Gastric Cancer – Looking for Therapeutic Advancement

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Schlag

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For the present issue of this journal a number of authors were asked their opinion of new developments in the surgical and multimodality treatment of gastric cancer. Now, as has been in the past, the extent of gastric resection takes a large portion of the discussion. Numerous arguments speak in favor of a generous indication for total gastrectomy. Admittedly, the chain of arguments is based mainly on historical experience of inhomogeneously treated patients. A definitive answer to the question of subtotal versus total gastrectomy as a standard procedure can only be given by a prospective randomized trial. The feasibility of such a study has been discussed repeatedly in the past. It is to the merit of F. Bozzetti that he has initiated such a trial incorporating a great number of patients. It will be a few years before this study is ready for evaluation. But the results will be an important and reliable basis for future indication regarding the extent of gastric resection. Until then, the resection lines of appearingly curable tumors will continue to be based on tumor location and differentiation, such as intestinal or diffuse type, according to the Lauren classification. Generally, it is agreed upon that total gastrectomy is indicated in diffuse type tumors of any location, as well as in intestinal tumors of the middle or upper third of the stomach. Hereby, it is understood, that total gastrectomy means the complete resection of the stomach including the greater and lesser omentum and systematic lymphadenectomy. Whereas subtotal gastrectomy is restricted to small intestinal type antrum tumors and includes also omentectomy and systematic lymphadenectomy. The resection lines follow the lesser curvature directly below the cardia, whereby only a small remainder of the gastric fundus is left in place (the so-called 4/5 resection).

The necessity of careful lymphadenectomy is undisputed today, but the extent of it is still under discussion. The systematic lymphadenectomy in gastric cancer is a means of extirpation of an anatomically widely branching lymph drainage area. The Japanese Society for Gastric Cancer has made some progress in the overall survival by standardising of lymphadenectomy. But it should not be overlooked that usually the stage-depending survival rates are compared, which are influenced by the intra- and postoperative staging. Somewhat exaggerated, it could be said that the extended lymphadenectomy only defines the prognostic groups better and does not really alter the

total prognosis of patients. It is therefore of great importance that Dutch surgeons acquired the proficiency of their Japanese colleagues and are now conducting a joint research on the benefits of standardized lymphadenectomy in a prospective randomized trial. The study design and quality controls are exceptional and inspiring because of their uncompromising clarity. The present study, led by C. van de Velde and J. J. Bonenkamp, could become a milestone in gastric cancer surgery. Nowadays, without doubt surgery is the only therapy leading to a cure of gastric cancer. On the other hand, we have to consider that probably extended lymphnode dissection influences the treatment results only marginally. If their efficacy was more evident and clear the

above mentioned studies would not be unnecessary and the dispute about the merits of this procedure would have been settled clearly and unequivocally.

Further strategies are needed to show how the prognosis of gastric cancer can be improved. The question remains whether this can be accomplished through multimodality therapies including cytostatic treatment regimes. A combination of new cytostatic agents and complex drug schedules have shown that gastric cancer is not as drug resistant as has been assumed in the past. Not all trials are as encouraging as the one reported by H. O. Klein¹, as a number of patients have experienced considerable side effects with the used regimes. Additional studies and follow-up will be required before all trials are mature enough to provide safe data of the various combinations and especially in its use in a preoperative setting. Unfortunately, the studies reported by M. Lise et al.¹ on adjuvant chemotherapy in patients with potentially curatively resected gastric cancer does not promise a very optimistic outlook. But the risk of such therapies are always with us and may also influence overall mortality.

The preferred local recurrence pattern may call for radiotherapy in combination with surgery. Their use has been limited because of a high radiation sensitivity of different organs of the upper abdomen. Intraoperative radiation (IORT) has become very interesting as it offers the advantage to move the sensitive tissues such as bile duct, duodenum and the small intestine out of the radiation field. M. J. Eble et al. have described the ratio-

¹ This paper will be published in one of the next issues.

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ality and the use of IORT in detail. The future will show, if by this procedure a real and relevant therapeutic gain can be reached. Therefore, at this time little advancement in the treatment of gastric cancer can be seen. The therapeutic concepts have not changed much in the past decade and follow a rather mechanistic and schematic path and show little consideration for cancer biology and various tumor risks. In general, therapeutic failures are accounted to an advanced tumor stage or to prognostically unfavorable factors which are not clarified sufficiently. Early diagnosis seems important even though the proportion of early gastric cancer has not increased in the past decade and the biology of early gastric cancer and its sequence to an advanced tumor stage remains unclear. There is hope for the future in a better molecular biological tumor understanding. Highly sophisticated studies probing the genome and transforming sequences extractable from human gastric carcinomas clearly open the door to new and exciting visions of the heterogeneity, the metastatic potential and hopefully also of the future therapy of gastric cancer.

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Ernährungstherapie bei Tumorkranken

Göttingen, 13. Juni 1992

Ort: Park-Hotel Ropeter, Göttingen

Organisation: Prof. Dr. med. Heim,

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