

Approaching the optimal transurethral resection of a bladder tumor

Optimal mesane tümörünün tam transüretral rezeksiyonuna yaklaşım

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ABSTRACT

A complete transurethral resection of a bladder tumor (TURBT) is essential for adequately diagnosing, staging, and treating bladder cancer. A TURBT is deceptively difficult and is a highly underappreciated procedure. An incomplete resection is the major reason for the high incidence of recurrence following initial transurethral resection and thus to the suboptimal care of our patients. Our objective was to review the pre-operative, intraoperative, and postoperative considerations for performing an optimal TURBT. The European Association of Urology (EAU), Society of International Urology (SIU), and The American Urological Association (AUA) guidelines emphasize a complete resection of all visible tumor during a TURBT. This review will emphasize the various techniques and treatments, including photodynamic cystoscopy, intravesical chemotherapy, and a perioperative checklist, that can be used to help to enable a complete resection and reduce the recurrence rate. A Medline/PubMed search was completed for original and review articles related to transurethral resection and the treatment of non-muscle-invasive bladder cancer (NMIBC). The major findings were analyzed and are presented from large prospective, retrospective, and review studies.

Key words: Bladder cancer; checklist; fluorescence cystoscopy; narrow band imaging; transurethral resection.

ÖZET

Mesane kanserinin yeterli şekilde teşhisi, evrelemesi ve tedavisi için mesane tümörünün tam transüretral rezeksiyonu (TURBT) esastır. TURBT aldatıcı biçimde zordur ve son derece az değer görmüş bir işlemdir. Tam olmayan bir rezeksiyon ilk transüretral rezeksiyon sonrası yüksek nüks insidansının başlıca nedenidir ve böylece hastalarımızın suboptimal bakımına neden olur. Amacımız optimal bir TURBT gerçekleştirmek için preoperatif, intraoperatif ve postoperatif konuları gözden geçirmektir. Avrupa Üroloji Birliği (EAU), Uluslararası Üroloji Derneği (SIU), ve Amerikan Üroloji Birliği (AUA) kılavuzları bir TURBT sırasında görünür tüm tümörün tam bir rezeksiyonunu vurgulamaktadır. Bu derleme tam bir rezeksiyonu sağlamaya ve nüks hızını azaltmaya yardımcı olmak için kullanılabilen fotodinamik sistoskopi, intravezikal kemoterapi ve bir perioperatif kontrol listesi dahil olmak üzere çeşitli teknikleri ve tedavileri vurgulayacaktır. Transüretral rezeksiyon ve kasa invaziv olmayan mesane kanseri (NMIBC) tedavisi ile ilgili özgün ve derleme yazıları için Medline/PubMed taraması tamamlanmıştır. Geniş prospektif, retrospektif ve derleme çalışmalarından gelen önemli bulgular analiz edilmiş ve sunulmuştur.

Anahtar kelimeler: Mesane kanseri; kontrol listesi; floresans sistoskopi; dar bantlı görüntüleme; transüretral rezeksiyon.

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Introduction

A transurethral resection of a bladder tumor (TURBT) is one of the most common and underappreciated operations in urology.^[1] Although it is thought of as an “easy” operation, it is increasingly recognized that the tumor is often incompletely resected, contributing to the high recurrence rate. Although it is highly understudied (a PubMed search for complications of radical prostatectomy versus TURBT produces 2964 and 55 results, respectively), TURBT is the mainstay of treatment for non-muscle-invasive bladder cancer

(NMIBC) - the 5th most common and most costly type of cancer to treat in Western society.^[2] The American Urological Association (AUA), European Association of Urology (EAU), and Society of International Urology (SIU) guidelines state that when possible, a complete resection of all bladder tumors should be performed.^[3-5] Multiple studies have reported between 30%-70% of residual cancer on repeat TUR.^[6,7] Even an apparently well-performed TURBT is not always complete, depending on the pathology of the tumor.^[8,9] There have been several technological advances to aid urologists, beginning with a periop-

erative checklist.^[10] We review these methods to enable practitioners to perform a complete TURBT.

Evidence Acquisition

An electronic database search was performed using PubMed and Medline for articles addressing the TURBT technique, the need for repeat TURBT, fluorescence cystoscopy (FC), narrow-band imaging (NBI) versus white light cystoscopy (WLC), and the use of intravesical chemotherapy in the immediate postoperative period for NMIBC. The recommendations from these articles were analyzed. The outcome of this analysis was used to generate recommendations to help improve considerations when performing TURBT for NMIBC.

Evidence Synthesis

Preoperative Considerations

History and Physical

As with any operation, the treatment begins in the outpatient setting. At this time, a full history is obtained, and a focused urological physical examination is performed. The history should include the patient's age, sex, past medical history, smoking history, history of bladder cancer or other malignancies, previous surgical history including endoscopic treatment and any intravesical therapy following the diagnosis of bladder cancer (BCa). A review of the patient's imaging studies is important to determine the status of the upper urinary tract.^[10]

A focused urologic physical exam should be performed, including the patient's performance status and body habitus. Obese patients can exhibit problems during a TURBT, as their abdominal girth may make it difficult to resect a tumor located in the anterior or posterior wall of the bladder. One must not forget to examine the prostate in men.^[10] The typical presentation for a patient with a bladder tumor is hematuria, and thus at least in our practice, the initial diagnosis is made at the time of an office flexible cystoscopy. At that time, the clinician documents the location, size, and configuration of the tumor. The use of a bladder diagram may be useful.^[11] The urologist has an immediate idea of the grade and stage, and with experience, the accuracy is quite good. Herr et al reported that 93% of TaG1 and 92% of TaG3 or T1G3 lesions were able to be correctly staged cystoscopically when compared with the final pathology.^[12] If this is the first diagnosis of a bladder tumor, the patient will go to the operating room for a TURBT under anesthesia. If this is a recurrence of a small apparent low grade Ta tumor, the lesion may be managed expectantly or safely cauterized in the office setting. The natural history of low-grade BCa has been validated in multiple studies dating back to 1987 by Jordan et al, continuing with Prout et al in 1992, and again by one of us through our own experience.^[10,12-16] Such tumors rarely threaten the life of a patient and should not be overtreated.

On the day of the operation, the history and physical exam should be reviewed. The case should be discussed with the anesthesiologist. The type of anesthesia is important. The patient should be fully relaxed so that the bladder can be filled to the desired amount (approximately 50%-70% of capacity). General anesthesia with complete neuromuscular blockade is often preferred, as it allows the patient to be paralyzed as needed intraoperatively and to recover quickly postoperatively. Spinal anesthesia is also a reasonable option as it ensures the patient will not move during the procedure and maximizes bladder relaxation. Although we have never used this technique, transvesical injection of the obturator nerve has been reported to be an effective method to block the adductor or obturator reflex.^[17] Lastly, in addition to the routine preoperative lab values, the team should review any history of anticoagulant therapy, which is common in elderly patients.^[10]

Intraoperative Considerations

Cystoscopy

A checklist can be used to ensure that all of the necessary equipment is available during the procedure and thus avoid delays while the patient is under anesthesia. It is a good habit to have a systematic way of performing a TURBT to ensure that no steps are missed. An optical dilator can be used during the initial part of the endoscopy to dilate the urethra under direct vision, to enter the bladder without urethral trauma, to avoid bleeding, and to allow adequate visualization of the prostatic urethra.^[18] Next, a 26F or 28F continuous flow resectoscope is inserted. Urine should be collected and sent for cytology based on the clinical scenario. A pancystoscopy is performed with both the 12- and 70-degree lenses. The bladder volume should be maintained at approximately 50%-70% of its capacity to avoid overdistention. This step is important, as a full bladder can flatten the mucosa and make it more difficult to visualize areas of carcinoma in situ (CIS). Again, a systematic approach should be taken during the cystoscopy. The ureteral orifices should be identified. When a tumor is found, its size and location should be documented.^[10,19] Brausi et al.^[11] emphasized using a bladder diagram to document the location of all tumors. With a programmatic emphasis on performing a complete TURBT and the use of a diagram, the authors observed that experienced surgeons were able to lower their recurrence rate.^[11] We utilize photography as well as written documentation to capture this information. In our experience, having a picture of the tumor in the patient's record is more informative than the dictated operative report.

Resection

A small papillary tumor can be removed either with cold cup biopsy forceps or by a standard TURBT. The cold cup technique eliminates cautery artifact, which improves the pathologist's ability to analyze the specimen. A larger tumor should be removed systematically with the electrocautery loop. The urologist can choose either monopolar or bipolar for the resection.

Our experience, as well as other reports, has found them equally safe and effective.^[20,21] We try to minimize cautery artifact and decide before each procedure on the needed depth of resection. We balance the importance of identifying the muscularis propria (MP) in the specimen against the risk of bladder perforation and of scarring of the bladder. MP is not required for the majority of patients who have a history of low grade Ta tumors yet is a requirement for patients who appear to have a high-grade tumor or during a repeat TURBT. Depending on the location of the tumor, a right angle or bladder wall loop should be selected. We prefer the right angle loop for a tumor at the trigone, bladder neck or anterior. The bladder wall or angled loop is ideal for tumors located on the posterior or lateral walls. When resecting a large tumor, it might aid the pathologist for the urologist to remove a separate specimen from the deep margin of the resection site.^[10] Sending a separate deep margin that includes the MP may improve decision-making and help ensure a complete resection. One needs to find the MP in the specimen for pT1 tumors for accurate staging. Herr and Donat observed residual tumor on re-resection in approximately 49% of cases without MP in the specimen compared with only 14% when it was present. The authors also found that for large tumors, a wider margin of resection helped with pathologic diagnosis, microscopic cancer control, and patient management.^[19] Jancke and colleagues reported that having at least an 8-mm margin of tumor-free urothelium around the lesion decreased the local recurrence rate from 58% to 19%.^[22] Multiple other studies exhibit a high rate of residual disease after the initial TUR. At re-resection (depending on tumor location and number), residual tumor was observed in up to 76% of patients; more inexperienced surgeons and multiple tumors were credited as having a large impact.^[6,23,24] It has been suggested that identifying and resecting all tumors that have MP in the specimen and have a low 3-month recurrence rate should be considered as markers of an adequate TURBT.^[25] A report from Jancke et al.^[26] indicated that more experienced surgeons perform a more complete resection and have lower recurrence rates. The authors looked at over 750 cases and found that faculty members had a recurrence rate of 60% versus 72% for residents at three months. These results were also observed by Mariappan et al.^[23] with a recurrence rate of 25% for experienced surgeons and 39% for less experienced surgeons. Brausi et al.^[27] reported that by increasing supervision and training in a residency program, the authors were able to decrease the recurrence rate from 28% to 16% at three months. After a resection is completed (including possible use of additional technology such as photodynamic cystoscopy or narrow band imaging), a 70-degree lens should be reinserted to ensure that no tumor remains and that adequate hemostasis is achieved.

Narrow Band Imaging (NBI)

Narrow Band Imaging is designed to aid in complete resection of bladder tumors. NBI consists of two bandwidths of light that are centered on blue, 415 nm, and green, 540 nm.^[28] The NBI is built into the light source and camera. By using only these

bandwidths, capillaries and other small blood vessels are more readily identified.^[29] Several studies demonstrate a higher detection of BCa and, more importantly, a higher recurrence-free survival when used during TURBT.^[30,31] The procedure does not require dye, has a higher detection rate, and has a comparable false-positive rate compared with white light cystoscopy (WLC).^[32] Herr et al.^[33] evaluated 103 patients with recurrent NMIBC, and although 87% of the recurrences were able to be seen with WLC, 100% of the lesions were visualized with NBI. Naselli et al.^[34] performed a prospective randomized control study powered to report a 10% difference in recurrence at 1 year and, indeed, found the recurrence risk using NBI versus WLC during TURBT to be 33% versus 51%, respectively. Montanari et al.^[35] later confirmed these results with a prospective trial that reported recurrence rates at 1 year of 35% with NBI compared with 50% with only WLC. In our experience, NBI is optimal in detecting residual papillary tumors after initially resecting with WLC. The procedure thus allows small tumors to be resected that may not have otherwise been found until the follow-up endoscopy and may have been considered new tumors.

Fluorescence cystoscopy (FC)

Another modality that can be used to help identify the 10-20% of bladder tumors that are overlooked with WLC is the use of a photosensitizing agent that is preferentially taken up by neoplastic cells.^[36] Hexylaminolevulinic acid (HAL) is an ester derivative of 5-aminolevulinic acid (5-ALA) and is the most commonly used photosensitizing agent. The 5-ALA or HAL is instilled into the bladder one hour preoperatively and removed at the time of the cystoscopy. Tumors may be identified by their red fluorescence when seen under the blue-violet light spectrum. Numerous studies have been performed investigating the additional detection rate of tumor, residual tumor at second resection, and recurrence-free survival with the use of 5-ALA and HAL.^[28,37-39] Grossman et al.^[40] and Jocham et al.^[41] both reported an approximately 11% increase in the detection rate of Ta tumors. The largest clinically important impact is on detection of CIS. Multiple studies reported an increase in its detection, ranging from 24%-44%.^[41-43] Another prospective randomized control trial revealed a median recurrence-free survival of 9.6 months in WLC compared with 16.4 months in FC.^[44] Geavlete et al.^[45] used HAL in high-risk bladder cancer and reported that at re-resection at 6 weeks, there was a short-term recurrence rate of 11% with FC versus 31% with WLC alone. Overall, the use of FC can prolong the time to recurrence in NMIBC.

Other considerations

Intraoperative complications are primarily limited to bladder perforation and bleeding. The complication rate ranges from 5%-43%; however, the majority of studies have reported values less than 15%. Neider et al.^[46] reported a 2.3% incidence of hematuria requiring transfusion in a residency setting. Additionally, the authors found the rate of bladder perforation

to be 3.5%. Bladder perforation is typically managed with an indwelling catheter; however, intraperitoneal bladder perforation carries a risk of peritoneal seeding of the tumor and should be managed by closing the defect if the rent is large.^[47] In our opinion, these rates are higher than what occurs with an experienced urologist. Bladder perforation should be rigorously avoided and, if necessary, should be conducted with great care, as significant hematuria should occur in <1% of cases.

Post-TURBT intravesical chemotherapy is recommended by the AUA, EAU, and the SIU.^[3-5] According to the International Bladder Cancer Group for low-risk NMIBC, there is an absolute risk reduction of recurrence of 17% with instillation of mitomycin C (MMC) into the bladder in the immediate postoperative period.^[48] Additional studies have confirmed these results and have compared MMC with other chemotherapeutic drugs that have been found to be less efficacious.^[47-50] The reasons for this risk reduction are likely multifactorial but are at least in part due to the reduction of the implantation of tumor cells, which is one of the causes of recurrence. It is our practice to instill MMC in the immediate postoperative period for all papillary tumors regardless of tumor grade as long as there is not a deep resection and a possibility of drug extravasation.

There are a multitude of considerations in performing an optimal TURBT. An incomplete resection is common and requires diligence and proper training like any other surgical procedure. Similar to what occurs in the airline cockpit, a perioperative checklist should be standard to ensure that the fundamentals of each case are reviewed and that the necessary procedure can be individualized for each patient. New technology can be used to aid in the complete resection of tumors and help ensure improved patient care.

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