

Retrospective review and long-term follow-up of radical cystectomy in a developing country

K. GAITONDE, A. GOYAL, S. NAGAONKAR, N. PATIL, D.R. SINGH and V. SRINIVAS
Department of Urology, PD Hinduja National Hospital and Medical Research Centre, Mumbai, India

Objective To retrospectively review the clinical data from patients undergoing radical cystectomy for bladder cancer, and to analyse the complications and survival rates associated with this operation in a developing country.

Patients and methods The study comprised 105 patients who underwent radical cystectomy from 1986 to 1993. Data were collected from retrospective reviews of hospital and physician's office records, and by contact with the patients. Metastatic status was evaluated before surgery and tumours staged using the Tumour-Nodes-Metastasis classification. The indication for surgery was histologically confirmed muscle invasion after transurethral resection biopsy, or endoscopically uncontrollable superficial disease. The data were analysed to assess the perioperative complications and long-term survival, with 5-year survival rates determined using Kaplan–Meier survival curves.

Results The complication rate was 27.6%; most of the complications were managed conservatively with good results and re-operation was required in only two patients. There were two deaths (1.9%) at 15–45 days after surgery, but none during surgery. Patients were divided into node-negative and node-positive groups for analysis and 5-year survival rates determined; for node-negative organ-confined disease (\leq pT3A) the

survival was 68% and for nonorgan-confined disease (\geq pT3B) 25%. The 5-year survival rate in the presence of nodal metastases was 13% for N1 and none for N2 disease. Six patients developed urethral recurrence, detected on follow-up urethral-wash cytology. Five of these patients underwent urethrectomy, and four of the six survived for 5 years. Pelvic recurrence occurred in five patients (4.7%), none of whom survived for 5 years.

Conclusion Radical cystectomy and pelvic lymph node dissection remains the mainstay of treatment in muscle-invasive bladder cancer. This is a relatively safe procedure with minimal morbidity and mortality; 68% of the present patients with organ-confined disease survived 5 years and 12 patients were alive at 10 years, indicating the effectiveness of this operation in selected cases. However, $<29\%$ of patients with nonorgan-confined and nodal metastatic disease survived 5 years, thereby implying the need for more effective adjuvant therapy in these patients. Radical cystectomy is a viable option in developing countries, with 5-year survival rates comparable with most large published series.

Keywords bladder cancer, radical cystectomy, survival, metastatic, nodes, developing country

Introduction

Radical cystectomy with pelvic lymph node dissection (PLND) is the standard treatment for muscle-invasive bladder cancer, a procedure popularized initially by Whitmore and Marshall [1]. The advent of improved surgical techniques, anaesthesia care and postoperative management has lowered the high complication and mortality rates previously associated with this operation [2–4]. Unrecognized distant metastases resulting in decreased survival occur in almost half of patients with high-grade tumours who undergo cystectomy [2,5]. However, radical cystectomy remains the most effective method for local control of muscle-invasive bladder cancer. In the present study we reviewed our experience

with this operation and analysed the results of a large series of patients in a developing country.

Patients and methods

All patients who underwent radical cystectomy from 1986 to 1993 at our institution were reviewed retrospectively. Data were collected by reviewing hospital and physician's office records, and by contacting the patients. Patients who underwent exploration and PLND but not cystectomy (because they had metastases detected on intraoperative frozen-section analysis of grossly enlarged lymph nodes) were excluded from the analysis. The extent of the PLND was from the bifurcation of the common iliac vessels superiorly up to the femoral ring

inferiorly, and from the external iliac artery laterally to the lateral fascia of the rectum medially.

Preoperative screening for metastatic disease included a chest X-ray, bone scan and abdominal/pelvic CT. Tumours were staged according to the TNM classification (1987). The indication for surgery was histologically confirmed muscle invasion after transurethral resection biopsy, or endoscopically uncontrollable superficial disease. All the procedures were undertaken by the same uro-oncologist. The perioperative complications and long-term survival were evaluated, with 5-year survival rates determined using Kaplan–Meier survival curves. In all, 105 patients underwent radical cystectomy with PLND, from 1986 to 1993 (male : female ratio 8.5 : 1, age range 32–74 years).

Results

The histopathological diagnosis was TCC in 98 patients, squamous cell carcinoma in five and adenocarcinoma in two; the pathological stage, grade and nodal status are shown in Table 1. Urinary diversion was as an ileal conduit in 103 patients and a Mainz II sigma rectum pouch in two. There were two deaths (1.9%) among the 105 patients at 15–45 days after surgery, but no deaths during surgery; the perioperative complications are detailed in Table 2.

Pelvic recurrence occurred in five patients (4.7%); all these were detected as an asymptomatic pelvic mass on follow-up ultrasonography within 6 months after surgery. The disease stage was pT3bN0 in three patients while two had nodal metastases detected on postoperative histopathological examination. Adjuvant chemotherapy was instituted in these patients but none survived for 5 years. Six patients developed a urethral

recurrence (5.7%), which was diagnosed on urethral-wash cytology during the follow-up. One of these patients presented with symptomatic urethral discharge and was subsequently diagnosed to have widespread metastatic disease precluding any surgical intervention. The other five patients underwent urethrectomy, with four of the six surviving for 5 years.

Patients were divided into node-negative and node-positive groups for analysis, and the 5-year survival rates determined; 88 patients had node-negative (N0) disease on postoperative histopathology of the PLND specimen (Table 3). Four patients had endoscopically uncontrollable and refractory pT1G3N0 tumours, and they underwent radical cystectomy and PLND, with three surviving for 5 years. Nodal metastases were detected in 17 patients; the primary bladder tumour stage in these patients was pT1 in one, pT3a in six, pT3b in seven and

Table 1 Pathological stage, grade and nodal status

Status	No. patients
Stage	
pT1	4
pT2	27
pT3a	44
pT3b	21
pT4	9
Grade	
1	1
2	12
3	72
4	20
Nodal	
pN0	88
pN1	15
pN2	2

Table 2 Perioperative complications (from [3])

Timing and type of complication	Number
Intraoperative	
Rectal injury	2
Myocardial ischaemia	1
Early postoperative	
Prolonged ileus	8
Subacute intestinal obstruction	2
Pelvic collection	1
Wound collection	9
Late postoperative	
Burst abdomen	1
Intestinal obstruction	1
Re-operations	2
Deaths	2

Table 3 Five-year survival in the various groups of patients

Group/ stage	No. patients	5-year survival, n (%)	Lost to follow-up
Node-negative			
pT1	4	3	–
pT2	26	21 (81)	1
pT3a	38	22 (58)	3
pT3b	14	4 (29)	2
pT4	6	1	–
Node-positive			
pN1	15	2 (13)	2
pN2	2	0	–
Node-negative			
organ-confined disease (\leq pT3a)	68	46 (68)	–
Nonorgan-confined (pT3b–pT4)	20	5 (25)	–
All stages	88	51 (58)	

pT4 in three; eight patients who were lost to follow-up were considered to have died, including one with pT2N0, three with pT3aN0 and one with pT3bN0 disease. Of the two patients with nodal metastases lost to follow-up, one had pT3aN1 and the other had pT3bN1 stage tumours (Table 3). Kaplan–Meier 5-year survival curves were determined for all 105 patients who underwent radical cystectomy and for the group of 88 who had node-negative disease, respectively (Fig. 1a,b).

Five-year survival was calculated for organ-confined (\leq pT3a) and nonorgan-confined (pT3b–pT4) disease in patients with node-negative status (Table 3). The 68 patients with organ-confined disease but no nodal metastases had a better 5-year survival rate (68%) than those with nonorgan-confined disease.

Discussion

Radical cystectomy and PLND has become the principal therapeutic treatment for muscle-invasive bladder cancer. In most large series the perioperative mortality rate from radical cystectomy is 2–5%, the reoperation rate 2–10% and the complication rate 25–35% [2–4]. In

the present series the complication rate was 27.6%. Most of the complications were managed conservatively, with good results, and reoperation was required in only two patients. Thus, radical cystectomy is a relatively safe procedure with minimal morbidity and mortality rates. If it is carried out meticulously, the complication rate can be reduced to acceptable levels and such surgery used routinely even in developing countries.

The general referral pattern in our urological practice results in most patients with haematuria being referred by their family physicians to a general urologist. If the tumour is superficial and easily resectable, then the general urologist manages the case. Only when the tumour becomes invasive and cannot be controlled endoscopically is the patient referred to a uro-oncologist. Hence most of the patients with bladder tumour treated in our institution have invasive disease. Our policy is to offer radical cystectomy as the treatment of choice and so we did not pre-select any subgroup for this procedure. During 1986–1993 we treated an additional 86 patients endoscopically for superficial bladder tumours, besides the 105 who underwent radical cystectomy, thus indicating that the bulk of bladder tumours referred to us were invasive; annually, we treat 20–25 patients with bladder cancer. Details from the tumour registry maintained by the city of Mumbai, India, show that the incidence of bladder cancer (documented in 1993) was 5.5 males/100 000 and 1.5 females/100 000 population [5].

The positive effect in low-stage tumours is reported in various series, with excellent survival rates [2,6–10]; the 5-year survival rates are 63–83% in T2 disease and 67–71% for T3a disease (Table 4). Radical cystectomy is occasionally required for superficial disease when all other methods fail. Five-year survival rates of 80–100% have been reported for refractory, endoscopically uncontrollable or high-grade superficial bladder tumours (pTa–pT1G3) [2,9]. In the present series there were four patients with endoscopically uncontrollable refractory pT1G3 tumours who underwent radical cystectomy, with three surviving for 5 years.

The effectiveness of radical cystectomy decreases with increasing stage of the disease [2,6–8,10,11]. The 5-year

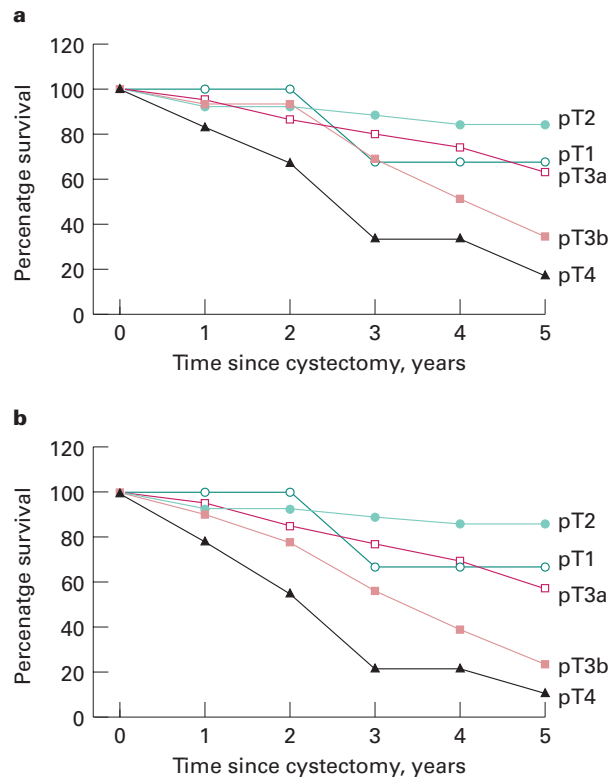


Fig. 1. Kaplan–Meier survival curves showing the 5-year survival of **a**, node-negative patients and **b**, all patients, with pathological disease stage (pT1, green open circle; pT2, light green closed circle; pT3a, red open square; pT3b, light red closed square; pT4, black triangle).

Table 4 Five-year survival rates in node-negative patients of differing pathological stage in reported series

Ref.	pT1	pT2	pT3a	pT3b	pT4
[11]	–	–	–	17	0
[6]	–	83	69	29	–
[7]	–	63	67	22	21
[8]	92	82	71	45	26
Present	75	81	58	29	17

survival rates in pT3b disease are 17–45% and in pT4 disease 0–21% (Table 4). The survival rates decrease rapidly as the primary tumour progressively invades the bladder wall, perivesical fat or adjacent structures. This may be related to the higher incidence of associated nodal metastases with increasing tumour stage.

Regional lymph node involvement is seen in 14–27% of patients with invasive tumours, resulting in decreased survival [9]. In the present series the 5-year survival rates were 13% for N1 and none for N2 disease. Few recent series have reported better survival (17–52%) with the greatest benefit in patients with a favourable stage (organ-confined disease) and/or microscopic lymph node involvement [2,12,13]. Survival seems to depend on the extent and bulk of nodal metastases, and the stage of the primary tumour. In view of these findings it might not be advisable to abandon radical cystectomy in patients with limited nodal involvement and tumour confined to the bladder wall. However, gross, palpable nodal disease still has a poor prognosis and might not warrant surgery.

Urethral recurrence occurs in 7–18% of cases in most series [2,14]; the early diagnosis and treatment of the recurrence might affect the prognosis. Symptomatic recurrences were shown to affect survival in one series [15]; six of the present patients developed urethral recurrence, which was detected on follow-up urethral-wash cytology. Urethrectomy in five of these six patients resulted in four surviving 5 years, and thus urethral-wash cytology after radical cystectomy seems advisable. Radical cystectomy is generally associated with pelvic recurrence rates of 10–20% [9] and indicates a poor prognosis. In the present series, pelvic recurrence occurred in five patients, none of whom survived for 5 years.

Despite improved survival in contemporary series, 50–70% of patients with tumour penetration into perivesical fat will have widespread metastatic disease, which will be apparent within \approx 30 months [2,6]. Most patients who die from bladder cancer after radical cystectomy succumb to metastatic disease. This indicates the need to develop effective adjuvant therapy, but studies suggest the effectiveness is variable. The search remains for a suitable adjuvant therapeutic agent which will increase survival.

Most patients in India have no health insurance and depend on their daily earnings to maintain a reasonable lifestyle. These patients are not so concerned about their body image but cannot afford complications and re-operations. Hence an ileal conduit, which is a well-established and durable option, is our diversion of choice. The high cost of intestinal staplers also makes various forms of continent diversion less attractive. As many of our patients live in villages and work in agriculture they

are uncomfortable with the idea of catheterizable pouches, because they have inadequate privacy, but they adapt very well to an ileal conduit. The Ostomy Association in Mumbai provides the patients with ileostomy bags (costing \$2.50 each) and the face-plate wafer, which adheres to the patient's abdominal wall, for \$0.25 per wafer. The patients reuse the ileostomy bag by washing it daily, so that each lasts them for \approx 3 weeks. The face-plate needs to be changed once weekly in the summer and every 8–10 days in winter, because of excessive sweating in summer, which causes the face-plate to loosen earlier. Thus, because the cost of the bags and wafers is subsidised (provided by the Ostomy Association) and as the patients are ingenious in reusing them, the ileal conduit is an economically viable option, at \approx \$4 per month. Former patients routinely counsel new patients so that they are mentally prepared for the operation and have help after discharge if they have any queries. As there is no full-time stoma therapy nursing clinic, this is the most practical method to manage stoma problems for each patient. For patients who are uncomfortable with an external stoma, we offer a Mainz II sigma rectum pouch, as this appears to have few complications and is best suited to our patients.

In conclusion, this retrospective analysis of 105 patients shows that radical cystectomy is a viable option in India, with 5-year survival rates comparable with most large series reported elsewhere.

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Authors

K. Gaitonde, MS, Urology Clinical Assistant.

D. Singh, MS, DNB(Urol), Urology Clinical Assistant.

A. Goyal, MS, Urology Clinical Assistant.

V. Srinivas, MS, FICS, FACS, MS(Can), Diplomate of the American Board of Urology, Consultant Urologic Oncologist.

S. Nagaonkar, MS, DNB, Urology Clinical Assistant.

N. Patil, MS, Urology Clinical Assistant.

Correspondence: V. Srinivas, PD Hinduja National Hospital & Medical Research Centre, Mahim, Mumbai 400016, India.

e-mail: dr_vsrinivas@hotmail.com

Abbreviation: PLND, pelvic lymph node dissection.