



Original article

Response to Treatment and Interval to Surgery After Preoperative Short-Course Radiotherapy in Rectal Cancer^{☆,☆☆}



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A B S T R A C T

Introduction: Preoperative short-course radiotherapy with immediate surgery improves local control in patients with rectal cancer. Tumor responses are smaller than those described with radiochemotherapy. Preliminary data associate this lower response to the short period until surgery. The aim of this study is to analyze the response to preoperative short-course radiotherapy and its correlation with the interval to surgery especially analyzing patients with mesorectal fascia involvement.

Methods: A total of 155 patients with locally advanced rectal cancer treated with preoperative radiotherapy (5×5 Gy) were retrospectively analyzed. Tumor response in terms of rates of complete pathological response, downstaging, tumor regression grading and status of the circumferential resection margin were quantified.

Results: The mean interval from radiotherapy to surgery was 23 days. The rate of complete pathological response was 2.2% and 28% experienced downstaging (stage decreased). No differences between these rates and interval to surgery were detected. Eighty-eight patients had magnetic resonance imaging for staging (in 31 patients the mesorectal fascia was involved). The mean time to surgery in patients with involvement of the fascia and R0 surgery was 27 days and 16 days if R1 (P=.016). The cutoff of 20 days reached the highest probability of achieving a free circumferential resection margin between patients with mesorectal fascia involvement, with no statistically significant differences: RR 3.036 95% CI=(0.691-13.328), P=.06.

Conclusions: After preoperative short-course radiotherapy, an interval >20 days enhances the likelihood of achieving a free circumferential resection margin in patients with mesorectal fascia involvement.

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Respuesta al tratamiento e intervalo de tiempo hasta la cirugía con radioterapia preoperatoria de curso corto en el cáncer de recto

RESUMEN

Palabras clave:

Cáncer de recto
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Introducción: La radioterapia preoperatoria de curso corto con cirugía inmediata, mejora el control local del cáncer rectal. Las respuestas que consigue son de menor magnitud que las descritas con radioquimioterapia. Datos preliminares asocian esta menor respuesta al corto periodo hasta la cirugía. El objetivo de este estudio es analizar la respuesta obtenida con el esquema preoperatorio de curso corto y su correlación con el tiempo hasta la cirugía, analizando especialmente a los pacientes con fascia mesorrectal afectada.

Métodos: Se analiza retrospectivamente a 155 pacientes tratados con radioterapia preoperatoria (5 × 5 Gy). Se cuantificó la respuesta tumoral en términos de tasas de respuesta completa patológica, reducción del estadio, grado de regresión tumoral y estado del margen de resección circunferencial.

Resultados: El intervalo medio radioterapia-cirugía fue de 23 días. Se alcanzaron respuestas completas patológicas en el 2,2% y reducción del estadio en el 28%. No se detectaron diferencias entre estas tasas y el intervalo hasta la cirugía. Ochenta y ocho pacientes tenían resonancia de estadificación (31 con fascia mesorrectal comprometida). La media de tiempo hasta la intervención en pacientes con fascia comprometida y cirugía R0 fue de 27 días y si R1 de 16 días ($p = 0,016$). El punto de corte de 20 días alcanzó la mayor probabilidad de lograr un margen circunferencial negativo entre los pacientes con fascia mesorrectal comprometida, aunque sin alcanzar significación estadística: RR 3,036, IC del 95% = 0,691–13,328, $p = 0,06$. **Conclusiones:** Tras la radioterapia preoperatoria de curso corto, un intervalo > 20 días potencia la probabilidad de lograr un margen de resección libre en pacientes con fascia mesorrectal comprometida.

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Introduction

Preoperative radiotherapy followed by total excision of the mesorectum continues to be the recommended treatment for locally advanced rectal cancer (LARC).¹ Preoperative regimens are less toxic and more effective for reducing local recurrences than postoperative treatment.^{2,3} There are 2 validated regimens: the so-called long regimen or chemoradiotherapy (CRTx) that administers 45–50.4 Gy in 25–28 daily fractions, associated with concomitant chemotherapy and followed by surgery deferred by 4–8 weeks²; and, preoperative short-course radiotherapy (SCRT) that administers 25 Gy in 5 fractions, without chemotherapy and immediate surgery in 1–7 days.⁴ These regimens have been extensively compared.^{5–7} A recent meta-analysis⁸ concluded that SCRT with immediate surgery is as effective as CRTx with deferred surgery in terms of overall and disease-free survival rates, local and distant control, and toxicity.⁸ There is no international consensus about the use of these 2 regimens in the context of LARC. While SCRT is widely implemented in northern Europe,¹ CRTx is the most widely used regimen in the US.

SCRT is more convenient for patients and more cost-effective for the Spanish national healthcare system.⁸ However, even though it has demonstrated similar rates of local control, the tumor reduction that is achieved is lower. A randomized trial⁵ reported complete pathologic

response (cPR) rates of 0.7% after SCRT and 16% with CRTx. This lower rate of cPR has been linked to minimal time intervals between the end of SCRT and interventions.⁹ Therefore, when tumor reduction is required prior to surgery, all clinical guidelines recommend a long CRTx¹ regimen in order to achieve free circumferential resection margins (CRM), which is a predictive factor for local control and survival.^{3,10} Nonetheless, in daily practice there are 2 patient subgroups (those with low performance status [PS] or comorbidities) that are not candidates for CRTx. The same is true for potentially resectable metastases, in which a 5-week regimen, together with a waiting period before surgery of 4–8 weeks, could allow the metastatic disease to progress. In these subgroups, even when found in resection margins, the multidisciplinary team frequently prescribes SCRT. Progressively, results are being reported that prolonging the time from the end of SCRT until surgery increases the tumor response obtained. Promoting this response is especially relevant in the subgroup of patients with compromised mesorectal fascia (MRF) on magnetic resonance imaging (MRI), which requires tumor reduction to achieve optimal surgical results.¹¹ There are trials currently underway,¹² but the optimal time interval before surgery has still not been identified.

The objective of this study is to analyze the local response obtained in the group of patients with LARC, cT3.4 and/or N+ treated at our hospital by means of SCRT and total mesorectal excision, especially analyzing patients with involvement of the MRF on MRI.

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