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Original Research

Are pathological high-risk features in locally advanced rectal cancer a useful selection tool for adjuvant chemotherapy?

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KEYWORDS
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Abstract ***Background:*** Several histological high-risk factors are used as an indication for adjuvant therapy in stage II colon cancer. Those and other factors, including lymphatic invasion, perineural invasion (PNI), venous invasion and tumour budding are associated with decreased outcome. In this study, we evaluated the prognostic and predictive values of these biomarkers in a cohort of rectal cancer patients.

Materials and methods: The trial-based cohort consisted of 221npTNM stage II–III rectal cancer patients, included in the PROCTOR/SCRIPT trial, a multicentre randomised phase III trial. Patients treated with neoadjuvant radiotherapy and TME surgery were randomised between adjuvant chemotherapy or observation. Lymphatic invasion, PNI, extramural venous invasion, intramural venous invasion and tumour budding were determined in standard tissue slides.

Results: The presence of PNI (HR 3.36; 95% CI 1.82–6.21), extramural vascular invasion (HR 1.93; 95% CI 1.17–3.19) and tumour budding (HR 1.83, 95% CI 1.11–3.03) was associated with a significant worse overall survival. The presence of ≥2 adverse biomarkers resulted in a stronger prediction of adverse outcome in terms of overall survival (HR 2.82; 95% CI 1.66–4.79), disease-free survival (HR 2.27; 95% CI 1.47–3.48), and distant recurrence (HR 2.51; 95% CI 1.56–4.02). None of these markers alone or combined predicted a beneficial effect of adjuvant chemotherapy.

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Discussion: We confirmed that several stage-independent biomarkers were significantly associated with a decreased outcome in rectal cancer patients. More importantly, these markers did not have predictive value and are thus not useful to select for adjuvant therapy in rectal cancer.

1. Introduction

Treatment regimens in patients with rectal cancer are primarily influenced by the tumour, node and metastasis (TNM) classification and the circumferential resection margin, which provide an estimation of the patient's prognosis [1]. Pathological staging is essential for planning the most appropriate treatment in patients with rectal cancer; however, outcome among patients with the same tumour stage differs significantly [2]. Consequently, it could be stated that conventional classification does not provide adequate individualised assessment.

For patients with stage III or high-risk stage II colon tumours, adjuvant chemotherapy is indicated after surgery [3,4]. The high-risk stage II colon tumour is mainly defined by histopathologic characteristics such as the presence of a T4 tumour, extramural vascular invasion (EMVI), poor differentiation, less than 10 harvested lymph nodes or patients who have had obstruction or perforation [3–5]. To optimise the delivery of adjuvant chemotherapy in rectal cancer, additional histological risk factors should be explored. Those factors include lymphatic invasion, perineural invasion (PNI), EMVI, intramural venous invasion (IMVI), and tumour budding, which are all associated with decreased clinical

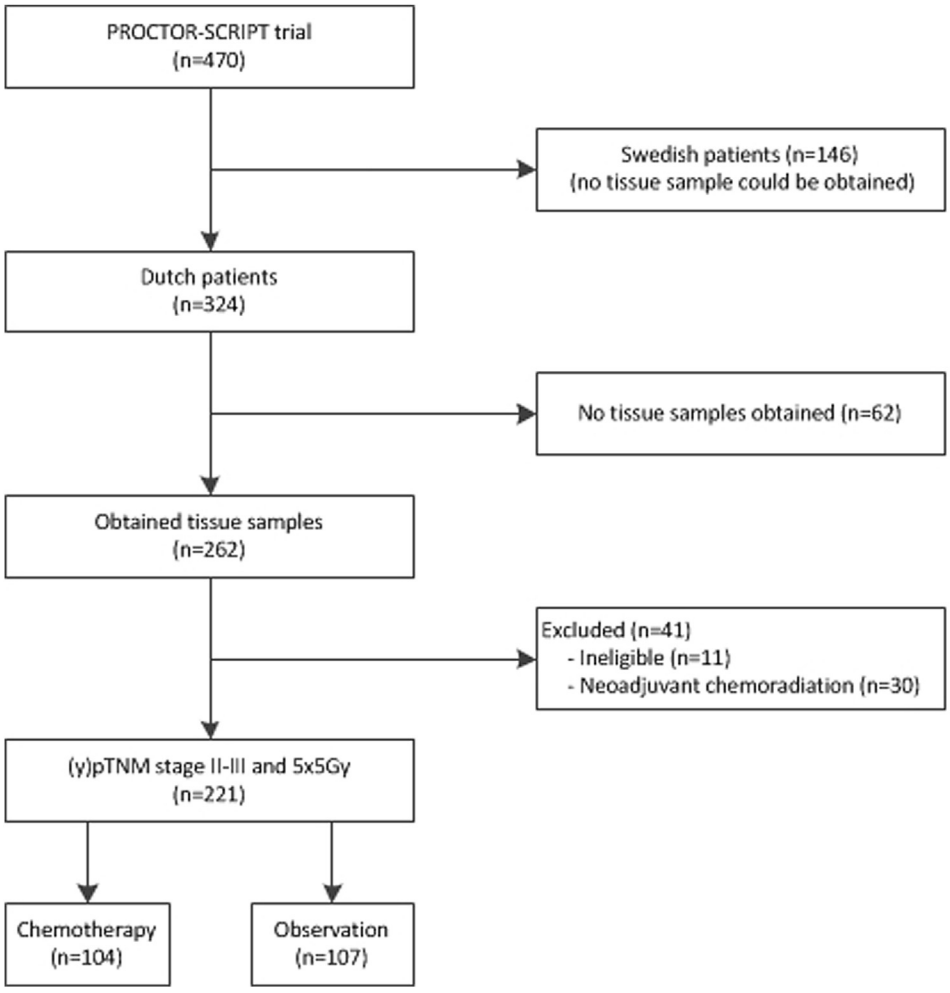

Fig. 1. Patient selection.