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Systematic Review of Factors Associated with the Utilization of Radical Cystectomy for Bladder Cancer

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Abstract

Context: Despite established guidelines for the treatment of muscle-invasive bladder cancer, it has been reported that radical cystectomy (RC) is markedly underused, especially among patients of advanced age and those with higher comorbidity burden and lower access to care. Understanding the interactions between patient, provider, and hospital factors may inform targeted interventions to optimize RC utilization.

Objective: To systematically review the literature regarding factors associated with RC utilization.

Evidence acquisition: A systematic search was conducted using Ovid and Medline according to Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines to identify studies between 1970 and 2017 reporting on RC utilization. Prospective and retrospective studies were included.

Evidence synthesis: There are no published randomized control trials on RC utilization. Variations in study quality and design precluded a formal statistical meta-analysis. RC receipt significantly depended on patient, provider, and hospital factors. Patient factors associated with lower RC use included advanced age, African American and Hispanic race/ethnicity, higher comorbidity burden, unmarried marital status, higher tumor stage and grade, and lower socioeconomic status. Provider factors associated with underutilization included lower surgeon volume and a metropolitan location. Finally, hospital factors associated with lower RC use included low hospital volume, nonacademic affiliation, and hospital location in the Midwest.

Conclusions: RC is reportedly underutilized. We found that age, race, marital status, socioeconomic factors, cancer severity, comorbidity burden, surgeon volume, and facility type and location significantly determined RC receipt. Improved understanding of the varying contributions of the risk factors according to patient, provider, and hospital determinants may assist in developing targeted interventions to improve RC utilization.

Patient summary: In this review we explored the clinical evidence for factors predicting the utilization of radical cystectomy for muscle-invasive bladder cancer. Many factors related to the patient, provider, and hospital determine whether patients receive this guideline-recommended treatment. However, there remains a lack of understanding on characterization and targeted interventions according to these levels, which may improve use.

Keywords

Radical cystectomy; Use; Utilization; Predictors

1. Introduction

Despite longstanding guidelines and being the standard of care treatment for muscle-invasive bladder cancer (MIBC), radical cystectomy (RC) has been markedly underused in a number of studies [1–3]. RC is associated with non-negligible morbidity and mortality that probably contribute to this underutilization, especially among the elderly and those with higher comorbidity burden [4]. Trimodal therapy (TMT), which combines maximal transurethral resection followed by concurrent chemotherapy and radiotherapy, has emerged as a bladder sparing treatment for MIBC [5]. Although there have been no randomized trials comparing TMT to RC, recent population-based studies using the National Cancer Data Base have reported inferior survival for TMT compared with RC [5,6]. RC remains the gold standard treatment for MIBC and patients with recurrent or refractory non–MIBC; however, several organizations—including the European Association of Urology—have updated guidelines supporting the use of radiotherapy combined with chemotherapy in selected patients with MIBC [7–9].

Against this backdrop, RC utilization rates remain as low as 6% across all age groups and 19–21% among patients aged ≥66 yr [1–3]. Given the limitations of administrative claims data, investigators have been unable to determine the extent to which patients are offered RC [3]. Patients aged ≥66 yr with higher comorbidity burden are less likely to undergo RC [1–3,10]; however, the independent role of patient, provider, and health care facility characteristics in access to RC has not been completely defined. Prior studies identified patient rurality and socioeconomic status, as well as the limited number of surgeons who perform RC, as potential sources of variation in care and survival outcomes [1,3]. The purpose of this systematic review was to comprehensively identify the factors associated with RC utilization.

2. Evidence acquisition

A systematic literature search was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement to identify studies reporting on RC utilization between 1970 and 2017 [11]. After the systematic review protocol was finalized, but before screening studies for inclusion, the protocol was registered in PROSPERO (www.crd.york.ac.uk/prospero) as CRD42018087866. PROSPERO only accepts registration of systematic reviews with a health-related outcome. A systematic review was conducted to identify studies of relevance for the following predefined research questions. (1) Do patient factors determine RC use? (2) Do provider factors determine RC use? (3) Do hospital factors determine RC use? The Ovid interface of Medline was searched along with a free-text manual search using one or several combinations of the following items: (“bladder”) AND (“cancer” OR “carcinoma” OR “tumour” OR “tumor” OR “neoplasm” OR “malignancy” OR “mass”) AND (“localized”) AND (“use” OR “utilization”) AND (“survival”) AND (“RC”). Studies included patients with localized disease defined as cT1–4a, N0, M0 bladder cancer. Studies on both MIBC and non-MIBC were included for review. Studies derived from similar administrative data sets and registries, alone or linked (i.e. NCDB, Surveillance, Epidemiology and End Results [SEER], and SEER-Medicare) were allowed. We permitted overlap of years of study, but excluded studies derived from similar data sets and time periods with similar inclusion and exclusion criteria. All selected articles were further searched to identify additional relevant articles. A total of 1801 studies were initially identified. The selection process was conducted in three stages. The first stage was initial screening of the title to identify eligible publications, including a search of publications in journals not listed in Medline to avoid missing any eligible study. In the second stage, publications were screened for eligibility according to the abstracts. The third stage was full-text assessment of the publications. For this systematic review, we excluded: (1) non-English articles; (2) review articles (without systematic review or meta-analysis); (3) editorials and case reports; and (4) repeated publications to avoid publication bias. We excluded review articles, as the interpretation of published results without systematic assessment or meta-analysis of data does not offer novel insights into RC use.

A total of 14 papers were considered for evidence synthesis (Tables 1–3). These studies were all retrospective and are therefore inevitably susceptible to the risk of selection bias. A Consolidated Standards of Reporting Trials diagram is provided in Figure 1.

3. Evidence synthesis

3.1. Use of RC

It has been reported that RC is markedly underused as a treatment modality for patients with MIBC [1–3]. For varying patient populations, utilization rates reported have been as low as 6% across all age groups, and 19–21% among patients aged ≥66 yr, with no noted change in more recent years [1–3]. At the same time, there has been an increase in the utilization of trimodal therapy (ie, maximal endoscopic resection, external beam radiation therapy, and chemotherapy) as a “bladder-sparing” treatment option [5].

3.2. Use of RC and patient factors

On examining patient factors associated with the use of RC, we consistently found that patients of advanced age are less likely to receive RC (Table 1). In particular, compared with patients aged 66–70 yr, those aged 71–80 yr (odds ratio [OR] 0.50, 95% confidence interval [CI] 0.40–0.61) and 81–90 yr (OR 0.23, 95% CI 0.18–0.30) were significantly less likely to undergo RC [3,5]. Casey et al. found that patients aged ≥75 yr were less likely to receive RC compared with patients aged 65–75 yr (30% vs 39%; $p < 0.001$) [5]. Moreover, approximately 1–10% of RCs are performed in patients aged >80 yr [12,13].

A higher number of comorbidities has likewise been associated with lower use of RC [1,3,5,10,13–16]. For patients with three or more comorbidities classified according to the Charlson comorbidity index, RC rates are as low as 2% [1]. We also identified several racial and ethnic disparities in RC use, including lower use among non-Hispanic black patients [2,3,5,13,14,16] and Hispanic men and women [2]. Bream et al. [13] found that Hispanic patients had a nearly 30% chance of undergoing RC (OR 0.71, 95% CI 0.53–0.94).

Another contributing factor to receipt of RC is marital status. Canter et al. [17] found that 71% of patients who received RC were married, compared with 61% of patients who received conservative management ($p < 0.001$). Williams et al. [3] noted a nearly 50% increase in the odds of RC among married patients (OR 1.47, 95% CI 1.14–1.91).

Additional socioeconomic factors that have a significant impact on RC use include education level and income. Patients living in counties with higher education levels, defined as the proportion of individuals with at least 4 yr of college, have higher odds of RC (college-educated: 21.3–29.7%, OR 1.47, 95% CI 1.27–1.70; 29.7–36.3%, OR 1.52, 95% CI 1.29–1.78; >36.3%, OR 1.23, 95% CI 1.04–1.44) [2]. Similarly, patient income impacts RC use. Patients living in ZIP codes with higher quartiles of median household income have higher rates of RC utilization [1,13]. Insurance type was associated with receipt of RC across numerous studies. Cahn et al. [5] found that Medicare beneficiaries experience higher rates of trimodal therapy versus RC use (OR 4.05, 95% CI 2.45–6.70) when compared with other insurers including Medicaid and private insurance/managed care.

Cancer severity was associated with patient receipt of RC. Chamie et al. [18] reported a decrease in RC utilization with increase in tumor stage from T2 through T4 across age groups. Konety et al. [19] showed varying RC rates according to clinical stage: for stage II, III, and IV the utilization rate was 22.7%, 49.0%, and 40.4%, respectively. Bream et al. [13] observed higher RC utilization among patients with a tumor stage T3 compared with T2 bladder cancer (OR 1.75, 95% CI 1.54–1.98), but a lower rate among patients with stage T4 bladder cancer (OR 0.61, 95% CI 0.53–0.71). Similarly, higher-grade bladder cancer was associated with higher use of RC [1,3]. Finally, it has been shown that the morphology of bladder cancer is significantly associated with receipt of RC [12]. Non-papillary vs. papillary urothelial carcinomas were significant predictors for advanced stage (II-IV) at presentation (64.2% vs. 24.2%, p<0.001), respectively [12]. In multivariable analysis controlling for stage, patients with papillary urothelial cell carcinoma were significantly less likely to undergo RC than patients with non-papillary urothelial carcinomas (OR 0.74, 95% CI 0.59–0.93; $p = 0.010$) [12]. Booth et al. [15] found that patients with squamous cell carcinomas were more likely to undergo RC compared with other histologies (OR 1.84, 95% CI 1.21–2.81) [15].

3.3. RC use and provider factors

Surgeon volume may be a surrogate for surgical quality [20]. Centralization of RC to high-volume surgeons who operate at high-volume centers has been initiated in other countries and led to increased RC use, better mortality, lower complication rates, and shorter hospital stays after centralization (Fig. 2) [21]. In the USA, the urologist density is associated with RC utilization: if the urologist density exceeds 60 urologists/1 000 000 residents, RC utilization is lower (OR 0.75, 95% CI 0.59–0.95) [3]. This suggests that increasing the number of urologists in a geographical area may not result in an increased in RC use if they do not offer the complex procedure. RC is significantly less likely to be performed in metropolitan counties compared to urban counties (OR 0.70, 95% CI 0.62–0.79; $p < 0.001$) [13]. There was no significant difference in RC use between rural and urban counties [13]. Patient distance from available RC providers impacts the receipt of RC. Among patients with stage 2 bladder cancer, there was an inverse relationship between distance from an RC provider and receipt of exenterative surgery (0–4 miles, 49%; 5–19 miles, 34%; 20–49 miles, 10%; ≥50 miles, 7%; $p = 0.003$; Table 2) [1]. Patients who had to travel outside their hospital service area to undergo RC care tended to come from ZIP codes with lower socioeconomic status indicators. Mossanen et al. [22] observed similar findings, as patients living in areas with lower socioeconomic status have a greater need to travel for complex urologic surgery such as RC. More than half of RC patients underwent RC outside their hospital service area and one-quarter outside their hospital referral region [22].

3.4. RC use and hospital factors

Utilization of RC has varied greatly depending on the facility type (Table 3). Specifically, several studies have demonstrated that academic institutions have the highest rates of RC compared with other hospital types [3,5,23]. Bream et al. [13] found that RC rates at comprehensive cancer centers (OR 0.42, 95% CI 0.38–0.46), community centers (OR 0.32, 95% CI 0.27–0.37), and other facilities (OR 0.39, 95% CI 0.28–0.55) were well below those at academic institutions ($p < 0.001$) [13]. Interestingly, comprehensive cancer centers are usually academic centers and the designation is separately coded in administrative data. Similarly, high-volume facilities perform higher rates of RC compared with intermediate- and low-volume facilities [13,23]. Bream et al. [13] reported a 70% higher odds of undergoing RC at a high-volume compared with a low-volume center (OR 1.72, 95% CI 1.53–1.92) [13].

Geographic heterogeneity in RC utilization has also been previously described. Most of these utilized the SEERs national cancer registry, which contains patient data from several state and regional cancer registries. It has been shown in numerous studies that the Midwestern registries, especially Iowa, have lower RC utilization [1–3,19]. Additional registries with lower RC utilization compared with other regions include rural Georgia and Connecticut [1,19].

3.5. Limitations

Although several studies have identified patient factors associated with RC use, associated provider and hospital factors and their intrinsic interactions remain poorly defined. Moreover, these data are derived from observational studies, which have inherent selection bias. This is important, as patient and provider decisions are vital elements that determine any treatment, but especially a complex surgical procedure such as RC. Consequently, the quality of evidence for this systemic review is proportional to the quality of evidence and data sources for the individual observational studies included in the analysis. Another major limitation is the lack of understanding of patient preferences, which may be a major driver for RC use. Given the limitations of observational data and the lack of randomized studies assessing RC use, we must rely on matching, restriction, and adjusted analyses (knowing the limitations of each) in deriving as much useful clinical information as possible.

4. Conclusions

Practice guidelines recommend RC as the standard of care treatment for MIBC; nevertheless, most observational studies reported that RC was markedly underused in their patient populations. Utilization rates were reportedly as low as 6% across age groups, and

19–21% among patients aged ≥66 yr. Patient age, race, marital status, socioeconomic status, cancer stage, grade, and tumor histology, comorbidity burden, surgeon volume, and facility type and location were factors that significantly affected RC receipt. Further efforts are needed to clarify the interactions between patient, surgeon, hospital, and environmental factors that influence RC utilization among patients for whom RC is deemed feasible. This may inform targeted implementation strategies to improve RC utilization and optimize health outcomes for patients with bladder cancer.

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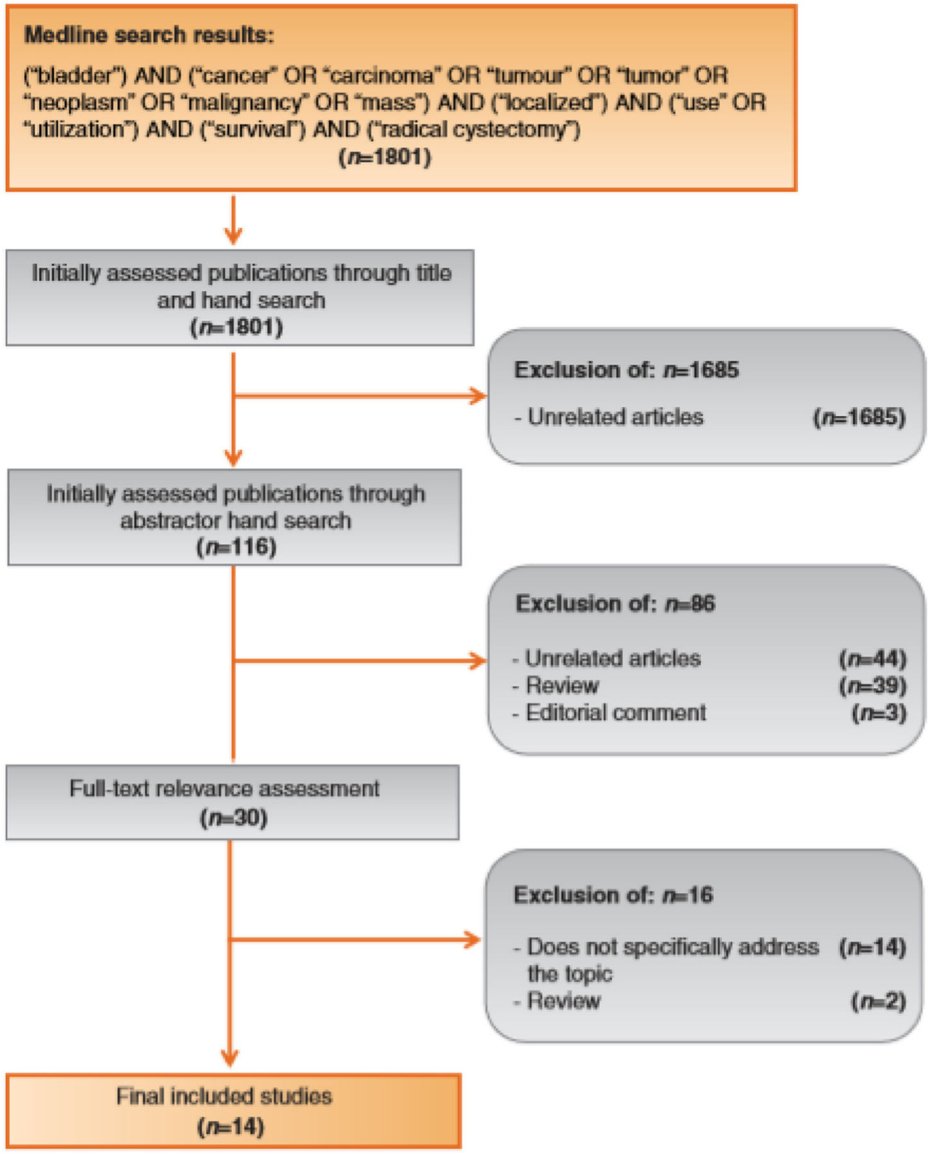

Fig. 1 –.

Consolidated Standards of Reporting Trials diagram showing the selection process for inclusion of studies in the review.

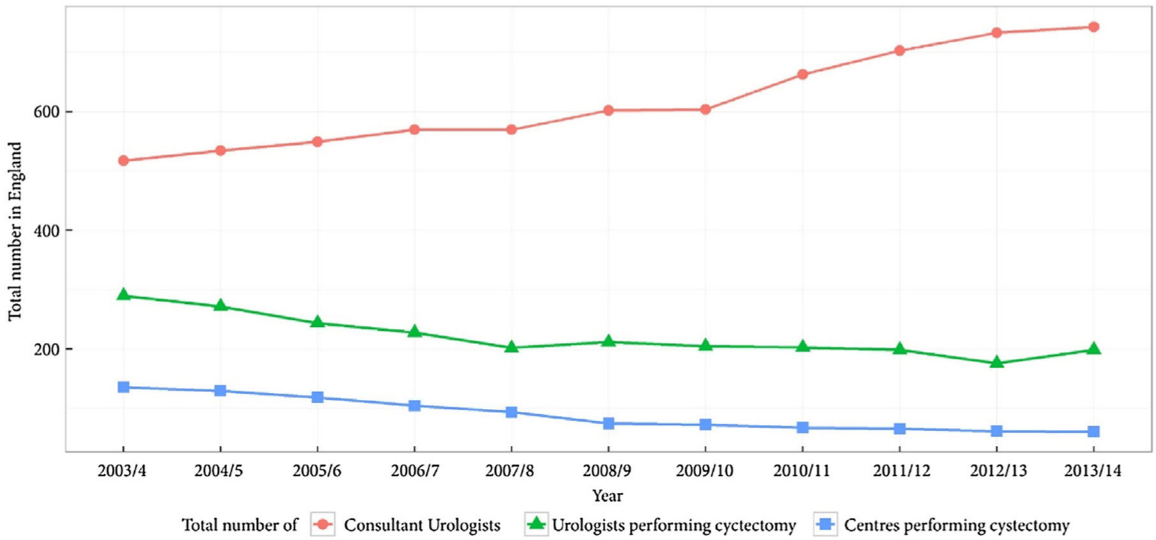

Fig. 2 –.

Number of providers, urologists, and urologists performing radical cystectomy in England from 2003 until 2014. In 2002, UK policymakers introduced the “Improving Outcomes Guidance”, in which a key recommendation was centralization of radical cystectomy to high-output centers. Reproduced with permission from Afshar et al. [21].

Table 1 –

Patient factors associated with utilization of radical cystectomy

Study	Source	Sample size	Age (yr)	Sex	Race	Insurance status	Marital status	Comorbidity	Cancer severity
Williams 2017 [2]	SEER	27 578	>80 vs<80: OR 0.23 [0.18–0.30]	NR	AA vs white: OR 0.79 [0.64–0.96]	NR	NR	NR	Stage III vs I: OR 29.1[23.9–35.3]
Cahn 2017 [5]	NCDB	32 300	>70 vs<50: OR 0.14 [0.09–0.22] >70 vs 51–60: OR 0.23 [0.18–0.29] >70 vs 61–70: OR 0.38 [0.33–0.44]	NSS	AAvs white: OR 1.54 [1.25–1.90]	MDC vs private: OR 4.05 [2.45–6.70]	NR	≥2 vs 0: OR 1.37 [1.14–1.64]	Stage III vs II: OR 0.28[0.25–0.32]
Booth 2014 [15]	Ontario Cancer Registry	5259	> 80 vs <50: OR 0.20[0.13–0.31] 70–79 vs <50: OR 0.49[0.31–0.76]	NSS	NR	NR	NR	1–2 vs 0: OR 0.53[0.47–0.61] ≥3 vs 0: OR 0.31[0.25–0.39]	NSS
Roghmann 2014 [16]	National Inpatient Sample	12 274	>80 vs <80: p<0.001	NR	NR	NR	NR	3+vs0 P<0.001	NR
Canter 2013 [17]	SEER	8467	>70 vs <70:p<0.001	NSS	NSS	NR	Married vs single: p<0.001	NR	NR
Barbiere 2011 [12]	ECRIC	4303	> 80 vs <50: OR 0.04[0.02–0.08] 71–80 vs <50: OR 0.34[0.21–0.55]	NSS	NR	NR	NR	NR	IV vs I: OR 3.15[2.28–4.36] III vs I: OR 5.38[3.85–7.52] II vs I: OR 3.11[2.39–4.04]
Gore 2010 [1]	SEER-Medicare	3262	>80 vs 66–69 yr: OR 0.10 [0.07–0.14]	NSS	NSS	NR	NSS	2 vs 0–1: OR 0.48[0.37–0.62] ≥3vs 0–1: OR 0.25 [0.14–0.45]	High vs low grade: OR 1.41[1.01–1.97]
Chamie 2008 [18]	SEER	10 807	<60 vs >79: p<0.002 60–69 vs >79: p<0.02	P<0.002	NSS	NR	NR	NR	T4vs T2: P<0.001
Konety 2003 [19]	SEER	16 976	≥85 vs 55–64: OR 0.14 [0.08–0.24] 75–84 vs 55–64: OR 0.51[0.38–0.67]	NSS	NSS	NR	NR	NR	IV vs I: OR 14.4[11.0–18.6] III vs I: OR 26.3 [19.8–35.0] II vs I: OR 14.3[11.1–18.4]
Parker 2018 [23]	NCDB	63 402	> 80 vs <60: OR 0.26[0.22–0.31]	NSS	NR	MDCvs uninsured: p<0.01	NR	NSS	Ta vs T1: p<0.01

Study	Source	Sample size	Age (yr)	Sex	Race	Insurance status	Marital status	Comorbidity	Cancer severity
Williams 2017 [3]	SEER-Medicare	3922	>80 vs 66–69: OR 0.15[0.12–0.19] 75–79 vs 66–69: OR 0.50[0.39–0.65] 70–74 vs 66–69: OR 0.73[0.56–0.94]	OR 1.87 [1.54–2.28]	AAvs white: OR 0.61 [0.40–0.94]	NR	OR 1.47 [1.141.91]	1 vs 0: OR 0.80[0.65–0.98] 2 vs 0: OR 0.42 [0.30–0.58] ≥3 vs 0: OR 0.41[0.29–0.57]	High vs low: OR 1.67[1.14–2.45]
Williams 2017 [10]	SEER-Medicare	9907	NR	Stage II: RR 1.48 [1.33–1.65] Stage III: RR:1.24 [1.13–1.37] Stage IV: RR 1.33 [1.19–1.49]	AA p<0.001 HSP p<0.001	NR	p<0.001	≥3 vs 0:p<0.001	IV vs II: p<0.007
Bream 2017 [13]	NCDB	18 945	80–84 vs 75–79: OR 0.58 [0.53–0.63] ≥85 vs 75–79: OR 0.12 [0.11–0.14]	NSS	AA vs white: OR 0.57 [0.46–0.70] HSP vs white: OR 0.71 [0.53–0.94]	NR	NR	≥2 vs 0: OR 0.70 [0.60–0.82]	T3 vs T2: OR 1.75[1.54–1.98] T4 vs T2: OR 0.61 [0.53–0.71]

AA = African American; ECRIC = Eastern Cancer Registration and Information Center; HSP = Hispanic; MDC = Medicare; NCDB = National Cancer Data Base; NR = not recorded; NSS = not statistically significant; OR = odds ratio [95% confidence interval]; RR = relative risk [95% confidence interval]; SEER: Surveillance, Epidemiology and End Results; SPARCS = Statewide Planning and Research Cooperative System.

Table 2 –

Provider factors associated with utilization of radical cystectomy

Study	Source	Sample size	Urologist density	Provider distance (miles)	Geography
Gore 2010 [1]	SEER-Medicare	3262	NSS	≥50 vs 0–4:OR 0.60[0.37–0.98]	NSS
Parker 2018 [23]	NCDB	63 402	NR	>17.4 vs <3.8: $p < 0.01$	Metropolitan vs rural: $p < 0.01$
Williams 2017 [3]	SEER-Medicare	3922	>60 vs <30/million: OR 0.75[0.59–0.95]	NR	NR

NCDB = National Cancer Data Base; NR = not recorded; NSS = not statistically significant; OR = odds ratio with 95% confidence interval in square brackets; SEER = Surveillance, Epidemiology and End Results.

Table 3 –

Hospital factors associated with utilization of radical cystectomy

Study	Source	Sample size	Hospital type	Hospital volume	Region
Cahn 2017 [5]	NCDB	32 300	Aca vs Comm: OR 2.51 [1.78–3.54] Aca vs CCC: OR 2.12 [1.68–2.69]	High vs low:OR 1.64 [1.18–2.27] High vs middle:OR 1.38[1.10–1.72]	NR
Roghmann 2014 [16]	NIS	12 274	Teaching vs nonteaching:$p<0.001$	NSS	NR
Parker 2018 [23]	NCDB	63 402	Aca vs Comm/CCC:$p<0.01$	High vs low:p<0.01	NSS
Bream 2017 [13]	NCDB	18 945	Aca vsCCC:OR 0.42 [0.38–0.46] Aca vs Comm: OR 0.32 [0.27–0.37]	Low vs high:OR 1.72 [1.53–1.92]	Midwest vs NE:OR 1.41[1.26–1.59] South vs NE:OR 1.14[1.01–1.28] West vs NE: OR 1.60[1.40–1.83]

Aca = academic; CCC = comprehensive cancer center; Comm = community center; NCDB = National Cancer Data Base; NE = Northeast; NIS = National Inpatient Sample; NR = not recorded; NSS = not statistically significant; OR = odds ratio with 95% confidence interval in square brackets; SEER = Surveillance, Epidemiology and End Results.