Prognostic Biomeasurements for Cancer

Subjects: Others

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Malnutrition can significantly affect disease progression and patient survival. The efficiency of weight loss and bioimpedance analysis (BIA)-derived measures in the evaluation of malnutrition, and disease progression and prognosis in patients with head and neck cancer (HNC) are an important area of research.

Keywords: cancer ; BIA ; BMI

1. Introduction

Malnutrition is a frequent finding in cancer patients, even at the time of diagnosis. Its incidence varies between 31–87%, depending on disease stage, histopathological type, treatment, and individual patient characteristics . Malnutrition can significantly affect disease progression and patient survival. Studies have shown that weight loss in cancer is associated with poor prognosis, poorer quality of life, increased treatment-related adverse effects, and reduced tumor response to treatment as well as lower physical activity levels.

Weight loss may develop due to either elevated energy requirements, low energy intake, or compromised nutrient absorption. In cancer patients, undernutrition may be attributed to various factors. In head and neck cancer (HNC) patients, weight loss before therapy is ascribed to several disease-related effects. More to the point, inflammation and catabolism, because of tumor, can lead to muscle wasting and body weight loss. On the other hand, tumor gastrointestinal obstruction can compromise both food intake and absorption as dysphagia, pain, and vomiting can be present. During treatment, eating-related side-effects (such as low appetite, early satiety, nausea and/or vomiting, oral and intestinal mucositis with dysphagia, diarrhea, hemorrhoids, anal fissures, and smell and taste changes) may not only affect total energy intake, but also nutrient absorption, deteriorating nutritional status, while patients' poor mental health state can diminish their food and energy intake.

Weight loss at diagnosis has been associated with shorter failure-free and overall survival, while being identified as an independent prognostic factor. In addition to this, weight loss during radiotherapy has been associated with more aggressive disease characteristics . Weight loss at the beginning of chemotherapy is associated with reduced response to treatment and increased toxicity. Currently, there is no definitive effective treatment for cancer-associated weight loss and cachexia , despite decades of research.

Body composition reflects the nutritional status. Bioimpedance analysis (BIA) is based on the body's tissue electrical properties, and is a non-invasive, time- and cost-effective technique to analyze and monitor body composition. The principles and applications as well as the drawbacks of BIA have been thoroughly explained by Kyle et al. as well as by Sergi et al.

BIA measures the resistance and reactance of the human body by recording the voltage drop in the applied current. The capacitance of the cell membranes (Cm/Reactance = 1/2 × π × frequency × capacitance) causes the current to lag behind the voltage, which creates a phase shift, quantified geometrically as the phase angle (PA, phase angle = arc − tangent reactance/resistance × 180◦ /π).

More to the point, "the membrane capacitance is proportional to the cell surface area and, together with the membrane resistance, determines the membrane time constant which dictates how fast the cell membrane potential responds to the flow of ion channel currents". Normal, pre-cancerous cells, and cancer cells have different electrical properties. Human oral cancer cells with higher tumorigenic abilities have exhibited higher Cm , while oral cancer progression has been associated with higher Cm of cancer cells . In biological systems, the smaller the quantity of the membranes equals greater capacitance .

Phase Angle (PA) and bioelectrical impedance vector analysis (BIVA—another graphical method for analyzing BIA raw data) are derived by reactance and resistance . Both PA and BIVA are considered to reflect both nutritional and hydration status, which are also considered as measures of cell membrane function and integrity .

BIA can be used to assess the body composition of patients of all ages, independently of their physical and mental health status, as this measurement is fast and easily obtainable, with patients only having to step on the scale-analyzer and hold the electrodes. BIA results and raw data are obtained almost immediately, with current body composition analyzers

displaying PA in their results. Notably, BIA is currently used in various clinical settings, from hospitals to dietetic clinics, hence it is easy to find a clinician or dietitian that has access to body composition analyzers. Additionally, most body composition analyzers are portable. On the other hand, the results of BIA are based on empirical regression equations derived from healthy individuals, who follow a protocol before the measurement, while the different regression equations derived from different populations may not aid in the interpretation of the results. The importance of adopting different cutoffs for patient populations has been highlighted. Monitoring of each patient's PA over time has also been suggested .

Due to the fact that the results of BIA are based on regression equations for healthy individuals, it has been proposed that raw data, derived by BIA, can be useful to other populations as a nutritional screening and assessment tool, and as a prognostic factor of clinical outcomes. PA is considered to be a useful prognostic tool across clinical settings, in critical condition patients, and especially in cancer patients. It has also been identified as a prognostic factor in colorectal and lung cancer patients as well as in advanced-stage cancer patients.

In addition to this, in healthy adults, PA has been significantly predicted from height, weight, muscle mass, and visceral fat , and increases with increasing body mass index (BMI) . During radiotherapy, weight loss has been associated with a decrease in PA. HNC is the seventh most common malignancy worldwide . At diagnosis, 3–52% of HNC patients are categorized as malnourished. During treatment, malnutrition is already present in 44–88% of patients.

Numerous studies have shown the role of different measures of nutritional status on prognosis and survival in HNC patients , highlighting the essential role of nutritional assessment as part of HNC management . In this aspect, various studies have been conducted to evaluate the role of easy-to-obtain measures of nutritional status in HNC patients.

In light of the above considerations, this review paper aims to critically summarize and discuss the currently available clinical data on the efficiency of easily obtainable nutritional status assessment tools such as weight loss and BIA measures in the evaluation of malnutrition in HNC patients, highlighting their role to affect disease progression and prognosis.

The PubMed database was thoroughly searched using relative keywords (weight loss, BIA, Bioimpedance Analysis, head and neck cancer, weight loss, BMI), in order to identify clinical studies that explore the role of BIA-derived raw data and weight loss on disease prognosis and progress as well as highlighting the role of BIA-derived raw data on assessing and predicting malnutrition. Inclusion criteria were:

• Studies in humans with HNC, where BIA was used to identify malnutrition and/or disease progression and patient prognosis;

• Studies that investigated the prognostic role of weight loss; and

• Written in English language.

Twenty-seven studies met the criteria. More specifically, six studies examined the prognostic role of tissue electrical properties in HNC patients; five examined the role of the tissue electrical properties on identifying malnutrition; four studies looked at the changes in the tissue electrical properties of HNC patients; and 12 examined the prognostic role of weight loss on survival and/or treatment outcomes.

2. Results

Method: The PubMed database was thoroughly searched, using relative keywords in order to identify clinical trials that investigated the role of BIA-derived measures and weight loss on the disease progression and prognosis of patients with HNC. Twenty-seven studies met the criteria. More specifically, six studies examined the prognostic role of the tissue electrical properties in HNC patients; five examined the role of the tissue electrical properties on identifying malnutrition; four studies looked at the changes in the tissue electrical properties of HNC patients; and 12 examined the prognostic role of weight loss on survival and/or treatment outcomes.Several studies have investigated the role of nutritional status tools on prognosis in HNC patients. Current studies investigating the potential of BIA-derived raw data have shown that phase angle (PA) and capacitance of the cell membrane may be considered prognostic factors of survival. Weight loss may be a prognostic factor for treatment toxicity and survival, despite some conflicting evidence. Further studies are recommended to clarify the role of BIA-derived measures on patients' nutritional status and the impact of PA on clinical outcomes as well as the prognostic role of weight loss.

3. Conclusions

As far as BIA is concerned, the majority of currently available studies have shown a good potential on its clinical use in HNC, in accordance with studies in other cancer patient populations.

Until now, it should be noted that few studies have investigated the prognostic potential of the raw data derived by BIA in this patient population, even though they can be easily obtained. The aforementioned studies have shown that both PA and capacitance of the Cm may be considered to be prognostic factors of patient survival in HNC. On the other hand,

there are some studies that have documented contradictory results concerning the potential of BIA and BIVA on predicting patients' malnutrition.

Even though three of the five studies reported encouraging results for the prediction of malnutrition, the exact role of PA on detecting malnutrition was deemed unclear in one study, and there was no predictive value in another. Moreover, in another study, PA could not differentiate malnourished from cachectic patients, while pre-treatment PA was not a predictive factor for cachexia during chemo-radiation treatment. In addition to this, a review by Rinaldi et al. showed that currently, in cancer patients, the agreement between PA and the SGA tool regarding malnutrition, is weak. Thus, further studies are needed in order to assess the association between malnutrition and altered tissue electrical properties as well as its subsequent prognostic role in HNC patients. Future studies evaluating the efficiency of BIA raw data may use more advanced body composition analyzers than those used in the currently available studies, since these analyzers are more accurate and display PA in their results. However, it is important to adopt specific cut-off points for PA for each patient population.

Considering weight loss, several studies have investigated its prognostic impact on patient survival and post-operative complications. Some studies have supported its prognostic value; however, other studies have shown a lack of prognostic capacity for weight loss in this patient population. It is important to note the heterogeneity of HNC in terms of affecting food intake, and thus outcomes regarding weight loss as well as the important role of cancer stage when analyzing the results. Great weight loss of >10% of initial body weight during treatment was found to be an independent predictive factor for one-year overall, disease-free, and disease-specific patient survival. Some studies have documented that pre-operative weight loss >10% was associated with greater five-year mortality, while pre-treatment weight loss was an independent prognostic factor for greater treatment failure, shorter locoregional recurrence-free survival, and distant metastasis-free survival as well as disease-specific and overall patient survival. On the other hand, other studies have failed to find an association between weight loss (at the beginning or after radiotherapy) and patient post-operative outcomes and survival.

Additionally, the two identified studies that concern treatment toxicity showed that weight loss and weight ratio were independent prognostic factors for late severe treatment-related toxicity. When taking BMI into account, one study found that, except for patients categorized as overweight and obese, high weight loss during radiation treatment was independently associated with poor nasopharyngeal carcinoma patient survival, with the impact being more prominent in underweight patients. In addition, another study in the same patient population did not find such an association as patients with significant weight loss did not have worse three-year clinical endpoints, even after adjusting for the impact of weight loss by BMI category.

In the past decades, tissue electrical properties have been studied in healthy individuals and patient populations. Adjunct BIA and weight loss monitoring are non-invasive, easy-to-use, and promising tools regarding the screening and assessment of the nutritional status of HNC patients, with prognostic value. A number of studies in other cancer patient populations highlight the prognostic role of PA and the utility of BIA, European Society fpr Parenteral and Enteral Nutrition (ESPEN) guidelines suggest the use of BIA in patients undergoing hematopoietic stem cell transplantation.

It is important to note that the majority of enrolled patients in the currently available studies were men, possibly due to the fact that HNC frequently effects more men than women[1]. However, future studies also need to address the role of different prognostic factors on clinical outcomes in women with HNC. More studies are also recommended in order to clarify the role of BIA-derived measures assessing nutritional status in HNC patients. Moreover, it is also important to examine the impact of deteriorating PA and BIVA measurements on patient survival and other crucial clinical outcomes such as post-operative complications and treatment-related toxicity. In addition to this, further studies can also focus on regression equations for cancer patient populations. Moreover, additional high-quality and well-designed studies, which take into account body composition and BMI, should be performed to accurately clarify the prognostic role of weight loss in HNC.

References

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