Short-term perioperative outcomes of patients treated with radical cystectomy for bladder cancer included in the National Surgical Quality Improvement Program (NSQIP) database

Giorgio Gandaglia, MD;[†] Briony Varda[*§] Akshay Sood,[¥] Daniel Pucheril, MD;[¥] Ramdev Konijeti, MD;[§] Jesse D. Sammon, MD;[¥] Shyam Sukumar, MD;[£] Mani Menon, MD;[¥] Maxine Sun, MD;[*] Steven L. Chang, MD;[§] Francesco Montorsi, MD;[†] Adam S. Kibel, MD;[§] Quoc-Dien Trinh, MD, FRCSC[§]*

Dr. Gandaglia and Dr. Varda equally contributed to the article.

[*]Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, QC; [†]Urological Research Institute, Vita-Salute San Raffaele University, San Raffaele Scientific Institute, Milan, Italy; [§]Division of Urologic Surgery and Center for Surgery and Public Health, Brigham and Women's Hospital / Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA; [¥]Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI; [£]Department of Urology, University of Minnesota, Minneapolis, MN

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Abstract

Introduction: We report the contemporary outcomes of radical cystectomy (RC) in patients with bladder cancer using a national, prospective perioperative database specifically developed to assess the quality of surgical care.

Methods: The National Surgical Quality Improvement Program (NSQIP) database was queried from 2006 to 2011 for RC. Data on postoperative complications, operative time, length of stay, blood transfusions, readmission, and mortality within 30 days from surgery were abstracted.

Results: Overall, 1094 patients undergoing RC were identified. Rates of overall complications, transfusions, prolonged length of hospitalization, readmission, and perioperative mortality were 31.1%, 34.4%, 25.9%, 20.2%, and 2.7%, respectively. Body mass index represented an independent predictor of overall complications on multivariate analysis ($p = 0.04$). Baseline comorbidity status was associated with increased odds of postoperative complications, prolonged operative time, transfusion, prolonged hospitalization, and perioperative mortality. In particular, patients with cardiovascular comorbidities were 2.4 times more likely to die within 30 days following cystectomy compared to their healthier counterparts ($p = 0.04$). Men had lower odds of prolonged operative time and blood transfusions ($p \leq 0.03$). Finally, the receipt of a continent urinary diversion was the only predictor of readmission ($p = 0.02$). Our results are limited by their retrospective nature and by the lack of adjustment for hospital and tumour volume.

Conclusions: Complications, transfusions, readmission, and perioperative mortality remain relatively common events in patients undergoing RC for bladder cancer. In an era where many advocate the need for prospective multi-institutional data collection as a means of improving quality of care, our study provides data on short-term outcomes after RC from a national quality improvement initiative.

Introduction

Open radical cystectomy (RC) currently represents the standard of care for the treatment of muscle-invasive bladder cancer.[1] Despite refinements in surgical technique and perioperative management, RC has been associated with a substantial risk of postoperative morbidity and mortality, where the rates of short-term complications and mortality.[1-7]

Identifying determinants of postoperative outcomes is crucial for individual risk-adjustment prior to RC. Several studies have reported predictors of complications, perioperative mortality, and readmission. However, these data are usually obtained from tertiary referral centres,[2,5-7] and therefore may not be generalizable to the American population. Recent population-based studies have reported nationwide outcomes for patients treated with RC for bladder cancer.[8-10] Despite their larger sample sizes, such studies are inherently limited by pre-selection bias, as well as errors in data collection, procedure classification and coding.[11,12]

To overcome these limitations, we sought to identify determinants of significant endpoints, such as postoperative complications, blood transfusions, prolonged operative time (pOT), prolonged length of stay (pLOS), perioperative mortality, and readmission using the American College of Surgeons (ACS) National Surgery Quality Improvement Program (NSQIP) database. The NSQIP was specifically developed to assess the quality of surgical care, and pro-

spectively collects perioperative data on preoperative risk factors, intraoperative variables, and 30-day postoperative mortality and morbidity for patients undergoing major surgical procedures in the United States. This database reliably detects complications and mortality in comparison to administrative databases or institutional series.[13-15]

Methods

Data source

The current study relied on the ACS NSQIP database. Per protocol, 252 Health Insurance Portability and Accountability Act (HIPAA)-compliant variables were collected for each encounter. These included patient demographic information, preoperative comorbidities risk factors, and laboratory results, intraoperative proceedings, as well as postoperative morbidity and mortality data for the subsequent 30-day period, where about 50% of complications occurred. Trained surgical clinical reviewers prospectively collected the data.

Study population

Overall, 1094 patients undergoing RC (Current Procedural Terminology [CPT] codes: 51590, 51595, and 51596) for bladder cancer (International Classification of Diseases 9th edition [ICD-9] codes: 188.x) between 2006 and 2011 were identified.

Covariates

For each patient, age at surgery, gender, body mass index (BMI), race, smoking status, alcohol consumption, preoperative comorbidity status, preoperative creatinine, albumin, hematocrit, receipt of neoadjuvant chemotherapy within 30 days before surgery, and type of urinary diversion were available. The Charlson comorbidity index (CCI) was calculated according to previously described methodology.[16,17] The glomerular filtration rate (GFR) was calculated using the Cockcroft-Gault equation. Multiple imputation was used to analyze missing data for the following covariates: BMI (n = 5), preoperative hematocrit (n = 31), and serum creatinine (n = 43).

Outcomes

Postoperative complications were classified under the following categories: cardiovascular (postoperative cardiac arrest, myocardial infarction, or cerebrovascular accident), pulmonary (pneumonia, need for postoperative reintubation, and need for ventilatory support >48 hours), thromboembolic (deep venous thrombosis and pulmonary embolism), septic (sepsis and septic shock), renal (acute renal failure and progressive renal insufficiency), urinary tract infections, and wound complications (superficial, deep, and organ space surgical site infections, and dehiscence), according to previously reported methodology.[18] Additional outcomes consisted of intraoperative transfusions, pOT, pLOS, readmission, and perioperative mortality. Postoperative transfusions were defined as any transfusion given from the time the patient left the operating room to 72 hours postoperatively. Prolonged operative time was defined as an operative time greater than the 75th percentile (≥422 minutes). Similarly, pLOS was defined as a LOS beyond the 75th percentile (≥11 days). Perioperative mortality was defined as death within 30 days after surgery. Data on the occurrence of 30-day readmission after surgery was only available for procedures performed on or after January 1, 2011.[19]

Statistical analyses

Descriptive statistics of categorical variables focused on frequencies and proportions. Means, medians and interquartile ranges were reported for continuously coded variables.

Multivariable logistic regression models tested the association between preoperative covariates and overall complications, pLOS, pOT, transfusion, and readmission rates. Covariates consisted of age at surgery, race, gender, BMI, smoking status, baseline comorbidities, GFR, albumin, hematocrit, neoadjuvant chemotherapy, and type of diversion. All statistical tests were performed using the R statistical package (version 3.0.2), with a two-sided significance level set at $p < 0.05$.

The Institutional Review Board exempted this study for review since it includes de-identified patients.

Results

Baseline characteristics

Overall, 1094 patients underwent RC at NSQIP participating hospitals between 2006 and 2011 (Table 1). The median age at surgery was 69 (interquartile range [IQR]: 61-76). Most patients were men (80.0%) and Caucasian (83.5%). Overall, 240 patients (21.9%) received continent diversion.

Short-term outcomes

Overall, 340 (31.1%) patients experienced at least 1 complication within 30 days. The most common postoperative complications were sepsis (14.2%), urinary tract infection (10.3%), and wound complications (10.3%). The median operative time was 331 minutes (IQR: 256-422). Overall, 425 (38.8%) patients received intraoperative blood transfusions. The median length of stay was 8 days (IQR: 7-11). Overall, 29 patients (2.7%) died within 30 days of surgery. Finally, 128 (20.2%) patients required readmission (Table 2).

Table 1. Baseline characteristics for 1094 patients treated with radical cystectomy between 2006 and 2011 (National Surgical Quality Improvement Program database)

	Total (n = 1094)
Age at diagnosis	
Median (IQR)	69 (61-76)
Gender, n (%)	
Female	219 (20.0)
Male	875 (80.0)
BMI, n (%)	
<25	340 (31.1)
25-30	406 (37.1)
>30	348 (31.8)
Race, n (%)	
White	914 (83.5)
Other	180 (16.5)
Smoking status, n (%)	
Non smoker	818 (74.8)
Current smoker	276 (25.2)
Alcohol, n (%)	
<2 drinks/day	1063 (97.2)
>2 drinks/day	31 (2.8)
Preoperative comorbidities, n (%)	
No comorbidities	337 (30.8)
Diabetes mellitus	204 (18.4)
Hypertension	650 (59.4)
Cardiovascular disease	134 (12.2)
Dyspnea	117 (10.7)
Other medical comorbidities	160 (14.6)
CCI	
0	772 (70.6)
1	278 (25.4)
≥2	44 (4.0)
Preoperative creatinine (mg/dL), n (%)	
<1.2	764 (69.8)
≥1.2	330 (30.2)
Preoperative albumin (g/dL, n (%)	
<3.0	75 (6.9)
≥3.0	1019 (93.1)
Preoperative hematocrit (%), n (%)	
<30	91 (8.3)
30-45	905 (82.7)
>45	98 (9.0)
Glomerular filtration rate (mL/min/1.73m2), n (%)	
≥60	763 (69.7)
30-59	288 (26.3)
<30	43 (3.9)
Neoadjuvant chemotherapy	48 (7.6)
Diversion, n (%)	
Continent Diversion	240 (21.9)
Other	854 (78.1)

BMI: body mass index; IQR: interquartile range; CCI: Charlson comorbidity index.

Multivariate analyses

Table 3 shows the multivariable logistic regression analyses evaluating the association between preoperative variables and postoperative outcomes.

Preoperative BMI, dyspnea, and unknown albumin were the only independent predictors of postoperative complications ($p = 0.01$). In particular, patients with a BMI >30 were 1.7 times more like to have postoperative complications compared to those with a BMI <25 ($p = 0.01$). Similarly, patients with dyspnea were 1.7 times more likely to experience complications compared to their counterparts without dyspnea ($p = 0.01$).

Age, race, BMI, hypertension, and continent diversion were significant predictors of the pOT ($p \leq 0.04$). Of note, patients receiving a continent diversion were 2.2 times more likely to have pOT compared to those receiving other diversions ($p < 0.001$).

Gender, preoperative hematocrit, and the presence of cardiovascular comorbidities were significant predictors of postoperative transfusion ($p \leq 0.03$). Men had a lower odds of blood transfusion compared to women ($p = 0.03$). Additionally, patients with cardiovascular comorbidity were 57% less likely to receive postoperative transfusion compared to their counterparts without cardiovascular comorbidities ($p = 0.03$).

Age at diagnosis, race, and the presence of comorbidities defined as other were the only predictors of pLOS ($p \leq 0.01$).

Urinary diversion type was the only predictor of readmission after discharge. Particularly, patients receiving a continent diversion were 49% more likely to be readmitted when compared to those patients who had other diversions ($p = 0.02$).

Finally, age at surgery and cardiovascular comorbidities were significant predictors of mortality within 30 days of surgery ($p \leq 0.04$). Specifically, patients with cardiovascular comorbidities were 2.4 times more likely to die within 30 days compared to their counterparts without cardiovascular comorbidities ($p = 0.04$).

Discussion

In the current study, we evaluated the contemporary rates and predictors of postoperative complications, pOT, transfusions, pLOS, readmission, and short-term mortality in a large cohort of patients included in the NSQIP database.

Several of our results are notable. First, we show that the risk of postoperative complications after RC for bladder cancer remains high in a contemporary cohort (up to 30%). This is consistent with complication rates reported in previous studies,[1,2,6,8,20] and corroborates the need for accurate identification of preoperative risk factors for potentially avoidable adverse events. Our results suggest that preoperative BMI represents a significant predictor of overall postoperative complications. Previous studies have linked increased BMI to a substantially higher risk of wound infection and dehiscence,[2,20] while others have suggested that construction of either urinary diversions or orthotopic bladder substitu-

Table 2. Intraoperative and postoperative outcomes for patients treated with radical cystectomy (RC) between 2006 and 2011 (National Surgical Quality Improvement Program NSQIP database)

	Overall	
Postoperative complications, n (%)		
Overall	340	(31.1)
Cardiovascular	15	(1.4)
Pulmonary	71	(6.5)
Thromboembolic	65	(5.9)
Septic	155	(14.2)
Renal failure	45	(4.1)
UTI	113	(10.3)
Wound	113	(10.3)
Median operative time (minutes; IQR)	331	(256-422)
Transfusions, n (%)	425	(38.8)
Median length of stay (days; IQR)	8	(7-11)
Readmission*, n (%)	128	(20.2)
Postoperative mortality, n (%)	29	(2.7)

*Readmission data only available for the year 2011 (n = 633); UTI: Urinary tract infections; IQR: Interquartile range.

tions in patients with higher BMIs poses a much greater technical difficulty.[21,22] Although we do not advocate that obesity should be considered a contraindication for surgery, these patients may do better in the care of an experienced urologist. Additionally, modifying surgical technique and using the appropriate surgical instruments are essential to minimizing the risk of adverse short-term outcomes in obese patients.[21] Finally, recent data supporting the use of multimodal chemotherapy and radiation in selected patients with muscle-invasive bladder cancer suggest that these patients need to be properly counselled of their alternatives before electing to undergo extirpative surgery.[23]

The high rate of readmission following cystectomy is another notable finding derived from this study. Specifically, more than 20% of the patients necessitated a hospital readmission within 30 days of surgery. This result complements those recently reported by Stimson and colleagues; these authors showed that most readmissions after RC occurred within 30 days (19.7%).[5] In multivariable analyses, type of urinary diversion was the only independent predictor of hospital readmission after hospital discharge in our cohort. Specifically, patients receiving a continent diversion were 1.5 times more likely to require readmission compared to those who underwent other diversions. However, the type of diversion was not associated with increased odds of 30-day overall complications. Thus, we hypothesized that patients receiving a continent diversion may be considered at higher risk of late postoperative complications, and thus of readmission after hospital discharge.

Another noteworthy finding was that comorbidity status was a significant predictor of perioperative complications, pOT, transfusion, pLOS, and mortality. Specifically, patients with dyspnea had higher odds of postoperative complications. Additionally, patients with cardiovascular comorbidities were 2.4 times more likely to die within 30 days following surgery compared to individuals without baseline cardiovascular diseases. Surprisingly, cardiovascular comorbidities were associated with lower odds of receiving blood transfusion. However, we suspect that this finding reflects more aggressive preoperative preparation of these patients.

When looking at the impact of baseline comorbidity status in published series, while the vast majority of the studies relied on the American Society for Anesthesiologists score, only a few studies comprehensively reported the impact of patient comorbidities on short-term outcomes after RC.[2,24] In the current study, the NSQIP database facilitated more accurate identification of the type of comorbidities, thus providing more clinically relevant information. For example, we were able to determine which specific comorbidities were associated with postoperative outcomes, instead of the overall comorbidity status as determined by a score relying on administrative data.

Our analyses failed to show a significant association between neoadjuvant chemotherapy and adverse postoperative outcomes. Several investigators have suggested that the underutilization of neoadjuvant chemotherapy prior to RC resides in patient and physician concerns regarding the increased risk of postoperative adverse outcomes.[25] However, our results together with recently published data suggest that efforts should be made to increase guideline compliant care with regard to the use of this therapeutic approach.[26,27]

It should also be noted that women were had higher odds of pOT and transfusions. This is in line with previous studies,[20,28] and highlights that RC might be more challenging in women.

Finally, we confirmed the unfavourable impact of older age on short-term postoperative outcomes. These observations may be explained by the established correlation between age and failure to rescue (i.e., death after the occurrence of a complication) in the context of RC.[29] Indeed, one may hypothesize that although advancing age is not associated with increased odds of complications, older and sicker patients are unable to recover when a complication does occur.[29]

From a practical perspective, our findings may be useful to develop preoperative strategies aimed at reducing perioperative morbidity and mortality in patients undergoing RC for bladder cancer. Indeed, reducing adverse events represents an important objective in the current state of health care, and would likely result in decreased expenditures related to the management of complications, transfusions, and readmissions following RC. In this context, individual preoperative risk assessment may facilitate better case selection, finally resulting in a decrease of adverse short-term outcomes.

The current study has its limitations. First, the lack of hospital and payer characteristic prevented assessment of

Table 3. Multivariable logistic regression analyses for intraoperative and postoperative outcomes for patients treated with radical cystectomy between 2006 and 2011 (National Surgical Quality Improvement Program database database)

	Overall complications OR (95% CI)	*p* value	Prolonged operative time OR (95% CI)	*p* value	Transfusion OR (95% CI)	*p* value	Prolonged LOS OR (95% CI)	*p* value	Readmission* OR (95% CI)	*p* value	Perioperative mortality OR (95% CI)	*p* value
Age at surgery	0.99 (0.98-1.01)	0.5	0.97 (0.96-0.99)	<0.001	1.01 (0.98-1.01)	0.9	1.04 (1.02-1.05)	<0.001	0.98 (0.96-1.01)	0.06	1.04 (1.01-1.1)	0.03
Race												
White	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Other	1.11 (0.78-1.59)	0.5	1.50 (1.03 -2.19)	0.03	1.11 (0.78-1.58)	0.6	1.61 (1.12-2.31)	0.01	0.61 (0.32-1.13)	0.1	1.33 (0.51-3.46)	0.5
Gender												
Female	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Male	1.24 (0.85-1.75)	0.2	0.65 (0.45-0.94)	0.02	0.70 (0.51-0.97)	0.03	0.84 (0.59-1.19)	0.3	0.97 (0.58-1.62)	0.9	0.58 (0.24-1.38)	0.2
BMI												
<25	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
25-30	1.04 (0.73-1.46)	0.9	1.08 (0.74-1.58)	0.4	0.80 (0.58-1.11)	0.2	1.14 (0.80-1.63)	0.4	1.12 (0.66-1.91)	0.6	0.71 (0.25-1.99)	0.5
>30	1.67 (1.16-2.42)	0.01	1.40 (1.01 -2.09)	0.04	0.78 (0.54-1.13)	0.2	1.26 (0.85-1.88)	0.2	1.44 (0.81-2.57)	0.2	1.54 (0.55-4.28)	0.4
Smoking status												
Non-smoker	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Current smoker	1.11 (0.80-1.54)	0.5	0.91 (0.64-1.29)	0.6	0.70 (0.51-1.01)	0.1	1.07 (0.75-1.52)	0.7	0.93 (0.56-1.54)	0.7	0.80 (0.27-2.34)	0.6
Preoperative comorbidities (Yes vs. No)												
Diabetes	1.28 (0.91-1.80)	0.2	1.06 (0.72-1.55)	0.8	1.03 (0.73-1.45)	0.8	0.87 (0.60-1.26)	0.5	1.12 (0.66-1.90)	0.6	0.63 (0.21-1.92)	0.4
Hypertension	0.81 (0.61-1.09)	0.2	1.49 (1.08-2.06)	0.01	1.14 (0.86-1.52)	0.3	1.00 (0.74-1.36)	0.9	1.21 (0.78-1.89)	0.4	0.56 (0.25-1.26)	0.1
Cardiovascular	1.02 (0.67-1.54)	0.9	1.02 (0.65-1.63)	0.9	0.63 (0.41-0.96)	0.03	0.89 (0.57-1.38)	0.6	0.73 (0.29-1.83)	0.5	2.41 (1.01-6.17)	0.04
Dyspnea	1.69 (1.11-2.59)	0.01	1.03 (0.65-1.62)	0.9	1.27 (0.83-1.96)	0.3	1.59 (1.08-2.33)	0.1	0.88 (0.39-1.49)	0.4	1.09 (0.34-3.44)	0.8
Other	1.10 (0.74-1.60)	0.6	1.18 (0.77-1.82)	0.6	0.86 (0.58-1.26)	0.4	1.58 (1.08-2.33)	0.02	0.76 (0.38-1.49)	0.3	0.69 (0.22-2.16)	0.6
Glomerular filtration rate												
≥60	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
30-59	1.27 (0.89-1.82)	0.2	0.76 (0.49-1.18)	0.2	1.28 (0.91-1.80)	0.1	1.21 (0.84-1.74)	0.3	0.97 (0.55-1.70)	0.9	1.44 (0.53-3.95)	0.4
<30	1.33 (0.64-2.76)	0.4	0.83 (0.34-2.02)	0.7	0.91 (0.44-1.87)	0.8	0.80 (0.36-1.79)	0.6	1.06 (0.27-4.11)	0.9	1.32 (0.15-11.82)	0.8
Preoperative albumin (g/dL)												
≥3.0	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
<3.0	1.06 (0.57-1.96)	0.8	0.75 (0.35-1.63)	0.5	0.99 (0.54-1.81)	0.9	1.35 (0.72-2.54)	0.4	1.18 (0.42-3.29)	0.7	1.72 (0.42-6.99)	0.6
Unknown	0.64 (0.48-0.85)	0.01	0.80 (0.59-1.09)	0.1	0.93 (0.70-1.22)	0.6	0.82 (0.61-1.11)	0.2	0.91 (0.59-1.40)	0.7	1.47 (0.61-3.01)	0.9
Hematocrit												
<30	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
30-45	0.72 (0.44-1.16)	0.1	1.05 (0.59-1.85)	0.8	0.52 (0.33-0.82)	0.01	0.81 (0.49-1.34)	0.4	0.94 (0.42-2.09)	0.8	1.47 (0.32-6.99)	0.6
>45	0.83 (0.43-1.59)	0.6	1.11 (0.52-2.35)	0.7	0.24 (0.12-0.51)	<0.001	0.81 (0.39-1.65)	0.5	1.12 (0.39-3.21)	0.8	0.92 (0.1-11.22)	0.9
Neoadjuvant chemotherapy												
No	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Yes	0.71 (0.46-1.11)	0.1	1.65 (0.95-2.88)	0.1	1.14 (0.67-1.94)	0.1	0.57 (0.29-1.13)	0.1	0.76 (0.35-1.67)	0.5	1.10 (0.2-5.11)	0.9
Diversion												
Other	1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Continent	1.21 (0.86-1.72)	0.2	2.16 (1.53-3.05)	<0.001	0.76 (0.53-1.08)	0.1	1.38 (0.95-2.02)	0.1	1.49 (1.03-2.41)	0.02	0.58 (0.16-2.13)	0.5

Readmission data only available for the year 2011 (n = 633); OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; LOS: length of stay.

the impact of hospital volume or other socioeconomic factors, such as insurance status on outcomes, as previously described.[30] Second, the NSQIP did not provide data on disease characteristics, such as tumour histology and stage, and therefore we could not adjust for these variables. However, previous studies failed to show higher complication rates for advanced diseases compared to localized tumours.[2,3,5,7] Nonetheless, further investigations are needed to comprehensively address this issue. Additionally, the NSQIP database lacked information regarding gastrointestinal complications, which has been shown to occur in a substantial proportion of patients after RC.[2,3,10,20] Nonetheless, the NSQIP data has been shown to reliably identify those complications that are most predictive of mortality. The lack of data beyond 30 days is another limitation.[5] Finally, the voluntary participation in NSQIP requires resources, which may select for larger, high-volume institutions, which are known to have lower rates of complications and readmission after RC.[8,29,30] For this reason, our results might not be generalizable to small rural hospitals.

Conclusion

Complications, transfusion, readmission, and mortality are relatively common events within 30 days following RC for bladder cancer. Age, baseline comorbidity status, BMI, and type of urinary diversion represent significant determinants of these outcomes. In an era where many advocate the need for prospective multi-institutional data collection as a means of improving quality of care, our study provides data on short-term outcomes after RC from a national quality improvement initiative.

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Competing interests: Dr. Gandaglia, Dr. Varda, Dr. Sood, Dr. Pucheril, Dr. Konijeti, Dr. Sammon, Dr. Sukumar, Dr. Menon, Dr. Sun, Dr. Chang, Dr. Montorsi and Dr. Kibel all declare no competing financial or personal interests. Dr. Trinh has received consultant fees from Intuitive Surgical Inc.

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Correspondence: Dr. Giorgio Gandaglia, Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Centre, 264 Blvd. Rene-Levesque E. #228, Montreal QC H2X 1P1; giorgio.gandaglia@gmail.com; giorgan10@libero.it