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Urol Clin N Am 32 (2005) 157–164

UROLOGIC
CLINICS
of North America

Surgical Factors in the Treatment of Superficial and Invasive Bladder Cancer

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Successful treatment of bladder cancer depends on multiple factors involving both tumor and patient. These include features of the primary tumor (tumor type, stage, and grade); tumor biology (capacity to recur, invade, and metastasize); patient characteristics (general health and quality-of-life concerns); and treatment strategy (selection and type). Surgery remains the predominant treatment of primary, recurrent, and locally advanced bladder tumors, and mounting evidence suggests that surgical factors related to the quality of surgery influence bladder cancer outcomes. Regarding surgery, who performs it and how well it is done for both superficial and invasive bladder cancer matters [1].

Superficial bladder tumors

Bladder tumors are diagnosed by transurethral biopsy and resection. Transurethral resection (TUR) is often regarded as a stochastic procedure that is diagnostic, but only sometimes therapeutic for superficial and minimally invasive bladder tumors. An initial TUR of bladder tumors has three main goals: (1) TUR provides pathologic material to determine the histologic type and grade of bladder tumor; (2) TUR determines the presence, depth, and type of tumor invasion; and (3) TUR aims to remove all visible superficial and invasive tumors. A more complete TUR provides more tissue for pathologic evaluation and results in better staging. Such information is critical because tumor stage, grade, extent, and pattern of growth direct additional therapy and influence prognosis. A better TUR also provides better local control of superficial tumors.

Prerequisite to successful control of superficial bladder tumors is complete eradication of disease by a thorough TUR done before intravesical therapy. TUR should be wide and deep, especially for papillary or nodular neoplasms suspected of invasion. Proof of this concept is illustrated by a study in which 35% of 462 patients undergoing a TUR had residual tumor in the tumor base and at least 2 cm lateral to visible tumor on wider resection [2]. Studies also show residual tumor at the first follow-up cystoscopy in 41% to 76% of patients [3–5], suggesting that the first resection is often incomplete. Early response to therapy (at 3 or 6 months) after TUR and intravesical therapy of superficial bladder tumors is the most powerful predictor of tumor recurrence and stage progression. Such information combined provides compelling evidence that the quality of the initial TUR is an integral component of treatment determining that first response and subsequent outcome.

How well TURs are performed for bladder tumors varies widely among urologists. For example, the presence of tumor at the first cystoscopy varied from 3% to 46% among a total of 2410 patients with superficial bladder tumors entered in multiple cooperative group trials. There was substantial difference between institutions and surgeons not explained by disease-related factors, suggesting that the quality of the TUR was responsible [6]. Even in the hands of experienced urologists, incomplete resection of minimally invasive bladder tumors is common. Of 71 patients with newly diagnosed stage T1 bladder cancers resected by the author, 18 (25%) had residual T1 disease found on contemporary

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0094-0143/05/$ - see front matter
doi:10.1016/j.ucl.2005.02.003

reresection 4 weeks later and 2 (3%) were upstaged to muscle invasion [7]. Another study showed that 40% of superficially invasive tumors had no muscle submitted or identified in the deep margins of resection [8], and a recent pathology review found that muscularis propria was missing in up to 51% of TUR specimens submitted by general urologists [9]. Proper execution of TUR is critical for primary tumor staging and determining definitive treatment. The pathologist can only evaluate what the urologist submits. Lack of a complete resection significantly increases the chance of understaging, early tumor recurrence, and stage progression of disease.

Second or restaging transurethral resection

Although most urologists agree that ideally initial TUR of bladder tumors should be thorough and complete, many factors confound the adequacy of resection, including multiplicity, size, location, and extent of tumor burden; capability and perseverance of the surgeon; and to some degree the body habitus of the patient. Because local tumor control and accurate tumor staging depend on complete TUR, a second or restaging TUR may be of value in evaluating patients with superficial bladder tumors. The purpose of a restaging TUR is to reduce the uncertainty of depth of tumor invasion, to control the primary tumors better, and to provide additional pathologic information that may help select appropriate treatment.

Table 1 shows results of a second TUR performed by the author in 96 consecutive cases 2 to 6 weeks after initial TUR by multiple referring urologists diagnosed superficial bladder tumors [8]. A significant proportion (75%) was found on the second TUR to have residual tumor: 31% had noninvasive tumor, 24% had submucosal invasion, and 20% were upstaged to muscle-invasive tumors. An incomplete initial resection was observed in 49% of stage T1 tumors when no muscle was submitted in the TUR specimen compared with 14% when muscle was identified. If cases of carcinoma in situ are excluded because complete TUR is less likely for such tumors, and one considers only the 76 patients with papillary Ta or T1 tumors, then 24% had no residual tumor found on restaging TUR, whereas 76% had residual tumor. Results of the second resection changed the strategy of tumor management in 33% of patients. Table 2 shows results from recently reported series of restaging TUR in patients with stage T1 bladder cancer [10]. Residual T1 tumor was present in 15% to 53% of cases, and another 4% to 29% were upstaged to muscle invasion. Collectively, these data show that a second or restaging TUR improves the quality of TUR, resulting in better assessment, local control, and staging accuracy of superficial bladder tumors.

Can a second TUR improve the treatment outcome of patients presenting with superficial bladder tumors? A recent long-term observational study showed that among a cohort of 124 consecutive patients, a restaging TUR found residual tumor in 33% of cases, and 81% of these were at the original tumor site [11]. After 5 years follow-up, 63% of the patients undergoing a second TUR had tumor-free bladders compared with 40% after a single TUR. Progression to muscle invasion was observed in only two (3%) patients after a restaging TUR. Another recent study suggests that a restaging TUR of high-risk

Table 1
Comparison of bladder tumor stage after first and second transurethral resections

Stage at first TUR	No. pts.	Stage at second TUR. No. pts. (%)			
		T0	Ta/Tis	T1	T2
Tis	20	6 (30)	8 (40)	4 (20)	2 (10)
Ta	18	5 (28)	7 (39)	5 (28)	1 (5)
T1	58	13 (22)	15 (26)	14 (24)	16 (28)
Muscle	35	9 (26)	11 (31)	10 (29)	5 (14)
No muscle	23	4 (17)	4 (17)	4 (17)	11 (49)
Totals	96	72 (75%)			

Abbreviation: TUR, transurethral resection.

Table 2
Bladder tumor stage after second transurethral resection of T1 tumors

Series	Year	No. patients	Stage at 2nd TUR			
			% T0	% Ta/Tis	% T1	% T2
Klan	1991	46		15	26	2
Herr	1999	58	22	26	24	28
Schwaibold	2000	60		17	24	5
Jakse	2001	42	35	17	24	24
Ozen	2001	28		18	53	29
Schips	2002	76	67	11	15	8
Rigaud	2002	52		16	17	4
Vogeli	2003	19		37	43	19