ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN-POLONIA
VOL. LX, N 1, 54 SECTIO D 2005

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Survival rate in patients with esophageal carcinoma treated with neoadjuvant chemotherapy followed by surgery

The incidence of adenocarcinoma of the esophagus is rising faster than any other malignancy. The prognosis of esophageal carcinoma is poor (9,10,11). About one-half of esophageal cancer patients present with locally advanced unresectable disease or distant metastasis (7). Single-modality or multi-modality therapy may be applied in patients with esophageal carcinoma. Chemotherapy, radiotherapy and surgical resections may be used (3,12,13). Surgical esophagectomy remains the preferred treatment for clinically localized thoracic esophageal carcinoma (3,7,10). Both chemo- and radiotherapy may be used as pre- or post-operative treatment (4). The evaluation of changes in neoplastic lesions in response to pharmacological treatment is en increasingly important task for radiologist(1).

The aim of the study was assessment of the patient survival depending on the degree of response to neoadjuvant chemotherapy.

MATERIAL AND METHODS

The material comprises a group of 47 men (aged 35–72 years) and five women (aged 40–54 years) with diagnosed esophageal carcinoma. In all patients CT examination of the esophagus was performed, using CT scanner Somatom AR. T by Siemens, in 5mm thick axial sections before and after administering contrast agent intravenously and orally. The control CT examination was performed in each patient after the proper course of neoadjuvant chemotherapy, using the same scanning protocol.

RESULTS

Adenocarcinoma was found in 16 patients and squamouscell carcinoma in 36. Twenty-five patients were in clinical stage II A, five patients in stage II B and 22 patients wwere in stage III. The narrowing of the esophageal lumen was found in 51 patients, with dilatation above the narrowing in 30 of them. The thickness of the esophageal wall was between 5–25mm (Fig. 1). The length of the tumor was clearly seen on MPR reconstructions (Fig. 2).

After chemotherapy the complete CT response (CR) was found in six patients (11.54%), and in three of them it was complete histopathological response. In 15 patients the partial response (PR) was found. In 21 patients there was no change (SD) after chemotherapy, and in 10 the progression was found (PD). The mean survival period was 31.33 months in CR group, 39.0 months in PR group, 16. 63 month in SD group and 10.56 months in PD group. Analysis of variance showed the statistically significant differences between mean survival period in a group with partial response and groups with stable disease and progression ($p=0.021$; Fig. 3).

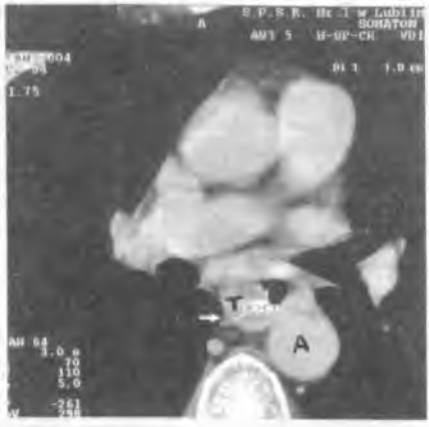

Fig. 1. Esophageal carcinoma; A– aorta, T – tumor

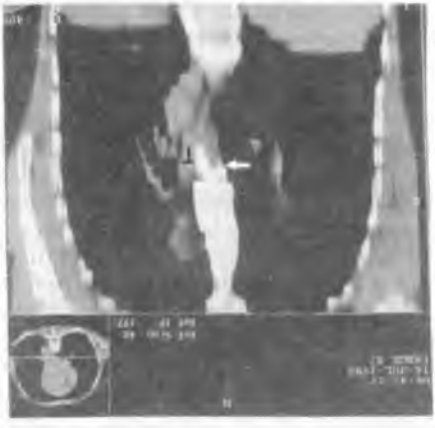

Fig. 2. Esophageal carcinoma – MPR reconstruction

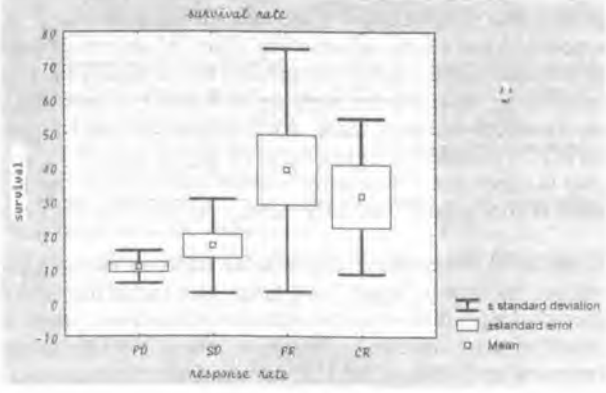

Fig. 3. Analysis of variance. Survival period clearly longer in patients with partial or complete response to neoadjuvant chemotherapy

Table 1. Analysis of variance. The mean survival period in group of different response to neoadjuvant chemotherapy

Marked differences are statistically significant p < 0.05000				
Response	PD	SD	PR	CR
	M=10.556	M=16,625	M=39.000	M=31.333
PD		0.521931	*0.006744*	0.088179
SD	0.521931		*0.013123*	0.180699
PR	*0.006744*	*0.013123*		0.500386
CR	0.088179	0.180699	0.500386	

DISCUSSION

Neoadjuvant treatment of esophageal cancer prior to surgery was thought to improve survival by reduction of the primary tumor lesion as well as of regional and systemic tumor spread. However until now, prospective randomized trials could not prove the effectiveness of chemotherapy in terms of prolonged survival or higher rate of cure (3,5). Single-agent therapy response in this disease is modest (10 to 40%), combination therapy has been more promising, with response rates between 50% and 70% for cisplatin-based doublets (2). One advantage of preoperative chemotherapy for esophageal cancer is the possibility of downstaging the primary tumor and hence enhancing resectibility, allowing a more conservative surgical approach, and also potentially improving local control. Another advantage is the ability to assess response to preoperative chmotherapy directly in the primary tumor, making the end point of adjuvant therapy more precise by identifying those patients who respond to chemotherapy and who might therefore benefit from postoperative chemotherapy. The most important advantage however is that early administration of chemotherapy facilitates treatment of subclinical metastatic disease at a time when chemotherapy is likely to have its greatest impact (6,8,9). Preoperative chemotherapty treatment should result in better drug delivery to the tumor as the local blood supply has not been disturbed by operative dissection. Distant control should be enhanced as remote micrometastases are treated early without having to wait for postsurgical recovery (2). Though radiographic improvement can be seen in up to one half of patients, two or three cycles (6–12 weeks) of chemotherapy are required, relief of dysphasia is slow and/or incomplete, and survival is anecdotal. Unfortunately, there is no way to select "responders" prior to beginning therapy, leaving 50% of patients without a hope of benefit from therapy (2).

The drawback of early systemic therapy, in general include the theoretical possibility of a growth advantage for tumor cells undergoing spontaneous mutation into chemotherapy-resistant tumor cells and the possibility of a delay in achieving effective local tumor control, increasing the risk of tumor spread from the primary during preoperative chemotherapy (4,5,6,12,13).

The standard method for assessing the response of a tumor to treatment is to determine its change in maximum cross-sectional area. Using WHO criteria for tumor response are as follows: • Complete response (CR) – complete disappearing of all known disease. • Partial response (PR) – at least 50% reduction in tumor size. • No change – stable disease (SD) – neither PR or PD. • Progression of the disease (PD) – greater than 25% increase in size of at least one lesion (or a new lesion) (1).

The survival depends on the response degree to neoadjuvant chemotherapy, and in groups with partial and complete response is longer. For a group with partial response the survival period is statistically significantly longer than in groups with stable disease and progression.

In attempt to establish more accurate evaluation criteria in 1994 the European Organization for Research and Treatment in Oncology, the US National Cancer Institute and the National Cancer Institute of Canada introduced new guidelines, called: Respond Evaluation Criteria in Solid Tumors (RECIST). While WHO criteria evaluated response to treatment by means of a bidimen-

sional evaluation, defined by the maximum axial diameter of the lesion, the new guidelines require a unidimensional evaluation, defined by the maximum axial diameter of the lesion, which is considered sufficient to assess the level of response to treatment. In RECIST the partial response is defined as a >30% decrease in the sum of the longest diameters of target lesions, progression is defined as a >20% increase in the sum of the longest diameters (1).

Chemotherapy offers the treatment of distant foci of tumor. However, the results from the use of chemotherapy as a single-line therapy have been disappointing. Both chemotherapy and radiation may be used as preor postoperative therapy (3).

CONCLUSIONS

CT enables precise assessment of esophageal carcinoma response to neoadjuvant chemotherapy. The WHO criteria of tumor response are the most widely used. The CT assessment provides the precise evaluation of the diameters of the tumor, and the presence of local and distal lymph node enlargement and metastases. The survival period depend directly on the response degree to neoadjuvant chemotherapy, and is longer for patients with partial or complete regression of the disease.

REFERENCES

1. Bellomi M. et al.: Evaluation of the response to the therapy of neoplastic lesions. Radiol. Med., 107, 450, 2004.
2. DeCamp M. M. Jr. et al.: Esophagectomy after induction chemoradiation. Chest, 116, 466S, 1999.
3. Entwistle J. W. C. et al.: Multimodality therapy for resectable Cancer of the thoracic esophagus. Ann. Thorac. Surg., 73, 1009, 2002.
4. Flamen P. et al: Position of positron emission tomography and other imaging diagnostic modalities in esophageal cancer. Q. J. Nucl. Med. Mol. Imaging, 48, 96, 2004
5. Heise J. W. et al.: Expense and benefit of neoadjuvant treatment in squamous cell carcinoma of the esophagus. BMC Cancer, 1, 20, 2001.
6. Kelsen D. P., Ilson D. H.: Chemotherapy and combined-modality therapy for esophageal cancer. Chest, 107, 224S, 1995.
7. Koshy M. et al.: Multiple management modalities in esophageal cancer: Epidemiology, presentation and progression, work-up. and surgical approaches. The Oncologist, 9, 137, 2004.
8. Koshy M. et al.: Multiple management modalities in esophageal cancer: Combined modality management approaches. The Oncologist, 9, 147, 2004.
9. Lerut T. et al.: Treatment of Esophageal Carcinoma, Chest, Supplement, 116, 463, 1999
10. Malthaner R.A. et al.: Neoadjuvant or adjuvant therapy for resectable esophageal cancer: a systematic review and meta-analysis. BMC Medicine, 2, 35, 2004.
11. Malthaner R.A. et al.: Neoadjuvant or adjuvant therapy for resectable esophageal cancer: a clinical practice guideline. BMC Cancer, 4, 67, 2004.
12. Shimada H. et al.: Treatment response and prognosis of patients after recurrence of esophageal cancer. Surgery, 133, 24, 2003.
13. Stein H. J. et al.: Esophageal cancer: patient evaluation and pre-treatment staging. Surgical Oncology, 10, 103, 2001.

SUMMARY

The aim of the study was presenting the use of CT in evaluating esophageal carcinoma response to neoadjuvant chemotherapy. The material comprises a group of 47 men (aged 35–72

years) and 5 women (aged 40–54 years) with diagnosed esophageal carcinoma. In all patients CT examination of the esophagus was performed, using CT scanner Somatom AR. T by Siemens, in 5 mm thick axial sections before and after administering contrast agent intravenously and orally. The control CT examination was performed in each patient after the proper course of neoadjuvant chemotherapy, using the same scanning protocol. Adenocarcinoma was found in 16 patients and squamouscell carcinoma in 36. Twenty-five patients were in clinical stage II A, five patients in stage II B and 22 patients were in stage III. The narrowing of the esophageal lumen was found in 51 patients, with dilatation above the narrowing in 30 of them. The thickness of the esophageal wall was between 5–25 mm. After chemotherapy the complete CT response was found in six patients (11.54%) (Fig. 1), and in three of them it was complete histopathological response. In 15 patients (28.85%) the partial response was found (Fig. 2). In seven patients minimal response was found. In 14 patients there was no change after chemotherapy (Fig. 3), and in 10 the progression was found (Fig. 4). Total response rate was 53.85%. Local lymph node enlargement was found in 23 patients. In four of them there were enlarged multiple lymph nodes. After chemotherapy the enlarged local lymph node were found in 17 patients. Conclusions: CT enables precise assessment of esophageal carcinoma response to neoadjuvant chemotherapy. The WHO criteria of tumor response are the most widely used. The CT assessment provides the precise evaluation of the diameters of the tumor, and the presence of local and distal lymph node enlargement and metastases. The survival period depends directly on the response degree to neoadjuvant chemotherapy, and is longer for patients with partial or complete regression of the disease.

Ocena przeżycia pacjentów z rakiem przełyku, leczonych przedoperacyjną chemioterapią

Celem pracy jest przedstawienie zastosowania TK w ocenie stopnia odpowiedzi na chemioterapię przedoperacyjną raka przełyku. Materiał obejmuje 47 mężczyzn i 5 kobiet z rakiem przełyku. U wszystkich pacjentów wykonano badanie TK przełyku przed i po przedoperacyjnej chemioterapii. Oceniano stopień odpowiedzi na leczenie przedoperacyjne. Po chemioterapii całkowitą odpowiedź TK stwierdzono u 6 pacjentów (11,54%), a 3 z nich miało całkowitą odpowiedź histopatologiczną. U 15 pacjentów (28.85%) stwierdzono częściową odpowiedź. U 7 pacjentów stwierdzono odpowiedź minimalną, u 14 brak zmian po leczeniu. U 10 pacjentów stwierdzono progresję choroby. Całkowity odsetek odpowiedzi na chemioterapię przedoperacyjną wynosi 53,85%. Wnioski: TK umożliwia precyzyjną ocenę stopnia zaawansowania raka przełyku oraz ocenę stopnia odpowiedzi na przedoperacyjną chemioterapię. Kryteria WHO stopnia odpowiedzi guza na leczenie są stosowane powszechnie. Przeżycie zależy bezpośrednio od stopnia odpowiedzi na chemioterapię i jest dłuższe dla pacjentów, u których stwierdzono częściową lub całkowitą regresję zmian.