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窄带成像技术联合放大内镜在早期胃癌诊断中的价值

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摘要 目的:评估比较窄带成像技术联合放大内镜(narrow band imaging-magnifying endoscopy, NBI-ME)在早期胃癌诊断中价值。**方法:**115例早期胃癌患者行NBI-ME观察,采集照片并做出内镜下诊断,于病灶最明显处取活检并行病理检查。所有患者接受内镜下治疗,术后行病理活检。分别计算NBI-ME、内镜活检诊断早期胃癌的敏感度、特异度、阳性预测值、阴性预测值、准确率。**结果:**115例患者纳入本研究,最终术后切除病理示低级别上皮内瘤变(low-grade neoplasia, LGIN)16例,高级别上皮内瘤变(high-grade neoplasia, HGIN)30例,分化型胃癌59例,未分化型胃癌10例。NBI-ME诊断早期胃癌的敏感度、特异度、阳性预测值、阴性预测值、准确率分别为98.0%、81.3%、97.0%、86.7%、95.7%,内镜活检的对应值分别为82.8%、87.5%、97.6%、45.2%、83.5%。NBI-ME诊断早期胃癌的敏感度及准确率均明显高于内镜活检($P<0.05$)。**结论:**NBI-ME对早期胃癌具有较高诊断价值。**关键词:**早期胃癌;窄带成像技术;放大内镜;病理;诊断

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Value of Narrow-band Imaging Combined with Magnifying Endoscopy in Diagnosis of Early Gastric Cancer

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ABSTRACT Objective: To evaluate the diagnostic performance of narrow-band imaging combined with magnifying endoscopy (NBI-ME) for diagnosis of early gastric cancer. **Methods:** Patients (115 cases) with early gastric lesions were enrolled in the study and examined by NBI-ME. Biopsy specimen was taken from suspicious lesions for pathological examination. All patients received endoscopic resection. The diagnostic ability of different methods will be compared. **Results:** A total of 115 patients in the study, 65 men and 50 women. The final pathology showed 16 cases of low grade intraepithelial neoplasia, high grade intraepithelial neoplasia in 30 cases, 59 cases of differentiated gastric cancer, and 10 cases of undifferentiated gastric cancer. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of NBI-ME for diagnosing early gastric cancer were 98.0%, 81.3%, 97.0%, 86.7%, 95.7%, respectively. The counterparts of endoscopic biopsy for diagnosing early gastric cancer were 82.8%, 87.5%, 97.6%, 45.2%, 83.5%, respectively. The sensitivity and accuracy of NBI-ME were significantly better than that of endoscopic biopsy ($P<0.05$). **Conclusions:** NBI-ME has value in diagnosis for early gastric cancer.

Key words: Early gastric cancer; Narrow-band imaging; Magnifying endoscopy; Pathology; Diagnosis**Chinese Library Classification (CLC):** R735.2 **Document code:** A**Article ID:** 1673-6273(2017)05-943-04

前言

早期胃癌,是指胃癌仅累及黏膜及黏膜下层,而无论有无淋巴结转移^[1]。早期胃癌预后良好,五年生存率超过90%^[2];而晚期胃癌预后较差,5年生存率仅为10%-20%^[3]。因此提高早期胃癌的诊断水平,将明显减少胃癌的病死率及改善患者的生存质量。而目前我国早期胃癌的诊治率低于10%,远远低于日本的70%,韩国50%。窄带成像技术(narrow band imaging, NBI)是近年来发展起来的内镜技术^[4],联合放大内镜(magnify-

ing endoscopy, ME)可以更清晰的显示黏膜表面的微细结构。本研究旨在评估NBI-ME与胃镜活检在早期胃癌诊断中的价值,探讨如何更好提高早期胃癌的诊断水平。

1 资料与方法

1.1 临床资料

收集2013年6月到2015年9月在青岛大学附属医院消化内镜中心行胃镜检查的患者。将普通白光下可疑早期胃癌的患者纳入本研究。排除以下情况:患者已确诊胃癌,进展期胃癌,胃癌术后;出血性疾病;存在严重的心肺等系统疾病,不能耐受胃镜检查;存在精神疾病不能合作者;拒绝接受进一步治疗者。最终本研究共纳入115例患者,其中男性65例,女性50例,年龄37~79岁,平均年龄(59.9±9.2)。经内镜黏膜下剥离术(endoscopic submucosal dissection, ESD)101例,内镜黏膜下切

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除术(endoscopic mucosal resection, EMR)14例,所有患者手术顺利,未出现严重的并发症及死亡病例。具体见表1。本研究通过青岛大学附属医院伦理委员会审批,入选患者均签署知情同意书。

表1 患者一般情况

Table 1 Clinicopathological characteristics of the patients

Patients	115
Sex (male/female)	65/50
Age (years)	59.9±9.2
Lesions	115
Mean lesion size (cm)	1.7(1-4)
Location	
Upper third of the stomach	18
Middle third of the stomach	35
Lower third of the stomach	62
Macroscopic type (Paris classification)	
II a	30
II b	17
II c	39
II a+II c	21
II c+II a	8
Final pathology	
LGIN	16
HGIN	30
Differentiated gastric cancer	59
Undifferentiated gastric cancer.	10

Note: LGIN, low grade intraepithelial neoplasia; HGIN, high grade intraepithelial neoplasia.

1.2 方法

本研究采用日本 Olympus 公司 GIF-H260Z 放大胃镜,主机采用 EVIS260 系统。所有患者胃镜检查当天空腹,术前20分钟口服二甲硅油 20 mL,术前10分钟口服盐酸利多卡因胶浆 10 mL,山莨菪碱 10 mg 肌注解痉。患者首先在普通白光下发现可疑病灶(颜色或形态改变)后,行 NBI-ME 观察并做出内镜下诊断,最后于病灶最明显处行标准活检 2 块。对于 NBI-ME 或内镜活检考虑早期胃癌的患者,行全腹 CT、超声内镜检查,明确肿瘤浸润及转移情况,综合评估病情,并向患者告知后决定内镜切除^[5],术后均行病理检查。

1.3 内镜分型

依据巴黎分型^[6],将早期胃癌分为三型,即隆起型(I型)、浅表型(II型)及凹陷型(III型)。其中浅表型(II型)又可分为浅表隆起型(II a)、浅表平坦型(II b)及浅表凹陷型(II c)。实际临床中又分为混合型(如 II a+II c、II c+III 等)。而在实际临床过程中,通过普通胃镜系统详细的观察,隆起型及凹陷型早期胃癌不难发现,但浅表型早期胃癌往往由于其类似胃炎改变,仍然难以发现^[7]。本研究我们主要选取浅表型(II型)及其混合型病灶。

1.4 本研究 NBI-ME 诊断早期胃癌标准

采用 Yao^[8]提出的"VS 分类系统",即(1)不规则的表面微结构(irregular microsurface pattern, IMSP)和明显的分界线(demarcation line, DL);(2)不规则的微血管(irregular microvascular pattern, IMVP)和明显的分界线(DL)。符合任意一条即可诊断为早期胃癌,反之为非癌性病变(图1)。

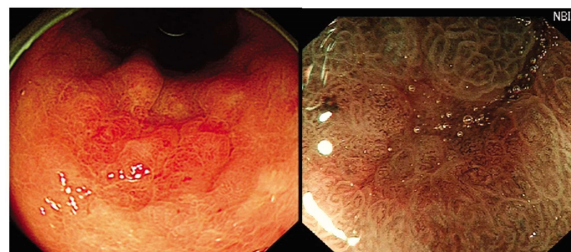


图1 内镜下胃体下部小弯近胃角处见一 II c 病变

Fig.1 Endoscopic findings of superficial depressed (0 IIc) type lesion in the gastric body

注:A:普通胃镜下于胃体发现一平坦略凹陷病变(II c),粘膜略发红,反光增强,不同于周围正常黏膜;B:NBI-ME 显示边界线存在,区域微血管不规则,微结构消失,诊断为胃癌

Note: A: Conventional white light imaging shows a slightly depressed lesion. The light reflection and color suggest different in surface morphology with background mucosa; B: ME-NBI: A clear demarcation line was noted between the lesion and the background mucosa. Within the demarcation line, an irregular microvascular pattern and an absent microsurface pattern are demonstrated. The lesion can be diagnosed as cancer by VS classification.

1.5 病理诊断

内镜发现的可疑病灶,在 NBI-ME 指导下行标准活检 2 块行病理检查;将内镜切除的整块组织送往病理科行病理检查。病理检查由我院同一位高资历病理医师完成。病理诊断参照修正的维也纳分类方法^[9],将高级别上皮内瘤变(C4)及以上者定义为胃癌,低级别上皮内瘤变(C3)及以下者定义为非癌性病变。

1.6 统计学处理

采用 SPSS 20.0 软件包进行数据的管理及统计分析,分别计算 NBI-ME、内镜活检诊断早期胃癌的准确率、敏感度、特异度、阳性预测值、阴性预测值,率的比较采用卡方检验,当 $P < 0.05$ 时,差异有统计学意义。

2 结果

NBI-ME 诊断早期胃癌 100 例,术后证实早期胃癌 97 例, LGIN3 例;非癌性病变 15 例,术后病理证实 LGIN13 例, HGIN2 例。内镜下活检诊断早期胃癌 84 例,术后病理证实 82 例为早期胃癌,2 例 LGIN;LGIN27 例,术后病理示 LGIN14 例, HGIN8 例,分化型胃癌 5 例;胃炎 4 例,术后证实为 HGIN3 例,分化型胃癌 1 例。以术后病理为诊断早期胃癌的金标准,分别计算 NBI-ME、内镜活检诊断早期胃癌的敏感度、特异度、阳性预测值、阴性预测值及准确率(见表2)。NBI-ME 与内镜活检相比,敏感度及准确率较好($P < 0.05$),两者特异度无统计学意义($P > 0.05$)。

表 2 不同方法对早期胃癌的诊断能力

Table 2 Diagnostic ability of NBI-ME and Endoscopic biopsy for early gastric cancer

Method	Sensitivity	Specificity	PPV	NPV	Accuracy
NBI-ME	98.0% ^a	81.3% ^b	97.0%	86.7%	95.7% ^a
Endoscopic biopsy	82.8%	87.5%	97.6%	45.2%	83.5%

Note: PPV, positive predictive value; NPV, negative predictive value.

^a $P < 0.05$, VS Endoscopic biopsy; ^b $P > 0.05$, VS Endoscopic biopsy.

3 讨论

降低胃癌的发病率及死亡率是我国面临的重大卫生问题^[10]。早期胃癌预后良好,因此提高早期胃癌的早诊早治是减少胃癌病死率的关键。而目前普通胃镜联合活检仍是我国诊断早期胃癌的主要方法,诊断水平明显落后于日本等发达国家。NBI 是近年来发展起来的新的内镜技术,通过滤光器滤掉普通内镜氙灯光源所发出红、蓝、绿中的宽带光谱,选择 415 nm、540 nm 的窄带光,显示黏膜表面微细结构和黏膜下血管较传统的白光模式内镜清楚,立体感更强^[4,11]。而以往研究多以胃镜活检病理作为最终病理结果,而已有研究表明普通胃镜活检与术后病理活检存在一定差异^[12-15],故本文以术后病理结果为金标准进一步评估 NBI-ME 在早期胃癌诊断中的价值。

本研究 NBI-ME 发现早期胃癌 100 例,术后证实早期胃癌 97 例, LGIN 3 例, 2 例早期胃癌漏诊。NBI-ME 的敏感度、阳性预测值、准确率较好,但特异度、阴性预测值不是很理想。据文献报道^[16] NBI-ME 诊断早期胃癌的敏感度、特异度、阳性预测值、阴性预测值、准确率分别为 73.7%、99.2%、93.3%、96.3%、96.0%,本研究准确率及特异度低于文献报道水平。可能因为早期胃癌的诊断水平往往与检查者的操作水平及对早期胃癌的认识水平有关。Mabe 等^[17] 研究表明对内镜医生进行 NBI-ME 培训可以提高早期胃癌诊断的准确率;另外,本研究选择病例均为浅表型早期胃癌,诊断本身也存在难度。本研究中 NBI-ME 将 3 例 LGIN 误诊为早期胃癌,这是导致我们特异度、阴性预测值、准确率下降的原因。有报道^[18] 43% 的 LGIN 存在 IMVP, 34% 的存在 IMSP, 23% 存在明确的 DL。因此, NBI-ME 下 LGIN 与早期胃癌的鉴别仍然比较困难。尽管 LGIN 是临床常见的胃癌前病变,但是其发展缓慢,因此新修正的维也纳分类标准^[9] 对于 LGIN 的处理建议是随访或内镜切除。对 LGIN 内科治疗后密切随访而非一概内镜切除,更符合我国的国情。

同时我们以术后切除病理为金标准比较了 NBI-ME 与内镜活检对早期胃癌的诊断能力。结果胃镜活检诊断早期胃癌 84 例, 术后病理证实 82 例为早期胃癌, 2 例 LGIN, 17 例早期胃癌漏诊。而术前活检漏诊的早期胃癌, NBI-ME 下全部符合早期胃癌诊断, NBI-ME 诊断早期胃癌的敏感度及准确率明显高于内镜活检($P < 0.05$)。但本研究中 NBI-ME 将 3 例 LGIN 诊断为早期胃癌,以至于特异度低于内镜活检,但两者的特异度没有统计学意义($P > 0.05$)。我们回顾了 NBI-ME 图片,正确诊断为早期胃癌的患者均具有明显的 IMVP 及 DL 或 IMSP 及 DL,而误诊的 3 例 LGIN 病变, NBI-ME 内镜下的这三种特异结构均难以把握,介于癌与非癌之间,呈 "不典型" 表现,而此时操

作者对早癌的认识及内镜经验往往决定了诊断的方向。而漏诊的 2 例患者,均因黏膜表面覆盖 "白色不透明物质" 影响了微血管及微结构的判断,后再次评估图片时均修正为早期胃癌。而胃镜活检诊断为 HGIN 的 2 例患者,术后病理却诊断为 LGIN,我们考虑可能为病变小而局限、内镜治疗过程中组织受破坏等原因。

目前普通胃镜联合活检是我国诊断早期胃癌的主要方法,但内镜活检由于取材浅而局限,具有随机性、盲目性、局限性,能多大程度上反应病灶整体情况存在争议。有报告内镜活检病理结果为 LGIN 的病变中, 10%~18% 的病变经内镜下切除后,病理提示为 HGIN 或早期胃癌^[19]。本研究中胃镜活检诊断慢性胃炎 4 例,术后诊断为 3 例 HGIN, 1 例分化型胃癌;而活检病理为 LGIN 的 13 例患者,术后病理为 8 例 HGIN, 5 例分化型胃癌。因此尚不能完全依据内镜活检病理结果决定病变的性质。本文研究表明 NBI-ME 对早期胃癌的诊断有较高的临床价值,但现行诊断标准仍比较主观,与 LGIN 的鉴别仍存在难度,且不能判断胃癌的浸润深度及分化程度^[20],因此尚不能取代组织活检。鉴于内镜活检与切除病理的差异, NBI-ME 具有较高的敏感度及准确率,对于 NBI-ME 下符合典型早期胃癌表现者无论胃镜活检如何,我们建议行内镜或手术进一步治疗;对于 NBI-ME 细微结构表现不典型的患者应结合胃镜活检综合决定患者的诊疗方案。然而本研究为单中心研究,纳入样本量相对较少,尚需要多中心大样本随机试验验证。

总之, NBI-ME 对早期胃癌有较高的诊断价值,对于 NBI-ME 典型早期胃癌患者无论内镜活检结果如何,建议行进一步治疗;对于 NBI-ME 下表现不典型的患者建议联合胃镜活检综合判断。

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