Does chemoradiotherapy after intended curative surgery increase survival of gastric cancer patients?

A Cuschieri

Chemo-radiotherapy after intended curative surgery for gastric cancer prolonged survival in patients with an adenocarcinoma of the stomach or gastro-oesophageal junction

The randomised controlled trial reported by MacDonald et al documents an impressive increase in overall survival with postoperative chemoradiotherapy compared with surgical resection of gastric cancer alone (36 months v 27 months). Of equal importance is the finding of a significant reduction in the hazard ratio for relapse (1.52, 95% CI 1.23–1.86; p<0.001). Although not the first randomised controlled trial to document a survival benefit from postoperative adjuvant therapy, it is the first to demonstrate a substantial survival advantage due to reduction of locally recurrent disease from postoperative adjuvant orthodoxy chemoradiation (425 mg fluorouracil/m² plus 20 mg leucovorin/m² for five days, followed by 45 000 cGy of radiation over a five week period) and brings hope to a depressing cancer with an unfavourable prognosis unless diagnosed at the T1 stage. Thus this North American randomised controlled trial merits close scrutiny.

The trial has adequate power and follow up, and analysis of the data seems appropriate. However, concerns have to be raised with respect to the non-standardised nature of the surgical resections in the randomised patients. The only surgery related requirements for eligibility to this multicentre study stipulated by the protocol were: (i) resection with curative intent; and (ii) en bloc resection of tumour with negative margins. The account carries no definition of what constituted “resection with curative intent” for the purpose of the study. It appears that patients were identified (and hence recruited into the trial) on completion of a single procedure by the surgeons defining the extent of lymphadenectomy. Thus there could not have been any serious attempt at standardisation/quality control of the resection. Consequently, there is a distinct possibility that this lack of standardisation of the surgical resection may have influenced the results in a spurious fashion, especially if the patients in the two arms had disease at different stages of advancement (pTNM). The characteristics of the patients in the two arms (see table 1 in the article) appear to be similar although the T stage is not defined (clinical or pathological) and a most unusual index of node involvement (percentage involvement) is used for comparison, rather than the standard level of nodal involvement used in gastric cancer studies (N1, N2, N3). Hence, unless the authors clarify these issues, we cannot be certain that this randomised controlled trial compared patients with equivalent stages of the disease and that an R0 (no macroscopic evidence of residual disease) resection was undertaken always and in both groups. Even so, confirmation by other randomised controlled trials on adjuvant postoperative chemoradiation is needed to reach the level III evidence that would mandate routine clinical usage.
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