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Efficacy of Transurethral Resection of the Bladder Tumor (TUR-BT) for Huge Bladder Cancer

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Abstract

There are no guidelines regarding whether to perform either a radical transurethral resection of the bladder tumor (TUR-BT) or a total cystectomy after TUR biopsy for huge bladder cancer, and this decision is entrusted to each institution. Of 439 patients in whom TUR-BT was performed from 2005 through 2009, the weight of the total resected volume was > 50 g in 6 patients, and among these 6 patients the following variables were compared: operating time, weight of resected volume, transfusion volume, presence or absence of hydronephrosis, preoperative urinary cytology, serum cytokeratin 19 fragment (CYFRA) level, intraoperative bladder compliance, and histopathological findings. The median age, operating time, weight of resected volume, transfusion volume, and length of follow-up were 72 years, 300 minutes, 88 g, 202 mL, 16 months, respectively. The serum CYFRA level in patients with muscle-invasive cancer (11.8 ng/mL) was higher than that in patients with non-muscle-invasive cancer (5.06 ng/mL). All patients with non-muscle-invasive bladder cancer survived without recurrence. Although the mean length of follow-up was only 16 months (5–59 months), the 1 patient who was followed up for 59 months had no recurrence. In cases of muscle-invasive bladder cancer, all patients, except for a relatively recent patient, have died. In cases without muscle invasion, lymph node metastasis, distal metastasis, or preoperative renal dysfunction accompanied by hydronephrosis, with favorable bladder compliance, we believe that radical TUR-BT should be actively performed to preserve the bladder. A second TUR-BT should be performed in cases of non-muscle-invasive cancer without G3 components to treat the huge bladder cancer.

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Key words: Huge bladder cancer, second transurethral resection of the bladder tumor, bladder preservation

Introduction

Bladder cancer is a common form of urothelial carcinoma, and accurate staging is important for therapy selection and prognosis in patients with bladder cancer. Thus, there is no doubt that transurethral resection of the bladder tumor (TUR-BT) is the gold standard for the initial treatment of bladder cancer. However, at present, there are no

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Table 1 Patient's characteristics in huge bladder tumor

No	Sex	Age	TUR-Bt	OT (min)	BT F (mL)	RV (g)	Com-plication	Pathological outcome	Hydro-nephrosis	Bladder com-pliance	CYFRA	Cytology	Follow-up (months)	Adjuvant therapy, out come
1	M	56	1st	325	420	98	DM, HT	UC, G2, pT1, INFα>β	(−)	favorable	4.1	Class V	59	BCG
			2nd	278	0	25		UC, G2, pT1, INFα>β						tumor free, alive
2	M	75	1st	230	420	150	HT, Angina	Neuroendocrine Ca, pT3b	(−)	poor	13.6	Class V	9	Total Cystectomy
														dead
3	M	84	1st	160	0	100	ARF	Undifferentiated Ca, G3, more than pT2	Bilateral severe	poor	4.8	Class V	4	No
														dead
4	M	68	1st	358	420	88	DM	UC G2>G1, pT1, INF α	(−)	favorable	8.5	Class V	12	BCG
			2nd	252	0	22		UC G2>G1, pT1, INF α						tumor free, alive
5	M	60	1st	481	0	133	DM	UC G1>G2, pT1, INF α, CIS G2	Lt mild	favorable	2.6	Class II	8	BCG
			2nd	361	140	55		UC G1>G2, pT1, INF α, CIS G2						tumor free, alive
6	F	91	1st	258	420	58	HT	UC G2>G3, more than pT1	Rt severe	favorable	17	Class IV	5	No
														residual tumor (+), alive

OT: operating time, BTF: blood transfusion, RV: resected volume, ARF: acute renal failure

guidelines regarding whether to perform either radical TUR-BT[1] or only total cystectomy after TUR biopsy for huge bladder cancer, and this decision is entrusted to each institution. To the best of our knowledge, there has not been any study investigating this issue. The decision of whether to preserve the bladder is a big problem for patients and medical staff. Mersenburger et al.[2] have reported that multimodality strategies for preserving the bladder might be a therapeutic option for carefully selected patients. At our institution, we have already tried to preserve the bladder in patients with muscle-invasive bladder cancer by performing radical TUR-BT and intra-arterial injection of anticancer agents.

In this study, we retrospectively analyzed TUR-BT procedures that were performed for huge bladder cancer (with the weight of the resected tissue > 50 g) at our institution, and we examined which cases should be treated with radical TUR-BT.

Patients and Methods

Of 439 patients in whom TUR-BT was performed from 2005 through 2009, the weight of the total resected tissue was greater than 50 g in 6 patients. The following variables were compared among these 6 patients: operating time, weight of resected tissue, transfusion volume, presence or absence of hydronephrosis, preoperative urinary cytology, serum cytokeratin 19 fragment (CYFRA) level, intraoperative bladder compliance, and histopathological findings. One urological pathologist performed all histopathological analyses. Postoperatively, urinary cytology and cystoscopy were performed every 3 months, and computed tomography (CT) was performed every 6 months to examine the upper urinary tract and look for recurrence and metastasis. Informed consent for radical TUR-BT was obtained from all patients.

Results

Table 1 shows the patients' characteristics. The median age, operating time per surgery, weight of resected tissue, transfusion volume, preoperative serum CYFRA, length of follow-up were 72 years (range, 56–91 years), 300 minutes (range, 160–481 minutes), 88 g (range, 22–150 g), 202 mL (range, 0–420 mL), 8.4 ng/mL (range, 2.6–17 ng/mL), and 16 months (range, 5–59 months), respectively. Preoperative urinary cytology was class V in 4 patients, IV in 1 patient, and II in 1 patient. As for histopathological findings, 4 patients had urothelial carcinoma, 1 patient had neuroendocrine cancer, and 1 patient had undifferentiated carcinoma. The length of follow-up ranged from 5 to 59 months (median: 16 months). Although the length of follow-up was short, all patients with non-muscle-invasive bladder cancer survived without recurrence. The 1 patient who was

Table 2 Levels of serum CYFRA, rate of hydoronephrosis, and presence of poor bladder compliance

	Serum CYFRA (ng/mL)	Hydronephrosis	Poor bladder compliance
Non-muscle Invasive bladder cancer	5.06 (2.6－8.5)	1/3 (33%)	0/3 (0%)
Muscle Invasive bladder cancer	11.8 (4.8－17)	2/3 (66%)	2/3 (33%)

followed up for 59 months has also had no recurrence. All patients with muscle-invasive bladder cancer, except for a relatively recent patient, have died.

We examined the preoperative serum level of CYFRA, the presence or absence of hydronephrosis, and bladder compliance between patients with non-muscle-invasive and muscle-invasive bladder cancer (**Table 2**). The serum CYFRA level in patients with muscle-invasive cancer (11.8 ng/mL) was higher than that in patients with non-muscle-invasive cancer (5.06 ng/mL). Hydronephrosis was more common in patients with muscle-invasive bladder cancer, and poor bladder compliance was also more common in patients with muscle-invasive bladder cancer.

Discussion

There is no doubt that TUR-BT is an important factor for non-muscle-invasive bladder cancer. How to use TUR-BT is an important issue for prognosis. The European Association of Urology states, "a complete and correct TUR is essential for the prognosis of the patients"[3]. However, with huge bladder cancer, it is difficult to ascertain invasiveness preoperatively, and the decision whether to perform radical TUR-BT is entrusted to physicians at each institution.

The problems of performing TUR-BT for huge bladder cancer are the large amount of blood loss and the long operating time. At our institution, the average operating time was 300 minutes, and the average volume of allogeneic blood transfusion was 202 mL. The major advantage of radical TUR-BT is bladder preservation, and at our institution, the bladder was preserved in 3 of the 6 patients. This result confirms the significance of radical TUR-BT for huge bladder cancer. The first case showed no recurrence for 59 months, thus supporting our rationale for radical TUR-BT for huge bladder cancer. In the other 3 cases of muscle-invasive bladder cancer, 1 patient was elderly and did not receive postoperative therapy, and another patient refused postoperative therapy; however, a third patient eventually underwent total cystectomy. In these 3 patients with muscle-invasive bladder cancer, total cystectomy should have been considered from the beginning instead of radical TUR-BT.

Diagnosing local invasion of bladder cancer is generally difficult. Tillou et al.[4] have reported that magnetic resonance imaging (MRI) can accurately distinguish non-muscle-invasive cancer and muscle-invasive cancer (80% sensitivity and 90% specificity). However, Assmy et al.[5] have documented a staging accuracy of 63.6% in distinguishing non-muscle-invasive cancer and muscle-invasive cancer. In the future, it will be necessary to perform MRI in all patients with huge bladder cancer to ascertain whether the cancer is invasive. According to our results, although the number of cases was small, poor bladder compliance due to cancer invasion into the muscle layer may be a preoperative indicator of invasiveness. While not numerically clear, our impression was that bladder compliance was poor in all patients with muscle-invasive bladder cancer. As shown in **Figure 1**, even when a bladder cancer is huge, the probability of bladder preservation is high if bladder compliance is favorable; therefore, and bladder compliance may be the best indicator.

In the TUR-BT, we adjusted the electric power to reduce blood loss. At first, we used a conventional method of TUR-BT at the surface of bladder cancers. We then changed the high-power coagulator mode and resected cancer body. Finally, we resected the muscle layer with the usual mode. These methods allow accurate diagnosis of the bladder cancer and bleeding control. However, it is difficult to perform TUR-BT without blood transfusion. In case 3, the tumor was

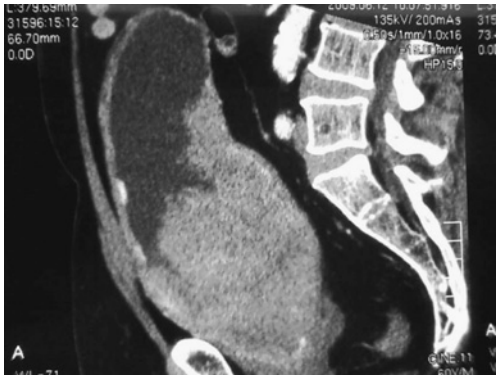

Fig. 1 Computed tomography (CT) finding. Huge bladder tumor can be seen, but the compliance of bladder seems to be favorable (case 5).

histopathologically diagnosed as a muscle-invasive undifferentiated G3 carcinoma, and in this unusual case, 100 g was resected with minimal bleeding. Furthermore, if bleeding cannot be controlled with TUR, transarterial embolization is required. Therefore, TUR should not be performed for patients with huge bladder cancer at institutions where transarterial embolization is unavailable.

At present, there is no established blood tumor marker for urothelial carcinoma. At our institution, we have investigated the usefulness of serum CYFRA as a maker for urothelial carcinoma based on the findings of Pariente et al.[6]. In a previous study[7], we used a CYFRA level of 2.6 ng/mL as a cut-off value. We have concluded that serum CYFRA is a useful marker in muscle-invasive bladder cancer. Andreadis et al.[8] have also concluded that serum CYFRA is a useful marker during chemotherapy, and at our institution, CYFRA has been used as a serum tumor marker for muscle-invasive urothelial carcinoma. We believe that serum CYFRA level might be used an indicator for the invasiveness of bladder cancer. Although the serum CYFRA of 1 patient with non-muscle-invasive bladder cancer was higher than in a patient with muscle-invasive bladder cancer, the mean serum CYFRA level of patients with muscle-invasive bladder cancer was higher than patients with non-muscle-invasive bladder cancer. It may be found that serum CYFRA is a muscle-invasive bladder cancer indicator by accumulating more cases.

Although the prognosis of non-muscle-invasive bladder cancer is generally considered favorable, we should be particularly cautious with T1 and G3 bladder cancer. Millan-Rodriguez et al.[9] have investigated the rates of recurrence, progression, and mortality in 1,529 patients with non-muscle-invasive bladder cancer. Multiple tumors, tumors ≥ 3 cm in diameter, and concomitant carcinoma in situ (CIS) were correlated with the rate of recurrence, and G3 cancer, multiple tumors, tumors ≥3 cm in diameter, and concomitant CIS were correlated with the rate of progression. However, G3 cancer and concomitant CIS were significant factors for the rate of cancer mortality, and the odds ratio for G3 cancer was 14. These findings clarify that G3 is a factor related to the most important parameters of progression and survival rate. We believe that an important factor in huge T1 bladder cancer is the absence of G3 components. Therefore, our patients in whom bladder preservation was possible did not have G3 components. In the future, it will be necessary to consider early systemic therapy for patients with preoperative cytology class V with G3 components.

Performing a second TUR has many advantages, including accurate pathological T stage diagnosis, minimal false-negative diagnosis, accurate diagnosis of recurrence, identification of patients with early progression requiring total cystectomy, achievement of favorable responses to bacillus Calmette-Guerin (BCG) therapy, and avoidance of BCG therapy, while decreasing the risk of recurrence. According to recent reports, the rate of detection of muscle invasion with a second TUR has been reported to be 3.8% to 10%[10–12]. The failure to perform a second TUR may result in the failure to detect muscle invasion. Based on these findings, the guidelines of the European Association of Urology and the American Urological Association now recommend a second TUR if pT1, G3 residual tumor is suspected. In the present study, a second TUR was performed in all cases of T1 tumors. Because these patients have not experienced recurrence or progression, we believe that TUR resulted in accurate staging and cure.

To prevent postoperative recurrence, anticancer agents and BCG are 2 therapeutic options. Many

studies and meta-analyses have shown that intravesical BCG therapy delays tumor recurrence and progression compared with treatment with mitomycin[13–15]. We also performed postoperative intravesical BCG therapy in all patients with pT1 disease. Because the area of bladder resection was broad, we were concerned about the side effects of BCG. However, BCG therapy was performed 6 times without any particularly severe side effects, and although the length of follow-up has been short, recurrence has not been observed.

For cases without muscle invasion, lymph node metastasis, distal metastasis, or preoperative renal dysfunction accompanied by hydronephrosis and with favorable bladder compliance, we believe that TUR-BT should be performed to preserve the bladder. For cases without G3 components and non-muscle-invasive cancer a second TUR-BT should be performed to cure the huge bladder cancer.

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