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Chapter 10

Cancer Treatment and Nutritional Deficiencies

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Abstract

Increasing cancer incidence and improved survival rates have seen the number of cancer survivors increase exponentially throughout the last few decades. As a consequence of this, cancer survivors may experience a number of permanent side effects from their cancer or the treatment. Traditionally, patient follow-up has been undertaken by oncological specialists with a major focus on possible cancer reoccurrence; however, this fails to identify or adequately address many patients' concerns regarding post-cancer treatment. For a majority of patients, nutrition during treatment and post-cancer diagnosis and treatment is an area they can control and change for their own health and well-being. The following chapter addresses nutrient deficiencies associated with certain cancers, chemotherapy agents, radiation and surgical procedures. Potential treatment protocols for different oncological stages post diagnosis are explored and conditions that may induce nutrient deficiencies and how they can be treated or decreased are explained.

Keywords: chemotherapy, radiation, cancer survivorship, nutrient deficiencies, well-being

1. Introduction

Increasing cancer incidence and improved survival rates have seen the number of cancer survivor's increase exponentially throughout the last few decades. As a consequence of this, cancer survivors may experience a number of permanent side effects from their cancer or the treatment [1]. Traditionally, patient follow-up has been undertaken by oncological specialists

with a major focus on possible cancer reoccurrence; however, this fails to identify or adequately address many patients' concerns regarding post-cancer treatment. For a majority of patients, nutrition during treatment and post-cancer diagnosis and treatment is an area they can control and change for their own health and well-being.

However, Zhang (2015) [2] published a study indicating that cancer survivors are usually motivated to improve their health but were found to have suboptimal diets. She examined the dietary intake of 1533 cancer survivors and 3075 individuals who had never had cancer. The researcher estimated the quality of the diets using the Health Eating Index, which is based on the United States government's 2010 Dietary Guidelines for Americans. The scores ranged from 0 to 100, with 0 indicating no adherence to 100 which is total adherence. After adjusting for age, sex and ethnicity, Zhang found that the group who had not had cancer had an average index of 48.3 and the cancer survivors on average indexed 47.2. It was found that cancer survivors in general from this population ate less fibre, more empty calories and more refined sugars and fats. In addition, they examined patients who had different types of cancer and found that those who had breast cancer had the healthier diets and those who had lung cancer had the worst diets. It was also identified that cancer treatment may cause people to have specific food cravings, or change the way food tastes. This may influence the food choices they make post treatment.

Nutritional deficiencies in people with cancer who are undergoing traditional oncology treatment are a critical component for the health and survival of patients with or after cancer diagnosis. To date, a majority of research and nutritional screening has focused on malnutrition and weight loss in relation to nutritional deficiencies. This nutritional assessment is essential for the diagnosis of nutritional compromise as nutritional deterioration has been found to be associated with adverse outcomes in terms of cancer prognosis such as response rate and survival [3]. The nutritional screening and identification for malnutrition has been well documented. However, this screening omits the general patient undergoing treatment for cancer who is not elderly, malnourished or losing weight. Patients who have lung, oesophagus, stomach, colon, rectum, liver and pancreas cancer have been found to be at greatest risk of weight loss and malnutrition [3].

However, breast and prostate cancer, which are two of the most common cancers, have been found to be associated with weight gain, not weight loss [4]. To date, nutritional screening of patients undergoing adjuvant or neo-adjuvant chemotherapy has not been conducted to ascertain nutritional status. Research into possible nutritional insufficiencies may provide an insight to assist clinicians in aiding patients to thrive with or after cancer. Moreover, individual research has identified a number of nutritional deficiencies that can occur from certain chemotherapeutic agents, radiation and surgery. Combining the research that has been conducted for people with cancer or post cancer may provide the information necessary for clinicians and patients post diagnosis and treatment to live a healthy, balanced life based on nutrient sufficiency, not deficiency.

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2. Background

Nutritional therapy for cancer requires a greater understanding of nutritional biochemistry, interactions as well as patients' expectations and disease impact. Nutritional analysis and early nutritional interventions (diet counselling, oral supplementation, enteral or total parenteral nutrition) may reduce, prevent or even reverse poor nutritional status, improve performance status and consequently affect their quality of life (QoL) [5]. The nutritional intervention may also depend on the type of cancer treatment, either curative or palliative. A nutritional intervention for a curative cancer treatment can have an additional role which is to increase the tolerance and response to the oncology treatment, decrease complications, reduce morbidity by optimizing the balance between energy expenditure and food intake, and decrease the possible risk of metastasis, whereas nutritional interventions for palliative care is aimed at improving the patients' QoL, controlling symptoms including vomiting, nausea, constipation and pain related to food intake [5].

Understanding the biochemistry associated with a patient who has a solid tumour versus a patient who is tumour-free post surgery/treatment is important for nutritional assessment. Cancer can have a major impact on a patient's physicality and psychological well-being. For example, proteolysis and lipolysis are accelerated while muscle protein synthesis is depressed in a person with a solid tumour. In addition, carbohydrate metabolism is modified by tumour growth such as an increased hepatic glucose production and Cori cycle activity and a reduction in insulin sensitivity in peripheral tissues. This results in a loss of lean body mass and fat tissue, causing an increase in energy expenditure and resulting in wasting [6, 7]. This type of cancer-related weight loss is different from simple starvation whereby normal refeeding can restore normal nutritional status. These tumour-associated metabolic abnormalities can frequently prevent the restoration of muscle mass and lead to cachexia due to complex interactions between pro-inflammatory cytokines and the host metabolism [8–10].

In addition to the effects of having a tumour, oncological treatments such as surgery, chemotherapy and radiotherapy can cause side effects and physiological changes that can affect food intake and nutritional status [11–14]. Moreover, the stress response from the treatment can have an effect on nutritional status and body composition. The changes in glucose metabolism, loss of muscle mass and increased fat distribution during chemotherapy also affect energy expenditure [15, 16]. In addition, the fatigue and nutritional status will vary depending on the patient who is assigned curative or palliative treatment.

A study conducted in 2015 on breast cancer patients analysed weight gain during adjuvant chemotherapy and survival. It was found that weight gain (between 1 and 12 kg) had a negative impact on both disease-free and overall survival rates [17]. Currently, the cause of weight gain during chemotherapy has not been revealed.

Individual nutrient deficiencies or insufficiencies can also occur during treatment. An example of this is vitamin D3. A systematic review published in 2013 found that 31% of cancer patients undergoing treatment were vitamin D3 deficient and 61% had insufficient levels [18]. The following chapter will investigate evidence-based research on nutrient deficiencies and insufficiencies during different phases of cancer treatment, stages and side effects of treatment.

3. Tumour-induced effects on nutritional status

The majority of research on tumour-induced effects on nutritional status is focused on cachexia or weight loss. Research has found that the progressive nutritional deterioration displayed in cachexia is different from starvation and is the result of the tumour burden on the body. The increased proteolysis and lipolysis is due to possible biochemical reactions in the body such as pro-inflammatory cytokine activation or specific molecules released by the tumour itself [19]. The proteolysis that is found in cachexia has also been found in cancer growth and can occur in individuals with a solid tumour who are not cachexic. The neoplasm or cancer growth can compromise the normal biochemical mechanisms that regulate muscle homeostasis, which results in the loss of muscle mass, functional impairment and compromised metabolism. The end result of this tumour-induced condition is enhanced muscle protein breakdown and amino acid release that sustains liver gluconeogenesis and tissue protein synthesis [20].

Research on individual nutrient deficiencies or insufficiencies has not been completed to date. It is uncertain at this stage if solid tumours cause nutrient deficiencies or nutrient insufficiencies. Further research is required to ascertain individual nutrient status of patients with cancer.

4. Nutritional implications from cancer therapies

Patients undergoing cancer treatment have been found to frequently experience malnutrition. The nutritional status of cancer patients varies depending on the treatment, the type of cancer and the ability to eat. A study on Indian patients published in 2015 investigated 57 cancer patients and evaluated them during treatment using a Patient-Generated Subjective Global Assessment (PG-SGA). The results found that 15.8% (9/57) were well nourished, 31.6% (18/57) were moderately or suspected of being malnourished and 52.6% (30/56) were found to be severely malnourished [21]. The researchers found that the highest malnutrition was in lip/oral cancer patients (33.3%) and that the prevalence of malnutrition was highest in patients during treatment (84.2%) [21].

Therefore, although not all nutrients have been researched to identify specific nutritional deficiencies or insufficiencies, it is highly likely that patients undergoing cancer treatment would have certain nutrient deficiencies or insufficiencies. These would vary just as patient responses to treatment vary as well.

4.1. Surgery

4.1.1. Head and neck cancers

Surgery for head and neck cancers includes tumours inside the sinuses, nose, mouth, salivary glands and down the throat including oesophageal cancer (Australian Cancer Research Foundation (ACRF)). The greatest impact on nutritional status from surgery for head and neck cancers is dysphasia (difficulty swallowing, approximately 14.7%) [22]. This impacts the patient's ability to eat and therefore nutrient intake. Research on specific nutrient deficiencies due to dysphasia has not occurred to date. Further research in this area is required.

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4.1.2. Gastrointestinal cancers

The gastrointestinal cancers involve surgery for stomach (gastric), bowel (colorectal), liver, oesophageal in some cases, pancreatic, anal, bile duct, gastrointestinal carcinoid, gallbladder and small intestinal cancers (ACRF). Depending on the cancer, location, staging and possible metastasis will depend on the implications on nutritional status.

A study published in 2016 investigated lean body mass after gastrointestinal surgery [23]. The loss of lean body mass has been found to decrease the compliance of adjuvant chemotherapy particularly in patients undergoing gastrectomy for gastric cancer. The researchers examined 485 patients. They found that the median loss of lean body mass was 4.7%. In 225 patients (46.4%), a lean body mass of 5% or more occurred. A statistical significance was found using both uni- and multivariate logistic analysis for severe lean body mass loss due to surgical complications including infection or fasting (odds ratio (OR) = 3.576; $p = 0.001$), total gastrectomy (OR: 2.522; $p = 0.0001$) and gender (OR: 1.929; $p = 0.001$) [23].

Hence, the identification of nutritional intervention requirements of patients undergoing surgery for gastrointestinal cancer is required. This is an important factor and could impact on patient adjuvant treatment compliance and possible survival post surgery.

4.1.3. General surgery considerations

All surgical interventions for cancer will have some form of nutritional impact on patients. Individual assessment of patients prior to and post surgery is important for patient health, compliance and health/well-being through treatment and post treatment.

Considering that a large percentage of cancer patients undergo surgery for a biopsy or to remove tumours, lymph nodes or de-bulking a neoplasm, the human body requires support for both minor and major surgeries. The body is an amazing machine when supported correctly. The main nutritional support required is based on decreasing inflammation, supporting the immune system and the body to fight infection.

Traditionally, it is suggested to avoid alcohol, tobacco, simple sugars, processed foods and recreational drugs prior to and post surgery [24, 25]. Smoking and hazardous drinking have been found to be the most common lifestyle risk factors that influence surgery complications [25]. In addition, avoiding nutrient supplementation that could increase the risk of bleeding such as fish oils, vitamin E, turmeric and herbs such as ginkgo should be stopped before 1 week.

Antibiotic use is common in surgery pre- or postoperatively [26, 27]. Prophylactic use of antibiotics has been to prevent the potential risk of infection postoperatively as pre- and perioperative antibiotics have been found to lower the infection rate [26]. To assist the recolonization of the microbiota, it is recommended to use pre- and probiotics [28].

Possible nutrient deficiencies pre- and postoperatively such as iron [29] need to be taken into consideration in addition to possible insufficiencies and nutrients to assist in healing such as vitamin C, zinc and amino acids such as proline and glycine [30, 31]. The prevalence of nutrient deficiencies postoperatively has been mainly focused on bariatric patients rather than on cancer patients [32]. However, nutrients found to be deficient in these patients may be

correlated to some cancer patients as a high percentage of patients with cancer have been found to have a higher body mass index (BMI) [33]. Therefore, nutrients such as vitamin D, which has been found to be deficient in approximately 57% of patients, vitamin B12, iron and folate, are best to be monitored pre- and postoperatively [32].

Hence, nutritional screening, management and support pre- and postoperatively assist the patient in chance for compliance through further interventional treatments in addition to survival.

4.2. Chemotherapy and immunotherapy

4.2.1. Identify certain nutrient deficiencies from chemotherapy administration

There are a large number of chemotherapy agents now on the market and are all divided into groups depending on their mechanism of action. Chemotherapy is often an effective treatment; however, each agent can cause particular side effects that can affect the person's health and well-being. Many of the new drugs now available do not cause the same severity of side effects and the new development in conventional medicine has helped to manage and reduce the main side effects of nausea, vomiting and leucopenia [34, 35].

Nutrient deficiencies that can occur from chemotherapy have limited research. A common side effect is chemotherapy-induced anaemia; however, this is not caused by low iron levels or deficiency. This side effect is due to the chemotherapy agent's mechanism of action on the development of red blood cells. Supplemental iron has been effective for an iron deficiency but not for chemotherapy-induced anaemia. Too much iron may promote tumour growth or worsen chemotherapy side effects. Therefore, iron supplementation should only be recommended if there is a diagnosed iron deficiency confirmed by pathology tests.

Vitamin B12 has been found to be deficient in certain individuals after chemotherapy [36]. A case study was presented in which a patient in a clinical trial for chemotherapy-induced peripheral neuropathy was found to be deficient in vitamin B12 post chemotherapy. This woman had normal vitamin B12 blood parameters pre-chemotherapy administration and again upon intramuscular vitamin B12 injection and supplemental vitamin B12 and 6 months after supplementation. Although this represents only one individual, it is possible that certain individuals may develop vitamin B12 deficiencies during chemotherapy, which may induce more severe presentation of other chemotherapy-induced side effects.

Hereditary disorders that cause haemolytic anaemias have also been found to induce a vitamin B12 deficiency, which require lifelong vitamin B12 administration [37]. These conditions need to be identified prior to chemotherapy administration to ensure that the patient is not in a deficient state. Another consideration is the use of protein pump inhibitors (PPI) and histamine H2-receptor antagonists as an association has been found with their use and a vitamin B12 deficiency [38]. PPIs are used during chemotherapy to assist with reflux and could have an impact on vitamin B12 absorption. In addition, metformin is another drug that has been found to decrease vitamin B12 and in combination with either histamine H2-receptor antagonists or PPIs, neuropathy due to vitamin B12 depletion has been found [39].

Another vitamin that has been found to be deficient during chemotherapy is vitamin D3. Teleni et al. in 2013 conducted a meta-analysis on vitamin D3 status in cancer patients [18]. They found that 31% of patients undergoing active treatment were deficient in vitamin D3 and 67% had insufficient levels. These findings and the awareness, impact and importance of vitamin D3 in the medical fraternity have now seen it being one nutrient that has been commonly prescribed to cancer patients undergoing treatment.

The main mineral that has been found to be deficient in patients undergoing chemotherapy such as cetuximab is magnesium [40]. Hypomagnesaemia has also been found in patients on PPIs particularly in combination with diuretics [41], which are common medications used in conjunction with chemotherapy agents. It is important to monitor magnesium levels in patients and potential oral supplementation may be required.

Research on nutrients to assist side effects from chemotherapy has continued; however, nutrients that are depleted during chemotherapy are still required. Potential nutrient deficiencies rather than macronutrient depletion may play an important role in patient mortality or morbidity. Further research is required to ascertain possible insufficiencies and deficiencies that could contribute to poor health and well-being of patients diagnosed with cancer and undergoing chemotherapy.

4.3. Radiation

Radiation, similar to chemotherapy, is considered to be an effective treatment against actively dividing cells. According to the American Cancer Society, more than 50% of all cancer patients undergo radiotherapy (www.cancer.org). Nutritional impact from radiation depends on where the person is receiving radiation. Head and neck cancers, lung cancer and gastrointestinal cancers have been found to have the greatest nutritional impact on cancer patients. The nutritional status of patients undergoing radiation therapy has been assessed, with specific nutritional indicators measured. One particular study focused on chemoradiotherapy on nasopharyngeal cancer. They found that after radiotherapy, 20.2% of patients had more than 10% weight loss. Statistically significant (p = 0.05) risk factors for poor nutritional status included old age, females, late stage of the disease, depression, high side effects and moderate nutritional status prior to radiotherapy [42]. It is advised that patients undergoing radiotherapy, particularly head and neck, gastrointestinal and lung cancer patients, be nutritionally assessed and intervention commenced to prevent malnutrition during treatment.

Individual nutrient screening of patients undergoing radiation is extremely limited. The main nutritional research on radiation is based on the prevention of malnutrition and weight loss, particularly for head and neck cancers. The importance of early nutritional management and intervention has been stipulated and implementation in hospitals has been encouraged [43]. Further research into individual nutrient deficiencies and insufficiencies during radiotherapy may also contribute to the health and outcome of cancer patients.

5. Nutritional screening

Effective nutritional screening, implementation of nutritional care plans and support are essential components for cancer patients. The screening and early detection of malnutrition is considered crucial in identifying patients at nutritional risk. A high prevalence of malnutrition has been identified in hospitalized cancer patients undergoing treatment, for example, colorectal cancer [44].

5.1. Current screening and assessment tools

Currently, there are a number of nutritional assessment tools used in clinical practice for cancer patients. The accuracy of diagnostic tools is based on sensitivity, specificity and positive- and negative-predictive values calculated on the likelihood that a given test result would be expected when the target condition is present compared with the likelihood of the same result if the condition was absent [44].

Tables 1 and **2** evaluate the nutritional tools available. The information has been obtained from the Queensland Government of Australia who conducted and published a malnutrition screening and assessment tool comparison in addition to a validated nutrition assessment tool comparison [45]. The screening tools evaluated used the parameters such as recent weight loss, poor intake/appetite and body weight measurements. It was found that all tools evaluated generally performed well. Choosing the correct nutritional screening tool will depend on various aspects such as complexity, sensitivity to that population group, who will be performing the screening, what actions will be undertaken and how the outcomes will be incorporated into the current facility procedures [45].

Name author, year	Setting and patient population	Nutrition assessment parameters	Rationale/clarification
Subjective Global Assessment (SGA) 1987 [46]	Setting: Acute [47–49] Rehab [50] community [51] Residential aged care [52] Patient group: Surgery [47] Geriatric [50–53] Oncology [48] Renal [49]	Medical history (weight, intake, GI symptoms, functional capacity) and physical examination Categories: 1. SGA A (well nourished) 2. SGA B (mild-moderate malnutrition) 3. SGA C (severe malnutrition	Requires training Easy to administer Good intra- and inter-rater reliability Patent-Generated
Subjective Global Assessment (PG-SGA) Ottery, F. 2005 [54]	Setting: Acute [55–57] Patient group: Oncology [55]	Medical history (weight, intake, symptoms, functional capacity, metabolic demand) and physical examination	Numerical score assists in monitoring changes in nutritional status

Name author, year	Setting and patient population	Nutrition assessment parameters	Rationale/clarification
http://pt-global.org/	Renal [56] Stroke [57]	Categories: SGA categories (A, B or C) as well as providing a numerical score for triaging. Global categories should be assessed as per SGA.	Easy to administer Scoring can be confusing requires training Patients can complete the first half of the tool by themselves
Mini-Nutritional Assessment (MNA) Guigoz Y et al. 1994 [58] http://www.mna-elderly.com/	Setting: Acute [58] Community [58] Rehab [58] Long-term care [58] Patient group: Geriatric [58]	Screening and assessment component includes diet history, anthropometry (weight history, height, MAC, CC), medical and functional status. Assessed based on numerical score as: - no nutritional risk - at risk of malnutrition or - malnourished	Lengthy Low specificity for screening section of tool in acute populations Can be difficult to obtain anthropometric data in this patient group

Table 1. Validated nutrition assessment tools: comparison guide [45].

Name author, year, country	Patient population	Nutrition screening parameters	Criteria for risk of malnutrition	When/by whom	Reliability established	Validity established
Malnutrition Screening Tool (MST) [59] Ferguson et al. (1999) Australia	Acute adults: inpatients and outpatients [59, 60] Elderly [61] Residential aged-care facilities [61]	Recent weight loss Recent poor intake	Score 0–1 for recent intake Score 0–4 for recent weight loss Total score: > 2 = at risk of malnutrition	Within 24 h of admission and weekly during admission. Medical, nursing, dietetic, admin staff; family, friends, patients themselves	Agreement by 2 Dieticians in 22/23 (96%) cases Kappa = 0.88 Agreement by a Dietician and Nutrition Assistant in 27/29 (93%) of cases Kappa = 0.84; and 31/32 (97%) of cases Kappa = 0.93	Compared with SGA and objective measures of nutrition assessment. Patients classified at high risk had longer length of stay. Sensitivity = 93% Specificity = 93%
Mini-Nutritional Assessment – Short Form (MNA-SF) [62] Rubenstein et	Elderly Best used in community, subacute or residential aged-care	Recent intake Recent weight loss Mobility Recent acute disease or psychological stress	Score 0–3 for each parameter Total score: <11 = at risk, continue with MNA	On admission and regularly not stated	Not reported	Compared to MNA and clinical nutritional status. Sensitivity = 97.9% Specificity = 100%

Name author, year, country	Patient population	Nutrition screening parameters	Criteria for risk of malnutrition	When/by whom	Reliability established	Validity established
al. (2001) United States	settings, rather than acute care [63]	Neuropsychological problems BMI				Diagnostic accuracy = 98.7% Compared with SGA in older inpatients Sensitivity = 100% Specificity = 52%2
Malnutrition Universal Screening Tool (MUST) [64] Malnutrition Advisory Group, BAPEN (2003) UK	Adults – acute and community	BMI Weight loss (%) Acute disease effect score	Score 0–3 for each parameter Total score: >2 = high risk 1 = medium risk 0 = low risk	Initial assessment and repeated regularly Able to be used by all staff	Internally consistent and reliable. Very good to excellent reproducibility Kappa = 0.8–1.0	Face validity, content validity, concurrent validity with other screening tools (MST and NRS) [65] Predicts mortality risk and increased length of stay and discharge destination in acute patients [66]
Nutrition Risk Screening (NRS-2002) [67] Kondrup et al. (2003) Denmark	Acute adult	% of recent weight loss % of recent poor intake BMI Severity of disease Elderly	Score 0–3 for each parameter Total score: >3 = start nutritional support	At admission and regularly during admission Medical and nursing staff	Good agreement between a Nurse, Dietician and Physician Kappa = 0.67	Retrospective and prospective analysis. Tool predicts higher likelihood of positive outcome from nutrition support and reduced length of stay among patients selected at risk by the screening tool and provided nutrition support.

Table 2. Comparison of malnutrition assessment and screening tools [45].

5.2. Nutritional deficiencies linked with specific cancers

5.2.1. Breast cancer

Breast cancer has been found to be the most frequently diagnosed cancer in women worldwide. It is estimated that 1.7 million cases and 521,000 deaths in 2012 were attributed to breast cancer and breast cancer alone accounts for 25% of all cancer cases and 15% of all cancer deaths among females [68]. There have been a number of different nutrient deficiencies or insufficiencies that have been attributed to an increased risk of breast cancer development. These include vitamin D3, iodine, folate, zinc, betacarotene and coenzyme Q10. **Table 3** shows the association of these nutrients and the risk of breast cancer.

Nutrient	Outcome
Coenzyme Q10	One study in 1998 investigated the role of coenzyme Q10 or ubiquinone in 200 women hospitalized for a biopsy and/or ablation of a breast tumour. They found that 80 patients (40%) with carcinomas and 120 patients (60%) with a non-malignant lesion had a coenzyme Q10 deficiency. There was also a correlation between the intensity of the deficiency and the prognosis of the breast cancer severity [69].
Folate	A lot of focus has been placed on the methylenetetrahydrofolate reductase (MTHFR) polymorphisms of late. A case-controlled study and pooled meta-analysis conducted in 2007 found that peri-menopausal ladies with the C677T polymorphism did have an increased risk of developing breast cancer [70].
Folate, zinc, betacarotene	A recent study in 2014 found that multiple genetic polymorphisms and/or deficiencies in folate, zinc and betacarotenes were associated with the triple negative breast cancer development, particularly in combination [71].
Iodine	Iodine was presented as a possible anti-proliferative agent for mammary glands in 2005 [72]. It has been found in both animal and human studies to exert a suppressive effect on the development and size of benign and cancer neoplasms [72]. As iodine stores in the thyroid and breast tissue, it exerts a protective action on the development of breast cancer. As hypothyroidism has been found to be high in breast cancer patients, it is proposed that low iodine levels may be considered a risk factor for breast cancer [73].
Selenium	In a meta-analysis conducted in 2014, an inverse relationship was found between selenium serum levels and the risk of breast cancer [74]. Therefore, maintaining selenium levels may decrease the risk of breast cancer for some women.
Vitamin D3	A vitamin D deficiency is highly prevalent among breast cancer females [75]. A vitamin D deficiency has been found in 99% of breast cancer females at diagnosis and approximately in 90% in healthy females [76]. Alcohol status and weight have an impact on vitamin D status and breast cancer risk [77].

Table 3. Nutrient deficiencies and breast cancer risk.

5.2.2. Prostate cancer

Nutrient	Outcome
Selenium	A systematic review and meta-analysis of selenium and prostate cancer found that the relationship between plasma/serum selenium and prostate cancer showed that the risk of developing prostate cancer decreased with increasing plasma/serum selenium levels (170 ng/mL) [78]. Further studies are required but there is a link between low selenium levels and prostate cancer risk.
Vitamin D3	Vitamin D3 (25(OH)D concentrations have been found to be inversely correlated with prostate cancer risk but not vitamin D–related polymorphisms or parathyroid hormone. This indicates that there is a possibility that low vitamin D3 blood pathology may pose a risk of prostate cancer risk [79]. No association has been found to vitamin D levels or vitamin D supplementation on prostate-specific antigen (PSA) levels [80]. It has been suggested that adding vitamin D supplementation might be an economical and safe way to possibly reduce the prostate cancer incidence and improve the cancer prognosis and outcome [81].
Vitamin E and trace minerals	As mentioned, a study on Nigerian prostate cancer males was conducted. This study showed that the levels of whole blood superoxide dismutase (SOD), vitamin E, serum selenium and zinc were significantly lower in prostate cancer patients. Therefore, the authors conclude that deficiencies in vitamin E, zinc and selenium may be risk factors for the development of prostate cancer [82].
Zinc	Human studies on zinc deficiencies and prostate cancer are limited. In vitro studies have found that a zinc deficiency does impact prostate cells and can compromise DNA integrity by impairing the function of zinc-containing proteins [83, 84]. One study conducted on Nigerian prostate cancer patients did find an association with a zinc deficiency and prostate cancer in addition to selenium and vitamin E deficiencies [82].

Table 4. Nutrient deficiencies linked with prostate cancer.

A majority of the population feel that prostate cancer is the most frequently diagnosed cancer in men worldwide, but in fact it is the second with 1.1 million new cases estimated to have occurred in 2012. However, it is the most frequently diagnosed cancer in men in developed countries. The incidence rates vary with the highest rates found in Australia/New Zealand, Northern America, Northern and Western Europe and some Caribbean nations. The lowest incidence rates are found in the Asian countries [68]. Nutrient deficiencies that have been studied and identified as potential risk factors include vitamin D3, selenium, zinc and vitamin E (**Table 4**).

5.2.3. Colon cancer

Colon or colorectal cancer is the third most commonly diagnosed cancer in males and second in females. It is estimated that 1.4 million cases and 693,000 deaths occurred in 2012 due to colorectal cancer. The highest incidence rates have been found in Australia/New Zealand, Europe and North America. The lowest incidence rates are found in Africa and South-Central Asia [68]. Nutrients that have been associated with an increased colon cancer risk include vitamin D3 and folate. Folic acid is controversial with a deficiency and if excess is linked with

colorectal cancer risk. In addition to specific nutrients, dietary factors are linked with colorectal cancer development as seen in **Table 5**.

Nutrient	Outcome
Fibre, low-fruit and -vegetable, high red and processed meat intake	Although not a specific nutrient, it has been well established that a diet low in fruits and vegetables, fibre and high in red and processed meat intake is a risk factor for colorectal cancer development [85–87].
Folic acid	Folic acid is a controversial nutrient for colorectal cancer. High levels have been associated with a reduced colorectal cancer risk; however, excessive folate levels may promote tumour progression [88]. These facts have prevented countries fortifying foods with folate due to the risk of colorectal cancer. Preventing a deficiency in folic acid is recommended as it is a risk factor for cancer development but monitoring levels to prevent excess is also recommended.
Selenium	Animal studies have found that a selenium deficiency can acerbate colitis and promote tumour development and progression in inflammatory carcinogenesis [89].
Vitamin D3	Vitamin D may protect and treat inflammatory bowel disease and assist colon cancer [90]. Vitamin D3 deficiency and insufficiency has been linked as a risk factor for colorectal cancer as found in observational studies in both human and experimental studies (animal and cell lines). The protection from vitamin D3 has been attributed its influence on cell proliferation, differentiation, apoptosis, DNA repair mechanism, inflammation and immune function [91]. A high prevalence of a vitamin D3 deficiency and insufficiency has been found in colorectal cancer patients [75].

Table 5. Nutrient deficiencies linked with colorectal cancer.

5.2.4. Lung cancer

Nutrient	Outcome
Selenium	Several epidemiological studies have shown an increased risk of lung cancer among adults with low blood levels of selenium; however, the results are inconsistent. One study conducted in the south-eastern United States found that there was a risk of lung cancer development in lower income and black Americans [92].
Vitamin A	Cigarette smoking has been directly associated with the development of lung cancer. It has been demonstrated that cigarette smoke significantly reduces retinoic acid in the lungs of rats and increases the formation of precancerous and cancerous lesions [93]. It has been found that this is attributed to two independent pathways, RARα- and RARβ-mediated pathways. Human studies are limited if a vitamin A deficiency increases the risk of lung cancer development if exposed to cigarette smoke.

Nutrient	Outcome
Vitamin D3	A high prevalence of low vitamin D3 has been found in lung cancer patients ranging from a mild deficiency to severe deficiencies [75].
Zinc	Human studies on zinc deficiency and lung cancer are limited. Cell culture work on human lung fibroblasts has found that a zinc deficiency can cause DNA instability and compromise its integrity and therefore may be important in the prevention of DNA damage and cancer [94].

Table 6. Nutrient deficiencies linked with lung cancer.

The popularity of breast and prostate cancer override the one cancer that is the most frequent cause of death among males in 2012 and is the leading cause of death in females in developed countries and second in less developed countries, lung cancer. The highest lung cancer incidence rates include Europe, Eastern Asia and Northern America and the lowest rates are in sub-Saharan Africa. Although smoking has high correlation with lung cancer development, a high prevalence of non-smoking individuals has been diagnosed with lung cancer. This high prevalence has been thought to reflect indoor air pollution, cooking fumes, exposure to occupational and environmental carcinogens such as asbestos, arsenic, radon and polycyclic aromatic hydrocarbons. Recently, outdoor pollution as also been attributed as a cause of lung cancer [68]. In addition, certain nutrients may also play a role in the development of lung cancer. These include vitamin D3, zinc, vitamin A and selenium as seen in **Table 6**.

6. Nutritional deficiencies and therapy for certain conditions linked with cancer treatment

Condition	Possible nutrient deficiency or insufficiency
Alteration of taste and smell	Zinc
Cachexia	Multiple nutrient deficiencies, protein, essential fats
Chemotherapy-induced peripheral neuropathy	Vitamin B12, vitamin B6, vitamin E, omega 3 fatty acid (DHA)
Dehydration	Water, electrolytes
Diarrhoea	Water, electrolytes, gut bacteria (lactobacillus, bifidus etc.)
Eczema/dermatitis	Essential fats, omega 3 fatty acids, vitamin E, vitamin D3, zinc, vitamin A
Hand and foot syndrome	Vitamin B6
Mucositis	Glutamine, vitamin A, zinc, glucosamine, vitamin C
Radiation-induced enteritis	Glutamine, vitamin A, zinc, glucosamine, vitamin C

Table 7. Potential nutritional deficiencies or insufficiencies for conditions linked with cancer treatment.

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Research into nutrient deficiencies linked with certain conditions is limited. Certain nutrients have been found to be insufficient or deficient for certain conditions and may assist the patient in managing the situation. **Table 7** lists some conditions and possible nutrients, which could be found to be deficient or insufficient. It may be beneficial to consider the replacement of these nutrients for patients, or at least pathological or physical assessment to check the status.

7. Nutrition for patients who have had treatment for curative cancer

Curative cancer treatment normally occurs after surgery and can be intense. The impact on the nutritional status of the patient strongly depends on the tumour site, stage and progression of the cancer, the risks of the active treatment and the base nutritional status of the patient. For example, a patient undergoing concurrent chemotherapy and radiation for head and neck or lung cancer has a higher risk of malnutrition and impact on nutritional status than a patient undergoing adjunct chemotherapy for breast cancer.

Nutritional assessment and management should be started at the time of diagnosis and monitored throughout active treatment and afterwards. An ideal nutritional intervention and management commences with the initial evaluation of the patient's nutritional status through preliminary assessment tools and blood pathology tests. Regular re-evaluation is required throughout the treatment and post treatment until a good nutritional status is restored.

8. Nutrition in advanced cancer/palliative

Advanced cancer or palliative treatment is defined as patients who have metastatic cancer or are not responsive to curative treatment [5]. The life expectancy for these patients can vary from 1 month to many years. Therefore, nutritional assessment and intervention will depend on the stage of the cancer, the individual's current state, controlling the symptoms, maintaining an adequate hydration state and maintaining or restoring the patients 'well-being'.

Body weight will vary depending on the person as weight gain can occur due to lack of mobility and fatigue or weight loss/cachexia towards the end of life. Oedema and ascites from the tumour sites can also cause discomfort and impact digestive ability. Nutritional intake can also influence the QoL of the patient [5]. Constant re-evaluation and nutritional options are required as the patient's physical state changes. Consideration of nutrient intake, supplementation and nutritional fluid replacements are all important for each stage. Optimal nutritional status may not be restored in some cases; however, maintaining nutritional status for as long as possible has been found to be beneficial for the patient's well-being and QoL [5].

9. Summary

Current treatment for cancer is focused on survival, cure or pain management of the patient through active treatments such as surgery, chemotherapy, immunotherapy, radiation or hormone treatment. The nutritional status of patients generally is not a major consideration of primary health professionals unless malnutrition or weight loss is present, or the treatment may induce malnutrition. However, with the increasing number of cancer survivors, base nutritional status, nutritional assessment and support need to be extended to all cancer patients prior, during and post active cancer treatment. Nutritional screening and assessment needs to be considered an essential component of all aspects of cancer treatment.

This increased likelihood of individuals with cancer living longer after treatment has seen 'cancer survivorship' become a popular concept amongst organizations, hospitals, institutions and researchers within the field of oncology. A cancer 'survivor' is commonly defined as any person who has been diagnosed with cancer from the time of diagnosis through the balance of their life [95], although, many parties advocate for use of the term to relate to individuals who have had a previous cancer diagnosis and are now pursing life 'after active treatment' [95]. There are three distinct phases of cancer survivorship: *time of diagnosis to active treatment, the transition from active treatment to extended survival* and *long-term survival* [96]. In 2013, the American Society of Clinical Oncology (ASCO) released its assessment of survivorship care in adults [97] and conducted its first Inaugural Survivorship Symposium this year, 2016, in San Francisco.

One of the main focuses of cancer survivorships is diet, nutrition, exercise and long-term side-effect management. From definition, this starts from cancer diagnosis. Potential nutrient deficiencies or insufficiencies are areas that need further attention as well as their possible impact on side effects experienced by patients. Integration of nutritional assessment and intervention can be achieved through the current medical system and should be an important component of cancer patient-centred care.

10. Further directions

- Investigation into nutrient deficiencies in newly diagnosed cancer patients with emphasis on the type of cancer, social and economic status, gender and culture.
- Future trials and/or nutritional monitoring, assessment and intervention throughout cancer patient's active treatment and post treatment.
- Research into how nutritional deficiencies or insufficiencies may affect patient side effects to treatment.
- Research into potential nutrient deficiencies and insufficiencies as risk factors for cancer development and their mechanisms of action in cell impairment and cancer initiation and progression.

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