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CLINICAL INVESTIGATION

Disease-Free Survival of Patients With Muscle-Invasive Bladder Cancer Treated With Radical Cystectomy Versus Bladder-Preserving Therapy: A Nationwide Study

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Purpose: Although level I evidence is lacking that radical cystectomy (RC) is superior to bladder-preserving therapy (BPT), RC is still advocated as the recommended treatment in patients with nonmetastatic muscle-invasive bladder cancer (MIBC). This study sought to compare the survival of patients with MIBC treated with BPT versus those treated with RC.

Methods and Materials: All patients with nonmetastatic MIBC diagnoses were identified via the population-based Netherlands Cancer Registry. Only patients treated with BPT or RC were included. The primary endpoint was 2-year disease-free

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Disclosures: none.

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survival (DFS), defined as time from start of treatment until locoregional recurrence, distant metastasis, or death. The secondary endpoint was overall survival (OS). Inverse propensity treatment weighting (IPTW) was used based on propensity scores to adjust for baseline differences between treatment groups. Survival was analyzed with Kaplan-Meier and Cox proportional hazards models.

Results: A total of 1432 patients were included, of whom 1101 underwent RC and 331, BPT. Median follow-up was 39 months (range, 27-51 months). The IPTW-adjusted 2-year DFS was 61.5% (95% CI, 53.5%-69.6%) with BPT and 55.3% (95% CI, 51.6%-59.1%) with RC, with an adjusted hazard ratio of 0.84 (95% CI, 0.69-1.05). The adjusted 2-year OS for patients treated with BPT versus RC was 74.0% (95% CI, 67.0%-80.9%) versus 66.0% (95% CI, 62.7%-68.8%), respectively, with an adjusted hazard ratio of 0.80 (95% CI, 0.64-0.98).

Conclusions: There was no statistically significant difference between the 2-year DFS of patients treated with BPT and RC. We propose that both RC and BPT should be offered as a curative treatment option to eligible patients with nonmetastatic MIBC.

Introduction

The recommended treatment for nonmetastatic muscle-invasive bladder cancer (MIBC) is cisplatin-based neoadjuvant chemotherapy followed by radical cystectomy (RC) with bilateral pelvic lymphadenectomy, according to both the European Association of Urology and the American Urological Association.[1,2] Radical cystectomy is, however, a major surgical procedure and is associated with high morbidity and a negative effect on quality of life.[3,4]

Organ-preserving treatment is considered a major development in clinical oncology and is accepted as standard curative treatment in several cancer types. Phase 3 randomized studies and large, prospective nonrandomized studies were the basis for introducing organ-preserving treatment as standard treatment of care for several tumor types. In MIBC, the available organ-preserving treatments, concurrent chemoradiation therapy (CRT) and external beam radiation therapy (EBRT) followed by brachytherapy, are currently mainly offered as an alternative treatment option to patients unfit to undergo surgery or motivated for organ preservation.[2]

Previous nonrandomized clinical studies have suggested that disease-free survival (DFS) after bladder-preserving treatment (BPT) with (chemo)radiation therapy or brachytherapy is equivalent to that of RC.[5-11] However, there is no completed randomized controlled trial comparing both modalities, and thus, level I evidence for noninferiority is lacking. The only randomized trial, the British SPARE trial, was closed prematurely because of poor accrual and noncompliance.[12] It is recognized that future randomized trials are unlikely to be successful, because patients are reluctant to be randomized between BPT versus removal of their bladder. Just recently, Zlotta et al compared outcomes after RC and BPT in a retrospective study including patients treated at 3 university hospitals in North America between 2005 and 2017.[13] They used propensity score matching and weighting as an alternative approach in the absence of randomization. In this historical cohort, they observed no difference in DFS and superior overall survival (OS) in the BPT group.

We initiated a large observational study at a nationwide level to compare outcomes between both treatments. We hypothesized that the 2-year DFS with BPT would be noninferior to that with RC in patients with nonmetastatic MIBC.

Methods and Materials

Cohort and patient selection

The Netherlands Cancer Registry is a nationwide registry collecting data on all patients with cancer diagnoses in the Netherlands. For patients who received bladder cancer diagnoses between November 2017 and November 2019, additional data were collected within the BlaZIB project, which is embedded in the Netherlands Cancer Registry. For full study details, see the published study protocol.[14] In line with national policy, treatment options for all patients with MIBC were discussed in a multidisciplinary meeting. The current CRAC (Comparison of Radical Cystectomy and Bladder sparing treatment in MIBC) study included all adult patients with nonmetastatic MIBC, stage cT2-4aN0/xM0/x, from the BlaZIB cohort with curative treatment advice and who received treatment with BPT or RC. The BPT group included patients treated with either concurrent CRT or a combination of EBRT followed by brachytherapy (BT refers to the combined EBRT and brachytherapy treatment). CRT was defined as radiation therapy dates overlapping with chemotherapy dates.

Neoadjuvant chemotherapy (NAC) was allowed, but patients with neoadjuvant EBRT were excluded. Only patients with a histology of (predominantly) urothelial carcinoma, based on the original pathology report, were included. Exclusion criteria were recurrent MIBC (after previous MIBC) and simultaneous other malignancy with a median life expectancy of less than 3 years.

Data collection and outcomes

The following variables were collected: patient characteristics (age, sex, Eastern Cooperative Oncology Group performance score, 1987 weighted Charlson Comorbidity Index [CCI] score, and social economic status [SES] as derived

from Statistics Netherlands based on the patient's full postal code), tumor characteristics (clinical T stage, tumor size, and hydronephrosis [absent, unilateral, or bilateral]), carcinoma in situ (CIS) (absent, focal, or extensive), multifocality (yes or no), treatment factors (completeness of transurethral resection [TUR]—macroscopic complete vs incomplete), treatment with RC or CRT or BT (including treatment details such as duration of surgery, number of lymph nodes, chemotherapy, and irradiation dose), type of hospital (academic or specialized hospital vs community hospital) in which the patient was diagnosed and/or treated, and use of NAC. Information on disease course (ie, disease recurrence, progression, and subsequent treatment) was complete at least until 2 years after diagnosis. Information on vital status was complete until January 31, 2022. Vital status was derived from annual linkage with the Personal Records Database, which provides data on dates of emigration and death for all inhabitants of the Netherlands.

The primary endpoint was DFS, defined as the time from RC or the first day of BPT until muscle-invasive locoregional recurrence, distant metastasis, or death. The secondary endpoint was OS. Muscle-invasive locoregional recurrence was defined as a persistent local tumor, or muscle-invasive recurrence, based on cystoscopy or imaging with or without the presence of regional lymph node metastasis on imaging or histology. Any nonregional lymph node metastasis or organ metastasis, as diagnosed by imaging or histology, was classified as distant metastasis.

Statistical analyses

Sample size calculation was prospectively performed based on noninferiority in DFS. We assumed a crude 2-year DFS of 70% for RC and 50% for BPT. The assumed difference between the crude rates was owed to an expected difference in case mix. By using propensity scores and accepting a maximum difference in DFS of 10% in the BPT group versus the RC group (the noninferiority limit), the minimum sample size to demonstrate noninferiority was 250 for the BPT group and 750 for the RC group (power, 81.5%; $\alpha = 5\%$).

An inverse probability treatment weighting (IPTW) approach based on a propensity score was used to correct for baseline differences between patients in the RC and BPT group. First, we estimated the propensity score (probability of treatment with RC) in a logistic regression model, using all baseline variables associated with both treatment and DFS. The final model included age, sex, CCI, performance status, SES, T stage, tumor size, CIS, hydronephrosis, completeness of TUR, NAC, and diagnosing hospital type. Inverse probability treatment weights were calculated and used to balance patients across treatment groups. The covariate balance between groups after IPTW was checked by calculating standardized differences. A standardized difference less than 0.1 indicates a negligible association and is considered optimal for balance after IPTW.[15]

Crude DFS and OS were estimated with the Kaplan Meier method. We computed Cox proportional hazards models using IPTW and adjusted for the following variables: age, sex, performance status, CCI index, SES, T stage, CIS, hydronephrosis, completeness of TUR, tumor size, multifocal tumors, NAC, and hospital type. We performed double adjustment to correct for any residual confounding bias after IPTW.[15] The proportional hazards assumption, formally tested using time-dependent explanatory variables in a Cox regression model, was violated in the Cox model for OS. We additionally performed a restricted mean survival time (RMST) analysis, which does not require the proportional hazards assumption. The RMST results in an absolute survival time by calculating the area under the survival curve up to a predefined time point. We used 12 months, 24 months, and 36 months, and additionally 48 months for OS, based on the availability of longer survival follow-up (FU).

Time was defined from treatment start to first event to avoid immortal time bias. All included patients had to be alive at treatment start, because they were included based on receiving either RC or BPT, and thus, no event could occur in the interval between diagnosis and treatment start. Patients were censored at the end of FU if alive. Clinical FU time was defined as the time between diagnosis and end of clinical data collection; survival FU was defined until last survival data linkage, in event-free patients.

Hazard ratios (HRs) with 95% confidence intervals (95% CIs) were calculated, with the RC group as the reference. Cumulative incidence was calculated using death as a competing event.

Prespecified subgroup analyses comparing RC with CRT were performed. Patients receiving BT were excluded because they were selected on favorable prognostic variables, such as smaller solitary tumors, and therefore were likely to have better outcomes.[16] To assess the influence of postoperative mortality, we performed a sensitivity analysis, excluding patients who died within 30 days after treatment start. All analyses were performed using SAS version 9.4.

Results

Population

A total of 2563 patients with nonmetastatic MIBC were identified within the BlaZIB cohort, of which 1432 patients were included in the CRAC study. Patient inclusion is illustrated in the CONSORT flowchart (Fig. 1). RC was performed in 1101 patients and 331 patients received BPT, of whom 43 patients received BT. In the RC group, 4 patients received adjuvant EBRT. Patient characteristics are described in Tables 1−3. The median age was 71 years (IQR, 64-76 years), and 74% were male patients. A large majority of the patients had clinical T2 tumors, and only 20% had concomitant CIS. In the RC group, a median of 15

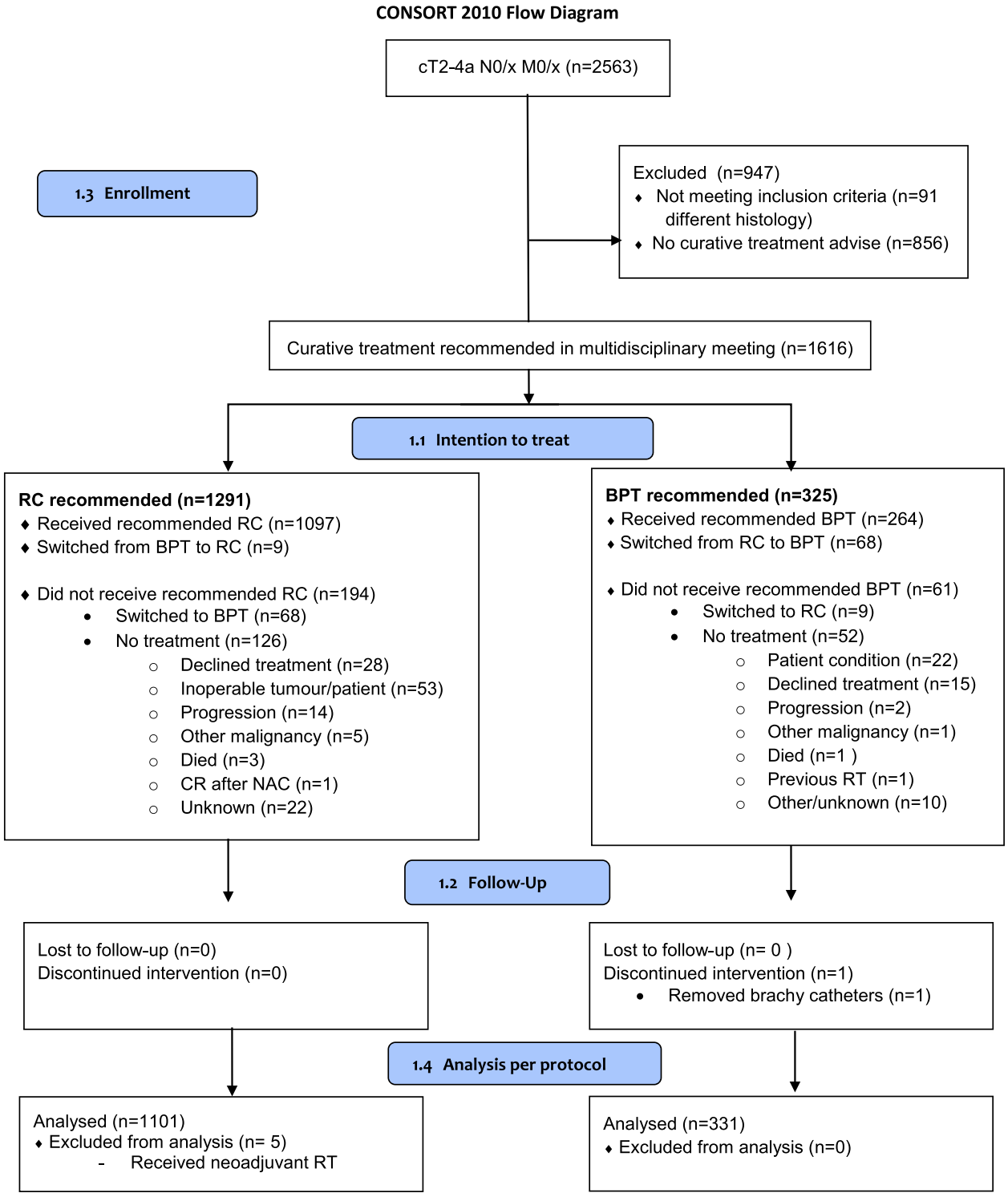

Fig. 1. CONSORT (Consolidated Standards of Reporting Trials) flowchart showing patient selection from the BlaZIB cohort.

(IQR, 10-21) lymph nodes were removed during lymphadenectomy, which revealed lymph node metastases in 261 patients (24%). In the unweighted population, a significantly higher proportion of patients treated with RC had tumors larger than 3 cm and hydronephrosis. The BPT group had a significantly higher proportion of patients aged 80 years or older and fewer patients with missing data on performance score. The weighted cohort was well balanced for all variables (standardized difference, <0.10). The median follow-up with detailed clinical data was 27 months (range, 1-47 months), and the median follow-up for survival data was 39 months (range, 27-51 months).

Table 1 Patient characteristics of 1432 patients with nonmetastatic muscle-invasive bladder cancer treated with radical surgery versus bladder-sparing treatment before and after inverse probability treatment weighting

	Patients						
		Unweighted			IPTW/weighted		
Characteristic	Total, no. (%)	RC, no. (%)	BPT, no. (%)	Standardized difference	RC, no. (%)	BPT, no. (%)	Standardized difference
Patients, no. (%)	1432 (100.0)	1101 (76.9)	331 (23.1)	—	1104 (77.6)	319 (22.4)	—
Age, median (IQR), y	71 (64-76)	70 (64-75)	73 (66-78)	−0.3153	70 (64-76)	71 (64-77)	−0.0259
Age category at diagnosis, y							
<60	202 (14.1)	166 (15.1)	36 (10.9)	0.3153	155 (14.0)	43 (13.5)	0.0331
60-69	426 (29.7)	338 (30.7)	88 (26.6)		331 (30.0)	94 (29.6)	
70-79	649 (45.3)	508 (46.1)	141 (42.6)		500 (45.3)	139 (43.7)	
≥80	155 (10.8)	89 (8.1)	66 (19.9)		118 (10.7)	42 (13.2)	
Male sex	1056 (73.7)	805 (73.1)	251 (75.8)	−0.0623	810 (73.4)	231 (72.4)	0.0229
ECOG performance score							
0	620 (43.3)	463 (42.1)	157 (47.4)	0.4808	473 (42.9)	150 (46.9)	0.0935
1	300 (20.9)	205 (18.6)	95 (28.7)		227 (20.6)	61 (19.0)	
2-3	40 (2.8)	20 (1.8)	20 (6.0)		40 (3.6)	11 (3.4)	
Missing	472 (33.0)	413 (37.5)	59 (17.8)		365 (33.0)	98 (30.8)	
CCI score							
0	629 (43.9)	497 (45.1)	132 (39.9)	0.1502	486 (44.0)	133 (41.7)	0.0491
1	383 (26.7)	294 (26.7)	89 (26.9)		291 (26.3)	91 (28.5)	
≥2	322 (22.5)	231 (21.0)	91 (27.5)		251 (22.7)	72 (22.6)	
Missing	98 (6.8)	79 (7.2)	19 (5.7)		77 (7.0)	23 (7.3)	
SES							
Low	370 (25.8)	292 (26.5)	78 (23.6)	0.1470	282 (25.5)	74 (23.3)	0.0798
Middle	562 (39.2)	443 (40.2)	119 (36.0)		430 (39.0)	124 (38.8)	
High	449 (31.4)	331 (30.1)	118 (35.6)		352 (31.9)	111 (34.8)	
Missing	51 (3.6)	35 (3.2)	16 (4.8)		40 (3.6)	10 (3.2)	
cT							
2	1004 (70.1)	764 (69.4)	240 (72.5)	0.1093	778 (70.5)	217 (68.0)	0.0467
3	350 (24.4)	275 (25.0)	75 (22.7)		269 (24.4)	84 (26.3)	
4	78 (5.4)	62 (5.6)	16 (4.8)		57 (5.2)	19 (5.8)	
Tumor size, cm							
<3	284 (19.8)	188 (17.1)	96 (29.0)	0.1093	217 (19.6)	66 (20.7)	0.0416
>3	227 (15.9)	186 (16.9)	41 (12.4)		178 (16.1)	53 (16.6)	
Missing	921 (64.3)	727 (66.0)	194 (58.6)		710 (64.3)	200 (62.8)	

Abbreviations: BPT = bladder-preserving therapy; CCI = Charlson Comorbidity Index; cT = clinical tumor stage; ECOG = Eastern Cooperative Oncology Group; IPTW = inverse probability treatment weighted; RC = radical cystectomy; SES = socioeconomic status.

Disease-free survival

At 2 years, there were 126 DFS events in the BPT population versus 450 in the RC population. This difference was not statistically different, with a crude HR of 0.88 (95% CI, 0.73-1.05).

Figure 2 shows the DFS and 95% CI for the weighted population by treatment group. The difference remained statistically nonsignificant in the adjusted analysis, with an adjusted HR of 0.84 (95% CI, 0.69-1.05). In the IPTW population, the 2-year DFS in the BPT and RC group was 61.5% (95% CI, 53.5%-69.6%) and 55.3% (95% CI, 51.6%-

Table 2 Patient and treatment characteristics of the CRAC study cohort, before and after inverse probability treatment weighting

	Patients						
Characteristic	Total, no. (%)	RC, no. (%)	BPT, no. (%)	Standardized difference	RC, no. (%)	BPT, no. (%)	Standardized difference
Patients, no. (%)	1432 (100.0)	1101 (77.3)	331 (23.1)	—	1104 (77.6)	319 (100.0)	—
CIS							
Absent	1052 (73.5)	779 (70.8)	273 (82.5)	0.3051	814 (73.7)	240 (75.2)	0.0254
Present	285 (19.9)	248 (22.5)	37 (11.2)		218 (19.8)	60 (18.8)	
Missing	95 (6.6)	74 (6.7)	21 (6.3)		72 (6.5)	19 (6.1)	
Hydronephrosis							
Absent	922 (64.4)	673 (61.1)	249 (75.2)	0.4727	705 (63.9)	206 (64.6)	0.0309
Present	338 (23.6)	304 (27.6)	34 (10.3)		259 (23.5)	75 (23.5)	
Missing	172 (12.0)	124 (11.3)	48 (14.5)		140 (12.7)	38 (12.0)	
Multifocal tumor							
Absent	953 (66.6)	728 (66.1)	225 (68.0)	0.0678	735 (66.5)	219 (68.8)	0.0491
Present	331 (23.1)	256 (23.3)	75 (22.7)		250 (22.6)	66 (20.6)	
Missing	148 (10.3)	117 (10.6)	31 (9.4)		120 (10.9)	34 (10.7)	
TUR resection							
Complete	306 (21.4)	195 (17.7)	111 (33.5)	0.4183	242 (21.9)	77 (24.2)	0.0836
Incomplete	587 (41.0)	490 (44.5)	97 (29.3)		446 (40.4)	114 (35.6)	
Unclear or missing	539 (37.6)	416 (37.8)	123 (37.2)		416 (37.7)	128 (40.2)	
Diagnosing hospital type							
Academic or research	385 (26.9)	257 (23.3)	128 (38.7)	−0.3361	298 (26.9)	86 (26.9)	0.0011
Nonacademic	1047 (73.1)	844 (76.7)	203 (61.3)		807 (73.1)	233 (73.2)	

Abbreviations: BPT = bladder-preserving therapy; CIS = carcinoma in situ; RC = radical cystectomy; TUR = transurethral resection.

59.1%), respectively. These results were in line with the RMST analysis results (Table E1).

Overall survival

At 2 years, fewer deaths were observed in the BPT population compared with the RC population: 90 versus 379. However, this difference was not statistically different, with a crude HR of 0.86 (95% CI, 0.70-1.05).

Figure 3 shows the OS and 95% CI for the weighted population by treatment group.

In the adjusted analyses, OS was significantly better in the BPT group compared with the RC group, with an adjusted HR of 0.80 (95% CI, 0.64-0.98). In the IPTW population, the 2-year OS for patients treated with BPT or RC was 74.0% (95% CI, 67.0%-80.9%) and 66.0% (95% CI, 62.7%-68.8%), respectively. These results were in line with the RMST analysis results (Table E2).

Disease recurrence

Nonmuscle invasive recurrence occurred in 21 patients (6.4%) in the BPT group. At 25 months, cumulative incidence of locoregional recurrence was 17% in the RC group and 27% in the BPT group (P = .0003). Salvage cystectomy was performed in 22 patients (6.6%), 19 in the CRT and 3 in the BT group. Ten patients received salvage cystectomy for residual tumor after CRT, 8 had MIBC recurrence, and 3 had nonmuscle invasive local recurrence; 1 cystectomy was performed as part of rectal cancer treatment. The median time to salvage cystectomy was 15.2 months. At 25 months, the cumulative incidence of distant metastases was 27% in the RC group and 20% in the BPT group (P = .0111).

Sensitivity analyses

In the sensitivity analyses, we excluded patients who died within 30 days after treatment start (n = 19). There was no

Table 3 Ttreatment characteristics of the CRAC study cohort, before and after inverse probability treatment weighting

Characteristic	Patients						
	Total, no. (%)	RC, no. (%)	BPT, no. (%)	Standardized difference	RC, no. (%)	BPT, no. (%)	Standardized difference
Patients, no. (%)	1432 (100.0)	1101 (77.3)	331 (23.1)	—	1104 (77.6)	319 (100.0)	—
Treatment							
Neoadjuvant chemotherapy	359 (25.1)	323 (29.3)	36 (10.9)	0.4733	277 (25.1)	81 (25.4)	−0.0039
RT schedule							
BED $\alpha/\beta10$ = 70.1 (20/55)	—	—	49 (14.8)	1.3594	—	39 (12.4)	1.3654
BED $\alpha/\beta10$ = 74.4 (25/60)	—	—	84 (25.4)		—	90 (28.2)	
BED $\alpha/\beta10$ = 76.8 (32/64)	—	—	31 (9.4)		—	34 (10.6)	
BED $\alpha/\beta10$ = 79.2 (33/66)	—	—	89 (26.9)		—	76 (23.9)	
20 fractions with brachytherapy boost	—	—	43 (13.0)		—	38 (12.0)	
Other schedule	—	—	35 (10.6)		—	42 (13.0)	
CRT chemotherapy regimen							
Capecitabin mitomycin	—	—	129 (39.0)	14.0712	—	135 (42.4)	9.9885
5-FU/mitomycin C	—	—	116 (35.0)		—	10 (32.8)	
Capecitabin	—	—	19 (5.7)		—	21 (6.5)	
Other schedule	—	—	25 (7.6)		—	21 (6.6)	
Only EBRT plus brachytherapy	—	—	42 (12.7)		—	37 (11.6)	

Abbreviations: 5-FU = 5-fluorouracil; BED = biologically effective dose; BPT = bladder-preserving therapy; CRT = concurrent chemotherapy and radiation therapy; EBRT = external beam radiation therapy; RC = radical cystectomy; RT = radiation therapy.

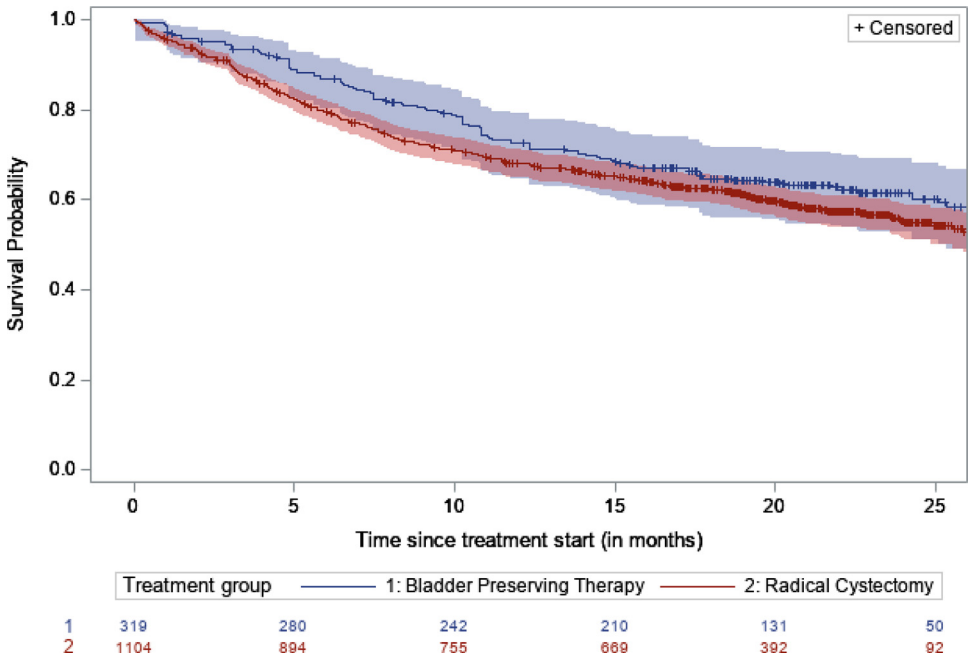

Fig. 2. Disease-free survival of the weighted population of patients with nonmetastatic muscle-invasive bladder cancer who underwent radical cystectomy versus bladder-sparing treatment, including 95% CIs and numbers at risk.

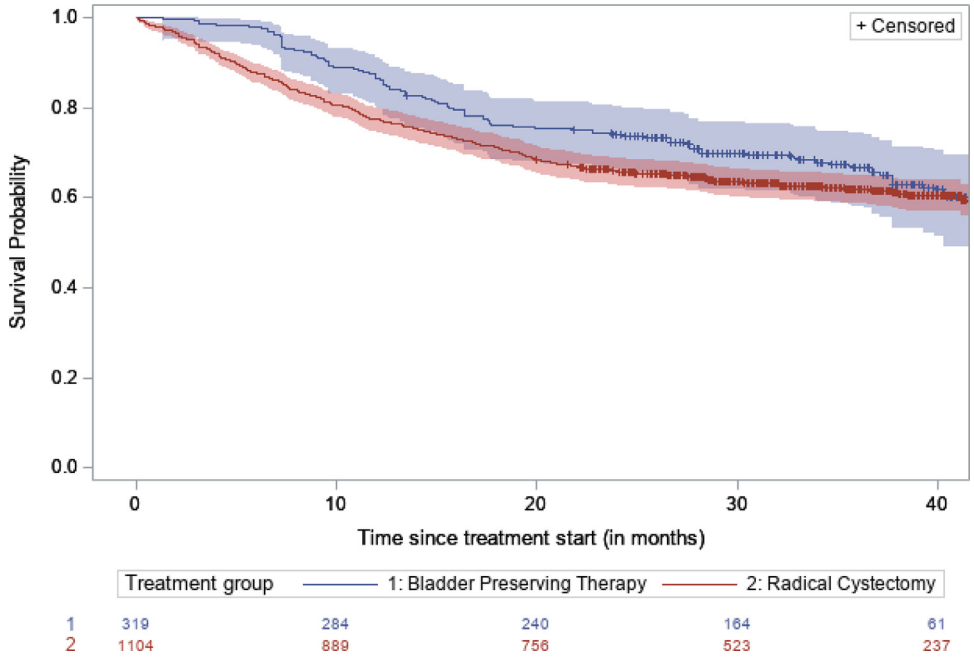

Fig. 3. Overall survival of the weighted population of patients with nonmetastatic muscle-invasive bladder cancer who underwent radical cystectomy versus bladder-sparing treatment, including 95% CIs and numbers at risk.

significant difference in the DFS and OS comparison (data not shown). There was no significant difference in the 2-yr DFS and OS between the RC and CRT group (adjusted HR, 0.87 [95% CI, 0.71-1.06] and 0.83 [95% CI, 0.67- 1.03], respectively).

Discussion

We performed a comprehensive nationwide observational cohort study comparing DFS between patients treated with RC and BPT. To correct for baseline differences between the 2 treatment groups, we performed propensity score weighted analyses. In the absence of a true randomized controlled trial, our IPTW approach optimizes ignorable treatment assignment and provides the best alternative evidence.[17] In both the crude and the adjusted analysis, the 2-year DFS was better in patients treated with BPT compared with those treated with RC, yet the difference was not statistically significant. In the IPTW analyses, OS was significantly better in the BPT group compared with the RC group.

Our study findings align with a very recent publication by Zlotta et al.[13] Their comparison yielded the same results, with no significant difference in DFS between the treatment groups and an overall survival benefit in the BPT group. However, they observed better absolute DFS and OS numbers in their entire cohort, which can likely be attributed to differences in patient selection, such as the setting and more restrictive inclusion criteria.

Previous studies comparing RC and BPT have mainly focused on OS. Softness et al performed an emulation of the SPARE trial using a propensity score analysis comparing OS across patients treated with NAC followed by RC versus NAC followed by trimodality treatment (TMT).[18] They found a 2-year OS of approximately 70% in both treatment groups, which is in line with our 2-year OS of 66% and 74% in the RC and BPT groups, respectively. Kumar et al observed similar 2-year OS of approximately 65% in patients treated with RC and patients treated with TMT with a platinum-based chemotherapeutic agent or mitomycin-C with 5-fluorouracil in a population of US veterans.[19] Interestingly, Seisen et al reported similar 2-year OS between RC and TMT, but survival in patients in the TMT group dropped 25 months after diagnosis.[8] If a similar time effect was present in our population, we would have expected to have seen evidence of this within our median follow-up of 39 months.

Disease-free survival has been reported in a randomized controlled trial by James et al comparing EBRT with CRT.[20] In the concurrent chemoradiation group, the 2-year DFS was 50%, which is comparable to the 57% 2-year DFS in our CRT group. In patients treated with RC, Sonpavde et al reported a 2-year DFS of 63%,[21] which is only slightly higher than the DFS we found (55%). This may be due to the selection of patients based on negative surgical margins. In our RC population, 9% had positive surgical margins, which are associated with higher risk of recurrence.[22]

In the BPT population in our study, 7% of patients received salvage cystectomy, which is comparable to previous reports. Patients treated with CRT in the randomized controlled trial by James et al had a 2-year cystectomy risk of 11.4%.[20] Kool et al report a salvage cystectomy risk of 8.8% in a multi-institutional Canadian cohort.[11]

There is no uniform definition that clearly distinguishes between regional and distant recurrences, and consequently, varying recurrence risks have been reported. In patients treated with RC, 5-year distant recurrence risks varied between 29% and 50%.[23,24] After BPT, Mak et al reported 5-year distant recurrence risks varying between 20% and 40%.[25] In our cohort, distant metastases were reported significantly more often after treatment with RC than BPT (25% vs 18%, respectively; P = .0079). A possible explanation may be underdiagnosis of metastases in the BPT group as a result of a difference in follow-up examinations. It is plausible that the frequency and extent of follow-up examinations were reduced in the older population of the BPT group.

Our study has several strengths. It was a large study, including all patients treated with either RC or BPT in the Netherlands in a 2-year period. The availability of extensive clinical data enabled correction for important confounders, and the linkage to the national death registry ensured reliable survival data. Furthermore, the use of IPTW is a proven method to reduce the inherent confounding by indication in observational data.[15] Despite the use of these analyses, the potential influence of unmeasured confounders cannot be excluded. Because this was an observational study, no standardized protocols for follow-up examinations were followed, which may have led to a difference in detection of disease recurrence between the 2 treatment groups.

Conclusion

In this nationwide study, we found better DFS in patients treated with BPT compared with those treated with RC, yet this was not statistically significant. The collective findings of Zlotta et al[13] and our study support the equivalence of RC and BPT in eradicating bladder cancer and preventing recurrence. Therefore, we propose to offer both treatment modalities to eligible patients. To further guide physicians and patients, other factors, such as patients' quality of life and the cost-effectiveness of these treatments, should be considered as well.

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