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Cardiac History and Risk of Post-Cystectomy Cardiac Complications

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Abstract

Objectives—Patients undergoing cystectomy often have significant baseline cardiac disease. Despite pre-operative medical optimization, post-operative cardiac complications remain a significant source of morbidity. We sought to evaluate risk factors for post-cystectomy cardiac complications (POCC).

Methods—A retrospective review of all radical cystectomies for bladder cancer from 1/2004 through 9/2006 was performed. Twelve pre-operative risk factors were evaluated including age, Charleson Co-morbidity index, type of urinary diversion, and prior cardiac history. All complications were recorded for 90 days post-operatively including myocardial infarction (MI) and new onset arrhythmia (NOA). Univariate and multivariate analysis were performed.

Results—283 patients underwent cystectomy for bladder cancer from 1/2004 to 9/2006. The median age of the cohort was 70 (35–90). 64 pts (23%) had a significant pre-operative cardiac history, including 18 (6%) with prior coronary artery bypass and 30 (11%) with a history of MI's. Thirty-one (11%) patients had either NOA (22, 8%) or MI (10, 4%); one had both. On univariate analysis, cardiac history, age, type of urinary diversion, and the Charleson co-morbidity index demonstrated significance. The risk of POCC was associated with ileal conduit urinary diversion (p=0.026, OR 5.58 [1.23–25.36]) and the Charleson Index score (p=0.030, OR 1.28 [1.024–1.60]) on multivariate analysis.

Conclusions—Multiple, inter-related factors may predict cardiac complications in the early post-operative period. Despite peri-operative optimization, patients with a prior cardiac history should be counseled regarding the increased risk of postoperative cardiac complications. The association between cardiac complications and ileal conduit diversion highlights the selection bias towards patients with pre-existing co-morbid disease.

Keywords

cystectomy; complications; cardiac; outcome

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Introduction

Radical cystectomy with urinary diversion is a standard treatment for invasive and high grade refractory non-muscle invasive urothelial carcinoma[1]. Increasing age is a major risk factor for both bladder cancer and cardiovascular disease[2]3. In a retrospective, coding based review of the Nationwide Inpatient Sample of the Health Care Utilization Project from 1998 to 2002[4] 5.3% and 12% of patients undergoing cystectomy had a history of congestive heart failure or arrhythmias, respectively, and these patients had a significant increased risk of post-operative, in-hospital complications.

The literature on risks of cardiac specific complications after radical cystectomy is fraught with small study populations, few reported events, and inconsistent definitions and methods for identifying and reporting complications. The range of reported cardiac complications after cystectomy is 1.4%–4.1%[4–10]. Assessment of patient ability to tolerate major surgery without complication can be complex and despite pre-operative medical screening, post-operative cardiac complications (POCC) remain a significant source of morbidity in cystectomy patients.

We sought to evaluate patient and operative risk factors for post-cystectomy cardiac complications.

Materials and Methods

Prior to initiating of this retrospective chart review, institutional review board approval was obtained. Identification of patients and all adverse events that occurred after surgery was done via our departmental database, retrospective review of inpatient and outpatient notes, imaging findings, billing records, and physician correspondence. We identified 283 consecutive patients who had undergone radical cystectomy and urinary diversion for urothelial carcinoma from January 2004 to September 2006. The majority of cases were performed by 5 surgeons. All patients underwent standard pre-operative history and physical exam. Additionally, cardiac clearance was obtained if the patient had a history of cardiac disease or if assessment was deemed necessary by the treating surgeon.

All patients were on a standardized post-operative care pathway that included medical and mechanical prophylaxis for vascular thromboembolism, however, deviations for co-morbid disease did occur as necessary. All patients received lovenox beginning on the day of surgery and continued for 30 days postoperatively. Patients with epidurals were given heparin on the day of surgery and were started on lovenox after removal of the epidural, usually on day 1 or 2 postoperatively. Patients with epidurals received heparin for the first dose followed by lovenox. POCCs were recorded for 90 days after discharge; all patients were included in the analysis irrespective of long term follow-up information. POCCs were graded according to the standard surgical complication classification system[11]: grade I (deviation from normal post-operative course without the need for pharmalogical, surgical, or radiologic intervention), grade II (requiring pharmacologic intervention); grade III (requiring surgical, endoscopic, or radiological intervention); grade IV (life-threatening, requiring intensive care monitoring); grade V (death).

Clinical, pathologic, and laboratory data were reviewed and recorded into a database. All POCC were reviewed. The following variables were analyzed to determine their value as predictors of POCCs: patient age, gender, body mass index (BMI), age-adjusted comorbidity index[12], American Academy of Anesthesiologist (ASA) score, prior cardiac history, pre-operative hemoglobin, operative time, intra-operative blood loss (estimated by the anaesthesiologist), fluid volume administered intra-operatively, type of urinary diversion, and use of neoadjuvant chemotherapy.

Prior cardiac history was defined as a history of one or more of the following: myocardial infarction (MI), cardiac stent, coronary artery bypass graft (CABG), or an ejection fraction (EF) <55%. EF was determined by echocardiography or cardiac catheterization within 4 months prior to surgery. Post-operative MI was defined by troponin elevation. New onset arrhythmia (NOA) was defined as any rhythm changes from the pre-operative ECG. BMI was defined as weight in kg/height in m^2. Choice of diversion was surgeon specific. Extended bilateral lymphadenectomy was routinely performed. Operative time was calculated from incision time to dressing application. Cardiac enzymes were obtained if the patient's clinical care required and at the discretion of the treating physician. Cardiac consultation was obtained post-operatively for any abnormal arrhythmia, troponin elevation, cardiac complaints, or occasionally due to increased pre-operative cardiac risk.

The Fisher's exact test and the chi-square test were used to evaluate the association between categorical variables. Differences in variables with a continuous distribution were assessed using non-parametric Students T-test. Multivariate analysis was conducted using stepwise logistic regression. Statistical significance in this study was set as $p \leq 0.05$. All reported p-values are two-sided. All analyses were performed with SPSS software (version 13.0, SPSS Inc., Chicago, IL).

Results

Of the 283 patients who underwent cystectomy for urothelial carcinoma, >90-day post-discharge data were available for 256 (90%) of the patients and no follow-up data were available for 3 (1%) of the patients. 152 (54%) patients had at least one post-operative complication. The 2 most common complications were wound issue (WI), which included infection, staple line erythema, dehiscence, or seroma, in 56 (20%) and ileus requiring total parental nutrition (TPN) in 38 (13%). There were no mortalities within the 90 day follow-up period.

Table 1 lists the demographic characteristics, operative variables, and cardiac risk factors assessed for the overall cohort and those that had a POCC. Variables with missing data elements included preoperative hemoglobin (n=27), EBL (n=11), and BMI (n=1). 31 (11%) patients had a POCC, either NOA (22 pts, 8%) or MI (10 pts, 4%); one patient had both. For those patients with NOA, the severity of the POCC was grade 2 in 9 patients, grade 3 in 10 patients, and grade 4 in 3 patients. All patients with an MI were considered to have a grade 4 complication. The median age of the cohort was 70 (35–90). Approximately one-third of patients (35%) had orthotopic urinary diversion. Univariate analysis demonstrated that age (p=<0.001), conduit urinary diversion (p=<0.001), comorbidity index (p=0.002), ASA (p=0.029), and prior cardiac history (p=0.011) were associated with POCC. Other factors evaluated, such as BMI, blood loss, volume of intravenous fluid, were not associated with POCC. Of the 30 patients with a history of previous MI, 4 had a post-operative MI (13%), compared to 6 of 253 (2%) with no prior history, p=0.002.

Approximately one-fourth of the patients, (64 patients, 23%) had a significant pre-operative cardiac history (table 2), including 18 (6%) with prior coronary artery bypass grafts, 21 (7%) with prior cardiac stents, 30 (11%) with a history of MI's, and 54 (19%) with ejection fraction <55%. Univariate analysis demonstrated an association of age (p=<0.001), comorbidity index (p=<0.001), and ASA (p=0.001) with a previous cardiac history. Patients with a previous cardiac history underwent conduit diversion more often than continent diversion (53 versus 11, p=0.001) and received neoadjuvant chemotherapy (25%) less frequently than those without a cardiac history (39%), p=0.039.

Ten patients had a post-operative MI and all ten had at least one other complication, including sepsis in 4 and WI in 3. The median time to occurrence/recognition of the MI was 3.5 days (1–12), and the median highest troponin elevation was 2.76 (0.05–12.21 ng/ml). Patients with post-operative MI had significant cardiac histories including CABG in 1, stenting in 5, MI in 4, and EJ <55% in 3. All patients with post-operative MI had undergone ileal conduit urinary diversion. Nine of the ten MI patients had pre-operative evaluation by either cardiology (5) or the internal medicine pre-operative assessment team (4) at our institution within 45 days of surgery. Pre-operatively, five of the ten patients had normal stress tests and 2 patients with abnormal stress tests underwent pre-cystectomy coronary artery stenting.

NOAs occurred in 22 patients (8%). 13 patients (62%) had at least one other complication, including WI in 5 (2 with fascial dehiscence) and ileus requiring TPN in 4 patients. The median time to occurrence/recognition of NOA was 3 days (0–11). 5 patients were symptomatic: 1 had chills, 1 anxiety, 1 respiratory failure, 1 shortness of breath, and 1 chest pain). 3 NOA occurred in post-operative holding prior to transfer to the floor. The arrhythmias consisted of 12 A-FIB, 4 with ventricular bigeminy or trigeminy, 1 with premature atrial contractions, 1 non-sustained ventricular tachycardia, 2 supra-ventricular tachycardia, and 1 transient mobitz type I block (2:1) intra-operatively which resolved. 15 patients were discharged with normal sinus rhythm and seven patients were discharged on therapeutic anti-coagulation (6 for atrial fibrillation and 1 for a lower extremity deep vein thrombosis). Patients with NOA had significant cardiac histories including 6 with previous history of arrhythmia, 4 with prior CABG, 4 with prior MI, 3 with prior stents, and 7 with EJ <55%. Ileal loop conduit diversion was the most common urinary diversion in patients who developed NOA (n=19/21).

There was a statistically significant difference in the duration of hospital stay for patients without a POCC versus those with a POCC (medians of 9 days and 17 days, respectively; p=0.006). The hospital stays for patients with MIs were significantly longer than those for patients with NOAs (medians of 29.5 days and 14.5 days, respectively; p=0.029).

The results of logistic regression analysis are shown in table 3. The risk of POCC was significantly associated with ileal conduit urinary diversion (p=0.026, OR 5.58 [1.23–25.36]) and comorbidityindex (p=0.030, OR 1.28 [1.024–1.60]), but not with a prior cardiac history.

Comment

This study highlights that patients which undergo cystectomy for bladder cancer often have significant medical co-morbidities. Almost one-quarter of the patients in this series had a pre-operatively identified significant cardiac history.

Our results demonstrate that multiple, inter-related factors may predict cardiac complications within the early post-operative period after cystectomy. We interpret the finding of ileal conduit urinary diversion being the most significant associated factor with POCC to reflect a selection bias due to surgeon preference of ileal conduit diversion in older patients with increased co-morbidities. Patients who underwent ileal conduit urinary diversion were older (median 71 vs. 56.5), underwent neoadjuvant chemotherapy more often (76 vs. 26), had higher Charleson index score (median 4 vs. 2.3) and ASA score (143 vs. 66 with ASA 3 and 27 vs. 3 with ASA 4), had lower pre-operative hemoglobin levels[13] (12.4 vs. 13.9), and were more likely to have a significant cardiac history (53 vs. 11) compared to patients who underwent orthotopic urinary diversion. BMI and EBL were relatively the same between these two groups.

The comorbidity index, which takes into account multiple patient history medical variables and age also demonstrated significance on multivariate analysis. We attribute this finding to both the breadth of medical co-morbidities included in this index and that fact that it is an age-

co-morbidity index. The age component addresses the potential of clinically unknown, but physiologically significant heart disease[3], specifically, coronary artery disease for MI.

Many patients in this study with known coronary artery disease (CAD) did not manifest a POCC. While most patients in our series who suffered a perioperative MI were evaluated preoperatively for cardiac clearance, 5 patients with negative stress tests and two patients with positive stress testing who underwent pre-cystectomy cardiac stenting had non-fatal MI's.

Our rates of 3.5% for MI and 8% for NOA (2.1% discharged on anticoagulation due to arrhythmia) are higher than in most published series[4–10]. Comparisons between studies are imprecise due to a lack of standardized definitions of cardiac events, lack of consistently reported cardiovascular co-morbidities, and the retrospective nature of most studies, including our own. It is also possible that the threshold to abandon cystectomy in the face of co-morbidities may vary among institutions. In a study by Knap et. al.[8], pre-operative cardiovascular co-morbidities were present in only 24/268 (9%) of patients. Five patients had post-op MI's (2%), and 4 were in patients over the age of 70 (p=0.007). Post-operative cardiac events are a cause of post-operative mortality. Quek et. al.[14] described 4 MI's and 2 fatal arrhythmia as the cause of death among 27 post-cystectomy deaths (2% of 1359 patients). Maffezzini et. al.[15] reported that three out of four post-operative MI's were fatal.

There are several obvious limitations to this retrospective review. Because multiple potential confounding medical and surgical factors can affect outcome, a much larger sample size is likely necessary to test the significance of all of the variables. Furthermore, many of the variables which may predict cardiac morbidity are interrelated which further complicates the analysis.

Physician interpretation of overall risk at the time of patient evaluation for surgery was not quantified in our study, and in patients with more severe co-morbidities, ileal conduit urinary diversion was preferentially performed. Selection bias against patients with severe medical co-morbidities inevitably occurs in any surgical series with those deemed too high risk for surgical intervention undergoing alternative therapy. In addition, potential confounding factors not accounted for such as the use of perioperative beta-blockers may influence our ability to assess patients risk for a cardiac event. Regardless of these limitations, our experience underscores the existing risk of cardiac complications, even in asymptomatic individuals, possibly because bladder cancer is a tobacco-related disease.

Future studies evaluating medical management and long term outcomes of patients with cardiac risks and histories need to be performed. First, the optimal peri-operative management of patients on anti-platelet agents or anticoagulation undergoing cystectomy is unknown[16]. Second, the long-term effects and potential increased future morbidity of a patient having a MI or NOA at the time of cystectomy need to be defined. Third, the potential impact of our internal medicine pre-operative assessment program on post-operative cardiac morbidity needs to be evaluated. Also, in a continuing effort to identify preoperative patient risk, research is ongoing evaluating energy reserve capacity using cardiopulmonary exercising testing in an attempt to correlate preoperative parameters of a patients' exercise energy reserve capacity to postoperative acute morbid outcomes. Fourth, there are clear differences in length of stay if patients had a cardiac complication, especially a MI. Whether this reflected an overall sicker patient due to increased pre-operative co-morbidity is possible, but identifying these patients pre-operatively and instituting more intensive pre and post-operative measures may decrease hospital stay and overall cost.

In our experience, no single or combination of factors were found to be reliable predictors of the risk of POCC after cystectomy, thus despite the availability of pre-operative data and

classification tools, urologists rely on their own medical judgment to assess which patients have “poor protoplasm” and, thus, are at the highest risk of a post-operative cardiac event.

Conclusions

Post-operative cardiac complications are a common source of morbidity in patients undergoing cystectomy with urinary diversion for bladder cancer. A significant proportion of patients undergoing cystectomy have a prior cardiac history or other medical characteristics which put them at risk for a POCC. Unfortunately, there is no simple, best predictor of POCC. This deficiency in prognostic potential has implications not only for patient care, but also for “quality of care”, an initiative supported by the federal government. For now, the data from this study can be used a guide for patient counseling. However, predictive factors need to be evaluated prospectively in larger cohorts. This can only be done once we are all working with a standard set of universally accepted definitions and severity scales.

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Table 1

Characteristics of Patients with a Post-Operative Cardiac Complication

		Overall	Cardiac Complication	P Value
Age		70 (35–90)	74 (54–90)	p=<0.001
Gender				p=0.797
	Male	237	27	
	Female	46	4	
BMI		27 (17.5–46.5)	29 (22–39)	p=0.219
Operative Time (hrs)		7.05 (3.38–16.58)	6.93 (3.77–12)	p=0.689
Operative Blood Loss		900cc (100cc–13750cc)	900cc (100cc–7L)	
Urinary Diversion				p=<0.001
	Conduit	185	29	
	Continent	98	2	
Pre-op Hemoglobin		13 (8.3–17.4)	12.7 (9.9–15.7)	p=0.322
Neoadjuvant Chemotherapy		102	11	p=1.00
Charleson Index		3.4 (0–9.9)	4.7 (0–8.7)	p=0.002
ASA				
	2	3	1	
	3	211	23	
	4	31	7	p=0.029
Prior Cardiac History		64	13	p=0.011
Ejection Fraction <55%		54	10	p=0.055
Prior CABG		18	2	p=0.940
Prior Cardiac Stent		21	7	p=0.004
Prior MI		30	10	p=0.002

Median Values and ranges shown. BMI = Body mass index. L = liters. ASA = American Academy of Anesthesiologists Score. CABG = Coronary artery bypass graft. MI = Myocardial infarction. Hemoglobin in grams/deciliter.

Table 2

Characteristics by Cardiac History

		Cardiac History	No Cardiac History	P Value
Gender				p=0.248
	Males	58	181	
	Females	6	38	
Age		71 (54–86)	68 (35–90)	p=<0.001
BMI		27.3 (17.5–39.2)	26.7 (17.9–46.5)	p=0.671
Charleson Index		4.3 (1.7–9.9)	3.15 (0–0.9)	p=<0.001
ASA				
	2	1	38	
	3	50	161	
	4	12	19	p=0.001
Pre-op Hemoglobin		13.2 (9.9–17.4)	13 (8.3–16.3)	p=0.173

ASA = American Academy of Anesthesiologists Score. BMI = Body Mass Index. Pre-op = pre-operative

Table 3

Multivariate Analysis for Risk of Post-Operative Cardiac Complications

Ileal Conduit Diversion	p=0.026, OR 5.58 [1.23–25.36]
Charleson Index	p=0.030, OR 1.28 [1.024–1.60]
Prior Cardiac History	p=0.143, OR 1.84 [0.81–4.17]