

STUDY THE VALUE OF ENDOSCOPIC ULTRASOUND IN THE DIAGNOSIS OF RECTAL CANCER STAGE

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SUMMARY

Objectives: To study the value of endoscopic ultrasound in the diagnosis of rectal cancer stage. *Subjects and methods:* Prospective, cross-sectional description study. 56 patients were diagnosed with rectal cancer by histopathology after surgery. *Results:*

- *Image of endoscopic ultrasound:* Most tumors invaded the muscle layer and serosa (together accounted for 37.5%). There were 5.4% of tumors invading the surrounding organs. 50% of tumors were in stage T3 and T4; 35.7% at T2; 33.9% had lymph node metastasis.

- *In the diagnosis of tumor invasion level:* Endoscopic ultrasound had a suitable degree of diagnosis with quite good histology with Kappa coefficient = 0.57; $p = 0.001$. Sensitivity, specificity and accuracy of endoscopic ultrasound were 80%; 92.2% and 91.07%, respectively.

- *In the diagnosis of lymph node metastasis:* Endoscopic ultrasound had a suitable degree of diagnosis of the disease level with histopathology with Kappa coefficient = 0.41; $p = 0.002$. Sensitivity, specificity and accuracy of endoscopic ultrasound were 66.7%; 78% and 75%, respectively.

Conclusion: Endoscopic ultrasound is a good method to diagnose, monitor and evaluate the stage of rectal tumors quickly, safely and accurately.

* *Keywords:* Rectal cancer; Histopathology; Endoscopic ultrasound.

INTRODUCTION

Evaluation of the stage of rectal cancer with endoscopic ultrasound (EUS) was first reported by Hildebrandt U and Feifel G in 1985 [8] and is now accepted as a method of initial selection to diagnose, monitor, evaluate the stage of rectal tumors quickly, safely and accurately [9]. According to studies by foreign authors, the accuracy of EUS in diagnosing invasive levels (T - according to TNM classification) of rectal cancer is 80 - 95% compared with CT (65 - 75%), and MRI (75 - 85%); in determining lymph node

metastasis of rectal cancer is about 70 - 75% compared with CT (55 - 65%) and MRI (60 - 70%) [6, 7]. Implementing a small needle biopsy (FNA) under the guidance of EUS increases the effectiveness of diagnosis of early stage T cases and suspects lymph nodes around the pot. Studies in Vietnam on EUS to diagnose the stage of rectal cancer are few and not systematic. Therefore, we conducted this study with aims: *Understanding the value of endoscopic ultrasound in the diagnosis of rectal cancer stage.*

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SUBJECTS AND METHODS

1. Subjects.

Including 54 rectal cancer patients diagnosed by histopathology after surgery, treatment at the E Hospital from January, 2013 to January, 2018.

** Standard selection:*

- Patient with rectal tumor was biopsy to diagnose rectal cancer.
- Performed rectal EUS before surgery.
- Surgical treatment at the E Hospital.
- Results of postoperative histopathology were rectal cancer.

** Exclusion criteria:*

- Patients did not meet the selection criteria.
- Patients with bleeding/coagulation disorder.
- Patients with acute and chronic diseases contraindicated to perform rectal endoscopy.

- Patients with rectal cancer no longer have surgery.
- The patient had no surgical treatment.
- Patient was previously treated (surgery, radiation, chemicals).
- Patients who did not perform rectal endoscopic ultrasound.
- Patients who did not agree to participate in the study.

2. Methods.

Cross-sectional descriptive study.

** Research targets:*

Characteristics of images of rectal EUS, assessment of tumor invasion, lymph node metastasis with postoperative histopathological results.

Data were processed by SPSS software 20.0.

RESEARCH RESULTS

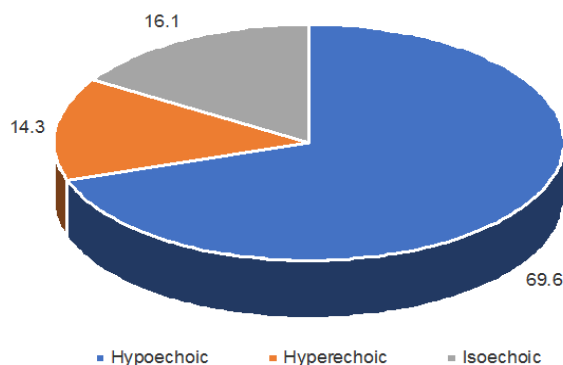


Figure 1: Echo characteristics of tumors on EUS.

Mostly tumors had echo poor properties (39 patients accounted for 69.6%).

** Tumor invasion characteristics on EUS:*

Submucosa layer: 8 patients (14.3%); muscle layer: 20 patients (35.7%); serosa and under the serosa: 20 patients (35.7%); fat layer: 5 patients (8.9%); surrounding organs: 3 patients (5.4%).

Most tumors invaded the muscle layer and serosa (together accounted for 35.7%).

Table 1: Characteristics of lymph node metastasis on EUS.

Characteristics of lymph node metastasis		No. of patients	Ratio %
Lymph node metastasis	No	37	66.1
	Yes	19	33.9
	Total	56	100.0
No. of lymph node	1 node	5	26.4
	2 nodes	7	36.8
	3 nodes	7	36.8
	Total	19	100.0
Size of node	1.02 ± 0.33 cm (0.6 - 2.1)		

EUS detected 19 cases (accounting for 33.9%) of lymph nodes around the rectal, in which 19/19 cases of lymph node ≤ 3.

Table 2: Classification of TNM stage by EUS.

Classification of TNM stage		No. of patients (n = 56)	Ratio %
T	T1	8	14.3
	T2	20	35.7
	T3	20	35.7
	T4	8	14.3
	Total	56	100.0
N	N0	37	66.1
	N1	19	33.9
	Total	56	100.0

50% of tumors had invaded the serosa and surpassed the serosa (T3 and T4); lymph node metastasis also accounted for 33.9%.

Table 3: Results of diagnosis of invasive levels with EUS with histopathology.

Histopathology	Localized		Invade surrounded organs		Total		p	Coefficient Kappa
	n	%	n	%	n	%		
SANS							0.001	0.57
Localized	47	92.2	1	20.0	48	85.7		
Invade surrounded organs	4	7.8	4	80.0	8	14.3		
Total	51	100.0	5	100.0	56	100.0		

EUS had level of good suitable diagnostic with histopathology with Kappa coefficient = 0.57; p = 0.001. Sensitivity, specificity and accuracy of EUS in the diagnosis of tumor invasion levels were 80%, 92.2% and 91.07%, respectively.

Table 4: Results of lymph node metastasis diagnosis on EUS with histopathology.

Histopathology	Lymph node no cancer		Lymph node cancer		Total		p	Coefficient Kappa
	n	%	n	%	n	%		
SANS								
Non-detected lymph node	32	78.0	5	33.3	37	66.1	0.002	0.41
Detected lymph node	9	22.0	10	66.7	19	33.9		
Total	41	100.0	15	100.0	56	100.0		

(: Test of Fisher's 2-side)*

EUS had level of suitable diagnostic accuracy with histopathology with Kappa coefficient = 0.41; p = 0.002. Sensitivity, specificity and accuracy of EUS in the diagnosis of lymph node metastasis were 66.7%; 78% and 75.0%, respectively.

DISCUSSION

1. Echo-density of tumors.

In our study, mostly tumors had hypoechoic property (69.6%). On EUS, tumors often appear as a hypoechoic block. It is difficult to determine the degree of tumor invasion when it develops to the junction between the two layers of the colon wall, for example: when the tumor is adjacent between the subserosa and the muscle layer (between T1 and T2) or between muscle and fat surround the rectum. A deep lesion at T1 stage may show abnormalities and the thickening of the submucosal layers on ultrasound causes difficulty when distinguishing from the surface of the tumor at stage T2. Explaining this, the authors suggested that the high resolution of the ultrasound probe can be detected but it is not possible to correctly distinguish the image of the hypoechoic inflammation around the tumor or whether it is a tumor. In addition, this also occurs when the tumor image is on a straight line twice or sharp

corners create a tangent image. This difference is most common for stage T2, but on EUS the tumor may appear as at stage.

2. The extent of the tumor invasion.

Evaluation of tumor invasion by EUS is based on the extent of invasion of the tumor compared to the rectal wall.

When conducting EUS for 56 cases of rectal tumors, we found that only 8 patients accounted for 14.3% of the tumor invaded the submucosal layer; and most tumors invaded the muscle and serosa (37.5% together). 8.9% of tumors invaded fatty tissue and 5.4% of tumors invaded the surrounding organs. Thus no cases of tumors were localized in the mucosa and muscularis, which means that no patients had indicated mucosal surface resection treatment by endoscopic but all had indications for thorough cutting surgery treatment.

Based on the determination of the extent of invasion of the tumor through the layers of rectum wall along with the

use of a high frequency probe 5 - 12 MHz, it is possible to evaluate the stage of cancer on ultrasound according to phase TNM:

+ Stage T0: There was no image of injury on ultrasound.

+ Stage T1: Limited lesions of the mucosa and submucosa, equivalent to the period of Tis and T1, on ultrasound images, small tumors were often separated from the muscle layer.

+ Stage T2: Tumor invaded the rectal muscle layer equivalent to T2.

+ Stage T3: Tumor invaded through muscle layer, equivalent to T3.

+ Stage T4: Tumor invaded the surrounding organization equivalent to T4.

Combining the above factors, when dividing the invasion level of tumor by TNM stage, we found that most tumors had invaded to the serosa and overcome serosa (T3 and T4), accounting for 50%; 35.7% of tumors were in stage T2 and 14.3% of tumors were in stage T1.

3. The degree of lymph node metastasis.

Lymph nodes appear as rounded or oval-shaped structures hypoechoic compared to fat around the rectum. Although metastatic lymph nodes tend to be larger than normal lymph nodes with a diameter of 3 - 5 mm, up to 50% of metastatic lymph nodes identified in histopathology may be less than 5 mm; up to 8% may be less than 2 mm [4]. In our study on endoscopic ultrasonography, 19 cases accounted for 33.9% with lymph nodes surround the rectum, in which 19/19 cases of lymph node number ≤ 3 .

Results of assessment of invasive levels of tumors in 56 cases, we found EUS with a suitable degree of diagnosis of good level with histopathology with Kappa coefficient = 0.57; $p = 0.001$. Sensitivity, specificity and accuracy of EUS in the diagnosis of tumor invasion level were 80%, 92.2%, and 91.07%.

Our research results were consistent with many other studies.

Ta Van Ngoc Duc et al (2018) [1] studied EUS before surgery in 30 patients with rectal cancer, the results showed the value of EUS in assessing the level of invasive tumors (stage T) compared with histopathology had a sensitivity of 96.15%, specificity 96.46%, accuracy of 93.33%.

In a meta-analysis of de Jong EA et al (2016) [5] in forty-six studies included 2,224 patients reached. Results showed that the gross accuracy for tumor invasion assessment was 75% for MRI, 82% for EUS and 83% for CT. If the T4 period was evaluated separately, the accuracy of EUS was 94%.

Waage J.E et al (2015) [11] studied 120 cases of rectum cancer to give results of sensitivity, specificity and accuracy (with 95%CI) in the diagnosis of adenocarcinoma respectively 0.96 (0.90 - 0.99), 0.62 (0.40 - 0.80) and 0.90 (0.83 - 0.94).

Badger SA et al [2] conducted research from October 1999 to May 2004, 95 rectal cancer patients were assessed for cancer stage according to TNM before EUS treatment by 1 doctor who performed EUS only. The results showed that the overall accuracy of the T-stage evaluation was 71.6%. Sensitivity, specificity, positive

predictive value and negative predictive value of EUS rated the T3 period were 96.6%, 33.3%, 70.4% and 85.7%, respectively.

Zammit M et al [12] studied 78 patients with rectum cancer without difficulty in the implementation of EUS, the accuracy in diagnosis of stage T was 80% and 77% for stage N. While at 39 patients, when implementing EUS, there were difficult problems such as causing rectal stenosis (23 patients), uncomfortable patients (8 patients), preparing patients before performing poor surgery (6 patients) and postoperative scarring (2 patients), the accuracy of the T-stage evaluation was 68%.

4. The value of endoscopic ultrasound in the diagnosis of lymph node metastasis.

Regional lymph node injury is one of the important factors in prognosis, so the treatment regimen will depend on lymphadenopathy. The problem is how to diagnose lymphadenopathy before surgery to build the best treatment regimen for patients. Methods such as rectal examination and endoscopic examination cannot assess lymphadenopathy. Diagnosis of anatomy is performed only after surgery, so it is valuable for retention.

The results of our study in 56 patients, after comparing with the histopathological results, showed that endoscopic ultrasound had a suitable degree of diagnosis with quite good histology with Kappa coefficient = 0.41; $p = 0.002$. Sensitivity, specificity and accuracy of EUS in diagnosis of lymph node metastasis were 66.7%; 78% and 75%.

The results of our research were consistent with the findings of other authors.

Ta Van Ngoc Duc et al (2018) [1] studied EUS before surgery in 30 patients with rectal cancer, the results showed the value of EUS in assessing the level of invasive tumors (stage N) compared with histopathology had 85.04% sensitivity, 88.04% specificity, 91.1% accuracy.

In a meta-analysis of de Jong E.A et al (2016) [5] in forty-six studies included 2,224 patients reached. Results showed that the accuracy for predicting the presence of lymph node metastasis was 72% for MRI, 72% for EUS and 65% for CT.

The study by Badger S.A et al [2] was conducted in 95 rectal cancer patients who were evaluated for cancer stage according to TNM before EUS treatment by a single EUS doctor. The results showed that the overall accuracy of the N-stage evaluation was 68.8%. Sensitivity, specificity, positive predictive value and negative predictive value of EUS assessing metastatic lymph nodes were 73.2%, 62.2%, 74.5% and 60.5%, respectively.

Landmanns R.G et al's study [10] conducted EUS in 938 rectal cancer patients, of which 134 patients were treated with thorough removal surgery, without treatment of accompanying radiation. The results showed that the accuracy and specificity of EUS in the evaluation of stage N was 70%. EUS is more likely to not detect small metastatic lymph nodes. The size of metastatic lymph nodes and the accuracy of EUS are related to stage T. Early rectal damage is more likely to have small metastatic lymph nodes but EUS is undetectable, which partly explains the

reason why is the high recurrence rate of rectal cancer patients only treated for surgical removal of the merely tumor.

Zammit M et al [12] studied the role of EUS in assessing invasive of tumors in patients with rectum cancer before surgical treatment. EUS is conducted by a single ultrasound doctor. The results showed that the accuracy of EUS in 78 patients was not difficult to implement EUS was 77%. Meanwhile, in 39 patients who performed EUS, they had problems such as rectal stenosis (23 patients), uncomfortable patients (8 patients), preparing patients before performing the procedure not good (6 patients), and postoperative scarring (2 patients) accuracy in the N-stage evaluation was only 67%.

The study by Bali C et al [3] conducted over a period of 4 years in 33 rectal cancer patients, who was assessed the pre-operative TNM stage and compared with the postoperative pathology results. The results showed that the accuracy of EUS in assessing the N stage was 59%.

CONCLUSION

Endoscopic ultrasound is a good method to diagnose, monitor and evaluate the stage of rectal tumors quickly, safely and accurately.

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