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Original Research Article

Accuracy Analysis of Narrow Band Imaging (NBI) Bronchoscopy Compared To White Light Bronchoscopy in the Diagnostics of Lung Tumours

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ABSTRACT

Background: Bronchoscopy plays an important role in the diagnostics of lung tumours. One of the technologies looking for their way in the diagnostics of pulmonary diseases is narrow band imaging. The aim of this study was to compare accuracy of examinations in the NBI and the white light (WL) modes in relation to biopsy results for the diagnoses of malignant tumour or severe dysplasia.
Methods and results: A group of 500 patients have undergone a bronchoscopic examination in the NBI mode and afterwards in the white light. Biopsies were taken from all areas with pathological findings in both the modes for histological examination. Pathological bronchoscopic images were detected in a total of 382 patients. Positive findings in both the NBI mode and the WL mode were detected in 331 patients (66.2%). Discordant NBI-/WL+ findings were detected in 29 cases (5.8%) and discordant NBI+/WL- findings were detected in 22 cases (4.4%). The relative sensitivity of NBI compared to WL is 1.06 ($p < 0.01$; NBI sensitivity is significantly higher). The relative rate of false positive results in NBI compared to WL is 0.91 ($p = 0.01$; the rate of false positive results is significantly lower in NBI).
Conclusions: The performed statistical evaluation shows a statistically significant increase in examination accuracy in NBI compared to WL. An NBI examination is able to differentiate between the necrotic avascular region of the tumour and the viable tissue very well even if an examination in the WL mode is not so explicit in this respect.

Key Words: Lung cancer; Bronchoscopy; Narrow band imaging

INTRODUCTION

Bronchoscopy plays an important role in the diagnostics of lung tumours. In the recent years, there has been a significant technological progress aiming at provision of the most detailed information possible on the structure of the bronchial mucosa, shape and character of vascular structures in the bronchial mucosa, and submucosal structures. One of the technologies looking for their way in the diagnostics of pulmonary diseases is narrow band imaging. [1]

NBI is a new technology of visualization of capillary patterns and bigger vessels in mucosa. Bronchial mucosa is illuminated by a combination of narrow spectra of the blue, green and red light with

wavelengths of 415, 540 and 600 nm. The depth of penetration of the light into the mucosa depends on the light's wavelength. Photons in the blue and green portions of the spectrum penetrate less deep and are selectively absorbed by hemoglobin – this enables visualisation of capillaries and small vessels located less deep in the mucosa. Photons of the red light penetrate deeper, beyond the hemoglobin absorption range, enabling visualization of bigger vessels located deeper. Vessels containing blood are visualized in dark colour; other structures of the mucosa are light. This enables visualization of vessels in the mucosa and differentiation between inflammation and pathological tumour vascularisation. [2]

Vascular structures are highlighted by using a special RGB (red, green and blue) rotating optical filter placed in the path of the white light emitted by a xenon lamp. Mucosa is illuminated by narrow beams with a given wavelength. The image is captured by a CCD chip and synthesized in a video processor. Subsequently, the image is displayed on an LCD monitor. [3]

The importance of NBI technology lies, above all, in the improvement of visualization of changes in the structure, architecture and frequency of vessels in bronchial mucosa. Angioneogenesis plays an important role in the growth of malignant tumours. New vessels differ in their morphology and frequency from the normal vascular structure of a healthy epithelium. [4-8] The detection of such changes may significantly improve the possibilities of diagnostics of premalignant and malignant processes in the epithelium of air passages.

The aim of this study was to compare accuracy of examinations in the NBI and the WL modes in relation to biopsy results for the diagnoses of malignant tumour or severe dysplasia.

MATERIALS AND METHODS

Group

500 bronchoscopic examinations were carried out in the NBI mode and afterwards in the white light. The group included 348 men (69.6%) and 152 women (30.4%). Indications for bronchoscopic examination included: pathological CT or x-ray findings – 420 (84.0%), hemoptysis – 33 (6.6%), follow-up after lung tumour surgery – 12 (2.4%), follow-up after chemotherapy and radiotherapy – 21 (4.2%), and follow-up after neoadjuvant chemotherapy –14 (2.8%).

Procedure

Bronchoscopic examinations were performed using the Olympus Evis Lucera system, which enables examination in the white light (WL), the NBI mode and the autofluorescence mode. The examinations were carried out under usual local anaesthesia in a bronchoscopy room with complete equipment necessary for flexible bronchoscopy. In order to eliminate mistakes caused by the bronchoscope touching the mucosa and subsequent bleeding, the patients were first examined in the NBI mode and only afterwards in the WL mode. The examiners evaluated changes in the structure, architecture and frequency of vessels visualized in the bronchial mucosa. Each pathological image was recorded by means of a DVD recorder and archived. Findings were evaluated by two physicians having experience with this diagnostic method. Samples were taken from areas with suspicious images of vascular changes, indicating possible malignity, for histological and cytological examination. The Evis Lucera bronchoscopy system enables biopsy material sampling during examination in the NBI mode.

Evaluation

Examiners evaluated the shape and size of vessels, their course, and the increase or decrease in the frequency of vascular structures. Pathological findings in the NBI

mode (NBI+) were divided, in compliance with works published by prominent world departments, [1,4,5,9] into 4 groups: 1) Image of "dotted" vessels with tortuous course, Figure 1; 2) Image of abrupt-ending vessels with disturbed architecture, Figure 2; 3) Avascular image typical for necrosis, Figure 3; and 4) Image of uniform multiplied vessels, Figure 4. The first two images reflect pathological changes in the morphology of vessels and disrupted vessel architecture originating in the process of neoangiogenesis in malignant growth. The image of avascular zones is typical for surface necrosis with poor vascular supply as may be seen on the surface of tissue with tumorous changes. The first three groups were suspected of malignancy. The fourth group was evaluated as inflammatory changes. We may observe increased vascular supply in such findings, but no changes in the morphology of the vessels. Samples were taken from the areas with pathological findings for histological and cytological examinations.

Pathological findings in the white light (WL+) were evaluated according to generally valid criteria for malignant pathological processes. [10]

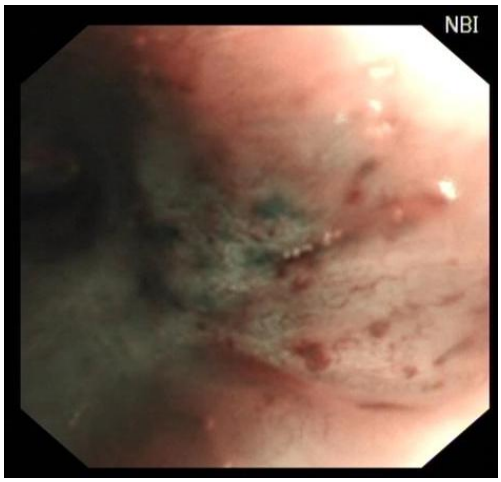

Figure 1. Image of "dotted" vessels with tortuous course.

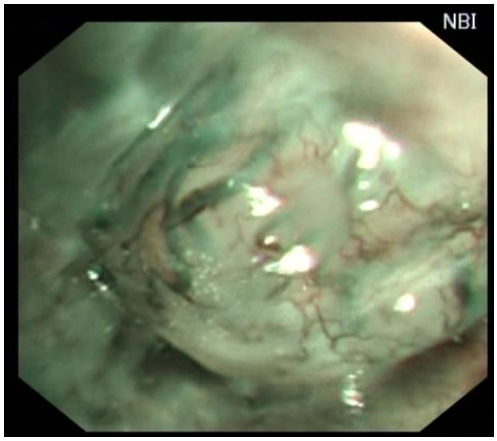

Figure 2. Image of abrupt-ending vessels with disturbed architecture.

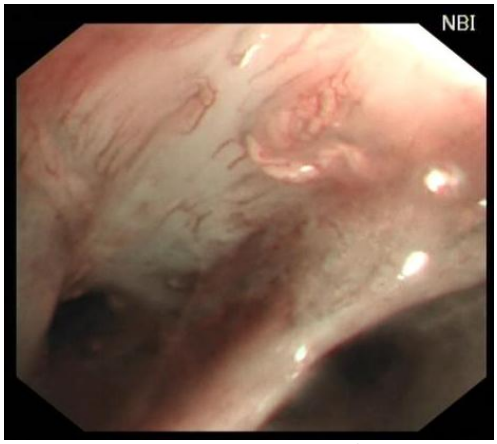

Figure 3. Avascular image typical for necrosis.

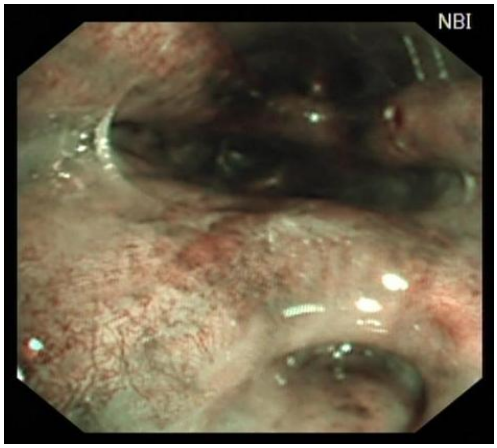

Figure 4. Image of uniform multiplied vessels.

Statistical Methods

The results of the histological and cytological examinations were evaluated with respect to relative sensitivity and

relative rate of false positive results in NBI compared to WL. [11] The statistical significance of the difference in sensitivity and specificity of the modes was determined by means of the McNemar's test. [12]

RESULTS

500 bronchoscopic examinations have been performed (table No. 1). Findings were negative in both the modes (NBI- and WL-) in 118 patients (23.6%).

Table 1: Division of Results of NBI/WL Bronchoscopic Examinations

Bronchoscopic Finding	Number of patients
NBI+/WL+ (positive finding)	331 (66.2)
NBI-/WL+ (discordant finding)	29 (5.8)
NBI+/WL- (discordant finding)	22 (4.4)
NBI-/WL- (negative finding)	118 (23.6)
Total	500
The values are given as n (%)	

Pathological bronchoscopic images were found in a total of 382 patients. Positive findings in both the NBI and the WL modes were detected in 331 patients (66.2%).

NBI-/WL+ discordant findings were detected in 29 cases (5.8%) and NBI+/WL- discordant findings were detected in 22 cases (4.4%). Biopsy examinations were performed in all cases with positive findings in both the modes or in just one mode (n = 382). Results of the histological examinations are presented in table No. 2. The positive predictive value of the NBI pathological findings, indicating malignity, was very high (97.5 %).

Table 2: Predictive Value of NBI/WL Bronchoscopic Findings

Bronchoscopic Finding	Histological Finding					
	Malignant Tumor	Severe Dysplasia	Inflammation	Benign Tumour	Negative Finding	Total
NBI+/WL+ suspected malignity	146 (95.4)	3 (2.0)	4 (2.6)	0	0	153
NBI+/WL+ suspected inflammation	1 (0.6)	5 (2.8)	162 (91.0)	0	10 (5.6)	178
NBI+/WL-	2 (9.1)	8 (36.4)	7 (31.8)	0	5 (22.7)	22
NBI-/WL+	0	0	13 (44.8)	9 (31.0)	7 (24.2)	29
Total	149	16	186	9	22	382
The values are given as n (%)						

The statistical evaluation focused on the comparison of examination accuracy in the NBI and the WL modes in relation to the biopsy results. Analyses of the relative sensitivity and the rate of false positive results in NBI compared to WL were carried out for histological or cytological findings of malignant tumours or severe dysplasia. The basic data for statistical processing are presented in table No. 3.

Table 3: Comparison of the Accuracy of NBI and WL Bronchoscopy. Patients who were negative in both modes (n = 118) did not undergo a histological examination and were not included in this evaluation.

	Histological examination POSITIVE for a malignant tumour or severe dysplasia			Histological examination NEGATIVE for a malignant tumour or severe dysplasia			TOTAL
	WL+	WL-	Total	WL+	WL-	Total	
NBI+	155	10	165	176	12	188	353
NBI-	0	-	0	29	-	29	29
TOTAL	155	10	165	205	12	217	382
The values are given as n							

The relative sensitivity of NBI compared to WL is 1.06 ($p < 0.01$; NBI sensitivity is significantly higher). The relative rate of false positive results in NBI compared to WL is 0.91 ($p = 0.01$; the rate of false positive results is significantly lower in NBI).

DISCUSSION

NBI very significantly improves visualization of vascular structures in

bronchial mucosa. The method enables significantly better evaluation of such structures than the white light. [13] This enables getting better information on the shape and frequency of vascular structures in the bronchial mucosa. Pioneering works, written especially by Japanese and German authors, have specified the principles for evaluation of pathological changes in vessels in mucosa with premalignant and malignant changes. [1,4,5,9] Such vascular structures may be found in apparently tumorous tissues even through tumour visualization by means of conventional white light bronchoscopy. The advantage of NBI in such cases lies certainly in the improvement of biopsy targeting to areas with pathological vascularization, which may be not-so-clearly-visible or even invisible in the white light. This improves examination yield. The results of our work also point out the high predictive value of NBI examinations for findings indicating malignity (97.5%).

Another important fact is the possibility of evaluating mucosa surrounding the tumorous tissue. The method enables detailed visualization of the vessels in the neighbourhood of the tumour, which is not possible in such detail in conventional white light bronchoscopy. The presence of pathological vascularization in the neighbourhood of the tumour helps to better identify the real borders of the malignant process. [14] Exact determination of the lesion extent is crucial for lung carcinoma staging and for determination of further therapeutic procedure. Inflammatory changes in the mucosa – occurring, for instance, in the neighbourhood of a tumour – may be differentiated from malignant changes by the shape and frequency of vessels.

Examinations in the NBI mode may be advantageously used for more accurate evaluation of changes in the mucosa which are not explicit in the white light – e.g. mucosal tubercles, mucosal edema, suspected mucosal infiltration, etc. The examination provides good information on vascular structures in such changed mucosa and enables further examination, especially biopsy from the area of suspicious changes.

The analyses of relative sensitivity and rate of false positive results in NBI compared to WL for histological or cytological findings of malignant tumours or severe dysplasia in our group point out that the relative sensitivity of NBI compared to WL is 1.06 ($p < 0.01$; NBI sensitivity is significantly higher). The relative rate of false positive results in NBI compared to WL in our group is 0.91 ($p = 0.01$; the rate of false positive results is significantly lower in NBI).

The performed statistical evaluation shows a statistically significant increase in examination accuracy in NBI compared to WL. An NBI examination is able to differentiate between the necrotic avascular region of the tumour and the viable tissue very well even if an examination in the WL mode is not so explicit in this respect. This results in a more accurate determination of the most suitable area for taking biopsy material.

The examination may play an important role in follow-up of patients after lung resection, chemotherapy and radiotherapy due to bronchogenic carcinoma. Mucosa of such patients, changed by post-surgical deformities, is frequently difficult to evaluate. A more detailed evaluation of the mucosa and its vascular structures may help in the detection of tumor recurrence or differentiation between inflammation and possible tumour recurrence. The method enables better determination of the area suitable for biopsy in such cases, too.

NBI bronchoscopy is also used for detection of early forms of lung tumours.

The examination is suitable for high-risk patients, smokers, and patients suffering from hemoptysis, with no explicit x-ray or CT findings. [4] A detailed evaluation of vessels in the bronchial mucosa of such patients may reveal anomalies which are invisible in the white light of conventional bronchoscopy. Targeted biopsy may subsequently detect severe dysplasia or carcinoma in situ. Modern video systems enable archiving of examination video recordings and saving photodocumentation of examinations in patients' cards in the computer. Such archived findings may be subsequently compared to control examinations carried out within the monitoring of the patients in a later period. This may be extremely important for early detection of malignant turnover of the disease. The role of modern bronchoscopic methods in the detection of early forms of lung tumours is subject to intensive research and the NBI method will certainly not be omitted. [15-24] Bronchoscopic high definition (HD) imaging using NBI imaging is a very promising new possibility in the diagnostics of lung tumours. The combination of these two methods enables to get a high-quality image of the vascular structures of the mucosa. First experience with this new method indicates that the method will enable even better detection of dysplastic changes than the current NBI. [25]

Differentiation between avascular necrotic tissue and other mucosa is relatively explicit; the difference is even bigger if there is tumorous tissue with pathological vascularization in the neighbourhood of the necrotic tissue. Histological examination of the viable tumorous tissue is important for the determination of the type of tumour; taking samples of necrotic materials frequently precludes histological examination. The possibility of taking biopsy samples directly during the NBI examination is seen as a great advantage, increasing biopsy yield and reducing the risk of undiagnosed sampling. [26,27]

A work concerned with the characteristic image of vascular anomalies in NBI for various histological types of lung carcinoma has been published recently. Statistically significant correlations were described between the histological type of squamous cell lung cancer (SCC) and the NBI image of tortuous vessels and abrupt-ending vessels, and between the histological type of adenocarcinoma and the NBI image of dotted vessels. [24,28]

A certain disadvantage of the method is the subjectivity of the evaluation of vascular changes. There are inexplicit and transient findings. Experience of examiners plays a very important role. In principle, each suspicious change should be verified by biopsy.

Another limitation to the examination is the presence of blood in the examined field. Even a minor bleeding may frequently hinder valid evaluation of the vascular changes. Difficulties may arise even by the bronchoscope touching the bronchial wall with subsequent minor bleeding. Therefore, it is necessary to start the examination in the NBI mode and only then continue in the white light. The first view of the intact mucosa is most important.

CONCLUSION

The first experience with this method shows that it helps in the detection of vascular anomalies in the bronchial mucosa, thus helping in the diagnostics of lung tumours. Above all, the method enables exact targeting of biological material sampling for histological and cytological examinations. It helps in the detection of submucosal tumours, tumour recurrence after surgery and determination of the tumour extent. The use of NBI bronchoscopy in the detection of early lung

tumour stages is subject to research. The first results in this respect are promising.

The performed statistical evaluation shows a statistically significant increase in examination accuracy as compared to WL. An NBI examination is able to differentiate between the necrotic avascular region of the tumour and the viable tissue very well even if an examination in the WL mode is not so explicit in this respect. This results in a more accurate determination of the most suitable area for taking biopsy material. The method significantly increases visibility of vascular structures in the mucosa. Evaluation of such changes is not always easy and requires significant experience of the examiner. NBI bronchoscopy helps in the detection of submucosal tumours and tumour recurrence after surgery. The method improves the possibility of determination of tumour extent before surgery and sometimes even improves the possibility of detection of early stages of lung tumours.

Better visualization of vascular anomalies in the bronchial mucosa improves the possibility of severe dysplasia detection. The clinical importance of such changes is not clear yet and is subject to intensive research.

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