

AB007. Stage III esophageal cancer: salvage resection after recurrence of definitive chemoradiation

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Abstract: Resectable stage III locally advanced esophageal cancer refers to T3–T4a or documented positive lymph node (LN). Nowadays, locally advanced esophageal squamous cell carcinoma (SCC) and adenocarcinoma are treated with multimodal strategy including surgery whenever possible. Both chemotherapy and radiotherapy are thought to improve survival and disease-free survival when they are followed by surgery. Both treatments have the potential to improve local control of the tumor with a significant downstaging, to favor the possibility of resection and to increase the potential to treat micrometastatic disease. To date, the best neoadjuvant treatment regimen has not been defined. But there is a global agreement that a standardized radical surgery remains the best option to achieve the best local control of the disease, to improve symptom of dysphagia and to obtain definitive pathological staging on pathological report. One of the recurrent critics of the strategy including neoadjuvant treatment followed by surgery remains the toxicity of surgery with its inherent postoperative mortality and morbidity. For these reasons, there is a variance in the perceived role of surgery to achieve local control instead of radiotherapy. Whatever the histological subtype, some oncologists have adopted definitive chemoradiotherapy (CRT) based on high-dose of radiation in order to reduce toxicity of surgery. With a dose of 60 Gy, complete response rate was 68% with an expected 3-year survival rate of 46%. These results have led two randomized trials conducting to compare definitive CRT with preoperative neoadjuvant CRT. Surgery appeared to improve local control of the disease with less dysphagia but overall survival was similar. Moreover, neoadjuvant CRT resulted in an increased rate of postoperative mortality. On the basis of these results, definitive CRT is now adopted in some institutions as a first line treatment, especially for SCC. In this situation, surgery is then considered as

a second line treatment in case of failure of definitive CRT in fit patients. Surgical treatment consists then in a salvage esophagectomy. There are numerous reasons why patients can be seen in this singular situation: some patients have never been referred to a surgeon and then have been treated with definitive intent to avoid surgery “by design”, others decline surgery, some others who were not candidates for surgery due to a bad performance status secondary to therapy. However local failure after definitive CRT remains problematic and can be considered in three different situations: (I) persistence of tumor after definitive CRT. This situation is defined when the tumor is detected within 3 months at the same site. Persistence rate after definitive CRT is estimated between 11 to 26% and remains associated with a poor prognosis (median survival: 9 months). In these situations, the patients are qualified as “non responders”. (II) Recurrence after definitive CRT. Locoregional recurrence is defined as cancer cells detected more than 3 months after completion of CRT. Near 50% of the patients have relapsed tumour at the primary site within 12 months. (III) Local toxicity or mechanical complication. Salvage surgery can be justified even if the proof of the recurrence is lacking because of local complications of definitive CRT such as radiation-induced strictures or perforation. Complete response (pT0N0M0) in the resected specimen after salvage esophagectomy is seen in 22% of patients suggesting that radiation-induced related complications can be another indication of such surgery. Whatever the situation, salvage esophagectomy stands out as the last curative option for selected patient who received high-dose of radiation and who are physiologically fit for surgery. Feasibility to perform salvage esophagectomy has been nowadays well reported. All medically fit patients with local regional recurrence after definitive CRT should be referred to a surgeon to consider resection. Current data on salvage surgery suggest that despite the increased morbidity (leakage, respiratory complications, graft necrosis) and mortality, a majority of patients are cured after salvage esophagectomy with an unexpected good long-term outcome. The decision to proceed with salvage esophagectomy is challenging and each individual case must be discussed at tumor board. Patients requiring salvage surgery should be referred to an experienced high-volume center. Even if surgery is proposed as a second line-treatment, oncological principles of surgery have to be strictly respected. Surgical resection must consist in an en bloc esophagectomy associated with an extended two-field LN dissection with the main objective to achieve a

complete R0 resection. Reviewing the previous radiation treatment plan is crucial. Esophagogastric anastomosis should be placed in the neck (above the radiation field) because of the high rate of leakage. When the stomach has received full-dose of radiation, alternative conduits have to be considered because of the risk of graft necrosis. The route of reconstruction (posterior mediastinum versus retrosternal route) depends on the potential bronchial injuries during the mediastinal dissection. Literature review indicates that results of salvage esophagectomy in patients having received a volume dose of radiation <55 Gy are similar, in term of mortality and morbidity, to those who have received a planned neoadjuvant treatment. However, for patients who received ≥ 55 Gy, in-hospital mortality, overall morbidity, anastomotic leak, surgical site infection

and pulmonary complications are dramatically increased. Given the numerous adverse events observed after high-dose of radiation ≥ 55 Gy, and second, the lack of good evidence supporting a high total radiation dose in term of local control or in term of survival, an upper limit threshold of 55 Gy should be considered in a definitive CRT strategy in order to not jeopardize the possibility of salvage surgery.

Keywords: Salvage esophagectomy; esophageal cancer; radiochemotherapy

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