



Fasting during chemotherapy

A statement by the Working Group on Prevention and Integrative Oncology (PRIO) in the German Cancer Society (DGEM), the German Society for Nutritional Medicine and the Association of Dietitians - German Federal Association (VDD).

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Abstract

For several years, there has been discussion about whether fasting periods of different lengths before, during, and after a chemotherapy cycle can reduce therapy-related side effects, increase therapy response, and improve patients' quality of life. In this context, the renunciation of food is supposed to strengthen healthy cells during treatment while better attacking cancer cells, which are supposed to be more susceptible to the therapy. When considering the current state of studies, meaningful clinical data are lacking due to methodological deficiencies, small numbers of participants, and heterogeneity of study interventions. Therefore, the authors of this statement conclude that no recommendation for fasting during chemotherapy should be made at this time.

Keywords: fasting, cancer, chemotherapy, tumor therapy, oncology, nutrition therapy

Introduction

Especially in oncology, there are various forms of nutrition for patients, which are supposed to support the sufferers during the therapy. One of these diets is a special form of fasting, which involves fasting periods of varying lengths before, during and after each chemotherapy cycle. By the renunciation of food, metabolic processes in the body should be altered, resulting in reduced chemotoxicity and side effects, increased efficacy of tumor therapies, and improved quality of life [1]. Although these effects initially sound promising, fasting periods provide for several days of food abstinence, the risks of which should be considered. In addition, the potential benefits have yet to be scientifically proven.

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Fasting – Definition

Fasting is understood as the (voluntary) renunciation of solid foods, high-energy drinks and stimulants such as caffeine and nicotine during a defined period of time that is individually adapted to the situation [2, 3]. Depending on the health status different forms of fasting can be distinguished: There is therapeutic fasting, preventive fasting and a fasting form for healthy individuals who choose this dietary form without therapeutic and medical intention [3].

Traditionally, fasting begins with an energy reduction to about 1,000 kcal for one day (d), followed by a fasting diet of 250–500 kcal/d through vegetable broth, fruit and vegetable juices, honey, and liquids such as herbal tea or water [2].

The targeted use of fasting has shown beneficial results in nutritional and metabolic dis-



eases (e.g. metabolic syndrome, hyperlipidemia), cardiovascular and nervous system diseases (e.g. hypertension, chronic pain syndrome) and psychological disorders (e.g. depressive mood) [3]. In recent years, this form of nutrition has also been attributed beneficial effects in oncology, without there being any clear data to support this.

Fasting in oncological patients

Regular periods of fasting are intended to protect oncology patients from chemotherapy and make tumor cells more sensitive to the therapy. In doing so, fasting is supposed to cause nutrient deprivation, which the healthy cells survive well and use their energy for maintenance and repair processes that contribute to chemotherapy resistance. At the same time, tumor cells are supposed to be unable to adapt to the fasting situation due to their mutations in tumor suppressor genes and mitogenic signaling pathways. As a result, chemotherapy drugs are supposed to cause increased DNA damage and apoptosis in tumor cells, while healthy cells remain unharmed [4]. As a result, there should be the widely discussed benefits of increased treatment response, reduced side effects, and also improved quality of life.

Based on five clinical studies, the guidelines of the specialized companies as well as two systematic reviews the working group nutrition of the Working Group Prevention and Integrative Oncology (PRIO) in the German Cancer Society, the German Society for Nutritional Medicine (DGEM) and the Association of Dietitians – German Federal association (VDD) comment on this as follows:

To the present time no scientific investigations are present, which prove that fasting before, during and/or after chemotherapy:

- can increase the therapeutic response of chemotherapies.
- can reduce toxicity and thus therapy-related side effects.
- improves the quality of life of patients compared to the guideline-based diet.

Clinical evidence

The postulated benefits of fasting are largely based on findings from animal studies. They report the reduced side effects, suppressed tumor progression, and even improved survival [5]. Such beneficial effects during chemotherapy are also claimed in randomized controlled trials in patients receiving chemotherapy, but these cannot be confirmed when critically examined:

1. A pilot randomized controlled trial examined the effects of fasting on quality of life during chemotherapy (36 h before to 24 h after) in gynecologic tumor patients. Participants were assigned in a crossover design to either short-term fasting ($n = 18$) or an isocaloric diet ($n = 16$) until half of their chemotherapy cycles, after which the two groups switched for the remaining chemotherapy cycles. The authors reported improved quality of life in the intervention group and good tolerance of the fasting period [6]. However, the study results should be viewed critically: Par-

ticipants in the intervention group received nutritional counseling on fasting as well as isocaloric diet and were also allowed to consume up to 350 kcal/d of energy. The lack of blinding during treatment allocation, the dropout rate of 30% in each case, and the lack of reproducibility in the second group in the crossover design significantly limit the validity of the study results.

2. A randomized controlled trial examined either a modified form of fasting ($n = 66$) or a standard diet ($n = 65$) three days before and on the day of neoadjuvant chemotherapy in breast cancer patients [7]. Comparing the interventions, this study differs from others in that the patients in the intervention group still consumed 1,200 kcal on day 1 and about 200 kcal/d on the following days in the form of a drinkable diet, soups and liquids. Nevertheless, the high dropout rate occurred: while approximately 92% of the control group adhered to their standard diet, only one-third of the patients (34%) adhered to the fasting periods for half of their chemotherapy cycles. Reasons given for early discontinuation of the fasting intervention included taste (51.0%), nausea (15.4%), and hunger (9.8%).

a. The first publication is about chemotherapy. While no significant differences in grade 3/4 toxicity are reported (75.4% vs. 65.6%; $p = 0.224$), the authors point to a trend in neutropenic fever (33.8% vs. 18.8%; $p = 0.052$) and neutropenia (50.8% vs. 34.4%; $p = 0.060$), however, without statistical significance. The study also showed that there was no improved pathologic complete remission (pCR), in which the results of the intervention and control groups did not differ (10.8% vs. 12.7%; $p = 0.735$), thus not confirming a better response to therapy [7].

b. The second publication of the study reported a positive effect of fasting on individual quality of life parameters, as assessed by the European Organisation for Research and Treatment of Cancer (EORTC) questionnaire [8]. Although individual parameters improved in the intervention and control groups, there was no difference between the study groups in any of the characteristics examined. Thus, fasting again showed no advantage over a standard diet.

3. A third study investigated another fasting form during chemotherapy (24 h before to 24 h after). Participants were assigned to



either the fasting group with only energy-free drinks ($n = 7$) or to a guideline-based dietary regimen ($n = 6$) [9]. The authors report good tolerance and lower toxicity, but their conclusions are limited by the very small number of participants, poor reporting of fasting tolerance, and patient-reported side effects alone in the absence of blinding.

4. Another study investigated different fasting times (24 h, 48 h, 72 h) in patients ($n = 20$) with different tumor types [10]. In addition to limited power due to the small study population, dropout rate of 35%, and lack of blinding, patients reported fatigue (77%), headache (46%), drowsiness (46%), and hypoglycemia (23%) as side effects of fasting.
5. A randomized controlled trial ($n = 24$) investigated a fasting regimen with only water intake (24 h before and 24 h after each chemotherapy cycle) compared with an isocaloric diet in gynecologic cancer patients [11]. Although good tolerance was reported, the intervention did not show significantly improved quality of life ($p = 0.71$), lower grade 3/4 side effects ($p = 0.49$), or improved treatment response (complete and partial treatment response $p = 1.0$ and 0.35 , respectively). Accordingly, fasting showed no advantage over a balanced diet regimen.

Regarding clinical trials, there are two systematic reviews evaluating fasting during chemotherapy. Given the paucity of studies, they essentially contain the studies already presented. One of the papers examined three of the studies, based on which the authors also question the current evidence. They conclude that the results in the studies are limited by the heterogeneous study population and by the study protocols [12].

The authors of a systematic review published in 2022 examined eight clinical trials, five of which meet our inclusion criteria and have already been critically reviewed in this statement. Even taking into account a case series, a controlled crossover study and a cohort study, the majority of the studies are of low quality and report heterogeneous results. Based on this, the authors are also unable to make a clinical recommendation for fasting, reinforcing our findings [13]. This is in accordance with the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline published in 2021. The experts do not make a recommendation for fasting due to the lack of evidence, either before, during, or after the application of anticancer drugs. They cite the weak evidence of positive effects from small case series and small randomized trials, but very good evidence on the risks of malnutrition [14]. The German Society of Nutritional Medicine (DGEM) also states in its guideline on nutrition in oncology [15]: "Dietary regimens that restrict food intake in patients with (impending) malnutrition can be potentially harmful and should be avoided."

Thus, the current state of studies on fasting during chemotherapy does not provide reliable data that would allow a positive recommendation for clinical practice. In contrast, there is a risk of malnutrition in terms of macronutrients and micronutrients, as well as negative effects on quality of life and increased occurrence of side effects that can potentially interfere with patient treatment.

Conclusion

Based on the study results to date, fasting before, during, and after chemotherapy is associated with no benefits but significant risks for cancer patients undergoing therapy. Due to the lack of clinical evidence, this dietary approach cannot be recommended for patients with oncologic disease.

- To improve chemotherapy-related side effects and quality of life, adequate side effect management and good patient care and counseling are needed.
- If patients decide to fast during their chemotherapy despite being informed appropriately, they should be closely supervised by a dietician or an appropriately qualified ecotrophologist/nutritionist.
- Patients with (impending) malnutrition should receive close-meshed nutritional therapy according to a standardized procedure. This includes nutrition screening and assessment, diagnosis of nutrition problems, setting of nutrition goals, intervention planning and implementation, and monitoring and evaluation. Nutrition therapy should be led by qualified nutritionists in a multidisciplinary team.

Conflict of interest

The authors declare that there is no conflict of interest

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