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EFFECT OF NEOADJUVANT CHEMORADIOTHERAPY ON POST OPERATIVE COMPLICATIONS FOLLOWING RESECTION FOR CARCINOMA ESOPHAGUS

Gastroenterology

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KEYWORDS

AIMS AND OBJECTIVES:

To assess the effect of neoadjuvant chemoradiotherapy (NACT) on anastomotic leakage and other postoperative events after esophageal cancer resection.

MATERIALS AND METHODS:

Study Population

Data from 70 consecutive adult patients operated on for carcinoma esophagus (including Siewert I OG junctional tumors) with curative intent at the Department of Surgical Gastroenterology, Thanjavur Medical College, between 2013 and 2018, were collected. Data collected included demographic parameters, details regarding perioperative and surgical treatment and postoperative outcomes. Patients receiving palliative chemotherapy were excluded. Those patients who received NACT (n = 24) were compared with those who underwent primary surgery (PS, n = 46).

Pre-treatment Workup

Pretherapeutic clinical tumor, node, metastasis (cTNM) classification was based on endoscopy and CT scan. Baseline investigations such as complete hemogram, blood sugar, urea and creatinine, esophageal carcinomaG were taken for all 70 patients.

Neoadjuvant Chemoradiotherapy

Briefly, NACT was used for patients with cT3/T4 tumors and/or cN+ disease. Neoadjuvant chemoradiotherapy, combining usually 5-fluorouracil and cisplatin administration for 2 to 4 cycles with concomitant 45 Gy of radiotherapy, and was used for locally advanced tumors.

Surgical Resection

Surgical resection was performed approximately 6 to 8 weeks after the completion of NACT. Briefly, curative surgical resection consisted of a transhiatal esophagectomy. For supracarinal tumors, cervical lymphadenectomies were performed.

Histopathological Analysis

Resections were designated R0 when removal was complete both macroscopically and microscopically, R1 in case of a microscopically positive resection margin and R2 in case of a macroscopically positive resection margin. All patients with pTNM stage IV were considered to have an R2 resection. Tumors showing a complete pathological response were graded as pTNM stage 0.

Endpoints of the Study

The primary objective was to evaluate the impact of NACT on anastomotic leak. Secondary objectives were to analyze the impact of NACT on 90- day postoperative morbidity and mortality, and on postoperative events such as pulmonary complications, conduit necrosis, chylothorax, bleeding, cardiovascular complications, thromboembolic events, sepsis, and reoperation.

Definitions of Complications

Anastomotic Leak was defined as a symptomatic (neck abscess, mediastinitis, or enteric contents in chest drainage) or asymptomatic disruption of the anastomosis (diagnosed by water soluble contrast swallow or endoscopy). Severity of complications was assessed according to the Dindo-Clavien classification, and only grade III/IV complications were considered for the analysis.

Among 70 consecutive patients operated on for carcinoma esophagus between 2012 and 2018 at Thanjavur Medical College, patients treated with neoadjuvant chemotherapy (NACT) (n = 24) were compared with those treated by primary surgery (n = 46).

RESULTS:

Patients in the NACT group were younger, with a higher prevalence of male sex, malnutrition, advanced tumor stage, squamous cell carcinoma when compared with the primary surgery group. Postoperative leak rates were 8.8% versus in the NACT group vs 10.6% in the primary surgery group, and 90-day postoperative mortality and morbidity rates between NACT group and primary surgery group were 9.3% versus 7.2% and 33.4% versus 32.1%, respectively. Pulmonary complication rates did not differ between groups (24.6% vs 22.5%), whereas chylothorax (2.5% vs 1.2%), cardiovascular complications (8.6% vs 0.1%), and thromboembolic events (8.6% vs 6.0%) were higher in the NACT group, with more chylothorax and trend toward more cardiovascular and thromboembolic events in the NACT group. Predictors of anastomotic leak were high American Society of Anesthesiologists (ASA) scores, supracarinal tumoral location, and performance status of the patients but not NACT.

DISCUSSION:

Addressing the issue of whether NACT increases the risk of anastomotic leak after esophageal carcinoma resection is important. If there is no increased risk, compromising oncological outcomes through avoidance of NACT is not justified. In the present study, we did not observe any significant increase in anastomotic leak rates after NACT in the entire study population. In addition, NACT was not identified as a predictor for anastomotic leak. Several recent studies and reviews have investigated the influence of NACT on anastomotic leak in esophageal carcinoma, and conflicting data have emerged. This is so for several reasons: the studies are underpowered to study such a rare event, some were not designed to study the incidence of anastomotic leak, the surgical techniques used vary widely, and in some studies groups are not comparable. In recent randomized studies comparing NACT with surgery alone, the rate of anastomotic leak has been reported to be higher after NACT (8% vs 0%) in one study, but similar between groups in both the CROSS trial and the FFCD 9901 trial. As reported by others and confirmed in the present study, high ASA scores, supracarinal tumor location, and cervical anastomosis were independent predictors of anastomotic leak but not NACT. In an exploratory subgroup analysis, NACT did not significantly impact on the anastomotic leak rate whatever could be the anastomotic location. Another issue is the impact of NACT on postoperative mortality and morbidity, also a highly debated topic with many conflicting results. Our results suggest that NACT does not have an impact on 90-day postoperative mortality and overall morbidity, including pulmonary complications, but does increase chylothorax rates with a trend toward more cardiovascular and thromboembolic complications. Neoadjuvant chemoradiotherapy has been frequently correlated with

increased pulmonary complications, whereas the pulmonary complication rates were similar between groups in the present study. It has been suggested that the means of radiotherapy administration and radiotherapy fractionation may minimize lung toxicity and low-dose volume may be more important in the prevention of pulmonary complications than high-dose volume. Whereas an increased risk of cardiovascular complications after NACT in esophageal carcinoma has been already reported, an increased risk of thromboembolic events is an emerging topic. In a recent prospective study, Byrne et al reported an increased activated procoagulant response after NACT. Moreover, it has been recently shown that platinum salts are responsible for a greater thrombogenic effect than other chemotherapy regimens. We identified a 3-fold increased risk of chylothorax after NACT. It is hypothesized that radiotherapy may induce a fibrotic environment, impairing the surgical dissection.

CONCLUSIONS:

Neoadjuvant chemoradiotherapy does not have an impact on the anastomotic leak rate after resection for esophageal cancer and consequently should not modify the therapeutic strategy.