



S0959-8049(96)00034-2

Short Communication

Contribution of Cervical Ultrasound and Ultrasound Fine-needle Aspiration Biopsy to the Staging of Thoracic Oesophageal Carcinoma

S. Bonvalot,¹ N. Bouvard,² P. Lothaire,¹ J. Maurel,¹ F. Galateau,³ P. Ségol¹ and M. Gignoux¹

Departments of ¹Digestive Surgery, ²Radiology and ³Pathology, Centre Hospitalo-Universitaire, Avenue de la Côte de Nacre, 14000 Caen, France

This study was performed to evaluate the use of cervical ultrasonography and ultrasound-guided fine-needle aspiration for pretherapeutic staging of oesophageal cancer. 50 patients with a thoracic-oesophageal cancer (upper third = 8, middle = 36, lower = 6), previously untreated, underwent cervical ultrasonography to detect supraclavicular lymph node metastases (LN). An ultrasound fine-needle aspiration biopsy was attempted in 12 cases of suspected LN. 26 patients were operated on, of which 13 had surgical exploration of the neck. All patients were followed after treatment with special attention to the supraclavicular area. 14 patients (28%) were ultrasonography positive, 5 of 8 in the upper third, 9 of 42 in the two other thirds. Of the 12 patients where a fine-needle biopsy was attempted, 9 showed neoplastic cells (75%). 5 patients had cervical metastatic LN at surgery, and 5 other patients demonstrated supraclavicular LN metastases during the follow-up. There was one false positive and six false negatives from cervical ultrasonography and two false negatives of UGFAB (ultrasound-guided fine-needle aspiration biopsy). The sensitivity and the specificity of the cervical ultrasonography were 68 and 97%, respectively. The pretherapeutic staging was modified: 7 patients initially stage II–III were regraded to stage IV. Cervical ultrasonography is a reliable method of assessment of supraclavicular LN in thoracic oesophageal carcinoma. Copyright © 1996 Elsevier Science Ltd

Key words: oesophageal cancer, staging, cervical ultrasound

Eur J Cancer, Vol. 32A, No. 5, pp. 893–895, 1996

INTRODUCTION

SUPRA-CLAVICULAR nodal metastases are a common indication of progression in thoracic oesophageal carcinoma, wherever the site of the tumour [1]. These nodes are considered as metastases (stage IV disease) according to the classification of the UICC 1987 [2]. Except in patients with enlarged palpable nodes, they are difficult to detect by conventional methods of staging. The present study was performed to evaluate the contribution of cervical ultrasonography and ultrasound-guided fine-needle aspiration biopsy (UGFAB) to the pretherapeutic staging of oesophageal cancers.

PATIENTS AND METHODS

50 consecutive patients with thoracic oesophageal cancer, previously untreated, were included in this study. 47 had

a squamous cell carcinoma and 3 had an adenocarcinoma developed on Barrett's oesophagus. Patients with carcinoma of the cervical oesophagus, with glandular carcinoma of the gastric cardia, and patients with a second primary of the oral cavity, larynx or pharynx were excluded. The site of the primary was the upper third in 8, middle third in 36 and the lower third in 6 cases. All patients had a pretherapeutic evaluation including endoscopy and barium swallow, chest X-ray, thoraco-abdominal computerised tomography and abdominal ultrasonography. Oesophageal endo-sonography was performed in 7 patients. Mediastinal and coeliac lymph node (LN) metastases were suspected if LNs were larger than 1 and 2 cm, respectively. 5 patients had enlarged, suspiciously firm supraclavicular LN at palpation, and 6 had visceral metastases. The pretherapeutic staging was established according to UICC (Table 1). Coeliac nodes were considered as regional nodes in case of adenocarcinoma of the lower third. In addition, all patients underwent ultrasonography of the

Correspondence to M. Gignoux.

Revised 2 Jan. 1996; accepted 16 Jan. 1996.

Table 1. Pretherapeutic staging according to the site of the tumour, before cervical ultrasonography

Stage (UICC 1987)	Upper (n = 8)	Middle (n = 36)	Lower (n = 6)
I	—	—	—
II A (n = 25)	1	21	3
II B (n = 3)	—	3	—
III (n = 10)	4	4	2
IV* (n = 12)	3 ¹	8 ²	1 ³

*Site of metastases: ¹Lung; coeliac; liver + supraclavicular + coeliac.

²Liver: 2; lung; coeliac: 2; supraclavicular; liver + supraclavicular; supraclavicular + coeliac. ³Supraclavicular.

neck using a 5 MHz transducer (Acuson). Pathological node was defined according to usual criteria [3]. Every node with a small to large axis greater than 0.5 was considered as suspect and an UGFAB, with a 22-gauge needle, was attempted, except for 2 cases with very deep nodes. Samples were spread on four slides and were immediately wet fixed with sprayed 95% ethyl alcohol for subsequent Papanicolaou staining. In addition, cell blocks were made with the remaining tissue from the needle and stained with haematoxylin and eosin.

26 patients were operated on and 25 were resected, 13 by abdominal and right thoracic approach and 12 by subtotal oesophagectomy and cervical anastomosis. One patient had an explorative cervicotomy showing fixed supraclavicular LN and was not resected. Overall, 13 patients had a cervical approach with exploration of supraclavicular and paraoesophageal LNs along recurrent nerves. The 25 unresected patients were treated by non-surgical means. The reasons of unresectability were locally advanced tumours (12 patients), visceral or coeliac metastases (9 patients), medical contraindications (2 patients), refusal (1 patient), and the patient with unresectable node at cervicotomy. There were no postoperative deaths. All patients were followed at least 12 months for surviving patients (mean 17 months) or until death. The site of progression was carefully checked with special attention to the subclavicular area. To evaluate the sensitivity and the specificity of cervical ultrasonography, supraclavicular LN were considered as metastatic either when UGFAB showed neoplastic cells, when cervical lymphadenectomy removed metastatic nodes, or when there was a clinical evidence of supraclavicular recurrence during the follow-up.

RESULTS

Clinical, ultrasonography and UGFAB findings in the cervical area are summarised in Table 2. 14 patients (28%) had

Table 2. Cervical lymph node metastases (LN) in the 50 cases of thoracic oesophageal cancer, as demonstrated by palpation, cervical ultrasonography and fine-needle aspiration biopsy

	Palpable LN	US +	UGFAB +
Upper third (n = 8)	1	5	4
Middle third (n = 36)	3	8	4
Lower third (n = 6)	1	1	1
Total (n = 50)	5	14	9

metastatic cervical LN according to the ultrasonography defined criteria, 5 of 8 in the upper third, 9 of 42 in the two other thirds. Out of the three adenocarcinomas (one in the middle, two in the lower), one had a positive ultrasonography. The site of cervical LN was indifferently right or left, or bilateral. If we considered the 45 patients having a negative clinical examination of the cervical area, ultrasonography was positive in 9 (20%). These nodes were invisible at CT scan or at endosonography. UGFAB was attempted in 12 and was positive in 9 (75%). There were no complications of the procedure (e.g. pneumothorax, bruising, vessel or nerve injury), nor implantation deposits along the needle tract during the follow-up. Among the three negative punctures, the diagnosis of cervical metastases became clinically evident during the follow-up in 2 patients; in the last patient, no pathological LN was found at surgery and he died of liver metastases 14 months after resection. This patient was the only one false positive of ultrasonography (Table 3). 2 patients had a positive ultrasonography but UGFAB was not done: in both cases, surgical exploration confirmed metastatic invasion of recurrent nerve lymphatic chain, and oesophageal resection was performed in 1 patient.

Among the 36 ultrasonography negative patients, 10 were submitted to a three-stage resection with cervical lymphadenectomy. In 3 of these, pathological examination showed one small metastatic LN (less than 10 mm) deeply located along the right recurrent nerve. These 3 patients died from recurrence at 12, 14 and 22 months. In one additional patient, surgical exploration was negative but cervical recurrence occurred 6 months later, confirmed by UGFAB, and the patient died at 9 months. Among the 26 remaining patients, 13 underwent an abdomino-thoracic oesophagectomy and 13 were treated by non-surgical means. 24 (9 living, 15 dead) showed no evidence of supraclavicular progression, and 2 patients presented at 5 and 6 months supraclavicular metastases assessed by both clinical and ultrasonography, and in one by UGFAB (Table 3). The sensitivity and the specificity of the cervical ultrasonography as regards supraclavicular LN metastases was 68 and 97%, respectively. 43 patients out of 50 were correctly assessed, giving an accuracy of 86%. In patients with negative clinical examination of the cervical area, sensitivity was 57%. Out of 38 stage II–III patients, the pretherapeutic staging was modified for 7 patients by using cervical ultrasonography. The rate of stage IV increased from

Table 3. Sensitivity and specificity of cervical ultrasonography in the detection of lymph nodes metastases

Positive ultrasonography (n = 14)	
True positive (n = 13)	UGFAB positive = 9 Positive surgical exploration = 2 Clinical progression = 2
False positive (n = 1)	UGFAB negative and no progression
Negative ultrasonography (n = 36)	
True negative (n = 30)	Negative surgical exploration and no further progression = 6 Absence of clinical progression = 24
False negative (n = 6)	Positive surgical exploration = 3 Negative surgical exploration but further clinical progression = 1 Clinical progression = 2

Table 4. Pretherapeutic staging according to the site of the tumour, after cervical ultrasonography

Stage (UICC 1987)	Upper (n = 8)	Middle (n = 36)	Lower (n = 6)
I	—	—	—
II A (n = 23)	1	19	3
II B (n = 2)	—	2	—
III (n = 6)	1	3	2
IV (n = 19)	6	12	1

24 to 38% overall, 37.5–75% in the upper third, 22–33% in the middle third (one false positive) (Table 4).

The influence of positive ultrasonography on the decision of treatment was examined. In 3 patients, mentioned above, with resectable tumour, positive ultrasonography led to explorative cervicotomy first (resection in 2). 5 patients with presumably resectable tumours (T3 with mediastinal or coeliac nodes) were referred to radiotherapy including cervical area. The 6 other patients had distant metastases or local extension contraindicating surgery.

DISCUSSION

The observed rates of positive cervical ultrasonography and positive UGFAB (28 and 18%, respectively) are similar to those of Van Overhagen and colleagues on 37 patients (27 and 19%) [4]. These authors mentioned three failures of UGFAB out of 10 patients. In this series, we observed five failures or technical impossibilities out of 14 patients, always with unpalpable nodes. The site of LNs, deeply situated near supraclavicular vessels, or a small diameter, especially in nodes along recurrent nerves, explain these failures of UGFAB. However, the high specificity of ultrasonography indicates that pathological criteria is not mandatory. The only ultrasonography false positive we observed concerned probably an inflammatory node, neither discovered at surgical exploration nor at further ultrasonography.

The originality of this study is the control by surgical exploration in 13 patients, and for the remaining by a careful follow-up, allowing the evaluation of sensitivity and specificity of cervical ultrasonography. Small pathological LNs situated behind the sternum are not detectable by ultrasonography (3 cases in this series). However, some bias must be considered: lymphadenectomy was limited to a sampling of the main suspect nodes, and was not an extensive procedure. Moreover, during the follow-up, subclinical cervical LNs can be missed, but a metastatic cervical LN initially absent can appear 5 or 6 months later. Nevertheless, we consider this appraising valuable and useful for the physician, even if the sensitivity is reduced because of the limits mentioned above.

Understaging is usual in oesophageal cancer with conventional methods of exploration, mainly as regards LN metastases. The sensitivity and the specificity of CT scan to detect mediastinal LN are 55 and 89%, respectively, and are not well documented in the cervical area [5]. Endosonography provides more information (sensitivity, 65–95%; accuracy, 68–81%), but the specificity is low [6, 7]. Furthermore, the concordance between observers is very low in the cervical area [8]. The Japanese classification individualises three main groups of cervical LN: para-oesophago-tracheal along the recurrent nerves, supraclavicular and deep cervical, below and

above the omohyoid muscle [9]. The former is the most difficult to detect in our experience, especially on the right side. These nodes should be considered as regional, not distant, in the staging of upper third thoracic tumours. In our study, the rate of cervical LN metastases in upper third carcinoma was 62.5%. Surgical series of resection with bilateral cervical lymphadenectomy show 35–56% of invaded nodes in the upper third tumours, 11–40% in the middle third, 8–23% in the lower third [10, 11]. Such metastases usually mean a poor prognosis, especially in the lower third, and the benefit of extensive three-field dissection remains controversial [11–13]. Nevertheless, when involvement of cervical LN is predicted, the cervical procedure should be performed first [14].

In conclusion, external cervical ultrasonography is a reliable method of assessment of metastatic LN in thoracic oesophageal carcinoma. Concurrent to other methods, it improves the pretherapeutic staging of the tumour and can modify the decision of treatment.

1. Mandard MA, Chasle J, Marnay J, *et al.* Autopsy findings in 111 cases of esophageal cancer. *Cancer* 1981, **48**, 329–335.
2. Hermanek P, Sobin LH eds. *International Union Against Cancer. TNM Classification of Malignant Tumours*, 4th edn. Berlin, Springer, 1987.
3. Tohnosu N, Onoda S, Isono K. Ultrasonographic evaluation of cervical lymph node metastases in esophageal cancer with special reference to the relationship between the short to long axis ratio (S/L) and the cancer content. *J Clin Ultrasound* 1989, **17**, 101–106.
4. Van Overhagen HV, Lameris JS, Zonderland HM, Tilanus HW, Pel RV, Schutte HE. Ultrasound and ultrasound-guided fine needle aspiration biopsy of supraclavicular lymph nodes in patients with esophageal carcinoma. *Cancer* 1991, **67**, 585–587.
5. Gayet B, Fria J, Cahuzac J, Fekete F. Intérêt de la tomodensitométrie dans le cancer de l'oesophage. Etude prospective et "aveugle". *Gastroenterol Clin Biol* 1988, **12**, 23–28.
6. Ziegler K, Sanft C, Zeitz M, *et al.* Evaluation of endosonography in TN staging of esophageal cancer. *Gut* 1991, **32**, 16–20.
7. Tio TL, Cohen P, Coene PP, Udding J, Den Hartog Jager FCA, Tytgat GNJ. Endosonography and computed tomography of esophageal carcinoma. Preoperative classification compared to the New (1987) TNM System. *Gastroenterology* 1989, **96**, 1478–1486.
8. Burtin P, Napoleon B, Palazzo L, Roseau G, Souquet JC, Cales P. Variabilité inter-observateurs de l'écho-endoscopie dans le bilan d'extension du cancer de l'oesophage et du cardia. *Gastroenterol Clin Biol* 1994, **18**, A41.
9. Japanese Society for Esophageal Diseases. Guidelines for the clinical and pathologic studies on carcinoma of the esophagus. *Jpn J Surg* 1976, **6**, 69–78.
10. Isono K, Sato H, Nakayama K. Results of a nationwide study on the three-field lymph node dissection of esophageal cancer. *Oncology* 1991, **48**, 411–420.
11. Peracchia A, Ruol A, Bardini R, Segalin A, Castoro C, Asolati M. Lymph node dissection for cancer of the thoracic esophagus: how extended should it be? *Dis Esophagus* 1992, **2**, 69–77.
12. Baba M, Natsugoe S, Kusano C, *et al.* Lymph node metastasis and the recurrence of esophageal carcinoma with emphasis on lymphadenectomy in the neck and superior mediastinum. *Jpn J Surg* 1995, **25**, 125–130.
13. Nishimaki T, Tanaka O, Suzuki T, Aizawa K, Hatakeyama K, Muto T. Clinical implications of cervical lymph node metastasis patterns in thoracic esophageal cancer. *Ann Surg* 1994, **220**, 775–781.
14. Matsubara T, Ueda M, Nakajima T. Preoperative assessment of lymph nodes in the prediction of disease spread and outcome in cancer of the thoracic oesophagus. *Br J Surg* 1995, **82**, 356–359.

Acknowledgement—The authors are grateful to L. Marlière for typing the manuscript.