

## Metabolic Management of Cancer

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### Abstract

**Background:** In light of the mitochondrial metabolic theory, cancer could be considered a metabolic disease. It has been suggested that cancer metabolic therapies, including ketogenic diets (KD) may be useful to exploit differences in metabolism from non-neoplastic cells. In this systematic review and meta-analysis of randomized controlled trials (RCTs) we aimed to investigate the efficacy of KD as an adjuvant therapy in the treatment of cancer compared to a traditional non-ketogenic diet.

**Methods:** In this study, databases such as MEDLINE/PubMed, Web of Science, SCOPUS, EMBASE, and Cochrane Central Register of Controlled Trials were searched. Only RCTs that involved cancer participants that were assigned to dietary interventions including a KD group and a control group (any non-ketogenic dietary intervention) were selected. Two reviewers independently extracted the data, and the meta-analysis was performed using a fixed effects model or random effects model depending on the I<sup>2</sup> value or p-value.

**Results:** This meta-analysis showed a significant reduction in weight (WMD = -3.58 kg; 95% CI: -6.24, -0.92; P = 0.008, BMI (WMD = -1.96 kg/m<sup>2</sup>; 95% CI: -2.83, -1.09; P < 0.001) and fat mass (WMD = -1.90; 95% CI: -3.57, -0.24; P = 0.025) with ketogenic diet. KD significantly decreased glucose (WMD = -9.52 mg/dl; 95% CI: -13.81, -5.23; P < 0.001) and IGF-1 (WMD = -16.27 ng/ml; 95% CI: -22.44, -10.09; P < 0.001). Furthermore, ketogenic diet induced ketosis by increasing  $\beta$ -hydroxybutyrate (WMD = 0.51 mmol/l; 95% CI: 0.11, 0.91; P = 0.012). There was a non-significant pooled effect of the ketogenic diet on insulin, C-reactive protein (CRP), lipid profile, kidney and liver function, and quality of life.

**Conclusion:** We found that KD might result in a greater reduction in glucose, IGF-1, ketosis, weight, BMI and fat mass in cancer patients compared to traditional non-ketogenic diets. According to our data, additional well-designed RCTs with larger sample sizes are needed to evaluate if KD can be routinely used as an adjuvant therapeutic component in cancer patients.

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