Is there a measurable association of epidural use at cystectomy and postoperative outcomes? A population-based study

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Abstract

Introduction: Thoracic epidural analgesia (TEA) is commonly used to manage postoperative pain and facilitate early mobilization after major intra-abdominal surgery. Evidence also suggests that regional anesthesia/analgesia may be associated with improved survival after cancer surgery. Here, we describe factors associated with TEA at the time of radical cystectomy (RC) for bladder cancer and its association with both short- and long-term outcomes in routine clinical practice.
Methods: All patients undergoing RC in the province of Ontario between 2004 and 2008 were identified using the Ontario Cancer Registry (OCR). Modified Poisson regression was used to describe factors associated with epidural use, while a Cox proportional hazards model describes associations between survival and TEA use.
Results: Over the five-year study period, 1628 patients were identified as receiving RC, 54% (n=887) of whom received TEA. Greater anesthesiologist volume (lowest volume providers relative risk [RR] 0.85, 95% confidence interval [CI] 0.75–0.96) and male sex (female sex RR 0.89, 95% CI 0.79–0.99) were independently associated with greater use of TEA. TEA use was not associated with improved short-term outcomes. In multivariable analysis, TEA was not associated with cancer-specific survival (hazard ratio [HR] 1.02, 95% CI 0.87–1.19; p=0.804) or overall survival (HR 0.91, 95% CI 0.80–1.03; p=0.136).
Conclusions: In routine clinical practice, 54% of RC patients received TEA and its use was associated with anesthesiologist provider volume. After controlling for patient, disease and provider variables, we were unable to demonstrate any effect on either short- or long-term outcomes at the time of RC.

Introduction

Radical cystectomy (RC) with urinary diversion for muscle-invasive bladder cancer (MIBC) has significant morbidity, particularly for the elderly.[1,2] Major complication rates approach 30%, even in centres of excellence.[3-5] However, RC — accompanied with an optimal pelvic lymph node dissection — performed in combination with perioperative chemotherapy remains the gold standard for MIBC management. Continuing efforts to reduce the morbidity of this major operation are paramount.

The role of anesthesia and analgesia in the perioperative care of MIBC patients would seem to be vital to favourable outcomes. Long considered the standard of care for major abdominal surgery,[6,7] intravenous patient-controlled analgesia (IV PCA) has been replaced by neuraxial analgesia, either thoracic epidural analgesia (TEA) or thoracic patient-controlled epidural analgesia (PCEA). In various surgical populations, studies have shown epidural analgesia as superior in terms of improving early outcomes, including improved perioperative pain control, decreased early complications, and decreased time to return of bowel function.[8,9] Recommendations for the Enhanced Recovery After Surgery (ERAS) programs therefore include TEA for large open abdominal procedures[10,11] and TEA is has been recommended as the postoperative analgesic technique of choice for MIBC patients undergoing RC.[12]

In addition to an improvement of early outcomes, there is a body of literature to suggest that perioperative regional analgesia may attenuate cancer recurrence. Early retrospective studies in breast, colon, and prostate cancer populations[13-15] reported improved recurrence- and metastasis-free survival in patients who received neuraxial analgesia. Despite these encouraging early findings and a plethora of basic science evidence to support the biologic plausibility,[16-18] more recent analyses have been less encouraging.[19,20] This phenomenon has not been specifically investigated in the RC population.

Population-based studies are able to provide further insight into outcomes in routine clinical practice. We undertook this contemporary, population-based study to describe the use of TEA at the time of RC in routine clinical practice and evaluate its association with short- and long-term outcomes.

Methods

We retrospectively examined factors associated with the use of TEA and its impact on outcomes in a population-based

cohort study of patients undergoing RC in the province of Ontario between 2004 and 2008. Patients who underwent RC were identified using the Ontario Cancer Registry (OCR). The OCR is a population-based registry capturing demographic and diagnostic data on at least 98% of incident cancer cases in the province of Ontario.[21] The OCR provided the following: International Classification of Disease site and histology codes, date of diagnosis, place of residence at diagnosis, vital status, date, and cause of death.

This registry data was then linked to a collection of administrative health databases, as previously described,[22] using unique encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences (ICES). Information about hospital care, physician providers, and surgical interventions were provided from the Canadian Institute for Health Information (CIHI). It is known that participation in the collection of separation records throughout the province of Ontario is consistent and complete.[23] Although information on pathological stage is missing in these datasets, a team of trained data abstractors reviewed pathology reports obtained from the OCR and entered variables according to a predefined study protocol.

Comorbidity was classified using the Charlson index[24] adapted by Deyo and colleagues.[25] Previously described methods of determining socioeconomic status were used.[22] Chemotherapy within 16 weeks after surgery was classified as adjuvant chemotherapy. Given provider volume's well-established measure of overall surgical quality,[26] we explored its association with epidural use. We also evaluated the association between anesthesiologist volumes and epidural use. Determination of surgeon and hospital volume was determined as previously described;[26] we used a similar approach to define anesthesiologist volume. As annual RC volume among anesthesiologists in Ontario was very low, we applied an a priori composite value that included both RC and similarly complex major colorectal procedures.

The study's primary objectives were to: 1) describe use of epidural analgesia in routine practice; 2) evaluate factors associated with practice; and 3) describe the association between epidural analgesia and patient outcome. Descriptive statistics were used to describe TEA use in this population. To examine factors associated with TEA use, a modified Poisson regression model was used. Logistic regression was used to examine factors associated with 90-day mortality. The Cox proportional hazards model was used to evaluate the association between patient-, disease- and treatment-related factors (including TEA use) with cancer-specific (CSS) and overall (OS) survival. Results were regarded as statistically significant with a p value of <0.05. SAS version 9.3 (SAS Institute, Cary, NC, U.S.) was used for all analyses. This study was approved by the Research Ethics Board at Queen's University, Kingston, ON, and the institutional review board at Sunnybrook Health Sciences Centre, Toronto, ON, Canada.

Results

During the study period of 2004–2008, 1628 patients had RC for bladder cancer in the province of Ontario. Table 1 describes the cohort based on whether or not they received TEA. Of the total cohort, 887 (54%) received a TEA, with several disease, patient, and provider characteristics associated with its use. In multivariable analysis, factors associated with TEA use included gender (p=0.029), nodal status (p=0.002), and anesthesiologist volume ($p \leq 0.001$) (Table 2). Women were less likely to receive an epidural than men (relative risk [RR] 0.89, 95% confidence interval [CI] 0.79–0.99). Status of a pelvic lymph node dissection, as determined by the surgical pathology report, was also associated with TEA use (RR 0.78, 95% CI 0.67–0.91). Finally, higher anesthesiologist volume was significantly associated with increased TEA use (lowest volume providers RR 0.85, 95% CI 0.75–0.96).

In a univariate analysis of outcomes (Table 3), we observed no difference in length of stay (LOS) between those who received a TEA and those who did not. There was no difference in either 30-day (p=0.161) or 90-day readmission rates (p=0.893) between the groups, nor was there a difference in 30-day mortality (p=0.438). There was a trend towards increased 90-day postoperative mortality in the non-epidural group (9%) compared to those with an epidural (7%), however, this did not reach significance (p=0.104). TEA was not associated with 90-day postoperative mortality in multivariable analysis (Table 4).

Although in univariate analysis, a trend towards improved five-year OS was observed in those who received an epidural vs. those who did not (41% vs. 37% respectively; p=0.127), multivariable analysis did not show a significant association between epidural and OS (Table 5). Furthermore, there was no difference between the groups in five-year CSS in univariate (p=0.937) or multivariable analyses (hazard ratio [HR] 1.02, 95% CI 0.87–1.19). Factors associated with long-term survival include age, comorbidity, extent of disease, surgeon volume, and use of adjuvant chemotherapy (Table 5).

Discussion

We report on neuraxial analgesia use among patients with bladder cancer treated with RC in routine clinical practice in the province of Ontario. In this retrospective, population-based study, we found that from 2004-2008 just over half of RC patients received TEA and higher-volume anesthesiologists were more likely to use TEA as a pain management strategy. TEA was also more commonly used in men than women. We found no association between TEA use and early or late patient outcomes in this population-based cohort.

Perhaps not unexpectedly, higher-volume anesthesia providers were more likely to use TEA. This supports evi-

Table 1. Characteristics of 1628 patients with bladder cancer treated with cystectomy in Ontario from 2004–2008

	All cases	Epidural		p value
	n=1628	Yes n=887	No n=741	
Age				0.495
20–59	239 (15%)	123 (14%)	116 (16%)	
60–69	386 (24%)	208 (23%)	178 (24%)	
70–79	646 (40%)	366 (41%)	280 (38%)	
80+	357 (22%)	190 (21%)	167 (23%)	
Patient-related				
Sex				0.005
Male	1,237 (76%)	698 (79%)	539 (73%)	
Female	391 (24%)	189 (21%)	202 (27%)	
Socioeconomic status*				0.534
Q1	289 (18%)	159 (18%)	130 (18%)	
Q2	360 (22%)	206 (23%)	154 (21%)	
Q3	396 (24%)	208 (23%)	188 (25%)	
Q4	314 (19%)	176 (20%)	138 (19%)	
Q5	269 (17%)	138 (16%)	131 (18%)	
Charlson comorbidity score				0.370
0	1,161 (71%)	623 (70%)	538 (73%)	
1	260 (16%)	152 (17%)	108 (15%)	
2+	207 (13%)	112 (13%)	95 (13%)	
Disease-related				
T stage				0.295
<T2	359 (22%)	194 (22%)	165 (22%)	
T2	320 (20%)	183 (21%)	137 (18%)	
T3	584 (36%)	302 (34%)	282 (38%)	
T4	365 (22%)	208 (23%)	157 (21%)	
N stage				0.003
N negative	952 (58%)	530 (60%)	422 (57%)	
N positive	455 (28%)	260 (29%)	195 (26%)	
NX	221 (14%)	97 (11%)	124 (17%)	
Treatment-related				
Adjuvant chemotherapy				0.458
Yes	282 (17%)	148 (17%)	134 (18%)	
No	1,346 (83%)	739 (83%)	607 (82%)	
Surgeon volume[&]				<0.001
Q1 (lowest)	276 (17%)	131 (15%)	145 (20%)	
Q2	387 (24%)	188 (21%)	199 (27%)	
Q3	434 (27%)	239 (27%)	195 (26%)	
Q4	528 (32%)	327 (37%)	201 (27%)	
Hospital volume[&]				<0.001
Q1 (lowest)	249 (15%)	127 (14%)	122 (16%)	
Q2	503 (31%)	230 (26%)	273 (37%)	
Q3	311 (19%)	197 (22%)	114 (15%)	
Q4	565 (35%)	333 (38%)	232 (31%)	
Anesthesiologist volume[#]				<0.001
Q1 (lowest)	403 (25%)	195 (22%)	208 (28%)	
Q2	366 (22%)	207 (23%)	159 (21%)	
Q3	362 (22%)	226 (25%)	136 (18%)	
Q4	457 (28%)	258 (29%)	199 (27%)	

*Q1 represents the communities where the poorest 20% of the Ontario population resided; [&]hospital and surgeon volume were classified based on the mean number of cystectomies done over a five-year study period (surgeon volume data were not available for <6 patients); [#]anesthesiologist volume was classified based on the mean number of cystectomy and colorectal resections over a five-year study period (volume data were not available for 40 patients).

dence that higher-volume centres are more adherent to care pathways and quality-of-care processes,[27] which are increasingly including use of regional — and specifically for intra-abdominal procedures — neuraxial analgesia. We felt it reasonable to use a composite value for anesthesiologist volume given the small RC volume of anesthesiologists in routine clinical practice. The finding that TEA use was less frequent in women is of interest and potentially highlights perceived inequities in management and outcomes of women with bladder cancer.[28]

Despite its recognized importance in early outcomes in related surgical populations,[8,9] there is a paucity of evidence supporting TEA-associated improvement of patient outcomes in RC. Evidence often quoted supporting use of TEA in reduction of short-term complications in RC come from the ERAS literature.[29] The ERAS studies are investigating several perioperative interventions simultaneously, so to attribute improvements in short-term complications to one aspect of the intervention — TEA — is not likely appropriate. Our best evidence then, must be extrapolated from mixed surgical populations.

Our findings are consistent with previous studies in the RC population showing no benefit to TEA in early outcomes. In their single-centre, retrospective analysis of 131 RC patients, Toren et al[30] noted no difference in early outcomes, including pain scores and LOS, between those who received IV PCA and PCEA. Gomez et al[31] similarly showed no differences in complications or survival between RC patients receiving IV PCA and TEA in their retrospective cohort of 274 patients. In a more recent series of 302 patients undergoing RC, aside from modest decreased amounts of total opioid requirement, Winer et al[32] observed no difference in early outcomes— including LOS, return of bowel function, and early complications — between those who received

Table 2. Variables associated with epidural among 1628* patients with bladder cancer treated with cystectomy in Ontario from 2004–008.

Characteristic	Epidural use (%)	Multivariable analysis	
		RR (95% CI)	p value
Patient-related			
Age			0.405
20–59 (n=239)	51%	Ref	
60–69 (n=386)	54%	1.06 (0.91–1.24)	
70–79 (n=646)	57%	1.12 (0.97–1.29)	
80+ (n=357)	53%	1.08 (0.92-1.26)	
Sex			0.029
Male (n=1237)	56%	Ref	
Female (n=391)	48%	0.89 (0.79–0.99)	
Charlson comorbidity score			0.547
0 (n=1161)	54%	Ref	
1 (n=260)	58%	1.07 (0.95–1.19)	
2+ (n=207)	54%	1.00 (0.88–1.14)	
Disease-related			
T stage			0.291
<T2 (n=359)	54%	Ref	
T2 (n=320)	57%	1.07 (0.94–1.22)	
T3 (n=584)	52%	0.95 (0.84–1.08)	
T4 (n=365)	57%	1.01 (0.88–1.16)	
N stage			0.002
N negative (n=952)	56%	Ref	
N positive (n=455)	57%	1.03 (0.93–1.14)	
NX (n=221)	44%	0.78 (0.67–0.91)	
Treatment-related			
Anesthesiologist volume[&]			<0.001
Q1 (n=403)	48%	0.85 (0.75–0.96)	
Q2 (n=366)	57%	1.00 (0.89–1.13)	
Q3 (n=362)	62%	1.12 (1.00–1.25)	
Q4 (n=457)	56%	Ref	

*Patients with NACT and/or preoperative RT (n=93) are removed from the analysis since stage of disease is not reliable; [&]anesthesiologist volume was classified based on the mean number of cystectomy and colorectal resections over a five-year study period (volume data were not available for 40 patients). CI: confidence interval; NACT: neoadjuvant chemotherapy RR: relative risk; RT: radiotherapy.

Table 3. Outcomes of 1628 patients with bladder cancer treated with cystectomy in Ontario from 2004-2008

	Epidural		p value
	Yes n=887	No n=741	
Outcome			
Mean LOS (days)	14	14	0.406
Median LOS (days)	10	10	0.651
30-day mortality	23 (3%)	24 (3%)	0.438
90-day mortality	63 (7%)	69 (9%)	0.104
30-day re-admission[#]	193 (22%)	183 (25%)	0.161
90-day re-admission[#]	306 (34%)	258 (35%)	0.893
5-year OS (95% CI)	41% (38–45%)	37% (34–41%)	0.127
5-year CSS (95% CI)*	52% (48–55%)	52% (48–56%)	0.937

[#]Numerator for hospital re-admission rate included cases discharged and re-admitted and those who died in hospital before discharge and cases never discharged at 30 and 90 days (denominator included all cases); *deaths within 90 days were not counted as CSS events. CSS: cancer-specific survival; LOS: length of stay; OS: overall survival.

epidural analgesia and those who received other perioperative pain management strategies.

Although early retrospective studies[13-15] suggesting attenuation of cancer recurrence for patients undergoing surgery receiving epidural analgesia were encouraging, the studies were all retrospective in nature and consisted of small sample sizes (n=129–655). Subsequent literature has been less promising and several recent studies have called into question the initial optimism regarding improved cancer outcomes.[19,20] Weingarten et al[33] recently published on their series of 129 patients undergoing RC with combined general anesthetic (GA) and TEA and compared to age-matched controls undergoing oncologic surgery with only GA. In this analysis, they found no association between TEA and cancer recurrence, OS, or CSS. To our knowledge, this small study is the only report that evaluates the association of long-term outcomes in bladder cancer patients to modes of analgesia used.

In our large population-based study, we found no strong evidence of association between TEA and long-term survival among patients treated with RC for bladder cancer. This observation is consistent with a recent, large, population-based study in gastric cancer using the Surveillance, Epidemiology, and End Results (SEER) Program/Medicare database.[19] Cummings et al showed no association between epidural use and cancer recurrence or survival in 2745 patients undergoing resection of gastric cancer.[19] Furthermore, Sun and colleagues[20] recently published a meta-analysis of 18 studies evaluating the impact of epidural anesthesia on cancer outcomes. Although no bladder cancer studies were included in the meta-analysis, they found that although epidurals were associated with improved OS (HR 0.84, 95% CI 0.75–0.94), it was not associated with reduced cancer recurrence (HR 0.91, 95% CI 0.70–1.18). It should be noted that all of the cited studies failed to control for provider volume, an important quality-of-care indicator, which we were able to include in our analysis. It is, therefore, plausible that the observed association between neuraxial analgesia and OS in previous reports reflect residual confounding rather than a true biologic effect.

Our study is limited by the fact that epidural use was only classified as yes/no using physician billing records and we do not have additional information regarding the extent and effectiveness of perioperative pain control. We were, therefore, unable to stratify our patients based on degree of epidural success. Furthermore, epidural 'failure' can be multifactorial and significant, yet difficult to determine retro-

Table 4. Variables associated with 90-day postoperative mortality among 1628* bladder cancer patients treated with cystectomy in Ontario from 2004–2008.

Characteristic	90-day mortality		
	90-day mortality	Multivariable analysis	
		OR (95% CI)	p value
Patient-related			<0.001
Age			
20–59 (n=239)	3%	Ref	
60–69 (n=386)	6%	2.08 (0.90–4.81)	
70–79 (n=646)	8%	2.44 (1.12–5.33)	
80+ (n=357)	14%	4.55 (2.06–10.08)	
Sex			0.962
Male (n=1237)	8%	Ref	
Female (n=391)	8%	0.99 (0.64–1.53)	
Charlson comorbidity score			0.242
0 (n=1161)	7%	Ref	
1 (n=260)	10%	1.28 (0.79–2.09)	
2+ (n=207)	13%	1.48 (0.90–2.42)	
Disease-related			
T stage			<0.001
<T2 (n=359)	4%	Ref	
T2 (n=320)	5%	1.24 (0.57–2.69)	
T3 (n=584)	8%	1.82 (0.95–3.50)	
T4 (n=365)	16%	3.86 (2.00–7.47)	
N stage			0.008
N negative (n=952)	5%	Ref	
N positive (n=455)	12%	1.91 (1.24–2.95)	
NX (n=221)	12%	1.75 (1.05–2.94)	
Treatment-related			
Surgeon volume[&]			0.042
Q1 (n=276)	11%	1.73 (0.98–3.05)	
Q2 (n=387)	7%	1.15 (0.66–2.02)	
Q3 (n=434)	11%	1.90 (1.15–3.15)	
Q4 (n=528)	5%	Ref	
Epidural			0.115
Yes (n=887)	7%	0.74 (0.51–1.08)	
No (n=741)	9%	Ref	

*Patients with NACT and/or preoperative RT (n=93) are removed from the analysis since stage of disease is not reliable; [&]surgeon volume was classified based on the mean number of cystectomies done over a five-year study period (surgeon volume data were not available for <6 patients). CI: confidence interval; NACT: neoadjuvant chemotherapy; OR: odds ratio; RT: radiotherapy.

spectively. We must assume that some patients would have received an epidural that did not function optimally or were misplaced entirely and were, therefore, transitioned to IV PCA; however, there is no way to capture this information from a database. We used related colorectal procedures in their total volume determination, as these procedures burden patients with similar amounts of perioperative pain and complications and similar skill-sets in managing these patients perioperatively are required. Finally, our study is further limited through unmeasured confounding variables present in any retrospective observational study. Despite this, our study includes all patients with bladder cancer treated with curative intent RC in the province of Ontario, minimizing the referral and selection biases of single-centre series or institution-based observational studies.

Conclusion

In this population-based cohort of cystectomy patients treated between 2004 and 2008, 56% (n=887) received TEA. High-volume providers used TEA more commonly. Our data was unable to demonstrate any association between epidural use and short-term outcomes or long-term survival among patients treated with RC in routine clinical practice.

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

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References

1. Leveridge MJ, Siemens DR, Mackillop WJ, et al. Radical cystectomy and adjuvant chemotherapy for bladder cancer in the elderly: A population-based study. *Urology* 2015;85:791-8. http://dx.doi.org/10.1016/j.urology.2014.12.027
2. Froehner M, Brausi MA, Herr HW, et al. Complications following radical cystectomy for bladder cancer in the elderly. *Eur Urol* 2009;56:443-54. http://dx.doi.org/10.1016/j.eururo.2009.05.008
3. Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: Long-term results in 1054 patients. *J Clin Oncol* 2001;19:666-75.
4. Novotny V, Hakenberg OW, Wiessner D, et al. Perioperative complications of radical cystectomy in a contemporary series. *Eur Urol* 2007;51:397-402. http://dx.doi.org/10.1016/j.eururo.2006.06.014
5. Stimson CJ, Chang SS, Barocas DA, et al. Early and late perioperative outcomes following radical cystectomy: 90-day readmissions, morbidity, and mortality in a contemporary series. *J Urol* 2010;184:1296-1300. http://dx.doi.org/10.1016/j.juro.2010.06.007
6. Hudcova J, McNicol E, Quah C, et al. Patient-controlled opioid analgesia vs. conventional opioid analgesia for postoperative pain. *Cochrane Database Syst Rev* 2006;Cd003348. http://dx.doi.org/10.1002/14651858.cd003348.pub2
7. Walder B, Schafer M, Henzi I, et al. Efficacy and safety of patient-controlled opioid analgesia for acute postoperative pain. A quantitative systematic review. *Acta Anaesthesiol Scand* 2001;45:795-804. http://dx.doi.org/10.1034/j.1399-6576.2001.045007795.x

Table 5. Factors associated with overall survival and cancer specific survival among 1628† patients with bladder cancer treated with cystectomy in Ontario from 2004–2008.

Characteristic	CSS			OS		
	5-year CSS	Multivariable analysis		5-year OS	Multivariable analysis	
		HR (95% CI)	p value		HR (95% CI)	p value
Patient-related						
Age			0.210			<0.001
20–59 (n=239)	58%	Ref		53%	Ref	
60–69 (n=386)	51%	1.22 (0.93–1.60)		45%	1.31 (1.04–1.65)	
70–79 (n=646)	48%	1.29 (1.00–1.65)		39%	1.46 (1.18–1.80)	
80+ (n=357)	40%	1.32 (1.00–1.75)		26%	1.78 (1.41–2.24)	
Sex			0.189			0.223
Male (n=1237)	50%	Ref		40%	Ref	
Female (n=391)	45%	1.13 (0.94–1.35)		37%	1.09 (0.95–1.27)	
Charlson comorbidity score			0.005			<0.001
0 (n=1161)	51%	Ref		43%	Ref	
1 (n=260)	49%	0.96 (0.77–1.19)		39%	1.01 (0.85–1.20)	
2+ (n=207)	31%	1.43 (1.14–1.79)		21%	1.56 (1.31–1.86)	
Disease-related						
T stage			<0.001			<0.001
<T2 (n=359)	78%	Ref		67%	Ref	
T2 (n=320)	61%	1.89 (1.36–2.61)		55%	1.54 (1.21–1.95)	
T3 (n=584)	38%	3.53 (2.65–4.71)		29%	2.65 (2.15–3.26)	
T4 (n=365)	22%	5.62 (4.15–7.61)		15%	4.30 (3.44–5.38)	
N stage			<0.001			<0.001
N negative (n=952)	63%	Ref		53%	Ref	
N positive (n=455)	26%	2.35 (1.93–2.86)		20%	2.24 (1.91–2.63)	
NX (n=221)	32%	1.95 (1.56–2.44)		24%	1.74 (1.45–2.09)	
Treatment-related						
Surgeon volume&			0.002			<0.001
Q1 (n=276)	43%	1.27 (1.00–1.61)		36%	1.25 (1.03–1.52)	
Q2 (n=387)	43%	1.51 (1.22–1.87)		34%	1.44 (1.21–1.71)	
Q3 (n=434)	43%	1.31 (1.06–1.63)		35%	1.38 (1.17–1.64)	
Q4 (n=528)	60%	Ref		50%	Ref	
Adjuvant chemotherapy			0.004			<0.001
Yes (n=282)	42%	0.72 (0.58–0.90)		35%	0.65 (0.54–0.79)	
No (n=1346)	50%	Ref		41%	Ref	
Epidural			0.804			0.136
Yes (n=887)	49%	1.02 (0.87–1.19)		41%	0.91 (0.80–1.03)	
No (n=741)	48%	Ref		37%	Ref	

†Patients with neoadjuvant chemotherapy and/or preoperative radiotherapy (n=93) are removed from the analysis since stage of disease is not reliable; &surgeon volume was classified based on the mean number of cystectomies done over a five-year study period (surgeon volume data were not available for <6 patients). CSS: cancer-specific survival: HR: hazard ratio; OS: overall survival.

8. Carli F, Trudel JL, Belliveau P. The effect of intraoperative thoracic epidural anesthesia and postoperative analgesia on bowel function after colorectal surgery: A prospective, randomized trial. *Dis Colon Rectum* 2001;44:1083-9. http://dx.doi.org/10.1007/BF02234626
9. Rigg JR, Jamrozik K, Myles PS, et al. Epidural anaesthesia and analgesia and outcome of major surgery: A randomized trial. *Lancet* 2002;359:1276-82. http://dx.doi.org/10.1016/S0140-6736(02)08266-1
10. Melnyk M, Casey RG, Black P, et al. Enhanced recovery after surgery (ERAS) protocols: Time to change practice? *Can Urol Assoc J* 2011;5:342-8. http://dx.doi.org/10.5489/cuaj.11002
11. Cerantola Y, Valerio M, Persson B, et al. Guidelines for perioperative care after radical cystectomy for bladder cancer: Enhanced Recovery After Surgery (ERAS) society recommendations. *Clin Nutr* 2013;32:879-87. http://dx.doi.org/10.1016/j.clnu.2013.09.014
12. Kassouf W, Aprikian A, Black P, et al. Recommendations for the improvement of bladder cancer quality of care in Canada: A consensus document reviewed and endorsed by Bladder Cancer Canada (BCC), Canadian Urologic Oncology Group (CUOG), and Canadian Urological Association (CUA), December 2015. *Can Urol Assoc J* 2016;10:E46-80. http://dx.doi.org/10.5489/cuaj.3583
13. Exadaktylos AK, Buggy DJ, Moriarty DC, et al. Can anesthetic technique for primary breast cancer surgery affect recurrence or metastasis? *Anesthesiology* 2006;105:660-4. http://dx.doi.org/10.1097/00000542-200610000-00008
14. Biki B, Mascha E, Moriarty DC, et al. Anesthetic technique for radical prostatectomy surgery affects cancer recurrence: A retrospective analysis. *Anesthesiology* 2008;109:180-7. http://dx.doi.org/10.1097/ALN.0b013e31817f5b73
15. Christopherson R, James KE, Tableman M, et al. Long-term survival after colon cancer surgery: A variation associated with choice of anesthesia. *Anesth Analg* 2008;107:325-32. http://dx.doi.org/10.1213/ane.0b013e3181770f55
16. Camara O, Kavallaris A, Noschel H, et al. Seeding of epithelial cells into circulation during surgery for breast cancer: The fate of malignant and benign mobilized cells. *World J Surg Oncol* 2006;4:67. http://dx.doi.org/10.1186/1477-7819-4-67
17. Dunn GP, Old LJ, Schreiber RD. The immunobiology of cancer immunosurveillance and immunoediting. *Immunity* 2004;21:137-48. http://dx.doi.org/10.1016/j.immuni.2004.07.017

18. O'Riain SC, Buggy DJ, Kerin MJ, et al. Inhibition of the stress response to breast cancer surgery by regional anesthesia and analgesia does not affect vascular endothelial growth factor and prostaglandin E2. *Anesth Analg* 2005;100:244-9. http://dx.doi.org/10.1213/01.ANE.0000143336.37946.7D
19. Cummings KC, Patel M, Than Htoo P, et al. A comparison of the effects of epidural analgesia vs. traditional pain management on outcomes after gastric cancer resection: A population-based study. *Reg Anesth Pain Med* 2014;39:200-7. http://dx.doi.org/10.1097/AAP.0000000000000079
20. Sun Y, Li T, Gan TJ. The effects of perioperative regional anesthesia and analgesia on cancer recurrence and survival after oncology surgery: A systematic review and meta-analysis. *Reg Anesth Pain Med* 2015;40:1-10. http://dx.doi.org/10.1097/AAP.0000000000000273
21. Robles SC, Marrett LD, Clarke EA, et al. An application of capture-recapture methods to the estimation of completeness of cancer registration. *J Clin Epidemiol* 1988;41:495-501. http://dx.doi.org/10.1016/0895-4356(88)90052-2
22. Booth CM, Li G, Zhang-Salomons, J, et al. The impact of socioeconomic status on stage of cancer at diagnosis and survival. *Cancer* 2010;116:4160-7. http://dx.doi.org/10.1002/cncr.25427
23. Williams J, Young W. A summary of studies on the quality of healthcare administrative databases in Canada. In: Goel V, Williams JI, Anderson GM, Blackstien-Hirsch P, Fooks C, Naylor CD (eds). *Patterns of healthcare in Ontario: The ICES Practice Atlas.* Ottawa: Canadian Medical Association, 1996:339-45.
24. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis* 1987;40:373-83. http://dx.doi.org/10.1016/0021-9681(87)90171-8
25. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992;45:613-9. http://dx.doi.org/10.1016/0895-4356(92)90133-8
26. Booth, CM, Siemens DR. Delivering high-quality care to patients with muscle-invasive bladder cancer: Insights from routine practice in Ontario. *Can Urol Assoc J* 2014;8:297-9. http://dx.doi.org/10.5489/cuaj.2339
27. Siemens DR, Mackillop WJ, Peng Y, et al. Processes of care and the impact of surgical volumes on cancer-specific survival: A population-based study in bladder cancer. *Urology* 2014;84:1049-57. http://dx.doi.org/10.1016/j.urology.2014.06.070
28. Patafio FM, Siemens DR, Wei X, et al. Is there a gender effect in bladder cancer? A population-based study of practice outcomes. *Can Urol Assoc J* 2015;9:269-74. http://dx.doi.org/10.5489/cuaj.2927
29. Maffezzini M, Campodonico F, Capponi G, et al. Fast-track surgery and technical nuances to reduce complications after radical cystectomy and intestinal urinary diversion with the modified Indiana pouch. *Surg Oncol* 2012;21:191-5. http://dx.doi.org/10.1016/j.suronc.2012.02.001
30. Toren P, Ladak S, McCluskey S, et al. Comparison of epidural and intravenous patient-controlled analgesia in patients undergoing radical cystectomy. *Can J Urol* 2009;16:4716-20.
31. Gomez AMA, Clarke C, Smith D, et al. Is postoperative epidural analgesia better than patient-controlled analgesia for radical cystectomy? *J Clin Urol* 2014;7:190-7. http://dx.doi.org/10.1177/2051415813500954
32. Winer AG, Sfakianos JP, Puttanniah VG, et al. Comparison of perioperative outcomes for epidural vs. intravenous patient-controlled analgesia after radical cystectomy. *Reg Anesth Pain Med* 2015;40:239-44. http://dx.doi.org/10.1097/AAP.0000000000000219
33. Weingarten TN, Taccolini AM, Ahle ST, et al. Perioperative management and oncological outcomes following radical cystectomy for bladder cancer: A matched retrospective cohort study. *Can J Anesth* 2016;63:584-95. http://dx.doi.org/10.1007/s12630-016-0599-9

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