Review

Preoperative Evaluation of Lymph Node Metastasis in Esophageal Cancer

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Lymph node metastasis (LMN) in esophageal cancer occurs from the superficial cancer and spreads wildly from the neck to the abdomen. Hence precise determination of LMN is essential when adequate treatments are employed. There are several reports about ultrasonic features of malignant lymph nodes (LNs), and in summary, reports of endoscopic ultrasonography (EUS) findings of malignant LNs showed they were more than 5-10 mm in diameter, with a distinct border, hypoechoic internal echo and round shape. Sensitivity, specificity and accuracies for the diagnosis of malignant LNs by EUS were 49-99%, 33-99% and 71-96%. The rates widely varied, because the accuracy of EUS's ability to determine malignancy were based on the evaluation of various echo features of LNs, and were dependent on the judgement of subjective observers. Therefore histological analysis is necessary for adequate treatments. Endoscopic ultrasonography guided fine-needle aspiration cytology (EUS-FNA) has been performed for the diagnosis of malignant LNs since 10 years. Results of those reports were sensitivity 81-97%, specificity 83-100% and accuracy 83-97%. EUS-FNA staging was better than EUS staging. Also clinically obvious complications by EUS-FNA have not been reported. Therefore published evidence showed that EUS-FNA is safe and useful for confirmation of malignant LNs. (Ann Thorac Cardiovasc Surg 2003; 9: 88–92)

Key words: endoscopic ultrasonography (EUS), endoscopic ultrasonography guided fine-needle aspiration cytology (EUS-FNA), diagnosis of lymph node metastasis (LNM)

Introduction

Lymph node metastasis (LNM) in esophageal cancer occurs from the superficial cancer and spreads from the neck, the mediastinum and the abdomen. There are several papers that have described the high incidence of LNM in esophageal cancer. The Japanese Society for Esophageal Diseases reported that around 60% of cases have LNM. Kajiyama et al.[1] reported that frequency of LNM in esophageal cancer was 22% in the neck, 34% in the upper mediastinum, 23% in midmediastinum, 20% in the lower mediastinum, and 38% in the upper area of the abdomen. Shiozaki et al.[2] reported that 46% of pT1 tumors have mediastinal lymph node (LN) involvement, 42% for the recurrent nerve chain nodes, 21% for the cervical nodes, 26% for the abdominal nodes, pT2 tumors have 53%, 40%, 20%, 33%, pT3 tumors have 73%, 43%, 28%, 60%, pT4 tumors have 83%, 58%, 50%, 75%, respectively. As the depth of tumor invasion is deeper, the frequency of nodal involvement increases. As to the tumor location, the rate of LNM of the upper thoracic esophageal cancer was higher in cervical and thoracic LN, the rate of LNM of middle thoracic esophageal cancer was wide spread from the cervical LN to the abdominal LN, the rate of LNM of lower thoracic esophageal cancer was higher in the abdominal LN and the thoracic LN. Hence the rate of LNM is influenced by tumor location but there is an overlap. Therefore precise determination of LNM in esophageal cancer is important for selection of adequate treatments. Several modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography, endoscopic ultrasonography (EUS), positron emission tomography (PET) have been employed for di-

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Table 1. EUS findings of nonmetastatic and metastatic LN[6]

	Nonmetastatic LN	Metastatic LN
Size (mm)		
Longest-D	8.5±5.4	10.8±6.5
Shortest-D	4.3±2.0	8.4±13.7
Morphology (%)		
Distinct border	24	76
Indistinct border	95	5
Heterogeneous internal echo	5	95
Homogeneous internal echo	90	10

EUS, endoscopic ultrasonography; LN, lymph node; D, diameter.

Table 2. Echo features of benign and malignant LN[9]

Echo features	Benign (%)	Malignant (%)
Size (≥1 cm)	74	94
Distinct margins	26	50
Shape		
Round	16	31
Oval	53	44
Triangle	26	6
Central echogenic area	21	0
Hypoechogenic nature	100	100
Mixed echogenicity	0	31

Table 3. Association between EUS features and LN histopathology[10]

	Benign	Malignant
Size of LN (mm)	1.4±0.1	1.7±0.1
Morphology (score)	9.9±0.3	11.9±0.3

Visual analog of LN						
Roundness		Irregular		Oval		Round
	Score	1	2	3	4	5
Echogenicity		Hyperechoic		Intermediate		Hypoechoic
	Score	1	2	3	4	5
Homogeneity		Heterogeneous		Intermediate		Homogeneous
	Score	1	2	3	4	5

agnosis of LNM, however, EUS provides higher accuracy among those modalities.[3-5] In this paper, the role of EUS for diagnosis of LNM has been reviewed.

EUS Feature of LNM

There are several papers describing malignant LNs. Murata et al.[6] reported the size and morphological EUS features of metastatic LNs. They were more than 5 mm in the shortest dimension, had a distinct border and heterogeneous hypoechoic internal echo (Table 1). Tio et al.[7] reported the criteria of LNM as hypoechoic clearly delineated nodes. Heintz et al.[8] described that the size of malignant LNs (10.1±5.3 mm) were significantly larger than benign nodes (7.4±2.9 mm). Comparing malignant and benign LNs,[9] in malignant nodes, there was a higher prevalence of nodes being larger than 1 cm, and having hypoechoic distinct margins and a round shape (Table 2). All visualized LNs were characterized according to standard EUS figures and scales were settled. Malignant LNs have higher scores than benign nodes (Table 3).[10] But the size of LNs between them was not much different. Summarizing those reports, malignant LNs should be more than 5-10 mm, hypoechoic, have a distinct border and a round shape (Fig. 1). However, some EUS features overlapped between benign and malignant LNs so that there are no firmly established criteria.

Accuracy of Determination of LNM

The overall results of EUS of LNM are shown in Table 4. Sensitivities are from 49 to 99%, specificities are from 33 to 99% and accuracies are from 71 to 96%.[6,7,11-20] Misjudgements on EUS can be due to inadequate scanning, such as nontraversable tumors and insufficient penetration. Therefore facilities which report a high rate of advanced tumors may be carrying out less accurate EUS in which case CT is superior to EUS.[3] When the specificity increases, the sensitivity lessens, it might be influenced by established EUS features of malignant LN. On the other hand, microscopic infiltration can cause false negative as inflammatory swelling LNs cause false negative results. Accordingly the accuracy of EUS was different depending on the facilities condition, the judgment of various observers and overlap between features of benign and malignant LNs.

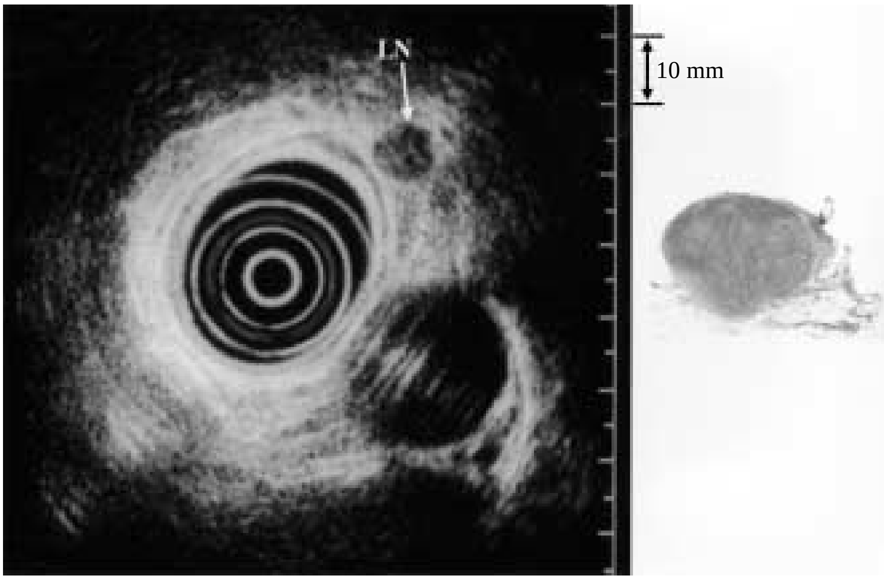

Fig. 1. EUS figure of malignant LN. Right: the LN of resected specimen.

Table 4. The results of published data for accuracy of EUS in LNM

Authors		No. of patient	Sensitivity (%)	Specificity (%)		Accuracy (%)
Murata et al. 1987[6]		222	87	90		89
Tio et al. 1990[7]		113	99	50		84
Fok et al. 1992[11]						
	CAN	98	58	76		71
	Med		85	86		
	Abd	45	62	86		
Dittler et al. 1993[12]		167	75	70		73
Murata et al. 1994[13]		328	85	91		90
Binmoeller et al. 1995[14]		38	90	44		79
Natsugoe et al. 1996[15]		37	80	88	T1	87
Shimizu et al. 1997[16]		82	49	99		95
Vickers et al. 1998[17]		49	97	54		86
Nishimaki et al. 1999[18]		224	78	60		72
Salminen et al. 1999[19]		32	95	33		72
Catalano et al. 1999[20]						73
	Med	149	79	63		
	CAN		83	98	FNA	96

CAN, celiac axis node; Med, mediastinum; Abd, abdomen; FNA, fine-needle aspiration cytology.

Endoscopic Ultrasonography Guided Fine-needle Aspiration Cytology (EUS-FNA)

Histological analysis of LNM is essential when indication for operation and LN dissection were determined or endoscopic treatments and less invasive treatments were introduced. For instance, when histological analysis was positive in the celiac node, operation could be avoided. Therefore video-assisted thoracoscopy and laparoscopy (VATS/LAP) were performed, and positive EUS results were 62% but VATS/LAP was 86%, 8 negative EUS results were confirmed and 6 positive by VATS/LAP.[21] The introduction of the curved linear array echoendoscope led to development of endoscopic ultrasonography guided fine-needle aspiration cytology (EUS-FNA) (Fig. 2). In 10 years, EUS-FNA has been introduced in the diagnosis of LNM. The decision for EUS-FNA was performed based on EUS appearance of the LN, such as suspected malignant or swelling. Adequate specimens for cytologic study were obtained in 90% of the procedures.[23] EUS-FNA produced sensitivity 81-97%, specificity 83-100% and accuracy 83-97% (Table5).[22-29] And the accuracy of EUS-

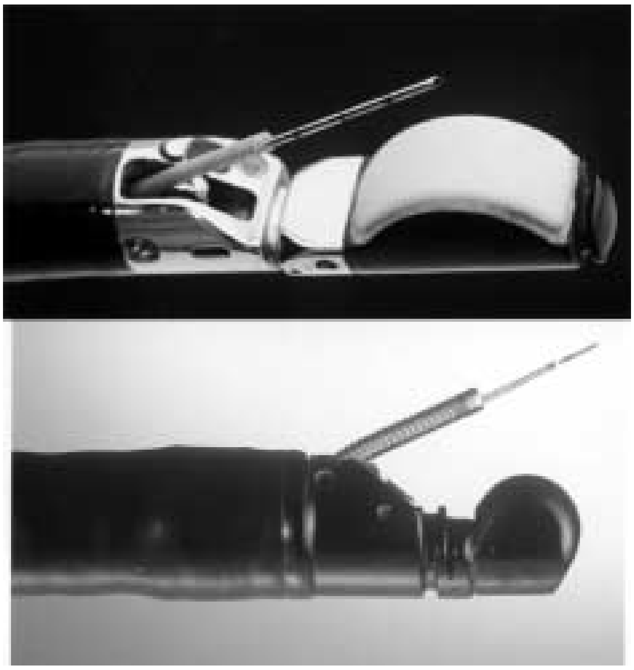

Fig. 2. The curved linear array echoendoscope led to EUS-FNA.

FNA is higher than that of EUS.[30] However, in patients whom have severe stenosis, the probe can not be passed and EUS-FNA is not possible, but dilation of the esophageal stenosis allows EUS-FNA to be performed, and accurate staging is possible.[31] There are no reports which describe severe complications caused by EUS-FNA. Furthermore, EUS-FNA may be a more cost-effective model than mediastinoscopy.[32]

In conclusion, EUS and EUS-FNA are safe and effective modalities for diagnosis of malignant LNs.

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Table 5. The results of published data for accuracy of EUS-FNA in LNM

Authors	No. of patient	Sensitivity (%)	Specificity (%)	Accuracy (%)
Giovannini et al. 1995[23]	24	81	100	83
Gress et al. 1997[24]	24	93	100	96
Hunerbein et al. 1998[25]	25	89	83	–
Silvestri et al. 1996[26]	26	89	100	92
Wiersema et al. 1998[27]	48	88	100	90
Williams et al. 1999[28]	60	87	100	90
Giovannini et al. 1999[29]	31	97	100	97

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