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Charlson comorbidity score is associated with readmission to the index operative hospital after radical cystectomy and correlates with 90-day mortality risk

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Abstract

Purpose Our objective was to determine perioperative variables associated with 30-day readmission to the index operative hospital after radical cystectomy for bladder cancer and subsequent survival outcomes.

Methods Retrospective cohort study utilizing the United States National Cancer Database from 2004–2015. All clinical stages undergoing radical cystectomy were analyzed. Exclusion criteria included clinical suspicion of nodal disease, metastasis, or preoperative radiation therapy. Multivariable logistic regression was used for 30-day readmission risk to the index hospital. Kaplan–Meier analysis and multivariable Cox regressions were used for survival outcomes.

Results 31,147 patients were identified and stratified by 30-day readmission ($n=2628$) or no readmission ($n=28{,}519$). Thirty-day readmission to the index surgery hospital was 8.4%. Groups were comparable in terms of age, gender, race, income, facility type, insurance, length of hospital stay, and pathologic stage. There were significantly more patients with higher Charlson comorbidity score in the readmission cohort. On logistic regression analysis, increasing Charlson score was the only predictor of 30-day readmission (OR 1.39–1.73, $p<0.001$). The 90-day mortality rate was 7.2% overall (7.0% no readmission vs 9.9% 30-day readmission, $p<0.001$). Cox regression analysis for mortality revealed increasing age (HR 1.04), higher Charlson score (HR 1.42–1.85), readmission within 30 days (HR 1.38) and pathologic stage pT ≥ 2 (HR 1.88–7.09, all $p<0.001$) as independent predictors of 90-day mortality.

Conclusions Increasing comorbidity is a strong predictor of readmission to the index surgery hospital after radical cystectomy. Readmission is associated with worsened mortality at 90 days.

Keywords Bladder cancer · Cystectomy · Patient readmission · Survival

Introduction

In 2018, it is estimated that bladder malignancy will comprise 4.6% of all cancer cases in the United States with an incidence of 81,190 cases and 17,240 deaths [1]. While treatment varies depending on severity and histologic subtype, muscle invasive bladder cancers and recurrent high-risk non-muscle invasive tumors are treated with radical cystectomy (RC). Radical cystectomy remains a morbid procedure with a high rate of postoperative complication, frequent readmission, and a significant risk of perioperative mortality [2]. Up to 67% of patients may experience a complication during the operative hospital stay, and those with complications have high rate of readmission [3, 4]. The most common causes of early readmission include upper urinary tract obstruction, pyelonephritis, intestinal obstruction, ileus, and metabolic acidosis [5].

Previous studies have defined expected rates of complications or death within 30 days of RC of approximately 30% and 3%, respectively [6, 7]. Rates of readmission after surgery are as high as 20% and tend to be associated with those who experience postoperative complications or have prolonged hospital stay [5]. Additionally, higher-volume operative centers tend to have improved outcomes leading to a push for centralization of RC; however, readmission after RC can occur at the index surgery hospital or outside referring institutions [8–11]. It remains unknown what the

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expected rate of readmission to the index surgical hospital is specifically for RC. We sought to determine the rate of 30-day readmission to the index hospital after RC from a national tumor registry and aimed to identify the preoperative and perioperative variables that are predictive of hospital readmission. Our primary outcome was index hospital readmission within 30 days of surgery, and our secondary outcome included all-cause mortality. We hypothesized that patients with increased age or significant comorbid conditions would have increased risk of readmission to the index hospital, as opposed to oncologic specific factors.

Materials and methods

Data source

The National Cancer Database (NCDB) is a joint project by the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The NCDB is the largest cancer registry in the world, gaining information from over 1500 hospitals around the country. Of all new cancer diagnoses nationwide, 70% are profiled in this database allowing access to staging information, patient characteristics, treatment outcomes, and more [12]. Retrospective data submitted to this database undergo significant quality assurance measures with annual internal validity reviews. Cases are submitted using standardized histopathological coding. All information collected is done so without direct patient identifiers and reported results are HIPAA compliant [13]. The data used in the study are derived from a de-identified NCDB file.

Study population

The NCDB bladder cancer dataset was queried for patients undergoing RC with clinically node-negative disease and no evidence of metastasis (cTanyN0M0) with any histology of bladder cancer. Patients were excluded if they received radiation therapy or were missing information regarding staging. All patients undergoing radical cystectomy were divided into two cohorts: no readmission or readmission within 30 days. All readmissions were to the index hospital where RC was performed. Readmission to outside institutions is not coded within the NCDB. Both groups were compared in terms of basic, clinical and pathologic parameters. Demographic information analyzed included age, gender, race, income status, distance traveled to facility, facility type, and insurance status. Of note, treatment facility type was categorized as low volume or high volume. Treatment facilities that accrued 500 or more newly diagnosed cancer cases per year were considered high volume (including academic centers); whereas, facilities with less than 500 were labeled low volume. Clinical information included Charlson comorbidity score [14, 15], clinical stage, and neoadjuvant chemotherapy information. Perioperative and survival parameters analyzed included time from diagnosis to surgery, length of hospital stay, pathologic staging, node positivity, presence of positive margins, length of follow-up, and mortality (overall, 30 , and 90 days).

Statistical analysis and outcome measure

Student's *t* test was performed for continuous variables, and Fischer's exact or Pearson's Chi-square tests for categorical variables. Multivariable logistic regression analysis was performed to identify predictors of 30-day readmission and Cox regression was used for mortality risk. Logistic regression analysis involved variables that were significantly different on unadjusted analysis and included days to cystectomy, Charlson score, clinical stage, neoadjuvant chemotherapy, and pathologic node-positive disease. Variables included in Cox regression for mortality analysis included age, Charlson score, neoadjuvant chemotherapy, 30-day readmission after surgery, and pathologic stage. Kaplan–Meier survival analysis was also completed for both the readmission and no-readmission cohorts. We utilized SPSS v25 (New York, United States) for all analyses, with p value of < 0.05 denoting statistical significance.

Results

A total of 31,147 patients were identified (Tables 1 and 2). The majority of patients were males (74.6%) and mean age of 67.8 ($\pm$ 10.5) years. The total rate of 30-day readmission to the index hospital was 8.4% ($n = 2628$). Two cohorts were created to analyze no readmission vs readmission within 30 days of surgery. The "no readmission" cohort contained data from 28,519 patients while the "readmission" cohort consisted of data from 2628 patients. Both groups were comparable in terms of age, gender, race, income status, distance traveled to facility, type of facility, insurance status, length of hospital stay, positive margins, pathologic stage, length of follow-up, overall mortality, or mortality within 30 days of surgery on the unadjusted analysis (all $p > 0.05$). There were significantly more patients with higher Charlson score in the readmission cohort ($p < 0.001$). For the "no readmission" cohort, 70% had a Charlson score of 0, 22.6% had a score of 1, 5.7% had a score of 2, and 1.6% had a score of 3+. In contrast, 61.8% of those in the readmission cohort had a score of 0, 28.2% had a score of 1, 7.5% had a score of 2, and 2.5% had 3+. A significantly higher number of patients with neoadjuvant chemotherapy were noted in the no-readmission cohort (41.2% vs 38.1%, $p = 0.002$). Time from diagnosis to cystectomy was longer for the no-readmission cohort

Table 1 Patient demographics and clinical tumor characteristics

Variable	All ($n=31,147$)	No readmission ($n=28,519$)	Readmission ($n=2628$)	p value
Mean age ± SD	67.8 ± 10.5	67.8 ± 10.5	67.9 ± 10.5	0.674
Male sex	23,245 (74.6%)	21,296 (74.7%)	1949 (74.2%)	0.575
Race				0.157
White	28,416 (92.2%)	26,017 (91.2%)	2399 (91.3%)	
Black	1736 (5.6%)	1577 (5.5%)	159 (6.1%)	
Other	995 (3.2%)	925 (3.2%)	70 (2.7%)	
Charlson				< 0.001
0	21,588 (69.3%)	19,965 (70.0%)	1623 (61.8%)	
1	7197 (23.1%)	6457 (22.6%)	740 (28.2%)	
2	1826 (5.9%)	1628 (5.7%)	198 (7.5%)	
3+	536 (1.7%)	469 (1.6%)	67 (2.5%)	
cT stage				0.026
Is	548 (1.8%)	514 (1.8%)	34 (1.3%)	
1	6324 (20.3%)	5781 (20.3%)	543 (20.7%)	
2	18,541 (59.5%)	16,925 (59.3%)	1616 (61.5%)	
3	3340 (10.7%)	3089 (10.8%)	251 (9.6%)	
4	2394 (7.7%)	2210 (7.7%)	184 (7.0%)	
cT 2–4	24,275 (77.9%)	22,224 (77.9%)	2051 (78.0%)	0.901
Income status				0.067
< $38,000	4767 (15.5%)	4343 (15.4%)	424 (16.3%)	
$38,000–47,999	7646 (24.9%)	7052 (25.1%)	594 (22.9%)	
$48,000–62,999	8592 (28.0%)	7836 (27.9%)	756 (29.1%)	
$63,000+	9718 (31.6%)	8895 (31.6%)	823 (31.7%)	
Unknown	424			
Distance traveled to facility (miles ± SD)	48.3 ± 130.4	48.5 ± 126.9	45.5 ± 163.9	0.533
Facility type				0.907
Low volume	4752 (15.3%)	4349 (15.2%)	403 (15.3%)	
High volume	26,395 (84.7%)	24,170 (84.8%)	2225 (84.7%)	
Insurance status				0.080
Uninsured	755 (2.4%)	709 (2.5%)	46 (1.8%)	
Private	9825 (31.5%)	9017 (31.6%)	808 (30.7%)	
Medicaid	1415 (4.5%)	1306 (4.6%)	109 (4.1%)	
Medicare	18,424 (59.2%)	16,814 (59.0%)	1610 (61.3%)	
Other govt	329 (1.1%)	304 (1.1%)	25 (1.0%)	
Unknown	399 (1.3%)	369 (1.3%)	30 (1.1%)	
Neoadjuvant chemotherapy	12,753 (40.9%)	11,753 (41.2%)	1000 (38.1%)	0.002

(87.5 vs. 84.1 days, $p=0.012$). On pathologic staging, the rate of node-positive disease was higher in the no-readmission cohort (25.4% vs. 23.6%, $p=0.044$). Mortality within 90 days of treatment was determined to be significantly increased in the group that required readmission (9.9% vs 7%, $p<0.001$).

On logistic regression analysis, we analyzed factors found to be significantly different on univariate analysis. This included time to cystectomy, Charlson score (CS), clinical stage, neoadjuvant chemotherapy, and pathologic node sensitivity. We noted that increasing CS was the only predictor of readmission within 30 days after surgery. Compared to patients with a CS of 0, patients with a CS of 1 were 1.39 times more likely to be readmitted; while, patients with CS of 2 were 1.46 times more likely, and a CS of 3 + were 1.73 times more likely ($p<0.001$ for all listed, Table 3). Given the difference in 90-day mortality, we performed a Cox regression including age, CS, neoadjuvant chemotherapy, 30-day readmission, and pathologic staging. Cox regression analysis for 90-day mortality revealed increasing age, higher CS, readmission within 30 days and pathologic stage $pT \geq 2$ as the independent predictors of 90-day mortality (Table 4). The utilization of neoadjuvant chemotherapy resulted in a significantly decreased risk of mortality in

Table 2 Perioperative and survival outcomes

Variable	All ($n=31,147$)	No readmission ($n=28,519$)	Readmission ($n=2628$)	p value
Days ± SD from diagnosis to RC	87.2 ± 74.6	87.5 ± 74.8	84.1 ± 82.0	0.012
Hospital stay (days ± SD)	9.6 ± 9.9	9.6 ± 10.0	10.2 ± 8.8	0.804
pT stage				0.675
0/a	1985 (6.4%)	1827 (6.4%)	158 (6.0%)	
1/is	4960 (15.9%)	4518 (15.8%)	442 (16.8%)	
2	8358 (26.8%)	7651 (26.8%)	707 (26.9%)	
3	10,699 (34.4%)	9812 (34.4%)	887 (33.8%)	
4	5145 (16.5%)	4711 (16.5%)	434 (16.5%)	
≥ pT2	24,202 (77.7%)	22,174 (77.8%)	2028 (77.2%)	0.494
pN+	7859 (25.2%)	7239 (25.4%)	620 (23.6%)	0.044
Positive margins	3612 (11.6%)	3288 (11.5%)	324 (12.3%)	0.226
Length of follow-up (months ± SD)	36.3 ± 29.8	36.5 ± 29.8	34.4 ± 29.1	0.215
Mortality	15,691 (50.4%)	14,334 (50.3%)	1357 (51.6%)	0.179
Within 30 days of RC	731 (2.6%)	678 (2.7%)	53 (2.3%)	0.505
Within 90 days of RC	1997 (7.2%)	1765 (7.0%)	232 (9.9%)	< 0.001

Table 3 Multivariable logistic regression for readmission

Variable	OR	95% CI low	95% CI high	p value
Days to cystectomy	1.000	0.999	1.000	0.174
Charlson Score (0 ref)				
1	1.393	1.271	1.528	< 0.001
2	1.463	1.250	1.713	< 0.001
3+	1.725	1.326	2.245	< 0.001
cT stage (cTis/1 ref)				
cT2	1.062	0.959	1.176	0.247
cT3	0.916	0.782	1.074	0.280
cT4	0.959	0.803	1.145	0.645
Neoadjuvant chemotherapy	0.928	0.845	1.020	0.121
pN+	0.931	0.844	1.027	0.151

Table 4 Multivariable cox regression for 90-day mortality

Variable	HR	95% CI low	95% CI high	p value
Age	1.037	1.032	1.042	< 0.001
Charlson Score (0 ref)				
1	1.416	1.273	1.574	< 0.001
2	1.749	1.482	2.065	< 0.001
3+	1.845	1.386	2.456	< 0.001
Neoadjuvant chemotherapy	0.432	0.386	0.484	< 0.001
30-day readmission	1.384	1.193	1.605	< 0.001
pT stage (pT0 ref)				
pT1	1.227	0.826	1.823	0.312
pT2	1.884	1.297	2.736	0.001
pT3	3.307	2.295	4.764	< 0.001
pT4	7.085	4.912	10.220	< 0.001

patients at 90 days (OR 0.43, $p<0.001$). Kaplan–Meier 5-year overall survival was performed comparing the two cohorts. We noted that patients who had no readmission resulted in 5-year OS of 41.4%; while, those with a 30-day readmission to the index hospital have 5-year OS of 39.0%. Furthermore, the median OS for patients with no readmission was 40.1 months and for patients with readmission was 37.2 months (log-rank $p=0.005$).

The trend of readmission over the study period is graphically displayed in Fig. 1. We noted relative stability of the readmission risk from 2004 to 2015, as the rate of readmission did not differ between those opposing years of study ($p=0.69$).

Discussion

Our contemporary analysis of the NCDB from 2004 to 2015 highlights the current landscape of readmission to the index surgical hospital after radical cystectomy. We note a readmission within 30 days of surgery that is 8.4% overall. On multivariable analysis, we find the independent risk of hospital readmission is driven by non-modifiable patient factors, specifically preoperative comorbidity. Notably, the risk of readmission is not affected by the use of neoadjuvant chemotherapy or oncologic factors such as stage or node positivity. Those that require hospital readmission to the index hospital within 30 days have decreased survival outcomes at 5 years, with significantly increased risk of mortality at 90 days. Our analysis adds to the current literature by examining a modern cohort of patients that confirms previous knowledge in a recent time frame, and we specifically identify rates of readmission to the index surgical hospital, which has not

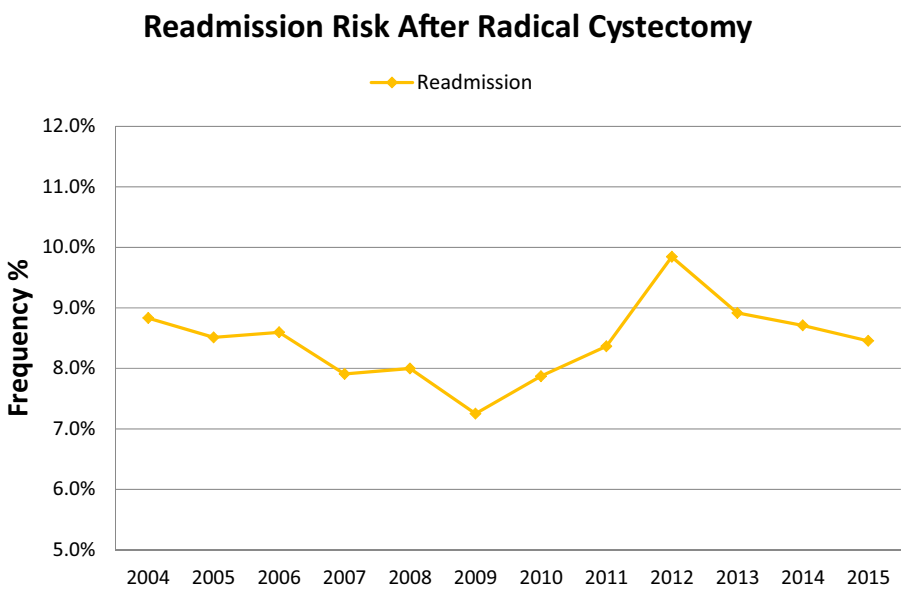

Fig. 1 Readmission risk after radical cystectomy over time

Variable	All (n=31147)	No Readmission (n=28519)	Readmission (n=2628)
2004	1404	1280 (91.2%)	124 (8.8%)
2005	1539	1408 (91.5%)	131 (8.5%)
2006	1652	1510 (91.4%)	142 (8.6%)
2007	1897	1747 (92.1%)	150 (7.9%)
2008	2713	2496 (92.0%)	217 (8.0%)
2009	3020	2801 (92.7%)	219 (7.3%)
2010	2986	2751 (92.1%)	235 (7.9%)
2011	2917	2673 (91.6%)	244 (8.4%)
2012	3017	2720 (90.2%)	297 (9.8%)
2013	3174	2891 (91.1%)	283 (8.9%)
2014	3398	3102 (91.3%)	296 (8.7%)
2015	3430	3140 (91.5%)	290 (8.5%)
Total	31147	28519 (91.6%)	2628 (8.4%)

been previously reported. Additionally, we found that hospital readmission risk has not varied over time and correlates with a risk of death at 90 days.

To our knowledge, our analysis is the first to report on 30-day readmission after RC to the index operative hospital. We identified a readmission rate of 8.4% to the index hospital, which is in contrast to the common reporting of a readmission risk that is as high as 30% when including readmissions to the non-operative hospital [16]. This can provide support during preoperative patient counseling, as approximately one out of three readmissions will happen at the index hospital; yet, the majority appear to occur at referring institutions. Our report is novel in this respect and provides new information regarding readmission data for patient counseling.

Previous research has noted that rates of readmission after radical cystectomy do not change over time, similar to our own analysis. These reports have typically shown an increased risk of readmission as high as 30% when examining all hospital readmissions; whereas, we noted an 8.5% readmission rate to the index surgical hospital [16]. Harraz et al [5] reported an 8.6% readmission rate within 90 days among 895 patients in Egypt; however, they did not look at 30-day readmission rate specifically. Three modern studies examining a 30-day readmission using large, multicenter databases determined the rate of 30-day readmission to be approximately 25% when including all readmitting centers [17–19]. Lorentz et al [17] has studied outcomes in a similar time frame (2011–2015), yet found a 30-day readmission rate almost three times higher than our analysis. This likely relates to the readmission data within the NCDB, as the NCDB does not capture data from outside referring institutions and only identifies readmissions to the index operative facility; thus, the readmission rate within NCDB is likely underreported overall. However, these discordant findings highlight the large variance in outcomes with cystectomy patients. Published data regarding 30-day readmission rates are variable, and our analysis provides a

large, contemporary, multi-center sample that may be useful in characterizing the overall readmission risk specifically to index hospitals performing RC.

We found CS to be the strongest predictor of 30-day readmission rate, emphasizing preoperative underlying patient comorbidity as a non-modifiable risk factor for poor outcomes. Other studies have identified this variable as a predictor of accessory discharge services, such as home health or nursing facilities [20]. Interestingly, readmission risk did not appear affected by patient age, despite the more advanced age of our cohort, as the mean age between groups was non-significant (67.8 vs 67.9 years, $p=0.674$). This may indicate that patient-specific comorbidity is the primary driver of readmission as opposed to individual patient age; however, further research would be helpful in a geriatric population. Stimson et al [21] also determined comorbidity to have association with 90-day readmission following RC. While specific comorbidities were not analyzed in this study, Minnillo et al [18] found an increased risk of 30-day readmission following RC in those with diabetes treated with medications and/or insulin as well as those with obesity. Similar to our findings, they ultimately concluded that those with more extensive comorbidities had higher readmissions. Other factors (both modifiable and not) associated with 30-day readmission in similar studies include discharge to post-acute care facility, receiving a continent urinary diversion, increasing age, pathologic T4 stage, positive surgical margin, perioperative blood transfusion, and prolonged surgical time [17, 22]. While pT4 was not determined to be a predictor of readmission in this population, it was a useful predictor of 90-day mortality. It may be reasonably inferred that increased comorbidities would increase risk of readmission, but awareness of associated risk can allow providers to assess which patients may benefit from closer observation during hospitalization and following discharge.

Neoadjuvant therapy was not found to alter risk of readmission at 30 days, nor did increased tumor staging or positive margins. Of note, there was an increased time from diagnosis to RC for the patients who did not have a readmission, and this likely translates to the increased use of neoadjuvant chemotherapy in the no-readmission cohort. Increased pT stage was not found to be associated with readmission at 90 days in another study, which is consistent with our findings [21]. In a study that analyzed length of hospital stay following readmission status post RC, neoadjuvant therapy did not have a protective role in decreasing hospital days either [19]. In appropriately selected patients, neoadjuvant therapy was recently found not to lead to increased short-term complications [23]. While its immediate short-term utility appears limited with regard to reducing readmission, findings support a significant association with decreased 90-day mortality. Providers should find these data encouraging, as the use of neoadjuvant chemotherapy or worsening pathology data do not increase the risk of readmission in these analyses. Importantly, previous literature has noted that patients with increased CS are less likely to receive neoadjuvant therapy, and this may be an unmeasured factor in our own analysis [24]. Although these patients may be less likely to tolerate neoadjuvant chemotherapy, they may benefit most from optimization as they have increased risk of future hospitalizations and subsequently increased mortality. As neoadjuvant therapy use associated with RC continues to become more prevalent through time, it will be important to find ways to safely implement among all populations [25].

For the entire study population of our analysis, the 90-day mortality was 7.2%. Based on other RC studies, reported mortality rate at 90 days ranges from 2.6 to 6.8%, lending credence to our findings [21]. Additionally, we noted that 90-day mortality in those that did not require readmission was 7%; while those who were readmitted to the index hospital within 30 days had a 90-day post-operative mortality rate of 9.9%, equating to a 41% relative risk increase of death in the 90-day period following surgery. There was also a 6% relative risk increase in 5-year mortality in those who were readmitted in 30 days. These findings are important as they stress the inherent increased risk of mortality associated with hospital readmission, especially when the readmission occurs at the index operative hospital. Although it is impossible to objectively measure within this dataset, it seems reasonable to assume that the most comorbid patients will require readmission to the index surgical hospital, as opposed to an outside referring institution, and this need for the index site correlates with an increased mortality risk. Providers should maintain close follow-up and have a high index of suspicion for patients with high CS, as they are at risk of readmission or mortality.

Limitations to this study exist. With any database, the quality of data is dependent on the quality of registry data entered [26]. Importantly, readmission data available to the NCDB are only recorded for the index hospital performing the initial operation, and it is estimated that up to approximately 30% of postoperative readmissions are to different facilities [27]. Thus, our quoted risk of readmission is underreporting the risk of all readmissions and equates only to a readmission risk to the initial operative institution. Furthermore, the NCDB does not capture data regarding reason for readmission, specifics of underlying comorbidity, or cancer-specific survival. Readmission risk may also be related to the type of urinary diversion performed, and this was not included within our analysis. The NCDB does not include specific perioperative outcomes such as estimated blood loss, transfusions, operative time, placement in the intensive care unit, or other perioperative complications. These could certainly increase the readmission risk and are not fully represented in the national dataset. However, our analysis provides data regarding readmission rates among

RC patients to the index operative institution and appears to have one of the largest study populations of those available. Additionally, we have identified novel evidence for the value of the Charlson Comorbidity Index in assessing short-term readmission risk and new evidence supporting the association of 30-day readmission with both 90-day and 5-year mortality.

Conclusion

Analysis of this large cohort of radical cystectomy patients reveals an 8.4% risk of readmission within 30 days to the index operative hospital after RC, which correlates with an increased risk of death at 90 days. Underlying medical comorbidity appears to drive this readmission risk. Utilization of this information can help to guide patient management following radical cystectomy.

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Compliance with ethical standards

Conflict of interest All listed authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent is not required due to the retrospective de-identified dataset from a national tumor registry.

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