

One year followup evaluation of hepatic triglycerides in colorectal cancer patients treated with adjuvant chemotherapy using ¹H magnetic resonance spectroscopy

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Purpose: Fatty liver disease is a reversible condition but it can also lead to permanent liver damage and scarring¹. Previous studies have suggested that hepatic steatosis might be associated with adjuvant or neo-adjuvant chemotherapy in colorectal cancer patients². The aim of this study was to evaluate hepatic triglyceride changes due to chemotherapy in colorectal cancer patients using ¹H-MR spectroscopy (MRS). We hypothesized that patients whose hepatic lipids became elevated during chemotherapy would experience recovery after completion of chemotherapy. This knowledge would alleviate concerns of both patient and physician regarding permanent effects of adjuvant chemotherapy.

Methods: Thirty-four colorectal cancer patients were studied prospectively. All patients were studied serially by ¹H MRS over a one year period. Twenty-one patients were treated with 12 cycles of FOLFOX (5-fluorouracil +leucovorin+oxaliplatin) over a period of 6 months. Thirteen patients received hepatic arterial infusion of floxuridine+decadron (HAI-FUDR) combined with systemic irinotecan (IRI) for the full one year period of the study. Single-voxel ¹H MRS exams were performed on a 1.5T GE Scanner prior to chemotherapy, at 6 months, and at 1 year. Sixteen patients who completed the 1 year evaluation are presented here. A point-resolved spectroscopy sequence was used to acquire a ¹H MR spectrum from a voxel of 8 cm³ volume in a single breath-hold without water suppression. Peak areas (PA) of water signal at 4.7 ppm and methylene lipid signal at 1.3 ppm were calculated using jMRUI. The fat water ratio was calculated as: $FFW = PA_{fat}/(PA_{water}+PA_{fat})$. A FFW change of 15% was considered significant based on our reproducibility study⁴.

Results: In the FOLFOX-treated population, 6 of 9 patients demonstrated an increase in hepatic lipids at the time of therapy completion (6 months) while the remaining 3 patients showed unchanged or slightly decreased lipids at 6 months. Of the six patients whose lipids had increased at 6 months, 4 demonstrated a trend toward recovery after no-treatment for six additional months. Two other patients experienced increased lipids at 6 months followed by another increase at 12 months despite the lack of treatment (red lines, Fig. 1). Both of these patients also experienced a significant increase in body mass index (BMI) with a weight gain of > 9 Kg and one's condition was further complicated by concurrent anti-HIV HAART treatment which has been related to steatosis (★). Finally, two of the patients in the FOLFOX group who had unchanged or slightly decreased lipids at 6 months, demonstrated elevated lipids at 12 months (gray lines, Fig. 1). Both of these patients also had increased BMI at that time. In the HAI-FUDR/IRI group, only 2 of 7 patients experienced an elevation in hepatic lipids during treatment. Recovery of lipids could not be evaluated in the HAI group because patients were on treatment throughout the study.

Discussion: In patients who experienced an increase in hepatic lipids while on FOLFOX treatment, there was a trend toward a return to baseline when the patient was off treatment for 6 months unless the patient gained weight during the off-treatment period. While 6 of 9 patients on FOLFOX experienced an increase in hepatic lipids during treatment, only 2 of 7 HAI-

FUDR/IRI patients demonstrated increased lipids. While these patient numbers are too low for detection of a significant difference, the data suggest that HAI-FUDR/IRI does not induce steatosis at a higher rate than FOLFOX. This was interesting because IRI has been linked to steatohepatitis². One possible explanation is that decadron which was co-administered during HAI treatment may protect against liver injury.

Conclusion: ¹H-MRS is a valuable, noninvasive technique which is ideal for serial evaluation of liver fat changes during and after chemotherapy. There is a trend toward a return of hepatic lipids to baseline levels after the patient completes chemotherapy unless the patient experiences significant weight gain. While a larger scale study is needed to confirm our data, our findings suggest that colorectal cancer patients who experience increased hepatic lipids while on FOLFOX chemotherapy will not have long term steatosis due to treatment.

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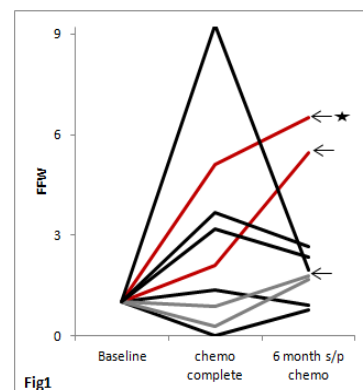


Figure 1. Hepatic lipids in patients treated with FOLFOX at baseline, completion of treatment and after 6 months off-treatment.