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The prognostic impact of lipid biosynthesis-associated markers, HSD17B2 and HMGCS2, in rectal cancer treated with neoadjuvant concurrent chemoradiotherapy.

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Abstract

Neoadjuvant concurrent chemoradiotherapy has been widely used for **rectal cancer** to improve local tumor control. The varied response of individual tumors encouraged us to search for useful biomarkers to predict the therapeutic response. The study was aimed to evaluate the **prognostic impact** of **lipid biosynthesis-associated** biomarkers in **rectal cancer** patients **treated** with preoperative **chemoradiotherapy**. Through analysis of the previously published gene expression profiling database focusing on genes associated with **lipid** biosynthesis, we found that **HSD17B2** and **HMGCS2** were the top two significantly upregulated genes in the non-responders. We further evaluated their expression by immunohistochemistry in the pre-treatment tumor specimens from 172 patients with **rectal cancer** and statistically analyzed the associations between their expression and various clinicopathological factors, as well as survival. High expression of **HMGCS2** or **HSD17B2** was significantly associated with advanced pre- and post-treatment tumor or nodal status ($P < 0.001$) and lower tumor regression grade ($P < 0.001$). More importantly, high expression of either **HMGCS2** or **HSD17B2** was of **prognostic** significance, with **HMGCS2** overexpression indicating poor prognosis for disease-free survival ($P = 0.0003$), local recurrence-free survival ($P = 0.0115$), and metastasis-free survival ($P = 0.0119$), while **HSD17B2** overexpression was associated with poor prognosis for disease-free survival ($P < 0.0001$), local recurrence-free survival ($P = 0.0009$), and metastasis-free survival ($P < 0.0001$). In multivariate analysis, only **HSD17B2** overexpression remained as an independent prognosticator for shorter disease-free survival ($P < 0.001$) and metastasis-free survival ($P = 0.008$). In conclusion, high expression of either **HSD17B2** or **HMGCS2** predicted poor susceptibility of **rectal cancer** to preoperative **chemoradiotherapy**. Both acted as promising **prognostic** factors, particularly **HSD17B2**.

KEYWORDS: CCRT; **Chemoradiotherapy**; **HMGCS2**; **HSD17B2**; **Rectal cancer**

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