RESEARCH ARTICLE

The applications of miniprobe endoscopic ultrasonography in the diagnosis and treatment of colorectal submucosal lesions

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Abstract

Objective: To evaluate the efficacy of miniprobe endoscopic ultrasonography for the diagnosis and adjuvant treatment of patients with colorectal submucosal lesions.

Method: The retrospective study was conducted at the Beijing Chao-Yang Hospital, Capital Medical University, China, and comprised data from January 1, 2016, to July 31, 2021, related to patients of either gender with colorectal submucosal lesions who underwent miniprobe endoscopic ultrasonography. The findings were compared with biopsy specimens and clinical diagnoses. Diagnostic features of miniprobe endoscopic ultrasonography were assessed along with its accuracy. Data was analysed using R 4.1.2.

Results: Of the 237 patients, 121(51.1%) were female and 116(48.9%) were male. The overall mean age was 55.6±12.9 years. Miniprobe endoscopic ultrasonography successfully imaged all 237(100%) colorectal submucosal lesions, and 188(79.3%) had consistent results compared to histopathological findings. The majority of lesions were <10mm 102(43.4%) or 10-19mm 84(35.7%) in size. Those detected with high echogenicity were 126(53.2%) and those with low/low-medium echogenicity were 83(35.0%). Tumour size 10-19mm and uneven echo quality significantly increased the accuracy of miniprobe endoscopic ultrasonography ($p<0.05$).

Conclusion: Miniprobe endoscopic ultrasonography was able to provide precise information about the size, layer of origin, echogenicity and border of colorectal submucosal lesions, and had a high accuracy in the differential diagnosis of such lesions.

Keywords: Ultrasonic endoscopy, Colorectal neoplasms, Diagnosis. (JPMA 73: 26; 2023)

DOI: https://doi.org/10.47391/JPMA.7017

Introduction

Colorectal submucosal lesions are protruding abnormalities that arise from the muscularis mucosa, submucosa, or muscularis propria, and are often unexpectedly detected during routine endoscopy. These lesions have a normal mucosal surface regardless of whether they originate intramurally or extramurally.[1] The prevalence of these lesions on routine endoscopy is unknown, but their occurrence rate is rather frequent at 1% during these procedures.[2,3] This rate tends to increase with the growth of colonoscopy for colorectal cancer screening. The most common types of colorectal submucosal lesions include neuroendocrine tumours (NETs), gastrointestinal stromal tumours (GISTs), lipomas, vascular lesions, and cystic lesions. Their treatment and prognosis vary, and while most are considered benign, some tumours, such as GISTs, have a strong propensity for malignant transformation.[4]

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Submission complete: 31-0-2022 **Review began:** 27-09-2022
Acceptance: 14-10-2023 **Review end:** 22-07-2023

However, colonoscopy has limited use in characterising colorectal submucosal lesions since it only allows for a visual evaluation of the surface of the colon lumen. The complex nature of these lesions is often not revealed. Endoscopic ultrasonography (EUS) has emerged as a reliable investigative procedure for performing an accurate differential diagnosis of gastric submucosal lesions and an ideal method for the evaluation of submucosal lesions due to its high resolution.[3,5,6] However, mainstream studies have focussed on assessing the detection effects of EUS on submucosal lesions of the upper digestive tract.[2,7,8] The radial and sectorial EUS is not widely used for the submucosal lesions of the lower digestive tract, such as colorectal submucosal lesions, due to the limitations of conventional EUS, including inflexible large tip diameters and instrument rigidity.

EUS of forward-viewing endoscopy has a tip that is too hard to pass the narrow or curved part of the colon and could cause complications, such as bleeding or perforation. Miniprobe endoscopic ultrasonography (mEUS) can overcome those shortcomings during the differential diagnosis of colorectal submucosal lesions since the mEUS probe can be passed through the working biopsy channel of a colonoscopy, and provide more flexibility in working in the colorectal environment. Additionally, mEUS can

provide precise indications by imaging the extrinsic compression, the size of intramural tumours, internal properties, originating wall layer, and the associated echostructure of the colorectal tracts.[9]

However, the clinical role of mEUS in differentiating various colorectal submucosal lesions and its adjuvant role in clinical treatment decisions are barely explored. There is scant data on certain aspects of the mEUS differentiating diagnosis and the management of colorectal submucosal lesions. Previous studies of mEUS only explored the applications of mEUS on a single tumour/submucosal lesion, and there is no systematic evidence on the comparison of the effects of mEUS across different submucosal lesions[2,6-16] The current study was planned to evaluate the efficacy of mEUS for the diagnosis and adjuvant treatment of patients with colorectal submucosal lesions.

Materials and Methods

The retrospective study was conducted at the Beijing Chao-Yang Hospital, Capital Medical University, China, and comprised data from January 1, 2016, to July 31, 2021, related to patients of either gender with colorectal submucosal lesions who underwent miniprobe endoscopic ultrasonography. The sample was raised using consecutive sampling technique. All patients had provided informed consent prior to undergoing the procedure. Data related to patients having had a colonoscopy to reach the terminal ileum, having an mEUS examination of submucosal bulge, and/or a pathological diagnosis of the submucosal bulge. Those who did not meet the criteria were excluded. The sample size was calculated using power analysis and was good enough for running multivariate regression analysis with nine dependent variables. This ensured that subsequent analyses were statistically reliable and valid.

An endoscopic ultrasonography system (Olympus CF-260/290, Tokyo, Japan) was used and a miniprobe (Olympus UM-3R 20 MHz, Tokyo, Japan) was introduced through the working channel after water infusion to immerse the lesion. The choice of the miniprobe might affect the localisation of submucosal lesions to be explored. In general, models with higher ultrasonic frequency have less penetration and higher resolution. An ultrasonic frequency of 20MHz was found suitable for high-resolution imaging of superficial lesions.

Demographic characteristics, imaging maximal diameter, margin characteristics, original layer, echotexture and histopathological identifications of the colorectal submucosal lesions were noted for each patient. The histopathology of the resected specimens and final clinical diagnosis were the standards that were used to confirm mEUS findings. The accuracy of mEUS was defined as the consistency with histopathological results or final clinical diagnosis. The data was divided into two groups. All cases in which mEUS diagnosis and pathological/clinical diagnosis were the same were in group A, and cases in which the diagnoses differed were in group B.

Data was analysed using R version 4.1.2. Continuous variables were expressed as mean and standard deviation (SD), whereas categorical variables were expressed as frequencies and percentages. The mEUS accuracy levels among different types of colorectal submucosal lesions were assessed using chi-square test. For the preliminary evaluation, univariate logistic regression analysis was performed to confirm how the clinical characteristics of those colorectal submucosal lesions influenced the accuracy of mEUS. Multivariate logistic regression analysis was performed to test the outcomes of the univariate logistic regression analysis. Findings were expressed in terms of odds ratios (ORs) and 95% confidence intervals (CIs). $P<0.05$ was taken as statistically significant.

Results

Of the 237 patients, 121(51.1%) were female and 116(48.9%) were male. The overall mean age was 55.6±12.9 years. The mEUS examination sessions were performed in various anatomic locations, with the rectum being the most common site (100, 42.2%), followed by the terminal ileum (64, 27.0%), transverse and descending colon (50, 21.1%), and left colon (21,8.9%). The mEUS successfully imaged all 237(100%) colorectal submucosal lesions, and 188(79.3%) had consistent results compared to histopathological

Figure-1 A: A 10*10mm colorectal submucosal lesion found in colon by colonoscopy.

Figure-1B: A 7.7*5.8mm colorectal submucosal lesion detected in the colon. Miniprobe endoscopic ultrasonography (mEUS) (20 MHZ) was performed. A homogenous hyperechoic mass with a distinct border arising from the submucosal layer was noted, and high-level echogenicity and lipoma was suspected.

Table-1: Descriptive data.

Number of patients	Level	Overall 237	Consistent 188	Differentiated 49	*p*-value
Location (%)	Left colon	21 (8.9)	18 (9.6)	3 (6.1)	0.001
	Rectum	100 (42.2)	67 (35.6)	33 (67.3)	
	Transverse colon	50 (21.1)	47 (25.0)	3 (6.1)	
	Terminal ileum	64 (27.0)	55 (29.3)	9 (18.4)	
	Multiple	2 (0.8)	1 (0.5)	1 (2.0)	
Size of tumour (%)	<10mm	102 (43.4)	74 (39.4)	28 (59.6)	0.012
	10-19mm	84 (35.7)	76 (40.4)	8 (17.0)	
	≥20mm	36 (15.3)	30 (16.0)	6 (12.8)	
	Other	13 (5.5)	8 (4.3)	5 (10.7)	
Originating layers (%)	Muscularis mucosa	40 (16.9)	29 (15.4)	11 (22.4)	0.042
	Submucosa	163 (68.8)	137 (72.9)	26 (53.1)	
	Muscularis propria	23 (9.7)	17 (9.0)	6 (12.2)	
	External/Full	2 (0.8)	1 (0.5)	1 (2.0)	
	Mucosal layer	7 (3.0)	3 (1.6)	4 (8.2)	
	Other	2 (0.8)	1 (0.5)	1 (2.0)	
Echogenicity (%)	Low / Low-medium	83 (35.0)	58 (30.9)	25 (51.0)	<0.001
	Medium-high	9 (3.8)	3 (1.6)	6 (12.2)	
	High	126 (53.2)	112 (59.6)	14 (28.6)	
	Pressure change	19 (8.0)	15 (8.0)	4 (8.2)	
Echo quality (%)	Even	137 (57.8)	119 (63.3)	18 (36.7)	0.001
	Uneven	86 (36.3)	57 (30.3)	29 (59.2)	
	Uneven with chamber structure	14 (5.9)	12 (6.4)	2 (4.1)	
Type of tumour (%)	Lipoma	122 (51.5)	112 (59.6)	10 (20.4)	0.023
	NETs	57 (21.5)	39 (20.7)	18(36.7)	
	Cystic lesions	19 (8.0)	12 (6.4)	7(14.3)	
	GISTs	10 (4.2)	8 (4.3)	2 (4.1)	
	Vascular lesions and others	29 (12.2)	17(3.7)	12(24.5)	

NET: Neuroendocrine tumour, GIST: Gastrointestinal stromal tumours.

Figure-2A: An 8*8mm colorectal submucosal lesion in the colon. The broad base is inactive, the surface is smooth and complete, and the texture is relatively hard.

findings. The majority of lesions were <10mm 102(43.4%) or 10-19mm 84(35.7%) in size. Those detected with high echogenicity were 126(53.2%) and those with low/low-medium echogenicity were 83(35.0%). Most of the colorectal submucosal lesions were managed based on mEUS interpretation (137, 57.8%).

Tumours with a large number of cases were classified according to lesion/tumour type, and the diagnostic accuracy was calculated for each tumour (Table 1). Lipomas were the most common colorectal submucosal lesions identified by mEUS (122,51.5%), had the highest accuracy rate of 59.6% among all the successfully identified cases (Figure 1A-B) 112(91.8%) of the lipomas were accurately diagnosed by mEUS. NETs (Figure 2A-B) were the second most frequently identified tumours by mEUS (57,21.5%), with an accuracy rate of 20.7% (Figure 2A-B). Cystic lesions were found in 19 (8.0%) patients, with a low/moderate accuracy rate of 6.4% (Figure 3A-B).

Univariate analysis showed higher mEUS accuracy in the rectum with higher/medium-high echogenicity, a size of 10-19mm, and an uneven echo with complicated structure, and all the diagnostic features independently correlated with mEUS detection accuracy (Table 2).

In the multivariate analysis, when all other conditions were well-controlled, tumour size 10-19 mm and uneven echo quality significantly increased the accuracy of mEUS ($p<0.05$). Specifically, the likelihood of unsuccessfully detecting a tumour size of 10-19 mm was 71.8% lower than the likelihood of unsuccessfully detecting a tumour size <10mm (OR: 0.292, 95% CI: 0.093,0.811). The likelihood of unsuccessfully detecting a lesion with uneven echo was 98.0% lower than the likelihood of unsuccessfully detecting a lesion with even echo (OR: 0.018, 95% CI: 0.0,0.321)(Table 3).

Figure-2B: A 6.7mm x 3.5mm colorectal submucosal lesion detected in the colon. Miniprobe endoscopic ultrasonography (mEUS) (20 MHZ) was performed. Lesions were located in the second layer with clear border and uneven low-level echogenicity was observed. Neuroendocrine tumours (NETs) were suspected.

Discussion

The current study is among the first to provide an evaluation of the applications of mEUS on detecting different types of colorectal submucosal lesions. The study confirmed the effectiveness of mEUS in detecting a specific type of colorectal submucosal lesions with a size of 10-19mm and having high echogenicity. However, mEUS

Figure-3A: A 2cm colorectal submucosal lesion in the transverse colon by colonoscopy. It had a smooth and transparent surface, soft texture, and was easily deformed under pressure.

Figure-3B: A 13 x 13.2mm colorectal submucosal lesion was detected. Miniprobe endoscopic ultrasonography (mEUS) (20 MHZ) was performed. The lesionwas located in the submucosa layer with clear border, No echo was observed. Cystic lesions were suspected.

had limited capability in identifying smaller lesions with low to moderate echogenicity and other complications. This finding is consistent with previous studies.[10-14] Large lesions (>20mm) may not be effectively identified during mEUS assessments due to poor imaging quality caused by ultrasound signal attenuation, angulation of a portion of the colon, or insufficient mEUS operating experience.

The diagnostic features identified in the current study can help determine the correct diagnosis and narrow the range of possible diagnoses for specific types of colorectal submucosal lesions. For intramural tumours, the nearest distance to the lesion should be measured accurately, followed by the observation of echogenicity and echotexture of the inner structure and tissues for a presumptive diagnosis. For instance, the ultrasound imaging characteristics of lipomas include the feel of a discrete, freely mobile, fluctuant, ovoid, or elliptical mass sized <20mm and showing a high level of echogenicity [15]. Based on the revealed mEUS diagnostic features, certain types of lesions, such as lipomas, can be diagnosed without further testing, including biopsy. The current study suggests that mEUS may be useful for preoperative diagnosis of certain types of benign subcutaneous lesions that can be removed endoscopically or observed without resection.

The study also supports the moderate/limited value of mEUS in differentiating submucosal lesions, with

Table-2: Univariate analysis results of diagnostic features of miniprobe endoscopic ultrasonography (mEUS).

Characteristic	mEUS accuracy		
	OR	95% CI	*p*-value
Location			<0.001
Left colon	—	—	
Rectum	2.96	0.92, 13.2	
Transverse colon	0.38	0.07, 2.23	
Terminal ileum	0.98	0.26, 4.78	
Size (mm)			0.011
<10	—	—	
10-19	2.64	0.31, 22.9	
≥20	0.53	0.18, 1.33	
Multiple sizes	1.32	0.26, 5.38	
Other	0.28	0.11, 0.62	
Originating			0.077
Muscularis mucosa	—	—	
Submucosa	0.5	0.23, 1.16	
Muscularis propria	0.93	0.28, 2.92	
External/Full	2.64	0.10, 70.7	
Mucosal layer	3.52	0.67, 20.4	
Other	2.64	0.10, 70.7	
Echogenicity			<0.001
Low/Low-medium	—	—	
Medium-high	4.64	1.13, 23.4	
High	0.29	0.14, 0.59	
Pressure change	0.62	0.16, 1.91	
Echo quality			0.001
Even	—	—	
Uneven with complicated structure	3.36	1.74, 6.66	
Uneven	1.1	0.16, 4.49	
Types of Tumours			<0.001
Lipoma	1.42	0.635,3.193	
Cystic lesions	0.16	0.023,0.595	
Vascular lesions and others	0.22	0.091,0.488	

OR: Odds ratio, CI: Confidence interval.

approximately 13% objectives of using EUS for non-invasive diagnosis of malignant tumours yet to be achieved.[16,17] The reported agreement between overall presumptive diagnoses based on EUS findings and biopsy results of submucosal lesions in the gastrointestinal tract for malignancy only reached an accuracy rate of 43% to 79%.[17,18] However, mEUS is still helpful in determining that further examination is required after careful endoscopic observation when colorectal submucosal lesions are found during colonoscopy. In addition, endoscopic ultrasonography-guided fine needle aspiration (FNA) and other imaging modalities can further help diagnose submucosal masses.

Regarding follow-up clinical treatment strategies, mEUS can be useful in determining the follow-up treatment for difficult-to-differentiate types of colorectal submucosal lesions. For example, the diagnosis of GISTs must be confirmed by pathology and immunohistochemistry (IHC)

Table-3: Multivariate analysis results of diagnostic features of miniprobe endoscopic ultrasonography (mEUS).

Characteristic	mEUS accuracy		
	OR	95% CI	*p*-value
Gender			
Male	2.332	0.989,5.813	0.059
Age (years)	0.998	0.965,1.033	0.919
Location			
Rectum	1.824	0.408,10.462	0.456
Transverse colon	0.512	0.078,3.571	0.477
Terminal ileum	1.105	0.217,6.992	0.908
Multi-locations	24.228	0.429,1548.557	0.107
Size of Tumour (mm)			
10-19	0.292	0.093,0.811	0.024
≥20	0.679	0.179,2.306	0.547
Multiple sizes	0.329	0.031,2.312	0.297
Others	3.704	0.181,95.788	0.393
Originating layers			
Submucosa	0.864	0.31,2.437	0.779
Muscularis propria	0.703	0.129,3.45	0.67
Mucosal layer	6.231	0.558,83.409	0.137
Other	0.576	0.006,39.282	0.794
Echogenicity			
Medium-high	5.977	1,40.888	0.053
High	14.505	1.088,483.052	0.067
Pressure change	6.28	0.409,194.33	0.217
Echo quality			
Uneven	0.604	0.145,2.479	0.481
Uneven with complicated structure	0.018	0,0.321	0.014
Type of tumour			
Lipoma	0.029	0.001,0.423	0.133
Cystic lesions			0.177
Vascular lesions and others			0.199

OR: Odds ratio, CI: Confidence interval.

examinations.[19] Along with other clinical examinations followed by clinical protocols, mEUS can provide information on the originating layers and sizes of the colorectal submucosal lesions.[20,21] For instance, leiomyosarcoma should be strongly suspected, and surgery should be considered when the tumour is observed >30mm in diameter and has an inhomogeneous internal echo during mEUS. The choice of treatment strategy, such as endoscopic submucosal dissection (ESD), endoscopic mucosal resection (EMR), or surgery, could rely on the previously collected information from mEUS.

Based on the findings, a management algorithm is recommended that may incorporate endoscopic and mEUS findings to guide clinical decision-making.

The current study has several limitations, including its retrospective design and the fact that it was conducted at a single centre using a single type of mEUS equipment. The accuracy of the ultrasound examination could vary depending on the operator's technological and clinical experience, available mEUS equipment, and patient compliance. In the future, it would be beneficial to explore the effects of mEUS across all types of colorectal submucosal lesions using different devices equipped with different ultrasonic frequencies and miniprobe choices. This would provide to be a more comprehensive understanding of the utility of mEUS in clinical practice. Further prospective studies involving multiple centres and larger sample sizes are needed to confirm the current findings and validate the proposed management algorithm.

Conclusions

The mEUS was able to provide precise information about the size, layer of origin, echogenicity and border of colorectal submucosal lesions, and had a high accuracy in the differential diagnosis of such lesions. The mEUS has the potential to be a valuable tool in the diagnosis and management of colorectal submucosal lesions.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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Author Contribution:

WZ, GL and XL: Conceived the study and designed the protocol.
WH, XL, RG, YG and JH: Data collection.
WZ, GL and XL: Statistical analysis, data interpretation.
WZ: Drafting, revision