A randomized controlled phase III multicenter study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer: ARTDECO study.

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Background: To analyze the effect of radiation dose escalation to the primary tumor on local control, locoregional control, survival and toxicity in definitive chemoradiation for esophageal cancer. Methods: Patients with clinical stage T2-4, N0-3, M0 carcinoma of the esophagus were randomized between a standard dose of 50.4 Gy/1.8 Gy/5,5 weeks to the tumor and regional lymph nodes (SD) versus the same dose combined with an integrated boost of 0,4 Gy per fraction (total 61,6 Gy) to the primary tumor (HD). Chemotherapy consisted of 6 weekly concurrent carboplatin (AUC 2) and paclitaxel (50 mg/m2) in both arms. The primary endpoint was local progression free survival (LPFS) and 260 patients were needed to detect a difference of 15% (power: 80%). Secondary endpoints were locoregional progression free survival (LRPFS), overall survival (OS) and toxicity. Patients were stratified for histological subtype. Results: Between September 2012 and June 2018, 260 patients were included. Reasons for inoperability were proximal localization and patient preference (44%), comorbidity (30%), unresectable lymph nodes (11%), T4 (5%), local recurrence 2% and combinations (7%). 61% of the patients had a squamous cell carcinoma (SCC) and 39% had an adenocarcinoma (AC). 94% completed radiation treatment and 85% had at least 5 courses chemotherapy. Median follow up time was 45 months. 3-year LPFS was 70% in the SD arm versus 76% in the HD arm (ns). LPFS for SCC and AC was 74% versus 81% and 62% versus 65% for SD and HD, resp. (ns). 3-year LRPFS was 53% and 63% for the SD and HD arm resp. (p = 0.08). 1 year any progression free survival was 60% for SCC and 50% for AC, without a significant difference between SD and HD (p = 0,5). 3-year OS was 41% versus 40% for SD and HD resp. Overall grade 4 and 5 CTC toxicity was 12% and 4% in the SD arm versus 14% and 10% in the HD arm, resp. Conclusions: In definitive chemoradiation for esophageal cancer, radiation dose escalation up to 61,6 Gy to the primary tumor did not result in a significant increase in local control over 50,4 Gy. Numerical improvement of locoregional control after HD was observed with an increase in toxicity and without improving OS.