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Delaying surgery after neoadjuvant chemoradiotherapy does not significantly influence postoperative morbidity or oncological outcome in patients with oesophageal adenocarcinoma

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Abstract

Background: Patients with resectable oesophageal cancer are treated with neoadjuvant chemoradiotherapy (nCRT) followed by surgery within 3–8 weeks. In practice, surgery is often delayed for various reasons. The aim of this study was to evaluate whether delaying surgery beyond 8 weeks has an effect on postoperative morbidity, long-term survival, and pathologic response in patients treated for oesophageal ADC.
Methods: Patients who underwent nCRT followed by surgery, for cT1-3, N0-3, M0 ADC between 2001 and 2014 were retrospectively included from a prospectively obtained database. Patients with a time from the end of nCRT to surgery (TTS) ≤8 weeks were compared with patients with a TTS >8 weeks.
Results: Of 190 patients, 65 had a TTS ≤8 weeks, and 125 had a TTS >8 weeks. Patient characteristics were comparable for both groups, but patients with TTS >8 weeks exhibited higher ASA scores ($p = 0.013$) and more comorbidities ($p = 0.007$). Multivariate analysis revealed that TTS did not significantly influence postoperative morbidity, pathologic complete response rates, and five-year survival rates (42% in patients with TTS ≤8 weeks and 37% in patients with TTS >8 weeks).
Conclusions: Delaying surgery beyond 8 weeks after nCRT did not significantly influence postoperative morbidity, pathologic response, and survival in patients with non-metastatic ADC. Therefore, it appears reasonable to postpone surgery beyond 8 weeks in patients who have not yet recovered from nCRT. However, if the patient is fit for surgery, postponing surgery does not have any additional advantages.

Keywords: Oesophageal adenocarcinoma; Neoadjuvant chemoradiotherapy; Interval; Postoperative outcome

Introduction

Neoadjuvant chemoradiotherapy (nCRT) followed by radical surgery improves overall survival and locoregional control in patients with non-metastatic locally advanced oesophageal cancer.[1–3] Postoperative morbidity rates after oesophagectomy vary between 26% and 66.7%.[4–6] Several factors influence postoperative morbidity rates, such as patient characteristics (age, smoking, and the presence of comorbidities) and surgical approach. Postoperative morbidity is also influenced by nCRT.[7,8] According to clinical guidelines, surgery is performed 3–8 weeks after completion of nCRT; this guideline is typically followed in randomised controlled trials.[9–11] This period allows acute inflammation to resolve following nCRT, patients to recuperate from neo-adjuvant treatment, and patients to be fit for surgery. In practice, however, surgery is often

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postponed beyond this timeframe due to the toxicity of nCRT and the patient condition. Time to surgery (TTS) may further depend on logistical reasons[12–14] and the patient's personal preference.

Delaying surgery may affect postoperative outcome given that nCRT is associated with inflammation and fibrosis in the surgical field.[15] Furthermore, radiation-induced fibrosis or radionecrosis could complicate surgery and postoperative recovery.[16] Finally, postponing surgery after nCRT may influence oncological outcome. On the one hand, a longer wait time could result in more tumour regression; however, this waiting period may lead to the progression of (systemic) disease.[15,17,18] In rectal cancer, postponing surgery beyond 8 weeks is associated with higher rates of pathologic complete response (pCR).[19–21] Additionally, postoperative morbidity, mortality, and overall survival were not significantly influenced by the interval between nCRT and surgery.[19–22]

Several studies suggest that patients with oesophageal squamous cell carcinoma (SCC) benefit more from nCRT than patients with adenocarcinoma (ADC). In the Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study (CROSS) trial, patients with SCC exhibited an increased pCR rate and better survival compared with patients with ADC.[3] Given its lower response rate, increasing TTS in ADC patients may have less of an influence on tumour regression compared with SCC patients. Little is known about the optimal timing of surgery after nCRT in ADC. Retrospective studies have shown conflicting results about whether or not delaying surgery is beneficial with respect to pathological response.[17,18,23–27] These studies, however, mainly focused on SSC of the oesophagus, whereas most tumours in the Western population currently are ADC. Kim et al.[17] performed a retrospective study in ADC patients, in which delaying surgery did not affect pathologic response. However, a recent study in SCC and ADC patients by Shapiro et al.[26] indicated that increasing TTS improved pathologic response with a trend towards more postoperative complications. Others however showed that delaying surgery beyond 8 weeks was not associated with more postoperative complications.[17,18,24–26]

The aim of this study was to evaluate the influence of the time period between nCRT and surgery on the postoperative course, pathological response, and long-term survival in patients with ADC.

Methods

A database of all patients with oesophageal cancer treated at the Catharina Hospital in Eindhoven in the Netherlands was obtained and retrospectively analysed for patients treated between 1 January, 2001 and 1 May, 2014. All data concerning diagnosis, treatment, and follow-up were recorded. In all patients, the standard work-up included a clinical examination, endoscopy with biopsies, endoscopic ultrasonography (EUS), ultrasonography or computer tomography (CT) of the cervical region, CT of the chest and abdomen, and a whole body positron emission tomography

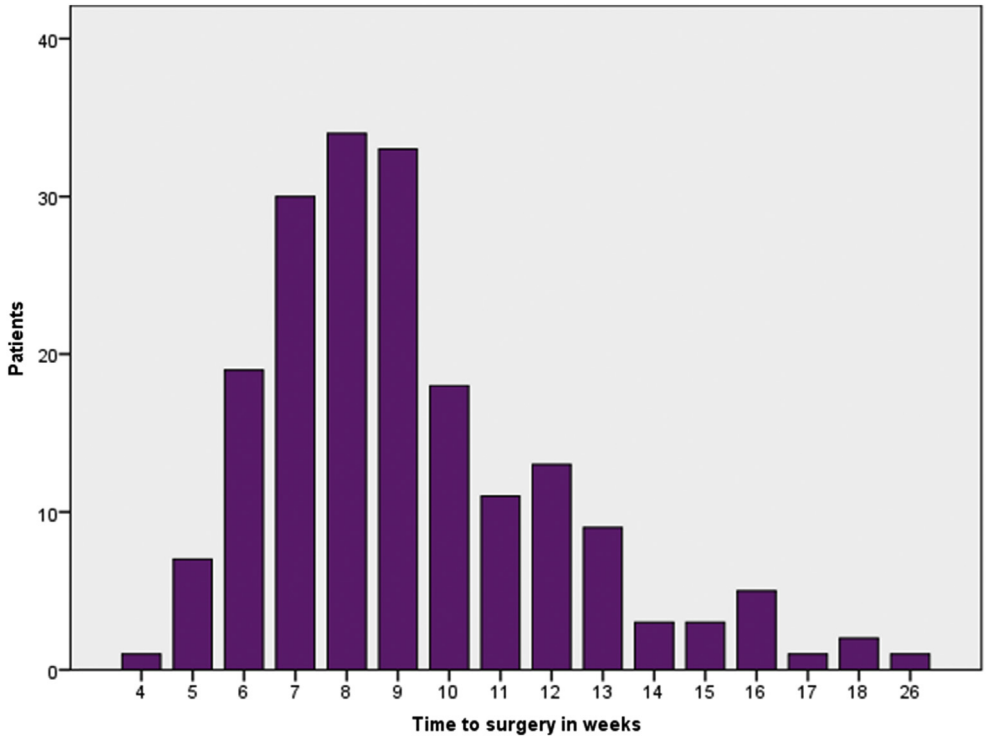

Figure 1. Distribution of the timing (in weeks) of oesophagectomy after completion of nCRT.