Short Term Complications post Radical Cystectomy South Egypt Cancer Institute: 5 years' experience

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Abstract

Background: Despite advances of surgical technique and perioperative management, radical cystectomy has been associated with a substantial risk of postoperative morbidity and mortality with variable rates of short-term complications and mortality. However, with meticulous patient selection, perioperative management and surgical procedures, it currently has acceptable low perioperative mortality rate and a low rate of complications which are manageable. The aim of this study was to define the surgical outcome of radical cystectomy for urinary bladder cancer management in the point of postoperative morbidities and mortalities related to different surgical procedures aiming to minimize them to achieve the best outcomes possible.

Method: This is a retrospective study of 456 patients who had underwent radical cystectomy at South Egypt Cancer Institute between a time period from January 2012 till December 2016, the data were collected from archive and cancer registration data base of surgical oncology department.

Results: The age of presentation was 57.7 ± 9.4 ranged from 34 to 87 years. Male to female ratio was 71.7%., 28.3% respectively. Sixteen percent of patients were hypertensive, 13.2% diabetic and 19.7% had liver cirrhosis. The average duration of hospital stay was 14.6±6.2 days and average operative time (hour) was 4.3±1.4 hours. Most of patients ($3/5^{th}$) showed backpressure on kidneys (63.2%). The commonest diversion performed after radical cystectomy was ileal conduit diversion (39%) then ureterocolic diversion (30.9%), followed by orthotopic diversion (14.9%) and ureterocutenous diversion (12.9%) with a few percentage with rectal bladder (2.2%). Only 7.9% of patients received neoadjuvant chemotherapy. Intra-operative complications were recognized in only 5.3% of patients. 64% of patients experienced one or more of post-operative complications within 90 day of surgery with the most common complication categories were sexual dysfunction (73.46%), genito-urinary (52.19%), gastro intestinal (48.25%), wound-related (41.25%), general (30%), lymphadenectomy-related (21%), pulmonary (6%) and psychological complications (2.6%).

Conclusion: Radical Cystectomy is a complex operation and has avoidable post-operative Morbidity and mortality. Various technical improvements of the surgical and anesthesia techniques, multi-disciplinary approach for correction/control of comorbidities and early postoperative rehabilitation have produced salutary effect in reducing the mortality.

Keywords: Bladder Cancer, Radical Cystectomy, Orthotopic diversion, Ileal conduit.

Introduction:

Radical cystectomy represents the standard treatment of muscle-invasive bladder cancer and non-muscle invasive bladder cancer (intra-vesical therapy). [1]

Despite advances of surgical technique and perioperative management, radical cystectomy has been associated with a substantial risk of postoperative morbidity and mortality with variable rates of short-term complications and mortality. [2]

However, with advances patient selection, perioperative management and surgical technique, it currently has acceptable low perioperative mortality rate and a low rate of complications which are manageable. [3]

Risk assessment tools, such as the modified Charlson Comorbidity Index, Cardiac Risk Index (Lee Criteria), and the American Society of Anesthesiologists Physicians Status Classification are widely adopted to counsel bladder cancer patients and guide selection of surgical candidates. [4]

A successful outcome with radical cystectomy depends upon surgical technique, safe extirpation of the bladder and on factors such as patient selection, coordinated perioperative care, and use of adjunctive treatments. [5]

The aim of our study was to define the surgical outcome of radical cystectomy in urinary bladder cancer management in the point of postoperative morbidities and mortalities related to different surgical procedures aiming to minimize them to achieve the best outcomes possible.

Patients and Methods:

Data Source:

This is a retrospective study of 456 patients who had underwent radical cystectomy at South Egypt Cancer Institute between a time period from January 2012 till December 2016, whom data were collected from archive and cancer registration data base of surgical oncology department.

Outcome Measures:

Descriptive variables including demographic data (Gender, Age, Co-morbidities, Average time of hospital stay and average time of operation) Type of procedure and early post-operative complications were documented.

Statistical analysis:

Numerical data were described with mean and standard deviation and categorical data with number and percentage. Numerical data were tested for normality and parametric t test was used for comparing normally distributed variables and Mann Whitney test for non-normally distributed variables. Chi-square/Fisher exact tests were used for testing proportion independence. P value was always two tailed and significant at 0.05 level.

Results:

Baseline Characteristics

Mean age at presentation was 57.7±9.4 and ranged from 34 to 87 years.

The average duration of hospital stay was 14.6±6.2 days and average operative time (hour) was 4.3±1.4 hours, table (1).

Males represented 71.7% and females represented 28.3 %. Sixteen percent of patients were hypertensive, 13.2% diabetic and 19.7% had liver cirrhosis, table (2).

Clinical Outcomes

More than 3/5th of patients showed backpressure on kidneys (63.2%). Commonest diversion performed after radical cystectomy was ileal-loop conduit diversion (39%) then ureterocolic diversion (30.9%), followed by orthotopic diversion (14.9%) and ureterocutenous diversion (12.9%) with a few percentage with rectal bladder (2.2%). Intra-operative complications were recognized in only 5.3% of patients. Only 7.9% of patients received neoadjuvant chemotherapy, table (3).

Overall, 64% of patients experienced one or more of post-operative complications within 90 day of surgery.

The most common complication categories were sexual dysfunction (73.46%), genito-urinary(52.19%),gastro-intestinal(48.25%),wound-related (41.25%), general(30%),lymphadenectomy-related(21%),pulmonary(6%)and psychological complications (2.6%) as shown in table (4).

The most common general complication encountered was metabolic acidosis in 16%of patients, while dehydration up to hypovolemic shock developed in 12% of patients. Only 2% of patients (9 patients) suffered from post-operative bleeding inform of active bleeding (6 patients, 1.3%) and localized pelvic hematoma (3 patients 0.7%). The general complication represent 30% of all post-operative complications, table (5).

Penile and Scrotal Edema was the most common genito-urinary complication encountered among male patients (27%).

Renal Impairment following Pyelonephritis, Acute Kidney Injury and Renal failure due to progressive deterioration of renal function presented in 18%of patients.as 13% of patients developed pyelonephritis, while 3% of the patients encountered Acute Kidney Injury. Only 2%of the patients went straight-forward to Renal Failure.

Ureteric Obstruction found in (3%) of the patients. on the other hand, Urinary Leak detected in (4.6%) of patients. subsequently the Genito-urinary complications represent 53% of all post-operative complications, table (6).

In view of complications of orthotopic diversions, 8.8% of patient encountered pouchits, while 13 patients started to become day-time continent (19%) with Mean post-void residual urine was (15-30ml) detected with using real-time MRI during micturition .while 82% of the patient still incontinent within the time period of 90 days after radical cystectomy and orthotopic urinary diversion. Only 3 patients suffered from urinary retention (4.4%) only one needed to insert a urinary catheter and another case required suprapubic catheter insertion. Also 11 patients experienced urinary leak post-operatively (16%) and kept under conservative measured and recovered smoothly. Furthermore, a case report of Neo-bladder Rectal Fistula (NRF) detected in our practice, table (7).

Post-operative ileus was the most common gastro-intestinal complication (15%) while hypo-albuminemia (decrease more than 1.5 g from basal serum albumin) developed in (30%) of patients. but, the intestinal leak which is the most serious gastrointestinal complication encountered in (3.3%) of patients. Subsequently gastrointestinal complications represent 48.5% of all post-operative complications, table (8).

Surgical Site Infection (SSI) developed in 19% of the patients, becoming the most common complication in this category. Wound dehiscence occurred in 33 patients (7.2%) while 8 patients escalated to Evisceration of intestinal content (1.7%), table (9).

Uncomplicated lymphocele was detected in 13% of patients which is the most common complication occurred due to pelvic lymphadenectomy, then came Deep Vein Thrombosis (DVT) in 6.6% of patients. Vascular (internal iliac vein) injuries encountered in 5 patients (1%), while nerve (obturator nerve) injuries occurred in 3 patients (0.6%), table (10).

Pneumonia is the most serious pulmonary complication developed in 23 patients (5%). while Acute Respiratory Distress Syndrome (ARDS) encountered in 5 patients (1%). subsequently Pulmonary complications represent 6% of all post-operative complications, table (11).

Sexual Dysfunction in both gender found in 73%in male patients (in form of Erectile Dysfunction) and

69%of female patients (in form of Dysparonia & Discomfort). Subsequently Sexual Dysfunction complications represent 73% of all post-operative complications, table (12).

Psychological complications found in 12 patients (2.6%) presented in 2 forms: Psychosis in 3 patients (0.7%) and Severe Depression with suicide attempts in 9 patients (2%) as shown in table (13).

Table (1): Base line characteristics in the study group

	Age (years)	**Length of hospital stay (days)**	**operative time (hour)**
N	456	456	456
Mean	57.7632	14.62	4.30
Std. Deviation	9.42809	6.206	1.392

Table (2): Gender & co-morbidities in the study group

	Count	**%**
Sex		
- Male	129	28.3
- Female	327	71.7
Hypertension	14.6275	166.4
Cirrhosis	90	19.7
Diabetes Mellitus	60	13.2

Table (3): Management of patients

	Count	**%**
Backpressure	288	63.2
Diversion		
- Radical Cystectomy & ureterocolic diversion	141	30.9
- Radical Cystectomy & uretero-cutenous diversion	59	12.9
- Radical Cystectomy & ileal conduit diversion	178	39.0
- Radical Cystectomy & orthotopic diversion	68	14.9
- Radical Cystectomy & rectal bladder diversion	10	2.2
Neo-adjuvant Chemotherapy	36	7.9
Intraoperative complications	24	5.3

Table (4): categories of post-operative complications

	Count	**%**
Genito-urinary complications	238	52.2
Gastrointestinal complications	220	48.2
Wound and skin complications	191	41.9
Lymphadenectomy related complications	97	21.3
Pulmonary complications	28	6.1
Sexual dysfunction (both gender)	335	73.5
Psychological complications	12	2.6

Table (5): Types of General complication

	Count	**%**
General complications	137	30.0
Dehydration	55	12.1
Metabolic acidosis	73	16.0
Bleeding		
- Active bleeding	6	1.3
- Localized pelvic hematoma	3	0.7

Table (6): Types of Genito-urinary complications

	Count	**%**
Genito-urinary complications	234	51.3
Pylonephritis	59	12.9
Acute Kidney Injury	13	2.9
Renal failure with persistent deterioration of renal function	9	2.0
Urinary leak	21	4.6
Ureteric obstruction with upper tract dilatation	14	3.1
Penile & scrotal edema (n=327)	88	26.9

Table (7): Complications related to orthotopic diversion

	Count	**%**
Pauchitis	6	8.8
Incontinence	55	80.9
Urinary retention	3	4.4
Urinary leak	11	16.18
Neo-bladder rectal fistula	1	1.47

Table (8): Gastro-Intestinal complications

	Count	%
Gastro-Intestinal complications	220	48.2
Ilieus	68	14.9
Intestinal leak	15	3.3
Hypoalbuminemia	136	29.8

Table (9): Wound and skin complications

	Count	%
Wound and skin complications	191	41.9
Surgical site infection	87	19.1
Dehiscence	33	7.2
Evisceration	8	1.8
Skin excoriation	50	11.0

Table (10): Lymphadenectomy related complications

	Count	%
lymphadenectomy related complications	97	21.3
Deep Venous Thrombosis	30	6.6
lymphocele	59	12.9
Vascular injury (int. iliac vein)	5	1.1
Nerve injury (obturator nerve)	3	0.7

Table (11): Pulmonary complications

	Count	%
Pulmonary complications	28	6.1
Pneumonia	23	5.0
Acute Respiratory Distress Syndrome	5	1.1

Table (12): Sexual dysfunctions

	Count	%
Sexual dysfunction	335	73.5
Erectile dysfunction (n=327) in males only	245	74.9
Dysparonia (n= 129) in females	90	69.8

Table (13): Psychological complications

	Count	%
Psychological complications	12	2.6
Psychosis	3	0.7
Severe depression with suicide attempts	9	2.0

Discussion:

In this study, the mean age of presentation was 57.7±9.4 ranged from 34 to 87 years , which agrees with another recent report from Egypt that found that the mean age of bladder cancer cases was 56.24 ± 11 [6]. This age is less than reported in the literature for other parts of the world; it was reported that the median ages at diagnosis for urothelial carcinoma was 69 years in males and 71 years in females [7].

The male to female ratio in this study was 71.7%, 28.3% respectively. This result is similar to male to female international ratio of 3:1 [8]. In this study, Sixteen percent of patients were hypertensive, 13.2% were diabetic and 19.7% had liver cirrhosis. The average duration of hospital stay was 14.6±6.2 days and average operative time (hour) was 4.3±1.4 hours.

Pang et al, showed that, three most common urinary diversions were orthotopic neobladder (44%), ileal conduit (31%) and ureterocutaneostomy (23%). Only 2.3% of patients accepted neo-adjuvant chemotherapy and only 18% of T3 and T4 patients accepted adjuvant chemotherapy [9]. But this study showed that the commonest diversion performed after radical cystectomy was ileal conduit diversion (39%) then ureterocolic diversion (30.9%), followed by orthotopic diversion (14.9%) and ureterocutenous diversion (12.9%) with a few percentage with rectal bladder (2.2%). Only 7.9% of patients received neoadjuvant chemotherapy.

The incidence of overall complication rates after radical cystectomy is 60%, and major complications are high, with an incidence of 10%. Radical cystectomy is one of the most challenging, complicated examples of urological surgery, treated with radical cystectomy. While, 64% of patients experienced one or more of complications within 90 day of surgery, 15% of them were high [10].

Shabsigh A, et al reported that the most common post-operative complication categories were gastrointestinal (29%), infectious (25%), wound-related (15%), and genitourinary (11%) , while that doesn't meet the study's results as the most common complication categories were sexual dysfunction (73.46%), genito-urinary (52.19%), gastro-intestinal (48.25%), wound-related (41.25%), general (30%), lymphadenectomy-related (21%), pulmonary(6%) and psychological complications (2.6%) the same study showed that the most common pulmonary complications were pneumonia (in 3.9% of patients)

and acute respiratory distress syndrome (in 3.3% of patients) related to decreased respiratory effort, atelectasis, bronchospasm, or pulmonary edema ,which came similar to our results with pneumonia in 5% of the patients and Acute Respiratory Distress Syndrome in 1% of the patients [11].

Gamé et al reported rates of the intraoperative, early and late postoperative complication rates were 38.4%, 46.5% and 16.4%, respectively, . In this study, intra-operative complications were recognized in only 5.3% of patients with insignificantly higher rate of early complications found in 48% of patients represented in wound infection was documented in 19.1%, deep venous thrombosis in 6%, urinary and intestinal leak (4.6% & 3.3% respectively) and ileus in 15% of patients [12].

In a study of 247 patients underwent radical cystectomy with urinary reconstruction, the most common causes for second readmission were ureteral stricture (30%), followed by urinary tract infection and dehydration (19% each) . Which came different than from the results in this study, dehydration and hypovolemic shock developed in 12% of patients and 8.8% of patient encountered urinary tract infection causing pouchitis. Only 3%of the patients developed image evidenced ureteric obstruction [13].

Osman Y et al reported that acute kidney injury developed in 46 (4.7%), patients after radical cystectomy. While 11 (1.1%), patients developed progressive deterioration of renal function [14].

Also, Takada et al., in a multi-institutional Study from Japan, reported an incidence of 0.5% of renal failure. Which came a little bit lower than what has been detected in this practice as acute kidney injury encountered in 13 patients (2.9%). However, 9 patients went unfortunately to renal failure [15].

Acute pyelonephritis is included as a common infectious complication, occurring in roughly 20%-25% of patients after radical cystectomy , but in our study renal impairment was less than these studies (17.8%)[10], [11].

V. Hernández et al. reported that Postoperative potency in men was significantly better than standard cystectomy in the sphincter preserving cystectomy groups in 6 studies comparing sphincter preserving cystectomy vs. radical cystectomy ($P < 0.05$), ranging 89.7%, 58.0% to 93.8% and 77.0% to 78.8% for prostate, and capsule or nerve-sparing techniques [16]. Only half of female patients have successful sexual intercourse after radical cystectomy; related issues can be ascribed to reduced vaginal lubrication caused by damage to autonomic nerves originating from the hypogastric plexus, inability to have orgasms, decreased sexual desire, and dyspareunia [17]. While in this study, erectile dysfunction was found in 75.7% of male patients and 69%of female patients (in form of dysparonia & discomfort).

Canadian cohort from academic centers, Yafi and colleagues reported rates of Peri-operative death (90 days) is 3.2% at 90 days. Our results were close with Peri-operative death (90 days) occurred in 3.9% of patients [18].

The nighttime continence rates for the same periods were 38.5%, 61.5%, and 78.8%. However, only. 13 patients started to become day-time continent (19%) with mean post-void residual urine was (15-30ml) detected with using real-time MRI during micturition .while 82% of the patient still incontinent within the time period of 90 days after radical cystectomy and orthotopic urinary diversion. But, it is so soon to delineate as in literatures, we can't get an accurate assessment the continent function before 6 months [19].

Urinary retention is more common in women with 43% of women compared to 20% of men requiring intermittent catheterization. However, in our study, only 3 patients suffered from urinary retention (4.4%) only one needed to insert a urinary catheter and another case required supra-pubic catheter insertion [20].

Upper tract dilatation due to uretero-ileal stenosis was seen in 13.5% of patients with image evidenced dilated pelvi-calyceal system. Only (3%) of the patients encountered ureteric obstruction with upper tract dilatation [21].

In a study by Henningsohn et al, 29 UTIs were more common in patients with neobladder (pouchitis) than in patients with other diversions (14% versus 6%). While, in this study (8.8%) of the neo-bladder patients showed signs of pouchitis [22].

Narushi Y et al. reported case of neobladder-rectal fistula that developed as an early postoperative complication of radical cystectomy and orthotopic neobladder construction procedures. Also we have a case report of neo-bladder Rectal Fistula (NRF) detected in our practice [23].

Bowel obstruction, for example, postoperative ileus, is a common complication and reported to affect 23%38% of early convalescent patients after radical cystectomy [10], [11].. However, these results came much lower than those reported studies (15%). Timothy Lyon et al found that the most common reasons for primary return to operative room were facial dehiscence (29%), bowel obstruction (21%), enteric anastomotic leak (9%), neobladder leak (5%) and uncontrolled hemorrhage (4%) [24].

But in this study, only 2% of patients (9 patients) suffered from post-operative bleeding inform of active bleeding (6 patients) as 1.3% and localized pelvic hematoma (3 patients) as 0.7%. Furthermore, intestinal leakage occurred in 3.3%of patients usually from ileo-ileal anastomosis.

The incidence of wound dehiscence or hernia, classified as wound-related complications, is reported to occur in 15%18% of patients [10], [11].

Wound complications were the main independent contributing risk factor to increased hospitalization, advancing age, a higher body mass index, and underlying comorbidities [25].

Gupta et al. concluded that an interrupted suture (as opposed to a continuous suture) in the fascia layer could lower the risk of wound dehiscence by half, following a meta-analysis of 23 randomized controlled trials [26].

Postoperative deep vein thrombosis and pulmonary embolism are life threatening conditions that account

for 3.5%8.0% of complications following radical cystectomy [27].

These results showed that 6.6% of patients had developed deep vein thrombosis within peri-operative period, none of them escalated to pulmonary embolism. The enhanced recovery after surgery *(*ERAS) program recommends the prophylactic management of venous thromboembolism by using a low-molecular weight heparin for 19-21 consecutive days after radical cystectomy. The use of intermittent pneumatic compression or a compression stocking and early ambulation after surgery is preferred and encouraged in the event of persistent postoperative bleeding or a high risk of bleeding [28]. Also, extended lymphadenectomy occasionally leads to complications, such as the formation of lymphocele or lymphedema [10], [11].

In this study,6% of the patients underwent Extended lymphectomy.12.9% of patients had developed uncomplicated lymphocele <2% required u/s guided aspiration or drainage ,there was statistical significance between lymph node positivity and relation to deep vein thrombosis & lymphocele with P value 0.017 and 0.023 respectively & with even higher statistical significant between number of retrieved lymph nodes and incidence of deep vein thrombosis & lymphocele with p value<0.001.but, Nevertheless, recent studies have shown survival gains from extended lymphadenectomy; there is a focus on the procedures and these apply to all bladder cancer patients. Consequently, the risk of lymphocele or lymphedema is increased. Thus, surgeons should take care to minimize injury to the adjunct tissue and ensure proper ligation or clipping of the lymphatic vessel to prevent lymphadenectomy-related complications [29],[30].

Obturator nerve injury (ONI) is a rare but important complication and has been reported to occur with a frequency of (0.7%) during pelvic lymphadenectomy. In these results, it was similar with incidence in 3 patients (0.6%). one of them was partial injury which is encountered during laparoscopic assisted radical cystectomy (LARC) [31].

Conclusion:

Open radical cystectomy still is the standard of care in treatment of urinary bladder cancer, with a great upcoming results with laparoscopic radical cystectomy.

Radical cystectomy is a complex operation and has avoidable post-operative morbidity and mortality. Some authors have reported measures to help reduce or prevent them. Various technical improvements in the surgical and anesthesia techniques, multi-disciplinary approach for correction/control of comorbidities and early postoperative rehabilitation have produced salutary effect in reducing the mortality.

Authors' contributions

DW, AZ, IA and MH conceived the study, participated in data collection, the study design and surgical technique. MH participated in data collection, sequence alignment and coordination and drafted the manuscript. All authors read and approved the final manuscript.

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