Role of narrow band imaging (NBI), in the treatment of non-polypoid colorectal lesions, with endoscopic mucosal resection (EMR).

A single-center experience

Luigi Sivero*, Serena Volpe*, Maurizio Gentile**, Stefania Sivero*, Speranza Iovino*, Nicola Gennarelli*, Alessia Chini*, Saverio Siciliano*

*Medical-Surgical Department of Diseases of the Digestive System, "Federico II" University of Naples, Naples, Italy
**Department of General and Specialistic Surgery, "Federico II" University of Naples, Naples, Italy

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BACKGROUND: *In this study, the authors evaluated the role of narrow band imaging endoscopy in the early detection of infiltration of the colon wall by flat and depressed lesions, highlighted during colonoscopy, to confirm the possibility of removal with Endoscopic Mucosal Resection (EMR).*
METHODS: *67 patients (37 males and 30 females) with non-polypoid colorectal lesions were included in this study. The location of the lesions, the size and possible infiltration of the colon wall were performed with a colonoscopy with NBI. Lesions without massive invasion were treated with an EMR.*
RESULTS: *NBI was found to be a sensitive, specific, and accurate technique in assessing any infiltration of the colon wall. Endoscopic resection of the mucous membrane was successfully performed in 62 patients, it was not possible to perform it in 5 patients, due to the lack of dissection, and they underwent surgery.*
CONCLUSIONS: *Non-polypoid colorectal lesions and early tumors can be treated with EMR. Certainly, early detection with Narrow Band Imaging endoscopy and subsequent endoscopic resection can reduce colorectal cancer mortality. Many studies have confirmed that these two methods have achieved important results comparable with surgical procedures.*

KEY WORDS: Endoscopic Mucosal Resection, Narrow Band Imaging, Therapy

Introduction

Narrow Band Imaging (NBI) is a method of image enhancement. It is an optical technology that processes images differently, compared to previous digital optical methods. In the development of NBI, the optical properties of living tissues have been deeply involved, starting from the previous endoscopic spectroscopy system (ESS). The first attempts were made using an optical fiber introduced into the operating channel of an endoscope; with the objective color data collected (spectral reflectance rates) from the stomach and colon, an algorithm was developed for their diagnostic application. Subsequently, a multispectral camera was used, with the possibility of acquiring spectroscopic images with a high radiant flux, using a light source with a central wavelength of 415 nm, capable to highlight the contrast of the capillaries, normally not detected by a white light [1]. Narrow Band Imaging (NBI) has set a new standard for cancer management [2].

The clinical benefits of Narrow Band Imaging are:
– greater accuracy for injury detection;
– higher detection rate of adenomas (up to 14% more) with NBI compared to conventional endoscopy [3]);
– higher detection rate of colorectal polyps (up to 29% more) with NBI compared to conventional endoscopy [3].

ABBREVIATIONS

ESS: Endoscopic spectroscopy system
EMR: Endoscopic Mucosal Resection
HP: Hyperplastic polyp
M: Mucosal cancer
MSM: Cancer With Massive Submucosal Invasion
NBI: Narrow Band Imaging
SSM: Slightly Invaded Submucosal Cancer
TA: Tubular adenoma
WLC: White light colonoscopy

A special narrow-band filter is passed through by the light of the NBI, and subsequently hits the tissues. The action of this filter is to eliminate all wavelengths except those from 415 nm in blue color and from 540 nm in green color, both correspond to the absorption spectrum of hemoglobin. This mechanism allows for greater contrast for superficial micro vessels which appear brown / black and in greater clarity of superficial mucosal structures [4]. In particular, the blue light, which has a lower penetration depth, improves the vision of the superficial capillary network, while the green light, which penetrates more deeply, highlights the submucosal vascular texture. Narrow-band imaging enables high-confidence optical diagnosis of colorectal lesions, especially flat and depressed ones.

Protruding, flat and depressed non-polypoid lesions of the colon account for 30-40% of all colorectal lesions and, given the ability to infiltrate the submucosa of the bowel early, their potential for malignancy is significantly higher than polypoid lesions [5,7].

The evolution of a neoplastic lesion of the colorectal passes from a non-invasive phase limited to the mucosa to an invasive one that first involves the submucosa and then affects the other layers of the wall [8,9].

The current macroscopic morphological classification of superficial neoplastic lesions is that of Paris [10] published in 2003, which distinguishes superficial lesions (type 0) into: polypoid or protruding and non-polypoid or non-protruding lesions, frequently detected thanks to the widespread screening of cancer of the colorectal.

Scientific works show that the early, non-invasive forms do not present lymph node metastases [11], therefore, are candidates for endoscopic resection, while submucosal neoplasms are accompanied by lymph node metastases in 6-12% of cases [12,13,14,15], therefore requiring, with some exceptions, a surgical resection with lymph node dissection for treatment with curative intent.

Endoscopic Mucosal Resection or mucosectomy (EMR) is now considered the first method of choice for the removal of flat colorectal polyps [16]. The main advantage of the method is that it is less invasive than tradition-al surgery, has fewer risks and fewer complications. The only disadvantage is that in polypoid lesions >20 mm it is not possible to remove the enbloc lesions, with a consequent increase in the risk of residual adenomatous tissue and therefore of recurrence, the same histological examination will have less accuracy in case of piece-meal removal.

Complications of EMR can be represented by bleeding, perforation, and strictures. Bleeding is the most common complication, it can be immediate in about 10% of cases or late in about 1.5-14% of cases, with manifestations up to 30 days after the procedure. Perforation occurs in up to 5% of EMRs. Most perforations are immediately diagnosed and treated endoscopically at the time of the procedure.

Materials and Methods.

In the period November 2017-December 2020 we recruited 67 patients (37 males and 30 females), with an average age of 65.4 years (47-81) from a series of patients undergoing colonoscopy in our endoscopic unit. The characteristics of these patients are listed in Table I. All patients were diagnosed with flat or depressed non-polypoid colorectal lesions, greater than 10 mm, according to the Paris endoscopic classification, identified by conventional colonoscopy. Lesions less than 10 mm in
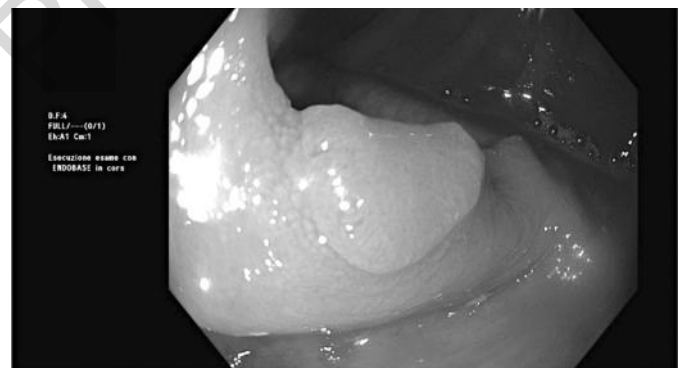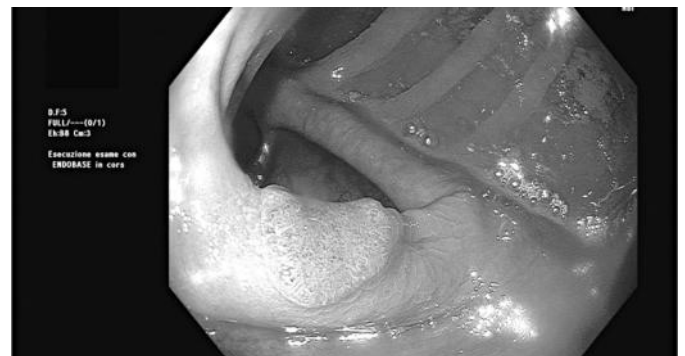

Fig. 1: Non-polypoid lesion (IIa) after WLC.

Fig. 2: Non-polypoid lesion (IIa) after NBI.

diameter were excluded, as they have a potentially hyperplastic or minimally infiltrating activity.

Endoscopic examinations were performed using a high-definition video colonoscope (CF-EZ1500DI with NBI Olympus, Tokyo, Japan), and all lesions were examined by NBI magnification.

After examination by white light endoscopy and identification of the target lesion, each patient underwent a lesion examination using the NBI system. The NBI magnification was used to visualize the surface details and the vascular network of the tumors. The NBI study of lesions was conducted using the green and blue wavelengths set at 540 and 415 nm, respectively. (Figs. 1,2). The lesions were then classified according to Kanao [14], as follows:

– type A, when the micro vessels were not observed or were extremely opaque.

– type B, when thin micro vessels were observed around the glandular crypts and clear pits could be observed through the micro vessel nest.

– type C, when the micro vessels were irregular, and the diameter or distribution of the vessels was heterogeneous.

Type C was divided into 3 subtypes (C1, C2, and C3) based on detailed magnification results of crypt visibility, vessel diameter, irregularity, and distribution:

– type C1, when the micro vessels included an irregular network, the wells observed through the micro vessels were slightly indistinct and the diameter or distribution of the vessels was homogeneous.

– type C2, when the micro vessels included an irregular network, the wells observed through the micro vessels were irregular and the diameter or distribution of the vessels was heterogeneous.

– type C3, when the pits of the microvessels were invisible, the irregular diameter of the vessel was thick, or the distribution of the vessels was heterogeneous and vascular areas were observed.

Type A and B lesions have been classified as neoplasms without invasion of the submucosa; type C1 and C2 as neoplasms with mild invasion of the submucosa (sSM); C3-type lesions have been classified as tumors with massive invasion of the submucosa (mSM).

Subsequently, during ordinary hospitalization and after obtaining informed consent, all identified lesions were subjected to endoscopic resection by EMR or surgery, and histologically evaluated.

The EMR technique was performed by injecting into the submucosa, with the use of a 23-gauge needle, a saline-epinephrine solution (0.9% saline and 0.001% epinephrine). The lesions were then removed in a single block using a combination of cutting and coagulation. The mucosectomy was performed successfully in 62 patients, it was not possible to intervene endoscopically in 5 patients, due to failure to detach the mucosa, and they

underwent surgical resection, in the latter a T2 adenocarcinoma was detected. We only had two bleeding complications that were treated endoscopically.

A single pathologist examined all the samples. Dysplasia was defined according to the modified Vienna criteria as low or high grade. The classification of invasive submucosal carcinoma was carried out according to previously reported criteria. Massive submucosal invasion (mSM) was defined as neoplastic cell proliferation extending into the submucosal layer >1000 µm. Pathological findings were then compared with NBI staging.

Results

A total of 83 colorectal lesions, meeting the inclusion criteria, were identified in 67 patients with a conventional colonoscopy. The lesions identified were: 1 of 50 patients, 2 of 16 patients and 3 of 1 patient, respectively. The characteristics of these injuries are listed in (Table I).

The relationships between NBI magnification classifications and histopathological diagnoses of colorectal cancers are listed in (Table II).

Discussion

Endoscopy with NBI is essential in the high-precision optical diagnosis of colorectal lesions, especially flat and depressed ones. Using wave frequencies, it can diagnose the level of invasion in the mucosa early, allowing their resection with an endoscopic technique, reducing the risks of surgery.

TABLE I - *Characteristics of patients and lesions*

Number of patients	67 (37 M, 30 F)
Average age	65.4 (47 – 81)
Number of lesions	83
Diameter mm (range)	18.2 (10 – 37)
Morphology	
IIA	51
IIB	2
IIC	4
IIA + IIC	19
IIC + IIA	7
Location	
Caecum	5
Ascending colon	19
Transverse colon	9
Descending colon	10
Sigma	18
Rectum	22
Histopathological diagnosis	
Hyperplastic polyp	12
Tubular adenoma	34
Mucosal cancer	16
Mildly invasive submucosal cancer	7
Cancer with massive submucosal invasion	14

TABLE II - *Relationship between NBI and histopathological diagnosis*

| NBI | HP | Histopathological diagnosis | | | |
		TA	M	sSM	mSM
Type A	12	4			
Type B		18	3		
Type C1		9	5		
Type C2		3	8	5	5
Type C3				2	9

HP hyperplastic polyp, TA tubular adenoma, M mucosal cancer; sSM cancer with mild submucosal invasion, mSM cancer with massive submucosal invasion.

EMR is considered a valid method for the endoscopic treatment of gastrointestinal cancers. In this study, flat or depressed colorectal lesions were treated with EMR. The total resection rate was 94%. The complete resection rate depends on the size of the lesions, for lesions >20 mm, the rate is significantly lower. The possibility of being able to perform an EMR was provided by the study with endoscopy with NBI, which evaluated the limits of invasion of the lesion.

Conclusions

With this study we evaluated the NBI in the evaluation of the infiltration of flat and depressed colorectal lesions before an endoscopic removal or surgery.
Estimating the depth of invasion of an early colorectal neoplastic lesion is of fundamental importance for a correct therapeutic strategy.
While NBI is an easy-to-use diagnostic technology that allows the endoscopist to switch between conventional and enhanced images with a single touch of an operating button on the endoscope handle, it also requires the expertise of a dedicated operator.
In our study, endoscopy with NBI was found to be effective and accurate in predicting deep submucosal infiltration in early flat and depressed colorectal neoplastic lesions and represents, in our opinion, an indispensable method for guiding the therapeutic choice.

Riassunto

In questo studio, gli autori hanno valutato il ruolo dell'endoscopia di imaging a banda stretta nella diagnosi precoce di infiltrazione della parete del colon da lesioni piatte e depresse, evidenziate durante la colonscopia, per confermare la possibilità di rimozione con resezione mucosa endoscopica (EMR).
METODO: In questo studio sono stati inclusi 67 pazienti (37 maschi e 30 femmine) con lesioni colo rettali non polipoidi. La localizzazione delle lesioni, le dimensioni e l'eventuale infiltrazione della parete del colon sono state eseguite con una colonscopia con NBI. Le lesioni senza massiccia invasione sono state trattate con un EMR.
RISULTATI: L'NBI è risultato essere una tecnica sensibile, specifica e accurata nella valutazione di qualsiasi infiltrazione della parete del colon. La resezione endoscopica della mucosa è stata eseguita con successo in 62 pazienti, non è stato possibile eseguirla in 5 pazienti, a causa della mancanza di dissezione, e sono stati sottoposti a intervento chirurgico.
CONCLUSIONI: Le lesioni colo-rettali non polipoidi e i tumori precoci possono essere trattati con EMR. Certamente, la diagnosi precoce con l'endoscopia Narrow Band Imaging e la successiva resezione endoscopica possono ridurre la mortalità per cancro del colon-retto. Molti studi hanno confermato che queste due metodiche hanno raggiunto importanti risultati paragonabili alle procedure chirurgiche.

References

1. Muto M, Yao K, Sano: *Atlas of endoscopy with narrow band imaging.* Springer, Japan, 2015.

2. Iwatate, M, Ikumoto T, Hattori S, Sano W, Sano Y, Fujimori T: *Nbi and nbi combined with magnifying colonoscopy.* Diagnostic and Therapeutic Endoscopy, 2012.

3. Pamudurthy V, Lodhia N, Konda VJA: *Advances in endoscopy for colorectal polyp detection and classification.* Proc (Bayl Univ Med Cent), 2019; 33(1):28-35.

4. East JE, Vleugels JL, Roelandt P, Bhandari P, Bisschops R, Dekker E, Hassan C, Horgan G, Kiesslich R, Longcroft-Wheaton G, Wilson A, Dumonceau JM: *Advanced endoscopic imaging: European society of gastrointestinal endoscopy (ESGE) technology review.* Endoscopy, 2016; 48(11):1029-45.

5. Rembacken BJ, Fujii T, Cairns A, Dixon MF, Yoshida S, Chalmers DM, Axon AT: *Flat and depressed colonic neoplasms: A prospective study of 1000 colonoscopies in the UK.* Lancet, 2000; 355(9211):1211-214.

6. Hurlstone DP, Cross SS, Adam I, Shorthouse AJ, Brown S, Sanders DS, Lobo AJ: *A prospective clinicopathological and endoscopic evaluation of flat and depressed colorectal lesions in the united kingdom.* Am J Gastroenterol, 2003; 98(11):2543-549.

7. Kudo SE, Kashida H: *Flat and depr,essed lesions of the colorectum.* Clin Gastroenterol Hepatol, 2005; 3(7 Suppl 1): S33-36.

8. Cooper HS: *Surgical pathology of endoscopically removed malignant polyps of the colon and rectum.* Am J Surg Pathol, 1983; 7(7):613-23.

9. Danzi M, Grimaldi L, De Capua Mᵇ, Tammaro N, Danzi R, Sivero L: *Obstructing left sided colorectal cancer. A retrospective single center study.* Ann Ital Chir, 2019; 90,2:121-126, 2019.

10. *The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002.* Gastrointest Endosc, 2003; 58(6 Suppl): S3-43.

11. Kitajima K, Fujimori T, Fujii S, Takeda J, Ohkura Y, Kawamata

H, Kumamoto T, Ishiguro S, Kato Y, Shimoda T, Iwashita A, Ajioka Y, Watanabe H, Watanabe T, Muto T, Nagasako K. *Correlations between lymph node metastasis and depth of submucosal invasion in submucosal invasive colorectal carcinoma: a Japanese collaborative study*. J Gastroenterol, 2004; 39(6):534-43.

12. Haggitt RC, Glotzbach RE, Soffer EE, Wruble LD: *Prognostic factors in colorectal carcinomas arising in adenomas: Implications for lesions removed by endoscopic polypectomy*. Gastroenterology, 1985; 89(2):328-36.

13. Minamoto T, Mai M, Ogino T, Sawaguchi K, Ohta T, Fujimoto T, Takahashi Y: *Early invasive colorectal carcinomas metastatic to the lymph node with attention to their nonpolypoid development*. Am J Gastroenterol, 1993; 88(7):1035-39.

14. Kanao H, Tanaka S, Oka S, Hirata M, Yoshida S, Chayama K: *Narrow-band imaging magnification predicts the histology and invasion depth of colorectal tumors*. Gastrointest Endosc, 2009; 69(3 Pt 2):631-36.

15. Nusko G, Mansmann U, Partzsch U, Altendorf-Hofmann A, Groitl H, Wittekind C, Ell C, Hahn EG: *Invasive carcinoma in colorectal adenomas: Multivariate analysis of patient and adenoma characteristics*. Endoscopy, 1997; 29(7):626-31.

16. Grgov S, Dugaliü P, Tomaševiü R, Tasiü Vojnosanit T: *Endoscopic mucosal resection of flat and sessile colorectal adenomas: Our experience with long-term follow-ups*. Pregl, 2014; 71(1):33-38.