Chulalongkorn Medical Journal

Volume 60
Issue 1 *January 2016*

Article 1

1-1-2016

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Chula Med J Vol. 60 No. 1 January-February 2016

Perioperative outcomes of open radical cystectomy in bladder carcinoma: King Chulalongkorn Memorial Hospital experiences

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Boonnam S, Panumatrassamee K, Opanuraks J, Santi-ngamkun A, Tantiwongse K, Ratchanon S, Bunyaratavej C, Usawachintachit M, Prasopsanti K. Perioperative outcomes of open radical cystectomy in bladder carcinoma: King Chulalongkorn Memorial Hospital experiences. Chula Med J 2016 Jan – Feb;60(1): 1 - 12

Background : *Radical cystectomy is the treatment of choice for muscle-invasive and refractory superficial bladder carcinoma.*

Objectives : *To report the perioperative outcomes and complications of open radical cystectomy.*

Materials and Methods : *We retrospectively reviewed all medical records of patients who underwent open radical cystectomy for bladder carcinoma at our hospital between January 2003 and June 2013. Patients' demographic data, operative outcomes and pathological study were recorded. Thirty-day postoperative complications were classified by modified Clavien Classification.*

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Results : *One hundred and forty-four patients with mean age of 64 years were included. There were 115 males and 29 females in this study. Nineteen patients had concomitant procedure (9 unilateral nephroureterectomy, 1 bilateral nephroureterectomy and 9 urethrectomy). Ileal conduit was the major procedure for urinary diversion (91.6%). Mean operative time was 340 minutes. Mean estimated blood loss was 2,177 ml. Postoperative complication rate was 83.3% included 17.4% of major complications (CCSC grade 3). The most common complications were electrolyte imbalance, anemia required transfusion and prolonged ileus. Four (2.8%) mortalities occurred from severe septicemia with multi-organ failure. The pathological study showed high grade transitional cell carcinoma (79%) was the most common cell type and 70.4% of patients were muscle invasive bladder carcinoma.*

Conclusion : *Although radical cystectomy had high complication rate, the majority of them minor complications and could be managed conservatively. It is, however, a standard treatment in muscle invasive bladder carcinoma.*

Keywords : *Bladder carcinoma, bladder tumor, complications, radical cystectomy.*

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Received for publication. March 5, 2015.

ศีลวัต บุญนำ, กมล ภานุมาตรัศมี, จุลินทร์ โอภานุรักษ์, อภิรักษ์ สันติงามกุล, กวิรัช ตันติวงษ์, สุพจน์ รัชชานนท์, ชนธีร์ บุณยะรัตเวช, มนินธ์ อัศวจินตจิตร์, เกรียงศักดิ์ ประสพสันติ. การศึกษาผลการรักษาและภาวะแทรกซ้อน ในช่วง 30 วันหลังการผ่าตัดกระเพาะปัสสาวะแบบแรดิคอลในผู้ป่วยเนื้องอกกระเพาะปัสสาวะ ในโรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2559 ม.ค. – ก.พ; 60(1): 1 – 12

เหตุผลของการทำวิจัย : *การผ่าตัดกระเพาะปัสสาวะแบบแรดิคอลในปัจจุบันถือเป็นการรักษาแบบมาตรฐานสำหรับมะเร็งกระเพาะปัสสาวะชนิดลุกลามกล้ามเนื้อกระเพาะปัสสาวะและชนิดไม่ลุกลามกล้ามเนื้อกระเพาะปัสสาวะที่ไม่สามารถรักษาด้วยวิธีการอื่นได้*

วัตถุประสงค์ : *เพื่อศึกษารายงานผลการรักษาและภาวะแทรกซ้อนในช่วง 30 วันหลังการผ่าตัดกระเพาะปัสสาวะแบบแรดิคอลแบบเปิดที่โรงพยาบาลจุฬาลงกรณ์*

รูปแบบการวิจัย : *การศึกษาวิจัยย้อนหลังเชิงพรรณนา*

สถานที่ทำการศึกษา : *โรงพยาบาลจุฬาลงกรณ์*

ตัวอย่างและวิธีการศึกษา : *ผู้ป่วยมะเร็งกระเพาะปัสสาวะทุกรายที่ได้นับการรักษาด้วยวิธีการผ่าตัดกระเพาะปัสสาวะแบบแรดิคอลแบบเปิดที่โรงพยาบาลจุฬาลงกรณ์ ตั้งแต่เดือนมกราคม พ.ศ. 2546 ถึง เดือนมิถุนายน พ.ศ. 2556 โดยทำการเก็บข้อมูลจากแฟ้มประวัติผู้ป่วยนอก และข้อมูลประวัติการเป็นผู้ป่วยใน*

ผลการศึกษา : *พบว่ามีผู้ป่วยที่เข้าเกณฑ์การศึกษาทั้งสิ้น 144 ราย เป็นชาย 115 ราย หญิง 29 ราย อายุเฉลี่ย 64 ปี ระยะเวลาผ่าตัดเฉลี่ย 340 นาที ประมาณการเสียเลือด 2,177 มิลลิลิตร พบภาวะแทรกซ้อนหลังผ่าตัดทั้งหมดร้อยละ 83.3 โดยเป็นภาวะแทรกซ้อนชนิดรุนแรงร้อยละ 17.4 ภาวะแทรกซ้อนที่พบบ่อยที่สุด ได้แก่ ภาวะระดับเกลือแร่ในเลือดผิดปกติ ภาวะซีดหลังผ่าตัด และภาวะท้องอืด ซึ่งถือเป็นภาวะแทรกซ้อนชนิดไม่รุนแรง พบมีอัตราการเสียชีวิตหลังผ่าตัดร้อยละ 2.8 สาเหตุการเสียชีวิตทั้งหมดเป็นจากการติดเชื้อรุนแรงในกระแสเลือด ผลการรายงานทางพยาธิวิทยาพบว่าร้อยละ 79 ของผู้ป่วยเป็นมะเร็งกระเพาะปัสสาวะชนิด ทรานซิชั่นนอลเซลล์แบบเกรดสูง และร้อยละ 70 ของผู้ป่วยเป็นชนิดลุกลามกล้ามเนื้อกระเพาะปัสสาวะ*

สรุป : *การผ่าตัดกระเพาะปัสสาวะแบบแรดิคอลนั้นมีอัตราการเกิดภาวะแทรกซ้อนได้สูง แต่ส่วนใหญ่เป็นเพียงภาวะแทรกซ้อนชนิดไม่รุนแรง และสามารถแก้ไขได้ด้วยการรักษาแบบประคับประคอง ปัจจุบันจึงยังถือเป็นวิธีมาตรฐานในการรักษามะเร็งกระเพาะปัสสาวะชนิดลุกลามกล้ามเนื้อกระเพาะปัสสาวะอยู่*

คำสำคัญ : *มะเร็งกระเพาะปัสสาวะ, ภาวะแทรกซ้อน, ผ่าตัดกระเพาะปัสสาวะแบบแรดิคอล.*

Bladder cancer is the second most common cancer of the genitourinary system. In Thailand, the incidence of bladder cancer is 4.4/100,000 in male and 1.2/100,000 in female. The incidence is high in old age. [1] The most common histopathology is transitional cell carcinoma (TCC). [2]

At present, radical cystectomy with pelvic lymph nodes dissection is still a standard treatment of muscle invasive bladder cancer and in non-muscle invasive bladder cancer that cannot be treated by bladder preservation therapy.[3] Radical cystectomy is a major surgery associated with high perioperative complications. Moreover, most of the patients were elderly and had medical comorbidities such as diabetes, hypertension and cardiac disease. Complications related to radical cystectomy varied from minor to major ones. The incidence of complication was 27.3 - 68% in the previous literatures with mortality rate 0.8 - 2%. [4 - 6]

Therefore, the objective of this study to report the perioperative outcomes including complications in our patients who underwent open radical cystectomy for bladder cancer at King Chulalongkorn Memorial Hospital within the last ten-years.

Materials and Methods

We retrospectively reviewed all medical records of 144 patients who underwent radical cystectomy for bladder carcinoma by open approach between January 2003 and June 2013 at King Chulalongkorn Memorial Hospital. Data were systemically collected according to the Martin criteria. [7] Analyzed parameters included age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, preoperative and surgical staging, previous surgical history, concomitant procedure, operative time, estimated blood loss (EBL), type of urinary diversion and length of stay. Categorical data were reported as count (%) and continuous data were reported as mean (SD) and median (IQR). All statistical analyses were performed using SPSS version 17.0.

Perioperative complication was defined as any complication that occurred within 30 days after surgery. Complications were categorized by Clavien-Dindo Classification of Surgical Complication (CCSC). CCSC grade 2 was defined as minor complication and CCSC grade > 2 was defined as major complication.[8] Prolonged ileus was defined as delayed recovery of the bowel function after surgery resulting in prolonged nasogastric tube decompression and/or requirement of parenteral nutrition. Pathologic staging (TNM) was classified following the American Joint Committee on Cancer (AJCC) 2002.[9]

We admitted the patients 2 days prior the surgery. Then, bowel preparation and prophylactic antibiotics were given to all patients. All procedures were performed under general anesthesia and the patients were monitored at the intensive care unit (ICU) after surgery.

Radical cystectomy was performed including the en bloc removal of the bladder with surrounding perivesical soft tissues, seminal vesicles and prostate in the male. In the female, the uterus, both ovaries and anterior vaginal wall were removed.[9] Standard bilateral pelvic lymph nodes dissection was routinely done. Urethrectomy in the male was performed in patients who had tumor that involved the prostate gland or urethra. Nephroureterectomy was concomitantly performed in patients with synchronous

upper urinary tract tumor. Urinary diversion was done with two main techniques: ileal conduit and ileal neobladder, depending on the surgeon and patient's preference. Ureteral stents were placed by using a feeding tube and removed postoperatively.

The study has been approved by the Institutional Review Board (IRB) of King Chulalongkorn Memorial Hospital (IRB number 628/57). All data were based on chart reviews.

Results

Patients' demographic data and operative outcomes are summarized in Table 1. The mean patients' age was 64.6 years. Most patients were male (79.9% : 20.1%). The mean BMI was 23.1 kg/m^2. No patient had ASA score 4 and 5 preoperatively.

Table 1. Patient characteristics and operative outcomes.

Variable	
Age, Year, Mean (SD)/ Median (IQR)	64.6(11.6)/ 66(58 - 74)
Gender	
Male	115(79.9%)
Female	29(20.1%)
Body mass index, Mean (SD)/ Median (IQR)	23.1(3.7)/ 23.5(20.4 - 25.2)
ASA*score	
1	23(15.9%)
2	96(66.7%)
3	25(17.4%)
Previous abdominal surgery	14(9.7%)
Number of previous TURBT*	
0	3(2.1%)
1	96(66.7%)
2	27(18.7%)
3	13(9%)
4	4(2.8%)
5	1(0.7%)
Pre-operative T stage*	
Non muscle invasive	26(18.1%)
Muscle invasive	118(81.9%)
Pre-operative histology (N = 138)	
Low grade transitional cell carcinoma	17(12.3%)
High grade transitional cell carcinoma	114(82.6%)
Adenocarcinoma	6(4.4%)
Carcinosarcoma	1(0.7%)
Data not available	6

Table 1. (Continuous) Patient characteristics and operative outcomes.

Variable	
Carcinoma in situ	5(3.5%)
Neo-adjuvant chemotherapy	1(0.7%)
Pre-operative radiotherapy	3(2.1%)
Concomitant procedure	
Urethrectomy in male	9(8%)
Unilateral nephroureterectomy	9(6.2%)
Bilateral nephroureterectomy	1(0.7%)
Urinary diversion (N = 142)	
Ileal conduit	133(93.7%)
Ileal neobladder	9(6.3%)
Operative time, minutes, Mean (SD)/ Median (IQR)	340(63)/ 340(300-385)
Estimated blood loss, ml, Mean (SD)/ Median (IQR)	2,177(1,898.8)/ 1,700(1,025-2,675)
Intraop. PRC* transfusion, Units, Mean (SD)/ Median (IQR)	3.4(2.6)/ 3(2-4)
ICU* stay, Day, Mean (SD)/ Median (IQR)	1.3(1.7)/ 1(1-1)
Length of stay, Day, Mean (SD)/ Median (IQR)	21(17)/ 16(12-23)
Time to start soft diet, Day, Mean (SD)/ Median (IQR)	9.2(5.2)/ 8(6-9)
Time to remove ureteric stent, Day, Mean (SD)/ Median (IQR)	14.3(4.7)/ 14(12-16)

*ASA (American Society of Anesthesiologists), TURBT (Transurethral Resection Bladder Tumor), T stage (Tumor staging according to 2002 TNM staging of bladder cancer), PRC (Packed Red Cell), ICU (Intensive Care Unit)

Preoperative tumor staging from tumor pathology and imaging study (Computed tomography or magnetic resonance imaging) showed muscle invasive bladder cancer in 110 cases (76.4%). The most common cell histology was high grade TCC (82.6%). Three patients had previous radiation treatment before surgery and one patient received neoadjuvant chemotherapy.

The mean operative time was 340 minutes: mean estimated blood loss 2,177 ml: mean intraoperative transfusion 3.4 units of packed red cell: mean postoperative ICU monitoring 1.3 days: and mean length stay 21 days. Ileal conduit was the most common type of urinary diversion (91.6%). Two patients with anephric stage after surgery had no urinary diversion.

Complications

Three hundred perioperative complications occurred in 120 patients (83.3%). Grades of complications are presented in Table 2: details of complications with management are presented in Table 3. The majority of complications were minor (66%). Four mortalities (Clavien grade 5) occurred in this study (2.8%); however, no intraoperative mortality occurred. The cause of death in all patients was severe septicemia with multiple organ failure.

Table 2. Perioperative complications classified by Clavien Classification (N = 144*)

Clavien classification	N (%)
No complication	24(16.7%)
Complication	120(83.3%)
Grade 1	39(27.1%)
Grade 2	56(38.9%)
Grade 3a	4(2.8%)
Grade 3b	11(7.6%)
Grade 4a	6(4.2%)
Grade 4b	0(0%)
Grade 5	4(2.8%)

*Highest grade of complication was used in patient who had more than one complication.

Table 3. Details of complication and management.

Clavien	Event of complication (n)	Management
1	Electrolyte imbalance (80)	Supportive treatment
	Wound infection (20)	Wound dressing
	Transient Cr rising (18)	Conservative treatment
	Diarrhea (10)	Supportive treatment
	Prolonged bowel ileus (6)	Conservative treatment
	Atelectasis (3)	Chest physiotherapy
	Pressure sore (2)	Wound dressing
	Upper GI bleeding (1)	Conservative treatment
2	Anemia (46)	Blood transfusion
	Prolonged bowel ileus (28)	Total parenteral nutrition
	Hypertension (17)	Medication
	Arrhythmia (7)	Medication
	Partial gut obstruction (6)	Conservative treatment
	Delerium (5)	Medication
	Urinary tract infection (7)	Antibiotic
	Deep vein thrombosis (2)	Anticoagulant
	Depression (1)	Medication
3a	Intra-abdominal collection (6)	Percutaneous drainage
	Upper GI bleeding (2)	Gastroscopy
	Arrhythmia (1)	Electro-conversion
	Deep vein thrombosis (1)	Inferior vena cava filter
	Pleural effusion (1)	Percutaneous drainage

Table 3. (Continuous) Details of complication and management.

Clavien	Event of complication (n)	Management
3b	Postoperative bleeding (6)	Laparotomy
	Wound dehiscence (5)	Re-suture wound
	Re-operation for off packing (1)	Laparotomy
	Bowel gangrene with anastomosis leakage (1)	Bowel resection
	Intra-abdominal collection (1)	Open drainage
	Pathologic fracture (1)	Internal fixation
	Entero-vaginal fistula (1)	Colostomy
	Entero-cutaneous fistula (1)	Laparotomy repair
	Lower GI bleeding (1)	Colonoscopy
4a	Respiratory failure (3)	ICU monitoring
	Cardiac arrest (1)	Cardiopulmonary resuscitation
	Congestive heart failure (1)	ICU monitoring
	Septic shock (1)	ICU monitoring
	Acute renal failure (1)	Dialysis
4b	Acute renal failure with multi-organ failure (1)	ICU monitoring
5	Septicemia with multi-organ failure (4)	-

Most common minor complication was electrolyte imbalance (*n* = 80), anemia required transfusion (*n* = 46) and prolonged bowel ileus required total parenteral nutrition (*n* = 28). Most common major complication was bleeding required re-laparotomy (*n* = 6) and intra-abdominal collection required percutaneous drainage (*n* = 6).

Histopathological reports

Surgical pathology reports are presented in Table 4. The most common histology was high grade TCC (84%). One hundred and seven patients (75.4%) had muscle-invasive bladder cancer (pT2). Carcinoma *in situ* (CIS) was presented in 21 patients (14.7%). Thirty-seven patients (25.7%) had nodal metastasis.

Discussion

Cancer of the bladder is the ninth most common malignancy worldwide.[10] The most common presenting symptom is painless hematuria. The choice of treatment depends on staging of the tumor by which it is divided into 2 groups: non-muscle invasive (superficial) and muscle-invasive bladder cancer. So far transurethral resection of bladder tumor (TUR-BT) and intravesicle agents are the treatments of choice for superficial bladder cancer while radical cystectomy is the treatment of choice for muscle invasive bladder cancer. [3, 9, 11]

From North America, Lavallee *et al*. [12] reported perioperative morbidity in 2,303 radical cystectomy patients. The overall complication rate was 55.3%. The most common complication was

Table 4. Surgical pathologic report.

Histologic type	N (%)
High grade transitional cell carcinoma	121(84%)
Low grade transitional cell carcinoma	15(10.4%)
Adenocarcinoma	5(3.5%)
Squamous cell carcinoma	1(0.7%)
Round cell tumor	1(0.7%)
Small cell neuroendocrine tumor	1(0.7%)
Carcinoma in situ	21(14.6%)
Pathologic T stage	
Ta	6(4.2%)
Tis	7(4.8%)
T1	22(15.3%)
T2a	24(16.7%)
T2b	16(11.1%)
T3a	19(13.2%)
T3b	27(18.8%)
T4a	23(15.9%)
pN stage	
N0	107(74.3%)
N1	18(12.5%)
N2	19(13.2%)

transfusion due to post-operative anemia (38%) and infectious-related complications (27.6%). Perioperative mortality was 2.9%. Stein *et al*. [13] also reported 2.5% perioperative mortality rate from 1,054 patients in radical cystectomy for invasive bladder carcinoma.

From East Asia, Takada *et al*.[6] studied the perioperative morbidity and mortality of radical cystectomy from multi-center in Japan. Their major complication was 17% and 30-day mortality rate was 0.8%. Cardiovascular morbidity and type of urinary diversion were the risk factors of major complications.

Nowadays, minimally-invasive surgery especially robot-assisted laparoscopic surgery plays an important role in Urology including radical cystectomy. Bochner *et al*.[14]reported a randomized clinical trial comparing the outcomes of radical cystectomy between open and robot-assisted approaches. The robot-assisted group had significantly lower intraoperative blood loss ($p = 0.027$) but longer operative time ($p < 0.001$). CCSC grade 2 - 5 was insignificant difference between the two groups (66% *vs* 62%, $p = 0.7$). Mortality rate was 1.7% with open approach while none in robot-assisted group. Most common complications were infection and postoperative ileus.

Santos *et al*. [15] studied the effect of hospital size and surgeon experience on the outcome of radical cystectomy. The risk of mortality was 13% reduction in high-volume hospital and 20% decrease in high-volume surgeon operated at a high-volume hospital.

The aim of our study is to report the outcomes of open radical cystectomy in a tertiary-care, referral hospital in Thailand. The complication rate in our series was 83.3% which was 17.4% of major complication and 2.8% of mortality.

Our overall complication rate was higher than in the previous literatures. We strictly reported any events that differed from the normal postoperative pattern as complication i.e. electrolyte imbalance, transient rising of serum creatinine and anemia that required transfusion which were not reported in others studies as complications. However, the majority of our complications were minor which could be managed conservatively. Patients with bladder cancer usually have low baseline hemoglobin level because of previous hematuria. Therefore, blood transfusion was expected when radical cystectomy was performed.

Limitation of our study was the retrospective descriptive study design. The procedures were performed by multiple surgeons that could affect the surgical outcomes. The oncological outcome was not assessed in this study, however.

Conclusion

Although radical cystectomy had high complication rate, majority was minor complication and could be managed conservatively. So far it still remains a standard treatment in muscle invasive bladder carcinoma.

Conflict of interest

All authors hereby declare no conflict of interest.

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