

Original Paper

NBI Guided TURBT in NMIBC Management - “The Right Path” to Better Tumor Ablation

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REZUMAT

NBI-TURBT în managementul NMIBC

Introducere și obiective: Managementul standard al cancerului vezical a fost adesea caracterizat de rezultate nesatisfăcătoare. Acest studiu prospectiv unicentric a comparat acuratețea diagnostică a cistoscopiei narrow band imaging (NBI) cu cea în lumină albă (WLC) la pacienții cu cancer vezical non-invaziv (NMIBC).

Material și metodă: Au fost incluse 81 de cazuri suspecte de NMIBC prezentând hematurie și/sau aspect ecografic sugestiv. Pacienții au fost evaluați prin cistoscopie standard și NBI. Tumorile vezicale vizibile în lumină albă au fost rezecate prin metoda transuretrală clasică (TURBT), iar rezecția în NBI a fost utilizată exclusiv pentru tumorile detectate exclusiv cu ajutorul acestei metode.

Rezultate: Cistoscopia NBI a decelat o rată substanțial crescută de detecție a leziunilor CIS precum și NMIBC în general. O proporție semnificativă de tumori adiționale a fost identificată în NBI indiferent de stadiul tumoral. Prin comparație cu cistoscopia convențională, pentru toate categoriile de pacienți cu NMIBC s-a obținut o rată de detecție tumorală crescută folosind NBI-ul. Specificitatea NBI-TURBT a fost marcată de mai multe rezultate fals-pozitive comparativ cu protocolul standard.

Concluzii: Cistoscopia și rezecția NBI s-au remarcat ca modalitate eficientă de creștere semnificativă a detecției NMIBC, optimizând astfel ablația tumorală. Cazurile și tumorile NMIBC diagnosticate exclusiv în NBI susțin această concluzie.

Cuvinte cheie: narrow band imaging, lumină albă, TURBT, NMIBC

ABSTRACT

Introduction & Objectives: The standard bladder cancer management was often marked by unsatisfactory outcomes. This prospective, single-center study compared the diagnostic accuracy specific for narrow band imaging (NBI) and respectively white light cystoscopy (WLC) among non-muscular invasive bladder cancer (NMIBC) patients.

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Materials & Methods: 81 consecutive NMIBC suspected cases were included based on the presence of hematuria and/or on ultrasound suspicious aspect. All patients were evaluated by both WLC and NBI cystoscopy. WL-visible lesions were removed by classical transurethral resection of bladder tumors (TURBT), while NBI resection was exclusively applied in tumors solely detected by this particular visualization method.

Results: Subsequent to NBI cystoscopy, substantially improved CIS and overall NMIBC patients' detection rates were determined. A significant proportion of additional lesions was identified in NBI regardless of the bladder cancer stage. Improved tumor detection rates were established for NBI when compared to white light concerning all NMIBC categories of patients. The more numerous false-positive results affected the NBI-TURBT related specificity compared to the standard investigation protocol.

Conclusions: NBI cystoscopy and TURBT were outlined as providing an efficient modality of significantly improving NMIBC detection, thus optimizing tumor ablation. The solely NBI diagnosed NMIBC cases and tumors largely supported this conclusion.

Key words: narrow band imaging, white light cystoscopy, TURBT, NMIBC

INTRODUCTION

Over the past few years, the conventional transurethral resection of bladder tumors (TURBT) has undergone increasing criticism among the international urological community due to its' inability to achieve a complete tumor ablation [1].

This substantial oncologic drawback has been mainly related to the limited sensitivity of the classical white light cystoscopy (WLC) [2]. In other words, the standard endoscopic assessment of the bladder was often outlined as insufficiently capable of accurately identifying all of the existing tumor formations [3].

Following this path of diagnostic improvement requirements, several optical enhancement modalities were introduced in an attempt to ameliorate tumor vision [4]. Among these, the hexaminolevulinate based photodynamic diagnostic (HAL-PDD) was supported by numerous publications as a remarkably efficient method of increasing tumor detection [5]. Unfortunately, the substantial costs implied by the expensive instillation agent prevented the technique from entering routine urological practice [6].

On the other hand, the narrow band imaging (NBI) technology, previously characterized by a spectacular impact on astronomy findings [7], was successfully adapted to the endoscopic evaluation of the bladder [8]. Basically, this type of cystoscopy benefited from a detailed visualization of the tumor specific vascular architecture leading towards a superior contrast between urothelial carcinomas and the normal mucosa [9].

Most importantly, progresses in terms of an adequate cystoscopic assessment of bladder lesions were defined as susceptible to providing the conditions for a superior tumor resection to be achieved [10]. As previously shown in the available literature, the discovery of additional flat and/or small size papillary malignancies may offer the chance for a reliably radical endoscopic removal of NMIBC (non-muscle invasive bladder cancer) formations to be consistently accomplished [11].

MATERIALS AND METHODS

The primary endpoint aim of the trial was to outline a diagnostic accuracy comparison between white light and NBI cystoscopy in bladder cancer patients based on their ability to provide the conditions for a complete urothelial carcinoma resection to be achieved. Practically speaking, both the NMIBC patients' as well as the tumors' related detection rates were established as significant parameters for the sensitivity of the two types of TURBT. The secondary endpoint was to determine the possible differences between these methods in relation with the particular tumor stage.

Between July and November 2014, a total of 81 consecutive bladder cancer suspected patients were included in a prospective, single center study. The inclusion criteria were represented by the presence of hematuria and/or ultrasound suspicious aspect for bladder tumors. The exclusion criteria consisted of severe associated co-morbidities preventing endoscopic surgery in general from being performed and massive hematuria affecting the cystoscopic quality

up to the point of extremely poor visibility.

The standard investigation protocol applied in all enrolled patients included general clinical examination, blood tests, urinalysis, abdominal ultrasound and intravenous pyelography or CT-scan. As general methodology, over the above mentioned period, all patients (60 men and 21 women with a mean age of 69.5 years – range 49 to 90) matching the respective criteria were consecutively enlisted in the study.

The surgical equipment consisted of the Visera II video system with both white light and NBI vision modes (Olympus Europa SE & CO KG), the ESG-400 bipolar generator (200 W for cutting and 120 W for coagulation), the 26F OES-Pro bipolar resectoscope, standard resection loops for tumor ablation and hemispherical shaped “button” electrodes for tumor bed coagulation carried out at the end of surgery.

The first stage of the diagnostic and treatment protocol performed in each patient was represented by a careful white light cystoscopic evaluation resulting in a WLC specific bladder map of all discovered lesions. Subsequently, the NBI assessment method of the mucosa leading to a separate map of all tumors found in this manner was completed (Fig. 1). The tumor removal process began with the conventional white light resection of all lesions marked on the WLC map. Afterwards, an NBI guided TURBT was applied for tumors exclusively identified based on the narrow band imaging-related bladder map (Fig. 2). In other words, this type of approach enabled an optimized standard TURBT to be carried out while providing the opportunity for NBI resection to specifically target lesions eventually overlooked by the white light endoscopy (Fig. 3).

While considering the subsequent pathological analysis of the resection specimens, the cases in which no malignant lesion was confirmed as well as those diagnosed with muscle-invasive bladder cancer (MIBC) cases were excluded from the trial. Finally, based on the NMIBC certified group of patients, the overall, CIS, pTa and pT1 case and tumor detection rates were determined for both therapeutic modalities.

RESULTS

The above described surgical steps in all involved patients were successfully followed. Based on the pathology findings, 13 of the 81 initially included cases



Figure 1. CIS lesion missed in white light and only found during NBI cystoscopy

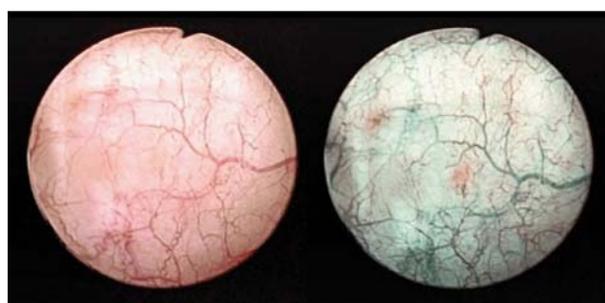


Figure 2. pTa tumor overlooked by WLC and solely identified in NBI mode

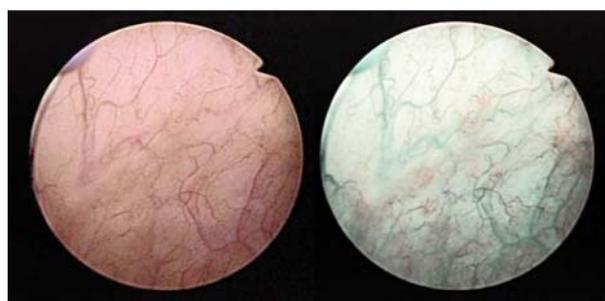


Figure 3. Multiple NMIBC lesions exclusively discovered when using NBI vision

were removed from the continuation of the study (3 patients with no bladder cancer lesions and 10 MIBC cases further referred for radical cystectomy). Consequently, the final targeted series was represented by 68 NMIBC patients diagnosed based on the cumulated results of the two diagnostic and treatment alternatives (6 CIS, 45 pTa and 17 pT1 cases).

On a patient related basis, by comparison to the standard white light protocol, the NBI guided cystoscopy/TURBT modality achieved improved CIS (100% versus 66.7%) and overall NMIBC (97.1% versus 89.7%) detection rates. Additionally, smaller differences in favor of the NBI evaluation were also established in pTa (95.6% versus 91.1%) and pT1

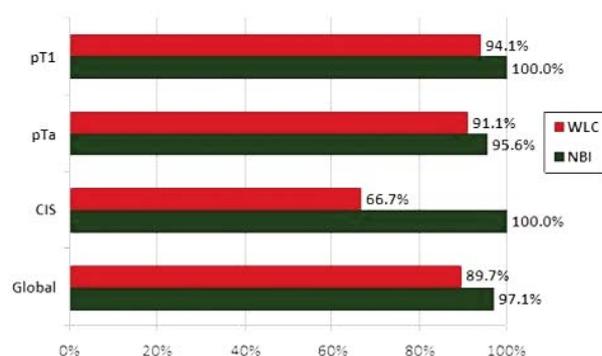


Figure 4. White light and NBI cystoscopy patients' detection rates

(100% versus 94.1%) cases (**Fig. 4**).

While summarizing the global pathology findings, a wider category of patients was defined as benefiting from the increased diagnostic accuracy of NBI visualization. Namely, besides the previously mentioned category of solely NBI discovered NMIBC cases, patients diagnosed by both methods but presenting supplementary tumors (predominantly in NBI) were identified. Consequently, when compared to WL, NBI resection was marked by a substantially higher proportion of additional tumor cases, regardless of tumor stage (26.5% versus 7.4% for overall NMIBC lesions, 50% versus 0% for CIS, 22.2% versus 8.9% for pTa and 29.4% versus 5.9% for pT1) (**Fig. 5**).

From the perspective of strictly focused tumor detection, the NBI specific lesions based diagnostic accuracy mode overcame the standard cystoscopy results for basically every NMIBC stage category (despite smaller differences for pT1 tumors). Ultimately, NBI cystoscopy was characterized by increased CIS (94.1% versus 58.8%), pTa (94% versus 83.2%), pT1 (96.8% versus 90.3%) and overall NMIBC (93.9% versus 81.9%) lesions' detection rates by comparison to the white light assessment (**Fig. 6**).

On the other hand, the specificity analysis shaded a somewhat different light over the potential drawbacks of the two diagnostic modalities. NBI cystoscopy was marked by a higher rate of false positive results when drawing a parallel to WLC (15.8% versus 10.7%), thus suggesting an increased proportion of unnecessary biopsies being taken.

DISCUSSION

Essentially, the bladder cancer optical enhance-

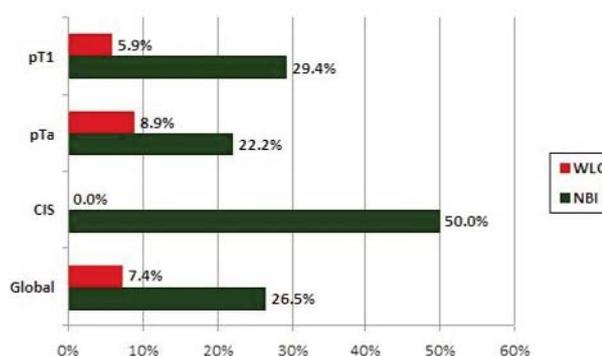


Figure 5. WLC versus NBI comparison regarding cases of additional tumors

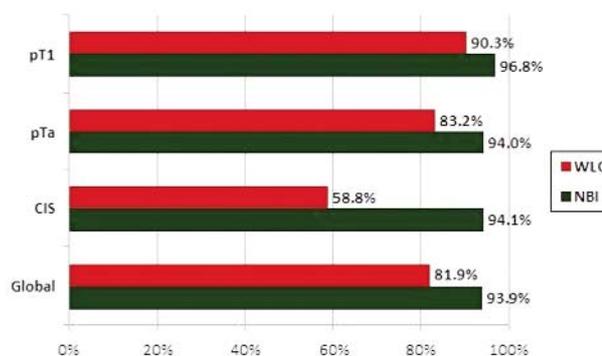


Figure 6. WLC–NBI diagnostic accuracy parallel concerning the tumors' detection rates

ment modalities were designed to provide a better contrast between urothelial carcinoma lesions and the normal mucosa background [12]. In fact, this goal was achieved by either using an intravesical instillation contrast agent subjective to increased absorption by malignant structures [13] or the application of narrowed bandwidths emphasizing the specific vascular architecture of bladder tumors [14]. Subjectively, both types of approach gained substantial visual detection advantages over the classical white light endoscopy [15, 16].

On the other hand, solid arguments in favor of the HAL-PDD and NBI cystoscopic techniques may only be established in the light of the actual evidence-based progresses accomplished in comparison with the standard WLC. The following discussion shall take into account the published findings related to blue light, narrow band imaging and classical cystoscopy within a parallel to the present data. Basically, the benefits offered by fluorescence and NBI endoscopic vision over WLC will be analyzed from the perspectives of the available literature and matched against this single center study. Generally

speaking, the question as to the viability of PDD and NBI should be answered “through the looking glass” of the eventual NMIBC oncologic progresses.

To begin with, in comparison with WLC, the hexaminolevulinate blue light cystoscopy was shown as emphasizing a superior detection rate of overall NMIBC tumors (96-97% versus 77-78% [17, 18]) and CIS lesions in particular (95-97% versus 58-68% [17, 18]). Most importantly, these figures were favorably matched by the NBI related published research, which underlined relatively similar outcomes while discussing an NBI versus standard cystoscopy parallel (92.7-94.7% versus 57.3-79.2% for overall NMIBC tumors and 89.7-93.1% versus 50-68.9% for CIS lesions [19, 20]). The presently analyzed trial successfully followed this path of improved tumor detection and confirmed the NBI superiority over WL concerning both categories of the above mentioned urothelial carcinomas (93.9% versus 81.9% and 94.1% versus 58.8%, respectively).

Last but not least, according to the available results, when compared to WLC sensitivity, the pTa tumors detection rate was consistently improved by both HAL-PDD (95% versus 83% [21]) and NBI cystoscopy (98.7% versus 83.5% [20]). The latter NBI related advantage was supported by findings of the present analysis, which described the ability of narrowed bandwidths vision to distinguish significantly more numerous pTa tumors than the white light assessment (94% versus 83.2%).

From another point of view, one of the main interests in bladder cancer diagnostic consists in the proportion of cases in which a certain endoscopic modality is capable of discovering supplementary lesions in comparison with the standard investigation protocol. A positive feedback from the literature data was outlined by the significantly higher proportion of NMIBC cases in which either blue light (26.6-41.5% versus 8.6-15.1% [3, 21]) and NBI (26.9-35.9% versus 2.9-7.3% [19, 20]) cystoscopy determined the presence of additional tumors when compared to conventional WLC. The present study obtained relatively similar outcomes, which emphasized the capability of NBI vision to discover a substantially increased number of lesions while drawing a parallel to the white light investigation (26.5% versus 7.4%, respectively).

The issue of the eventually lower specificity characterizing the relatively new and more sensitive cystoscopic enhancement alternatives was often addressed by the already available trials. From this

perspective, a constantly increased rate of false positive results with regard to both fluorescence (29-39% versus 17-31% [21, 22]) and NBI (28-31.6% versus 21-24.5% [19, 20]) cystoscopy when compared to white light was underlined. The same principle was supported by the present findings, which also expressed a drawback in the NBI approach when facing a classical WLC' comparison in terms of the more numerous unnecessarily biopsies taken (15.8% versus 10.7%, respectively).

Overall, it may be stated that, based on the previously published data together with the presented prospective trial, NBI cystoscopy was characterized by a reliable and constant increase in diagnostic accuracy when considering the standard cystoscopy, at the cost of reduced specificity [15]. Most importantly, the HAL-PDD available figures generally matched NBI outcomes throughout the literature as far as the above mentioned parameters were concerned [12]. Therefore, while considering the substantially higher costs implied by the use of an exogenous contrast medium during blue light fluorescence cystoscopy [4], the NBI modality may constitute a strong competitor for the so far extensively documented fluorescence diagnostic superiority. Naturally, on the long term, more extensive studies will have to clarify the balance between the two methods.

CONCLUSIONS

The present data supported the NBI-TURBT superiority in terms of achieving a superior urothelial carcinomas ablation. To begin with, more than 1 in 10 NMIBC patients benefited from a correct bladder cancer diagnostic and consequent endoscopic therapy solely due to NBI cystoscopy. Further more in this regard, an important proportion of CIS cases was exclusively detected while using narrow band imaging.

From the perspective of supplementary lesions being eventually found, NBI resection was emphasized as capable of identifying an increased number of bladder cancer formations, regardless of the tumor stage. As of such, a substantial share of the NMIBC studied patients group was determined as having pathologically confirmed additional tumors during the NBI assessment and subsequent removal.

The NBI related diagnostic advantages over conventional cystoscopy were further confirmed by the significantly improved tumor-based detection

rates characterizing the CIS, pTa, pT1 as well as overall NMIBC cases. Still, the somewhat increased rate of false positive results outlined a potential drawback of the NBI transurethral approach.

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