Exploring the Role of a Lifestyle Intervention on Peri-Prostatic Adipose Tissue and Fat Metabolism in Men with Prostate Cancer

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Introduction. Excess visceral fat and altered lipid metabolism are linked to prostate cancer progression. We assessed whether weight loss intervention using diet and exercise modifies dietary fatty acid intake, PPAT fatty acid composition and signaling, and the plasma sphingolipid signature in men with prostate cancer.

Methods. In a phase II trial, 40 men scheduled for prostatectomy were randomized to an intervention (n = 20) or control (n = 20). The intervention group followed a diet and exercise regimen for 4-16 weeks pre-surgery and six months post-surgery, while controls received standard care and educational materials. Blood samples, dietary records, and health metrics were collected at baseline (4-16 weeks pre-surgery), one week pre-surgery, and six months post-surgery. PPAT biopsies were obtained at surgery. Fatty acid profiles were measured using flame-ionization gas chromatography. RNA from third-passage adipose stromal cells was analyzed with the nCounter® PanCancer Immune Panel, and plasma sphingolipids were quantified via quadrupole time-of-flight mass spectrometry.

Results. The intervention resulted in a 5.5% body weight loss. Although dietary fatty acid intake changed relative to controls, these alterations did not correlate with changes in PPAT fatty acid composition. ASC transcriptomic analysis revealed decreased COLEC12 and increased IL-17F expression; Ingenuity Pathway Analysis predicted inhibited leptin and IL-6 signaling in the intervention group. Plasma sphingolipid score significantly decreased in the intervention arm.

Conclusions. Weight loss induced significant dietary, transcriptomic, and metabolic alterations, downregulating pathways associated with prostate cancer progression. The improved plasma sphingolipid signature suggests that lipid metabolism changes may protect against prostate cancer progression.

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