

The changing pattern of mortality and morbidity from radical cystectomy

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Objectives To examine the morbidity and mortality of radical cystectomy as currently practised, and to compare the findings with historical data.

Patients and methods The operative mortality and early and late complications were recorded in 101 consecutive patients (median age 65 years, range 38–81; 33 aged >70 years) undergoing radical cystectomy between April 1992 and October 1997. Fifteen patients had relapsed after previous radical radiotherapy.

Results The median postoperative stay was 14 days (range 8–44). There were two deaths within 60 days of surgery (of patients aged 46 and 59 years) from respiratory failure and sepsis, respectively. The mortality in the elderly was not more than in other age groups. The early morbidity included two cases of lower limb insufficiency, both in the salvage cystectomy group, where the morbidity was significantly

higher than in those undergoing primary cystectomy (chi-squared, $P < 0.01$). Three patients underwent early re-exploration. There were four clinically significant episodes of deep vein thrombosis and two pulmonary emboli that were not fatal.

Conclusion As currently practised, radical cystectomy is associated with a lower mortality (<2%) and morbidity than described previously. The added morbidity of salvage cystectomy and the acceptable mortality of primary cystectomy suggests that the treatment of choice for muscle-invasive disease is primary cystectomy, with external beam radiotherapy reserved for those patients unfit for major surgical intervention. Age alone should no longer be considered a contraindication to cystectomy.

Keywords Cystectomy, mortality, morbidity, bladder cancer, age, surgery

Introduction

The annual overall incidence of bladder cancer in the UK is 34.0 for men and 13.3 for women per 100 000 population, and the incidence rises rapidly after the sixth decade of life [1]. Although the pattern of disease presentation throughout the Western world is fairly uniform, as assessed from published reports, the approach to muscle-invasive disease in the UK has been primarily conservative, whereas in continental Europe and North America, primary cystectomy has been more common. Indeed, it has been reported that a significant proportion of patients in the UK, particularly the older patient, with muscle-invasive carcinoma of the bladder is not being offered definitive surgical therapy [2]. Significant factors in the risk-benefit analysis of any operative intervention, particularly one as major as cystectomy, are the perceived mortality and morbidity of the procedure. Bloom *et al.* [3] reported the 60-day mortality of cystectomy as 8% overall and 11% in those over 65 years old.

In 1992, all inpatient urological activity in Sheffield moved to a single institution, with the appointment of three new consultants, each with a different subspecialist interest [4]. This resulted in the vast majority of patients with invasive bladder cancer being managed by one consultant with a declared interest in uro-oncology. The purpose of the present observational study was to examine critically the morbidity and mortality of current radical cystectomy in such a setting and to compare this with historical data to determine any differences.

Patients and methods

The study comprised all patients undergoing radical cystectomy and urinary diversion over a 5-year period (April 1992 to October 1997) under the care of one urological consultant with a special interest in uro-oncology. The database was compiled from pathology and theatre records, with cross-reference to hospital inpatient activity data; 101 patients (75 men and 26 women) undergoing radical cystectomy were identified in this period. The case-records were examined for the duration of anaesthesia, intraoperative complications,

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morbidity in the first 60 days after surgery, duration of inpatient stay and records of previous radiotherapy for carcinoma of the bladder. The Blood Transfusion Service database was searched for the period covering the operation and inpatient stay to identify transfusion requirements. The median age of the patients was 65 years (range 38–81). Table 1 outlines the analysis of comorbidity and previous radiotherapy by age group. Fifteen patients had relapsed after previous radical radiotherapy; of the 101 patients eight underwent radical cystectomy with a continent diversion (Indiana pouch) and the remainder had ileal loop diversion (93%) after their radical cystectomy.

Results

The final pathological findings recorded are shown in Table 2; the vast majority of tumours were TCC. Two patients died within 60 days after surgery; the first was a 46-year-old man with a squamous cell carcinoma (SCC) and severe ankylosing spondylitis causing respiratory compromise. Despite elective tracheostomy at the time of cystectomy and admission to the intensive care unit, he died from respiratory failure within a week of surgery. The second patient was a 59-year-old man who developed a leak at the uretero-ileal anastomosis. Despite re-exploration, he developed sepsis and died 2 weeks after his initial operation. Neither patient had undergone previous radiotherapy. It was accepted at the outset that the first patient (with SCC) was a high-risk candidate and he was counselled accordingly. Because of his disease (pT3 SCC) it was considered that of the therapies available, cystectomy would provide the best chance of 'cure'. The second patient (stage pT3b) had no obvious premorbid problems except mild peripheral vascular disease. This latter patient probably illustrates the true mortality associated with cystectomy and urinary diversion.

Twenty-two (22%) patients had an adverse event after surgery and these were broadly categorized into one of six areas (Table 3). Previous radical radiotherapy had a

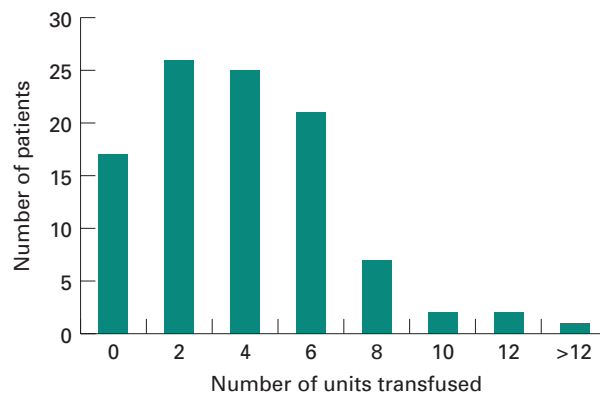


Fig. 1. Transfusion requirements during and after surgery in the 101 patients undergoing radical cystectomy.

significant effect on the overall incidence of an adverse event after cystectomy (chi-square, $P < 0.01$). There were two cases of acute vascular compromise of the lower limb, identified either before or immediately after surgery. In both cases the limbs were salvaged by bypass grafting in one and balloon angioplasty in the other. Three patients required re-exploration within 24 h of cystectomy, two for continuing bleeding and one for obstructed ureteric stents. Figure 1 shows the transfusion requirements for the patients. The median (range) transfusion volume was 3 (0–19) units; 12 patients required ≥ 8 units and 17 required no blood products, either during or after surgery. There was no obvious pattern between transfusion requirement and the incidence of post-operative problems. Thrombo-embolic phenomena occurred in six patients, with four clinically significant proximal deep vein thromboses and two cases of pulmonary emboli that were not fatal. Four patients required parenteral nutrition after surgery for 5–14 days; the indications for this were prolonged ileus in two, preoperative hypo-albuminaemia in one and intra-abdominal sepsis in one.

Discussion

The operative mortality of cystectomy in the present patients was considerably lower than that described in previous British series [3,5]. There was no correlation

Table 1 Pre-existing comorbidity in study population subdivided according to age

Comorbidity	Age (years)		
	<60	60–69	>70
Number	33	35	33
Cardiac	1	4	5
Vascular	1	3	4
Respiratory	1	4	4
Previous radiotherapy	3	6	6

Table 2 Final pathological staging and cell type in 101 patients undergoing radical cystectomy for carcinoma of the bladder

Tumour type	CIS only	PTa/PT1	PT2	PT3/4	Total
TCC	3	6	44	42	95
Squamous cell			1	2	3
Adenocarcinoma			1		1
Anaplastic carcinoma			1	1	2

Table 3 Adverse events after cystectomy; there was a significantly higher overall incidence of adverse events in those receiving radiotherapy before cystectomy than in those not (chi-squared, $P < 0.01$)

Complication	Previous radiotherapy	No previous radiotherapy
Number	15	86
Sepsis	3	5
Prolonged ileus	1	2
Thrombo-embolic	2	4
Uretero-ileal anastomotic leak	0	1*
Respiratory failure	0	1*
Vascular	2	0
Re-exploration	0	4
Overall, <i>n</i> (%)	8 (53)	14 (16)

*The two patients who died after surgery.

between either mortality or morbidity and age at cystectomy. In the only randomized study to date, Bloom *et al.* [3] concluded that cystectomy gave better results than radiotherapy in the younger patient (< 65 years) but was associated with a high mortality (11%) in those over 65 years old. Interestingly, patients over 70 years of age were not included in that study. Thomas and Riddle [5] described similar results for postoperative mortality. These reports have had a significant influence on British urological practice. In marked contrast, the present study found no relationship between age and operative mortality. Hendry reported similar findings to the present in 1986 [6], but did not discuss the issue of age. A brief examination of published studies supports our view that there has been a steady reduction in the mortality associated with cystectomy. The present overall mortality of 1.9% is consistent with that described in other recent series (Table 4). There has been about an eight-fold reduction in mortality from this operation over the past three decades. The reasons for this are not immediately apparent, but there have been several changes in both surgical and anaesthetic management, and in patient characteristics. The operative technique has changed a little, with better recognition of the vascular anatomy of the bladder and prostate, particularly given experience with radical prostatectomy. However, probably the most significant factor is the rapid improvement in anaesthetic technique and the improved perioperative care which accompanies the rational concentration of resources in subspecialist teams. All patients undergoing radical cystectomy at our unit are routinely admitted to a high-dependency unit after surgery for 1–3 nights. Central venous pressure and invasive arterial pressure are routinely monitored during and after surgery. Parenteral nutrition is not given

routinely but is instituted only if the patient has not recommenced oral feeding by the fifth postoperative day. Only four of the present patients required total parenteral nutrition. The value of such feeding is controversial, with published evidence both supporting its use [7] and suggesting increased morbidity in those who are fed parenterally [8].

Of patient characteristics, the mean life expectancy has been increasing throughout this century; currently a 65-year-old man can expect to live a further 14.6 years and a woman a further 18.2 years [14]. This implies that the population is in general healthier and better able to cope with the demands of major surgery. The rising incidence of carcinoma of the bladder must also be considered and anecdotally more patients in their seventies are presenting with disease that is potentially curable by radical surgery than previously. The management of the elderly patient with invasive bladder cancer remains a challenge. However Stroumbakis *et al.* [15] described an overall postoperative mortality of 4.5% in an octogenarian population ($n = 44$). In such a group, with 78% having significant comorbidity, this would seem an acceptable value for a potentially life-saving procedure. Similarly, Figueroa *et al.* [16] reported no mortality in 52 patients aged ≥ 80 years undergoing radical cystectomy. These authors suggested that in a properly selected group, age alone should no longer be viewed as a contraindication to cystectomy, as has been suggested previously.

In any surgical series there is a large element of patient selection and the present study is no exception. The selection criteria applied in the current series was that anyone with a potentially curative invasive bladder tumour was offered cystectomy and urinary diversion either via ileal conduit (in 93) or a continent diversion (in eight), if they were deemed fit for anaesthesia; no arbitrary age limit was applied. There is no reason why recent series are any more selective than previous studies and we therefore contend that the reduction in mortality is real. We have no accurate estimate of the number of patients undergoing radical or palliative radiotherapy in this period, but acknowledge that our usual practice is to refer those patients who are considered unfit for, or unlikely to benefit from, radical surgery for radiotherapy. However, we do contend that fitness for anaesthesia is the main factor determining the 30- or 60-day outcome. All patients in the present series were managed by one urological consultant and were anaesthetized by one of two anaesthetic consultants, who therefore developed considerable expertise with such patients.

The complication rate for radical cystectomy and urinary diversion is reported to be 17–32% [13,17], with sepsis, intestinal obstruction and thrombo-embolic events being the most common. Although the complication rate for salvage cystectomy was higher than for primary

Table 4 Historic and contemporary series of radical cystectomy showing the recent reduction in mortality

Study	Study period	No. of patients	Overall mortality (%)	Mortality in selected group (%)
[9]	1952–64	46	20	–
[10]	1948–55	230	14	–
[11]	1967–73	50	14	20 for salvage cystectomy
[3]	1966–75	189	7.8	11 in those aged 65–70
[5]	1970–80	100	7	12 in the over 65 age group
[12]	1971–77	165	2.4	8.1 for salvage cystectomy
[13]	1979–87	261	1.8	–
Present	1992–96	101	1.9	No increased mortality with age or with salvage cystectomy

cystectomy in the present study, there was no increased mortality in the irradiated group. The present adverse events, i.e. lower limb ischaemia, seem not to have been reported previously. Both cases occurred in patients who had previously undergone external beam radiotherapy. It is recognized [18] that radiotherapy may accelerate atherosclerosis and it is possible that the increased morbidity identified in previously irradiated patients is a consequence primarily of vascular intimal damage.

In conclusion, the added morbidity of salvage cystectomy and the acceptable mortality of primary cystectomy shown in this series suggests that currently the treatment of choice for muscle-invasive disease may be primary cystectomy, with external beam radiotherapy reserved for those patients unfit for major surgical intervention. These results agree with those of other contemporary series, in that anaesthetic fitness rather than chronological age should determine treatment selection. The concentration of resources by subspecialization in larger units increases the consistency of care and may contribute to the improved perioperative survival observed in recent years.

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