Cancer Imaging (2003) **3,** 96–100
DOI: 10.1102/1470-7330.2003.0009

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REVIEW

Patterns of recurrence of bladder carcinoma following radical cystectomy

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Date accepted for publication 14 February 2003

Abstract

The purpose of this study was to describe the imaging features and patterns of disease in patients with recurrent bladder carcinoma following radical cystectomy.

A retrospective review was made of the CT and MR findings in 42 patients (33 male, 9 female, mean age 65.1 years) with histologically verified transitional cell carcinoma of the bladder, who developed recurrent disease following radical cystectomy. Histology confirmed T2 disease in 7 patients, T3 disease in 26 patients and T4 disease in 9 patients. The tumour grade was G3 in 38 patients and G2 in 4 patients. The CT ($n = 42$) and MR imaging ($n = 9$) obtained at disease relapse were reviewed, noting the sites of disease recurrence and their imaging appearances.

The mean time to recurrence following cystectomy was 14.6 months (range 2–50 months). Patients with T2 disease had a significantly longer time to recurrence compared with patients with T3 or T4 disease (22.7 vs. 13.0 months, student t-test, $P < 0.05$). The most common pattern of recurrence was pelvic lymphadenopathy (55%). Retroperitoneal lymphadenopathy was common (33%) and was the only site of nodal disease in 10%. Local pelvic recurrence (45%) appeared as a soft tissue mass, which involved muscle, urethra or vagina. Sites of distant metastasis included the liver (19%), bone (12%) and lungs (10%). Liver metastasis was associated with nodal disease in the majority (80%).

The sites of recurrence of bladder cancer following radical cystectomy are described. Pelvic lymph node involvement is the most frequent site of disease recurrence despite the fact that pelvic lymph node dissection is performed as part of the standard procedure of radical cystectomy.

Keywords: *Bladder carcinoma; CT; MRI.*

Introduction

Bladder cancer is the most common cancer of the urinary tract with a peak incidence between the sixth and the seventh decade[1,2]. It is three times more common in men than women, accounting for 4.5% of all new malignant neoplasms and 1.9% of cancer deaths in the US[2].

Radical cystectomy is the treatment of choice for muscle invasive tumours, as it offers the best chance of cure, but may also be considered as first-line treatment in cases of superficial tumours with severe anaplasia. Surgery involves en bloc excision of the bladder, prostate and seminal vesicles with pelvic nodal dissection.

As the bladder is completely removed at radical cystectomy, urinary diversion becomes necessary. This may take the form of cutaneous ureterostomy, ileal conduit with ureteroileocutaneostomy, ureterosigmoidostomy or orthotopic neobladder reconstruction with ileal or ileocaecal segments. Orthotopic neobladder reconstruction is now the procedure of choice if the urethral sphincter can be conserved at surgery without compromise to the clearance of tumour[3].

The risk of disease relapse following radical cystectomy is reportedly 5–70%, with the majority occurring within 2 years of surgery[4,5]. Despite the significant

risk of relapse, there is a paucity of data describing the imaging features of recurrent bladder cancer following surgery. Hence, it was the aim of our study to describe the imaging features and patterns of disease in patients with recurrent bladder carcinoma following radical cystectomy.

Materials and methods

Patient population

Using the hospital information system, a database search revealed 42 patients with histologically verified transitional cell carcinoma of the bladder, who developed recurrent disease following radical cystectomy between 1997 and 2001. There were 33 males and 9 females, with a mean age of 65.1 years (range 40–80 years). 13 out of 42 patients had received pre-operative radiation treatment prior to surgery.

Histopathology following radical cystectomy confirmed T2 (according to TNM staging system) disease in 7 patients, T3 disease in 26 patients and T4 disease in 9 patients. The tumour grade was grade III in 38 patients and grade II in 4 patients.

Histological proof of disease relapse was available in 10 patients from percutaneous biopsies. The remaining 32 had presumptive diagnosis of disease relapse based on the clinical and imaging findings.

Imaging review

A retrospective review was made of the CT ($n = 42$) and MR imaging ($n = 9$) obtained at the time of diagnosis of disease relapse. Axial CT images were obtained following intravenous and oral contrast administration, using a spiral CT system (Siemens' Somatom, Erhlanger, Germany) with 8 mm collimation, 8 mm reconstruction and a scan pitch of 1.5. MR imaging was performed on a 1.5 T system (Siemens' Vision, Erhlanger, Germany) using T1- and T2-weighted axial images, supplemented with T2-weighted sagittal and coronal images. Dynamic intravenous gadolinium-enhanced T1-weighted images were also acquired in 3 patients.

The CT and MR imaging were reviewed to determine the sites and patterns of disease relapse. For nodal disease, the appearance, size and location of lymphadenopathy were recorded. Lymph nodes greater than 8 mm in size were considered enlarged[6]. For local pelvic recurrence, the extent and appearance of disease were evaluated. Involvement of pelvic structures such as the vagina, urethra, rectum and pelvic sidewall muscles were noted. The presence and sites of metastatic disease on imaging were tabulated.

Results

Time to recurrence

The mean time from cystectomy to recurrence was 14.6 months (range 2–50 months). The mean time to recurrence was shorter for patients with stage T3 or T4 disease (mean = 12.9 months) compared to those with stage T2 disease (mean = 22.7 months) ($P < 0.05$, student's t-test).

Lymphadenopathy

Despite pelvic nodal dissection, pelvic lymph node was the most common site of disease relapse (23/42; 55%). Pelvic nodal relapse was not associated with local pelvic soft tissue recurrence in the majority (14/23). The mean nodal size was 3.6 cm (range 2–8 cm) and the nodes were of homogeneous soft tissue density on CT (Fig. 1).

Figure 1 **Pelvic nodal relapse. In this 45-year-old man with previous cystectomy, note surgical clips along the pelvic sidewall from previous nodal dissection. There was urinary diversion by an ileal conduit (not shown) and the tip of the urinary bag was visible over the right lower abdominal wall. A 2 cm left internal iliac lymph node was detected along the left pelvic sidewall (arrow).**

The frequency of pelvic nodal group involvement was as follows: common iliac nodes (13/42; 31%), external iliac nodes (11/42; 26%), obturator nodes (11/42; 26%), hypogastric nodes (4/42; 12%), internal iliac nodes (4/42; 12%), inguinal nodes (4/42; 12%) and lateral sacral nodes (2/42; 5%).

Abdominal retroperitoneal lymphadenopathy occurred in 14/42 (33%). The majority (10/42) of cases had associated pelvic nodal disease. However, retroperitoneal lymphadenopathy (Fig. 2) was an isolated finding in 4/42 (10%). Of these, only two cases had received previous pelvic irradiation.

Local pelvic soft tissue recurrence

Local soft tissue recurrence was detected in 19/42 (45%) of cases. 11/19 (58%) presented as a circumscribed soft tissue mass (Fig. 3), while 8/19 (42%) appeared

as ill-defined soft tissue thickening within the pelvis (Fig. 4). Involvement of adjacent structures, such as the vagina (2/19), urethra (2/19), pelvic sidewall (2/19), anterior abdominal wall (1/19), seminal vesicle (1/19) and spermatic cord (Fig. 5) (1/19) could be identified on imaging. Local recurrence was associated with pelvic lymphadenopathy in 9/19 (47%).

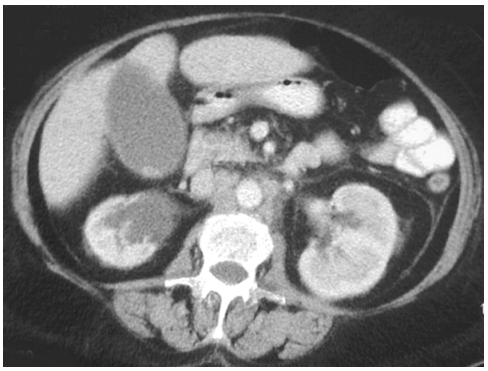

Figure 2 **Retroperitoneal lymphadenopathy. In this 60-year-old lady with isolated nodal relapse within the retroperitoneum, note the circumaortic lymph nodes. There was mild right hydronephrosis resulting from the ileal conduit urinary diversion (not shown).**

Distant metastasis

Distant metastases were present in 18/42 (47%) patients at the time of disease of relapse. The most frequent sites of metastatic disease included the liver (8/42; 19%), the bones (5/42; 12%) and the lungs (4/42; 10%). Involvement of the peritoneum (1/42), brain (1/42), pancreas (1/42) and adrenal glands (1/42) was more unusual.

80% (6/8) of patients with liver metastases had associated nodal disease, either within the pelvis or retroperitoneum (Fig. 6).

Discussion

Radical cystectomy provides the best treatment option in patients with muscle invasive bladder carcinoma. However, patients with extra-vesicular involvement, nodal metastases, lymphatic or vascular permeation, pelvic visceral invasion and p53 gene deletion[7], have a high risk of relapse following radical surgery.

The tumour stage is predictive of the likelihood of disease recurrence. Slaton *et al.*[4] found that for stages T1, T2, and T3 bladder cancer, recurrence occurred in 5, 20 and 40% of patients respectively following surgery. In another study, the rate of recurrence in patients with locally advanced disease (37%) was reportedly twice that of organ-confined disease (18%)[8].

The tumour stage also has an association with the onset of relapse following surgery. In our study, patients with stages T3 and T4 disease had a shorter mean time to recurrence compared to patients with stage T2 disease (12.9 vs. 22.7 months, $P < 0.05$). The reported median time to recurrence following cystectomy is approximately 10–12 months, although this ranges widely between 1 and 100 months[4,5]. The majority of local recurrence occurs within 2 years of surgery (54–82%)[4,5]. Patients with a lower stage disease prior to cystectomy recurred later than those with a higher stage disease. In one series[4], patients with pT1, pT2 and pT3 disease prior to cystectomy had a median time to recurrence of 53, 19 and 12 months respectively.

Imaging has an important role in detecting and defining the sites of recurrent disease. However, familiarity with the range and variety of post-surgical changes and the normal appearances of the urinary diversion procedures is crucial to the interpretation of imaging studies.

Despite pelvic nodal dissection, which is carried out routinely as part of the radical cystectomy procedure, we found pelvic lymphadenopathy to be the most frequent site of relapse, occurring in 55% of our cases. The majority (14/23) of these cases were not associated with local soft tissue recurrence. On imaging, pelvic nodal disease was usually 2 cm or greater in size, and typically appeared as homogeneous soft tissue attenuation on CT. Although the external iliac nodes, obturator nodes and hypogastric lymph nodes are dissected and removed at surgery, the common iliac chain, the internal iliac chain and pre-sacral lymph nodes are usually undisturbed. Not surprisingly, we found that pelvic nodal relapse occurred most frequently along the common iliac group of lymph nodes.

Retroperitoneal lymphadenopathy was also common (33%). Although the majority of cases of retroperitoneal lymphadenopathy were associated with pelvic nodal disease, they were an isolated finding in 10%. Only half of the cases with isolated retroperitoneal nodal disease had previous history of pelvic irradiation, and no association could be found between the occurrence of isolated retroperitoneal lymphadenopathy and previous pelvic radiotherapy treatment.

Pelvic soft tissue recurrence was found in 45% of our cases. The majority of pelvic soft tissue recurrence in our study appeared as a circumscribed soft tissue mass (58%), although diffuse soft tissue thickening was also common (42%). Local relapse may be subtle on imaging, and detection of disease can be made more difficult by the persistent but variable asymmetrical soft tissue changes following surgery. Hence, it is imperative to compare each new scan with previous imaging to scrutinise for any interval change. In addition, locally recurrent lesions may be indistinct on CT, resulting in underestimation of the size and extent of the lesion. In these cases, dynamic gadolinium-enhanced MR imaging has been proposed as a method to help distinguish the abnormal tumour tissue from its surroundings[9].

Ellis *et al.*[10] reported that recurrence at cystectomy sites tended to be associated with pelvic lymphadenopa-

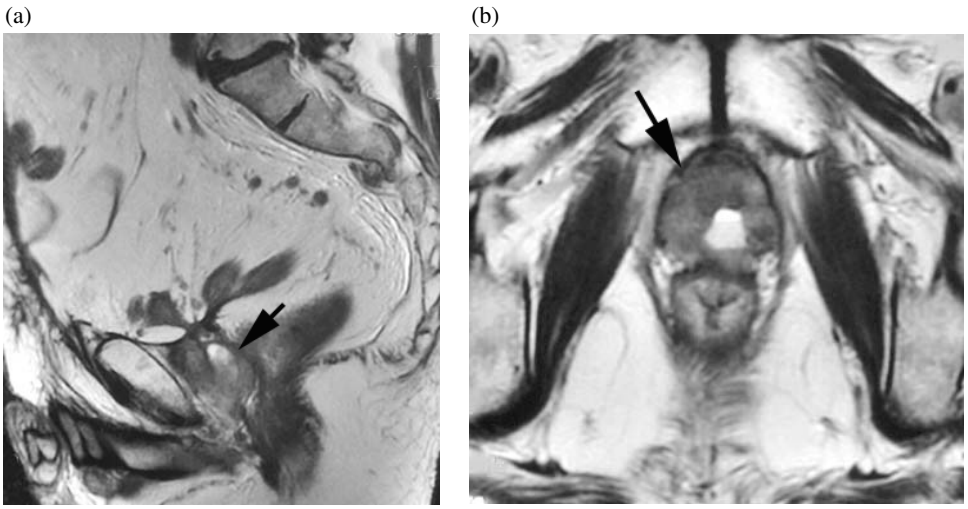

Figure 3 **Urethral recurrence. (a) Sagittal and (b) axial T1-weighted images; an intermediate signal mass arising from the urethra (arrows) due to disease recurrence.**

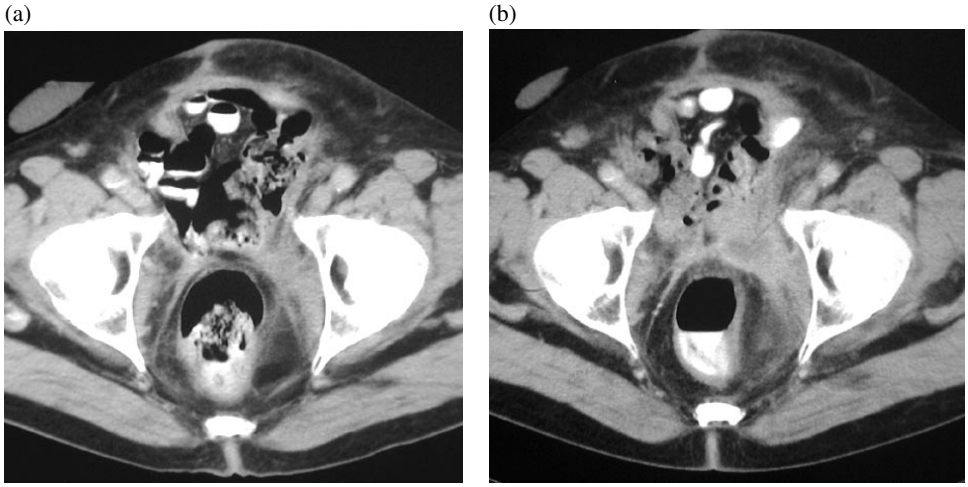

Figure 4 **Pelvic sidewall recurrence. (a) Post-contrast axial CT through the lower pelvis showing ill-defined soft tissue thickening, which was inseparable from the left obturator internus muscle. (b) A repeat CT through the same level 3 months later showed an increase in the soft tissue along the left pelvic sidewall. A biopsy confirmed the presence of disease relapse.**

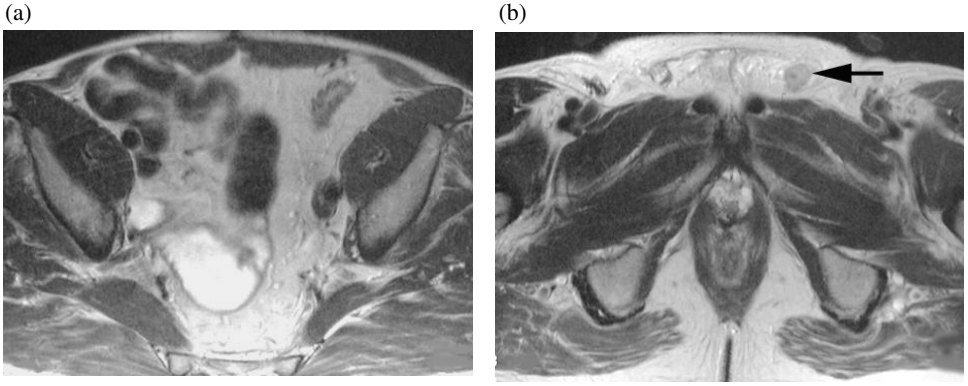

Figure 5 **Left spermatic cord recurrence. (a) T2-weighted axial image showing an orthotopic neobladder within the pelvis. (b) T2-weighted axial image taken at a lower level showed abnormal thickening of the left spermatic cord of intermediate signal (arrow). Disease relapse was confirmed at surgery.**

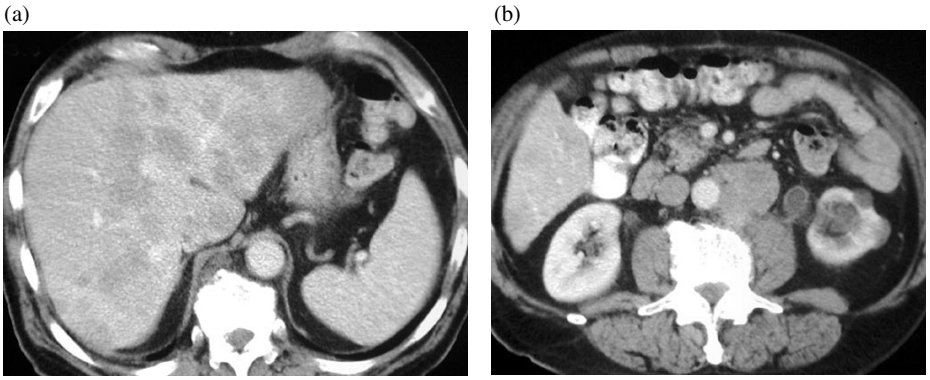

Figure 6 **Liver metastases. (a) Axial CT following intravenous contrast showing multiple low attenuation metastases within the liver. (b) A CT section taken from the mid-abdomen revealed concomitant bulky left paraortic nodal disease.**

thy and absence of lymphadenopathy in these circumstances was unusual. In our study, local recurrent disease was associated with nodal disease in only 47%, a figure that is substantially lower than the 80% observed by Ellis *et al.*[10].

Bladder cancer can metastasise widely, but their imaging appearances are indistinguishable from metastases arising from other primary tumours[11,12]. The most common sites of metastatic disease in our study were the liver (19%), bones (12%) and lungs (10%). Interestingly, the majority of patients with liver metastases had coexisting nodal disease within the pelvis or abdomen.

Most of the cases of relapse in our study have been detected through surveillance imaging following cystectomy. However, the usefulness of surveillance CT after cystectomy remains a subject of controversy. One report suggests that routine CT surveillance identifies only 14% of recurrences that are not symptomatic or apparent on physical examination[5]. Another suggested that CT could detect up to 30% of those with pelvic or retroperitoneal recurrence before the development of symptoms[4].

Montie[13] has proposed a surveillance program for recurrent transitional cell carcinoma following radical cystectomy. CT of the abdomen and pelvis at 6, 12, and 24 months is recommended, regardless of the stage of the primary tumour. Slaton *et al.*[4], however, advocate follow-up CT imaging in patients with primary T3 tumour but not in those with lower stage primary disease. Surveillance CT imaging should include both the pelvis and abdomen, since recurrence may be apparent only on the abdominal portion of the scan in up to 13% of patients[11,12].

Conclusions

The patterns of relapse of bladder cancer following radical cystectomy have been described. Despite pelvic nodal dissection, pelvic lymph node was the most frequent site of disease relapse following radical cystectomy for transitional cell carcinoma of the bladder. Local pelvic recurrence was also common, and may present as a circumscribed mass or diffuse soft tissue thickening. Retroperitoneal lymphadenopathy was an isolated finding in 10%. The liver was the most frequent site of metastatic disease and was usually associated with nodal disease.

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