Ressecção transuretral da bexiga convencional assistida por *Narrow Band Imaging*: Melhores taxas de detecção e tratamento?

NBI-assisted TURBT: Does it improve detection and treatment rates?

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Resumo

Objetivos: De acordo com a literatura, cerca de 40 a 70% dos tumores da bexiga sem invasão muscular recidivam após a terapêutica inicial. Grande parte das recidivas precoces devem-se a ressecções transuretrais vesicais (RTU-V) incompletas de pequenas lesões não identificadas. O NBI (*Narrow Band Imaging*) foi desenvolvido com o objectivo de potenciar a definição de pequenas lesões vesicais. Os autores pretendem confirmar este desígnio e avaliar em que medida o NBI poderá minimizar recidivas tumorais ou alterar a conduta terapêutica.

Material e Métodos: Estudo prospectivo efetuado no Serviço de Urologia do Hospital Geral do Centro Hospitalar e Universitário de Coimbra em doentes que foram submetidos a RTU-V convencional assistida por NBI.

Resultados: Estudo efetuado em 33 doentes com neoplasias vesicais primárias ou recidivadas. O NBI colocou em evidência lesões adicionais em 18 doentes (54,5%) e nada acrescentou em 15 (45,5%). Dos 18 doentes com lesões adicionais identificadas por NBI, 10 apresentavam lesões benignas (56%) e 8 carcinomas de células de transição (CCT) (44%). O número de indivíduos diagnosticados com tumores malignos adicionais com NBI foi de 8/33 (24,2%). Com os resultados obtidos foi possível inferir para a população geral através do cálculo dos intervalos de confiança para proporções. Com um nível de confiança de 95%, podemos dizer que, na população, o NBI vai permitir remover tumores malignos adicionais em cerca de 9,6% a 38,9% dos indivíduos. Dos doentes diagnosticados com CCT por RTU-V convencional 30,7% (8/26) apresentavam lesões malignas adicionais evidenciadas com NBI. Em 6 desses doentes os tumores identificados por NBI eram de estadio semelhante ou inferior ao das lesões ressecadas com luz branca. Em 2 doentes o uso do NBI permitiu uma subida no estadio dos tumores ressecados com luz branca, alterando, deste modo, a conduta terapêutica adjuvante.

Conclusões: Apesar da elevada taxa de falsos positivos, a combinação de luz branca e NBI parece permitir uma optimização diagnóstica e consequentemente terapêutica dos tumores da bexiga. Os valores percentuais inferidos para a população geral parecem justificar, por si só, a utilização de RTU-V assistida por NBI. No entanto, mais estudos prospectivos, randomizados e multicêntricos, com uma amostra maior e seguimento mais alargado no tempo são necessários para se concluir acerca do benefício da utilização sistemática do NBI associado à RTU-V convencional.

Palavras-chave: Neoplasia vesical, narrow band imaging, cistoscopia, ressecção transuretral

Abstract

Objectives: *According to the literature, about 40 to 70% of non-muscle invasive bladder tumors (BT) recur after initial treatment. Much of the early recur-*

rences are due to incomplete transurethral resection (TUR) due to minor neglected lesions. NBI (Narrow Band Imaging) was developed with the goal of enhancing the definition of small lesions of the bladder. The authors intend to confirm this purpose and assess the extent to which the NBI may prevent recurrences or change future therapeutic strategy by upstaging or upgrading of bladder cancer lesions.

Materials and Methods: *Prospective study performed in patients submitted to NBI assisted TURBT at the Urology Department of the Hospital Geral of the Centro Hospitalar e Universitário de Coimbra. With the results achieved it was possible to infer to the general population by calculating confidence intervals for proportions.*

Results: *A total of 33 patients with primary or recurrent bladder tumors were included. NBI has highlighted additional lesions in 18 patients (54.5%) and added nothing in 15 patients (45.5%). Of the 18 patients with additional lesions identified by NBI, 10 had benign lesions (56%) and 8 TCC (44%). The number of individuals diagnosed with additional malignant tumors with NBI was 8/33 (24.2%). With a confidence level of 95%, we could say that in the general population, NBI will allow further remove of malignant tumors by about 9.6% to 38.9% of the patients. 30.7% (8/26) of patients diagnosed with TCC by conventional TURBT had additional malignant lesions evidenced by NBI. In six of these patients the tumors identified by NBI were similar to or below the stage of resected lesions with white light color (WLC). In two patients the use of NBI enabled the upstaging of tumors resected with WLC, changing thus the adjuvant therapy.*

Conclusions: *Despite the high rate of false positives, the combination of white light and NBI appears to allow a better diagnostic and therapeutic attitude of bladder tumors, especially non-muscle-invasive ones. The values extrapolated to the general population seem to justify, by itself, the use of NBI assisted TURBT. However, more prospective, eventually multicenter and randomized studies, with more patients and extended follow-up are needed to conclude on the benefit of systematic use of NBI associated with conventional WLC.*

Keywords: *bladder cancer, narrow band imaging, cystoscopy, TURBT, transurethral ressection*

Introduction

Bladder cancer is a frequent disease and represents the second most common genitourinary neoplasm[1]. Because of its high prevalence, recurrence and low relative mortality the cost of the treatment of bladder cancer is one of highest between all cancers[2]. According to the literature, about 40 to 70% of non-muscle invasive bladder tumors (BT) relapse after initial treatment[3, 4]. While white light cystoscopy (WLC) is considered the gold standard for the detection of BT and for the visualization of tumor in TURBT, its sensitivity and specificity are not entirely satisfactory. Remnant tumors have been found in up to 43% of secondary ressections[5]. Many of the early recurrences are due to incomplete transurethral ressection (TUR) due to minor neglected lesions. Recent years have witnessed a technological development in order to improve diagnostic accuracy and efficacy by preventing relapses and recurrent hospitalizations and surgeries. Photodynamic diagnosis with blue light cystoscopy after instillation of hexaminolevulinic acid allows, according to recent prospective studies, an additional detection of 20% of all tumors and 23% of carcinoma *in situ* (Cis). However, the need for instillation of a fluorescent agent, the window of opportunity and the cost of the equipment and products raises doubt about the cost-effectiveness of the procedure.

Narrow-band imaging (NBI) is an optical image enhancement technology that narrows the bandwidth of the light output from the *Olympus Lucera* sequential RGB endoscopy system to 415 nm and 540 nm. This narrow bandwidth of light is strongly absorbed by haemoglobin and penetrates only the surface of tissue, increasing the visibility of capillaries and other delicate tissue surface structures by enhancing contrast between the two[6, 7, 8]. NBI enhances contrast between superficial tumors and normal mucosa[9, 10, 11]. It doesn't need previous instillation of photodynamic agent and individual variation among urologists including a novice using NBI cystoscopy to evaluate patients for recurrent bladder tumors is minimal[10]. NBI (Narrow Band Imaging) was developed with the goal of enhancing the definition of small lesions of the bladder that could be missed during white light cystoscopy. The authors intend to confirm this purpose and assess the extent to which the NBI may prevent recurrences or change the therapy by upstaging or upgrading of bladder cancer lesions.

Materials and Methods

Between December 2010 and March 2011 we conducted a prospective controlled within-patient comparison of standard WLC and NBI cystoscopy and TURBT at the Hospital Geral do Centro Hospitalar e Universitário de Coimbra, in Coimbra. Included patients had clinical indication to undergo

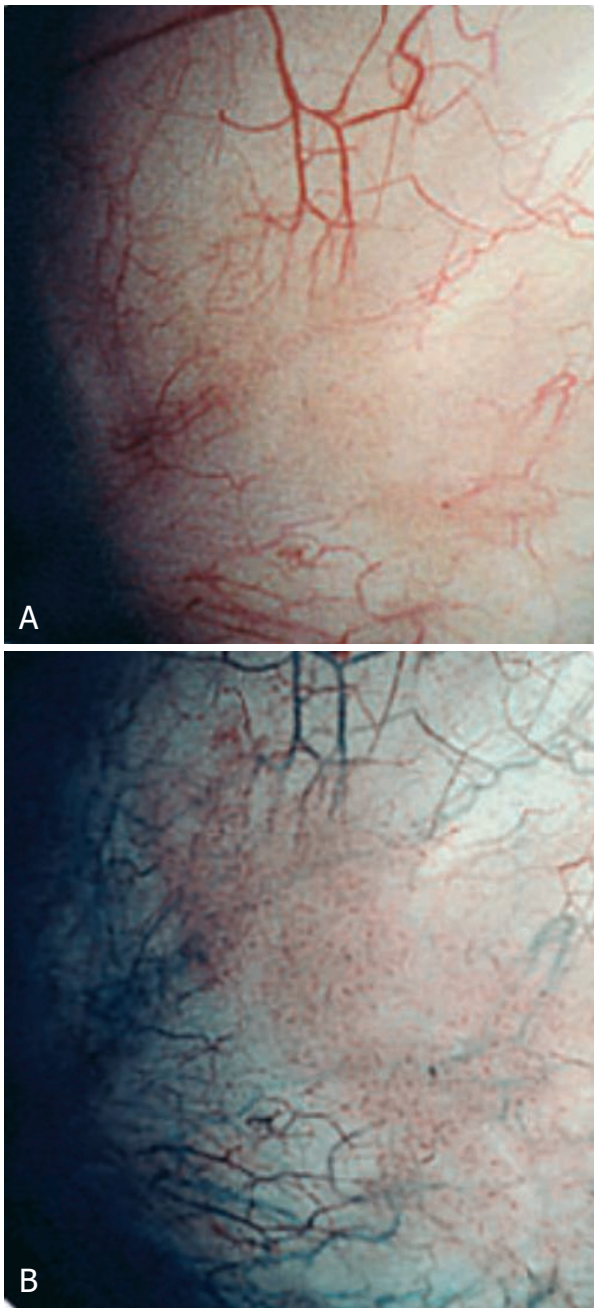

Figure 1) Different view of a bladder tumour with WLC (A) vs. NBI (B)

to a NBI cystoscopy after TURBT with WLC. Two randomized surgeons, who identified, independently, suspected areas with WLC and NBI after TURBT WLC, performed this study. These areas were resected and sent separately (WLC positive lesions and NBI positive lesions) for the pathologist. A single pathologist reviewed all the cases in order to avoid bias. With the results achieved it was possible to infer to the general population by using the formula for calculation of the confidence intervals for proportions. The materials used were an Olympus® Narrow-Band Imaging Evis Exera II™ Universal Platform with a HDTV 1080i monitor and HD OTV-S7ProH-HD-L08E camera and a Monopolar Storz® resectoscope Ch24F. Every patient received a single postoperative Mitomicin C vesical instillation until 6 hours after the procedure.

Results

NBI provided a clearer view of the bladder capillaries vessels as well as camouflaged small or flat bladder lesions by enhancing their contrast (figure 1A e 1B).

This study included 33 patients from whom 25 were men (76%) and 8 were women (24%) with a mean age of 72 ± 14 years (Mean ± Standard Deviation) (table 1). Primary lesions were found for 66.7% (n=22) of the included patients, 30.3% (n=10) of patients had recurrent lesions and one patient (3.0%) was submitted to a re-TURBT (table 2). Patients with recurrent lesions had a history of 3 ± 1 previous TURBTs (table 2). 36% of the patients had lesions bigger than 3 cm (table 3) with variegated morphology (table 4). NBI has highlighted additional lesions in 18 patients (54.5%) (figure 1). In 10

Characteristics (N=33)	n (%)
Male	25 (75.8)
Female	8 (24.2)
Age; years (Mean±Standard Deviation)	72 ± 14

Table 1) Patients' demographic characteristics

Primary vs. Recurrent Lesions	
Primary Lesions	22 (67%)
Recurrent Lesions	10 (30%)
Number of Previous TURBTs	3 ± 1
Re-TURBT	1 (3%)

Table 2) Proportion of patients with primary and recurrent lesions

Size of lesions (N=33)	N (%)
< 3 cm	21 (63.6)
≥ 3 cm	12 (36.4)

Table 3) Size of the lesions with white light cystoscopy (WLC)

Morphology (N=33)	N (%)
Papillary	12 (36.4)
Sessile	12 (36.4)
Flat	6 (18.2%)
Mixed	2 (6.0%)
TURBT Scar	1 (3.0%)

Table 4) Morphology of the Lesions with white light cystoscopy (WLC)

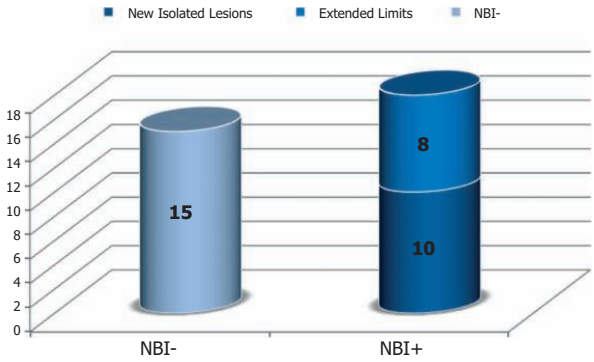

Figure 1) Detected lesions with NBI

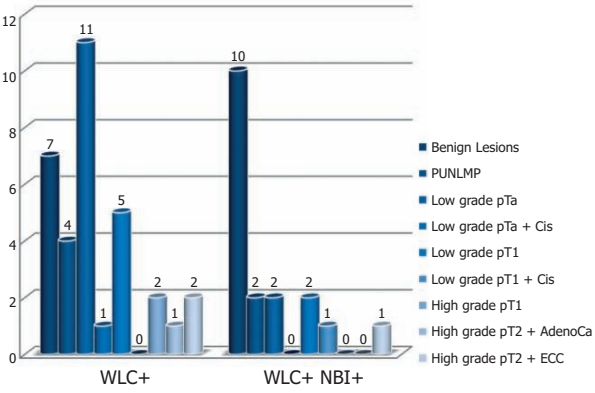

Figure 2) Pathology of the WLC only detected lesions vs. the WLC and NBI detected lesions

of the included patients, additional lesions were independent (30.3%) and in 8 patients additional lesions were found in the borders of previously resected lesions by WLC (24.2%) (figure 1). Benign/ /inflammatory lesions were diagnosed for 7 patients (21.2%) and transitional cell carcinoma was found in 26 patients (78.8%) with WLC (figure 2). From the 18 patients with additional lesions identified by NBI, 10 presented benign lesions (55.6%) and 8 presented TCC (44.4%). The number of individuals diagnosed with additional malignant tumors with NBI was 8 (24.2%). From the 26 patients diagnosed with TCC by conventional TURBT, 30.7% (n=8) had additional malignant lesions evidenced by NBI (figure 2). In 6 of these patients the tumors identified by NBI were similar to or below the stage of resected lesions with WLC. In 2 patients the use of NBI enabled the upstaging of tumors resected with WLC, changing thus the adjuvant therapy (in 1 case from follow-up only to adjuvant Mitomicin C and in another case from Mitomicin C to BCG) (table 5). There were no perioperative complications or immediate postoperative complications.

WLC NMIBC Lesions (n= 23)	
Additional Malignant Lesions detected with NBI (Total)	7/23 (30,4%)
Same or Lower Stage/Grade	5 (21,7%)
Upstaging or Upgrading PUNLMP] Low grade pT1 Low grade pT1 [Low grade pT1 + Cis	2 (8,7%)

Table 5) Importance of the NBI detected malignant lesions

Discussion

Of the 18 patients with NBI detected additional lesions, only 8 had malignant lesions (false positive rate of 56%). By using the formula for general population extrapolation, we can state, with a confidence interval of 95%, that: NBI will detect more lesions in 37,6% to 71,5% of the patients, between individuals with positive NBI, there is a ratio of 21,1% and 66,9% that will have malignant lesions and NBI will detect more malignant lesions in diagnosed ones by WLC in 11,6% to 49,2% of the patients. The false positive rate may vary between 33,1% and 78,9%. This high rate of false positives may be due, in part, to artifacts produced during white light TURBT. Even though, NBI may change management in 0% to 20,2% of the patients diagnosed with a malignant lesion. Despite the high rate of false positives, the combination of white light and NBI appears to allow a better diagnostic and therapeutic attitude of bladder tumors, especially non-muscle-invasive ones. The results of our study are comparable to the data obtained from previous studies[4,6,8,10,11] but have the clear limitation of a small cohort.

Conclusions

The values extrapolated to the general population seem to justify, by it, the use of NBI assisted TURBT. However, more prospective, multicenter and randomized studies, with larger samples and extended follow-up are needed to reduce the extrapolated intervals and to conclude on the benefit of systematic use of NBI associated with conventional WLC or its equivalency to PDD.

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