

The association between diet and health-related quality of life in cancer patients

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Abstract

Although it is known that diet is a risk factor for various types of cancer, the association of diet during or after treatment with outcomes like health-related quality of life are less clear. This review aims to give an overview of dietary patterns and their association with HRQoL in cancer patients, both during and after treatment. The ketogenic diet seems to have great potential in the treatment of cancer, because of its anti-tumor effect and improvement of QoL. Subsequently, fasting during chemotherapy might improve HRQoL and several illness domains in cancer patients. Studies have shown that the Mediterranean diet is able to improve HRQoL in prostate and breast cancer patients undergoing treatment and in breast cancer survivors. Currently, bigger studies and intervention studies are needed to proof causality between certain diets and the health-related quality of life in cancer patients.

Introduction

Currently, one of the biggest morbidities in the world is cancer. Due to its wide variety of forms it is placing a high burden on global society (Fitzmaurice et al., 2017). Although, cancer has always been known as an age-associated disease, currently, it is seen as the biggest cause of premature death, where most of the cancers seem to develop under the influence of western lifestyles (Jemal et al., 2008). Factors like obesity, diabetes and chronic inflammation have been associated with a higher risk of development and mortality of certain cancer forms (Gallagher & LeRoith, 2015; Holly, Zeng, & Perks, 2013; Jaffee et al., 2017).

As previously shown by several studies, the diet seems to play a crucial role in the development of cancer. One of these studies, performed by Hodge et al, used a large cohort study in Australia and looked at the Mediterranean diet score (MDS) and the occurrence of lung cancer. In this study, they found a higher MDS, which indicates a healthier diet, associated with a lower risk for lung cancer (Hodge et al., 2016). Another study that highlights the relation between the diet and cancer development, is the study by Takato et al. In this Chinese cohort study, an association between vitamin-containing foods (like fruit and vegetables) and lung cancer was found (Takata et al., 2013).

Moreover, breast cancer was shown to be more prevalent in alcohol usage and lower in dietary patterns rich in plant foods and low in refined carbohydrates, like the Mediterranean diet (Toledo et al., 2015). While a food pattern high in whole grains, fibres, fruits and vegetables was shown to lower the risk on colorectal cancer development. The consumption of fish might lower the risk for liver cancer. Next to this, the regular intake of processed or grilled meat was shown to increase the risk for gastric cancer (Aicr & WCRF, 2012; Rock et al., 2020).

Although it has been shown that diet has an influence on cancer development, most of the association with diet during or after cancer treatment are less clear. An important end-point measure of cancer treatment is the health-related quality of life (HRQoL) of the patients. The HRQoL is defined by how well an individual functions in their life and his or her perceived wellbeing in physical, mental and social domains of health. Because of the heavy treatment, HRQoL is often low in cancer patients. Since the HRQoL cannot be measured by biomarkers, it is determined by means of a questionnaire (Karimi & Brazier, 2016) (Martin & Amin, 2017).

Recent studies have already shown that changes in physical activity, smoking habits, diet and weight management help to improve health-related quality of life (HRQoL)

in survivors of cancer (Clinton, Giovannucci, & Hursting, 2020). However, there is currently no clear overview of how different dietary patterns are associated with HRQoL in cancer patients.

Therefore this review aims to give an overview of the evidence about diets and health-related quality of life in cancer patients, during and after treatment. A search strategy containing search terms regarding diet, cancer and quality of life was used in Pubmed. In the context of this search, diet is defined as a certain food pattern that is followed over period, like the Mediterranean diet. An overview of the articles, resulting from the search, is shown in Appendix 2.

Ketogenic diet in cancer treatments.

In the ketogenic diet, the carbohydrate (CHO) intake is reduced and replaced by fats, leading to the formation of ketone bodies. This results in a shift in energy usage of the body. Normally the human body thrives on glucose, however, cancer cells also get their energy from glucose. Therefore, the ketogenic diet might be a promising way to surpass this principle. Unlike normal cells, cancer cells are not able to use ketones as an energy source. It is thought that the ketogenic diet is able to starve cancer cells of the energy needed for proliferation (Cohen, Fontaine, Arend, Soleymani, & Gower, 2018; Weber et al., 2020).

Recent studies have shown that the ketogenic diet might protect healthy cells from chemotherapy and increases the toxic effects towards the cancer cells. Although, the efficacy could be influenced by cancer type and genetic background. The antitumor effects of the ketogenic diet are determined by preclinical studies, where they found decrease tumor size and higher survival rates in the mice, during chemotherapy and radiation treatment (Klement, 2018; Weber et al., 2020). Moreover the ketogenic diet was shown to reduce inflammation and the diet did not give side effects (Youm et al., 2015).

Most importantly, the KD diet was shown to improve quality of life in cancer patients undergoing treatment. Khodabakshi et al performed an interventional study in 80 patients with locally advanced and metastatic

breast cancer, undergoing chemotherapy. In the study, the ketogenic diet consisted of 6% calories from CHO, 19% from protein, 20% from medium-chain triglyceride (MCT) oil and 55% from fat. MCT oil, an odorless and tasteless saturated fat, does not require enzymes for digestion. It is easily converted to ketones in the liver and thereby enhances ketosis.

In their study, they saw a decreased hunger, weight and body fat mass in the KD group after 6 of weeks intervention. These factors might be explained by the high fat content of the diet. High fat intake slows down digestion, resulting in a decreased hunger perception and weight loss. Next to this, physical activity levels in the patients were significantly higher, compared to control. These factors are especially favorable in obese patients. QoL was assessed by the EORTC QLQ-C30 questionnaires, at baseline, after 6 weeks and at the end of the study. Overall, the diet led to a global increase in HRQoL in patients treated for breast cancer. Assessed by physical and role functioning. A downside of this study is the relatively short study period of 12 weeks, since the transition into ketosis already takes 2 weeks (Khodabakhshi, Seyfried, Kalamian, Beheshti, & Davoodi, 2020).

In contrast to the study of Khodabakshi et al, Cohen et al did not find an effect of the ketogenic diet on appetite or weight loss, in patients with ovarian cancer, treated by chemotherapy or radiation. A possible explanation for this can be the fact that only 25% of the patients in this study was undergoing chemotherapy. In this study, the ketogenic diet consisted of 5% energy from CHO, 25% from protein and 70% from fats. Both groups were constructed to not alter the amount of energy intake. After 12 weeks of intervention, a significant ($p=0.02$) increase of physical activity and energy level was found in the KD group. Next to this, a significant ($p=0.04$) between group increase in physical functioning was observed. No changes in mental functioning were observed. Overall, this study resulted in an improvement of Health-related quality of life. Although positive effects of the diet were found, this study only lasted 12 weeks and therefore more studies are needed (Cohen et al., 2018).

Augustus et al, performed a randomized control trial in stage 2 and 3 cancer patients, undergoing chemotherapy, in the Caribbean (N=40). The patients were randomized 1:1 to receive a ketogenic or control diet for 16 weeks. In this study, the ketogenic diet consisted of 10% CHO, 15% protein and 75% fats, with a total of 2000 kcal. The main source of fats in this study was medium chain triglycerides. After the intervention period, a significant decrease in BMI ($p=0.04$), patients health ($p=0.001$) and overall QoL scores ($p=0.001$) was observed. Next to this, a self-reported improvement on mental health was observed in the KD group (Augustus, Granderson, & Rocke, 2021).

Although it is becoming increasingly evident that the ketogenic diet has anti-tumor effects and can improve the quality of life in cancer patients, it is not being prescribed as a standard treatment improvement. Since the diet is hard to follow, some patients might feel restricted by it, which can have a negative effect on the patients perceived HRQoL (Bauersfeld et al., 2018). Next to this, most studies are only looking at short-term effects. No long-term studies on large patients groups are currently being performed. In order to make better conclusion about the use of KD in cancer treatments, bigger studies and more interventional studies need to be conducted. Despite this, the diet has great potential to be used in the treatment of cancer.

Fasting as an addition to chemotherapy.

It has been known that a 20-40% reduction of calorie intake is able to protect the body against oxidative stress and aging. Because of this, it is hypothesized that calorie restriction is also able to protect patients from the toxic effects of chemotherapy (Lee et al., 2012; Longo & Fontana, 2010). Currently, several studies have looked at the effect of short-term fasting on QoL during chemotherapy treatment.

Like Bauersfeld et al, who performed a randomized control trial in 50 breast and ovarian cancer patients, undergoing chemotherapy. The intervention group was asked to fast, starting 36h before and ending 24h after 6 cycles of chemotherapy. The total

fasting period was 60h, during which the patients received unlimited amounts of water and herbal tea, 200 cl vegetable juice and small portions of vegetable broth (about 350 kcal per day). This intervention resulted in a significantly less compromised HRQoL and reduced fatigue level after chemotherapy, compared to baseline. Next to this, the patients reported a better tolerance to chemotherapy and declared to voluntarily continue the fasting during the following chemotherapy cycles (Bauersfeld et al., 2018).

Riedinger et al, looked at the effect of water only fasting during chemotherapy in gynecologic cancer patients. In this randomized control trial, 20 patients were asked to maintain a water-only fasting period, starting 24h before and ending 24h after each chemotherapy cycle. The participants were allowed to stay hydrated with water, black coffee and tea. The quality of life score was determined by the NCCN FACT FOSI-18 QoL questionnaire. The study demonstrated that fasting is safe and feasible in the patient group. The fasting treatment did not lead to any side effects or significant weight loss, even though this patient group is normally already at risk for malnutrition. Most importantly, a significantly improvement in QoL score was found in the fasting group, compared to baseline. As also shown in figure 1, where the bars show the change in QoL compared to baseline and the line shows the mean QoL score. As can be concluded from this study, water-only fasting can be seen as a safe strategy to improve QoL in gynecologic cancer patients, receiving chemotherapy (Riedinger et al., 2020).

Lugtenberg et al, demonstrated the effect of fasting in stage two and three breast cancer patients, undergoing chemotherapy (N=130). The patients were randomized, to receive fasting intervention or a normal diet. The fasting started 3 day prior to until the day of chemotherapy. QoL was assessed by means of the EORTC-QLQ-C30 questionnaire.

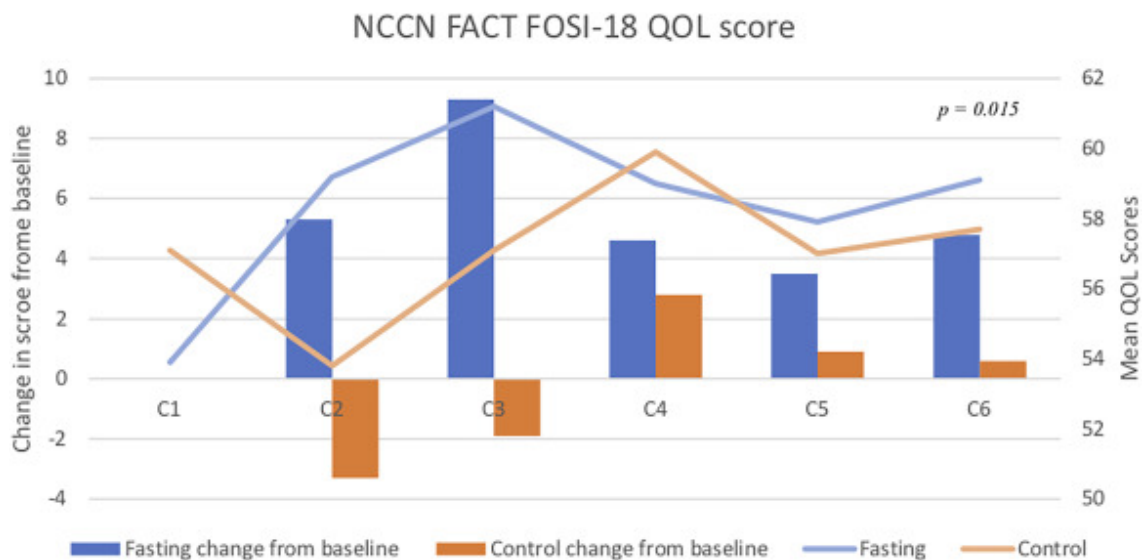


Figure 1: Quality of life scores, after fasting during chemotherapy cycles. Line represents mean Qol scores, according to right axis. Bars represent differences in Qol from baseline score, according to left axis (Riedinger et al., 2020).

Patients undergoing the fasting intervention showed a significant improvement in Qol over time; fasting patients gave better emotional and physical score as well as lower nausea and fatigue scores, compared to normal diet. In addition to this, they were less concerned about the possible side effects of treatment, compared to patients on normal diet (Lugtenberg et al., 2021).

To summarize, fasting prior and during chemotherapy seems to improve Qol and several illness domains in cancer patients. No side effects were observed by the fasting. Overall, fasting was shown to be a feasible way to improve treatment for all patients undergoing chemotherapy.

The Mediterranean diet in cancer treatment

The Mediterranean diet (MD) is characterized by high consumption of plant based foods (Fruit, vegetables, nuts, whole grains and olive oil) and low amounts of milk, red meat and sugars (Willett et al., 1995). For several decades, the diet has already been associated with a reduced risk of chronic diseases, like cardiovascular and neurodegenerative disease. Recent evidence suggest a possible role for the MD in the prevention of cancer (Giacosa et al., 2013; Michels, Mohllajee, Roset-Bahmanyar, Beehler, & Moysich, 2007; Trichopoulou, Costacou, Bamia, & Trichopoulos, 2009; Turati et al., 2018).

It is thought that the protective properties of the diet lie in the high levels of antioxidants and fibers in the diet. Bonaccio et al, studied the effects of the MD in a large cohort study of healthy individuals in Italy (N=16.937). In this study, people were randomly recruited and asked to fill out food frequency questionnaire, to evaluate dietary intake patterns and the short form health survey (SF-36), to evaluate health-related Qol. In this study, they found that a higher health-related quality of life was associated with a high adherence to the Mediterranean eating pattern. Although, the relationship was more potent in mental health than for physical health (Bonaccio et al., 2013). A big strength of this study is the cohort study itself, were a big amount of data can be collected from a large group of participants. Although cohorts also have limitations, since no interventions are performed no real causality can be found. Therefore cohort studies should be combined with interventional studies, to really study the effects on Qol.

Some studies have also suggested that the Mediterranean diet is also able to improve Qol in cancer patients. Both for patients being treated and in cancer survivors. Several studies looked at the effect of MD during cancer treatment, like Montagnese et al.

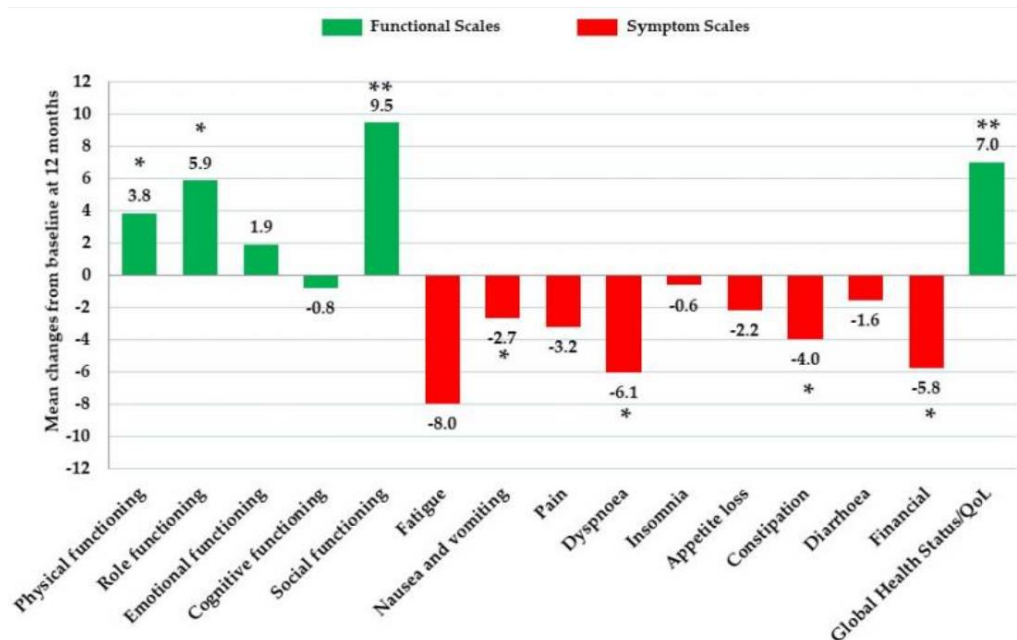


Figure 2: Mean changes in quality of life (QoL) by the Mediterranean diet in breast cancer patients. Significant increases in functional scales (green). Significant decrease of symptom scales (Red). Results in a significant increase in quality of life. ($P < 0,05$; $** < 0,001$) (Montagnese et al., 2021).

Montagnese et al, conducted an intervention study in patients with breast cancer, to evaluate quality of life after following a Mediterranean diet for 12 months. The adherence to the diet and QoL was assessed by means of questionnaires. After 12 months, a significant improvement in quality of life was found, compared to the baseline (figure 2). Which was assessed by significant improvements in several domains of health status, like physical ($p=0.5$) and social ($p=0.001$) functioning. Next to this, a significant decrease in symptoms like nausea ($p=0.5$), pain and appetite loss was shown, compared to the baseline. Other factors that were shown to improve, were the functional scales for body image and future prospective. These factors are commonly low in patients with cancer, therefore, the diet might be a good way to improve the QoL feeling in breast cancer patients (Montagnese et al., 2021).

Baguley et al, performed a randomized control study in patients being treated for prostate cancer. In this study, twenty-three men received a Mediterranean diet for 12 weeks, after which the QoL was determined. The MD consisted of <10% energy from saturated fat, 2 serving of fruit a day, 5 serving of vegetables a day, 30gr fiber a day, 3 serving fish per week, 2 serving dairy a day, 1 serving nuts/seeds a day, less than 2 units of alcohol

per week and elimination of red meat. Although red wine is normally present in a Mediterranean diet, it might have a negative effect on the cancer and is therefore not used in this study. This study concluded that MD is a safe and feasible intervention for man being treated for prostate cancer. Most importantly, a significant improvement of QoL was observed, compared to baseline and the control group. This was evaluated by a reduction in body mass and a improvement of mental health, vitality and emotional wellbeing (Baguley, Skinner, Jenkins, & Wright, 2021).

When looking at the current evidence, it is clear that the Mediterranean diet might be helpful during the treatment of cancer. However, most studies are too short or include little amount of patients, therefore larger studies are needed.

The Mediterranean diet in cancer survivors

Although cancer treatment can be effective, the risk for recurrence is still pressing. Next to this, the burden of cancer and its treatment can have a big negative effect on the HRQoL in cancer survivors. The Mediterranean diet might be an important factor in cancer survivors, to prevent recurrence and improve Health-related quality of life after cancer treatment. Like Ruiz-Vozmediano et al showed with their interventional study in breast cancer

survivors, who completed their treatment more than 12 months before. In this study, 75 survivors were randomized to receive the a life-style intervention or no intervention. In this study, the intervention consisted of dietary training and promotion of physical activity. The participants received workshops about healthy eating patterns, which promoted positive effects of certain food groups (fruit, vegetables, nuts, grains, fish, diary products, etc) and the negative effects of others (processed meats, high-fat products, etc). Next to this, recommendations were given about components to be avoided, like sugary and alcoholic drinks and reduction of salt. During the whole intervention period, meetings were organized to promote healthy cooking and share recipes between participants.

At the end of the follow-up, it was concluded that the promotion of healthy lifestyle significantly improved adherence to MD and weight control. Moreover, the results indicated that an MD intervention is able to improve QoL in breast cancer survivors, on both physical and social functioning. Which was assessed by an significant improvement of fatigue, physical condition and weight loss ($p=0.027$, 0.028 , 0.05 respectively) in the participants. Before the intervention, a majority of participants was overweight or even obese. Since overweight is seen as a risk factor for breast cancer and worse outcome, the MD intervention might be a potential to prevent recurrence of (breast) cancer (Ruiz-Vozmediano et al., 2020).

This effect of the MD diet on QoL in breast cancer survivors was also observed by Cho et al in South-Korea. Cho et al, performed an 8 week randomized control trial on 75 breast cancer survivors. For the MD group, participants were asked to increase the intake of certain food groups, like olive oil, fruits, vegetables, fish, nuts. They had to avoid processed meat, sugary drinks and sweets. After the intervention period, the QoL was determined by means of the EORTC QLQ-C30 questionnaire. At beginning, during and after the study some body measurements were taken, to analyze the full effect of the Mediterranean diet. The MD diet was shown to facilitate significant weight loss and improve

metabolic parameters, next to an improvement of QoL (Cho et al., 2020).

Porciello et al, conducted a randomized control trial in breast cancer survivors, to determine the dietary effect on breast cancer recurrence (N=309) in Italy. In order to determine the adherence to the Mediterranean diet, the PREDIMED questionnaire was used. The Health-related QoL was determined by means of 3 questionnaires, of which the EORTC QLQ-C30 is the most used. This study found that a greater adherence to the diet was associated with a significant lower pain and insomnia level, a higher physical functioning, health status and mental health in patients with a history of breast cancer, resulting in a significant better quality of life in these patients. Next to this, the dietary pattern was associated with reduced mortality and lower incidence of chronic diseases, including cardiovascular disease, diabetes and recurrence of cancer (Porciello et al., 2020).

To summarize, it is clear that the Mediterranean diet is able to improve quality of life in prostate and breast cancer patients undergoing treatment and in breast cancer survivors. Although, most of the shown effects seem to results from the weight loss following on the MD. Moreover, the current studies are commonly small and short, which makes a weak evidence. Therefore, more and bigger studies are needed, while also looking at different forms of cancer, to get a better overview of the effects of the diet on quality of life in cancer.

Other dietary interventions in (malnourished) cancer patients.

Patients with cancer mostly suffer from an impaired nutritional status or even malnutrition, which is also one of the factors that contributes to a worsened outcome of surgery or cancer treatment. It is known that cachexia is one of the leading causes of a decrease in quality of life (Bozzetti & Mariani, 2009; Fearon et al., 2011). The optimal nutritional management could contribute to tolerability of the oncological treatment and therefore lead to an improvement in the patients quality of life (Buskermolen et al., 2012; Capuano et al., 2010).

Zietarska et al, looked into the effect of a high protein diet on cancer related cachexia. In this study 100 patients with colorectal cancer and subsequently pre-cachexia were randomized to the intervention or control group. The intervention group received high-energy, high-protein, oral liquid nutritional supplements, two times 125 ml per day, over a period of 12 weeks. One portion contained 300 kcal, 18g of protein, carbohydrates, lipids, vitamins and minerals. The study indicated that a high protein diet in pre-cachexic patients improves nutritional status. In addition, the use of high protein diet resulted in an increased appetite in the patients, which led to an improvement of QoL. Next to this, serum albumin was significantly increased in patients undergoing the high protein diet (Ziętarska, Krawczyk-Lipiec, Kraj, Zaucha, & Małgorzewicz, 2017). Studies suggest that higher serum albumin levels are associated with fewer complications after treatment, improved prognosis and lower mortality rates (Arrieta et al., 2010; Borda et al., 2014). Overall, the study of Zietarska demonstrates that a high protein diet can significantly improve quality of life in patients with cancer cachexia (Ziętarska et al., 2017).

Leedo et al, looked at the effect of home delivery meal service of energy and protein rich meals to 40 malnourished patients suffering from lung cancer and receiving treatment. In this study, patients received 1 main dish, containing 450 kcal and 18 gr proteins and 1 snack per day. After 12 weeks, the Global QoL of the patients was determined by means of the EORTC QLQ-C30 questionnaire. Next to this, several other outcome measures were assessed, like the functional, symptom and depression score. Although no significant changes in outcome measures were found, this study did find an overall improvement of QoL in the intervention group, compared to control. Next to this, a positive relation between protein intake and QoL ($p=0.0006$) and for body weight ($p=0.02$) was found. A negative correlation was found between protein intake and symptoms scores ($p=0.002$) (Leedo et al., 2017).

Cotogna et al, looked at the effect of home parental nutrition (HPN) feeding on quality of life in advanced cancer patients.

Since HPN might prolong survival rates in incurable cancer patients, little is known about their QoL during this last period of life. This prospective, double-centre study looked at 110 cancer patients that were receiving HPN. Most patients had gastrointestinal cancers, were severely malnourished and had advanced stage cancer. The patients were closely monitored by physicians and caregivers. HPN was delivered 10 to 14h per day at night, using standard all-in-one bags. All patients were followed until withdrawal of HPN, for every possible reason. The QoL of the patients was tested by means of the EORTC QLQ-C30 questionnaire, in the presence of a physician or caregiver.

The study showed a significant improvement of global QoL, physical and emotional functioning, as well as increased appetite and a lower fatigue level ($p=0.001$, 0.001 , 0.001 , 0.004 and 0.02 respectively). The improvement of QoL by the nutrition seemed to be better in patients still undergoing treatment, compared to those without treatment. To conclude, this study demonstrated that HPN is associated with an improvement of QoL in advanced cancer patients, to make their end period of life more bearable (Cotogna et al., 2017).

Although these current studies seem to highlight a connection between high protein meals to improve quality of life in (malnourished) cancer patients, most studies only look at 12 weeks intervention period. Therefore longer studies with more participants are needed to prove real causality.

Significant dietary patterns in cancer treatment

Although a specific diet seems important, the habits of certain dietary patterns are more common and thus easier to adapt to. Therefore, looking at patterns might give a better and bigger overview of dietary effects on quality of life in cancer patients.

Gigic et al, looked at the possible associations between common dietary patterns and the quality of life, in colorectal cancer patients. For this study, data from a multicentre, international cohort, initially developed by the Fred Hutchinson Cancer Research Centre in Seattle USA, was used. Patients with available food frequency questionnaire (FFQ) data at 12 months post-

surgery and at baseline and 12 months follow-up QoL data, were included in the study, to find possible food patterns and its effect on QoL. Next to this, newly-diagnosed colorectal cancer patients were recruited, to investigate predictors of cancer recurrence, survival rates and health-related QoL.

Several food patterns were observed in this study, of which some were not observed before in other studies. Like the “bread&butter” pattern, which reflects high scores in bread, butter and margarine. This pattern was associated with a continuous loss of appetite ($p=0.05$) and a lack of interest in diet. Previous studies have shown that lack of appetite in early stage of disease was significantly associated with lower survival rates ($p=0.01$) and a low QoL level ($p=0.02$) (Fournier et al., 2016).

Participants with a high consumption of a “western” diet, reported an increase in constipation ($p=0.01$) and diarrhoea ($p=0.04$) over time, compared to other patterns. This might be explained by the facts that the western diet does not contain foods rich in dietary fibres, which is crucial for the intestine. The western food pattern commonly contains high amounts of processed meats, potatoes and sugars. Moreover, these patients were less likely to improve their global QoL status ($p=0.04$) and physical functioning ($p=0.1$).

In contrast to this, high “food&vegetable” dietary pattern scores were associated with an improved diarrhoea ($p=0.01$) score. Since dietary fibres, mostly found in fruits, vegetables and whole grains are known to protect against constipation and diarrhoea. Next to this, a positive association between the healthy diet (fruit and vegetable rich) and quality of life as well as physical functioning was found.

To summarize, it is clear that certain dietary patterns can influence the quality of life over time, in colorectal cancer patients. While a “western” pattern can negatively affect QoL, a diet rich in fruit and vegetables seems to be beneficial for the patients QoL (Gigic et al., 2018). This information could be used to instruct cancer patients, that don't want to change their whole diet. Adapting into a food pattern rich in fruit and vegetables might be more feasible for most cancer patients.

Conclusion

The aim of this review was to acquire a better overview of the knowledge about dietary patterns and their association with health-related quality of life in cancer patients and survivors. While (lack of) quality of life is an important aspect in cancer patients, most studies do not look at a quality of life, which makes this review of great importance.

Although it is clear that the ketogenic diet is able to improve HRQoL in cancer patients, more extensive studies are needed to determine the full potential of the diet. The current studies suggest that implementing the KD in cancer treatments is safe and feasible, for overall weight management and improvement of HRQoL, both mentally and physically.

Short-term fasting might even be more feasible for cancer patients undergoing chemotherapy. Studies have shown that fasting prior and during chemotherapy seems to improve certain QoL and illness domains in cancer patients, while no side effects were shown. Therefore, fasting seems to be a feasible way to improve cancer treatment.

The Mediterranean diet is commonly studied in relation to breast cancer, where it has the promising ability to improve HRQoL, both during and after treatment. However, the possible potential in other cancers still needs to be studied.

To summarize, it is clear that diet can be seen as a promising way to improve quality of life in cancer patients. Although the way to determine HRQoL sometimes differs between studies, which might result in less reliable results. Most studies use the EORTC QLQ-C30, while some studies look at other QoL questionnaires. Currently, more research is required to discover the full potential of diets and dietary patterns can have on health-related QoL.

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Appendix 1: Search strategy

Before writing the essay, a search strategy was set up in order to discover the most important articles in the field.

Table 1: Search strategy used for the study

| | Cancer | Nutrition | Quality of life |
|-------------------|---|--|--|
| MeSH | "Neoplasms" | "Diet" | "Quality of life" |
| Text words [tiab] | Neoplasm* Cancer* Tumor* Malignan* "Oncolog*" | Healthy diet Diet Nutrition* Healthy nutrition Eating healthy Healthy eating index* HEI Food pattern* | Quality of life QoL Living quality EORTC QLQ |
| N** | 4,586,616 | 675,917 | 383,523 |

("Neoplasms" [MeSH] OR "Neoplasm*" [tiab] OR "Cancer*" [tiab] OR "Tumor*" [tiab] OR "Malign*" [tiab] OR "Oncolog*" [tiab])

AND

("Diet" [MeSH] OR "Healthy diet" [tiab] OR "Diet" [tiab] OR "Nutrition" [tiab] OR "Healthy nutrition" [tiab] OR "Eating healthy" [tiab] OR "Healthy eating index*" [tiab] OR "HEI" [tiab] OR "Food pattern*" [tiab])

AND

("Quality of life" [MeSH] OR "Quality of life" [tiab] OR "QoL" [tiab] OR "living quality" [tiab] OR "EORTC" [tiab] OR "QLQ" [tiab])

8 December 2021: N= 2,824

Without reviews: 346 results

New more focused search strategy

Mediterranean diet

("Neoplasms" [MeSH] OR "Neoplasm*" [tiab] OR "Cancer*" [tiab] OR "Tumor*" [tiab] OR "Malign*" [tiab] OR "Oncolog*" [tiab])

AND

("Mediterranean diet" [tiab] OR "MDS" [tiab])

AND

("Quality of life"[MeSH] OR "Quality of life"[tiab] OR "QoL" [tiab] OR "living quality" [tiab] OR "EORTC" [tiab] OR "QLQ" [tiab])

21 December 2021: N=276

Without reviews: 24

Ketogenic diet

("Neoplasms" [MeSH] OR "Neoplasm*" [tiab] OR "Cancer*" [tiab] OR "Tumor*" [tiab] OR "Malign*" [tiab] OR "Oncolog*" [tiab])

AND

("Ketogenic diet" [tiab] OR "Keto diet" [tiab] OR "Fasting" [tiab] OR "Short-term fasting" [tiab])

AND

("Quality of life"[MeSH] OR "Quality of life"[tiab] OR "QoL" [tiab] OR "living quality" [tiab] OR "EORTC" [tiab] OR "QLQ" [tiab])

21 December 2021: 194 results

Without reviews: 39

Appendix 2: Sorting of articles

The articles that came forward from the search strategy, ordered on subject.

| Subject | Auteur | Year | Type of cancer | During or after treatment | Results of study | PMID | Type of study |
|---------------------------------|--------------|------|-----------------------------|---------------------------|---|----------|--------------------------|
| Ketogenic diet | Weber | 2020 | Several cancers | During standard treatment | Increase in QoI | 31399389 | Review |
| Keto/ fasting | Plotti | 2020 | Several cancers | During radiation | Reduction of drug toxicity and improving QoI | 33197913 | Review |
| Short-term fasting | Bauersfeld | 2018 | Breast and ovarian cancer | During | Fasting improves QoI | 29699509 | Cross-over pilot study |
| Ketogenic diet | Cohen | 2018 | Ovarian cancer | During | Significant benefits that improve QoI | 30200193 | Randomized control study |
| Ketogenic diet | Khodabakhshi | 2020 | Breast cancer | During | Improved QoI in patients | 32828130 | Randomized control trial |
| Fasting | Riedinger | 2020 | Breast cancer | During chemo | Clinical relevant improvement of QoI | 32958269 | Randomized control trial |
| Fasting | Lugtenberg | 2021 | Breast cancer | During chemo | Improved QoI and illness perception | 33179154 | Phase 2 direct trial |
| Ketogenic diet | Augustus | 2020 | Stage 2 and 3 cancer | During | Great improvement of QoI and mental health | 32791011 | Randomized control trial |
| Mediterranean diet | Porciello | 2020 | Breast cancer | During chemotherapy | Improve of QoI | 33031478 | Multicenter trial |
| Mediterranean diet | Montagnese | 2021 | Breast cancer survivors | After | Positive impact on QoI | 33396551 | Intervention study |
| Mediterranean diet | Cho | 2020 | Breast cancer survivors | After | Significant weight loss and improvement of QoI | 33061494 | Randomized control trial |
| Mediterranean diet | Vozmediano | 2020 | Breast cancer survivors | After | Significant improvement of QoI | 32462950 | Randomized trial |
| Mediterranean diet | Baguley | 2020 | Prostate cancer | During ADT | Significant improvement of QoI | 32534948 | Randomized control trial |
| Diet | Mehra | 2017 | Cancer survivors | After | Healthy diet improves QoI | 28992860 | Review |
| Dietary guidelines | Lee | 2019 | Colorectal cancer survivors | After | Patients with family that promoted healthy diet showed improved QoI | 31464383 | Cross-sectional study |
| Dietary patterns | Gigic | 2018 | Colorectal cancer patients | During | Western diet negative for QoI, while fruit and vegetables can improve QoI | 29244538 | Intervention study |
| Nutritional intervention | Anderson | 2017 | Cachexia cancer patients | During | Early intervention can improve QoI | 28138933 | Review |

| | | | | | | | |
|--------------------------------|-------------|------|---|------------------------|--|----------|---------------------------------|
| Dietary patterns | Kim | 2021 | Cachexia cancer patients | During | Improvement in Qol | 33718995 | Review |
| High protein | Zeitaska | 2017 | Precachectic cancer patients | | Higher nutritional status, no changes in Qol | 29019951 | Randomized study |
| Home parental nutrition | Cotogni | 2017 | Advanced (gastrointestinal) cancer patients | End stage of treatment | Significant improvement of Qol | 28557362 | Prospective double centre study |
| Home enteral nutrition | Campos | 2021 | Cancer patients that need HEN | During | Route of entry influences Qol | 32459026 | Questionnaires |
| Parenteral nutrition | Muscaritoli | 2012 | Advanced (gastrointestinal) cancer patients | End stage of treatment | Enhancement of Qol | 22365185 | Review |