Morbidity and mortality of octogenarians following open radical cystectomy using a standardized reporting system

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Introduction: Recent evidence suggests that radical cystectomy may be underutilized in elderly patients, despite literature supporting acceptable morbidity/ mortality in this population. However, there is a paucity of literature reporting complications in a standardized manner. Therefore, we evaluated the morbidity and mortality of octogenarians treated with radical cystectomy using the modified Clavien complication reporting system. **Materials and methods:** We retrospectively reviewed 443 consecutive patients undergoing radical cystectomy at our institution between January 2000 and April 2010. Patients who underwent cystectomy for benign conditions were excluded, leaving 359 for analysis. Baseline demographic and perioperative data were reviewed and all complications were graded. We compared the outcomes of our octogenarian population (n = 43) against our younger population (n = 316).

Results: There was no difference between octogenarians and the younger cohort for overall complication rates (86% versus 83%, p = 0.91), or major (33% versus 30%, p = 0.93) or minor (81% versus 80%, p = 0.91) complications. The younger group was more likely to encounter a late complication (41.5% versus 23.3%, p = 0.03). Those 80 years and older trended toward more intraoperative complications (21% versus 10%, p = 0.07). The older group also had a greater propensity for neurological complications (26% versus 11%, p = 0.02), but there was no difference in CVA (2% versus 3%, p = 0.22). There was no difference in mortality rates between the older and younger cohort (2.3% versus 0.9%, p = 0.95).

Conclusions: Radical cystectomy is a morbid procedure regardless of patient age. Age alone should not preclude radical cystectomy in the elderly.

Key Words: surgical complications, bladder cancer, transitional cell carcinoma, octogenarians, urothelial carcinoma

Introduction

Given the morbidity of radical cystectomy, many surgeons have questioned its benefit in elderly patients, opting for less aggressive therapy.[1-3] However, multiple authors have reported a strikingly wide range of morbidity rates, depending on criteria for complication reporting and time frame, making accurate patient counseling and informed consent difficult.[4] Four prior studies have used the Clavien system to grade complications and have shown discordant results regarding whether or not the elderly have similar morbidity and mortality rates as younger patients.[5-8] Similar discordance is present in other previous studies not using the Clavien system.[4,8-16] Some studies have concluded there is a significant increase in complications and/or death rates in the elderly, while others have refuted these findings. For this reason, we performed the fifth Clavien system based analysis of cystectomy in the elderly to further

clarify whether an aggressive or conservative approach is warranted for octogenarians. We reviewed data from patients undergoing radical cystectomy in the last 10 years at our institution.

Materials and methods

Upon Institutional Review Board approval, we conducted a retrospective chart review of patients undergoing radical cystectomy at our institution from January 2000 to April 2010. Patients undergoing cystectomy for indications other than bladder malignancy were excluded. Standard preoperative work up included routine serum chemistries, chest x-ray and CT of the abdomen and pelvis. Preoperative variables were reviewed, including age, sex, race, body mass index, revised cardiac risk index, prior abdominal surgery, prior pelvic radiation, neoadjuvant chemotherapy, preoperative hydronephrosis, COPD, congestive heart failure, hypertension, serum creatinine, and smoking history. Operative variables included type of urinary diversion, extent of lymph node dissection, lymph node positivity, estimated blood loss, intraoperative transfusion, and packed red blood cell units received. Postoperative data included admission to intensive care unit (ICU), length of ICU admission, reoperation, length of hospital admission, follow up duration, recurrence rates and complications.

Operative and postoperative complications were recorded and defined from the time of the procedure through the most recent follow up. Complications were classified based on a 5-grade modification of the Clavien system: 0, no event observed; 1, oral medications or bedside intervention; 2, intravenous medications, total parenteral nutrition, enteral nutrition or blood transfusion; 3, interventional radiology, therapeutic endoscopy, intubation, angiography or operation; 4, residual and lasting disability requiring major rehabilitation or organ resection; 5, death.[17,18] Death was recorded for those who expired in-house or whose death was recorded in our electronic medical record.

Complications were subdivided into minor (Clavien grades 1-2) or major (Clavien grades 3-5), and stratified into 11 system-based categories: respiratory, neurological, gastrointestinal, genitourinary, cardiac, endocrine, thromboembolic, renal, infection, vascular, and other.[5,6] Patients were dichotomized by age (< 80, ≥ 80). All statistical analysis was conducted using SAS Institute's StatView commercially available software, version 5.0.1. Student's t-test was used to compare means and a z-test was used to compare percentages. Variables were assumed to be normally distributed. P values < 0.05 were considered significant.

Results

Demographics

A total of 443 patient charts were screened and 359 met inclusion criteria, of which 348 had urothelial carcinoma, 9 had squamous cell carcinoma and 2 had adenocarcinoma of the bladder. Forty-three (12%) were older than age 80 at the time of surgery. Octogenarians were less likely to have received neoadjuvant chemotherapy (0% versus 17%, p = 0.02) and had a lower incidence of COPD (2% versus 14%, p = 0.04). However, octogenarians more commonly had hypertension (74% versus 57%, p = 0.04), higher creatinine level (1.5 versus 1.2, p = 0.0002), and an American Society of Anesthesiologists (ASA) score > 2 (79% versus 54%, p = 0.002) prior to surgery. They also trended toward revised cardiac risk indices > 2 (49% versus 33%, p = 0.06) and a higher frequency of prior abdominal surgery (63% versus 43%, p = 0.07). There were no significant differences with respect to race, body mass index, obesity, prior pelvic radiation, preoperative hydronephrosis, and congestive heart failure, Table 1. Overall, 57.1% of our patients had an ASA score > 2 at the time of cystectomy.

Intraoperative

Octogenarians were less likely to undergo lymph node dissection (88% versus 98%, p = 0.02) and more likely to receive a non-continent urinary diversion (100% versus 70%, p = 0.001) and blood transfusions (65% versus 39%, p = 0.02). However, there was no difference in estimated blood loss or number of packed red blood cell units received between the two groups.

Hospitalization

Postoperative admission to the ICU and duration of ICU stay were not significantly different between groups. There was also no significant difference regarding rates of reoperation, total length of hospital admission, average length of follow up, and prevalence of metastasis/recurrence, Table 2.

Complications

There were no differences between age groups with respect to overall, early, major or minor complication rates. However, those younger than 80 were more likely to incur a late complication (41.5% versus 23.3%, p = 0.03). The older cohort trended toward more intraoperative complications (21% versus 10%, p = 0.07). When stratified by organ system, octogenarians were more likely to have a neurologic complication (26% versus 11%, p = 0.02); however, rates of cerebrovascular accidents were not significantly different. There

TABLE 1. **Patient demographics**

	< 80 years n = 316	≥ 80 years n = 43	p value
Mean age (SD)	66.1 (9.6)	82.7 (2.1)	**< 0.0001**
Male (%)	87	74	0.07
Female (%)	13	26	0.07
Caucasian (%)	85	91	0.52
Mean BMI (SD)	28.7 (5.8)	27.3 (3.5)	0.13
BMI > 30 (%)	33	19	0.09
Revised cardiac risk index ≥ 2 (%)	33	49	0.06
Prior abdominal surgery (%)	47	63	0.07
Neoadjuvant chemo (%)	17	0	**0.02**
Prior pelvic radiation (%)	7	7	0.99
Preoperative hydronephrosis (%)	24	30	0.35
COPD (%)	14	2	**0.04**
CHF (%)	4	12	0.11
HTN (%)	57	74	**0.04**
Mean preoperative serum creatinine (SD)	1.2 (0.4)	1.5 (0.9)	**0.0002**
Past or current smokers (%)	81	60	**0.03**
ASA score > 2 (%)	54	79	**0.002**

SD = standard deviation; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CHF = congestive heart failure; HTN = hypertension; ASA = American Society of Anesthesiologists

TABLE 2. **Intraoperative, immediate postoperative hospitalization, and post-hospitalization data**

	< 80 years n = 316	≥ 80 years n = 43	p value
Intraoperative data			
Lymph node dissections (%)	98	88	**0.02**
Positive lymph nodes (%)	27	29	0.99
Non-continent diversions (%)	70	100	**0.001**
Mean EBL (SD)	1216 (919)	1470 (1562)	0.125
Intraoperative transfusion (%)	39	65	**0.02**
Mean units PRBCs received (SD)	3.3 (2.3)	4.0 (4.5)	0.25
Hospitalization data			
Admitted to ICU (%)	24	37	0.10
Mean ICU stay (SD)	2.6 (3.1)	1.8 (0.8)	0.36
Reoperation (%)	7	5	0.87
Mean LOS days postoperatively (SD)	11.9 (14.7)	11.0 (5.7)	0.70
Post-hospitalization data			
Average follow up, months (SD)	21.6 (23)	15.3 (20.4)	0.09
Metastasis/recurrence (%)	27	30	0.72

SD = standard deviation; EBL = estimated blood loss; PRBCs = packed red blood cells; ICU = intensive care unit; LOS = length of stay

TABLE 3. **Complications data including intraoperative, major, minor, systems-based, and mortality**

	< 80 years n = 316	≥ 80 years n = 43	p value
Complications by grade (%)			
Any	83.5	86	0.91
Intraoperative	9.8	20.9	0.07
Minor (grade 1-2)[1]	79.4	81.4	0.98
Major (grade 3-5)[1]	32.9	30.2	0.93
Complications by systems (%)			
Respiratory	7.6	14.0	0.26
Neurological	11.1	25.6	**0.02**
CVA	3	2	0.22
Gastrointestinal	36.7	30.2	0.55
Other	20.3	20.9	0.99
Genitourinary	58.2	41.9	0.06
Cardiac	17.4	27.9	0.13
Endocrine	1.3	4.7	0.51
Thromboembolic	10.8	7.0	0.60
Renal	11.1	9.3	0.90
Infection	11.4	9.3	0.90
Vascular	0.9	0	0.93
Mortality (%)			
Intraoperative mortality	0	0	1.00
30-day mortality	0.9	2.3	0.40
90-day mortality	1.6	4.7	0.20

[1]within 90 days

were no differences in complications involving the respiratory, gastrointestinal, cardiac, endocrine, renal, or vascular systems. The younger cohort trended toward fewer genitourinary complications than the older cohort (42% versus 58%, p = 0.06). Rates of infection, thromboembolic events, and other complications were not significantly different between the two groups. There was no difference in intraoperative, 30 day, or 90 day mortality, Table 3.

Discussion

Radical cystectomy is a morbid procedure, regardless of age, often justified by the dismal prognosis of untreated muscle invasive disease.[19] Contemporary mortality rates are approximately 2% with complication rates ranging from 24% to 64%, associated with patient age, comorbidities, and procedure complexity.[4-8,9] Generalization from these data is difficult, as variable reporting methods, complication time-frames, and definitions of "elderly" (ages 65-80) were used.[4,9-11] Mortality would seem easier to assess with rates for the elderly ranging from 0%-11%, but different studies

have reported on intraoperative, 30 day and 90 day mortality, or a combination of the three.[4,6,17,19-22] Analyses of the Surveillance, Epidemiology and End Results (SEER) database show that patient age influences the use of cystectomy suggesting that urologists are reluctant to perform such a morbid surgery on an elderly population.[1,2] However, disagreement persists as to whether our oldest patients (specifically those > 80) have complication and mortality rates differing significantly from younger patients.

Using the modified Clavien grading system, we found no significant difference in complications between octogenarians and younger patients (86% versus 83%, p = 0.91) even when stratified into minor (Grades 1-2) and major (Grades 3-5) complications (81% versus 80%, p = 0.98; 30% versus 33%, p = 0.93 respectively). These findings are in agreement with other groups using the modified Clavien system such as Novara and Donat et al who found no difference in mortality based on age, while Shabsigh et al reported that age was an independent predictor of major though not overall complication rate.[5-7] In groups not using the modified Clavien system, similar discrepancies

are noted with both Boström and Clark et al reporting increased complications with age, but both Fairey and May et al found no such correlation.[9-13]

When categorized by organ system, we found no significant differences between octogenarians and younger patients, except with neurologic complications (26% versus 11%, p = 0.02). Donat et al also found neurologic complications to be significantly increased in octogenarians although they also noted increased cardiac complications, which we did not observe.[5]

Although our overall and major complication rates were higher than those previously published (83.8%, with a major complication rate of 32.6%), our 30 day mortality rates were less (1.1%), with no significant difference between octogenarians and younger patients (2.3% versus 0.9%, p = 0.40). Using data from the SEER database, Isbam and Liberman both found that advanced age was associated with significantly higher 90 day mortality rates.[21,22] On the contrary, using an age 80 cut off, our results suggest there is not a significant difference between the two cohorts with respect to 30 day (2.3% versus 0.9%; p = 0.40) or 90 day mortality (4.7% versus 1.6%; p = 0.20).

Though our octogenarian cohort showed no statistical difference with complications compared to our younger patients, there are many differences between the groups limiting the generalizability of this study. First, our octogenarians were less likely to receive neoadjuvant chemotherapy (0% versus 17%, p = 0.02). While this is a striking difference, it is not surprising given other published data.[14,23] Second, there was a variable degree of surgical aggressiveness between cohorts, as demonstrated by statistically lower rates of lymphadenectomy (88% versus 98%, p = 0.02) and continent diversions (0% versus 30%, p = 0.001) in octogenarians. These differences likely represent a deliberate attempt by the surgeon to mitigate potential morbidity in an elderly population. Third, our older cohort was more morbid than our younger population based on ASA scores > 2 (79% versus 54%, p = 0.002). Fourth, while our overall complication rate was much higher than previously reported, our liberal definition of complications, including anxiety, atelectasis, delirium, hypokalemia, hypovolemia, hyperglycemia, hyperkalemia, intractable hiccups, nausea, poor pain control, postoperative confusion/agitation, vomiting, and wheezing may have contributed to our elevated reported rate. Furthermore, other studies utilizing the modified Clavien system only reported complications up to 90 days, whereas our data reports complications over the entire duration of follow up (median [IQR] of 13 months, range 4-32). Lastly, another potential limiting factor may be selection bias regarding which octogenarians received radical cystectomy.

When considering candidates for radical cystectomy our inclusion criteria have generally been the following: life expectancy ≥ 3 years, EF > 20%, ECOG ≤ 2, can discontinue clopidogrel or warfarin for 1-2 weeks, and creatinine < 3. We generally exclude those with high risk cardiac features, active dementia, metastatic disease, CVA within one year, or significant hepatic impairment (ascites or encephalopathy). Additionally, our study is limited by its retrospective nature and inclusion of various types of bladder cancer, though the vast majority was urothelial.

Conclusions

Radical cystectomy is a morbid procedure, fraught with many potential complications. Our data supports the growing body of literature suggesting similar complication and mortality rates in the elderly; however, we advocate for wide-spread use of standardized complication reporting utilizing the modified Clavien system. While a large volume of research has been published on the risks of cystectomy in the elderly, inter-study comparison and validation is difficult given the variability in reporting methodologies. Regardless, despite differences in treatment decisions between age groups, radical cystectomy should continue to be the standard of care for advanced bladder cancer, even in an elderly population. □

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