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Resumo	Rectal cancer (RC) is a gastrointestinal cancer with a poor prognosis. While some studies have shown metabolic reprogramming to be linked to RC development, it is difficult to define biomolecules, like lipids, that help to understand cancer progression and response to therapy. The present study investigated the relative lipid abundance in tumoral tissue associated with neoadjuvant therapy response using untargeted liquid chromatography–mass spectrometry lipidomics. Locally advanced rectal cancer (LARC) patients (n = 13), clinically staged as T3–4 were biopsied before neoadjuvant chemoradiotherapy (nCRT). Tissue samples collected before nCRT (staging) and afterwards (restaging) were analyzed to discover lipidomic differences in RC cancerous tissue from Responders (n = 7) and Non-responders (n = 6) to nCRT. The limma method was used to test differences between groups and to select relevant feature lipids from tissue samples. Simple glycosphingolipids and differences in some residues of glycerophospholipids were more abundant in the Non-responder group before and after nCRT. Oxidized glycerophospholipids were more abundant in samples of Non-responders, especially those collected after nCRT. This work identified potential lipids in tissue samples that take part in, or may explain, nCRT failure. These results could potentially provide a lipid-based explanation for nCRT response and also help in understanding the molecular basis of RC and nCRT effects on the tissue matrix.
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