HOW TO OPTIMIZE TURB

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ABSTRACT

Transurethral resection of the bladder (TURB) is an apparently easy endourological operation familiar to all urologists. Often considered a less formidable procedure, on the contrary TURB is rather demanding from an oncologic point of view. The results of TURB are limited by the risk of tumor understaging and the high recurrence rate. The major prerequisite for optimal oncological outcomes is a systematically and meticulously performed TURB by a well-trained urologist. It is important to be systematic and to follow updated guidelines, as well as to use modern equipments, including bipolar resectoscopes, new telescopes and high-definition video systems. Urologists should also be aware of promising innovations in imaging techniquesand their possible benefits, with particular reference to the photodynamic diagnosis (PDD)-aided cystoscopy and TURB.

1. Introduction

Transurethral resection of the bladder (TURB) is an apparently easy endourological operation familiar to all urologists. Often considered a less formidable procedure, on the contrary TURB is rather demanding from an oncologic point of view. If performed correctly it may allow long-term control of bladder cancer; if performed unproperly it may not achieve its diagnostic and therapeutic goals, i.e. the complete removal of the tumor tissue, when feasible, in absence of perioperative complications and an accurate pathologic evaluation of the resected tissue for a reliable TNM staging and histologic grading, fundamental for planning the appropriate therapeutic approach.

It has been demonstrated that many of the so-called early recurrences are in fact persistent tumors that were overlooked and left behind during resection.Even more importantly, inaccurate diagnosis, in particular understaging, can adversely affect the survival of the patient.In a series of more than 1000 patients affected by first diagnosed T1G3 bladder cancer who underwent early cystectomy more than 33% had a non-organ-confined disease, almost 50% were understaged by TURB and about 35% died of metastases at 48 months.[1-3]

For all these reasons it is evident that quality of TURB is crucial. A low grade/low stage bladder cancer may forgive an incomplete TURB without heavy consequences for the prognosis of

the patient, except for the need for an early endoscopic retreatment of a lesion which is not a recurrence but rather residual disease.[4]In the case of a muscle-invasive bladder cancer TURB may well be incomplete because of the bulk of the tumor and just have a staging role, being the damage of leaving some bladder cancer behind limited by the fact that the patient will early undergo radical surgery. But the respect of the cornerstones of a good TURB (completeness and good quality of the resected tissue) becomes of the utmost importance for the heterogeneous group of the non-muscle-invasive bladder cancers on the whole[5], including both "kitten" and"tigers", exhibiting a wide range of recurrence, progression and survival rates. This is why TURB should be maximally optimized by the use of a variety of means, helping the surgeon to satisfy all the clinically required requisites.

2. **Step by step standardization of TURB**

TURB should be performed systematically and meticulously. Aproposal for a transurethral resection of bladder tumor checklist has also been recently published.A well-trained urologist should carry it out and teach it step by step to residents and less experienced urologists. A careful TURB additionally minimizes perioperative morbidity, avoiding problems like bladder overdistension, overlooked perforations or damage of ureteral orifices.[1,6] **SEE Video**

2.1 **Completeness in depth**

Small tumors can be resected en bloc. Tumors >1 cm should be resected obtaining separate samples of the bulk of tumor and of the tumor base, performing a deep resection including the detrusor muscle and avoiding carbonization of the tissue.[1,7]

Re-TURB two to six weeks after initial TURB can improve recurrence-free survival and tumor staging, and is recommended in all T1 or high-grade tumors, when the pathologist reports that the specimen contains no detrusor muscle, or when the urologist is not sure that the first resection is complete, especially in case of extensive or multiple tumors.[7]

Maximal bladder TURB, possibly visibly complete, needs to be carried out if a bladder preserving multimodality treatment (TURB followed by sequential chemotherapy and radiotherapy protocols) is planned.[8]

2.1 Completeness in extension

Separate samples of multiple lesions should never be mixed. Margins of the normal appearing tissue surrounding bulky lesions should also be obtained. Biopsies of all suspicious areas should be obtained in order to rule out carcinoma in situ. The limited value of normal appearing areas biopsies associated with negative cytology and/or papillary tumors has been recognized, on the contrary biopsies from normally looking mucosa in patients with positive cytology and/or non-papillary tumors prostatic are recommended.[1] Prostatic urethra sampling of suspicious areas is important to exclude carcinoma in situ, because none of the possible negative prognostic factors should be overlooked or missed.[9]

3. **Correct staging of the disease**

Bimanual palpation under anesthesia (positive in case of cT3 or more) should always be performed during TURB, giving a clinical idea of the staging of the disease.[1]

Obtaining good quality tissue for pathologists and ordered, separated samples of all the lesions and the margins is then fundamental. Burning artifacts due to the excessive use of the monopolar electrocautery may interfere not only with the finest evaluations[10,11](like lymphovascular invasion or immunohistochemistry for specific markers) but also with the basic staging and grading of the bladder cancer.[7,12] The absence of the detrusor muscle will limit the value of the histopathological response.[1]

4. **How to optimize TURB**

White-light TURB is the gold standard for primary diagnosis and management of bladder cancer, but unfortunately as currently performed it is an oncologically imperfect surgery,whereby only the visible tumor tissue is removed in pieces. For this reason all devices and modern equipmens to optimize endoscopic vision and resection should be employed, including bipolar resectoscopes, new telescopes and high-definition video systems.

4.1 **Bipolar TURB**

Real bipolar electrosurgery offers a number of advantages. First of all, the current does not flow through the body of the patient to reach the neutral electrode on the leg, so it produces no interference with cardiac pacemakers. Saline as irrigation solution is used, allowing large tumors resections without risk of TUR syndrome. The low resistance of the saline solution allows an elevated initial input of energy (100 microsec), optimizing conductivity and energy release according to the impedence of the tissue to the cut (additionally down-regulated by the Magic Box). Only low voltages are employed: maximum 1200V for cutting, permitting precise and fine bladder tissue resection,and 450V for coagulation, with asignificantly reduced (141 vs. 287 micron) coagulation depth, avoiding thermal damage (40-70°C) to neighbouring tissues and carbonization of the samples to be sent to the pathologist. Additionally, the flow of the current from the active to the neutral electrode located on the same resection loop is strictly limited to the target area, preventing obturator nerve stimulation and the related risk of bladder inadvertent perforation. A less aggressive and more precise coagulation can reduce the risk of bleeding, also in its delayed manifestation. Dedicated loops for en-bloc resection and posterior wall lesions have been conceived, in order to facilitate the procedure and limit the complications thanks to a more ergonomic design.[13]

4.2 **High resolution video systems**

High resolution may allow to recognize with increased accuracy the bladder tissues (mucosa, submucosa, detrusor and adventitia) and thus to perform an optimal TURB including the detrusor for a correct staging. The increased aspect ratio (from 4:3 of the standard definition to the 16:9 of the high definition) broadens the field of vision of about 36%, especially if the zoom of the videocamera is fully open, and this is useful especially in case of multifocal bladder lesions. More resolution (2,073,600 pixels, five times more than standard definition) means more contrast and more light intensity, especially with three-chips cameras. The colour contrast generates a quasi-three-dimensional vision, avoiding to miss small bladder tumors and to assess post-TURB outcomes like vesical perforations.[14,15]

4.3 **A new generation of optical diagnostics for bladder cancer**

Urologists should be aware of promising innovations in the field of the imaging techniques, and of their possible benefits.Enhancements to endoscopic imaging offer the hope of improving detection and characterization of malignant lesions in the bladder.

Photodynamic diagnosis (PDD), using as fluorescent dye the protoporphyrin 5-aminolevulinic acid instilled into the bladder and visualized under blue light, can aid in the detection of CIS as well as in the identification of papillary tumors. A PDD-aided TURB in experienced hands may be able to guide resection of tumor tissue at the edge of what might be otherwise considered a complete margin.[16]For all these reasons PDD cystoscopy/TURB has been introduced in the 2012 EAU guidelines with a level of evidence 2a.

Narrow-band imaging (NBI)improves the contrast between abnormal and normal bladder mucosa by restricting the optical spectrum used for examination by means of filters narrowing the bandwidth.[17]The **Storz Professional Image Enhancement System (SPIES)** is also based on a computed virtual chromoendoscopy processing the color components by means of three specific filters.

Optical coherence tomography (OCT) is a novel technology providing real-time, high-resolution, cross-sectional imaging of biological tissues, accurately distinguishing benign and malignant bladder lesions, and precisely staging Ta, T1 or T2.[18]

Confocal laser endomicroscopy (CLE) requires either intravenous or intravesical administration of fluorescein and has the ability to distinguish normal urothelium form low- amd high-grade tumors, based on cellular architecture cystoscopy.[19]

Raman spectroscopy (RS) measures the molecular components of tissue objectively in qualitative and quantitative ways.[20]

OCT, CLE and RS aim at providing a real-time, minimally invasive, objective prediction of the histopathologic diagnosis, whereas PDD, NBI and SPIES aim at improving visualization of bladder tumors.

REFERENCES

1. Babjuk M (2009) Transurethral resection of non-muscle-invasive bladder cancer. EurUrolSuppl 8:542-548
2. FritscheHM, Burger M, Svatek RS et al (2010) Characteristics and outcomes of patients with clinical T1 grade 3 urothelial carcinoma treated with radical cystectomy: results from an international cohort. EurUrol57:300-309
3. Turker P, Bostrom PJ, Wroclawski ML et al (2012) Upstaging of urothelial cancer at the time of radical cystectomy: factors associated with upstaging and its effect on outcome. BJU Int 110:804-11
4. Pruthi RS, Baldwin N, Bhalani V, Wallen EM (2008) Conservative management of low risk bladder tumors. J Urol 179:87-90
5. Serretta V (2009) T1HG bladder tumours: so many papers, do we need them? Yes, we do! EurUrol 56:911-913
6. Pan D, Soloway MS (2012) The importance of transurethral resection in managing patients with urothelial cancer in the bladder: proposal for a transurethral resection of bladder tumor checklist. EurUrol 61:1199-1203
7. Babjuk M, Oosterlinck W, Sylvester R, Kaasinen E, Böhle A, Palou-Redorta J, Rouprêt M. EAU guidelines on non-muscle-invasive urothelialcarcinoma of the bladder, the 2011 update. Eur Urol. 2011 59(6):997-1008
8. deVere White RW, Lara PN, Goldman B et al (2009) A sequential treatment approach to myoinvasiveurothelial cancer: a phase II Southwest Oncology Group Trial (S0219) J Urol 181:2476-2481
9. Palou J, Sylvester RJ, Faba OR et al (2012) Female gender and carcinoma in situ in the prostatic urethra are prognostic factors for recurrence, progression, and disease-specific mortality in T1G3 bladder cancer patients treated with Bacillus Calmette-Guérin. EurUrol62:118-125
10. Zhang M, Tao R, Zhang C, Shen Z (2010) Lymphovascular invasion and the presence of more than three tumors are associated with poor outcomes of muscle-invasive bladder cancer after bladder-conserving therapies. Urology 76:902-907
11. Ha YS, Kim JS, Yoon HY et al (2012)Novel combination markers for predicting progression of nonmuscle invasive bladder cancer. Int J Cancer 15;131:E501-7
12. Van RhijnBW, van Leenders GJ, Ooms BCet al (2010) The pathologist's mean grade is constant and individualizes the prognostic value of bladder cancer grading. EurUrol 57:1052-7
13. Del Rosso A, Pace G, Masciovecchio S et al (2012) Plasmakinetic bipolar versus monopolar transurethral resection of non-muscle invasive bladder cancer: A single center randomized controlled trial.Int J Urol, in press

14. Falk V, Mintz D, Grünenfelder J et al (2001) Influence of three-dimensional vision on surgical telemanipulator performance.SurgEndosc 15:1282-1288
15. van Bergen P, Kunert W, Buess GF The effect of high-definition imaging on surgical task efficiency in minimally invasive surgery: an experimental comparison between three-dimensional imaging and direct vision through a stereoscopic TEM rectoscope.SurgEndosc 14:71-4
16. Kausch I, Sommerauer M, Montorsi F et al (2010) Photodynamic diagnosis in non-muscle-invasive bladder cancer: a systematic review and cumulative analysis of prospective studies.EurUrol 57:595-606
17. Naselli A, Introini C, Timossi L et al (2012) A randomized prospective trial to assess the impact of transurethral resection in narrow band imaging modality on non-muscle-invasive bladder cancer recurrence.EurUrol 61:908-13
18. Lerner SP, Goh AC, Tresser NJ, Shen SS (2008) Optical coherence tomography as an adjunct to white light cystoscopy for intravesical real-time imaging and staging of bladder cancer. Urology 72:133-137
19. Wu K, Liu JJ, Adams W et al (2011) Dynamic real-time microscopy of the urinary tract using confocal laser endomicroscopy. Urology 78:225-31
20. Shapiro A, Gofrit ON, Pizov G et al (2011) Raman molecular imaging: a novel spectroscopic technique for diagnosis of bladder cancer in urine specimens.EurUrol 59:106-12

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