, Dyba T, Randi G, Bettio M, et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and

25 major cancers in 2018. *Eur J Cancer*. 2018;103:356-87. DOI:10.1016/j.ejca.2018.07.005.

2. Gakis G, Efstathiou J, Lerner SP, Cookson MS, Keegan KA, Guru KA, et al. ICUD-EAU International Consultation on Bladder Cancer 2012: Radical cystectomy and bladder preservation for muscle-invasive urothelial carcinoma of the bladder. *Eur Urol*. 2013;63(1):45-57. DOI:10.1016/j.eururo.2012.08.009.
3. Novara G, De Marco V, Aragona M, Boscolo-Berto R, Cavalleri S, Artibani W, et al. Complications and mortality after radical cystectomy for bladder transitional cell cancer. *J Urol*. 2009;182(3):914-21. DOI:10.1016/j.juro.2009.05.032.
4. Donat SM, Shabsigh A, Savage C, Cronin AM, Bochner BH, Dalbagni G, et al. Potential impact of postoperative early complications on the timing of adjuvant chemotherapy in patients undergoing radical cystectomy: a high-volume tertiary cancer center experience. *Eur Urol*. 2009;55(1):177-85. DOI:10.1016/j.eururo.2008.07.018.
5. Gerharz EW, Mansson A, Hunt S, Skinner EC, Mansson W. Quality of life after cystectomy and urinary diversion: an evidence based analysis. *J Urol*. 2005;174(5):1729-36. DOI:10.1097/01.ju.0000176463.40530.05.
6. Henningsohn L, Steven K, Kallestrup EB, Steineck G. Distressful symptoms and well-being after radical cystectomy and orthotopic bladder substitution compared with a matched control population. *J Urol*. 2002;168(1):168-74; discussion 174-5. DOI:10.1016/s0022-5347(05)64854-9.
7. Shipley WU, Kaufman DS, Zehr E, Heney NM, Lane SC, Thakral HK, et al. Selective bladder preservation by combined modality protocol treatment: long-term outcomes of 190 patients with invasive bladder cancer. *Urology*.

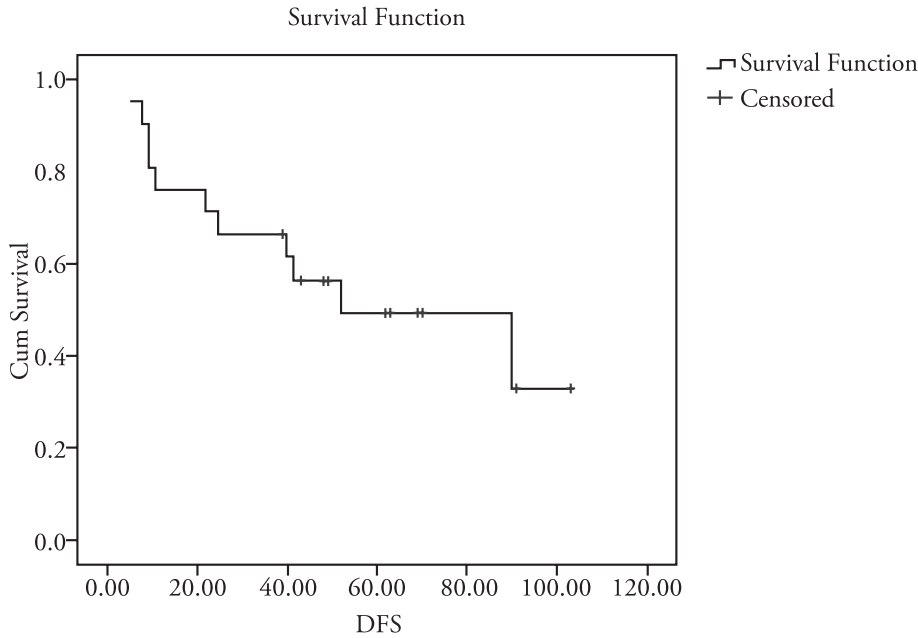


Figure 1: Disease free survival of salvage cystectomy

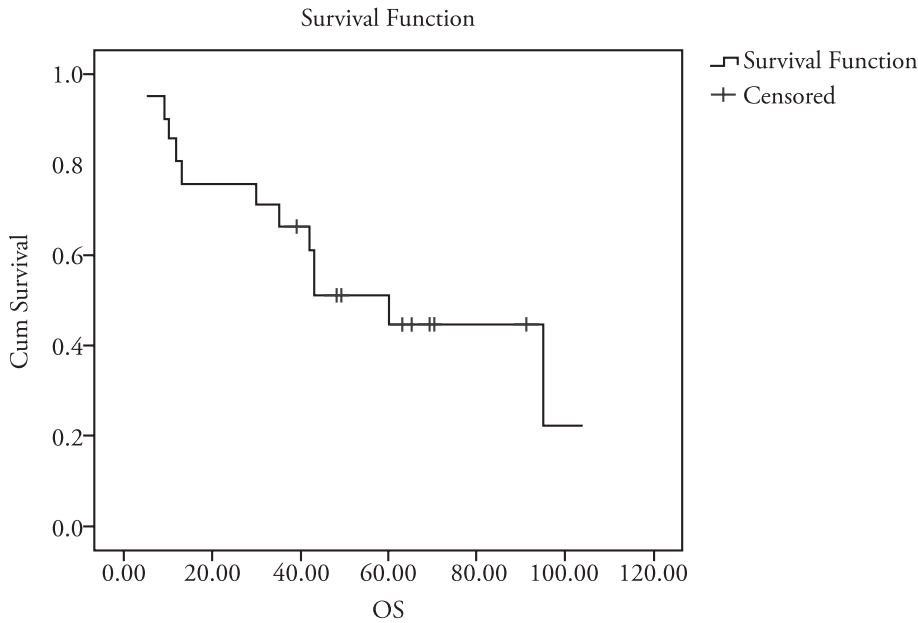


Figure 2: Overall survival of salvage cystectomy

Organ conservation in invasive bladder cancer by transurethral resection, chemotherapy and radiation: results of a urodynamic and quality of life study on long-term survivors. *J Urol.* 2003;170(5):1772-6. DOI:10.1097/01.ju.0000093721.23249.c3.

11. Dixon AK, Deane AM, Doyle PT. Computed tomography and magnetic resonance imaging before salvage cystectomy. *Br J Urol.* 1990;66(1):42-6. DOI:10.1111/j.1464-410x.1990.tb14863.x.
12. Droller MJ, Walsh PC. Therapeutic efficacy of salvage cystectomy. Do results reflect natural history of bladder cancer? *Urology.* 1983;22(2):118-22. DOI:10.1016/0090-4295(83)90489-2.
13. Nieuwenhuijzen JA, Horenblas S, Meinhart W, van Tinteren H, Moonen LM. Salvage cystectomy after failure of interstitial radiotherapy and external beam radiotherapy for bladder cancer. *BJU Int.* 2004;94(6):793-7. DOI:10.1111/j.1464-410x.2004.05034.x.
14. Eswara JR, Efstathiou JA, Heney NM, Paly J, Kaufman DS, McDougal WS, et al. Complications and long-term results of salvage cystectomy after failed bladder sparing therapy for muscle invasive bladder cancer. *J Urol.* 2012;187(2):463-8. DOI:10.1016/j.juro.2011.09.159.
15. Efstathiou JA, Spiegel DY, Shipley WU, et al. Long-term outcomes of selective bladder preservation by combined-modality therapy for invasive bladder cancer: the MGH experience. *Eur Urol.* 2012;61:705e711. DOI:10.1016/j.eururo.2011.11.010
16. Bochner BH, Figueroa AJ, Skinner EC, Lieskovsky G, Petrovich Z, Boyd SD, Skinner DG. Salvage radical cystoprostatectomy and orthotopic urinary diversion following radiation failure. *J Urol.* 1998;160(1):29-33. DOI:10.1016/s0022-5347(01)63018-0
17. Wammack R, Wricke C, Hohenfellner R.

- 2002;60(1):62-7; discussion 67-8. DOI:10.1016/s0090-4295(02)01650-3.
8. Schuster TG, Marcovich R, Sheffield J, Montie JE, Lee CT. Radical cystectomy for bladder cancer after definitive prostate cancer treatment. *Urology.* 2003 Feb;61(2):342-7; discussion 347. DOI:10.1016/s0090-4295(02)02272-0.
9. Efstathiou JA, Bae K, Shipley WU, Kaufman DS, Hagan MP, Heney NM, et al. Late pelvic toxicity after bladder-sparing therapy in patients with invasive bladder cancer: RTOG 89-03, 95-06, 97-06, 99-06. *J Clin Oncol.* 2009;27(25):4055-61. DOI:10.1200/JCO.2008.19.5776.
10. Zietman AL, Sacco D, Skowronski U, Gomery P, Kaufman DS, Clark JA, et al.

Long-term results of ileocecal continent urinary diversion in patients treated with and without previous pelvic irradiation. J Urol. 2002;167(5):2058-62.

DOI:10.1016/S0022-5347(05)65083-5.
18. Eisenberg MS, Dorin RP, Bartsch G, Cai J, Miranda G, Skinner EC. Ear-

ly complications of cystectomy after high dose pelvic radiation. J Urol. 2010;184(6):2264-9. DOI:10.1016/j.juro.2010.08.007.

Author's Contribution

SF conceived the idea, collected the data and contributed in article writing. AA, SA, YM and ZAC contributed in collection of data. MAB conducted the statistical analysis and KM revised the manuscript for the final review.. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.