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Opinion paper

The importance of protein sources to support muscle anabolism in cancer: An expert group opinion

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SUMMARY

This opinion paper presents a short review of the potential impact of protein on muscle anabolism in cancer, which is associated with better patient outcomes. Protein source is a topic of interest for patients and clinicians, partly due to recent emphasis on the supposed non-beneficial effect of proteins; therefore, misconceptions involving animal-based (e.g., meat, fish, dairy) and plant-based (e.g., legumes) proteins in cancer are acknowledged and addressed. Although the optimal dietary amino acid composition to support muscle health in cancer is yet to be established, animal-based proteins have a composition that offers superior anabolic potential, compared to plant-derived proteins. Thus, animal-based foods should represent the majority (i.e., ≥65%) of protein intake during active cancer treatment. A diet rich in plant-derived proteins may support muscle anabolism in cancer, albeit requiring a larger quantity of protein to fulfill the optimal amino acid intake. We caution that translating dietary recommendations for cancer prevention to cancer treatment may be inadequate to support the pro-inflammatory and catabolic nature of the disease. We further caution against initiating an exclusively plant-based (i.e., vegan) diet upon a diagnosis of cancer, given the presence of elevated protein requirements and risk of inadequate protein intake to support muscle anabolism. Amino acid combination and the long-term sustainability of a dietary pattern void of animal-based foods requires careful and laborious management of protein intake for patients with cancer. Ultimately, a dietary amino acid composition that promotes muscle anabolism is optimally obtained through combination of animal- and plant-based protein sources.

Abbreviations: AICR, American Institute for Cancer Research; CI, confidence interval; DIAAS, digestible indispensable amino acid score; MPB, muscle protein breakdown; MPS, muscle protein synthesis; PDCAAS, protein digestibility corrected amino acid score; RDA, recommended dietary allowance; WCRF, World Cancer Research Fund.

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1. Introduction

Cancer is a leading cause of mortality worldwide and is the main cause of premature death in much of the Western Hemisphere and Western Europe [1]. Early and continued optimization of nutritional status, including elevated protein requirements [2,3], is crucial to prevent and minimize negative health outcomes (e.g., muscle loss) often observed in cancer. Optimal nutrition is a hallmark of successful cancer treatment as it can alleviate symptom burden, improve health and quality of life, and support survivorship [4–7].

Many people with cancer recognize the importance of nutrition and are often motivated to make lifestyle changes and improve their dietary choices [8–10]. However, access to regulated nutrition professionals in outpatient cancer centers is sparse, and only those with, or at significant risk for, depleted nutritional status are likely to be referred to a registered dietitian/nutritionist [11]. As such, the burden to seek dietary advice is often placed on the patient.

Self-guided dietary changes, including restricting or eliminating animal foods (e.g., meat and/or dairy) are common in cancer [9,12] and often used by patients in an attempt to "cure the cancer" or alleviate symptoms [13,14]. A Dutch study showed that people with cancer ($n = 239$) reported decreasing their meat intake and increasing intake of plant-based foods following a cancer diagnosis [15]. Similarly, a group of 1458 patients with stage I-IV colorectal cancer reported several dietary changes, including decreased meat and increased fruit, vegetables, fibers, wholegrains and fish consumption [14]. Decreased meat intake ($n = 376$) was more prevalent than increased fish consumption ($n = 342$), although these dietary changes were not quantified in relation to total protein intake [14], and thus the effect of habitual dietary change on protein intake was unclear. A study of the NutriNet-Santé cohort ($n = 696$) found that changes following a diagnosis of cancer included decreased vegetable, dairy, meat, soy, and alcohol consumption which cumulatively resulted in significantly lower total protein intake (-17.4 ± 12.5 g/day; $p < 0.0001$), compared with pre-diagnosis [16]. Dietary changes post-diagnosis resulting in decreased protein intake have also been observed in patients with breast cancer [17]. Although some of these changes are beneficial to overall health (e.g., decreased alcohol consumption), a diet containing exclusively (i.e., vegan diet) or predominantly (i.e., vegetarian diet) plant-based foods is concerning due primarily to the importance of animal-based protein for skeletal muscle health.

Acknowledging that healthy populations in the Americas, Europe, and Oceania achieve much of their protein intake from animal sources [18], the above-mentioned dietary changes should not be overlooked, nor the consequences underestimated. Aside from veganism, all diets contain a mixture of animal- and plant-based proteins. Initiating a dietary pattern that restricts or eliminates animal-based foods without careful consideration for increased protein needs may hinder optimal nutritional status following a diagnosis of cancer, especially related to the ability to sustain muscle mass. Dietary proteins provide essential amino acids required for muscle health. Muscle loss is a prominent problem experienced by people with cancer despite the increasing prevalence of obesity [19,20] and impacts prognosis and clinical outcomes [21–23]. Loss of muscle is a defining feature of malnutrition, which has several consequences ranging from economic [24] to physical burdens [23], and also of cancer cachexia, a debilitating multifactorial syndrome that results in functional debilitation and mortality [25]. Muscle loss occurs to varying degrees across stages and types of disease, body weight or weight stability/change, and leads to detrimental clinical outcomes, including lower tolerance to treatment and decreased survival [20–23,26]. In fact, low muscle mass is emerging as a clinical marker of biological age, the latter of which has been proposed as an important consideration when prescribing anti-cancer therapies [27].

Given the importance of muscle health in the oncologic setting and the notion that cancer is a catalyst for dietary change, we aimed to address the potential impact of protein sources (i.e., animal- and plant-based) on muscle anabolism in cancer and suggest an optimal ratio of intake. Herein, animal-based proteins include beef, pork, chicken, fish, eggs, milk, cheese, etc. This opinion paper is a narrative review and expert group understanding of available data. Search term categories included 'protein', 'muscle', and 'cancer'. Key concepts are summarized in Box 1.

2. Protein intake and muscle mass

Whole-body skeletal muscle mass is dependent on rates of muscle protein synthesis (MPS) and muscle protein breakdown (MPB), collectively termed muscle protein turnover [28–30]. In a healthy state, MPS and MPB are constantly changing in relation to food intake to maintain muscle mass [30]. To achieve muscle anabolism (i.e., growth), MPS on average must chronically exceed MPB to obtain a positive net protein balance. The homeostatic state of muscle protein turnover is disrupted in pro-inflammatory conditions such as cancer [30,31]. Upregulation of ubiquitin-proteasome/autophagy pathways [32] and a decline in MPS [33] results in increased degradation of intracellular proteins and subsequently loss of muscle mass [34]. Reduced protein intake because of inflammation-related anorexia and the adverse effects of cancer therapy further contribute to muscle loss [35,36]. In addition, muscle protein synthesis is greatly affected by protein intake and level of physical activity [29,37–40], which are often diminished in cancer [41–43], further exacerbating catabolism.

The nutritional value of protein is determined by the quantity and quality of constituent amino acids [44]. Amino acids are the dietary anabolic drivers of muscle mass accretion but vary in quality and do not equally promote anabolism [45,46]. The Protein Digestibility Corrected Amino Acid Score (PDCAAS) is indicative of essential amino acid content and digestibility of proteins [47]. Since the PDCAAS was developed, another measure of protein quality was introduced: The Digestible Indispensable Amino Acid Score (DIAAS) [48]. Notably, these scores do not suggest true skeletal muscle anabolic response to a particular amino acid but do provide a proxy method of quality comparison between proteins [28]. Dietary proteins have varying amino acid profiles whereby animal-based proteins offer greater anabolic stimuli when compared with plant-based alternatives [28,49,50]. Plant-based proteins are less digestible (i.e., lower PDCAAS) than animal-based proteins [47,51]. Other key differences between animal and plant proteins are highlighted in Fig. 1.

Soy protein isolate (i.e., a purified form of soy) is the plant-based protein that is an exception (high PDCAAS) as the absence of anti-nutritional factors in the isolated form of soy increases the digestibility of this product compared to soy protein in whole foods [51,52]. As with whole foods, animal-based protein supplements (e.g., whey) offer increased MPS and superior anabolic potential compared with plant-based protein powders, including soy protein isolate (PDCAAS 1.0) [28,53]. The decreased anabolic potential of plant-proteins (including soy) may be due to increased amino acid oxidation, decreased MPS, and lower leucine content compared to animal proteins [49,53]. The presence of anti-nutritional factors (e.g., trypsin inhibitors, tannins, phytates) may negatively impact digestibility and availability of amino acids in plant-proteins [52]. Plant-based proteins resist proteolysis in the gastrointestinal tract (i.e., decreasing their digestibility) due to their difference in structure when compared with animal-based proteins [54], which may be especially concerning for people suffering from gastrointestinal cancers (e.g., small bowel, pancreas, gastro-esophageal).

Box 1
Key Messages

- People with cancer need more protein than healthy individuals.
- Animal proteins provide greater anabolic stimuli compared with plant-based protein foods and are, therefore, better for muscle health.
- A combination of animal (≥65% of protein intake) and plant proteins is likely to be optimal for supporting muscle health and avoiding malnutrition during the treatment of cancer.
- Eliminating animal proteins (i.e., vegan diet) is not a recommended dietary change to pursue during active treatment of cancer.
- During active treatment of cancer, the goals of nutritional intake shift and do not necessarily parallel the recommendations for cancer prevention and post-treatment.
- Theoretical arguments suggesting that nutrition feeds the tumor are not supported by evidence and should not be a reason to alter food choice.
- Individuals following well planned and balanced exclusively (i.e., vegan) or predominantly (i.e., vegetarian) plant-based diets for personal reasons (e.g., religious, ethical) may be able to support muscle health during treatment of cancer although a professional nutrition assessment is highly recommended.

Given the equally high protein quality (PDCAAS 1.0) of soy protein isolate as most animal proteins (e.g., whey), the role of soy for muscle health is a topic of interest [28,55]. Regardless, soy protein appears to be inferior to animal-based proteins at stimulating MPS and overall muscle anabolism in healthy older adults [49,53]. Leucine is a key regulator [45] and possibly the sole stimulator [56–59] of MPS. Leucine is also the most potent stimulator, compared with other essential amino acids, of the mTOR pathway — an essential anabolic pathway [46]. Animal-based proteins generally contain more leucine than plant-based proteins except for maize (corn), which in spite of its high leucine content is not a complete protein [18]. The role of collagenous animal proteins in muscle health has also been investigated. Collagen is an anomaly in the context of animal-based proteins because it completely lacks the essential amino acid tryptophan, rendering it incomplete and thus having a DIAAS of 0 [51,60]. A review of the literature suggests that MPS does not appear to be stimulated with collagen supplementation [51] although acute experiments with collagen also are difficult to interpret as tryptophan attached to albumin can temporarily provide tryptophan [61]. Future research in this area is needed; at this time, we do not recommend collagen supplementation for the specific purpose of muscle anabolism. Notably, despite the potential role of specific protein sources or nutrients, most dietary guidelines consider total protein intake rather than the amino acid composition of dietary protein.

3. Anabolic potential and protein source in cancer

The anabolic potential of skeletal muscle during cancer is controversial; studies indicate both anabolic resistance [62,63] and retained anabolic potential [19,62,64,65]. The etiology of cancer-associated muscle loss is complex and not fully understood despite its well-documented prevalence [20,63,64]. Cancer therapy often includes surgery, which can have a drastic and negative impact on skeletal muscle. The loss of muscle in the perioperative period can stem from bedrest, the catabolic stress of the surgery itself, and diminished nutritional intake [63]. A small study in patients with colorectal cancer found that compared to healthy counterparts, those with cancer presented significantly less lean mass (which includes muscle mass) in their lower extremities before surgery [63]. Compared with the pre-operative period, those undergoing tumor resection had further lower lean leg mass loss post-operatively [63]. The benefits of nutrition therapy post-operatively and upon discharge continue to be doubted despite increasing acceptance of Enhanced Recovery After Surgery [66]. Although perioperative nutritional therapy alone may not alleviate all nutritional challenges in patients undergoing surgery for cancer, marginal gains achieved throughout the cancer trajectory have the capacity to improve clinically relevant outcomes [66]. Hence, small improvements in nutritional status should not be discounted if they do not amount to clinically meaningful changes in isolation as the additive effect of small improvements over time have the potential to bring about clinically significant positive change [66].

Animal-based proteins are of major importance during the active treatment of cancer to preclude detrimental loss of muscle and promote muscle anabolism. Only a few amino acid kinetic studies investigated whole-body protein synthesis and balance in cancer over the last decade [62,67–69], as reviewed by Antoun & Raynard [70]. Bozetti & Bozetti [71] previously reviewed the same topic and cited studies that suggested increased [72–74] or decreased/no change [73] in whole-body protein synthesis

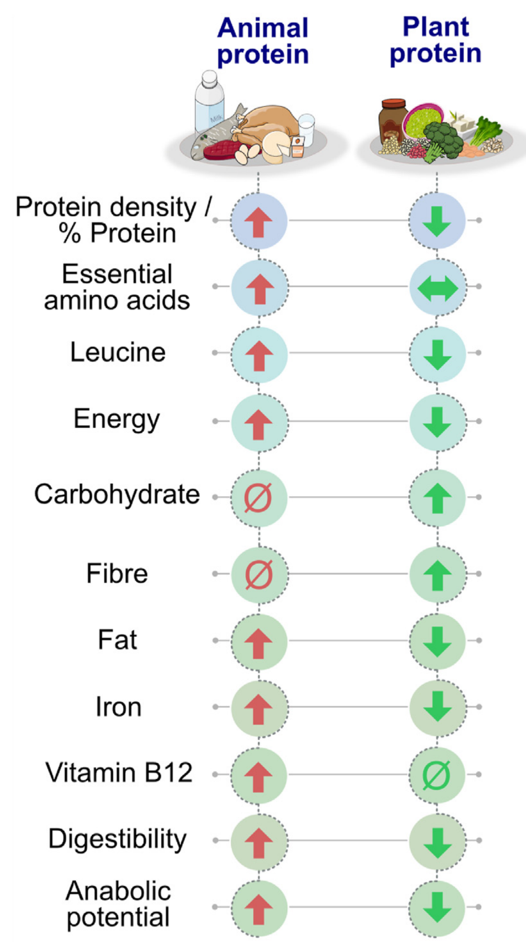

Fig. 1. Visual comparison of select key nutritional differences between animal and plant proteins. Legend: ↑: higher; ↓: lower; ↔: variable; Ø: none. Images retrieved from smart.servier.com.

following amino acid infusions in persons with cancer. Although these studies forecast the effects of mimicking whole-food diets on muscle change, translating results from amino acid kinetics to whole-body anabolism is difficult, as whole-body protein turnover does not necessarily equate to skeletal muscle protein anabolism [70]. A study using a cachectic pig model that compared the effects of a dairy with dairy/plant combination diet on skeletal muscle anabolic response to feeding found that despite the diets having equal leucine content, the dairy/plant diet was not effective in inducing an anabolic response to feeding; in contrast, the whey protein diet was [75]. A study investigating the effects of leucine on tumor-bearing mice suggested that supplemental leucine may protect muscle from disease-induced wasting [76], although to our knowledge, a similar study is yet to be conducted in humans.

The role of the mTOR pathway in mediating amino acid-induced skeletal muscle anabolism is well-established. Nevertheless, the mTORC1 pathway is also involved in negative forms of anabolism, including tumor growth, such that some fear nutritionally-derived anabolic stimuli (e.g., protein) may also fuel or be associated with tumor growth [77]. Despite amino acids having heterogeneous effects on tumor growth in humans, the effect of protein intake on tumor growth has not been substantiated [78]. In general, international guidelines on nutrition in cancer acknowledge that theoretical arguments suggesting that nutrition feeds the tumor are not supported by evidence and should not be a reason to alter nutrition delivery [2].

4. Protein in nutrition oncology guidelines (during curative or palliative cancer treatment)

Protein intake in cancer is highly variable, and many patients do not meet the minimum recommended intake [41,42,79,80]. Nutritional oncology guidelines recommend a minimum intake of 1.0 g protein/kg body weight/d but suggest a target consumption of 1.2–2.0 g/kg/d [2]. These guidelines are similar to those for older adults, which recommend at least 1.0–1.2 g/kg/d, acknowledging that those with acute or chronic illness require more protein (1.2–1.5 g/kg/d) [81]. Given that targeting guideline-based protein levels with individualized nutrition support improves clinical outcomes in cancer [7] and that increased total protein intake in adults over the age of 65 years (similar to the median age of a cancer diagnosis) has a protective effect [82], it appears that total protein intake should be a co-primary consideration in addition to protein quality. Notably, historical concerns regarding the supposed negative impact of protein on kidney health are unfounded. Higher protein intakes ($\geq$2.0 g/kg/d) are safe for people with healthy kidney function [2,44] and may reduce mortality in critically ill patients [83], although those with pre-existing kidney disease should maintain a lower intake [84,85].

Protein intake recommendations in cancer are notably higher than the recommended dietary allowance (RDA) of 0.8 g/kg/d for the healthy population, determined by nitrogen balance studies [86]. These studies primarily used high-quality proteins with a PDCAAS of 1.0 (e.g., animal-based proteins or soy protein isolate) [28,86–88]. Based on the methodology used to determine the RDA, this value should be considered a minimum amount needed to attain nitrogen balance rather than an amount sufficient to promote muscle maintenance or anabolism [44]. Conversely, the recommendations for patients with cancer are primarily based on expert opinions given the paucity of studies that investigated nitrogen balance or the impact of protein intake on clinical outcomes [2]. As oncology recommendations were derived from protein metabolism studies [2,62,89,90], the guidelines also acknowledge that the optimal amino acid composition for patients with cancer remains unknown [2].

The risk of malnutrition varies in people with cancer [91], especially between the curative and palliative setting, although the potential benefit of animal protein is present given the association of low muscle mass with malnutrition [23]. Studies employing isotopic tracer methods are needed to determine specific amino acid requirements in oncology settings [92]; for example, the indicator amino acid oxidation method is one technique that could be used to determine total protein requirements in a non-invasive manner [93]. Additionally, challenges of understanding optimal protein quantity and amino acid composition for muscle mass maintenance or anabolism are compounded by gut dysfunction, which is observed in patients with cancer, resulting in decreased protein digestion of oral food intake and absorption [94,95]. The reduction in protein digestion negatively impacts systemic amino acid availability and leads to increased quantity of undigested proteins in the colon [94,95]. The latter can alter microbial metabolism and generate harmful metabolites which may negatively affect muscle health [94,95].

5. Additional considerations and current evidence of animal- and plant-based protein intake during cancer treatment

One of the ten World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR) recommendations for *prevention* of cancer is to follow the remaining nine recommendations for those *diagnosed* with cancer [96]. Translating dietary recommendations for prevention of cancer to patients with active cancer may provide insufficient nutritional targets and, therefore, suboptimal nutritional status. Some dietary strategies for prevention of cancer might result in worse outcomes once a diagnosis of cancer is made. Although controversial, red meat may be positively associated with the incidence of colon cancer, although the association may be inversely related to colon cancer mortality [97]. In a cohort of 992 patients with stage III colon cancer, restricted red and processed meat intake was associated with increased risk of death [97]. Additionally, diet quality was not associated with overall survival in a cohort of 1284 patients with metastatic colorectal cancer [98]. We propose that once a diagnosis of cancer is made, the goals of nutritional intake shift and do not necessarily parallel the recommendations for cancer prevention and post-treatment (survivors).

When considering protein sources, one concern regarding an exclusively, or even predominantly, plant-based diet during active treatment of cancer is the feasibility of obtaining adequate dietary amino acid intake to sustain functional muscle reserves, especially given the high risk of malnutrition in this population [91] (Fig. 3). Cancer therapy is frequently accompanied by nutrition-impact symptoms (e.g., nausea, anorexia, taste alterations) that can affect food intake and compound muscle catabolism [99,100]. Early satiation can also contribute to decreased oral intake and may be influenced by nutrients in the diet (e.g., protein, fiber). As discussed, protein intake is essential for muscle health in cancer, although caloric intake is also vital for optimizing nutrition in this vulnerable population. In older adults, essential amino acid supplementation has been proposed as a complementary measure, in addition to protein intake, that does not impact satiety, optimizes the ability to meet nutritional requirements, and promotes muscle health [101]. The efficacy of essential amino acid supplementation requires further investigation in clinical settings, including cancer. Similarly, although the satiating effect of protein has been studied in other populations, how a predominantly plant-*vs.* animal-based diet affects satiety is unknown in people with cancer or at risk of malnutrition [102]. Regardless of satiating effects, a larger volume of plant-based proteins than animal-based products is required to obtain adequate amino acid intake [103]. It follows that the higher quality of animal-based proteins provides adequate protein intake from a smaller volume of food [28], as shown in Fig. 2.

Despite some insight into protein intake in this population, studies investigating protein quality or types of protein consumed are lacking [2]. In healthy middle-aged women, those consuming ~68% of their protein from animal sources (animal:plant protein intake ratio 2.09) had significantly higher muscle mass compared with vegetarians consuming ~55% of their protein from animal sources (animal:plant protein intake ratio 1.23) [104]. Given the paucity of research on optimal ratio of protein sources in cancer, interpretations can be drawn from studies in populations at similar risk of malnutrition as those undergoing treatment of cancer to provide insight and a starting point into appropriate nutrition needed to optimize health in cancer. In older adults with comorbidities, at least 65% of protein intake from high-quality protein (i.e., animal-based protein) is needed to avoid malnutrition [105]. Additionally, factors similar to those seen in people undergoing treatment of cancer (e.g., missing a meal, taste alterations) were independently associated with inadequate intake of ≥1 essential amino acid and subsequently greater risk of malnutrition [105]. Given the paucity of this type of research in cancer and the similarity in malnutrition risk and nutrition impact symptoms between populations, we propose that inferences be drawn and a minimum of 65% of protein intake from animal sources be considered as an optimal starting point to support muscle anabolism for people undergoing active cancer treatment. Future trials should seek to determine the optimal animal:plant protein ratio to support muscle mass in cancer.

Ongoing trials are investigating protein needs [106] and the clinical impact of increased protein [107,108] or amino acid [109,110] intake on muscle in people with cancer. The impact of protein on muscle strength is also an important consideration in cancer given that muscle weakness can occur without loss of muscle mass [31]. A review that focused on nutritional interventions for muscle strength in cancer found no studies that compared plant-with animal-based diet interventions [111]. Clinical trials related to protein source and muscle anabolism in cancer primarily focused on MPS and MPB rather than whole-body lean mass response and its impact on clinical outcomes. A paradox exists in current research whereby humans consume predominately whole foods, yet research has focused on specific amino acids and their contribution to muscle protein turnover. Pragmatic studies employing a whole-food approach exploring the influence of protein sources on whole-body skeletal muscle anabolism are needed to guide future nutrition recommendations.

It is our opinion that in catabolic disease states such as cancer, the attributes of animal-based proteins contribute to optimal nutrition care and can be safely included in the diet. We acknowledge various reasons (ethical, religious, planetary, health, etc.) for choosing a plant-based diet. Those already consuming a balanced exclusively or predominantly plant-based diet may achieve adequate nutritional intake to support health, although appropriate knowledge of diet diversity is needed to ensure higher protein needs are met [112,113]. Initiating an unbalanced exclusively or predominantly plant-based dietary pattern during active treatment of cancer may impact negatively on the ability to achieve optimal protein intake. In contrast, a dietary pattern that combines protein from animal- and plant-based sources is, in our view, more likely to be the most suitable option for optimal health.

Lastly, although not the focus of this paper, and regardless of protein sources in the diet, exercise is a viable proponent of a multimodal approach to supporting muscle health in cancer. It is

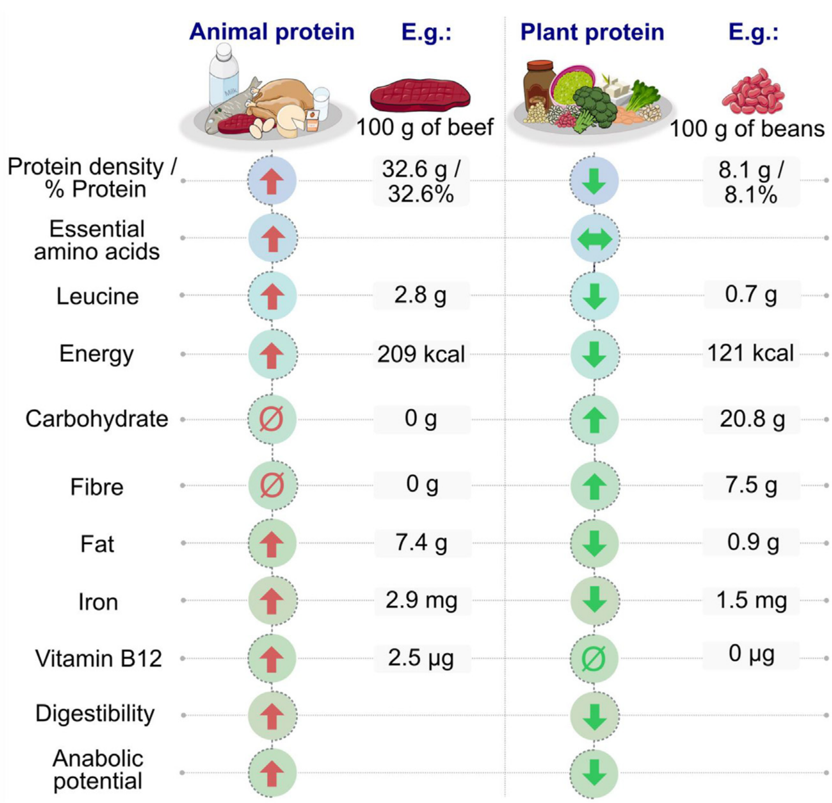

Fig. 2. Select nutritional differences between animal and plant proteins are highlighted with food examples. Animal proteins include beef, pork, chicken, fish, eggs, milk, cheese, etc. Plant proteins include beans, lentils, soy, nuts, etc. Legend: ↑: higher; ↓: lower; ↔: variable; Ø: none. Images retrieved from smart.servier.com. Canadian Nutrient File food codes: beef – 6112; beans – 7085.

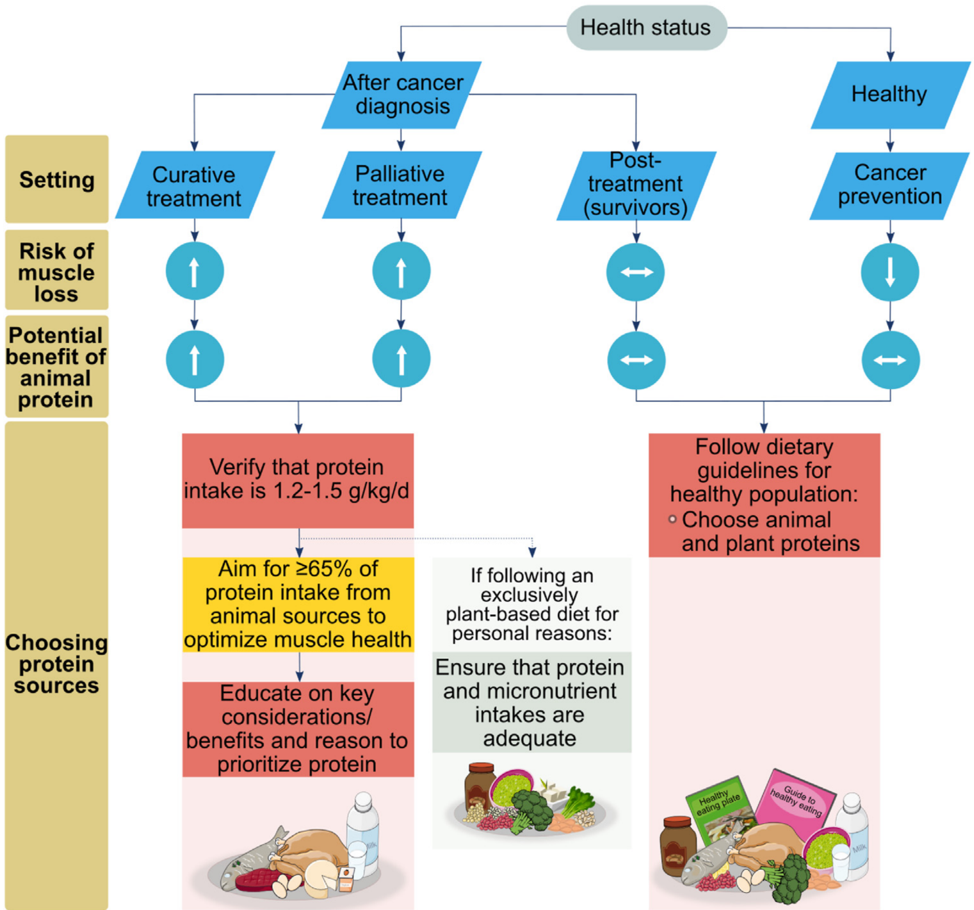

Fig. 3. Flowchart of important nutrition-related considerations based on health status. Legend: ↑: increased; ↓: decreased; ↔: neutral; animal proteins: beef, pork, chicken, fish, eggs, milk, cheese, etc.; plant proteins: beans, lentils, soy, nuts, etc. Images retrieved from smart.servier.com.

safe during and after treatment and is encouraged [2,114]. The role of resistance exercise and nutrition to mitigate muscle loss in pro-catabolic states has been extensively reviewed, emphasizing the importance of a multimodal approach to muscle health [115–117].

6. Dietary guidelines for healthy populations (for cancer prevention and post-treatment)

National dietary guidelines for healthy populations (including prevention of cancer and post-treatment) have increasingly emphasized plant-based foods for overall health, chronic disease prevention, and sustainability [118–121]. The WCRF/AICR has ten recommendations related to diet, nutrition, and physical activity for prevention of cancer. In line with select national dietary guidelines worldwide, the WCRF/AICR recommends limiting consumption of red and processed meat [96]. Although guidelines explicitly state not to avoid meat consumption entirely, the layperson may be inclined to adopt an exclusively or predominantly plant-based diet based on recommendations for cancer prevention. A review of the literature could not confirm that substituting animal-based proteins with plant-based options reduced the risk of developing cancer [122]. The limited and conflicting evidence of protein sources challenges the ability to draw confident conclusions; thus, the positive and negatives effects of these types of foods must be weighed in relation to health priorities [123–126]. Elimination of specific foods or food groups without supportive substitution is concerning as nutritional considerations of dietary intake are complex and should not be dichotomized as ‘good’ or ‘bad’. Protein needs for prevention of cancer and post-cancer treatment may not be elevated compared with protein needs during active cancer treatment, therefore the former can likely be reasonably achieved with predominantly plant-based foods given the lower risk for malnutrition and muscle loss in this population (Fig. 3). Thus, obtaining ≥65% of protein from animal sources may not be essential to sustain muscle mass in this healthy population. In general, protein intake from animal- and plant-based sources is highly variable. One study in healthy adults found that self-reported vegetarians ($n = 2370$) consumed 50.9% of their protein (g) from animal sources, whereas meat eaters ($n = 90{,}664$) ingested 70.8% of protein from animal sources [127]. Regardless of self-reported diet strategies, the definition of a predominantly plant-based diet remains controversial, compounding the challenge of determining optimal ratios of protein intake based on nutritional needs.

An important consideration is that the response of skeletal muscle to dietary anabolic stimuli may be blunted with age and, thus, older adults may have increased protein needs [81]. Moreover, increased protein intake is protective against mortality in adults over the age of 65 years [82]. Additional considerations for older adults with cancer include age-associated changes in appetite regulation, lack of hunger, a decline in taste and smell, reduced central and peripheral drive to eat, delayed gastric emptying and deteriorating dentition [128]. These are why animal protein intake decreases with age, and the feasibility of adequate plant-protein intake in older adults may be compromised [49].

7. General benefits of plant-based proteins

Dietary guidelines for chronic disease prevention do not account for the source of protein, despite its importance given the diverse protein intake patterns observed worldwide [18]. As illustrated in Figs. 1 and 2, plant-based proteins are higher in essential fatty acids and fiber, whereas they are lower in protein, essential amino acids, and certain micronutrients (e.g., iron, vitamin B_{12}, zinc) [129].

Globally, plant-based options are the predominant source of protein [18,49]. Compared with animal counterparts, plant-based proteins are more environmentally sustainable, requiring fewer resources (e.g., land and water) and producing lower levels of greenhouse-gas emissions [119,130]. As such, many people are adopting an exclusively or predominantly plant-based diet, regardless of health status [119,131]. For example, national and international oncology groups support incorporating soy-based foods as a part of a healthy diet for prevention of cancer and during active treatment [132,133]. The high isoflavone content of soy continues to foster unfounded concerns regarding a potential link between soy intake and negative health outcomes relating to hormone production [122,132,134]. Soy intake has not been linked to cancer occurrence or recurrence; conversely, the isoflavones have anti-inflammatory properties that may decrease the risk of cancer occurrence [122,135].

In the absence of disease, it is possible to maintain a healthy diet without consuming animal products if eliminating the latter is substituted with alternatives that contain adequate essential nutrients [136]. Importantly, a regulated health care professional who is a nutrition expert (e.g., registered dietitian/nutritionist) should be consulted before making any drastic dietary changes. These professionals can counsel patients and provide strategies to achieve adequate intake, especially those who are already following an exclusively or predominantly plant-based diet while undergoing oncologic treatment.

8. Conclusion

We argue that the inclusion of anabolic-stimulating animal proteins like beef, pork, chicken, fish, eggs, milk, cheese, etc. is key to achieving clinical benefits related to muscle anabolism in cancer, especially given the higher protein needs due to the pro-inflammatory nature of the disease, low intake levels, and deconditioning of these patients. Drastic changes to food choice such as eliminating animal products from the diet may negatively interfere with the quality and quantity of protein intake if not properly substituted in the diet and do not align with international nutritional oncology guidelines. Without adequate substitution with other foods, nutritional status may be compromised if meat-derived proteins are reduced or eliminated. We support the increased incorporation of plant-based proteins. However, we caution that a dichotomous approach to eating that eliminates animal products may lead to inferior anabolic stimuli and greater quantity and variability of protein sources needed to achieve skeletal muscle anabolism, especially once diagnosed with cancer. Thus, we propose that in the oncologic setting, a minimum of 65% of protein intake should be derived from animal sources as an initial starting point although further research in this area is needed. Following successful cancer treatment, increased consumption of plant-based proteins may be adequate to sustain muscle health but requires careful planning if substituting animal products in the diet. Dietary changes can be optimized with the help of a registered dietitian/nutritionist.

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Author contributions

All authors were responsible for conceptualization, writing and review/editing the manuscript. K.L.F wrote the first draft.

Conflict of interest

K.L.F has no conflicts to declare.

J.A. reports receiving honoraria from Baxter, B. Braun, Berg-Apotheke, Falk, Fresenius-Kabi, Helsinn, Nestlè and Nutricia.

P.J.A. reports consultancy fees and research income from Abbott Nutrition and Fresenius-Kabi.

M.P.K.J.E has no conflicts to declare.

T.J.M.G. reports receiving consulting fees for honoraria for lectures at industry-sponsored events; consulting fees from Nestlé Health Science and Nutricia.

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