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Surgical Results of Upper Thoracic Esophageal Carcinoma

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Background. Due to its anatomical location, carcinoma of the upper thoracic esophagus (i.e. below the thoracic inlet and above the carina) often results in early invasion of adjacent structures and precludes radical resection. The prognosis of carcinoma of the upper thoracic esophagus was considered worse than that of distal esophagus. There are few studies specifically addressing the prognostic factors in the surgical treatment for carcinoma in this location. Herein we report a retrospective study conducted to analyze the result of surgical treatment for carcinoma of the upper thoracic esophagus.

Methods. From January 1983 to December 2002, 298 cases were diagnosed with upper thoracic esophageal carcinoma in our institute. Among them, 78 cases underwent operation with curative intent and were enrolled for study.

Results. The tumors were stage I in 7.7%, stage II in 42.3%, stage III in 33.3% and stage IV in 12.8%. The postoperative morbidity and mortality rates were 59.0% and 6.8%, respectively. Pulmonary complication was the most common morbidity and also the leading cause of postoperative death. The overall median survival time after surgery was 13.1 months. The 1-, 3- and 5-year survival rates were 53.9%, 28.7% and 21.4%, respectively. There was an improvement in surgical result over time. The 5-year survival rate improved from 13.6% in the earlier 10-year period to 37.6% in the latter 10-year period ($p = 0.0493$). Univariate analysis revealed 5 positive prognostic factors: tumor length ($p = 0.0012$), pT status ($p = 0.0274$), pN status ($p = 0.001$), pathologic stage ($p = 0.0322$) and R category ($p = 0.0009$). Multivariate analysis identified pN status, R category and tumor length as independent prognostic indicators. In patients receiving neoadjuvant therapy, the 5-year survival rate after surgery was 23.4%, which was similar to those undergoing surgery alone ($p = 0.5174$). For patients with advanced tumor stages (ie. pT > 3, pN > 0, pM > 0) or with residual tumors ($R_{1/2}$ resection), the 5-year survival rates were significantly different in patients with and without postoperative adjuvant chemoradiation therapy (16.0% *vs.* 0%, $p = 0.0045$).

Conclusions. For carcinomas in the upper thoracic esophagus, the prognosis was dismal. Surgical resection remains the treatment of choice. In addition to lower resectability, the postoperative morbidity and mortality rates were relatively high. The length of tumor extension, status of lymph node involvement and radicality of surgery were independent prognostic factors.

Carcinoma of the esophagus is one of the most lethal malignant tumors, and it occurs frequently among the Chinese.[1,2] According to the official annual report of the Department of Heath in Taiwan, carcinoma of the esophagus was the ninth leading cause of cancer death in the population and the sixth leading cause in male gender in 2002. The incidence and death rate of carcinoma of the esophagus have been significantly rising during the past years. Annually, about 1-thousand deaths, i.e. 4.85 cases per 100,000 of population, were attributed to this disease in Taiwan.[3]

Surgical resection remains the mainstay of treatment

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for esophageal carcinoma. However, the disease is often far advanced at the time it is detected, and only a small number of patients are considered for curative resection and long-term survival. The results of treatment for esophageal carcinoma are generally unsatisfactory despite the advances in surgical techniques, the attempt to increase the radicality of nodal dissection, and the application of combined multimodal therapy.[4-7]

Due to its anatomical location in the upper mediastinum, carcinoma of the upper thoracic esophagus (i.e., below the thoracic inlet and above the level of the carina) often results in early involvement to the nearby structures and cervical lymph nodes. The intimate relationship between the esophagus and the airway, aortic arch, and recurrent laryngeal nerve in this region precludes wide local excision. Moreover, an extended lymphadenectomy is technically demanding and carries additional risks. The prognosis of upper thoracic esophageal carcinoma was reported to be worse than that in the distal esophagus.[8-10] In addition, the sensitivity to radiotherapy might differ from that in lower esophageal carcinoma.

Because carcinomas arising from the proximal esophagus are relatively uncommon, there are few studies available addressing the factors that influence the outcomes of treatment. In this study, we present our 20-year experience in treating upper thoracic esophageal carcinomas and analyze the parameters related to surgical results.

METHODS

Patients

Between January 1983 and December 2002, there were 298 cases of carcinoma of the upper thoracic esophagus diagnosed in our institute. Among them, 78 patients (26.2%) underwent surgical resection and were enrolled in this study. The preoperative assessments for these patients consisted of a detailed history-taking and physical examination, routine blood cell counts and biochemical studies, esophagogastroscopy with biopsy, barium esophagography, chest roentgenography and computed tomography, sonography of the abdomen and neck, and radioisotopic scanning of whole body bone. Bronchoscopy was performed routinely to exclude ingrowth of tumor into the mucosa of upper airways. All patients were operated on with curative intent. The tumors were staged after the operation according to the current TNM system of the American Joint Committee on Cancer (AJCC).[11]

After treatment, all patients were followed up regularly with systemic examinations of biochemical tests, chest radiography, sonography of abdomen and neck, and whole body bone radioisotope scans in 3- to 6-month intervals. The records of these 78 patients were analyzed retrospectively for the demographic characteristics, symptoms, and data regarding resection methods, pathologic findings, and hospital course.

Surgery

The surgical procedures have been described previously.[1] In brief, the majority of patients underwent a subtotal esophagectomy with locoregional mediastinal lymph node dissection through a right thoracotomy, followed by a combined midline laparotomy and left neck incision where upper abdominal and left cervical lymphadenectomy were carried out and then the esophageal reconstruction was established. Right cervical lymphadenectomy was not routinely performed unless involvement of cervical lymph node was suspected by preoperative sonography or computed tomography of the neck. In patients with poor cardiopulmonary function or unsatisfactory general condition, transhiatal esophagectomy was carried out. A feeding jejunostomy was placed routinely in all patients.

Adjuvant therapy

In eligible patients with locally advanced disease (pT4), regional lymph node metastasis (pN1), or evidence of gross or microscopic residual tumor, postoperative adjuvant radiotherapy or chemotherapy was administered if the patient agreed and the condition permitted. The total prescribed dose of irradiation ranged from 50 to 60Gy, depending on the patient's condition. Concurrent chemotherapy usually consisted of a platinum-based combination regimen of choice.[12] The adjuvant therapy was generally instituted 3 to 4 weeks after esophagectomy.

Statistical analyses

Survival analyses were performed using the Kaplan-

Meier method. Comparisons of survival between groups were assessed by log-rank test. Differences of clinicopathologic variables among groups were calculated using chi-squared test, Student's *t*-test or Mann-Whitney *U*-test when appropriate. Multivariate analysis with a stepwise Cox regression model was conducted to evaluate the significance of age, sex, length of tumor, T factor, N factor, M factor, overall pTNM stage, and R category as independent prognostic factors. A p value less than 0.05 was considered statistically significant. All the analyses were performed with SPSS software version 10.0 (SPSS Inc., Chicago, IL).

RESULTS

Clinicopathologic characteristics

Over a 20-year period, a total of 78 patients underwent surgical resection for cancers in the upper thoracic esophagus. The mean age of patients was 66 years (range, 37 to 80 years), with a male-to-female ratio of 12:1. The demographics and the modes of surgical procedure with regard to 2 consecutive time periods (period I from 1983 to 1992; period II from 1993 to 2002) are outlined in Table 1. The rate of surgical resection was 27.6% (45/163 patients) in period I, and 24.4% (33/135 patients) in period II. The surgical approaches included thoracotomy for 70 patients (89.7%), transhiatal approach for 7 (9.0%), and partial sternotomy for 1 patient (1.3%). For reconstruction of intestinal continuity, the stomach was utilized as a substitute for reconstruction in 71 patients (91.0%) whereas the left side colon was used in 7 patients (9.0%). The reconstruction was conducted through the retrosternal route in 70 patients (89.7%), and via the posterior mediastinum in the remainder. A radical resection (R_0 resection) was achieved in 51 cases (65.4%). In 18 patients (23.1%), macroscopic residual tumor (R_2 resection) was evident at operation. In the remaining 9 patients (11.5%), microscopic tumor involvement in the margin of resection (R_1 resection) was shown on pathological examination of the resected specimen. The percentage of R_0 resection was 72.7% in period II compared with 60.0% in period I ($p = 0.17$). Overall, neoadjuvant therapy was given to 16 patients (20.5%), including 13

Table 1. Patient demographics and tumor characteristics

	Total (n = 78)	Period I* (n = 45)	Period II* (n = 33)	*p value*
Sex (%)				
Male	72 (92.3)	43 (95.6)	29 (87.9)	0.21
Female	6 (7.7)	2 (4.4)	4 (12.1)	
Mean age (SD)	63.8 (9.4)	62.0 (7.7)	66.1 (11.1)	0.22
Median follow-up months (SD)	13.1 (42.5)	12.9 (47.4)	15.5 (35.2)	0.63
Mode of resection (%)				
Thoracotomy	70 (89.7)	42 (93.3)	28 (84.8)	
Transhiatal	7 (9.0)	2 (4.4)	5 (15.2)	
Partial sternotomy	1 (1.3)	1 (2.2)	0 (0)	0.16
Reconstruction (%)				
Stomach	71 (91.0)	40 (88.9)	31 (93.9)	
Colon	7 (9.0)	5 (11.1)	2 (6.1)	0.43
Route of reconstruction (%)				
Retrosternal	71 (91.0)	43 (95.6)	28 (84.8)	
Posterior mediastinal	7 (9.0)	2 (4.4)	5 (15.2)	0.10
R category (%)				
R0	51 (65.4)	27 (60.0)	24 (72.7)	
R1/2	27 (34.6)	18 (40.0)	9 (27.3)	0.17
Neoadjuvant Chemoradiotherapy (%)				
Yes	16 (20.5)	13 (28.9)	3 (9.1)	
No	62 (79.5)	32 (71.1)	30 (90.9)	0.03

*Period I = 1983~1992; Period II = 1993~2002.

cases in period I (13/45 patients, 28.9%) and 3 in period II (3/33 patients, 9.1%). The period I group had a significantly higher rate of receiving neoadjuvant therapies than the period II group ($p = 0.03$). Otherwise there was no difference in sex, age, types of surgical resection and R categories between these 2 period groups.

The most common clinical manifestations included swallowing disturbance, weight loss and substernal pain (Table 2). The presence of symptoms was not shown to be related to the stages of tumor or clinical outcomes.

The histological classifications of the tumors were all squamous cell carcinoma in our study. The pathologic T, N, M categories and stages for to the 2 time periods are summarized in Table 3. As compared with period I, the period II group was associated with earlier pT status and overall pTNM stage ($p = 0.002$, $p = 0.003$, respectively). The proportion of pT0 and pT1 tumors in period II (21.2%) was approximately 3 times higher than that in period I (6.7%), whereas the proportion of pT4 tumors in period II (12.1%) was about half that in period I (26.7%). There was no difference in pN status and pM status between these 2 period groups ($p = 0.84$ and 0.48 respectively).

In terms of the status of lymph node metastasis with regard to pT category, regional lymph node metastases were 3 times more frequently found in patients with pT3~4 stage than in pT0~2 stage (42.1% *vs.* 14.3%, $p = 0.016$). Metastases to other organs were detected at operation in 5 patients, 2 metastasizing to the lungs, 2 to the celiac lymph nodes and 1 being found in the thyroid gland.

Forty-six patients (59.0%) developed 1 or more postoperative complications listed in Table 4. Pulmonary complication, namely pneumonia and respiratory failure, was the most frequent postoperative complication. It occurred in 22 patients (28.2%). Thirty patients (38.5%) had 1 or more surgical complications. Among them, 15 patients (19.2%) had a cervical anastomotic leakage and

Table 2. The presenting symptoms

Symptoms	n	%
Swallowing disturbance	70	89.7
Weight loss	27	34.6
Substernal pain	18	23.1
Regurgitation	7	9.0
Choking	5	6.4
Cough	3	3.8
Heart burn	2	2.6
Hoarseness	2	2.6
Hiccup	1	1.3

Table 3. Pathologic T, N, M category and stage with regard to two periods

		Total (n = 78)	Period I* (n = 45)	Period II* (n = 33)	*p value*
pT					
	T0	3 (3.8%)	3 (6.7%)	0 (0.0%)	
	T1	7 (9.0%)	0 (0.0%)	7 (21.2%)	
	T2	11 (14.1%)	6 (13.3%)	5 (15.2%)	
	T3	41 (52.6%)	24 (53.3%)	17 (51.5%)	
	T4	16 (20.5%)	12 (26.7%)	4 (12.1%)	0.002
pN					
	N0	51 (65.4%)	29 (64.4%)	22 (66.7%)	
	N1	27 (34.6%)	16 (35.6%)	11 (33.3%)	0.84
pM					
	M0	68 (87.2%)	41 (91.1%)	27 (81.8%)	
	M1	5 (6.4%)	2 (4.4%)	3 (9.1%)	
	M1a	5 (6.4%)	2 (4.4%)	3 (9.1%)	0.48
Stage					
	Stage 0	3 (3.8%)	3 (6.7%)	0 (0%)	
	Stage I	6 (7.7%)	0 (0%)	6 (18.4%)	
	Stage IIa	31 (39.7%)	17 (37.8%)	14 (42.4%)	
	Stage IIb	2 (2.6%)	2 (4.4%)	0 (0%)	
	Stage III	26 (33.3%)	19 (42.2%)	7 (21.2%)	
	Stage IVa	5 (6.4%)	2 (4.4%)	3 (9.1%)	
	Stage 1Vb	5 (6.4%)	2 (4.4%)	3 (9.1%)	0.003

* Period I = 1983~1992; Period II = 1993~2002.

Table 4. Postoperative complications

	n	(%)
Medical		
Pulmonary complications	22	(28.2)
Pneumonia	12	(15.4)
Respiratory failure	10	(12.8)
Cardiac arrhythmia	2	(2.6)
Acute renal failure	2	(2.6)
Myocardial infarction	1	(1.3)
Surgical		
Cervical anastomotic leakage	15	(19.2)
Vocal cord paralysis	13	(16.7)
Unilateral	11	(14.1)
Bilateral	2	(2.6)
Chylothorax	5	(6.4)
Hemorrhage	1	(1.3)

13 patients (16.7%) developed vocal cord paralysis. Of the 15 patients with cervical anastomotic leaks, only 1 patient required revision of the cervical anastomosis. The remaining 14 patients were treated conservatively and the leakage closed spontaneously. Postoperative vocal cord paralysis was unilateral in 11 patients and bilateral in 2 cases, all of whom had a pT3/T4 tumor. Five patients (3.8%) developed chylothorax. Among them, 4 cases resolved with conservative management and 1 patient underwent thoracotomy and ligation of the thoracic duct. The median postoperative hospital stay was 27.0 days (range, 9 to 87 days), 16.5 days for patients without complications and 33.0 days for patients with 1 or more postoperative complications ($p < 0.001$). There were 4 cases of 30-day mortality (6.8%). Three died of pulmonary complications and 1 of acute myocardial infarction.

Survival and prognostic factors

Follow-up was completed in all patients. The median follow-up time was 13.1 months, ranging from 0.4 to 223.9 months. The overall median survival time was 13.1 months; the cumulative 1-, 3- and 5-year survival rates were 53.9%, 28.7% and 21.4%, respectively, which were significantly better than in the non-surgical group ($p < 0.0001$, Fig. 1). When the result was analyzed with regard to 2 periods, a better outcome was observed in period II (Fig. 2). Excluding 30-day mortality, the 1-, 3- and 5-year survival rates in period I were 54.6%, 20.5%, and 13.6%, comparing to 60.0%, 45.5%, and 37.6% in period II ($p = 0.0493$). The difference in survival was even more prominent when only pN0 cases were taken for comparison (5-year survival rate 14.8% *vs*. 57.5%, $p = 0.003$).

The relationships between clinicopathological characteristics and prognosis are summarized in Table 5. Tumor length, pT status, pN status, pathologic stage and R category were significantly correlated with survival. For patients with tumor less than 4 cm in length, the prognosis was favorable. The median survival time of these patients was 38.2 months, compared with 9.7 months for patients with tumor 4 cm or more in length ($p = 0.0012$, Fig. 3A). Patients with earlier pT (ie. pT0/T1/T2), pN (ie. pN0) status and pTNM stage tended to have better outcomes after surgery ($p = 0.0274$, $p = 0.0010$, $p = 0.0322$ respectively, Figs. 3B-D). The radicality of surgery was significantly related to survival. For patients with R_0 resection, the median survival was 28.3 months, which declined to 9.2 and 7.9 months, respectively, for patients with R_1 and R_2 resections. The 5-year survival rates were 32.3, 12.7 and 5.6%, respectively ($p = 0.0009$, Fig. 3E). Six factors with p value less than 0.1 in univariate survival analyses (ie. tumor length, pT, pN, PM status, pTNM stage and R category) were selected for entry into multivariate survival analysis with a

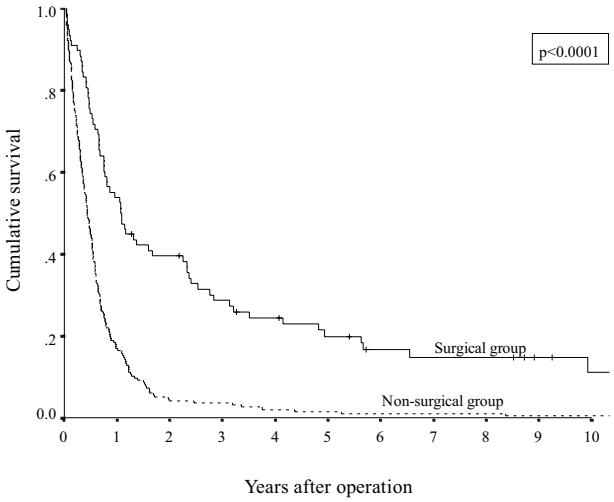

Fig. 1. Overall survival curves for patients with upper thoracic esophageal cancer, undergoing esophagectomy (surgical group, n = 78) or non-surgical treatment (non-surgical group, n = 220) between 1983 and 2002.

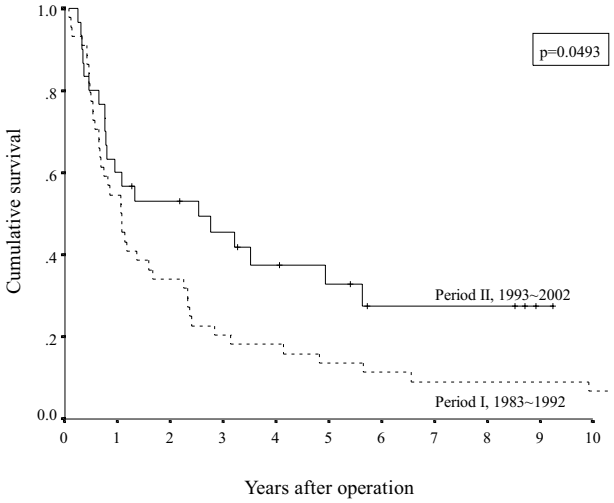

Fig. 2. Survival curves (excluding 30-day mortality) with respect to time periods. Period I: 1983~1992, Period II: 1993~2002.

Table 5. Relationships between clinicopathological characteristics and prognosis by univariate analysis

		No. of patients	Median survival (months)	Survival rate (%)			*p* value
				1-year	3-year	5-year	
Age at presentation							
Age ≥ 65	Yes	44	11.6	50.0	31.3	23.3	
	No	34	13.1	58.8	25.1	18.8	0.9153
Symptoms/Signs							
Swallowing disturbance	Yes	70	12.9	52.9	25.3	17.6	
	No	8	60.1	62.5	62.5	62.5	0.1169
Weight loss	Yes	27	11.6	48.2	29.6	18.5	
	No	51	13.9	56.9	27.9	23.2	0.9639
Tumor length							
≥ 4 cm		50	9.7	46.0	14.9	8.5	
< 4 cm		28	38.2	67.9	53.3	45.0	0.0012
pT stage							
T0/T1/T2		21	34.5	71.4	49.7	44.2	
T3/T4		57	10.4	47.4	21.1	14.0	0.0274
pN stage							
N0		51	20.3	64.7	38.1	31.5	
N1		27	7.9	33.3	11.1	3.7	0.0010
pM stage							
M0		68	13.9	55.9	29.9	23.2	
M1		10	9.4	20.0	0.0	0.0	0.0694
Pathological stage							
I		9	60.1	83.3	83.3	83.3	
II		33	16.0	57.6	30.3	27.3	
III		26	7.9	42.3	19.2	7.7	
IV		10	9.4	44.4	20.0	10.0	0.0322
R category							
R_0		51	28.3	68.6	37.9	29.1	
R_1		9	9.2	11.1	11.1	11.1	
R_2		18	7.9	33.3	11.1	5.6	0.0009
Neoadjuvant therapy							
Yes		16	16.6	56.3	37.5	23.4	
No		62	12.9	53.2	26.4	20.9	0.5174

stepwise Cox regression model. Tumor length, pN status and R category were identified as independent prognostic factors (Table 6).

Preoperative chemo-radiotherapy (CRT) was performed in 16 patients. Nevertheless, it did not affect the prognosis significantly ($p = 0.5174$, Fig. 4A). For patients with advanced stage of tumor (ie. PT > 3, pN > 0 or pM > 0) or with microscopic or macroscopic residual tumors (R_1 or R_2 resection), postoperative adjuvant CRT conferred beneficial effect on prognosis (Fig. 4B). The median survival time was 5.5 months for patients with surgery alone and 12.8 months for those undergoing surgery plus postoperative CRT. The 1-, 3-, 5-year survival rates in the 2 groups were 21.1%, 10.5%, 0% and 52.0%, 24.0%, 16.0%, respectively ($p = 0.0045$).

Table 6. Multivariate analysis of prognostic factors

	Relative risk	95% CI	*p* value
Tumor length			
< 4 cm	1		
≥ 4 cm	1.842	1.012 - 3.353	0.045
pT status			
pT0/T1/T2	1		
pT3/T4	1.355	0.650 - 2.824	0.417
pN status			
pN0	1		
pN1	1.937	1.146 - 3.275	0.014
pM status			
pM0	1		
pM1a/b	1.088	0.494 - 2.396	0.835
pTNM stage			
Stage I/II	1		
Stage III/IV	1.543	0.683 - 3.488	0.297
R category			
R_0 resection	1		
R_1/R_2 resection	1.951	1.129 - 3.369	0.017

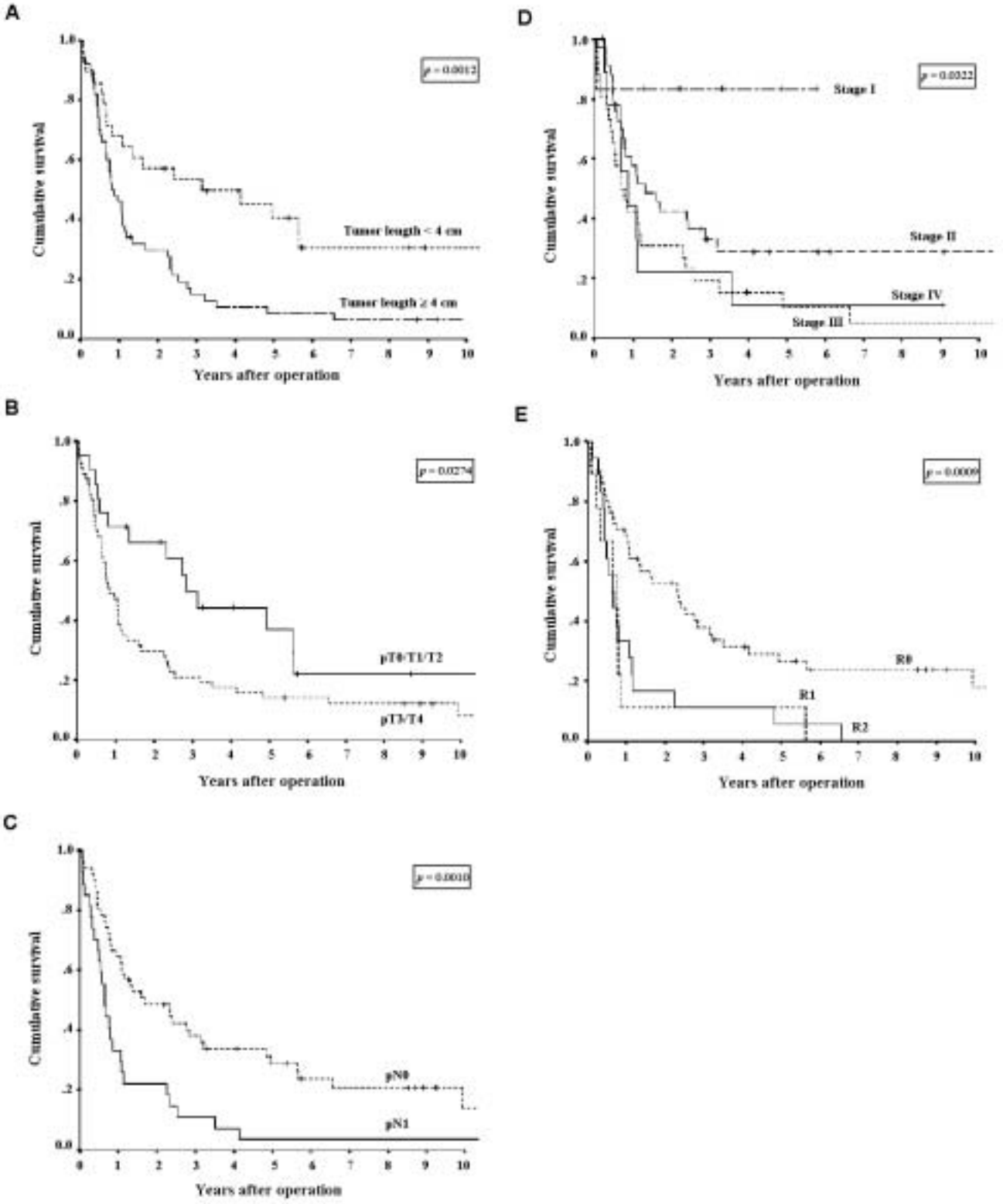

Fig. 3. Survival curves with regard to clinicopathologic variables: the length of tumor (**A**), the depth of tumor invasion (**B**), regional lymph node status (**C**), pathologic-TNM stage (**D**), and radicality of surgery (**E**).

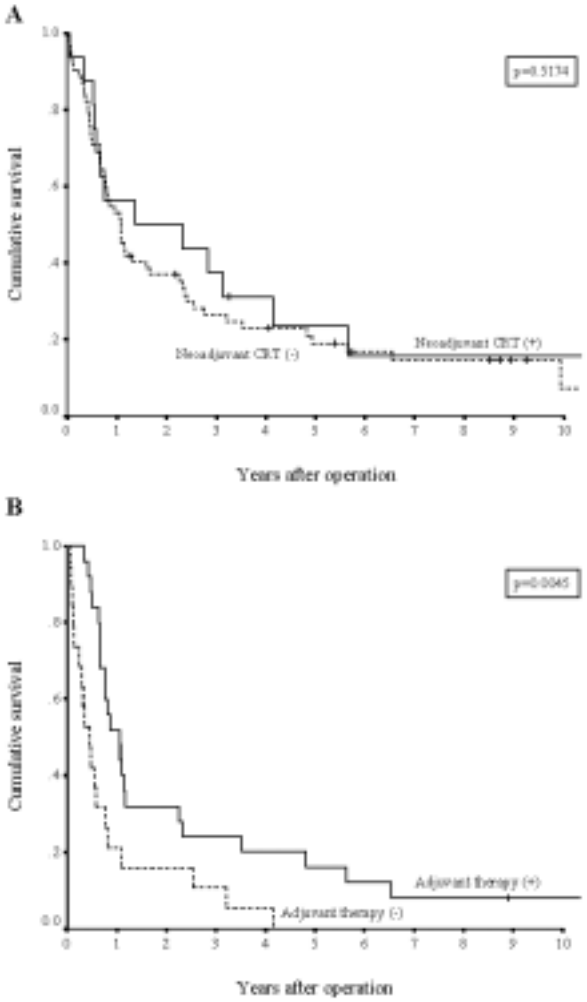

Fig. 4. Effect of neoadjuvant chemo-radiotherapy (CRT) on overall survival (**A**), and postoperative adjuvant therapy on prognosis of patients with advanced tumor stages, ie. pT4, pN1 or pM1, or with residual tumors, ie. R_1 or R_2 resections (**B**).

DISCUSSION

It has been reported that the survival of patients with upper thoracic esophageal carcinoma is worse than that of patients with a carcinoma at other sites of the thoracic esophagus.[8-10] In our study, the median survival time after surgical resection was 13.1 months, and the 1-, 3- and 5-year survival rates were 53.9%, 28.7% and 21.4%, respectively, which were comparable to the results of previous studies.[9,10] Moreover, our study showed a significant improvement in the outcomes of surgical treatment over time. The 5-year survival rate after surgery improved from 13.6% in period I (from 1983 to 1992) to 37.6% in period II (from 1993 to 2002). This improvement in surgical outcome may be explained partly by the earlier tumor stages of the patients operated (Table 3), which might be due to earlier diagnosis and more stringent selection criteria for surgery in the latter period. Additionally, for patients with the same pN0 stage, the 5-year survival rate after surgery had improved significantly, from 14.8% in period I to 59.6% in period II (p = 0.013). The improved surgical results might be explained by the advances in locoregional disease control and accurate tumor staging as well as the introduction of en-bloc resection around the early 1990s.

Postoperative complications had been reported in as high as 61.5 to 71.4% of patients undergoing surgery for the upper thoracic esophageal carcinomas.[8,10,13] The morbidity rates were higher than that in distal esophageal carcinomas, reflecting the disease characteristics and the technical difficulties in surgery of the proximal esophagus. In the present study, the overall postoperative complication rate was 59.0%, which was higher than the average complication rates after surgery for esophageal carcinomas at all levels in our previous study.[1,2,7] Pulmonary complication was the most frequent postoperative complication and also the leading cause of surgical mortality. It was shown that the use of postoperative epidural analgesia and bronchoscopy (for clearance of pulmonary secretion) could reduce postoperative pulmonary complications and hospital death rate.[14] Now both measures are the common practices in our institute. Moreover, our previous study also showed the nutrition status to be an important determinant of postoperative pulmonary complications.[12] Therefore, for performance of such a high-morbidity surgery, preoperative nutrition support and utmost perioperative care must be taken to prevent pulmonary complications.

Surgical complications (complications directly related to surgical procedures) occurred in 38.5% of patients. Although the rate was high, most of the complications were minor ones and were managed with conservative measures. Only 2 patients required additional surgical interventions, including 1 case undergoing revision of cervical esophagogastrostomy because of persistent anastomotic leakage and another patient receiving second thoracotomy and thoracic duct ligation to treat chylothorax. Overall, the surgical mortality rate (death

within 30 days) was 6.8%, which was similar to the average 30-day mortality rate after surgery for esophageal carcinoma in our previous study.[1,7] When 30-day mortalities were excluded, the 5-year survival rate for patients who developed postoperative complications was 19.6%, which was similar to 22.5% for patients without postoperative complications (p = 0.74). This indicated that long-term survival was not significantly affected by the occurrence of early postoperative complications.

Several clinicopathological parameters have been demonstrated to be related to the outcome after surgery for esophageal carcinoma, including pTNM staging, tumor length, number of involved lymph nodes, ratio of positive lymph nodes, tumor differentiation, body weight change, and serum levels of CRP, SCC antigen and soluble interleukin-2 receptor-α.[1,2,15-20] Nonetheless, there are only a few studies specifically addressing the prognostic factors of upper thoracic esophageal carcinomas. In the present study, univariate analysis revealed 5 factors (i.e. the length of tumor, pT status, pN status, pathologic stage and R category) to be related to patient survival. Multivariate analysis identified 3 independent prognostic indicators: pN status, R category and tumor length. The importance of lymph node status as an independent prognostic factor was in accordance with other studies previously reported.[16,21] It is well recognized that radical resection of esophageal carcinomas above the tracheal bifurcation may be compromised because of the proximity of the trachea and the recurrent laryngeal nerves. The rate for R_0 resection was reported to be lower in patients with a proximal tumor than distal group.[8,10] In our study, curative resection (R_0) was achieved in 51 patients (65.4%). The prognosis of patients with non-curative (R_1/R_2) resection was dismal, with median survival of less than 10 months (9.2 months for R_1 resection, and 7.9 months for R_2 resection). The most common cause of R_1/R_2 resection was due to invasion of the tumor to the trachea or bronchus. There have been a few studies proposing an aggressive surgical approach for esophageal carcinoma with airway invasion.[22, 23] However, our data suggested that if a residual tumor is to be anticipated following surgery, an aggressive surgical approach might not be warranted due to its poor result, high recurrence rate and associated morbidities. Instead, our previous study indicated that multimodal therapy might be better for this group of patients.[12] A recent study analyzing 10,441 patients of esophageal carcinomas in the United States had shown the significance of tumor length as a positive prognostic factor and proposed a new TNM classification system in which the pT subclassifications were redefined using both the depth of tumor invasion and the length of tumor extension as parameters.[16] In the present study, the length of tumor also constituted an independent prognostic factor. The surgical result was favorable if the tumor length was less than 4 cm.

The effect of neoadjuvant chemoradiotherapy on the treatment of esophageal carcinomas remains controversial. Some randomized studies concluded that neoadjuvant therapy had no beneficial effects on survival,[24,25] while others did show promising results.[26] In a study focusing on the role of preoperative chemoradiotherapy in the management of upper thoracic esophageal squamous cell carcinoma, Tsujinaka, *et al*. showed that preoperative chemo-irradiation therapy contributed to downstaging of the tumors, but no significant survival benefit was observed.[27] In our series, there was no significant difference in survival between the 2 groups of patients with or without neoadjuvant therapy. However, since this was a retrospective analysis, the patient selection might be biased and the treatment programs were not uniform, so the survival benefit could not be adequately assessed. In terms of postoperative adjuvant therapy, our study showed a beneficial effect on survival among patients with advanced stages or with residual tumors. The result was in accordance with a recent multi-center randomized controlled trial concerning the effect of postoperative adjuvant chemotherapy.[28]

In conclusion, our study demonstrated that the prognosis of patients with upper thoracic esophageal carcinoma remains poor. Surgery could offer an opportunity for long-term survival but was associated with a high morbidity rate. Pulmonary complication was the leading cause of surgical mortality, and it should be prevented with adequate preoperative nutrition support and utmost perioperative care. An improvement in surgical result over time has been observed during the past 20 years, which may reflect the advances and refinement in surgical procedures, resulting in better locoregional disease control. The length of tumor extension, status of lymph node involvement and radicality of surgery were the 3

most important prognostic factors. In this retrospective study, preoperative neoadjuvant therapy added no survival benefit, but postoperative chemo-irradiation therapy might confer beneficial effects to patients with a tumor of advanced stages or with residual tumors after surgery.

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