World J. Surg. 28, 680–685, 2004
DOI: 10.1007/s00268-004-6865-y

WORLD
Journal of
SURGERY

Clinical Significance of Serum Carcinoembryonic Antigen, Carbohydrate Antigen 19-9, and Squamous Cell Carcinoma Antigen Levels in Esophageal Cancer Patients

Shin-ichi Kosugi, M.D., Tadashi Nishimaki, M.D., Tatsuo Kanda, M.D., Satoru Nakagawa, M.D., Manabu Ohashi, M.D., Katsuyoshi Hatakeyama, M.D.

Department of Regeneration and Transplant Medicine, Division of Digestive and General Surgery, Graduate School of Medical and Dental Science, Niigata University, 1-757 Asahimachi-dori, Niigata 951-8510, Japan

Published Online: June 4, 2004

Abstract. Serum carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19-9, and squamous cell carcinoma (SCC) antigen levels were assessed to determine if their levels are useful for staging esophageal cancer preoperatively and for predicting patient survival after esophagectomy. Hence their seropositivity was investigated for a correlation with resectability, clinicopathologic parameters of tumor progression, and treatment outcomes in patients with unresectable esophageal cancer ($n = 63$) and those undergoing esophagectomy for resectable disease ($n = 267$). Abnormal elevation of serum SCC antigen levels showed a significant correlation with resectability ($p < 0.0001$), depth of tumor invasion ($p < 0.0001$), lymph node status ($p = 0.0015$), TNM stage ($p < 0.0001$), lymphatic invasion ($p = 0.0019$), blood vessel invasion ($p = 0.0079$), and poor survival after esophagectomy ($p = 0.0061$). A significant relation ($p = 0.0145$) was found between elevated serum CEA levels and distant metastasis, whereas the seropositivity of CA 19-9 showed no association with resectability, tumor progression, or patient survival. These results indicate that abnormal elevation of serum SCC antigen is a useful predictor of advanced esophageal cancer associated with poor survival after esophagectomy.

Treatment outcomes of patients with esophageal cancer have been poor even after radical esophagectomy [1] because the disease has already progressed to an advanced stage by the time it is diagnosed, rendering most cases incurable. Consequently, various tumor markers have been used in attempts to detect esophageal cancer at an early stage. Carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19-9, and squamous cell carcinoma (SCC) antigen are some of the tumor markers commonly used in the management of patients with esophageal cancer [2–4]. Many studies have reported that tumor markers have limited utility in the early detection of esophageal cancer; the sensitivities of these tumor markers are unacceptably low, particularly in cases of early esophageal cancer [4, 5]. However, it is not yet known whether preoperative serum levels of CEA, CA 19-9, and SCC antigen are predictive of resectability, curability, or long-term survival after esophagectomy in patients with esophageal cancer. Furthermore, it is not known whether the preoperative serum levels of these tumor markers are significant predictors of postoperative outcomes independent of the clinicopathologic factors that serve as a major component of the TNM staging system [6].

Therefore the purposes of the present study were to (1) clarify which clinicopathologic factors associated with tumor progression correlate with preoperative serum levels of CEA, CA 19-9, or SCC (or any combination thereof); (2) evaluate the usefulness of these tumor markers for predicting resectability, curability, or postoperative survival and if these prognostic factors are independent of the clinicopathologic factors known to be authentic prognostic indicators; and (3) determine the role of the preoperative serum levels of these tumor markers in managing patients with esophageal cancer.

Patients and Methods

Patients

Between 1992 and 1999 a total of 359 patients were admitted to the Division of Digestive and General Surgery, Niigata University for treatment of esophageal cancer. The ages of these patients ranged from 40 to 91 years (average 65.2 years). There were 318 men and 41 women. At our institution since 1992, serum levels of CEA, CA 19-9, and SCC antigen have been routinely measured in patients with esophageal cancer prior to treatment.

Of the 359 patients, 83 did not undergo esophagectomy. In most of the 83 cases it was due to the advanced status of the disease, which was evidenced by direct involvement of adjacent vital organs via local tumor extension ($n = 54$) or the presence of distant organ metastasis ($n = 12$); in others, it was due to poor performance status ($n = 15$); and in several, it was due to the patients' refusal to undergo the operation ($n = 5$). These 83 patients underwent feeding gastrostomy or jejunostomy ($n = 21$); endoscopic stent implantation ($n = 9$); chemotherapy, radiotherapy, or both ($n = 73$); or no further treatment ($n = 10$). Altogether, 63 patients in whom esoph-

Correspondence to: Shin-ichi Kosugi, M.D., e-mail: sugishin@med.niigata-u.ac.jp

agectomy could not be performed because of advanced disease were included in the present study as the NR group.

The remaining 276 patients underwent tumor removal by esophagectomy ($n = 267$) or endoscopic mucosal resection ($n = 9$). The 267 patients undergoing esophagectomy were included in the present study as the ER group. Of these 267 patients, 251 underwent transthoracic esophagectomy with bilateral cervical, mediastinal, and abdominal lymphadenectomy ($n = 73$) or with mediastinal and abdominal lymphadenectomy ($n = 57$); and 118 underwent transhiatal esophagectomy with lower mediastinal and abdominal lymphadenectomy for thoracic esophageal cancer. The remaining 16 patients underwent total esophagectomy through the transhiatal approach with cervical lymphadenectomy for carcinoma of the cervical esophagus.

Preoperative Staging

Chest radiography, esophagography, esophagoscopy, endoscopic ultrasonography, percutaneous ultrasonography, and computed tomography were routinely performed to stage the esophageal tumors. Cases showing distant organ metastasis or definite direct involvement of adjacent vital organs by local tumor extension by any of these diagnostic modalities were regarded as unresectable. Magnetic resonance imaging, bronchofiberoscopy, or bone scintigraphy was additionally performed if indicated for the determination of individual resectability.

Tumors

All 330 patients included in the present study had squamous cell carcinoma. In the 267 patients of the ER group, anatomic subsites, histopathologic grading, the depth of the primary tumor, and stage grouping were defined by the TNM classification of the International Union Against cancer (UICC) [6]. The quality of tumor clearance was determined using the residual tumor (R) classification of the UICC-TNM classification [6]: Cases with no residual tumor, microscopic residual tumor, or macroscopic residual tumor after tumor resection were classified as R0, R1, or R2, respectively. In addition, the presence or absence of lymph node metastasis, intramural metastasis [7], lymphatic invasion, and blood vessel invasion were histologically examined in the ER group. Based on the results of our earlier study [8], the number of positive nodes per patient (0, 1–4, ≥ 5) was also assessed as a prognostic factor after esophagectomy. These clinicopathologic variables were determined by pathologíc examination of the resected specimens. These 267 cases were classified into 12 cases of stage 0, 60 cases of stage I, 32 cases of stage IIA, 28 cases of stage IIB, 90 cases of stage III, and 45 cases of stage IV disease.

For the 63 patients of the NR group, stages were determined using imaging techniques. These 63 cases included 46 cases of stage III disease and 17 cases of stage IV disease.

Tumor Markers

Serum concentrations of CEA, CA 19-9, and SCC antigen were measured in all patients before the initiation of treatment for esophageal cancer. They were assessed in 61, 59, and 53 patients of the NR group, respectively, and in 266, 262, and 245 patients of the ER group, respectively.

The SCC antigen was measured by the SCC antigen microparticle enzyme immunoassay (EIA) (Dainabot, Tokyo, Japan). The cutoff value for SCC antigen was determined to be 1.5 ng/ml, as previously reported [9]. CEA and CA 19-9 were measured by EIA using a Lumipulse 1200 (Fujirebio, Tokyo, Japan) with cutoff values of 5 ng/ml and 37 U/ml, respectively.

Table 1. Seropositivity of CEA, CA 19-9, and SCC in the ER and NR groups.

Tumor marker	ER group ($n = 267$)	NR group ($n = 63$)
CEA	87/266 (32.7%)	25/61 (41.0%)
CA 19-9	23/262 (8.8%)	4/59 (6.8%)
SCC	75/245 (30.6%)*	35/53 (66.0%)*

Results are the seropositivity rates.

CEA: carcinoembryonic antigen; CA: carbohydrate antigen; SCC: squamous cell carcinoma; ER: patients undergoing esophagectomy; NR: patients in whom esophagectomy could not be performed owing to advanced disease.

*$p < 0.0001$.

Statistical Analysis

Differences in frequency were detected by the χ^2 test. In the ER group, survival rates were calculated from the time of tumor resection until death or the latest follow-up for surviving patients using the Kaplan-Meier method. The equality of the survival curves was assessed using the generalized Wilcoxon test. Follow-up data were available for all patients of the ER group, with a median follow-up period of 33 months (range 1–98 months). Cox's proportional hazard model was used for multivariate survival analysis. A value of $p < 0.05$ was considered significant. All analyses were performed with StatView J4.11 (Abacus Concepts, Berkeley, CA, USA).

Results

Relation between Serum Tumor Marker Level and Resectability

The median values of serum CEA, CA 19-9, and SCC antigen concentrations were 4.0 ng/ml (0.7–74.7 ng/ml), 11.0 IU/ml (2.0–63.0 IU/ml), and 2.0 ng/ml (0.3–46.1 ng/ml), respectively, in the NR group. Abnormal elevations of serum CEA, CA 19-9, and SCC antigen levels beyond the respective cutoff values was observed in 41.0%, 6.8%, and 66.0% of the patients in this group (Table 1). The median serum CEA, CA 19-9, and SCC antigen concentrations were 3.5 ng/ml (0.9–464.5 ng/ml), 11.0 IU/ml (2.0–1696.0 IU/ml), and 1.0 ng/ml (0.3–60.7 ng/ml), respectively, in the ER group. Abnormal elevations of the respective tumor markers in the sera were found in 32.7%, 8.8%, and 30.6%, respectively, of the ER patients (Table 1). The positive rate of serum SCC antigen assessment was significantly higher in the NR group than in the ER group ($p < 0.0001$). However, no significant difference was detected in the positive rate of either serum CEA or CA 19-9 between these two groups.

Correlations between Serum Tumor Marker Levels and Clinicopathologic Variables

Positive rates for serum CEA, CA 19-9, and SCC antigen in the ER group are shown in Table 2, according to patient gender, primary site, histopathologic grading, depth of the primary tumor, lymph node status, disease stage, presence or absence of distant organ

Table 2. Positive rates of serum CEA, CA 19-9, and SCC levels according to clinicopathologic variables in the ER group.

	CEA		CEA 19-9		SCC	
Variable	Positive	*p*	Positive	*p*	Positive	*p*
Gender		NS		NS		NS
Male	79/232 (34.1%)		21/228 (9.2%)		65/213 (30.5%)	
Female	8/34 (23.5%)		2/34 (5.9%)		10/32 (31.3%)	
Tumor location		NS		NS		0.0103
Cervical	4/16 (25.0%)		1/14 (7.1%)		8/15 (53.3%)	
Upper thoracic	9/15 (60.0%)		1/15 (6.7%)		1/14 (7.1%)	
Middle thoracic	40/125 (32.0%)		11/123 (8.9%)		29/117 (24.8%)	
Lower thoracic	34/110 (30.9%)		10/110 (9.1%)		37/99 (37.4%)	
Histopathologic grading		NS		NS		0.0392
Well differentiated (G1)	27/78 (34.6%)		8/75 (10.7%)		30/69 (43.5%)	
Moderately differentiated (G2)	44/146 (30.1%)		13/145 (9.0%)		38/140 (27.1%)	
Poorly differentiated (G3)	12/30 (40.0%)		2/30 (6.7%)		6/29 (20.7%)	
Undifferentiated (G4)	1/4 (25.0%)		0/4		0/2	
Depth of invasion (pT)		NS		NS		<0.0001
Tis, T0, T1	33/101 (32.7%)		6/101 (5.9%)		9/91 (9.9%)	
T2	5/14 (35.7%)		2/14 (14.3%)		4/13 (30.8%)	
T3	39/120 (32.5%)		13/117 (11.1%)		46/111 (30.8)	
T4	10/31 (32.3%)		2/30 (6.7%)		16/30 (53.3%)	
Lymph node involvement (pN)		NS		NS		0.0015
N0	35/111 (31.5%)		10/110 (9.1%)		18/98 (18.4%)	
N1	52/153 (33.3%)		13/150 (8.7%)		57/145 (39.3%)	
Metastatic nodes (pN –no.)						
Negative	35/111 (31.5%)		10/110 (9.1%)		18/98 (18.4%)	
≤ 4	30/104 (28.8%)		7/101 (6.9%)		34/98 (35.7%)	
≥ 5	21/49 (42.9%)		6/49 (12.2%)		22/47 (46.8%)	
Distant metastasis (pM)		0.0145		NS		NS
M0	65/221 (29.4%)		21/218 (9.6%)		61/202 (30.2%)	
M1	22/45 (48.9%)		2/44 (4.5%)		14/43 (32.6%)	
Stage (TNM)		NS		NS		<0.0001
0,1	21/72 (29.2%)		5/72 (6.9%)		7/65 (10.8%)	
IIA, IIB	21/60 (35.0%)		7/59 (11.9%)		13/54 (24.0%)	
III	23/89 (25.8%)		9/87 (10.3%)		41/83 (49.4%)	
IV, IVA, IVB	22/4567 (48.9%)		2/44 (4.5%)		14/43 (32.6%)	
Lymphatic invasion		NS		NS		0.0019
Negative	28/107 (26.2%)		6/105 (5.7%)		19/98 (19.4%)	
Positive	59/158 (37.3%)		17/156 (10.9%)		56/147 (38.1%)	
Blood vessel invasion		NS		NS		0.0079
Negative	46/148 (31.1%)		11/146 (7.5%)		31/134 (23.1%)	
Positive	41/117 (35.0%)		12/115 (10.4%)		44/111 (39.6%)	
Intramural metastasis (IM)		NS		NS		NS
Absence	69/216 (31.9%)		19/213 (8.9%)		55/197 (27.9%)	
Presence	18/50 (36.0%)		4/49 (8.2%)		20/48 (41.7%)	
Residual tumor		NS		NS		NS
R0	73/230 (31.7%)		20/228 (8.8%)		62/209 (29.7%)	
R1, R2	14/36 (38.9%)		3/34 (8.8%)		13/36 (36.1%)	

metastasis, lymphatic invasion, blood vessel invasion, intramural metastasis, and postoperative residual tumor status. There were strong correlations between serum SCC antigen positivity and tumor location ($p = 0.0103$), depth of the primary tumor ($p < 0.0001$), nodal metastasis ($p = 0.0015$), number of metastatic nodes ($p = 0.0010$), disease stage ($p < 0.0001$), histopathologic grading ($p = 0.0392$), blood vessel invasion ($p = 0.0079$), and lymphatic invasion ($p = 0.0019$). Serum CEA positivity showed a significant correlation with distant organ metastasis ($p = 0.0145$). No significant association was observed between serum CA 19-9 positivity and any of the clinicopathologic variables.

Relations between Serum Tumor Marker Levels and Patient Outcome

The overall survival rate was 45.1% at five years after tumor resection in the ER group. Survival curves of the ER group patients according to the preoperative serum CEA, CA 19-9, and SCC antigen levels are shown in Figure 1. The survival curve of patients with a positive SCC antigen assay was significantly worse than that of patients with a negative SCC antigen assay ($p = 0.0061$). However, relative to the positive or negative results of preoperative CEA and CA 19-9 assessment, no significant differences in patient survival were observed.

Significant Prognostic Factors

Univariate analysis showed that the depth of the primary tumor invasion, lymph node metastasis, number of positive nodes, distant organ metastasis, disease stage, lymphatic invasion, blood vessel invasion, intramural metastasis, and postoperative residual tumor status, in addition to the positivity of the preoperative serum SCC assay, were significant prognostic factors in the ER group (Table 3). Of these prognostic factors revealed by univariate analysis, the depth of the primary tumor invasion, number of metastatic nodes,

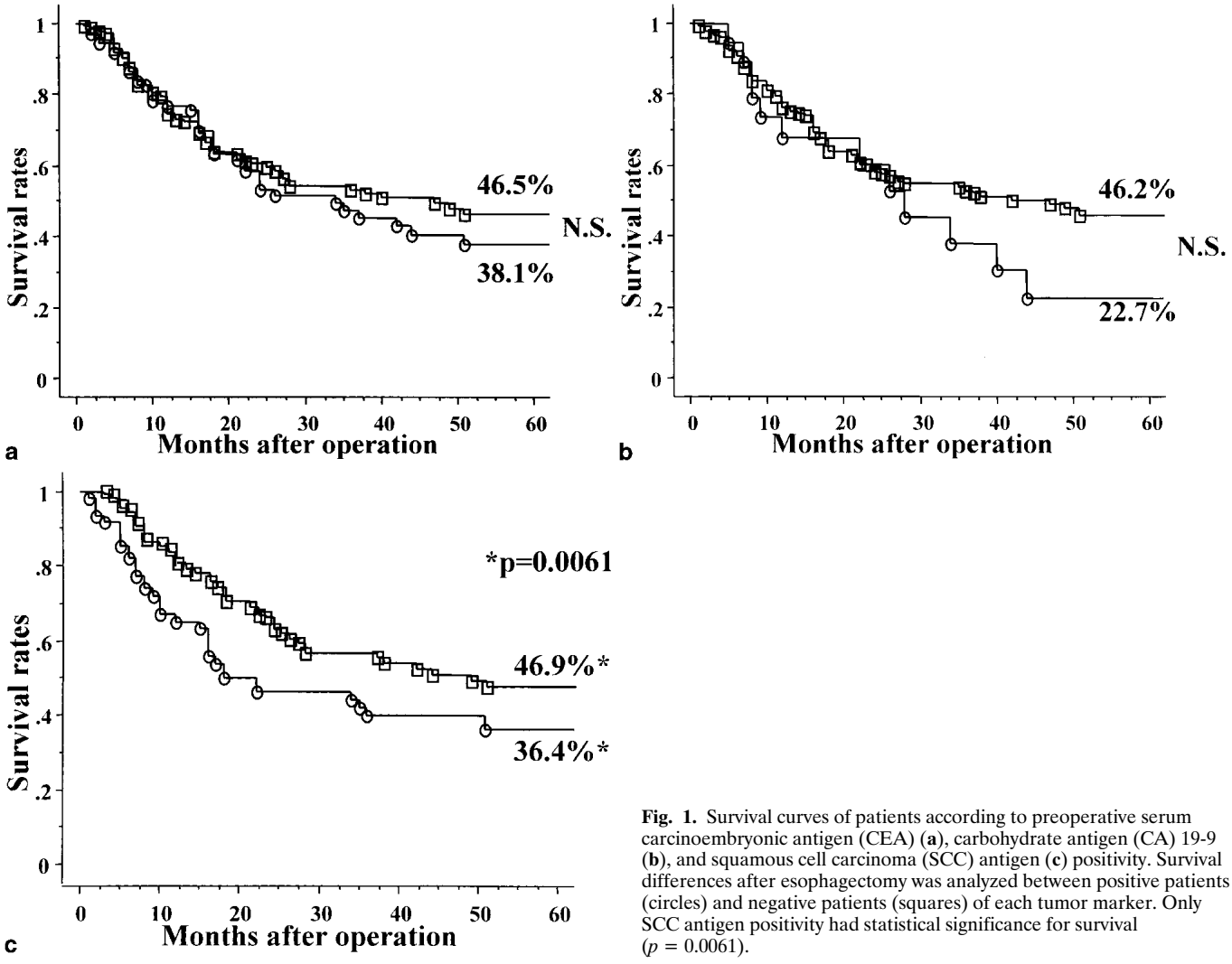

Fig. 1. Survival curves of patients according to preoperative serum carcinoembryonic antigen (CEA) (**a**), carbohydrate antigen (CA) 19-9 (**b**), and squamous cell carcinoma (SCC) antigen (**c**) positivity. Survival differences after esophagectomy was analyzed between positive patients (circles) and negative patients (squares) of each tumor marker. Only SCC antigen positivity had statistical significance for survival ($p = 0.0061$).

Table 3. Univariate analysis of prognostic factors in the ER group.

Variable	5-year survival (%)	*p*
pT (T1/T2/T3/T4)	79.8/34.9/27.1/18.0	< 0.0001
pN (N0/N1)	70.4/27.1	< 0.0001
pN no. (N0/1–4/≥ 5)	70.4/36.8/8.1	< 0.0001
pM (M0/M1)	48.5/17.9	< 0.0001
Stage (I/II/III/IV)	86.2/56.7/21.4/17.9	< 0.0001
Lymphatic invasion (−/+)	58.4/34.5	< 0.0001
Blood vessel invasion (−/+)	59.6/25.6	< 0.0001
IM (−/+)	50.6/13.9	< 0.0001
Residual tumor (R0/R1/R2)	50.1/25.0/3.5	< 0.0001
Serum SCC antigen positivity (−/+)	48.5/34.6	0.0061

IM: intramural metastasis.

Table 4. Multivariate analysis of prognostic factors in the ER group.

Variables	Exponent	*p*	95% CI
Depth of invasion			
T2	2.807	0.0733	0.907–8.689
T3	3.949	0.0006	1.805–8.639
T4	5.816	0.0002	2.270–14.898
No. of metastatic nodes			
≤ 4	1.943	0.0536	0.990–3.814
≥ 5	3.824	0.0009	1.728–8.462
Intramural metastasis present	2.079	0.0025	1.295–3.340
SCC antigen positivity	0.917	0.7122	0.578–1.454

CI: confidence interval.

and intramural metastasis were shown by multivariate analysis to be independent prognostic factors (Table 4). An elevated preoperative serum SCC antigen level, however, was not found to be a significant independent prognostic factor.

Discussion

Esophageal cancer is one of the most difficult malignancies to cure regardless of the treatment modality. To improve treatment outcome, several tumor markers assessed in patient sera have been tested for their utility in screening, diagnosis, establishing prognosis, monitoring treatment, and detecting relapse in patients with esophageal cancer [10]. CEA, CA 19-9, and SCC antigen are several of the tumor markers commonly used in the management of esophageal cancer patients [2–4]. Although some studies have reported that CYFRA 21-1 has higher sensitivity for detecting esophageal cancer than other tumor markers [11–13], the sensitivity of CEA, CA 19-9, SCC antigen, and even CYFRA 21-1 has been re-

ported to be less than 10% in patients with early esophageal cancer [4], suggesting that these tests have limited utility for detecting this disease at an early stage. However, whether the assessment of serum levels of these tumor markers prior to the initiation of treatment is useful for staging esophageal cancer or for predicting survival after esophagectomy remains unclear.

Previous studies have suggested the potential usefulness of CEA and CA 19-9 when screening or monitoring disease recurrence and response to treatment [2, 3]. Gion et al. reported that the CEA assay showed a positive rate of 27.1% and was directly related to the clinical stage in patients with esophageal cancer [14]. In contrast, Clark et al. found no relation between preoperative CEA elevation and tumor stage or patient survival [15]. In the present study, seropositivity of CEA and CA 19-9 before treatment had no correlation with resectability, most clinicopathologic parameters of tumor progression, or patient survival. In accord with the results of our study, Kim et al. found that the CEA level did not predict resectability or survival in patients with esophageal cancer [16]. However, the present study revealed a significant relation between preoperative elevation of serum CEA levels and the presence of clinically inapparent distant metastases. Our findings are similar to those of Munck-Wikland et al., who reported that the appearance of distant metastases was associated with increased CEA levels [2]. In addition, Sanders et al. reported that the abnormal elevation of serum CEA levels may reflect the metastatic potential of esophageal cancer cells [17].

In the present study, in contrast to the preoperative serum levels of CEA and CA 19-9, those of SCC antigen exhibited significant correlation with resectability, location of the primary tumor, histopathologic grading, and clinicopathologic parameters of tumor progression, including depth of tumor invasion, lymph node status, TNM stage, lymphatic invasion, and blood vessel invasion. Although judging resectability based on preoperative serum SCC antigen levels is not practical, it may serve as an ancillary tool to predict resectability. Distribution of the disease stage revealed that the NR patients had significantly more advanced disease than did the ER patients ($p < 0.0001$). This may explain the significantly higher rates of serum SCC antigen positivity in the former group than in the latter group. Both mucosal and submucosal carcinomas of the esophagus are defined as T1 tumors by the UICC's TNM classification system. However, recent studies have demonstrated that esophageal T1 tumors comprise an oncologically heterogeneous subgroup; that is, mucosal carcinomas are usually a local disease associated with excellent treatment results, whereas submucosal carcinomas frequently display extraesophageal spread associated with a significantly worse prognosis than that of the mucosal tumors [18]. On the other hand, the prognosis of patients with T4 esophageal carcinoma is extremely poor. When the data from patients with mucosal carcinomas and T4 tumors were eliminated and survival rates were recalculated in the remaining ER group, univariate analysis showed that the positivity of the preoperative serum SCC antigen assay was not a significant prognostic factor ($p = 0.1558$, data not shown). Because a strong correlation between serum SCC positivity and the depth of the primary tumor was observed, there may be no significant difference in patient survival relative to the positive or negative results of preoperative SCC antigen assessment in patients without T4 tumors. Our findings are similar to those of Nakamura et al., who found a significant correlation between preoperative serum SCC antigen levels and TNM stage in patients with esophageal cancer [4]. On the other hand, Kawaguchi et al. found no relation between the serum SCC antigen levels and the TNM stage [12]. Their study sample was smaller than that used in the study of Nakamura et al. [4]. The findings in the present study may partly explain the contradictory results.

The present study revealed that elevated preoperative levels of serum SCC antigen indicated an adverse outcome regarding patient survival after esophagectomy. To our knowledge, such a prognostic impact of serum SCC antigen levels has not been previously reported. The fact that our study sample was larger and the follow-up period after esophagectomy longer than in previous studies might account for the fact that the prognostic significance of preoperative serum SCC antigen levels in patients with esophageal cancer was detected. We did not find preoperative seropositivity of SCC antigen to be an independent prognostic factor by multivariate analysis, although our findings reconfirmed that the depth of tumor invasion, number of positive nodes, and intramural metastasis were independent prognostic factors. However, these results may not necessarily diminish the utility of preoperative serum SCC antigen assessment because the amount of elevation of these factors regarding the degree of tumor spread is often difficult even by the current imaging techniques prior to esophageal resection, particularly in patients with resectable esophageal cancer [19]. Nishimaki and associates reported that preoperative stage grouping was only 56% accurate for resectable, localized esophageal cancer [19]. Therefore preoperative serum SCC antigen levels may be a useful prognostic predictor in these cases although not independent of the clinicopathologic factors known to be authentic prognostic indicators. Furthermore, measurement of serum SCC antigen levels is convenient as well as less expensive.

Recently, CYFRA 21-1, which is recognized as a soluble cytokeratin-19 fragment, has been tested for its clinical utility in patients with esophageal cancer. Some investigators have reported that serum CYFRA 21-1 levels are superior to SCC antigen levels because the former are more sensitive and correlate more significantly with tumor progression [11–13]. Notably, other researchers have found that CYFRA 21-1 is not superior to CEA or SCC antigen, particularly in patients with superficial esophageal cancer [5]. Nakamura et al., for example, reported finding a significant correlation between serum CYFRA 21-1 and SCC antigen levels in patients with esophageal cancer [4]. Although further study, enrolling a large number of patients, is needed to determine the most useful tumor marker in the management of patients with esophageal cancer, the present study suggests that preoperative assessment of serum SCC antigen levels is useful for staging esophageal cancer as an ancillary tool to assess the extent of disease.

Conclusions

An abnormal elevation of the serum SCC antigen level is a useful predictor of advanced esophageal cancer associated with poor survival after esophagectomy. Serum CEA levels may be of use in predicting clinically inapparent distant metastasis. Preoperative assessment of serum CA 19-9 levels, in contrast, has no clinical significance in the management of patients with esophageal cancer.

Résumé. Afin de clarifier si l'évaluation préopératoire des taux de l'ACE, du CA 19-9 et du SCC étaient utiles pour le staging et pour prédire la survie des patients après oesophagectomie, on a analysé la séropositivité de ces marqueurs et on a corrélé les résultats avec la résecabilité, les paramètres cliniques et pathologiques de la progression tumorale ainsi qu'avec

l'évolution chez les patients, respectivement, porteurs d'un cancer non résecable de l'oesophage ($n = 63$) et ayant eu une oesophagectomie pour maladie réséquable ($n = 267$). Une élévation anormale de SCC était corrélée de façon statistiquement significative avec la résecabilité ($p < 0.0001$), la profondeur de l'invasion tumorale ($p < 0.0001$), l'état ganglionnaire lymphatique ($p = 0.0015$), le stade TNM ($p < 0.0001$), l'invasion lymphatique ($p = 0.0019$), l'invasion vasculaire ($p = 0.0079$), et la survie après oesophagectomie ($p = 0.0061$). On a retrouvé une corrélation significative ($p = 0.0145$) entre le taux élevé d'ACE dans le sérum et l'existence de métastases à distance. Cependant, aucune association entre la séropositivité de l'antigène CA 19-9 et la réséquabilité, la progression tumorale ou la survie n'a pu être mise en évidence. Ces résultats indiquent que l'élévation anormale de SCC dans le sérum est un facteur prédictif utile d'un cancer avancé de l'oesophage, et qu'elle est associée à une survie médiocre après oesophagectomie.

Resumen. El trabajo tiene como objetivo el averiguar si en el preoperatorio los niveles séricos de CEA, CA 19-9, y SCC son útiles para la estadificación del cáncer de esófago y para pronosticar la supervivencia de los pacientes tratados mediante esofaguectomía. Investigamos si la positividad sérica de estos marcadores tumorales se correlacionaba con la tasa de resecabilidad, parámetros clínicopatológicos de la extensión tumoral y resultados del tratamiento, tanto en pacientes con cáncer irresecable ($n = 63$) como resecable ($n = 267$). Una elevación anormal de los niveles séricos del SCC mostró una correlación significativa con la resecabilidad ($p < 0.0001$), profundidad de la invasión tumoral ($p < 0.0001$), afectación ganglionar ($p = 0.0015$), estadificación TNM ($p < 0.0001$) invasión linfática ($p = 0.0019$), de los vasos sanguíneos ($p = 0.0079$) y escasa supervivencia tras la esofaguectomía ($p = 0.0061$). Una correlación significativa se constató entre los niveles séricos elevados de CEA y las metástasis a distancia. Sin embargo, la positividad sérica del CA19-9 no mostró relación alguna con la resecabilidad, extensión tumoral y supervivencia de los pacientes. Nuestros resultados demuestran que la elevación anormal en suero del marcador tumoral SCC constituye un factor pronóstico útil en el cáncer avanzado de esófago, asociándose a una corta supervivencia tras esofaguectomía.

References

1. Nishimaki T, Suzuki T, Suzuki S, et al. Outcomes of extended radical esophagectomy for thoracic esophageal cancer. J. Am. Coll. Surg. 1998; 186:306–312
2. Munck-Wikland E, Kuylenstierna R, Londholm J, et al. Carcinoembryonic antigen, CA 19-9, and CA 50 in monitoring human squamous cell carcinoma of the esophagus. Anticancer Res. 1990;10:703–708
3. McKnight A, Mannell A, Shperling I. The role of carbohydrate antigen 19-9 as a tumor marker of oesophageal cancer. Br. J. Cancer 1989;60: 249–251
4. Nakamura T, Ide H, Eguchi R, et al. CYFRA 21-1 as a tumor marker for squamous cell carcinoma. Dis. Esophagus 1998;11:35–39
5. Shimada H, Takeda A, Arima M, et al. Serum p53 antibody is a useful tumor marker in superficial esophageal squamous cell carcinoma. Cancer 2000;89:1677–1683
6. Sobin LH, Wittekind Ch. TNM Classification of Malignant Tumours, 5th edition, New York, Wiley-Liss, 1997
7. Nishimaki T, Suzuki T, Tanaka Y, et al. Intramural metastases from thoracic esophageal cancer: local indicators of advanced disease. World J. Surg. 1996;20:32–37
8. Nishimaki T, Tanaka O, Suzuki T, et al. Patterns of lymphatic spread in thoracic esophageal cancer. Cancer 1994;74:4–11
9. Mino-Miyagawa N, Kimura Y, Hamamoto K. Tumor-antigen 4: its immunohistochemical distribution and tissue and serum concentrations in squamous cell carcinoma of the lung and esophagus. Cancer 1990;66: 1505–1512
10. Bates SE. Clinical applications of serum tumor markers. Ann. Intern. Med. 1991;115:623–638
11. Yamamoto K, Oka M, Hayashi H, et al. CYFRA 21-1 is a useful marker for esophageal squamous cell carcinoma. Cancer 1997;79:1647–1655
12. Kawaguchi H, Ohno S, Miyazaki M, et al. CYFRA 21-1 determination in patients with esophageal squamous cell carcinoma: clinical utility for detection of recurrences. Cancer 2000;89:1413–1417
13. Brockmann JG, St. Nottberg H, Glodny B, et al. Analysis of serum CYFRA 21-1 concentration in patients with esophageal cancer. Anticancer Res. 2000;20:4899–4904
14. Gion M, Tremolada C, Mione R, et al. Tumor markers in serum of patients with primary squamous cell carcinoma of the esophagus. Tumori 1989;75:489–493
15. Clark GW, Ireland AP, Hagen JA, et al. Carcinoembryonic antigen measurements in the management of esophageal cancer: an indicator of subclinical recurrence. Am. J. Surg. 1995;170:597–600
16. Kim YH, Ajani JA, Ota DM, et al. Value of serial carcinoembryonic antigen levels in patients with resectable adenocarcinoma of the esophagus and stomach. Cancer 1995;75:451–456
17. Sanders DS, Wilson CA, Bryant FJ, et al. Classification and localization of carcinoembryonic antigen (CEA) related antigen expression in normal oesophageal squamous mucosa and squamous carcinoma. Gut 1994;35:1022–1025
18. Nishimaki T, Suzuki T, Kanda T, et al. Extended radical esophagectomy for superficially invasive carcinoma of the esophagus. Surgery 1999;125:142–147
19. Nishimaki T, Tanaka O, Ando N, et al. Evaluation of the accuracy of preoperative staging in thoracic esophageal cancer. Ann. Thorac. Surg. 1999;68:2059–2064