ORIGINAL ARTICLE

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Invasive non-urachal adenocarcinoma of the bladder: analysis of the National Cancer Database

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Abstract

Purpose To review the United States National Cancer Database (NCDB) from 2004 to 2015 and analyze survival outcomes of invasive non-urachal adenocarcinoma based on treatment modality.

Methods The NCDB 2004–2015 bladder dataset was queried for adenocarcinoma histology, excluding urachal variant, and limited to patients with clinical stage T2–T4 disease. Treatment modality was categorized as no treatment, cystectomy (partial or radical), external beam radiation therapy (EBRT), or EBRT plus cystectomy. Our primary outcome was overall survival. Cox regression (CR) and Kaplan–Meier (KM) analysis were performed.

Results 851 patients were identified with invasive (cT2–T4) adenocarcinoma of the bladder. Treatment modalities included 398 (47.8%) no treatment, 298 (35.8%) cystectomy, 124 (14.9%) EBRT, and 31 (3.7%) EBRT plus cystectomy. On KM analysis excluding those with metastatic disease, the 5-year survival was significantly better ($p < 0.001$) for patients who underwent cystectomy (39.6%), versus no treatment (21.0%), EBRT (18.6%), or EBRT plus cystectomy (26.9%) (log rank, $p < 0.001$). On CR for mortality, age (HR 1.030, $p < 0.001$), Charlson score 1 (HR 1.287, $p = 0.034$), cT4 (HR 1.768, $p < 0.001$), and receiving treatment at a low-volume center (HR 1.289, $p = 0.026$) were associated with worsened survival; however, cystectomy (HR 0.593, $p < 0.001$) was the only factor associated with improved survival. For those undergoing cystectomy, the mean length of stay was 8.5 days and the 30-day readmission rate was 7.0%.

Conclusions Invasive non-urachal adenocarcinoma of the bladder is a rare diagnosis. Survival benefits in patients without metastatic disease are seen only in those patients undergoing definitive surgery.

Keywords Bladder cancer · Adenocarcinoma · Invasive · Survival

Introduction

Bladder cancer is one of the most common but deadliest malignancies [1]. While many malignancies have seen notable improvements in survival outcomes, 5-year survival for bladder cancer has only increased by 6% since 1975 [1]. These poor survival outcomes are in part due to a high presentation of muscle-invasive or advanced disease. Muscle-invasive bladder cancer accounts for 25% of all diagnosed bladder cancers and portends a poor prognosis, even after therapy. Evidence-based treatment algorithms have been established incorporating surgical extirpation (radical cystectomy) and bladder preservation (radiation therapy) for urothelial cell carcinoma; however, guidelines for pure variant histology are currently lacking [2].

Less than 10% of patients diagnosed with bladder cancer have a non-urothelial histologic variant, which is associated with worse outcomes [3]. Additionally, there is a paucity of data regarding treatment modalities and their effects on survival outcomes for variant histology. Treatment algorithms specific to adenocarcinoma of the bladder (ACB) have not been established and, instead, rely on those formulated for urothelial cancer (UC) [3]. Unlike pure UC, ACB has a perceived resistance to chemotherapy while its sensitivity to radiation is still being debated [2, 4, 5]. Instead, earlier surgical intervention is recommended, but at best is only an "expert opinion." These deficiencies in evidence-based practice amount to 5-year survival rates of around 35% for primary non-urachal ACB [6]. Prior database reviews have demonstrated similar cancer-specific mortality (CSM) in

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patients diagnosed with ACB versus UC who underwent radical cystectomy (RC), although results have not been consistent [3, 7, 8].

In this population-based study, we reviewed the National Cancer Database (NCDB) for patients with invasive, non-urachal ACB (clinical stage T2–T4 disease) and analyzed survival outcomes for ACB based on varying treatment modalities. Our aim was to determine the differences in survival outcomes of those patients who received definitive treatment, including cystectomy and/or radiotherapy, versus those who received no treatment.

Methods

Data source

The National Cancer Database (NCDB) is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The NCDB includes data from all cancer patients treated at participating Commission on Cancer-accredited institutions and is estimated to capture over 70% of new cancer cases in the USA [9]. Standardized coding definitions are utilized, and the data are freely available to participating institutions after application for projects are submitted and accepted by the NCDB. The data used in the study are derived from a de-identified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator.

Study population

The NCDB was queried for patients with ACB (histology code 8140), including clinical stage T2–T4 disease between 2004 and 2015. Patients with missing survival time were excluded. To rule out patients with urachal variant of adenocarcinoma, we excluded those with International Classification of Diseases topographical code C67.7 (urachal) from the primary location category. We identified 851 patients age $\geq$ 18 years meeting inclusion criteria (Fig. 1). The study population was categorized by definitive treatment type for purposes of analysis. Treatment categories included cystectomy (radical or partial cystectomy), external beam radiation therapy (EBRT), EBRT plus cystectomy, or no definitive treatment. Sub-categorization was performed for those with or without clinical metastasis (cM0 or cM+).

Patient demographic variables included age, race, gender, Charlson comorbidity index, clinical TNM stage, income status, treatment facility type, and insurance status. Treatment facility type was categorized as low volume or high volume. Treatment facilities that accessioned 500 or more
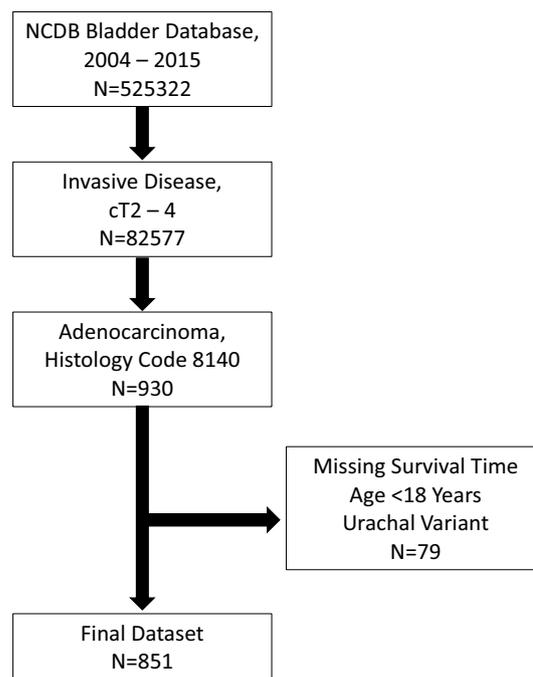

Fig. 1 Study flow diagram

newly diagnosed cancer cases per year were considered to be high volume, whereas facilities with less than 500 were labeled low volume. Post-treatment outcomes included pathologic T stage and nodal status (for surgical patients only), all-cause mortality (within 30 days of treatment, 90 days of treatment, and at last follow-up), and length of follow-up.

Statistical analysis and outcome measure

One-way ANOVA or Student's T test was performed for continuous variables, and Fischer's exact or Pearson Chi square tests for categorical variables to compare differences in patient demographics, clinical characteristics, and survival outcomes. Multivariable analysis was performed using Cox regression to identify risk factors for mortality. Kaplan–Meier analysis was performed for survival outcome by treatment type. We utilized SPSS v24 (New York, USA) for all analyses, with p value of < 0.05 denoting statistical significance. Our primary outcome was overall survival, stratified by treatment type.

Results

Patient demographics and clinical tumor characteristics

Table 1 highlights the demographic and clinical tumor variables. The patient population totaled 851 with 398 (47.8%)

Table 1 Patient demographics and clinical tumor characteristics

Variable	All (n = 851)	No Trx (n = 398)	Surgery (n = 298)	EBRT (n = 124)	EBRT + Surg (n = 31)	p value
Mean age	68.2 ± 13.6	70.0 ± 14.1	64.4 ± 12.3	73.1 ± 12.3	61.5 ± 12.2	< 0.001
Race						0.053
White	663 (77.9%)	312 (78.4%)	237 (79.5%)	92 (74.2%)	22 (71.0%)	
Black	149 (17.5%)	74 (18.6%)	40 (13.4%)	27 (21.8%)	8 (25.8%)	
Other	39 (4.6%)	12 (3.0%)	21 (7.0%)	5 (4.0%)	1 (3.2%)	
Male sex	524 (61.6%)	245 (61.6%)	186 (62.4%)	77 (62.1%)	16 (51.6%)	0.705
Charlson						0.801
0	605 (71.1%)	284 (71.4%)	210 (70.5%)	89 (71.8%)	22 (71.0%)	
1	175 (20.6%)	79 (19.8%)	64 (21.5%)	25 (20.2%)	7 (22.6%)	
2	47 (5.5%)	25 (6.3%)	12 (4.0%)	8 (6.5%)	2 (6.5%)	
3 +	24 (2.8%)	10 (2.5%)	12 (4.0%)	(1.6%)	0 (0%)	
cT stage						< 0.001
2	50 (59.9%)	236 (59.3%)	193 (64.8%)	71 (57.3%)	10 (32.3%)	
3	123 (14.5%)	35 (8.8%)	65 (21.8%)	15 (12.1%)	8 (25.8%)	
4	218 (25.6%)	127 (31.9%)	40 (13.4%)	38 (30.6%)	13 (41.9%)	
cN +	99 (11.6%)	56 (14.1%)	22 (7.4%)	17 (13.7%)	4 (12.9%)	0.044
cM +	139 (16.3%)	105 (26.4%)	6 (2.0%)	26 (21.0%)	2 (6.5%)	< 0.001
Income status						0.239
< $38,000	185 (22.1%)	84 (21.4%)	58 (19.8%)	34 (28.1%)	9 (30.0%)	
$38,000–47,999	194 (23.2%)	86 (21.9%)	77 (26.3%)	23 (19.0%)	8 (26.7%)	
$48,000–62,999	244 (29.2%)	122 (31.0%)	75 (25.6%)	38 (31.4%)	9 (30.0%)	
$63,000 +	214 (25.6%)	101 (25.7%)	83 (28.3%)	26 (21.5%)	4 (13.3%)	
Unknown	14	5	5	3	1	
Facility type						0.271
Low volume	190 (22.3%)	100 (25.1%)	58 (19.5%)	27 (21.8%)	5 (16.1%)	
High volume	661 (77.7%)	298 (74.9%)	240 (80.5%)	97 (78.2%)	26 (83.9%)	
Insurance status						< 0.001
Uninsured	25 (2.9%)	15 (3.8%)	6 (2.0%)	2 (1.6%)	2 (6.5%)	0.266
Private insurance	242 (28.4%)	95 (23.9%)	109 (36.6%)	28 (22.6%)	10 (32.3%)	
Medicaid	62 (7.3%)	31 (7.8%)	24 (8.1%)	2 (1.6%)	5 (16.1%)	
Medicare	494 (58.0%)	241 (60.6%)	153 (51.3%)	89 (71.8%)	11 (35.5%)	
Other govt	11 (1.3%)	4 (1.0%)	3 (1.0%)	1 (0.8%)	3 (9.7%)	
Unknown	17 (2.0%)	12 (3.0%)	3 (1.0%)	2 (1.6%)	0 (0%)	

No trx no treatment, *Surgery* any cystectomy, *EBRT* external beam radiation therapy, *EBRT + Surg* external beam radiation therapy and any cystectomy

undergoing no definitive treatment, 298 (35.8%) cystectomy, 124 (14.9%) EBRT, and 31 (3.7%) EBRT plus cystectomy. The mean age of our cohort was 68.2 years (SD ± 13.6), while those undergoing cystectomy were on average younger at 64.4 (SD ± 12.3) years. There was no statistically significant difference in race or Charlson score between treatment modalities (p = 0.053 and 0.801, respectively). A total of 99 patients had clinically node-positive disease (cN +) and 139 had metastatic disease (cM +). The cN + sub-population was less likely to undergo cystectomy alone with 56 (56.5%), 22 (22.2%), 17 (17.1%), and 4 (4.0%) choosing no treatment, cystectomy, EBRT, or EBRT plus cystectomy, respectively (p = 0.044). The trend for the cM + group was similar with

105 (75.5%) forgoing treatment, while 6 (4.3%) opted for surgery, 26 (18.7%) EBRT, and 2 (1.4%) EBRT plus cystectomy (p < 0.001).

Perioperative survival outcomes

Operative and survival outcomes are noted in Table 2. Of the 298 surgical patients who underwent cystectomy, 21 (7.0%) had an unplanned 30-day readmission. Within the cystectomy arm, the rate of partial cystectomy was 29.5%, while in the EBRT plus cystectomy arm the rate of partial cystectomy was 19.4%. The mean perioperative hospital stay was 8.5 ± 12.3 days after surgical intervention. The

Table 2 Perioperative and survival outcomes

Variable	All (n = 851)	No Trx (n = 398)	Surgery (n = 298)	EBRT (n = 124)	EBRT + Surg (n = 31)	p value
Unplanned 30-day readmission after surgery	N/A	N/A	21 (7.0%)	N/A	0 (0%)	
Hospital stay	N/A	N/A	8.5 ± 12.3	N/A	8.8 ± 8.4	
Partial cystectomy	N/A	N/A	88 (29.5%)	N/A	6 (19.4%)	
pT stage						
< 2			9 (3.0%)		0 (0%)	
2			74 (24.8%)		2 (6.5%)	
3			118 (39.6%)		9 (29.0%)	
4			52 (17.4%)		16 (51.6%)	
Unknown		398 (100%)	45 (15.1%)	124 (100%)	4 (12.9%)	
pN +	N/A	N/A	65 (21.8%)	N/A	9 (29.0%)	
Length of follow-up (months)	27.8 ± 29.1	20.2 ± 26.0	39.0 ± 31.5	23.2 ± 22.4	37.5 ± 31.6	< 0.001
Mortality (all pts)	568 (66.7%)	292 (73.4%)	156 (52.3%)	100 (80.6%)	20 (64.5%)	< 0.001
Within 30 days of treatment	28 (4.1%)	20 (6.8%)	5 (1.9%)	3 (3.3%)	0 (0%)	0.046
Within 90 days of treatment	77 (11.3%)	57 (19.4%)	16 (5.9%)	4 (4.4%)	0 (0%)	< 0.001
Mortality (exclude cM +)	444/712 (62.4%)	200/293 (68.3%)	151/292 (51.7%)	75/98 (76.5%)	18/29 (62.1%)	< 0.001

No trx no treatment, *Surgery* any cystectomy, *EBRT* external beam radiation therapy, *EBRT + Surg* external beam radiation therapy and any cystectomy

Table 3 Multivariable cox regression analysis for overall mortality with non-urachal adenocarcinoma of the bladder, including all patients with cT2–4 disease

Variable	HR	95% CI low	95% CI high	p value
Age (continuous)	1.029	1.022	1.036	< 0.001
Charlson score (0 ref)				
1	1.213	0.988	1.490	0.065
2	1.153	0.799	1.663	0.447
3 +	1.888	1.168	3.051	0.010
cT stage (cT2 ref)				
3	1.068	0.827	1.380	0.613
4	1.336	1.083	1.648	0.007
cN +	1.430	1.103	1.854	0.007
cM +	2.374	1.875	3.008	< 0.001
Low-volume center	1.279	1.048	1.561	0.016
Uninsured	1.246	0.734	2.115	0.416
Treatment (no treatment ref)				
Cystectomy	0.584	0.471	0.724	< 0.001
EBRT	0.875	0.694	1.103	0.259
EBRT + cystectomy	0.609	0.383	0.968	0.036

HR hazard ratio, *CI* confidence interval

average length of follow-up in months was 27.8 ± 29.1 for the entire cohort. Those choosing intervention were more likely to have a longer follow-up with cystectomy patients following up for 39.0 ± 31.5 months, EBRT with cystectomy for 37.5 ± 31.6 months, those forgoing treatment followed up for 20.2 ± 26.0 months, and finally EBRT patients for

23.4 ± 22.4 ($p < 0.001$). Pathologic tumor stages for cystectomy patients was 9 (3.0%) for < pT2, 74 (24.8%) pT2, 118 (39.6%) pT3, and 52 (17.4%) for pT4, while 45 (15.1%) had an unknown tumor pathologic stage. While cN + disease was seen in only 22 (7.3%) patients choosing surgery, after surgery pathologic evaluation led to nodal-positive disease found in 65 (21.8%) patients.

Multivariable analysis

Cox regression was performed for all clinical stages with patient demographics and clinical tumor characteristics to determine the effects on mortality (Table 3). A statistically significant increased risk on mortality was seen for increasing age (HR 1.029; 1.022–1.036, 95% CI). In comparison to patients with cT2 disease those with cT4 were associated with worsened mortality (HR 1.336; 1.083–1.648, 95% CI). As expected, clinical node positivity (HR 1.430; 1.103–1.854, 95% CI) and metastatic disease increased the risk of mortality (HR 2.374; 1.875–3.008, 95% CI). Patients receiving care at low-volume centers were also at increased risk of mortality (HR 1.279, 1.048–1.561, 95% CI). Of note, the only treatment found to have an independent beneficial effect on overall mortality was surgical extirpation, including cystectomy (HR 0.584, 0.471–0.724, 95% CI) and EBRT + cystectomy (HR 0.609; 0.383–0.968, 95% CI). EBRT alone did not carry any survival benefit ($p = 0.259$). Charlson scores of 1, 2, or uninsured status did not contribute to survival outcomes. Charlson score of

Table 4 Multivariable cox regression analysis for overall mortality with non-urachal adenocarcinoma of the bladder, including all patients with cT2–4 disease but excluding patients with cM +

Variable	HR	95% CI low	95% CI high	p value
Age (continuous)	1.030	1.022	1.039	< 0.001
Charlson score (0 ref)				
1	1.287	1.020	1.624	0.034
2	1.031	0.685	1.551	0.884
3 +	1.713	0.994	2.952	0.053
cT stage (cT2 ref)				
3	1.076	0.811	1.426	0.612
4	1.768	1.402	2.230	< 0.001
cN +	1.243	0.875	1.765	0.225
Low-volume center	1.289	1.031	1.611	0.026
Uninsured	1.157	0.605	2.214	0.660
Treatment (no treatment ref)				
Cystectomy	0.593	0.472	0.744	< 0.001
EBRT	0.850	0.649	1.114	0.240
EBRT + cystectomy	0.647	0.394	1.063	0.086

HR hazard ratio, *CI* confidence interval

3 + was associated with a worsened outcome (HR 1.888; 1.168–3.051, 95% CI).

The Cox regression was repeated excluding patients with cM + disease (Table 4) revealing differences in factors contributing to survival in this sub-population. Age, cT4 disease, and low-volume centers continued to be associated with worsened mortality. The only statistically significant contributor to a reduction in mortality risk was cystectomy (HR 0.593; 0.472–0.744, 95% CI). Notably, surgery + EBRT lost its statistical significance when excluding cM + ($p = 0.086$). Meanwhile, variables such as Charlson score of 3 + and node positivity lost their statistical significance in this particular cohort ($p = 0.053$ and 0.225 respectively).

Kaplan–Meier analysis

Kaplan–Meier analysis was performed on our patient population demonstrating an improved 5-year overall survival for patients undergoing cystectomy in comparison to no treatment, EBRT, or EBRT with cystectomy (log-rank $p < 0.001$, Fig. 2). At time points of 2 and 5 years, the overall survival for treatment modalities were 31.6 and 15.5% for no treatment, 65.6 and 39.1% for cystectomy, 35.6 and 14.4% for EBRT, and 61.1 and 24.7% for EBRT with cystectomy. When excluding patients who had cM + disease, the largest detriment to survival outcomes at 5 years was seen in patients undergoing no treatment (log-rank $p < 0.001$, Fig. 3). Results when excluding those with cM + disease for 2- and 5-year overall survival rates were 39.1 and 21.0% for no treatment, 66.3 and 39.6% for

cystectomy, 44.2 and 18.6% for EBRT, and 62.2 and 26.9% for EBRT with cystectomy.

Treatment utilization over time

Figure 4 highlights the use of each treatment modality during the study period. The majority of patients (46.8%) received no definitive treatment. With regard to treatment, 35.0% received cystectomy, while 14.6% received EBRT and 3.6% underwent EBRT with cystectomy.

Discussion

We conducted the largest retrospective review of overall survival, relative to treatment modalities, in non-urachal ACB. Five-year overall survival was superior for patients undergoing cystectomy versus no treatment, EBRT, or EBRT plus cystectomy. In fact, cystectomy was the only statistically significant variable found to decrease mortality risk on multivariable analysis. ACB is an uncommon variant histology that suffers from lack of randomized data to guide treatment; however, despite the limitations of this retrospective dataset, our analysis adds support to the best-known evidence available. Clinicians should consider surgical treatment when technically feasible.

Patients afflicted with urothelial variant of non-metastatic muscle-invasive bladder cancer are directed to neoadjuvant chemotherapy (NAC) followed by RC [2, 10]. A meta-analysis of randomized phase III trials denotes an absolute survival benefit of 8% at 5 years when undergoing cisplatin-based NAC [11]. Meanwhile, the role of radiation therapy has shown survival benefit in retrospective analyses, but it has yet to show reliable improvements in mortality in a randomized trial when compared to RC [10]. On the other hand, treatment for non-urothelial variants is less clear and extrapolated from UC outcomes or based on retrospective, single institution series [2, 12, 13]. Upfront cystectomy is currently the treatment of choice, whereas radiotherapy has proved beneficial only in select studies [2, 5]. Furthermore, chemotherapy has failed to demonstrate a statistically significant benefit [4, 14, 18]. Based on treatment effects, it is evident that UC and ACB behave differently. Scarcity of data regarding ACB is due to its rarity, as it only occurs in 0.5–2% of patients diagnosed with bladder cancer [14].

The NCDB has been examined in the past to elucidate outcomes and prognosis based on histology [15]. Between 1998 and 2014, ACB was found in 2781 patients, representing 1.7% of all bladder cancer diagnoses. Not accounting for specific treatment or stage, 5-year overall survival was 36.2% during this time frame, highlighting the poor prognosis of this variant histology. Notably, treatment modality was not sub-categorized and the location of disease (urachal

Fig. 2 Kaplan Meier—overall survival (all patients)

Variable	2 year OS	SD	5 year OS	SD
No Treatment	31.6%	2.5	15.5%	2.2
Cystectomy	65.6%	3.0	39.1%	3.3
EBRT	35.6%	4.5	14.4%	3.5
EBRT+Cystectomy	61.1%	9.2	24.7%	8.8

Log rank p<0.001
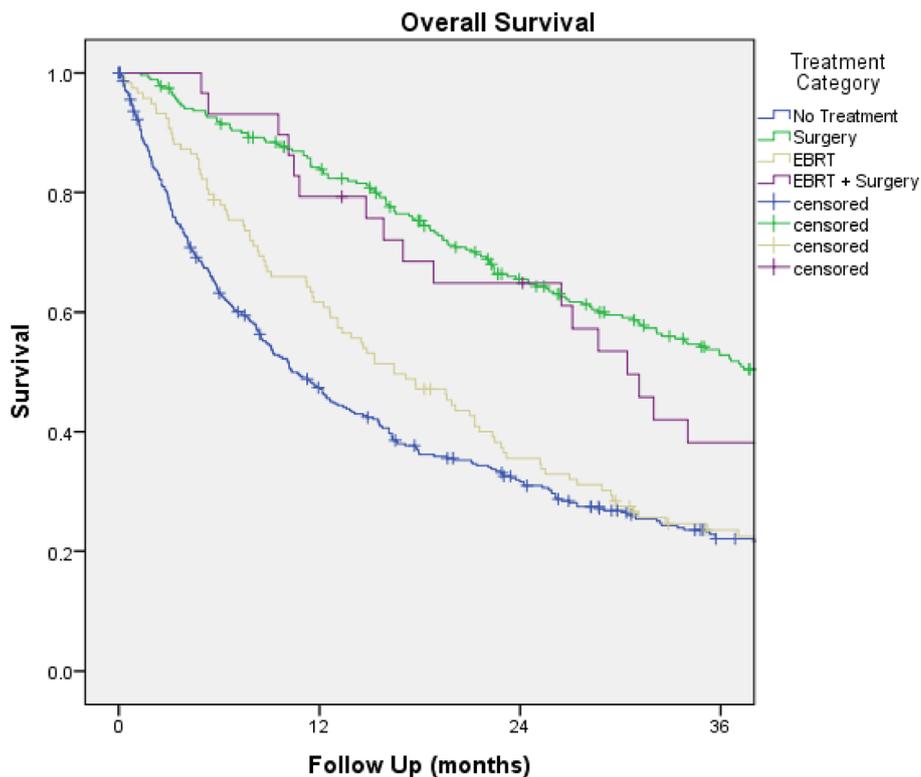
Variable	# at risk			
No Treatment	363	101	33	3
Cystectomy	270	157	62	8
EBRT	118	40	12	0
EBRT+Cystectomy	29	18	6	1
Time	0 months	24 months	60 months	120 months

versus non-urachal) was not specified in the prior analysis. Within our analysis between 2004 and 2015, the incidence of surgical extirpation for non-urachal ACB has increased from 32.6 to 40.0%, suggesting a changing therapeutic landscape. Our analysis adds to this ongoing discussion, as we stratify mortality based on treatment type and focus on non-urachal, invasive disease.

Wright et al. looked at 1374 patients with non-urachal ACB and found a 5-year survival rate of 35% [6]. Of those, 888 patients underwent treatment with TURBT (55%), partial (16%) or radical cystectomy (28%). Within this analysis, the comparison of 5-year survival included a 15% rate of distant metastasis; however, in our own analysis when including those with M + disease in our study, 5-year survival was still greater (39.1%). Furthermore, this incongruity is likely attributed to the significant proportion of patients

undergoing TURBT, which was associated with a hazard ratio of 1.83 (1.42–2.34, CI 95%) when compared to RC. While no evidence-based guidelines exist, TURBT is not a suggested treatment option [2, 10]. Krasnow et al. examined combination treatment consisting of maximal TURBT in addition to radiation and chemotherapy, finding no difference in overall survival between UC versus UC containing variant histology [16]. Importantly, it should be noted that these patients possessed mixed, and not pure, histology, consisting of an unspecified percentage of ACB, making its extrapolation complex. Our analysis, on the other hand, contains patients with pure ACB and sub-stratifies survival outcomes for those with and without distant metastases.

The effects of NAC followed by RC on median overall survival in clinically localized ACB with limited pelvic lymph node burden were examined by Vetterlein et al.
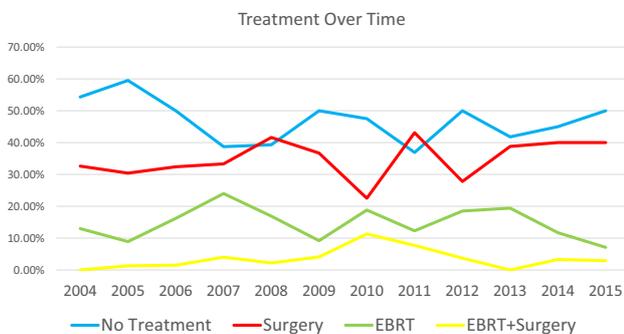
Fig. 3 Kaplan Meier—overall survival (excludes cM + patients)

Variable	2 year OS	SD	5 year OS	SD
No Treatment	39.1%	3.1	21.0%	2.9
Cystectomy	66.3%	3.0	39.6%	3.4
EBRT	44.2%	5.2	18.6%	4.4
EBRT+Cystectomy	62.2%	9.5	26.9%	9.4

Log rank p<0.001
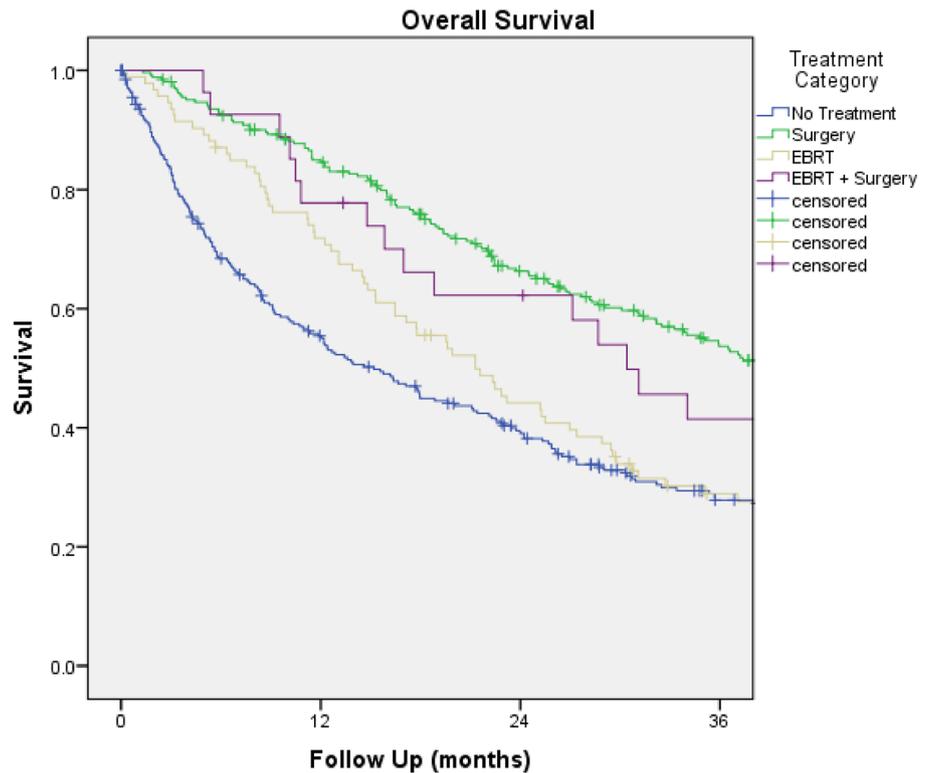
Variable	# at risk			
No Treatment	267	91	31	3
Cystectomy	264	154	61	8
EBRT	93	39	12	0
EBRT+Cystectomy	27	16	6	1
Time	0 months	24 months	60 months	120 months

Fig. 4 Treatment over time

[17]. They found the addition of NAC did not contribute to a statistically significant improvement on median overall survival. Non-operative therapy has been repeatedly unsuccessful in demonstrating survival benefits over RC. Yet, 14.5% of patients in our dataset chose a therapy with unreliable supportive evidence, while another 47.8% underwent no treatment. It is likely that the poor survival outcomes associated with ACB are somewhat attributable to a significant proportion of patients not undergoing the current recommended treatment. Additionally, our retrospective analysis does not provide clinical data to understand the reason behind the choice of treatment modality. Lughezzani et al. proved the possibility of similar cancer-specific mortality, when correcting for grade and stage, in patients with UC versus ACB if surgical extirpation is undertaken; however, their results have not been dependably corroborated [3, 7,

8]. Studies continue to examine treatment effects on varying survival end points, but comparative studies between these therapies are lacking.

Our review of the NCDB contains its own limitations, similar to any other retrospective review. There is inherent selection bias, which plays a significant role in our survival analysis. The underlying reason why some patients chose surgery, EBRT, or no treatment is unknown, and there are many possible confounding variables that are not measured. One can assume that those patients with the lowest burden of disease and highest performance status will be more likely to receive definitive therapy, whereas those patients who are at highest risk of mortality will most likely not pursue definitive treatment. We attempted to mitigate this bias by performing multi-variable Cox regression analysis and stratifying by presence of metastatic disease, but regardless our findings must be viewed in this retrospective context. Additionally, specific details regarding the gradation of histologic homogeneity within these tumors, not reported in the NCDB, should be considered as it may allow prognostic stratification [18]. The percentage of a particular histology within the specimen to warrant a particular code is dependent on the individual pathologist, presenting inter-observer variability. The study is further limited by its retrospective nature allowing discovery of only association, not causation, and the unclear temporal relationship between time from diagnosis to therapeutic intervention. Lastly, the NCDB does not address cancer-specific survival, instead only collecting overall survival; so, the relationship between treatment and cancer-related mortality is unknown. Despite these limitations, our analysis is the largest review in the current literature focused on invasive non-urachal ACB with overall survival outcomes and is strengthened by its focus on invasive disease stratified by multiple treatment types.

Conclusions

ACB is a rare malignancy found in 0.5–2% of patients diagnosed with bladder cancer and has disparate outcomes [6]. Surgery is underutilized for invasive ACB, and bladder preservation with radiation therapy has no objective survival benefit. Our NCDB data analysis demonstrates improved survival outcomes for patients undergoing definitive surgical extirpation, compared to other treatment modalities; thus, surgery remains the mainstay of treatment with invasive non-urachal ACB.

Compliance with ethical standards

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