Perioperative outcomes after radical cystectomy at NCI-designated centres: Are they any better?

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Cite as: *Can Urol Assoc J* 2015;9(5-6):207-12. http://dx.doi.org/10.5489/cuaj.2621
Published online June 15, 2015.

Abstract

Introduction: In 1971, the National Cancer Institute (NCI) introduced a network of NCI-designated Cancer Centers (CC), which underwent a comprehensive approval process relying on research, education and prevention activities. In this study, we examine the effect of CC status on perioperative outcomes after radical cystectomy (RC).

Methods: Within the Nationwide Inpatient Sample, we focused on RC performed from 2006 to 2010. As all recognized centres were residency teaching institutions, we stratified according to teaching and CC-teaching status. We examined the rates of in-hospital mortality, intra- and postoperative complications, prolonged length of hospital stay, as well as blood transfusion. Multivariable logistic regression analyses were further adjusted for confounding factors.

Results: Overall, 22 840 RC patients (5451 at non-teaching, 10 857 at residency teaching, 6532 at CC-teaching institutions) were identified. Patients treated at residency teaching and CC-teaching institutions were younger, had less comorbidities, and more likely to have private insurance. In multivariable analyses, patients treated at residency and CC-teaching institutions were less likely to experience postoperative complications (odds ratio [OR] 0.73 and 0.66, respectively) and blood transfusions (OR 0.77 and 0.53, respectively) relative to patients treated at non-teaching institutions. In addition, CC patients were also less likely to experience in-hospital mortality (OR 0.61, all $p < 0.001$) as compared to non-teaching institutions.

Conclusions: On average, patients treated at residency and CC-teaching institutions are less likely to experience unfavourable outcomes after RC. Moreover, patients treated at CC fared better than patients treated at residency teaching institutions. Our findings acknowledge the quality of RC care at accredited centres.

Introduction

Radical cystectomy (RC) is the treatment of choice for patients with muscle-invasive bladder cancer.[1,2] Though perioperative outcomes have undoubtedly improved in recent years,[3] RC still carries substantial morbidity and mortality, with a 3-month mortality rate of 1% to 3% and with about 50% of patients experiencing a postoperative complication.[4-6] Certain patient characteristics, such as lower patient age and baseline comorbidity profile higher surgeon and hospital volume,[3,7] as well as institutional teaching status,[8] have been associated with favourable perioperative outcomes.

In 1937, the National Cancer Institute (NCI) was formed by the United States Congress to conduct and foster cancer research.[9] During the 1960s, the NCI introduced a network of NCI-designated Cancer Centers (CC), leading to the official establishment of the NCI CC branch by the National Cancer Act in 1971.[9] These CC undergo a comprehensive approval process of all oncology departments, simultaneously necessitating regular re-accreditation based on standards of basic and clinical research, specialized training for scientists, physicians and surgeons, as well as cancer prevention and public education.[9,10]

Although the quality of surgical cancer care is not assessed in the review process, it is generally assumed that these centres might offer treatment of a superior quality compared to non-NCI designated centres.[10] However, there are only a few reports comparing postoperative outcomes after major oncologic surgery between NCI-designated CC and those without such designation.[11,12] These studies analyzed historic cohorts of patients treated in the previous decade and found that postoperative mortality rates after visceral[11,12] and thoracic surgery were lower in NCI-designated CC.[11,12] Importantly, no difference in operative mortality was seen for RC,[11] and in any case, perioperative outcomes were not assessed as the primary endpoint in either study.

We therefore decided to examine, at a population level, the effect of CC status on perioperative outcomes after RC. Our working hypothesis is that regionalization of care to designated CC has led to improved outcomes at these centers.

Methods

Data source

We relied on the Nationwide Inpatient Sample (NIS) database, which was developed as part of the Health Cost and Utilization Project (HCUP).[13]

Sample population

Patients with a primary diagnosis of bladder cancer were identified via ICD-9-CM code 188 (bladder cancer) in the 5 most contemporary years of the NIS (2006–2010). Those with a RC procedure code (International Classification of Diseases, 9th Edition, Clinical Modification [ICD-9-CM] code 57.71 and 57.79) and a urinary diversion by ileal conduit (ICD-9-CM56.51) or neobladder (ICD-9-CM57.87) were abstracted. Patients with missing data on indication, urinary diversion, gender, age, socioeconomic status according to ZIP and expected primary payer for treatment were excluded from further analysis.

Baseline patient characteristics

Patient characteristics included age at surgery, gender, race, and year of surgery. Patients who were younger than 18 years of age were removed from the analyses.

Patient comorbidity was calculated using a validated algorithm (categorized as 0–1, 2, ≥3).[14] Patients' ZIP income was classified into 4 groups: (1) <$25 000; (2) $25 000–$34 999; (3) $35 000–$44 999; and (4) ≥$45 000.[15] Insurance status was based on the expected primary payer (Medicare, Medicaid, private, and other, including uninsured patients).

Hospital characteristics

Hospital volume was defined according to previously described methodology as the number of cystectomies performed annually, namely the number of procedures performed overall divided by the number of years the hospital performed the operation, for the entire study period and based on the current database.[16]

Hospital location was defined as rural or urban. Institutional teaching status was obtained from the American Hospital Association (AHA) Survey of Hospitals. A hospital is considered to be a teaching hospital if it has an American Medical Association-approved residency program, is a member of the Council of Teaching Hospitals, or has a ratio of full-time equivalent interns and residents to beds of 0.25 or higher.

Detailed information on accredited institutions was obtained from the website of the NCI.[9] The NIS hospital universe was then searched for all hospitals related to the institutions listed in the aforementioned website. Of the 67 accredited NCI programs, 26 were identified within our database. This difference is caused by multiple reasons. Not all states are included in the NIS and some do not provide hospital information at all. In addition, the NIS is supposed to provide a representative sample of the states included. Therefore not all hospitals within the states which do provide hospital information are included in the NIS. Since all accredited institutions were also teaching institutions, we were able to stratify teaching status into three categories: non-teaching, teaching without accredited NCI program (teaching) and NCI accredited teaching CC (CC-teaching). To minimize confounding factors, patients from states in which hospital identification was not provided were excluded, resulting in 22 840 eligible cases for subsequent analyses. While sampling weights are typically incorporated into NIS population-based studies, we elected not to perform weighted analyses in the current study due to the large number of excluded patients.

In-hospital complications

Overall complications (intra- and postoperative complications) and blood transfusions were evaluated using ICD-9 diagnostic and procedural codes according to previous methodology.[3,7] Blood transfusion recipients were identified using the ICD-9 procedure codes: 99.02, 99.04. For statistical analysis purposes, we stratified patients by 0 vs. 1 or greater complications.

Length of stay, and in-hospital mortality

Length of stay was calculated by subtracting the admission date from the discharge date.[17,18] Same-day stays, coded as 0, were excluded from current analysis. In-hospital mortality information was coded from disposition of the patient. Patients with missing or invalid length of stay or in-hospital mortality status were not considered within the current study. A prolonged length of hospital stay was defined as length of stay above the median (9 days).

Statistical analysis

Frequencies and proportions as well as means, medians and ranges were generated for categorical and continuously coded variables, respectively. The chi-square and Kruskal-Wallis tests were used to compare the statistical significance of differences in proportions and medians, respectively.

Subsequently, we relied on univariable and multivariable logistic regression models adjusted for clustering to quantify the effect of institutional teaching/CC status on complications, prolonger length of stay, and in-hospital mortality. After Bonferroni correction, all tests were two-sided with a statistical significance set at $p < 0.003$. Analyses were con-

ducted using the statistical package for R (the R foundation for Statistical Computing, version 2.15.2).

Results

Baseline descriptives

Overall, 22 840 patients who underwent RC for bladder cancer were recorded within the NIS (2006–2010). Of those, 5451 (23.9%) were treated at non-teaching institutions, whereas 17 389 patients were treated at institutions with a residency program. The last group could be subdivided by CC status (teaching vs. CC-teaching) with 10 857 (47.5%) and 6532 (28.6%) patients, respectively (Table 1).

Intra- and postoperative outcomes

Intraoperative and postoperative outcomes recorded during hospital stay are shown in Table 2. In multivariable analyses

Table 1. Demographic characteristics of patients treated with radical cystectomy for bladder cancer, stratified according to institutional teaching and NCI-designated cancer center status, Nationwide Inpatient Sample, 2006–2010

Characteristic	Non-teaching	Teaching	CC-teaching	Total	*p* value†
No. patients, %	5451 (23.9)	10857 (47.5)	6532 (28.6)	22840 (100)	-
No. hospitals, %	306 (56.0)	214 (39.2)	26 (4.8)	546 (100)	-
Age (year), mean (median)	70.1 (72.0)	68.7 (70.0)	68.6 (70.0)	69.0 (70.0)	<0.001
Hospital volume, mean (median)	5.7 (4)	17.2 (13.0)	55.9 (42.0)	25.4 (14.0)	<0.001
Patients, % per column					
Age, groups					
<55	7.3	10.0	9.3	9.2	<0.001
55–64	20.5	22.3	24.0	22.4	
65–74	34.3	34.3	35.0	34.5	
>75	37.9	33.4	31.7	34.0	
Gender					
Male	82.6	83.2	87.7	84.4	<0.001
Female	17.4	16.8	12.3	15.6	
Race					
White	72.6	71.4	78.1	73.6	<0.001
Non-white	7.5	11.9	11.2	10.7	
Unspecified	19.8	16.7	10.7	15.7	
Elixhauser comorbidity index					
0–1	36.7	37.8	42.3	38.8	<0.001
2–3	46.5	47.7	46.2	47.0	
>3	16.8	14.6	11.5	14.2	
ZIP code income quartile, $					
1–24 999	18.6	17.0	14.7	16.7	<0.001
25 000–34 999	26.9	24.4	24.9	25.1	
35 000–44 999	26.3	28.0	24.8	26.7	
≥45 000	28.3	30.6	35.6	31.5	
Primary payer					
Medicare	66.3	61.8	63.1	63.3	<0.001
Medicaid/other	6.7	9.2	6.6	7.9	
Private	27.0	28.9	30.3	28.9	
Urinary diversion					
neobladder	6.0	9.2	20.7	11.7	<0.001
Ileal conduit	94.0	90.8	79.3	88.3	
Hospital location					
Rural	10.9	3.3	4.8	5.5	<0.001
Urban	89.1	96.7	95.2	94.5	

†chi² test; NCI: National Cancer Institute; CC: NCI-designated Cancer Center.

Table 2. Intraoperative and postoperative outcomes during hospitalization stratified according to institutional teaching and CC-teaching status (no. patients, %)

	Non-teaching	Teaching	CC-teaching	Total	*p* value
	5451 (23.9)	10857 (47.5)	6532 (28.6)	22840 (100)	
Intraoperative complication	166 (3.0)	363 (3.3)	168 (2.6)	697 (3.1)	0.017
Postoperative complication					
Overall	2080 (38.2)	3235 (29.8)	1776 (27.2)	7091 (31.0)	<0.001
Digestive	1262 (23.2)	1764 (16.2)	934 (14.3)	3960 (17.3)	<0.001
Respiratory	201 (3.7)	214 (2.0)	92 (1.4)	507 (2.2)	<0.001
Hemorrhage	202 (3.7)	363 (3.3)	234 (3.6)	799 (3.5)	0.449
Cardiac	230 (4.2)	429 (4.0)	264 (4.0)	923 (4.0)	0.714
Infectious	236 (4.3)	381 (3.5)	273 (4.2)	890 (3.9)	0.014
Vascular	40 (0.7)	51 (0.5)	32 (0.5)	123 (0.5)	0.077
Seroma	29 (0.5)	62 (0.6)	28 (0.4)	119 (0.5)	0.447
Operative wound	242 (4.4)	370 (3.4)	154 (2.4)	766 (3.4)	<0.001
Fistula	33 (0.6)	74 (0.7)	25 (0.4)	132 (0.6)	0.040
Genitourinary	138 (2.5)	282 (2.6)	158 (2.4)	578 (2.5)	0.768
Shock	42 (0.8)	84 (0.8)	70 (1.1)	196 (0.9)	0.086
Blood transfusion	2099 (37.9)	3795 (35.3)	2196 (33.7)	8090 (35.5)	<0.001
Length of hospital stay >9 days	2214 (40.6)	4289 (39.5)	2298 (28.6)	8801 (38.5)	<0.001
In-hospital mortality	139 (2.5)	260 (2.4)	94 (1.4)	493 (2.2)	<0.001

CC: NCI-designated Cancer Center; NCI: National Cancer Institute.

(Table 3), patients treated at teaching and CC-teaching institutions were less likely to experience overall postoperative complications (odds ratio [OR] 0.73 and 0.66, respectively) or in-hospital death (OR 0.61, all $p \leq 0.001$). No difference according to teaching/CC status could be demonstrated for intraoperative complications and prolonged length of stay.

Additional multivariable analyses using teaching hospitals without NCI as a reference confirmed that patients treated at NCI designated hospitals were less likely to die (OR 0.58) or to experience blood transfusion (OR 0.66), as well as overall complications (OR 0.86, all $p < 0.001$).

Hospital volume was associated with a lower likelihood of postoperative shock and prolonged length of stay (OR 0.98, OR 0.99, both $p < 0.001$), as demonstrated by improved outcomes per additional procedure performed per institution. Interestingly, higher hospital volume was associated with a higher likelihood of respiratory, cardiac, infectious, vascular, urinary complications, as well as blood transfusion (all OR 1.01, $p \leq 0.006$). An incremental change in overall postoperative, digestive, hemorrhage, seroma, wound complications, or in-hospital mortality was not demonstrated as hospital volume increased.

Table 3. Multivariable analyses of perioperative outcomes† adjusted for age, gender, year of surgery, race, Elixhauser comorbidity index, hospital location, insurance status, income status, urinary diversion and hospital volume

	Teaching vs. non-teaching		CC-teaching vs. non-teaching	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Intraoperative complication	1.000 (0.896–1.117)	0.995	0.960 (0.805–1.145)	0.648
Postoperative complication				
Overall	0.728 (0.669–0.791)	<0.001	0.663 (0.596–0.738)	<0.001
Digestive	0.675 (0.608–0.749)	<0.001	0.582 (0.511–0.664)	<0.001
Respiratory	0.485 (0.393–0.598)	<0.001	0.229 (0.163–0.323)	<0.001
Hemorrhage	0.916 (0.756–1.110)	0.370	0.954 (0.705–1.292)	0.763
Cardiac	0.851 (0.714–1.015)	0.072	0.557 (0.450–0.688)	<0.001
Infectious	0.773 (0.653–0.915)	0.003	0.728 (0.592–0.896)	0.003
Vascular	0.554 (0.349–0.879)	0.012	0.337 (0.181–0.627)	0.001
Seroma	1.064 (0.686–1.650)	0.782	0.880 (0.447–1.732)	0.711
Operative wound	0.774 (0.652–0.919)	0.003	0.529 (0.391–0.714)	<0.001
Genitourinary	0.913 (0.735–1.135)	0.412	0.680 (0.483–0.957)	0.027
Shock	1.297 (0.869–1.936)	0.202	3.245 (2.020–5.213)	<0.001
Blood transfusion	0.774 (0.693–0.864)	<0.001	0.527 (0.419–0.663)	<0.001
Length of hospital stay >9 days	1.033 (0.952–1.122)	0.436	1.090 (0.947–1.255)	0.229
In-hospital mortality	0.984 (0.786–1.231)	0.885	0.609 (0.456–0.815)	0.001

†A model for prediction of perioperative fistula was not performed due to insufficient number of events observed for each subgroup. CC: NCI-designated Cancer Center; CI: confidence interval; stay; NCI: National Cancer Institute; OR: odds ratio.

Discussion

Despite undoubted improvement in recent years,[3] RC is still associated with significant morbidity and mortality, due to its technically demanding nature as well as the need for specialized postoperative care.[4-6] Given the increasing regionalization of RC to high-volume, academic centres,[19] we felt it was important to validate this move by comparing outcomes at teaching and non-teaching institutions and particularly to confirm whether improved outcomes are seen at NCI-designated CC, as has already been shown for other major oncologic surgery.[11,12]

Our analysis raised several noteworthy findings. Firstly, to our knowledge, we are the first to demonstrate superior perioperative outcomes after RC at centres with NCI designation. Specifically, overall postoperative (OR 0.66), digestive (OR 0.58), respiratory (OR 0.23), infectious (OR 0.73), vascular (OR 0.34), and wound (OR 0.53) complications, as well as in-hospital mortality (OR 0.61, all $p \leq 0.003$) were lower at NCI-designated CC compared to non-teaching centres. Moreover, the above held true when comparing NCI CC to other residency teaching hospitals, thereby somewhat validating the premier nature of CC.

The only previous study addressing this specific question compared surgical mortality and survival rates of a large Medicare population undergoing different types of cancer surgery, including RC.[11] Although a trend towards lower adjusted surgical mortality at NCI CC was seen for RC, this was not significant. This is likely explained by the fact that the study was based on a historical cohort (1994–1999) compared to our more contemporary cohort (2006–2010), reflecting the benefits of regionalization of RC as well as general improvements in surgical technique and postoperative care over the past decade. That said, control groups in both studies differed in the numbers of RC performed.

There are numerous potential reasons as to why patients treated at NCI-designated CC are more likely to experience favourable outcomes. It may be due to superior surgical care at these centres, or more careful patient selection for RC given the highly-developed infrastructure at a CC, with regular multidisciplinary tumour boards and ease of access to preoperative consultations and pre- and postoperative imaging tests.[10,11] The benefits gained by greater experience in managing higher-risk patients with advanced bladder cancer may also be a contributory factor.[10,11] Additionally, multispecialty-performed surgery, if needed, might be more easily planned and conducted at CC.

Previous studies have investigated the impact of residency versus accredited fellowship teaching status, and non-academic versus academic institutions on outcomes after urooncologic and other cancer surgery.[20-22] These have broadly supported the hypothesis that patients treated at the latter centres experience more favourable outcomes. As the proportion of physicians with fellowship training at academic institutions is putatively higher at NCI-designated CC, this may facilitate the achievement of superior perioperative outcomes at these centres.

Yet, although we did adjust for all confounders available in the data source, our results may be subject to selection bias. Healthier and more mobile patients, who are at a lower risk of surgical morbidity and mortality, might be more likely to travel to a centre of excellence or high repute, thereby providing an inherent advantage to CC.[11] Nevertheless, selection bias is unlikely to entirely account for our findings.

Interestingly, after adjusting for confounders, hospital volume was not generally related with improved outcomes, exerting marginal impact compared to hospital teaching/CC status (1%–2%). This may shed further light on the volume-outcome relationship for patients undergoing RC, since it raises the possibility that the overall nature of the service provided by a CC, and not merely the number of procedures performed, is responsible for the outcome benefits seen.

Our study has several limitations, aside from the inherent drawbacks of conducting an observational, retrospective analysis. Despite accounting for major differences between patient groups, we were unable to control for other variables, including patient, disease, surgeon, treatment (extent of node dissection/utilization of perioperative chemotherapy) and socioeconomic characteristics. For instance, those with more aggressive disease may be referred to particular types of institution, while socioeconomic factors affect access to care. Additionally, although we did use the latest updated list of designated CC, as per the NCI website,[9] NCI accreditation status could have changed over the years of study, while our sample was only able to capture less than 40% of all NCI-designated CC. Further, restriction of our analyses to the most contemporary years of the NIS minimizes this effect. Finally, the NIS only supplies in-hospital data and since length of stay differs from patient to patient, we were unable to generate analyses for standardized lengths of follow-up.

Conclusion

Our results indicate that a more favourable postoperative complication profile and lower in-hospital mortality after RC should be expected at teaching and CC-teaching institutions. Specifically, the risk of unfavourable outcomes after RC was lower at NCI-designated CC compared to other teaching institutions, after adjustment for potential confounders. This emphasizes the quality of care provided at accredited CC for patients undergoing RC for bladder cancer.

Competing interests: The authors declare no competing financial or personal interests.

This paper has been peer-reviewed.

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Continued from page 163

NCCN guidelines from the general consensus of the other guidelines rather than a deviation of the Canadian guidelines.

These Canadian guidelines take a weak stance on the European Organisation for the Research on the Treatment of Cancer (EORTC) prospective randomized trial demonstrating an overall survival advantage for radical nephrectomy over partial nephrectomy in 541 patients with a renal mass ≤5 cm in diameter.[10] The overall survival difference (81.1% vs. 75.7% at 5 years; hazard ratio 1.50 with 95% confidence interval 1.03–2.16) was significant on an intention-to-treat (ITT) analysis, but not when restricted to patients with pathologically confirmed renal cell carcinoma. Since the histologic diagnosis of renal cell carcinoma is not generally made until after partial nephrectomy because pre-operative biopsy has not been widely adopted, the ITT analysis is the clinically more relevant one. It appears easy to disregard this level one evidence without critical analysis of the results. While we are reluctant to give up the purported advantage of preserving renal function despite the results of this EORTC trial, should they not at least dissuade the urologist from performing technically very challenging partial nephrectomies? Interestingly, the NCCN guidelines do not even refer to this paper,[2] and the EAU guidelines completely disregard any controversy with the simple statement: "In a prematurely closed randomized study of RCC < 5 cm, comparing PN and RN, there was no difference in OS in the targeted population."[3] At least the controversy has been acknowledged in the Canadian guidelines.

Competing interests: Dr. Black is currently a member of the advisory boards for AbbVie and Astellas. He is also a member of the Speaker's bureau for AbbVie. He is participating in clinical trials with Janseen, Ferring, Astellas, and Amgen and is receiving consulting fees from Cubist. He is also part of the clinical trial design team for Roche/Genentech.

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