Original Article

Accuracy of detecting recurrent rate of NMIBC by NBI and WLC: the prospective study

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Narrow-band imaging cystoscopy, white light cystoscopy, non-muscle invasive bladder cancer, transurethral resection of bladder tumors

Abstract

Objective: The aim of this study was to investigate the accuracy of narrow-band imaging cystoscopy (NBI) in cases of recurrent non-muscle invasive bladder cancer (NMIBC) compared to standard white light cystoscopy (WLC).

Materials and Methods: All NMIBC patients at Rajavithi Hospital, Thailand were enrolled onto this single-center prospective cohort study. The patients were diagnosed by transurethral resection of bladder tumor (TURBT) then underwent both WLC and NBI carried out by the same two urologists. Cold cup biopsy was performed for all visible lesions.

Results: A total of 67 NMIBC patients were enrolled onto the study. The male to female ratio was 3.5 : 1, the mean age was 69.2±10.7 years, and stage Ta and T1 were 56.7% and 43.3% respectively. Papillary urothelial neoplasm of low malignant potential (PUNLMP), low and high grade were 3.0%, 37.3%, and 59.7% respectively. The NBI significantly improved the detection rate of NMIBC and carcinoma in situ (CIS) in comparison to standard WLC (100.0% versus 80.0% and 100.0% versus 0.0% respectively). Also, NBI cystoscopy resulted in significantly superior detection rates for CIS and overall tumors. However, specificity was lower (84.0% versus 93.0%) and the false positive rates of NBI were higher than WLC (15.7% versus 7.01%).

Conclusion: NBI cystoscopy is an alternative procedure for patients with recurrent NMIBC, with significant levels of improvement regarding tumor detection. This technique may lead to better outcomes from early treatment.

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Introduction

Bladder cancer is the 11th most common malignancy worldwide[1] and the 6th most common cancer in Thailand.[2] Bladder cancer is divided into two types: non-muscle invasive bladder cancer (NMIBC) (75%) and muscle-invasive bladder cancer (MIBC) (25%).[1]

The current standard technique for diagnosis is white light cystoscopy (WLC) and urine cytology. Transurethral resection of bladder tumor (TURBT) is the key to confirmation of the diagnosis and pathological staging.[3] However

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WLC has limitations, and has a high recurrence rate. A small and flat lesion that was a tumor or carcinoma in situ (CIS) which had been overlooked at the initial investigation and also during the intra-operative phase can result in tumor recurrence.[4] EAU guidelines recommended biopsy of any abnormal looking urothelium, or even random biopsy of normal mucosa in case of potential positive cytology.[5]

Therefore, better detection methods have been established to reduce the impact of these lesions.[6] More recently narrow-band imaging (NBI) has been playing a significant role. The wavelength of the NBI which resulted in peak absorption by hemoglobin and allowed greater visual clarity of the microvessels than WLC was 390-445 nm. NBI can detect small lesions or CIS that are difficult to find.[7] NBI is useful in the detection of early-stage cancer in gastrointestinal endoscopy and is therefore expected to play an important role in detection of NMIBC.[8] However, to date, this technique is not routinely used for diagnosis.[6] This prospective, experimental trial will compare the sensitivity of the detection of NMIBC between NBI and WLC in a 1 year period.

Materials and Methods

Study population and procedures

This study was approved by the ethics committee at Rajavithi Hospital, Thailand (Study Number: 045/2021). All patients were informed about the trial and gave consent prior to the procedure. A total of 67 patients with a preliminary diagnosis of superficial bladder cancer were enrolled; 52 patients were male, 15 were female, and the age range was from 35 to 95. Each patient underwent both WLC and NBI in sequence by two different experienced urologists. After the patient was placed in the lithotomy position, the first urologist used WLC and then the second one performed NBI within 5 minutes of the first technique. Both urologists were blinded to the result's of the other to prevent bias. Rigid cystoscope's (Model EXERA II CV-180, Olympus Medical systems, Tokyo, Japan) that can be switched from WLC to NBI were used in this study. After each urologist completed the cystoscopy and recorded the suspected area under WLC and NBI in a mapped form, biopsies were conducted in accordance with the record form (1 biopsy from each lesion). The specimens were put in tagged containers and transferred to a pathologist who was blinded to the collection method. The sensitivity and specificity of WLC and NBI cystoscopy was compared from the results of biopsies.

Study design

Prospective controlled trial

Study population

1. Inclusion criteria: Patients with a preliminary diagnosis of non-muscle invasive bladder cancer by TURBT
2. Exclusion criteria: No tumor lesions found in cystoscopy

Outcome measures and statistics

The primary outcome was to compare the sensitivity and specificity of NBI cystoscopy and WLC cystoscopy for detection of recurrent NMIBC or CIS. The secondary outcome was to compare the differences in the positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio. The data were analyzed using SPSS Statistics Version 22.0. (IBM Corp., Chicago, IL, USA). Data were presented as mean and standard deviation (SD) unless otherwise noted. Measure of agreement was calculated by Kappa.

Results

The demographic data in the study are detailed in Table 1. A total of 67 patients were enrolled onto this study. Positive and negative results were based on pathological results. The Kappa statistic (0.71 $p < 0.001$) indicates that there was substantially significant agreement between the findings of the WLC and NBI techniques. According to the WLC results, number of diagnoses by directional cystoscopic examination with biopsy positive were 12 and 8, respectively. The number of diagnoses by directional cystoscopic examination and biopsy positive were 19 and 10, respectively from NBI.

A total 10 patients from 67 patients were confirmed as having recurrent bladder cancer by pathological report. A total of 2 patients were detected using NBI only, whereas 8 patients was detected using both WLC and NBI (Table 2). Regarding the pathological stage in 10 patients; 5 patients were pTa, 3 patients were pT1, and 2 patients pTis.

The diagnostic efficiency of WLC and NBI cystoscopy was calculated by the sensitivity, specificity, positive predictive values, negative predictive values, positive likelihood ratio, and negative likelihood ratio (Table 3). In these 67 patients, the sensitivities of NBI and WLC were 100.0% and 80.0%, respectively, the specificities of NBI and WLC were 84.0% and 93.0%, respectively; the false positive rates of NBI and WLC were 15.7% and 7.0%, respectively; the positive predictive values of NBI and WLC were 52.6% and 66.7%, respectively; the negative predictive values of NBI and WLC were 100.0% and 96.4%, respectively; the positive likelihood ratio of NBI and WLC were 6.33 and 11.44, respectively; and the negative likelihood ratio of NBI and WLC were 0 and 0.22 respectively.

Pathological grading in 10 patients; 1 patient was papillary urothelial neoplasm of low malignant potential (PUNLMP) (10.0%), 1 patient was low grade (10.0%), 2 patients were CIS (20.0%) and 6 patients were high grade (60.0%). The overall detection rates for patients with CIS was significantly improved as a result of NBI in comparison with WLC (100.0% versus 0.0%) (Figure 1)

After intravesical BCG therapy, NBI was positive in 4 patients; 1 patient (25.0%) had a positive biopsy. Intravesical BCG may increase false positive rates of NBI, but these findings were not significant.

Table 1. Demographic and clinical characteristics of the study patients

Characteristics	Total (N=67)
Gender, n (%)	
Male	52 (77.6)
Female	15 (22.4)
Age (years)	
Mean±SD	69±10.7
Co-morbidity, n (%)	35 (52.2)
Diabetes Meletus	10 (28.6)
Dyslipidemia	8 (22.9)
Hypertension	27 (77.1)
Other	15 (42.9)
Smoker, n (%)	19 (28.4)
Alcohol drinker, n (%)	11 (16.4)
Tumor staging, n (%)	
Ta	38 (56.7)
T1	29 (43.3)
Tumor grading, n (%)	
PUNLMP	2 (3.0)
Low grade	25 (37.3)
High grade	40 (59.7)

SD = standard deviation, PUNLMP = papillary urothelial neoplasm of low malignant potential

Discussion

Non-muscle invasive bladder cancer has a high rate of recurrence. Incomplete tumor removal is one of the reasons for early recurrence. Therefore, new technology such as narrow band imaging has been developed to improve the detection rate of NMIBC

NBI uses the light at wavelengths of 390 - 445 nm that absorbed by hemoglobin and more clearly seen the microvessels than with WLC. NBI can improve the detection of small lesions

Table 2. Cystoscopy results

Cystoscopy results	Number of cases of biopsy, n	Tumor n (%)	No tumor n (%)
WLC+, NBI+	12	8 (66.7)	4 (33.3)
WLC-, NBI+	7	2 (28.6)	5 (71.4)
WLC+, NBI-	0	0 (0.0)	0 (0.0)

WLC = white light cystoscopy, NBI = narrow band imaging cystoscopy

Table 3. Results of the multivariate analysis

Characteristics	Sensitivity (%)	Specificity (%)	95%CI	PPV	NPV	+LH	-LH
WLC	80.0	92.98	44.39-97.48	66.67	96.36	11.44	0.22
NBI	100.0	84.21	69.15-100	52.63	100.0	6.33	0.00

WLC = white light cystoscopy, NBI = narrow band imaging cystoscopy

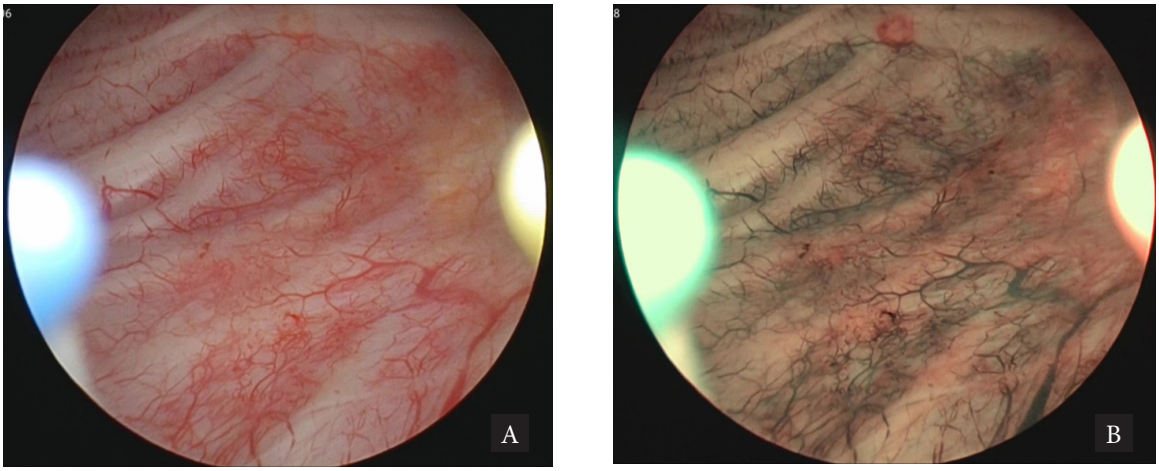


Figure 1. Carcinoma in situ lesion visible in narrow-band imaging (B) not seen in white light cystoscopy (A)

or CIS that are not easily seen with WLC. The main advantages of NBI are that there are no contraindications for the patient. Moreover, this technique is simple and does not increase the cost of therapy.[9]

Recent reports have indicated that NBI cystoscopy is more effective than WLC for the detection of the recurrence of bladder cancer. In a study by Zhangqun et al, 124 of 167 (74.3%) recurrent bladder cancer samples were diagnosed using both WLC and NBI. Forty one (24.5%) were detected using only NBI and 2 (1.2%) were detected using only WLC.[10] Zhangqun et al. reported that NBI could improve the sensitivity of the diagnosis of recurrent bladder cancer. Li et al calculated that NBI facilitated the detection of recurrence in an additional 17.0% of patients (95% confidence interval [CI], 10.0–25.0%) and an additional 24.0% of tumors (95% CI, 17.0–31.0%).[11] The disease recurrence shows that the use of NBI versus WLC improves the detection of recurrence by 15.0-32.0%, with time to recurrence of 29 and 13 months, respectively. In addition, a significantly greater rate of tumor detection was achieved with NBI cystoscopy than with WLC in a study by Geavlete et al. (94.9% vs. 84.3%, respectively).[12]

In our study, the primary outcome is a comparison of the sensitivity and specificity between NBI and WLC. The order of the WLC or NBI inspections was conducted by two urologists. After each urologist completed the cystoscopy and mapped the suspected area identified under WLC and NBI, biopsies were conducted according to their findings (1 biopsy in each lesion). Both urologists were blinded from perception of the other's results to prevent bias.

The findings of our study indicate that NBI cystoscopy could be used to improve the detection of non-muscle invasive bladder cancer. In particular, early stage tumors or carcinomas in situ could be more clearly observed under NBI cystoscopy. However, although NBI significantly improved the sensitivity of diagnosis, the procedure resulted in a lower specificity and higher false positive rate than WLC. Intravesical BCG may increase the false positive rate of NBI, but the results were not significant.

Although NBI cystoscopy has a high sensitivity, a few limitations of this study merit consideration. The accuracy of NBI and WLC were operator dependent with regard to the detection of tumors as well as to other subjective factors. The number of patients of this study was lower than expected, future research studies could enroll more patients.

Conclusions

NBI cystoscopy showed significantly improved detection rates of NMIBC and CIS in comparison to WLC. However, the rate of false-positive results was higher for NBI.

In conclusion, NBI cystoscopy is an alternative procedure for the treatment of NMIBC patients, in order to improve tumor detection. This approach also provides a substantial improvement in postoperative therapeutic management of bladder cancer.

Conflicts of Interest

The authors declare no conflicts of interest.

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