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Commentary

Treatment of gastroesophageal junction tumors: A Commentary

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Abstract

In the 1990s, Siewert defined a new entity: tumors of the gastric esophagus junction. It encompasses esophageal and gastric tumors, regardless of their histological type. Recently this classification has changed, in the new AJCC classification, but the controversy remains: how to approach these tumors? To data their approach is different, according to the differents centers. The authors intend to carry out a short review on the theme

Key words: gastric esophagus junction, adenocarcinoma, squamous cell carcinoma

Discussion

In the 1990s, Siewert defined tumors of the gastric esophagus junction (GEJ), as those whose epicenter is located in the proximal or distal 5 cm in relation to the anatomical transition line between the esophagus and the stomach (cardia). There are 3 subtypes that, in 2000, were defined as:

Type I- tumor in the distal esophagus, which can infiltrate JEG from above;

Type II- tumor in the junctional area, with JEG origin;

Type III - sub-cardial tumor, which infiltrates JEG or distal esophagus from below.

In 2017, with the 8th American Joint Committee on Cancer (AJCC) classification, tumors type I and II were classified as esophageal and type III as gastric tumors for staging purposes. As for their approach, the controversy remains: treat as esophageal, gastric tumors or as an entity of their own? In most centers tumours Siewrt type I and II are treated as esophegeal and type III as gastric tumours, but the the controversy keeps.

Endoscopic techniques play an important role in the treatment of GEJ tumors in the early stages, with lower morbidity than surgical techniques. Currently, surgery remains a cornerstone of the treatment of GEJ tumors, with the correct selection of patients being fundamental and, in the vast majority of patients, a neoadjuvant or perioperative treatment. In fact, multiple clinical trials involving patients with adenocarcinomas (AD) of the esophagus and stomach and squamous cell carcinomas (SCC) of the esophagus, demonstrated a clear benefit in overall survival (OS) and progression-free survival (PFS) in doing a neoadjuvant or perioperative treatment compared with surgery only. Of the more recent studies, CROSS and FLOT stand out for their excellent results and, above all, for making the choice of pre / peri-operative treatment increasingly individualized for each patient.

In the CROSS study patients with AD or SCC of the esophagus or GEJ (24%), locally advanced, T1N1; T2-3N0-1, patients were randomized between radiotherapy (RT) (41.4 Gy) concomitant with preoperative chemotherapy (carboplatin / paclitaxel) follow by surgery 4 to 6 weeks after and surgery only. After a folllow up of 45,4 months (m) OS was best in the first arm (49 vs 24 m), also PFS (37,7 vs 16,2 m) and the % of complete ressection (R0) were better (92 vs 69%). The number of complete pathological responses (pCR) was particulary good in the SCCs (49%), being 23% in the AD. This study made RT / QT as the most frequent option in the preoperative treatment in the GEJ SCC, also maintaining as very valid in the AD.

In the FLOT study, which included gastric AD ≥ cT2 and / or N +, the perioperative treatment with FLOT (fluorouracil, leucoverine, oxaliplatin, docetaxel), 4 cycles, before and after compared with ECF (epirubicin, cisplatin, 5 Fluorouracil (5FU) / capecitabine), 3/4 cycles before and after surgery. The results showed a clear benefit for the FLOT with increase of pCR (16 vs 6%), PFS (30 vs 18 m) and OS (50 vs 35 m), with OS rates at 3 years of 57 vs 48% becoming the new peri-operative standard in gastric AD and an option in GEJ AD. Radical radiotherapy / chemotherapy is also an option for surgery. In this situation, the most consensual chemotherapy is a platinum a associated with a fluoropyrimidine.

In metastatic disease, OS at 5 years is less than 10%. The performance of chemotherapy is a ssociated with an increase in OS and quality of life (QL) when compared to the best symptomatic treatment (BSC). There is no consensus regarding the best chemotherapy scheme in the first line (L). Poly-chemother-

apy schemes are associated with an increase in OS; the most commonly used are platinum and fluoropyrimidine based doublets. In patients with better performance status is to consider triple therapy. In adenocarcinomas with HER2 overexpression trastuzumab should be considered. The chemotherapies options of 2nd L are more consensual. In adenocarcinomas, ramucirumab, alone or in combination with paclitaxel, demonstrated an increase in OS, PFS and QL, making it the most valid option. Schemes with irinotecan or taxanes are also options, both in AD and SCC. Recently, the use of pembrolizumab was validated after progression in 2 or more lines in AD with microsatellite instability. The nivolumab revealed, in the Asian population, also very encouraging results after 2 or more lines.

Currently, several clinical trials are underway to clarify which are the best options, whether in the early stages, locally advanced and / or metastatic [1-6].

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