What Is the Role of Surgery in Multimodality Treatment of Localized Oesophageal Cancer?

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Despite improved surgical techniques, which increased the rate of complete tumour resection (RO resection) and improved perioperative management, which reduced perioperative morbidity and mortality, the prognosis of patients with oesophageal cancer has not essentially changed over the past four decades. In the Western countries 5-year survival rates have remained below 10% [1, 2]. This reflects the fact that even if the disease is still localized, about 70% of the patients present with T3/T4 and/or N-positive lesions at the time of diagnosis, where these tumours are usually beyond of cure by standard treatment, e.g. surgery or radiotherapy.

As a consequence, multimodality treatment has gained increasing interest within the past 15 years, and the question has been raised, if surgery definitively adds some benefit to the outcome of patients with localized oesophageal cancer. Recent investigations with combined treatment modalities including surgery showed that neither the combination of pre-/postoperative radiotherapy with surgery nor preoperative chemotherapy were able to significantly influence the prognosis of patients with localized oesophageal cancer [3]. On the other hand, a randomized trial of the Radiation Therapy Oncology Group (RTOG) proved that concurrent chemotherapy (cisplatin, 5-fluorouracil) and radiation (50 Gy) is superior to radiotherapy alone (60 Gy) in terms of local tumour control, distant recurrence and overall survival [4]. This prompted investigators – particularly in the U.S. – to state that the use of concurrent chemoradiotherapy (without surgery) should be recommended for patients with localized oesophageal cancer.

However, there may be some important pitfalls in the interpretation of the published data on multimodality treatment. (1) The terms localized or local-regional oesophageal cancer include patients with much different prognosis by standard treatment. Most trials did not differentiate between more early or 'potentially resectable' tumours, which means tumour stages T1-2 NX MO (UICC, [5]) and 'locally advanced' tumours, comprising tumour stages T3-4 N0-1 MO. The latter can hardly be cured by surgery, whereas in patients with T1/2 NO tumours 5-year survival rates of about 40% may be achieved after surgery. (2) Most trials basing on clinical staging did not include modern staging procedures. The assessment

of tumour infiltration and lymph node involvement by computed tomography or magnetic resonance imaging without endoscopic ultrasound does not reach a sensitivity of more than 50%. Thus, data of phase-II trials with and without surgery should be compared very carefully. (3) Many authors mixed results achieved in oesophageal carcinoma of different histology. Although retrospective analyses of combined treatment modalities usually could not show a prognostic difference between squamous cell and adenocarcinoma, future trials should focus on one distinct

histology. This is rather because of the histology than because of the tumour localization. Adenocarcinomas mostly occur below the tracheal bifurcation, where complete tumour resection as well as intra-ab-dominal lymph node metastases are much more likely. From this point of view it seems wise to treat this tumour entity similar to gastric cancers and to generally include surgery into the treatment.

So, what can we conclude from the published data regarding the role of surgery in squamous cell carcinoma of the oesophagus, when taking into consideration all these issues?

Potentially Resectable Tumours (T1-2 **IMO-1** MO)

In the Western countries, only 20% of the tumours were discovered in these early stages. Surgery offers the patients a probability of survival at 5 years of 40-50%, with a perioperative mortality rate of 5% and less in experienced centres. So far, there is no evidence that perioperative chemo/radiotherapy might improve these results [3]. Four randomized trials showed that a subgroup of patients who responded to preoperative chemotherapy had a distinct benefit compared to those with surgery alone. But this was not true for the whole study population. A couple of phase-II and -III trials with definitive chemoradiation (in part compared to radiation) achieved 3- and 5-year survival rates of about 40% and 15-30%, respectively. A major problem of all these studies, including the RTOG trial [4], was the high rate of local recurrence of about 50% within 2 years. Thus, surgery remains the central treatment modality in these tumour stages for operable patients. Moreover, outside of randomized trials

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perioperative chemo-/radiotherapy can not be recommended, so far.

Locally Advanced Tumours (T3-4 **NO-1** MO)

Surgery usually does not offer a curative chance to patients with locally advanced disease. Less than 50% of the tumours can be completely resected, and even after R0 resection 90% of the patients will die of recurrent disease. Therefore, surgery should not be designated as standard treatment in this clinical situation. By now, no reliable data are available about definitive chemoradiotherapy in patients with clearly locally advanced tumours, because most papers reported on mixed results with more early stages. Despite the absence of data from randomized trials, preoperative chemoradiotherapy seems to be a promising strategy for improving the patient's outcome. Recent investigations reported on 3-year survival rates of 30% in locally advanced carcinomas, with local recurrences in less than 20% of the resected patients [6].

Local control represents an important goal in oesophageal cancer, because swallowing function is critical for providing good quality of life for the patients.

Moreover, well-designed preoperative chemoradiation (30-40 Gy) led to pathologic complete responses in about 30% of the patients undergoing subsequent surgery. Another 20% showed only microscopic residual tumour at resection, which might be destroyed by increased radiation dose (> 60 Gy). Thus, a definite portion of the patients may not need surgery. Unfortunately, our current assessment techniques do not allow to identify these patients preoperatively. Some study groups tried to solve this problem by operating only patients with objective response to preoperative treatment. But these patients in particular have a good chance for pathologic complete remission and therefore may be candidates for definitive chemoradiation without surgery.

At present, we do not know what is the role of surgery in locally advanced oesophageal cancer. To answer this important question we have the obligation to treat our patients within well-

designed, multicentric randomized trials, comparing multi-modality treatment with and without surgery.

References

CA – Cancer Stat 1995;45:8-30.

Müller JM, Erasmⁱ H, Stelzner M, Zieren^U, Pichl^{maier} H: Surgical therapy of oesophageal carcinoma. Br J Surg 1990;77:845-857.

Ilson DH, Kelsen DP: Combined modality therapy in the treatment of esophageal cancer. Semin Oncol 1994;4:493-507.

4Herskovic A, Martz K, Al-Sarraf M, Leichman L, Brindle J, Vaitkevicius V, Cooper J, Byhardt R, Davis L, Emami B: Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. N Engl J Med 1992;326:1593-1598.

5 Hermanek P, Sobin LH (eds): TNM Classification of Malignant Tumours. 4th ed, 2nd revision. Berlin, Springer, 1992, pp 40-42.

6 Stahl M, Wilke H, Fink U, Stuschke M, Walz MK, Siewert JR, Molls M, Fett W, Makoski HB, Breuer N, Schmidt U, Sack H, Eigler FW, Seeber S: Combined preoperative chemotherapy and radiotherapy in patients with locally advanced esophageal cancer: Interim analysis of a phase II trial. J Clin Oncol (in press).

Erratum

Im ONKOLOGIE-Sonderheft 3 zu Band 18, November 1995, «Aktiv gegen den Krebs: Früherkennung und Vorbeugung» ist in der Arbeit von M. Schröder: «Häufigkeit der zufälligen Malignomdiagnose im internistischen Krankengut einer Klinik der Regelversorgung» auf Seite 19, Zeile 10 in der linken Spalte die Zahl 71 durch «Sieben» zu ersetzen. Der Satz muß richtig lauten: «Sieben der 219 Männer waren an der Prostata transurethral reseziert worden mit gutartiger Histologie.»

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