

Laparoscopic Radical Cystectomy in a Low-Middle Income Country: A 5-Year Review of a Single Institution; Operative Data, Oncologic Results and Morbidity

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Abstract

Introduction and Objective: Laparoscopic radical cystectomy (LRC) is an alternative to open approach with lower morbidity and better oncologic outcome. We aim to share our experience on laparoscopic radical cystectomy and to evaluate our morbidity and oncological outcome in our settings. **Methodology:** An observational study in the Douala Medico-Surgical Urology Centre on 5 patients who underwent laparoscopic cystectomy with or without lymph node dissection and external urine diversion between April 2014 to July 2016 was conducted. The overall survival rate was subsequently estimated. **Results:** Four men and one woman underwent laparoscopic radical cystectomy during the 5-year study period with a mean age of 54.5-year-old. Three patients were submitted to ileal conduits, one to neobladders, and one patient to uretero-cutaneostomies. The mean operative time was 300 ± 17 minutes and the mean length of hospital stay was 9 ± 3 days. Three patients had minor complications according to Clavien and Dindo Classification treated conservatively without need for further operation. Four patients had transitional cell carcinoma and one Squamous cell carcinoma types. Everyone had negative resection margin while only two had negative lymph node. The median survival years in our study was 2.5 years, the overall survival rates at 2 years were 60%, 40% at 3 years and 20 at 5 years. 2 patients die after one year due to renal failure and intercurrent disease. **Conclusion:** Laparoscopic radical cystectomy is a safe and effective approach for the treatment of bladder cancer in a low-middle income country.

tectomy carried lower morbidity and cancerological outcome compare to open surgery making it a good alternative for bladder oncologic surgery.

Keywords

Radical Cystectomy, Laparoscopy, Oncology Findings, Bladder Cancer

1. Background

Radical cystectomy (RC) with pelvic lymph node dissection and urinary diversion is the preferred treatment for non-metastatic muscle-invasive bladder cancer (BC), and for some cases of high-risk non-muscle-invasive BC, in patients fit for major surgery [1]. RC is a comprehensive procedure that involves surgery to several organ systems and as a result it is associated with high postoperative morbidity and mortality. This procedure can be performed by laparotomy, laparoscopy or robot-assisted surgery [2].

The classic approach is the open surgery which has evolved since its first description nearly 80 years ago [2] [3]. Perioperative outcomes have slowly improved, but overall, 90-days complication rates have been reported to be as high as 65% [4]. Morbidity can particularly correlate with urinary diversion technique [5]. Laparoscopic techniques were first used for radical cystectomy in 1992 for neurologic bladder then in 1993, Sanchez De Badajoz introduce this approach in the treatment of bladder cancer due to its benefits such as reduce postoperative pain, less blood loss, shorter hospital stays, earlier return to normal activity and cosmetic benefits [6] [7] [8].

The frequency of radical cystectomy worldwide is not-well known. Approximately 2100 cystectomies are performed in each year in England among which 37.9% are Laparoscopic Radical Cystectomy (LRC) [9]. In hospital-based studies, there were 185 cystectomies perform over 4 years in Japan [10]. Whereas, in Africa, from 2007 to 2013 a single South African centre performed Thirty (30) patients LRC and 32 ORCS [11]. In Egypt, LRC was completed for 47 patients [12]. Improvements in perioperative care, anesthesia, and surgical technique have led to a decrease in postoperative mortality with rates from 20% in the late 1970s to currently between 2.5% and 7.9% [13] [14].

Bladder cancer is diagnosed based on a bladder biopsy histologic analysis after white light or fluorescent cystoscopy [15]. The biopsy histology results, combined with the imaging work-up and a detailed exploration of the entire urinary tract, allow to classify patients into 3 main therapeutic and prognostic groups [15]: non-muscle invasive bladder cancer ($T^* < a$, T is and T1 lesions 2); Muscle-invasive bladder cancer ($T^* \geq 2$) and Metastatic bladder cancer. Moreover, this classification allows us to determine the therapeutic management of patients with urothelial bladder carcinoma. Therefore, palliative chemotherapy is indicated in patients with metastatic disease [16]. For Non-muscle-invasive bladder cancer,

treatment will consist of a complete transurethral resection of bladder tumour followed by intravesical therapy with some agents. Under certain circumstances, radical cystectomy may be indicated [17].

Higher surgical volume is associated with improved outcomes [18] [19], but the magnitude of this effect remains controversial. While several studies emphasize the importance of the surgeon's experience [18], the influence of treating institution and perioperative management might be additional key factors to reduce in-hospital morbidity and mortality [19].

Significant worldwide involvement has advanced the Laparoscopic radical cystectomy (LRC) technique from initial single case report to compelling more sophisticated series with reproducible procedures, therefore LRC is enhancing as an acceptable treatment replacement of ORC. In Africa this approach is still very little used due to the cost of surgery and the socio-economic level of the patients [20]. From our literately review, data on LRC series in low-middle income countries are available. Therefore, we will report our centre 5-year experience with LRC and LND and urinary diversion operative results, morbidity and oncological outcome to improve the knowledge gap between our region and the world.

2. Methodology

2.1. Type of Study, Location

A 5 patient's case series was carried out in the Douala Medico-Surgical Urology Centre as an observational descriptive cohort study. This is specialised urology centre, which has 5 urological surgeons among who an experienced laparoscopic surgeon who frequently perform several laparoscopic procedures, including radical cystectomies.

2.2. Study Population, Study Period, Sampling, Inclusion and Exclusion Criteria

In this Case series study, all patients who met the selection criteria during April 2014 to July 2016 were recruited regardless of gender, age and race. Patients with pathologically confirmed bladder cancer who underwent laparoscopic radical cystectomy and pelvic lymph node dissection and urinary diversion were included. We excluded: patients who did not consent, patients who underwent open cystectomy, patients with metastatic disease and those who were lost to follow-up at the end of treatment.

2.3. Procedures

Diagnosis and staging: The diagnosis of bladder cancer was made on the basis of the result of a transurethral bladder biopsy providing oncological evidence of the tumor and histological grading. Patients were staged using the 2017 TNM classification [20]. All patients had abdominal and pelvic CT scans to complete the staging.

Complications: The complications were classified according to the Clavien-

Dindo classification (CDC) of surgical complications. We considered CDC I and II as minor complications and CDC III and above as major complications.

Operative technique: With the patient under general anaesthesia and Trendelenburg position, a 10 mm umbilical port is placed using lift abdominal technique. This allows introduction of a 10 mm 30° lens. Under direct vision pneumoperitoneum is induced. Right and left 5 mm port are placed 4 to 6 cm superior to the pubic symphysis below the camera port, just lateral to the respective rectus muscles bilaterally and symmetrically to allow introduction of 5mm trocars. The fourth port (12-mm right assistance port) is placed approximately 5 cm above the right anterior superior iliac spine in the mid-axillary line. We start with Lymph node dissection to remove bilateral obturator and iliac lymphadenectomies. We then proceeded with identification and dissection of the ureters follow by posterior dissection then anterior dissection to extract the bladder. For urine diversion we did mini-laparotomy under direct visual control. There were not specific criteria for choosing the type of diversion, this choice was made by the surgeon and patients after discussing the risks and benefits of each type of diversion on each individual situation. A 14 French drain is left in the abdominal cavity after surgery.

Outcome Measures and Analysis: The outcome measures evaluated the patients' demographics, cystectomy pathology grading, operative time, conversion rate, urinary diversion method, length of hospital stay, rehospitalisation, adjuvant chemotherapy and complication rates.

Follow-up: Patients were seen in clinic one month postoperatively, then every three months for the first year, then every six months for the next year, then on a yearly basis. Follow-up investigations consisted of transabdominal ultrasound, CT scan and LAB Tests including FBC, Serum electrolyte, CRP, Urine culture and sensitivity, renal and liver functions Tests

Ethical considerations: Before the start of recruitment, we obtained clearance from the ethical review board of the institution. Written informed consent was obtained from patients for publication of this case series and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal. Any identifying material has been removed, including the patient's name, date of entry, face or any distinctive features on the pictures taken. The collected data has been codified and stored in strict respect for the privacy of patients.

3. Results

3.1. Clinical Manifestations, Risks Factors, Diagnosis, Staging

A total of 5 patients with bladder tumours who underwent LRC were included in the study. The majority of patient were men (4 men to 1 woman) with a mean age of 54.5 years ranging from 34 to 74 years (**Table 1**). The histologic type for 4 of our patients was Urothelial carcinoma while one who 3 years earlier was diagnosed with a muscle invasive Urothelial tumour had an Urothelial carcinoma with epidermoid differentiation. In this latter, an endoscopic resection was per-

formed, with histologically healthy margins; then, Bacillus Calmette Guerin (BCG) immunotherapy therapy was then initiated. Regarding risk factors, apart from BCG therapy, only 1 patient was a smoker (Table 1). All presented with muscle-invasive form of the disease ($T^* \geq 2$). One patient presented with a bladder tumour alongside a concurrent renal pelvis tumour. A staging computer tomography proven organ confined tumour cT2N0M0 for 2 patients, lymph node extension for two patients (cT2N1M0) who also had lymph node involvement and the last one had an extravesical tumour cT3N0M0.

3.2. Treatment Protocol, Surgery and Postoperative Follow Up

Base on the preoperative histologic results, RC was practice because of muscular invasive disease ($T^* \geq 2$) in 100% of the cases; in one patient radical cystectomy was associated with a right ureteronephrectomy (Table 2). All the procedures were done through laparoscopic approach with mini-invasive laparotomy urine diversion, there were no conversion. With respect to the type of urinary derivation, Ileal conduit was performed in 3 patients out 5 patients, while orthotopic

Table 1. Clinical and histological characteristics of patients.

Patient	Age (Years)	Sex	Risks factors	Comorbidities	Clinical manifestations	Grade (G)	TNM	Stage
Patient X	32	M	None	None	Painless gross haematuria	G2	cT ₂ N ₀ M ₀	IIIA
Patient Y	47	F	Tobacco	None	Painless gross haematuria	G3	cT ₃ N ₁ M ₀	IIIA
Patient Z	62	M	None	None	Painless gross haematuria with voiding symptoms	G2	cT ₂ N ₀ M ₀	II
Patient M	62	M	BCG Therapy	PMH of Non-infiltrative bladder cancer	Painless gross haematuria	G3	cT ₂ N ₀ M ₀	II
Patient B	74	M	None	None	Painless gross haematuria	G3	cT ₂ N ₁ M ₀	IIIA

Abbreviations: BCG: Bacillus Calmette-Guérin; PMH: Past Medical History; TNM: Tumour, Node, Metastasis; c: clinical.

Table 2. Distribution and description of surgical intervention, urine diversion, length of stay, operative time and complications.

Patient	Type of resection	Type of urinary diversion	Operative Time (minutes)	Hospital Stay (Days)	Complication (grade)*	Timeframe of complication (days)
Patient X	Cystoprostatectomy	Ileal Conduits (Briker)	260	6	Grade I	8
Patient Y	Anterior pelvectomy and right ureteronephrectomy	Uretero-cutaneostomy	350	12	Grade IV	10
Patient Z	Cystoprostatectomy	Orthotopic neobladder	310	10	Grade IV	9
Patient M	Cystoprostatectomy	Ileal Conduits (Briker)	270	9	Grade I	7
Patient B	Cystoprostatectomy	Ileal Conduits (Briker)	310	8	Grade II	10

*Graded according to Clavien-Didon classification of surgical complications [25].

Table 3. Distribution and detailed description clinical and pathologic stage, histology result, adjuvant chemotherapy and margin.

Patient	Age (Years)	Clinical stage	Pathological stage	Histology	Margin	Adjuvant chemotherapy	Survival years
Patient X	32	G2cT2N0M0	G2pT2N0M0	Transitional carcinoma	Negative	Gemcitabine-cisplatin	5
Patient Y	47	G3cT3N1Mx	G3PT3N1Mx	Transitional carcinoma	Negative	Gemcitabine-cisplatin	1
Patient Z	62	G2cT2N0M0	G1pT2N1M0	Transitional carcinoma	Negative	G2	1
Patient M	62	G3cT2N0M0	G3pT2N0M0	Transitional carcinoma with epidermoid differentiation	Negative	Gemcitabine-cisplatin	1
Patient B	74	G3cT2N1M0	G2pT3N1M0	Transitional carcinoma	Negative	Gemcitabine-cisplatin	4

neobladder and ureterocutaneostomies. was done for 1 patient each. The mean operative time was 300 min, the mean length of stay was 9 days, no patient dies during the surgery nor was rehospitalise within 30 days postoperatively.

The pathological staging post cystectomy is on (Table 3). Only two patients had similar clinical and pathological stages. However, 3 patients had positive lymph node and received adjuvant chemotherapy with gemcitabine and cisplatin. Transitional cell carcinoma was the histologic diagnosis in the cystectomy specimen, one had an associated epidermoid tumour. All specimens had negative surgical margin.

3.3. Complications and Survival Rates

Minor complications (Clavien-Dindo 1 to 2) within 10 days of cystectomy occurred in all patients, in details grade I: 2 cases of vomiting manage with antiemetic, 2 cases of paralytic ileus manage with fluid rehydration and electrolyte and a case of abdominal sepsis due to Surgical Site infection manage at the bed side with dressing. In regard to late complication, patients with Incontinent urine diversion (Briker), there was no complication such as renal failure or urolithiasis base on clinical and paraclinical continuous evaluation after 4 years follow up.

The patient with orthotopic bladder, reported 80% daytime continence after 6 months.

The follow-up period lasted approximately 30 months. The median survival years in our study was 2.5 years, the overall survival rates (Table 3) at 2 years were 60%, 40% at 3 years and 20 at 5years. 2 patients die after one year due to renal failure and intercurrent disease (gastroenteritis).

4. Discussion

Bladder cancer is a cancer of the elderly. The median age at diagnosis is 73 years [21]. In subSaharan Africa, the age at diagnosis varies between 65 and 75 years for urothelial carcinomas and 45 to 65 years for squamous cell carcinomas (SCC) [22]. In our series, the population was younger, with ages between 34 and 74 years. Even those according to the literature bladder tumour are rare before the age of 40 years accounting only for 1% - 4% of all cases. The ratio of male to

female in the present study was 4:1.

In Africa, Squamous Cell Carcinoma is often encountered in the context of schistosomiasis. The predominant histological type in our series was TCC, only one case of associated SCC was diagnosed in a patient with a history of intravesical Bacillus Calmette-Guerin (BCG) immunotherapy. Indeed, the risk factors identified for SCC are mainly chronic cystitis from various causes: bladder calculi, recurrent urinary tract infections, schistosomiasis, BCG and pelvic irradiation. Smoking and prolonged use of cyclophosphamide have also been cited [23].

Radical Cystectomy with pelvic lymphadenectomy is the gold standard treatment for muscle-invasive bladder cancer [2] [16]. The operative goals of the surgery are to ensure negative surgical margin and an adequate Lymph node dissection (LND) [2]. Other cystectomy indications include non-invasive bladder tumours that are either recurrent, high grade, SCC or multifocal [2] [17].

During radical cystectomy, several procedures may be combined depending on the stage of the disease. Anterior or posterior pelvicotomy may be associated, as well as nephro-ureterectomy. In our series one patient presented with a multifocal urothelial tumour diagnosed after a Uroscan. Indeed, patients with pelvic and ureteral urothelial tumours have an associated bladder tumour in 17% of cases at the time of diagnosis [21] [24].

LRC is an emerging technique which has been proposed as an alternative to ORC minimally-invasive. The goal of this minimally-invasive approach is to reproduce the oncologic results of an open procedure while reducing postoperative morbidity and length of hospital stay [8]. The laparoscopic approach has various benefits, enclosing less blood loss, a shorter hospital stay, and equivalent complication rates.

However, the longer operating time and having to overcome the learning curve are disadvantages. Since the first laparoscopy procedure a lot of centres have published their series sharing their experience. Our study reports data on our 5-year experience with LRC. Laparoscopy is hardly performed because of its high cost. In our study, only 5 patients underwent the procedure. All of these patients had health insurance, which covered most expenses related to the procedure.

We have no rehospitalisation nor perioperative death in our series, this could be explained by the size and the close monitoring benefited from our multidisciplinary team. Indeed, the early perioperative mortality rate in RC is relatively low, around 1.2% - 3.2% [17].

In terms of surgical management, the reconstruction of the urinary tract either with orthotopic or heterotopic, continent or incontinent urinary diversions represent an important step, which will affect the patient's quality of life forever. Therefore, the choice of urine diversion technique should be made in accordance with the patient based on the surgeon's skills. In our institution we used three types of urine diversion: Bricker, neobladder and ureterocutaneous ostomy. The ileal conduit was the most practiced technique, this choice was driven by the patient's option and sur-

geon experience.

Following RC, adjuvant chemotherapy may be introduced for patients. Indications are a pT3 or T4 stage after cystectomy, or a positive node [17]. In our series, 4 of the 5 patients had an indication for adjuvant chemotherapy. No patient benefited from peri-operative radiotherapy.

As stated in previous literature early complications, defined as the ones affecting patients within 30 days of surgery, and their rate ranged from 20% - 57% [2]. In our study, the overall morbidity rate in this series was 100%. A significant decrease in the incidence rate of complications has been shown to occur as the learning curve increases. Therefore, the EAU recommends a minimum of 10 RCs per institution per year [17]. We encounter only minor complications according to Clavien-Didon especially Grade I representing 80% of them which occurred within the 10 postoperative days. The overall postoperative mortality rate was null, the mean follow-up period of 30 months with a median survival rate of 2.5 years. In terms of 5 years survival rate, we report a rate of 60% at 2 years 40% at 3 years and 20% at 5 years. This survival rate can be link to the limited number of patients we had and length of our follow-up also knowing that proficiency of the surgeon and hospital volume also relate to survival outcomes. After all, time will tell us the full potential of LRC within our centre and his potential as an alternative to ORC in low-middle income countries as us.

5. Conclusions

RC plays a central role in the multimodal therapy of patients with high risk NMIBC and MIBC. With this study documenting the early experience of LRC in our centre we were able to conclude that LRC is associated less blood loss, less analgesic consumption, reduce morbidity and mortality. ORC is associated with shorter operative time. The two options are similar in terms of complication rates and oncological outcomes. After establishment of an adequate learning curve and equipment, LRC is a feasible and safe option in our setting. Therefore, is should be proposed to patient with bladder cancer as a therapeutic option as an alternative to ORC. However, the cost of this approach remains high in our context.

Knowing the number of patients who subsequently underwent LRC at our centre since the completion of this study, it is clear that the number of potential participants for a future study may allow for more definitive statements to be made regarding which modality may provide better outcomes especially in a comparative study. The volume of RC currently being performed at our centre may allow for a prospective study design, thereby producing more robust evidence, which may guide practice in the future.

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Declarations

What is known about the subject: Laparoscopic radical cystectomy is an emerging minimally invasive approach which has been proposed as an alternative to open radical cystectomy. This procedure is most often performed in high income countries.

What our study brings back: This study brings as addition: The indication, feasibility and outcomes of the treatment of invasive bladder cancer by laparoscopy in a resource-limited environment.

Availability of Data and Materials

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study

Ethical Considerations

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

A copy of the written consent is available for review by the Editor-in-Chief of this journal. Any identifying material has been removed, including the patient's name, date of entry, face or any distinctive features on the pictures taken.

Authors' Contributions

ASNM, LHD and LWT, contributed in design of the study and writing of the manuscript BNN, LOM, MDB and JPF contributed in critical reading BNN, collected the pictures, and obtained the patient's consent.

All authors have read and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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List of Abbreviations

BCG	Bacillus Calmette-Guérin
c	Clinical
CDC	Clavien-Dindo Classification
CT	Computerized Tomography
EAU	European Association of Urology
F	French
LND	Lymph Node Dissection
LRC	Laparoscopic Radical Cystectomy
min	Minute
ORC	Open Radical Cystectomy
p	Pathology
PMH	Past Medical History
RC	Radical Cystectomy
SCC	Squamous Cell Carcinoma
TCC	Transitional Cell Carcinoma
TNM	Tumor, Node, Metastasis
UC	Urothelial Carcinoma