

Pathological Profile, Early Complications, Functional and Oncological Outcome after Radical Cystectomy - Ileal Conduit for Bladder Cancer Patients in Sanglah General Hospital between January 2013 and December 2016

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Abstract

Citation: Wayan Y, Ayu PD, Gde OAA, Wayan N, Widyadharma IPE. Pathological Profile, Early Complications, Functional and Oncological Outcome after Radical Cystectomy - Ileal Conduit for Bladder Cancer Patients in Sanglah General Hospital between January 2013 and December 2016. Open Access Maced J Med Sci. <https://doi.org/10.3889/oamjms.2018.384>

Keywords: Bladder cancer; Radical cystectomy; Ileal conduit; The oncological outcome

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Received: 29-Jul-2018; **Revised:** 08-Sep-2018; **Accepted:** 09-Sep-2018; **Online first:** 23-Sep-2018

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Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

BACKGROUND: Radical cystectomy is the standard treatment for nonmetastatic bladder cancer (muscle-invasive and selective superficial bladder cancer). There are many types of urinary diversion after this procedure; the ileal conduit is the most and simplest one.

AIM: To assess clinical, pathological profile, early complication, functional and oncological outcome after radical cystectomy and ileal conduit for muscle-invasive bladder cancer patients.

METHOD: Between January 2013 and December 2016, there were 68 patients diagnosed with bladder cancer. From those patients, 24 (35.29%) patients had been performed radical cystectomy with ileal conduit type for urinary diversion (100%). Patients demographic, clinical and pathological profile, early postoperative complication, functional and oncological outcome were collected from the medical record.

RESULT: Among the 24 patients who underwent radical cystectomy, 20 patients were male (83.3%) with the mean age was 57.3 y.o (33–77 y.o). Twelve patients (50%) showed pT4 and pT2 respectively. Based on pathological result 20 patient (83.34%) had the urothelial carcinoma, three patients (12.5%) had squamous cell carcinoma, and one patient (4.1%) had adenocarcinoma. Two patients (8.3%) got neoadjuvant chemotherapy, and nine patient (37.5%) of patients followed adjuvant chemotherapy after surgery. Wound dehiscence, fistula enterocutan, prolong ileus, leakage anastomosis and sepsis were kind of complication after surgery. One year's survival rate is 84%, mortality rate 20.8% and a recurrence rate of 20.8% in 4 years follow up.

CONCLUSION: Radical cystectomy and ileal conduit type of urinary diversion still become the preferable procedure for nonmetastatic bladder cancer with good functional and oncological outcome.

Introduction

Radical cystectomy with bilateral pelvic lymphadenectomy is the standard treatment for muscle-invasive and high-risk non-muscle-invasive urothelial carcinoma of the bladder. There are numerous choices for urinary diversion after radical cystectomy; ileal conduit continues to be the most common form of urinary diversion [1] [2].

Improvements in surgical techniques and modern perioperative care have substantially decreased the rate of perioperative complications and lowered the operative mortality rate. However, this

procedure remains complication-prone and is associated with significant perioperative and long-term morbidity ranging from 19% to 64% according to different series [3]. In several large series, the overall recurrence-free survival at five years for patients undergoing cystectomy approaches 70%, ranging from 50 to 60% for stage 3 or 4 tumours and 89 % for stage 2 tumours [3] [4].

Countless retrospective studies unquestionably support radical cystectomy excellent oncologic outcomes and satisfactory postoperative quality of life (QoL) at long-term follow-up. Although much of the clinical evidence coming from these studies are of low quality, major international

guidelines strongly recommend radical cystectomy as the elective treatment for muscle-invasive bladder cancer. For more than 30 years, the ileal conduit (IC) has been considered the “standard” urinary diversion method for most patients submitted to radical cystectomies. It is recognised as the most clinically adequate, reliable, and cost-effective solution.

Some complications are strictly related to IC and have been distinguished between early (before 90 days) and late (after 90 days). Early complication related to bowel complication such as intestinal anastomosis related, ureteral ileal anastomosis leakage, enteric fistula, bowel obstruction, prolonged ileus and conduit necrosis, whereas late complication related to stoma complication such as abdominal wall related, conduit stenosis, ureters enteric anastomosis stricture also Hydronephrosis, kidney failure, and metabolic changes [5].

This study aimed to investigate the clinical, pathological profile and complications related to radical cystectomy and ileal conduit patients with bladder cancer in Sanglah general hospital, Denpasar Bali.

Methods

From January 2013 to December 2016, there were 68 patients had been diagnosed with bladder cancer, 59 patient had the urothelial carcinoma, four patient had squamous cell carcinoma, five patient had adenocarcinoma. 30 patient already underwent chemotherapy, three patient had a partial cystectomy, and 24 patient (35.3%) had been performed radical cystectomies with following ileal conduit type or Bricker's procedure type of urinary diversion, remain of it 11 patient (16.17%) had refused for treated. We carried out a retrospective study by reviewing the medical records of those 24 patients who treated with open radical cystectomies and ileal conduit type for urinary diversion. Follow up on those patients continued until January 2017. Data were collected through follow-up visits in outpatient clinics, evaluated by the following history included: age and comorbid (diabetes mellitus, hypertension, ischemic heart disease), operative details, histopathological type and grading also the history of neoadjuvant and adjuvant chemotherapy were recorded. We were also collecting postoperative early complications and late complications, at early complications, we divided into diversion related and not diversion related. With a minimum follow up 6-month patients were routinely seen in the outpatient clinic for stoma care, oncologic follow-up and also late complications after the procedure.

Results

Pre characteristics database showed 20 patients (83.4%) was male, with the median age was 57.3 y.o (32-77 y.o). All patients came to the hospital with chief complained initiated gross hematuria or blood clot retention, some of them complained of dysuria too, 33.3% patients had suffered from UTI (Urinary Tract Infection), 20.83% patients had bladder stone and some suffered systemic comorbidities such as cardiovascular diseases (29.2%), type II diabetes Mellitus (8.3%) and prior renal failure (37.5%). Based on clinical, 20.83% patients with staging cT2 tumour preoperatively, 33.3% patients had cT3 and 45.83% with cT4. There is only two patient (8.33%) had neoadjuvant chemotherapy.

Table 1: Preoperative characteristic of bladder cancer patients who underwent radical cystectomies

Variables Preoperative	Result
Sex (%)	
Male	20 (83.4%)
Female	4 (16.6%)
Mean age (range)	± 57.3 y.o (33–77 y.o)
Chief complain	Hematuria (100%)
Local comorbidities (%)	
UTI	8 (33.3%)
Bladder stone	5 (20.83%)
Bladder diverticula	2 (8.34%)
Surgical history of bladder	3 (12.5%)
Systemic comorbidities (%)	
Cardiovascular comorbidity	7 (29.2%)
DM type II	2 (8.3%)
Chronic kidney failure	9 (37.5%)
Clinical staging (%)	
T1	-
T2	5 (20.83%)
T3	8 (33.3%)
T4	11 (45.83%)
Neoadjuvant Chemotherapy	2 (8.33%)

From perioperative data showed that the mean operation time was 351 minutes (310-435 minutes), and mean intraoperative blood loss was 1070cc (500 – 2500cc). 91.66% of patients performed bilateral pelvic lymph dissection. There was, two patients (8.33%) died one month after surgery because of sepsis.

Table 2: Perioperative data from patients with radical cystectomies

Variables Perioperative	Result
Mean Operation time (range)	± 351minutes (310-435 minutes)
Mean intra operative blood loss (range)	±1070 cc (500-2500 cc)
Pelvic Lymph dissection bilateral	
Yes	22 (91.66%)
No	2 (8.34%)

From postoperative and follow up data in the outpatient clinic we found that 50% patient showed pT4, and 50% had pT2, there is no pT3, 83.34% patients showed with transitional Cell ca (TCC) and one patient with a synchronous tumour with TCC and acinar adenocarcinoma prostate, 70.83% was high-grade carcinoma. In all cases, nine patients (37.5%) undergo adjuvant chemotherapy.

Table 3: Postoperative characteristics data from patients with radical cystectomies

Variables Postoperative	Result
Pelvic Lymph dissection (%)	
Yes	22 (91.66)
No	2 (8.34)
Pathological staging (%)	
pT1	-
pT2	12 (50%)
pT3	-
pT4	12 (50%)
Lymph Node Pathological	
pN0	13 (54.2%)
pN1	6 (25%)
pN2	3 (12.5%)
pNx	2 (8.3%)
Pathological type (%)	
TCC	20 (83.34%)
SCC	3 (12.5%)
Adenocarcinoma	1 (4.16%)
Pathological grading (%)	
Low grade	4 (16.7%)
Moderate grade	3 (12.5%)
High grade	17 (70.83%)
Adjuvant Chemotherapy	9 (37.5)

About the postoperative complication, we divided into an early and late complication, which early was taken 3 months after surgery and late was taken 3 months after surgery. Early complication related to bowel complication such as intestinal anastomosis related, ureteral ileal anastomosis leakage, enteric fistula, bowel obstruction, prolonged ileus and conduit necrosis, whereas late complication related to stoma complication such as abdominal wall related, conduit stenosis, ureters enteric anastomosis stricture also Hydronephrosis, kidney failure, and metabolic changes [5]. From the early complication include one patient had fistula enterocutan and 20.8% suffered prolonged ileus. Fifteen patients still alive in minimum follow up 12 months had a survival rate of 84%. Mortality rate 20.8%, causes of death shown at table 4: one patient (4.16%) died 2 months after surgery because of ileus, One patient (4.16%) died 1 year after surgery because of recurrence and metastasis, and one patient (4.16%) died 21 months after surgery because of metastasis. Recurrence happens in five patients (20.8%), 4 with local recurrence and 1 with distant metastasis. The distant metastasis went through bone metastasis.

Table 4: Complication characteristics from patients with radical cystectomies

Variables	Result
Early complication (%)	
Bowel related	
Prolonged ileus	5 (20.8%)
Fistula enterocutan	1 (4.16%)
Sepsis (<3 month)	2 (8.34%)
Late Complication (%)	
Stoma-related	
Ureter stenosis	1 (4.16%)
Electrolytes imbalance	1 (4.16%)
Wound dehiscence	5 (20.8%)
A hernia incisional	1 (4.16%)
Survive (>12 months)	15 (84%)
Mortality rate	5 (20.8%)
Cause of Mortality rate	
Sepsis	2 (8.34%)
Metastasis	2 (8.34%)
Ileus	1 (4.16%)
Recurrence	5 (20.8%)

Discussion

Radical cystectomy with pelvic lymph node dissection provides the best cancer-specific survival for muscle-invasive urothelial cancer and is the standard treatment, with 10-year recurrence-free survival rates of 50–59% and overall survival rates of around 45% [6] [7] [8] [9]. The primary goals in the selection of a urinary diversion are to provide the patient with the diversion that results in the best local cancer control, the lowest potential for both short and long-term complications and the best quality of life while still allowing the timely completion of chemotherapy and therapeutic goals [10]. Recently, many options for urinary diversion after radical cystectomy, but in our study ileal conduit still considered the "standard" urinary diversion for nonmetastatic bladder cancer. It is universally recognised as being the most clinically adequate, cost and time effective, and reliable solution in long-term. Other option for urinary diversion like neobladder still not yet performed in our institution because of for developing country like Indonesia, many patients with bladder cancer came from intermediate low social state and poor education so that ileal conduit type more acceptable than neobladder. However, a form of incontinent urinary diversion (ICUD) is the method of choice in elderly patients, and in those with high comorbidity (American Society of Anaesthesiologist Score [ASA] > 3), Ileal Conduit remains the preferred method [11].

Radical cystectomy with ileal conduit type of diversion entails simultaneous surgery on the urinary tract, intestines, and lymph nodes; hence, complications frequently occur after this extensive procedure. According to the literature, the incidence of such secondary conditions varies widely (from 19% to 64%). Hollenbeck et al., studied data on 2538 cases obtained from the National Quality Improvement Program, which is a prospective quality management initiative of 123 US Department of Veterans Affairs medical centres, and the results of that evaluation showed that 30.5% of the patients had at least one complication at 30-day follow-up after RC [12] [13] [14]. From postoperative data and follow up outpatient clinic we found that 50% patient had pT4, and 50% had pT2, there is no pT3. Based on pathological result 20 patient (83.34%) had urothelial carcinoma, 3 patient (12.5%) had squamous cell carcinoma, and 1 patient (4.1%) had adenocarcinoma, and one patient had a synchronous tumour with TCC and acinar adenocarcinoma prostate, 70.83% was high-grade carcinoma, while Enein et al. study showed TCC 59.5%, SCC 36%, and Adenocarcinoma 2%, moderate grade 56.5% and T3 46.5% [15].

Fifty percent of our patients came with the high stadium, more than stadium II of cancer, and not few of them came with metastatic bladder cancer. At the time of diagnosis, almost all high-grade bladder

cancer are muscle invasive. It is because of minimum information about cancer especially bladder cancer in our society, and low awareness about it, so there always almost all of the patients came with late bladder cancer. The decision to perform immediate radical surgery depends on several factors, including ASA, age, and life expectancy.

In our study the average patient loses 500ml to 2500 ml of blood during RC, indicating that this type of surgery often leads to considerable loss of blood and, consequently, to transfusions. Blood transfusions are associated with major complications and with high total hospital costs for RC [16] [17].

It is noteworthy that all patients in this study had a minimum follow up, and some of them, not well recorded and loss of follow up also. From complication data, we divided into an early and late complication, early taken before 3 months after surgery and late is made 3 months after surgery. From the early complication, only one patient had ureter stenosis, 20.8% had wound dehiscence, 20.8% patients had prolonged ileus, and 1 (4.1%) had an incisional hernia. The earliest complications in our study were wound dehiscence, it is probably because of bad hygiene, hypoalbuminemia, late immobilisation, and some of our patients had systemic comorbidities like diabetes mellitus type II. Kim et al., have searched about early and late complication, their study showed during the median follow-up of 46.6 months, early, and late morbidities were 29.5% and 19.8%, and complication-related mortalities were 2.2 and 6.6%, respectively [18].

Feared complications immediately after RC include internal anastomotic leak and urinary extravasation caused by anastomotic or reservoir leakage. In a prospectively randomised study [19], perioperative stenting was found to decrease urinary leakage. Even in the absence of available evidence, it seems wise to recommend that drains be left in place until anastomotic integrity is established in the intestinal and urinary tracts. Due to the relatively low extravasation rate associated with RC, it is probably not necessary to perform routine postoperative urography or stentograms in patients with a normal postoperative course [16]. Gastrointestinal events probably represent the most common type of complication during the period after RC. Postoperative intestinal anastomotic leakage has been described in 3% of patients [20], Compared to urinary or intestinal leakage, intestinal obstruction is more common as a complication of RC, and it was found to affect 23% of patients in a recent cystectomy series [20]. Infectious events are the second most common complications of RC, constituting 25% of all early complications within 90 d of the surgery, according to a recent investigation [20]. Adequate perioperative antimicrobial prophylaxis to prevent postoperative infectious complications is standard practice in the care of surgery patients, but information is lacking concerning the optimal schedule in conjunction with RC. Wound-related complications,

primarily dehiscence in the early postoperative period, constitute 15% of all early complications of RC [20]. However, when using a midline incision, several factors might affect the incidence of wound separation, including operational, technical issues. In contrast, a recent meta-analysis of 23 randomised studies comparing the interrupted and continuous methods of laparotomy wound closure demonstrated that the interrupted technique was associated with significantly less dehiscence (odds ratio: 0.58), whereas there was no difference concerning hernia risk [21].

In our study, Recurrence has arisen in 5 cases, 4 with local recurrence and 1 with distant metastasis while in a study by Jian et al., there was local recurrence in 9 patients (5.3%), distant metastasis in 23 patients (13.5%) and both in two patients (1.2%) [21].

Five patients (20.8%) had died from various causes; one patient (4.16%) died 2 months after surgery because of ileus, two patient (8.33%) died before one month after surgery because of sepsis, One patient (4.16%) died 1 year after surgery because of recurrence and metastasis, and One patient (4.16%) died 21 months after surgery because of metastasis, while in the study of Jian et al., there were 28 of 171 patients (16.4%) had died from various causes, 20 from metastasis and 8 from causes unrelated to the tumor (two from upper gastrointestinal bleeding, two from myocardial infarction, two from pneumonia, one from stroke and one from a car accident) [21].

Improvements in surgical techniques and modern perioperative care have substantially decreased the rate of perioperative complications and lowered the operative mortality rate. However, this procedure remains complication-prone and is associated with significant perioperative and long-term morbidity ranging from 19% to 64% according to different series. The Ileal conduit remains the most frequent form of urinary diversion, published first in 1952 and became popular and is still the Gold Standard. The technique proved to be quick, safe and straightforward compared to neobladder [11].

In conclusion, the Ileal Conduit can still be considered an appropriate surgical solution after Radical Cystectomy in most patients because of the relative simplicity of the surgical technique, the acceptable complication rate, and the satisfactory postoperative Quality of Life. Our patients still need to be follow up till next 5-10 years after surgery, to maintain the late complications after surgery. After all, yet to be our job to give more education and information about cancer issue, to raise awareness and to reduce morbidity, and gained the better quality of life for cancer patients. Careful patient selection, strict adherence to proper surgical technique and appropriate life-long follow-up are of paramount

importance in the successful management of patients undergoing radical cystectomy for bladder cancer.

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