Survival analysis comparing bladder preservation techniques in octogenarians with muscle-invasive bladder cancer

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Background: The gold standard treatment for localized muscle-invasive bladder cancer (MIBC) is neoadjuvant chemotherapy with radical cystectomy (RC). Guidelines suggest concurrent chemoradiation (CRT) could be considered as an alternative, and partial cystectomy (PC) may be considered in carefully selected individuals. The bladder preservation strategies are gaining popularity, and due to the concerns about morbidity associated with RC and limited life expectancy, the octogenarian population is exploring strategies that help preserve bladder function. Hence, it is crucial to understand the outcome of various bladder preservation strategies. Using the National Cancer Database (NCDB), we compared the overall survival (OS) of octogenarians treated with PC and CRT.

Methods: We retrospectively evaluated the octogenarians with localized MIBC (cT2N0M0) ≤5 cm and urothelial histology between 2004 and 2018. Our analytic cohorts were the PC cohort, which included patients who underwent PC, and the CRT cohort, which included patients who received chemotherapy and radiotherapy within a 90-day timeframe. After propensity-matching with race and ethnicity, gender, facility type, median income, comorbidity index, and tumor grade, we compared the OS between PC and CRT cohorts.

Results: A total of 1,038 were octogenarians who met our selection criteria. Among them, 248 (23.8%) underwent PC, and 790 (76.2%) received CRT. In the PC cohort, tumors were located predominantly in the dome (34.3%) and anterior wall (10.5%), while in the CRT cohort, tumors were in the trigone (8.4%), lateral (22.0%) and posterior walls (10.6%). The median OS for the matched PC and CRT cohort was 38.3 and 32.9 months, respectively (P=0.66). Multivariate Cox regression showed no difference in survival hazards between PC and CRT [hazard ratio =1.07 (95% confidence interval: 0.82–1.39)] (P=0.63).

Conclusions: Our study comparing PC and CRT in octogenarians with T2 ≤5 cm tumors showed that PC had comparable OS to CRT. Therefore, PC can be considered a viable option in carefully selected octogenarians.

Keywords: Bladder preservation; partial cystectomy (PC); chemoradiation (CRT); octogenarians; elderly

Introduction

In the United States, bladder cancer is ranked as the 6th most common cancer, and globally, it is ranked 10th, accounting for 2% to 3% of all malignancies (1). The median age at diagnosis of bladder cancer is 73 years, and approximately 20% to 30% of patients were identified with muscle-invasive bladder cancer (MIBC) at the time of diagnosis (2,3). About 71.4% of individuals above 65 years are diagnosed with bladder cancer with a higher incidence at 85 years (4). It was estimated that in 2023, approximately 82,300 newly diagnosed cases and 16,700 deaths were secondary to bladder cancer (5). Over decades, the average life expectancy of an individual has been increasing. The life expectancy for older adults above 80 years old is 8 to 10 years and may vary depending on the associated co-morbidities. In the United States, the life expectancy for men and women aged 80 years old is 7 and 9.1 years, respectively (6,7). In recent years, many individuals in their eighties are undergoing major surgeries due to improvements in the healthcare system and increased life expectancy. Therefore, it is crucial to understand the outcomes of various treatments in octogenarians.

Neoadjuvant chemotherapy with radical cystectomy (RC) is the standard of care for MIBC, and its effectiveness has been well-established (8,9). As bladder preservation protocols like chemoradiation (CRT) are gaining popularity, and due to factors like morbidity associated with RC and life expectancy for age, some elderly populations prefer strategies that help preserve bladder function. Guidelines suggest RC as the preferred first-line treatment and concurrent CRT as an alternative in MIBC. Similarly, partial cystectomy (PC) is suggested as a viable option in carefully selected individuals with solitary lesions and no carcinoma *in situ* (10). Until the mid-1980s, PC was used in good numbers to treat bladder cancer. With the lack of definitive indication and the concern about oncological and survival outcomes, the usage of PC was limited. Studies have compared survival outcomes between RC and PC and observed that PC may have comparable outcomes in carefully selected individuals with structured criteria (11-14). Similarly, studies have shown that CRT and RC may have comparable oncological and survival outcomes (15,16). Therefore, as an option for bladder preservation, it is essential to understand the outcomes of PC and CRT among the elderly population. Our study uses the National Cancer Database (NCDB) to evaluate the survival outcomes among octogenarians treated with PC and CRT. We present this article in accordance with the STROBE reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-24-602/rc).

Methods

Patient selection

Our retrospective study focused on elderly individuals aged 80 years old and above diagnosed with MIBC and urothelial histology between 2004 and 2018. Our selection criteria included patients having cT2N0M0 with tumor size ≤5 cm and urothelial histology. We gathered data from the National Cancer Database (NCDB), which covers nearly 70% of newly diagnosed cancer cases in the United States (17). The study employed deidentified participant user files, which comply with the Health Insurance Portability and Accountability Act regulations. Quality checks are conducted annually to validate the data. Since the data used are publicly available upon request and are deidentified, re-identification is unlikely, and as the data do not involve direct human subjects, institutional review board approval and informed consent were deemed not required (17,18). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). We divided our primary cohort into two categories based on

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Highlight box

Key findings
- Among bladder preservation strategies, partial cystectomy (PC) and chemoradiation (CRT) had comparable overall survival among the octogenarian population with muscle-invasive urothelial bladder carcinoma

What was recommended and what is new?
- Concurrent CRT is considered an alternative to radical cystectomy, which is the preferred first-line treatment for muscle-invasive bladder cancer.
- Our study using the National Cancer Database observed that PC had comparable survival outcomes to CRT in carefully selected octogenarians with well-defined criteria.

What is the implication, and what should change now?
- Among carefully selected octogenarians concerned about bladder preservation, these findings could encourage and help with patient counseling and shared decision-making. As the overall survival with PC is comparable with CRT, PC may be considered a viable option in carefully selected octogenarians with muscle-invasive bladder cancer, but it needs further exploration.
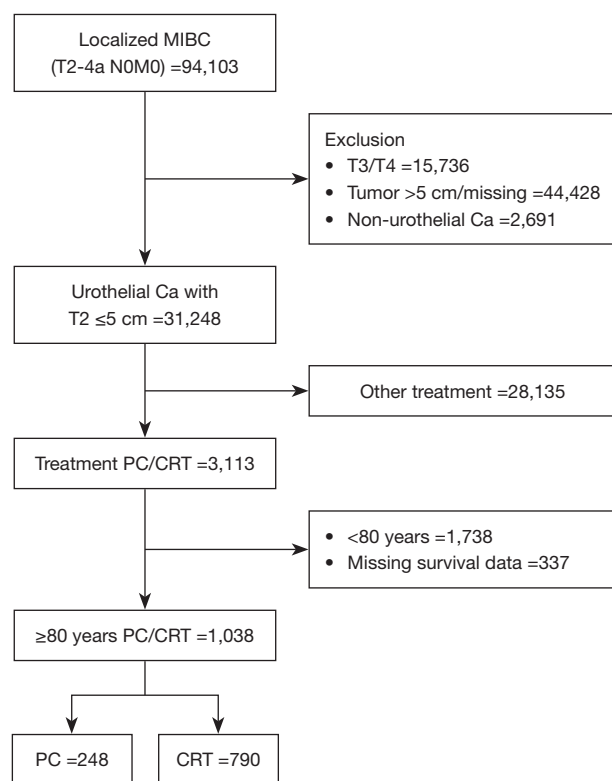

Figure 1 Study population for partial cystectomy and chemoradiation in octogenarians. PC, partial cystectomy; CRT, chemoradiation; MIBC, muscle-invasive bladder cancer; Ca, carcinoma.

the intervention: PC and CRT cohorts. The PC cohort included those who underwent PC (coded as PC), and the CRT cohort included individuals who received both chemotherapy and radiation of ≥39.6 Gy within the 90-day timeframe (19). We excluded cases with variant histology, those who underwent cystectomy, carcinoma *in situ*, hydronephrosis, and those with missing data on chemotherapy, radiotherapy, or follow-up. Our final study population included 3,113 octogenarians who met our inclusion and exclusion criteria (*Figure 1*).

Statistical analyses

We analyzed sociodemographic factors like race and ethnicity, gender, insurance, median income, and treatment facility and clinical factors like clinical stage, tumor size, tumor grade, and comorbidity score 30- and 90-day mortality to compare both treatment cohorts. Ethnicity was categorized as Hispanic, non-Hispanic, and others. Race was simplified into white, black, and others.

This simplification was performed because of the few patients representing other categories. The clinical and sociodemographic information was evaluated using the Chi-squared test and contingency tables. Propensity score matching with Mahalanobis distance was performed to match both intervention cohorts and to minimize the effect of confounders. Variables like race and ethnicity, gender, comorbidity score, facility type, median income, and tumor grade were used for matching. Kaplan-Meier survival analyses with log-rank test and multivariate Cox regression analyses were used to compare the survival outcomes between both treatment modalities. A P value of <0.05 was defined as a statistically significant difference in all parts of the analyses. We performed the statistical analysis using SAS software, version 9.4.

Results

A total of 671,462 patients were diagnosed with bladder cancer between 2004 and 2018, with 94,103 having localized MIBC and urothelial histology (*Figure 1*). Among them, 3,113 had T2 tumors ≤5 cm and underwent PC or CRT. Among them, 1,038 were octogenarians who met our selection criteria. In this population, 248 (23.8%) had undergone PC, and 790 (76.2%) underwent CRT (*Figure 1*). The mean [± standard deviation (SD)] for age of patients treated with PC and CRT was 84.1 (±3.2) and 84.4 (±3.0) years, and the mean (± SD) for follow-up was 40.2 (±32.6) months and 35 (±28.7) months, respectively. After propensity-matching, each cohort had 248 patients. Our analysis (*Table 1*) showed that the location of tumors in PC and CRT cohorts were 85 (34.3%) and 46 (5.8%) in the dome, 1 (0.4%), and 66 (8.4%) in the trigone, 33 (13.3%) and 174 (22.0%) were in the lateral wall, 19 (7.7%) and 84 (10.6%) were in the posterior wall of the bladder, 26 (10.5%) and 43 (5.4%) were in the anterior wall (P<0.001). The 30-day mortality was 1.2% *vs*. 0%, and the 90-day mortality was 3.2% *vs*. 0.6% in patients who underwent PC and CRT, respectively (P<0.001). Among those who underwent PC, 13 (5.2%) received adjuvant radiation, and 34 (13.7%) received adjuvant chemotherapy. There was no statistically significant difference in gender, race, ethnicity, median income, insurance, facility type, comorbidity index, tumor grade, and 30-day readmission.

Kaplan-Meier survival analysis showed the median overall survival (OS) for the unmatched population of PC and CRT cohorts (*Figure 2A*) was 38.3 [95% confidence interval (CI): 31.6–46.7] and 33.5 (95% CI: 29.9–38.6) months (P=0.40),

Table 1 Socio-demographics parameters of matched and unmatched population of PC and CRT among octogenarians

Variables	Unmatched population			Matched population		
	PC (N=248)	CRT (N=790)	P value	PC (N=248)	CRT (N=248)	P value
Sex			0.87			0.99
Male	177 (71.4)	568 (71.9)		177 (71.4)	177 (71.4)	
Female	71 (28.6)	222 (28.1)		71 (28.6)	71 (28.6)	
Race			0.84			0.71
White	228 (91.9)	724 (91.6)		228 (91.9)	232 (93.5)	
Black	11 (4.4)	41 (5.2)		11 (4.4)	10 (4.0)	
Others	9 (3.6)	25 (3.2)		9 (3.6)	6 (2.4)	
Ethnicity			0.45			0.80
Non-Hispanic	238 (96.0)	742 (93.9)		238 (96.0)	237 (95.6)	
Hispanic	3 (1.2)	12 (1.5)		3 (1.2)	2 (0.8)	
Others	7 (2.8)	36 (4.6)		7 (2.8)	9 (3.6)	
Insurance			0.74			0.84
Private	20 (8.1)	62 (7.8)		20 (8.1)	16 (6.5)	
Medicare	224 (90.3)	706 (89.4)		224 (90.3)	226 (91.1)	
Others	2 (0.8)	14 (1.8)		2 (0.8)	3 (1.2)	
Unknown	2 (0.8)	8 (1.0)		2 (0.8)	3 (1.2)	
Median income			0.88			0.84
<$46,277	27 (10.9)	93 (11.8)		27 (10.9)	27 (10.9)	
$46,277–$57,856	51 (20.6)	167 (21.1)		51 (20.6)	50 (20.2)	
$57,857–$74,062	58 (23.4)	178 (22.5)		58 (23.4)	50 (20.2)	
≥$74,063	85 (34.3)	282 (35.7)		85 (34.3)	87 (35.1)	
Unknown	27 (10.9)	70 (8.9)		27 (10.9)	34 (13.7)	
Facility type			0.22			0.86
Community CP	21 (8.5)	75 (9.5)		21 (8.5)	16 (6.5)	
Comprehensive CCP	108 (43.5)	369 (46.7)		108 (43.5)	109 (44.0)	
Academic program	70 (28.2)	172 (21.8)		70 (28.2)	72 (29.0)	
Integrated network	49 (19.8)	174 (22.0)		49 (19.8)	51 (20.6)	
Comorbidity index			0.76			0.76
CCI 0	155 (62.5)	498 (63.0)		155 (62.5)	165 (66.5)	
CCI 1	59 (23.8)	199 (25.2)		59 (23.8)	55 (22.2)	
CCI 2	24 (9.7)	60 (7.6)		24 (9.7)	21 (8.5)	
CCI 3	10 (4.0)	33 (4.2)		10 (4.0)	7 (2.8)	
30-days readmission			0.16			0.22
No admission	224 (90.3)	738 (93.4)		224 (90.3)	236 (95.2)	
Unplanned	10 (4.0)	15 (1.9)		10 (4.0)	5 (2.0)	
Planned	7 (2.8)	13 (1.6)		7 (2.8)	4 (1.6)	
Unknown	7 (2.8)	24 (3.0)		7 (2.8)	3 (1.2)	

Table 1 (*continued*)

Table 1 (*continued*)

Variables	Unmatched population			Matched population		
	PC (N=248)	CRT (N=790)	P value	PC (N=248)	CRT (N=248)	P value
Tumor location			<0.001			<0.001
Trigone	1 (0.4)	66 (8.4)		1 (0.4)	20 (8.1)	
Dome	85 (34.3)	46 (5.8)		85 (34.3)	15 (6.0)	
Lateral wall	33 (13.3)	174 (22.0)		33 (13.3)	54 (21.8)	
Anterior wall	26 (10.5)	43 (5.4)		26 (10.5)	11 (4.4)	
Posterior wall	19 (7.7)	84 (10.6)		19 (7.7)	27 (10.9)	
Others	33 (13.3)	157 (19.9)		33 (13.3)	49 (19.7)	
Bladder NOS	51 (20.6)	220 (27.8)		51 (20.6)	72 (29.0)	
Tumor grade			0.70			0.41
Grade II	6 (2.4)	15 (1.9)		6 (2.4)	2 (0.8)	
Grade III	93 (37.5)	275 (34.8)		93 (37.5)	107 (43.1)	
Grade IV	130 (52.4)	422 (53.4)		130 (52.4)	121 (48.8)	
Unknown	19 (7.7)	78 (9.9)		19 (7.7)	18 (7.3)	
30-day mortality			<0.001			0.049
Alive	245 (98.8)	787 (99.6)		245 (98.8)	247 (99.6)	
Dead	3 (1.2)	0 (0.0)		3 (1.2)	0 (0.0)	
Missing	0 (0)	3 (0.4)		0 (0)	1 (0.4)	
90-day mortality			<0.001			0.01
Alive	240 (96.8)	783 (99.1)		240 (96.8)	246 (99.2)	
Dead	8 (3.2)	5 (0.6)		8 (3.2)	1 (0.4)	
Missing	0 (0)	2 (0.3)		0 (0)	1 (0.4)	

Data are presented as n (%). PC, partial cystectomy; CRT, chemoradiation; CP, Cancer Program; CCP, Community Cancer Program; NOS, not specified; CCI, Charlson-Deyo Comorbidity Index.
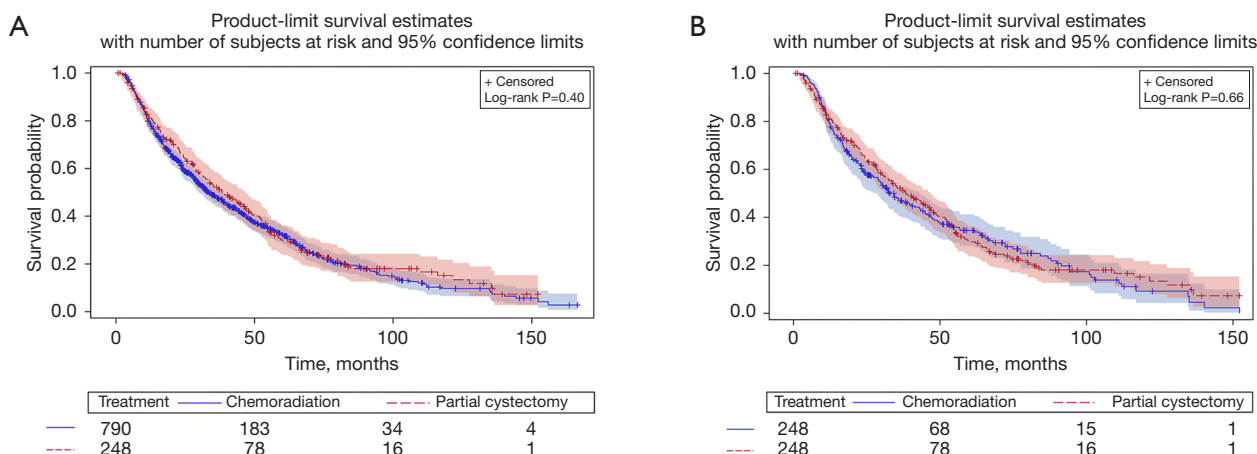

Figure 2 Overall survival comparing unmatched (A) and matched (B) populations of partial cystectomy and chemoradiation among octogenarians with muscle-invasive bladder cancer.

Table 2 Multivariate Cox regression for the matched PC and CRT cohorts

Parameter	Hazard ratio (95% CI)	P value
Treatment (*vs.* PC)		
CRT	1.07 (0.82–1.39)	0.63
Sex (*vs.* male)		
Female	0.70 (0.53–0.91)	0.008
Race (*vs.* White)		
Black	0.82 (0.46–1.45)	0.49
Unknown	0.56 (0.24–1.28)	0.17
Ethnicity (*vs.* non-Hispanic)		
Hispanic	2.01 (0.73–5.51)	0.18
Unknown	1.33 (0.72–2.46)	0.36
Insurance (*vs.* private)		
Medicare	0.86 (0.54–1.37)	0.53
Others	0.52 (0.09–2.90)	0.45
Unknown	1.82 (0.51–6.54)	0.36
Facility type (*vs.* community CP)		
Comprehensive CCP	0.83 (0.53–1.30)	0.42
Academic program	0.66 (0.41–1.06)	0.09
Integrated network	0.83 (0.50–1.37)	0.46
Comorbidity index (*vs.* CCI 0)		
CCI 1	1.12 (0.83–1.52)	0.44
CCI 2	1.97 (1.32–2.94)	<0.001
CCI 3	3.09 (1.64–5.83)	<0.001
Tumor location (*vs.* trigone)		
Dome	0.92 (0.45–1.86)	0.81
Lateral wall	0.96 (0.49–1.87)	0.90
Anterior wall	1.13 (0.53–2.39)	0.76
Posterior wall	0.65 (0.31–1.35)	0.25
Other	0.90 (0.44–1.84)	0.77
Bladder NOS	1.06 (0.55–2.03)	0.87
Tumor grade (*vs.* grade IV)		
Grade II	0.23 (0.01–4.55)	0.34
Grade III	0.85 (0.66–1.09)	0.20
Unknown	0.75 (0.48–1.19)	0.22

PC, partial cystectomy; CRT, chemoradiation; CI, confidence interval; CP, Community Program; CCP, Cancer Community Program; NOS, not specified; CCI, Charlson-Deyo Comorbidity Index.

and the matched population (*Figure 2B*) was 38.3 (95% CI: 31.6–46.7) and 32.9 (95% CI: 28.8–43.3) months (P=0.66), respectively. Multivariate Cox regression analysis for the matched population (*Table 2*) showed there was no significant difference in the risk of mortality between PC and CRT cohorts [hazard ratio =1.07 (95% CI: 0.82–1.39)] (P=0.63). Similarly, there was no significant difference in mortality risk based on tumor location. However, females had a reduced risk of mortality compared to males, and the mortality risk increased with an increase in the comorbidity index. No significant difference in the mortality risk was seen in race, ethnicity, insurance, facility type, tumor location, and tumor grade.

Discussion

In our study comparing the survival outcomes of PC and CRT in T2 ≤5 cm tumors among octogenarians, we observed there was no significant difference in survival between patients undergoing PC and CRT. Tumors in the dome and anterior wall had predominantly undergone PC, while tumors in the lateral and posterior walls underwent CRT. The 30- and 90-day mortality rates were higher in PC compared to CRT. Patients with an increase in the comorbidity index had an increased mortality risk. However, there was no difference in mortality risk based on race, ethnicity, facility type, tumor location, and tumor grade.

Studies have evaluated the effectiveness of PC in MIBC with different settings. Peak *et al.* observed that in patients with bladder cancer, 7% to 10% underwent PC, and 2.8% of them had MIBC. They stated that only 5–10% of patients with MIBC were suitable for PC, and selecting more appropriate patients with timely radiotherapy and chemotherapy could yield better outcomes (20). A study by Kassouf *et al.* observed that 5-year disease-specific survival (DSS) and OS for PC were 87% and 67%, respectively, and superficial tumors, clinical T-stage, and adjuvant chemotherapy were associated with higher recurrence-free survival (RFS) (21). Knoedler *et al.* noted no significant difference between PC and RC with regard to 10-year cancer-specific survival (CSS) (58% *vs.* 63%, P=0.63), but the retreatment rate for PC was 18.6% (22). In a study by Zhang *et al.* on localized MIBC, the 5-year OS for PC with intravesical chemotherapy was 44.6% and stated that PC with intravesical chemotherapy could achieve a comparable tumor control to RC in patients with solitary lesions (23). These studies highlight that PC may offer survival benefits

with structured selection criteria. We studied T2 ≤5 cm tumors among octogenarians and observed that OS for PC was non-inferior to CRT, suggesting PC could offer beneficial survival outcomes in carefully selected individuals with well-defined criteria.

In our study, we observed that tumors primarily located in the lateral and posterior walls predominantly underwent CRT, while those in the dome of the bladder underwent PC, which could have been a potential bias. However, there was no difference in the mortality risk based on tumor location. Many studies have reported that CRT has considerable oncological and survival outcomes. de Ruiter *et al.* observed that CRT is a safe and effective treatment in nonmetastatic MIBC, with an initial cystoscopy showing a 90% complete response and a 5-year DSS and OS in 50% of patients (24). Jiang *et al.*, in their study on neoadjuvant chemotherapy with CRT, observed that cisplatin-tolerating patients had better 2-year DSS and OS (25). A study by Kotha *et al.* on elderly with MIBC with urothelial histology from the US Veteran Affairs National Database observed that CRT is effective with a 6-year OS rate of 25.7% (26). In our study on octogenarians, we observed that CRT had a 5-year OS of 32.2%. Studies have shown that low-volume solitary lesions, T2 tumors, no carcinoma *in situ*, and nodal metastasis are suitable for bladder-sparing and improving survival outcomes (27). In our research on bladder preservation, PC and CRT both had comparable survival outcomes. Therefore, the lack of well-structured selection criteria and concerns about oncological and survival outcomes could have possibly limited the utilization of PC.

Su *et al.*, in their Surveillance, Epidemiology, and End Results (SEER) database study, compared PC and trimodality therapy as bladder preservation strategies and observed that PC had better survival outcomes than the trimodality approach with a median OS of 41 and 21 months, respectively (28). Our study on the octogenarians who underwent PC with stringent selection criteria like T2 tumors ≤5 cm with no carcinoma *in situ* had comparable survival outcomes to CRT, suggesting PC could be considered in carefully selected individuals. In a tetra modality treatment protocol by Kijima *et al.*, patients treated with induction CRT and consolidative PC had a 5-year CSS rate of 83% and OS of 77% (29). In another study on tetra modality treatment on elderly aged 75 and above, they observed that 5-year RFS and CSS were 98% and 95%, respectively (30). In our study, limited data was available on patients treated with adjuvant therapies

following PC. Therefore, additional survival benefits that may be achieved by combining PC with adjuvant chemotherapy and radiation need further exploration.

This study had several limitations, including its retrospective design. A propensity-score matched analysis was performed to limit the influence of possible confounding factors and selection bias, but they cannot be eliminated entirely. The findings from a study on databases need careful interpretation. The study's results underscore the necessity for further evaluation of the impact of PC on carefully selected individuals in this population subset. Oncological outcomes and chemotherapy information, like RFS, CSS, chemotherapy dose, and regimen, and also information on focality, and urine cytology were unavailable. Due to the availability of limited information on the adjuvant therapies following PC in this patient population, further studies evaluating the impact of radiation and chemotherapy are required. Details on salvage cystectomy and depth of transurethral resection were also not available. Future studies combining these treatment modalities with well-structured selection criteria to evaluate the oncological outcomes and their effectiveness could help us understand the role of PC in bladder preservation strategy among elderly individuals. These findings could help encourage collaborative decision-making among the healthier elderly population concerned about preserving bladder function.

Conclusions

In our study on PC and CRT among octogenarians with T2 tumors ≤5 cm, we observed PC and CRT had comparable OS. Therefore, PC can be considered a viable option in a carefully selected octogenarian population. PC as a bladder preservation strategy with adjuvant chemotherapy and radiation may provide additional survival benefits, which need further exploration.

Acknowledgments

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tau.

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