

Role of Neoadjuvant Chemoradiotherapy in Management of Carcinoma Esophagus.

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ABSTRACT

Several randomized trials and meta-analyses has shown survival benefit of neoadjuvant chemo-radiotherapy (CT-RT) as compared to surgery alone in resectable adenocarcinoma of esophagus, however benefit might be less as reported due to various shortcomings of the studies. Adjuvant CT-RT could also be used in such cases.

Keywords: adenocarcinoma, esophagus, neoadjuvant chemoradiotherapy.

INTRODUCTION

Neoadjuvant chemo-radiotherapy (CT-RT) followed by surgery is now considered as standard of care in resectable middle third and lower third carcinoma esophagus based on results of various randomized trials and meta-analyses. However certain important facts about these evidences must be reconsidered.

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DISCUSSION

Walsh et al in 1996 presented the results of a randomized trial comparing pre-operative chemoradiation followed by surgery with surgery alone in resectable adenocarcinoma of esophagus.^[1] Patients were randomized to receive either cisplatin and 5-FU with concurrent radiation followed by surgery or surgery alone. Three-year survival was 32% in multimodality arm (MMT) vs 6% in surgery alone arm and the difference was significant (p=.01). Recent update of this trial has shown persistence of this survival benefit with MMT compared to surgery alone in resectable adenocarcinoma (AC) and was replicated in squamous cell carcinoma (SCC) also (the results of SCC were not mentioned earlier). But there are two main flaws of this trial. First patient's pre-treatment stratification was not done according to clinical T and N staging, so we do not know that these characteristics were equally

balanced or not in the two groups. Second the sample size in the study to get the significant results for both the groups (i.e SCC and AC) was less than that actually planned.

Results of another important trial, CROSS (Chemoradiotherapy for esophageal cancer followed by Surgery Study) by van Hagen et al has shown significantly better median survival and 3-year survival in favour of MMT arm (MMT vs Surgery : Median survival: 49.4 vs 24 months, 3- year survival : 58% vs 44%). But this trial also has several drawbacks like better median survival observed than expected (median survival; combined arm vs surgery: 22 vs 16 months) indicating need for greater sample size, stratification not done according to tumour grade, PET/PET-CT (was used only for staging in some patients which may led to unequal N characteristics in the two groups) and only 23% patients having SCC.^[2] So considering these things, the amount of benefit might be less than reported.

An updated meta-analysis of 24 randomized trials (including resectable esophageal cancers) by Sjoquist et al revealed that as compared to surgery alone, an absolute survival benefit of +8.7% with neoadjuvant CRT and 5.1% with neoadjuvant CT at 2-years was observed but a clear advantage of neoadjuvant CRT over neoadjuvant CT could not be established.^[3] A phase III randomized POET trial (Preoperative chemotherapy, or Radiochemotherapy in Esophagogastric Adenocarcinoma) by Stahl et al comparing the above two groups reported that as compared to preoperative CT, preoperative CRT was associated with higher pathological complete response rates (2% vs 16%; p=.03), local control (59% vs 76%; p=.06) and 3-year survival (28% vs

47%; p=.07). However the study was underpowered as it was closed earlier due to poor accrual.^[4]

A study by Macdonald et al including 556 patients has showed that in adenocarcinoma (stage IB-IV) of gastroesophageal junction and stomach, postoperative adjuvant chemoradiation significantly improves overall survival as compared to surgery alone (36 months vs 27 months respectively). An update of this study has demonstrated that even after 10 years of median follow-up, survival benefit persisted with combined modality group.^[5]

CONCLUSION

Neo-adjuvant CT-RT followed by surgery is better than surgery alone in management of resectable adenocarcinomas of oesophagus, however the benefit might be less than reported due to several shortcomings of the studies. Adjuvant CT-RT after surgery might be used as an alternative to neo-adjuvant CT-RT.

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