The risks of cancer after bladder replacement or diversion

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Cancer following bladder replacement or diversion is a significant issue and can undo even the very best surgical reconstructions. In this article the author describes which procedures carry the highest risk, and what efforts can be made to reduce the risk and catch cancers at an early stage if they do occur.

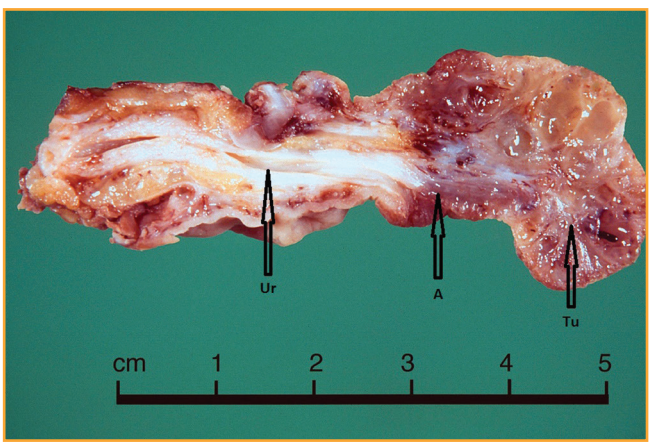

Figure 1. Fresh surgical specimen of a resected ureterosigmoidostomy. The anastomosis (A) of the ureter (Ur) to the colon is the site of an adenocarcinoma (Tu)

The standard diversion method for urine until the early 1950s was to transfer the ureters into the sigmoid colon to make a ureterosigmoidostomy (U/sig). This accidentally created the ideal conditions for neoplasia in a urinary diversion. It is now known that the mixture of urine and faeces acting on an anastomosis between urothelium and colonic mucosa will produce a tumour of the anastomosis (Figure 1). In experimental animal and human diversions and reconstructions, without one or more of these four components the risk of neoplasia is considerably reduced.

The exposure of the anastomosis needed to initiate the neoplastic process may be as short as nine months, but it takes a mean of 25 years (range 14–49) to produce a malignant adenocarcinoma (18 years for a benign adenoma). It is thought that about five years is needed for the benign lesions to become malignant. The risk of any neoplasia for patients having a U/sig is 22% at 20 years and 30% at 30 years.[1]

There are neoplasms in almost all urinary diversions and reservoirs that are not sited at the anastomosis (6% of neoplasms in U/sigs), including adenocarcinomas, neuro-endocrine tumours, lymphomas and squamous carcinomas. They do not fit particular patterns and may be unrelated to the altered urinary system. The small number of follow-up series of anastomosis of the ureter directly to the skin (cutaneous ureterostomy) has not reported any primary cancers.

ILEAL CONDUITS AND RESERVOIRS

Reconstructions with fewer than the combination of four components (urothelium joining colon, urine and faeces) do have a lower risk. Ileum in the gastrointestinal tract is a very rare site for malignant tumours. When used as a conduit or reservoir for urine they are

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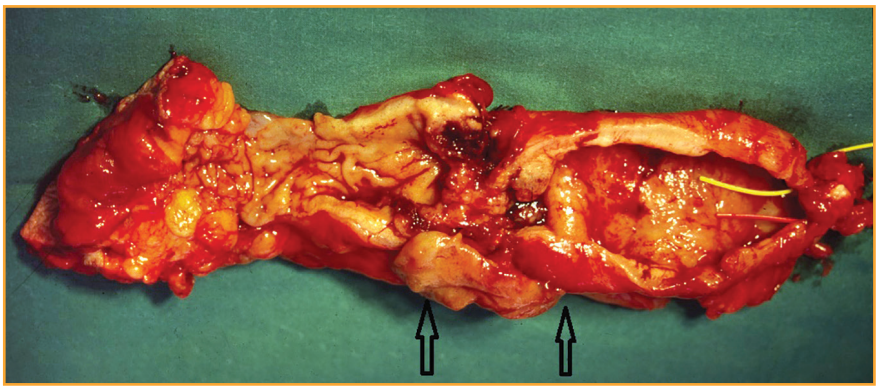

Figure 2. Fresh surgical specimen of an ileal conduit. It has been opened longitudinally. There is an obstructing adenocarcinoma in the central portion, remote from the ureters which have had yellow and red stents passed through them

likewise rare. In a German review of 37 years of follow-up from 44 clinics, the incidence of anastomotic tumour was 0.05% for ileal neobladders and 0.02% for ileal conduits, though one was a desmoid tumour.[2] There are also reports of non-anastomotic adenocarcinomas in conduits (Figure 2). For self-catheterisable ileo-caecal pouches there were three tumours in 2181 patients (1.14%), but only one was an adenocarcinoma. The time from surgery to neoplasia diagnosis was 1 to 37 years.[2]

The carcinogenic agent in U/sigs is unproven but may be an N-nitroso compound. These compounds are also found in ileal reservoirs when infection is present but not when the urine is sterile.[3] It is possible that the intermittent exposure to N-nitroso compounds may initiate anastomotic neoplasms with longer follow-up; however, there is no evidence for this so far.

COLON CONDUITS AND RESERVOIRS

Colon is less used than ileum for conduits and neobladders, making the incidence figures for tumours less accurate. In the German review there was one adenocarcinoma in a conduit at 40 years of follow-up and one benign tumour in a colonic neobladder (0.04%).

COMPLEX RESERVOIRS

The more complex the reconstruction, the higher is the neoplastic risk, especially when large bowel is incorporated. When an ileal patch is added on to a native bladder (clam cystoplasty), the risk goes up to 1.17% between 1 and 21 years. In a clam for a benign but chronic inflammatory disease of the bladder, such as bilharzia, tuberculosis or radiation, the neoplastic risk is higher; in an Egyptian series the figure was 3 in 54 patients (5.5%), but with a mean latency of 22 years.[4]

Continent catheterisable reservoirs have a higher risk than those based on urethral voiding or conduits. Nonetheless, all of these neoplasms are rare and only 50% are related to ureteric anastomosis.

NON-URINARY AND METASTATIC CANCERS

The organs used to replace the lower urinary tract are at risk of their own characteristic neoplasms, irrespective of contact with urine. This is particularly so with large bowel. Most non-anastomotic neoplasms in patients with U/sigs are adenocarcinomas. The sigmoid is the most common site of colonic carcinoma, especially in patients under 40 years old – highly relevant to those whose diversion was done in childhood. However, all of the large bowel is at risk. Figure 3 shows an example of a patient with an adenocarcinoma of the right colon used as a reservoir, and who was found to have multiple pre-malignant polyps elsewhere in the colon.

Most urinary diversions are done for pelvic malignancy, and metastases or local recurrence can occur in the reconstruction. The most common reconstruction of the lower urinary tract is made from ileum or colon anastomosed to the native urethra following cystectomy for carcinoma (orthotopic neobladder). The biggest cancer risk with this arrangement is recurrence of the original transitional cell carcinoma in the urethra. Data from series before orthotopic reconstruction was widely practised give that risk as 9% to 13% at five years and 17% to 27% at 10 years.[5,6]

More recently, lower urethral recurrence rates have been reported, especially after orthotopic reconstruction. However, it is still possible to find a range of risk from 1.4% to 18% at five years. There must be a selection bias in the various series to produce such a wide variation; in particular, longer follow-up gives a higher incidence. Curiously, the risk seems to be lower with an orthotopic neobladder compared to an ileal conduit diversion leaving the urethra *in situ* (4% and 8% respectively at 13 years median follow-up).[7]

Although there are differences of opinion in the literature, it is probable that involvement of the prostate, especially of the stroma, is a risk factor. Higher grade tumours and extensive carcinoma *in situ*

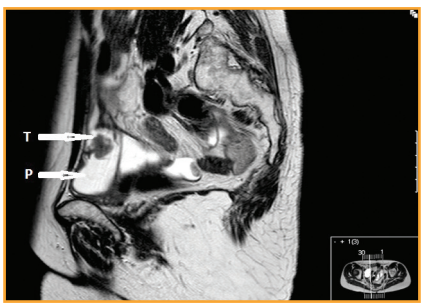

Figure 3. Sagittal MRI scan showing a right colon pouch (P) with a pedunculated adenocarcinoma (T). On colonoscopy the patient was found to have pre-malignant polyps at other sites in the large bowel. The pouch tumour was considered to be a part of colonic malignancy and unconnected with the reconstruction

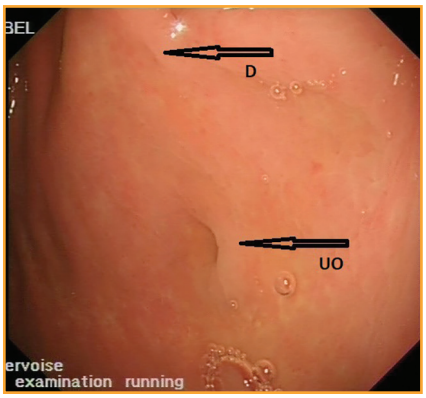

Figure 4. Sigmoidoscopic view of a normal ureteric orifice (UO) in a patient with a Mainz II type ureterosigmoidostomy. The bowel has an irregular surface; a similar looking dimple (D) is not a ureteric orifice. In supra-pubic catheterisable diversions it is seldom possible to get an endoscope bigger than 12fg through the channel, which gives a smaller field of vision and the orifice is more difficult to see

also increase the risk. In patients who have prostatic involvement and elect for an ileal conduit, urethral recurrence is found in 24%. Assuming that these data are correct, there is no justification for leaving the urethra behind if it is not going to be used for urination.[7] Reconstructions are seldom the site of truly metastatic disease, but it can occur.

SCREENING

It is standard practice to screen for neoplasms in patients with U/sigs or its variations, such as the Mainz II. Flexible sigmoidoscopy is recommended annually from the twelfth year.[8] As a result, virtually all tumours are found at a benign stage and can be managed with local excision, assuming that the patient wants to continue with a U/sig.

The latent period for neoplasms in other reconstructions is so long and the tumours so rare that screening would produce numerous negative results. It is largely in the follow-up of children that useful data have been accumulated, and it has been disappointing. In this group the risk of neoplasia in an augmented bladder (the largest group) is 1.5% per decade, mainly in those born with exstrophy or spina bifida.[9] Very few cases are anastomotic tumours. The others have usually been highly aggressive and rapidly fatal malignancies found through the onset of symptoms between any screening tests. Neither screening endoscopy nor urine cytology have been useful tests for early detection.[10]

With continent catheterisable reservoirs, endoscopy through the stoma is difficult, because the instruments have a small field of vision and there are no recognisable landmarks in the bowel wall. The ureteric orifice can be very difficult to see (Figure 4). It is not easy to exclude a neoplasm with confidence.

All patients with urinary diversions and reconstructions should have a urological review at least annually. A urinary tract ultrasound should be included, among other things. However, the main indication is to look for stones, which are far more common than tumours – any tumour present should be found. This was case with the patient in Figure 3 who was entirely symptomless.

CONCLUSIONS

There are two broad types of neoplasm in urinary diversions and reconstructions. The most common is the anastomotic adenoma associated with the U/sig and its variations. The adenomas undergo malignant transformation over a mean of five years and account for 94% of neoplasms found in this group.

For any other reconstruction and diversion, the risk of neoplasia is seldom more than 1% with a latency of up to 50 years. About a half of all cases are adenomas or adenocarcinomas at the anastomosis between transitional and intestinal epithelia. The other half are a disparate group of various histologies remote from any anastomosis. For patients having an orthotopic neobladder the risk of recurrence in the urethra is uncertain; possibly around 4% at 10 years. Urethral recurrence has a poor prognosis and patients should be advised of this risk in counselling before undergoing cystectomy.

For all of these neoplasms, the risk increases with time. Where screening is possible, it should never be abandoned. Where it is not possible, clinicians should always investigate the standard symptoms of urological malignancy promptly: it is not normal to have visible blood in the urine of a patient with a reconstruction or conduit.

KEY POINTS

- **The maximum risk of neoplasia in a urinary diversion occurs when there is an anastomosis of urothelium to colon that is exposed to both urine and faeces, as in ureterosigmoidostomies**
- **Anastomotic cancers are much less common when one or more of these four components are absent**
- **Other neoplasms in diversions or reconstructions are rare and only 50% of them are anastomotic; the other 50% may be unrelated to the diversion/ reconstruction**
- **Screening of patients with ureterosigmoidostomies for anastomotic cancer by flexible sigmoidoscopy is standard of care, as they are so common and there is a mean five-year pre-malignant interval**
- **Other malignancies are not amenable to screening**

Acknowledgements
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Declaration of interests: *none declared.*

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