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MEASUREMENT OF BODY COMPOSITION AND ITS SIGNIFICANCE IN TREATMENT OF ONCOLOGICAL PATIENTS

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Summary

Body composition changes could indicate health conditions and potential health risks. Although several methods are currently available for quantitative assessment, each has limitations. Indirect methods are most frequently used because of their availability and simplicity. One of those methods, which found wide use in clinical trials and everyday clinical practice and was found to be of great value in oncology patients, is bioelectrical impedance (BIA). Assessed muscle volume and mass, measured by BIA, were associated with chemotherapy toxicity and overall prognosis, regardless of the primary tumor site. It has been shown that calculated phase angle could be a strong prognostic factor for a particular endpoint and an independent prognostic factor in patients with advanced malignancies. Body composition was also found to correlate with the quality of life (QoL) of patients with cancer, and several studies have shown a significant impact on various QoL subdomains. Measuring body composition and the information it provides could be used for the development of different clinical interventions that can help cancer patients live longer and better lives.

KEYWORDS: *body composition; bioelectrical impedance; cancer; sarcopenia*

BODY COMPOSITION MEASUREMENT

Body composition assesses the proportion of individual components: water, fat, bone, and muscle tissue in the body. Assessment of the ratio of individual body components and evaluation of nutritional status are essential for physicians because they could indicate the presence of health conditions and potential health risks. Measuring body composition is particularly important in assessing and treating obesity and related diseases, such as metabolic disorders and cardiovascular diseases. Still, it has also been shown to be helpful in the treatment of some other diseases, such as kidney disease, malignancies, and anorexia(1). Repeated measurement of body composition allows monitoring of changes in health status and assessing the effectiveness of dietary and other therapeutic interventions(1,2).

METHODS FOR MEASURING BODY COMPOSITION

Although several methods are currently available for quantitative body composition assessment, each has limitations regarding the technical characteristics and information it provides. All methods are based on assumptions about tissue density, electrolyte and water concentration, and interrelationships between body and tissue components and their distribution in healthy individuals(3). Direct methods analyze the body from the atomic to the cellular level. These methods are not widely available; they have many technical requirements and, therefore, can only be carried out

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in laboratories with adequate equipment (total body water measurement based on isotope dilution, total body measurement based on the measurement of naturally radioactive potassium 40 in the body, etc.)(4–7). Criterion methods measure the properties of the body, such as density, and describe the quantity and distribution of skeletal, muscle, and adipose tissue using X-rays or magnetic fields (densitometry, computed tomography, magnetic resonance)(8–11).

They are less technically demanding than direct body measurement methods but more expensive and often unavailable in everyday clinical practice for this purpose. With indirect methods, we do not measure but only assess the body composition (anthropometric measurements – weighing, height measurements, measurements of the circumference of the abdomen and skin fold, calculation of body mass index, and bioelectric impedance analysis). They are easily performed, inexpensive, and widely available. Individual characteristics and some health conditions could greatly affect the results of indirect measurements. Hence, errors in body composition estimation are expected more often with these methods(12,13).

Bioelectrical impedance (BIA) in clinical practice Basic principles of bioelectrical impedance are based on two assumptions. The first one relies on the fact that the human body mainly comprises water (around 55% of total body water is intracellular, and about 45% is extracellular) and ions, which are good electrical conductors(14). Muscles and bones are less conductive, while adipose tissue is the least conductive part of the body and provides the most significant resistance to electric current(15). This method measures different body components' resistance (impedance) when conducting an alternating electric current of very low strength. In practice, body impedance is defined by a drop in voltage recorded when a constant current of low power and constant frequency (800 μA, 50 kHz) passes between two electrodes in contact with the subject's palms and/or feet. Lean tissue rich in water and electrolytes has the lowest impedance. In contrast, adipose tissue has the highest, and the amount of lean tissue and body fat can be indirectly calculated from this difference(16). The obtained resistance index is proportional to the total body water volume and is used as an independent variable in regression equations to predict body composition. The final result of bioelectrical impedance analysis (BIA) is an estimation of the amount of total body water (TBW), fat-free body mass (FFM), and total body fat(17–19). The second basic principle of the BIA model is based on the assumption that the human body behaves as a cylindrical ion conductor with a homogenous composition, constant cross-sectional area, and uniform distribution of current density(20). BIA measures the resistance to the flow of an electric current through the total body fluid. Thus, the total conductive volume – V (represented by TBW or FFM) is directly related to the square length of the conductor – S and inversely correlated with the resistance of the cross-section area of the conductor – R. At the same time, p stands for the specific receptiveness of the conductor, which generates the equation: $V = p \times S2/R$. Based on this presumption, solely arms and legs contribute to 47-50% of the total body resistance (despite contributing only 4-17% of body weight), while the trunk, which carries 50% of the body weight, contributes only 5-12% of the total body resistance(14). The main disadvantage of this method in everyday practice is that bioelectrical impedance analyzers use equations based on biological relationships within the particular population to describe statistical associations(21). The relationship between the obtained bioelectrical data and TBW, including the validity of the method itself, can be influenced by gender, age, race, ethnicity, phase of the menstrual cycle, type of disease, amount of fat in an individual, etc. Produced BIA equations are population-specific and useful only in subjects who match the comparative (reference) population by the size and shape of their body. When used in a population with different characteristics, these methods could yield wrong results with an average error of up to 8%(22,23). In a review article by Heyward and Wagner, who examined the reliability and validity of different equations when measuring BIA, it was shown that BIA results are incorrect when generalized equations are applied in different ethnic groups (24). Body composition diversities between ethnic groups could be explained by different adipose tissue quantity and distribution, average body weight, and different body proportions(25–27). Other factors influencing BIA results are food and beverage intake, physical activity before measurements, health conditions that impact fluid and electrolyte balance, environmental factors, and the subject's characteristics(28-34). Considering the above, the

BIA method is unsuitable for measuring body composition in extensive international epidemiological studies involving a heterogeneous population of subjects, given that predictive equations have not yet been defined for individual ethnic groups. Therefore, the validity of the results obtained is questionable. In smaller studies including homogeneous populations (same ethnicity, sex, age, level of physical activity, or health status), it is possible to assess the body's composition with a high-reliability level with this method(35). BIA advantages are low cost, simple conduction of measurements with minimal requirements for the subjects, and safety (it is not recommended in patients with pacemakers).

MEASUREMENT OF BODY COMPOSITION IN ONCOLOGICAL PATIENTS

Body composition has relatively recently begun to be studied as part of oncological studies in different types of tumors in the context of metabolism of various anti-tumor drugs, assessment of the response to treatment and its tolerability and, consequently, the overall prognosis of malignant disease depending on the proportion of individual body components(36-38).

Skeletal muscles and adipose tissue estimation using computed tomography (CT) imaging became popular in larger oncology centers because of its availability, high accuracy, and moderate expenses, especially in patients with metastatic disease, mainly because most of these patients undergo initial CT or MRI staging before cancer treatment, on which body composition can be measured(39). CT has become the preferred standard for providing information on body compositional changes, especially those associated with cancer cachexia(40). In particular, fat and muscle area at the L3 vertebra level are highly correlated to other measures of body composition, and serial imaging enables longitudinal assessment of changes in body composition following treatment that cannot be captured by conventional anthropomorphic measurements(41,42). One of the measures recently highlighted as relevant in predicting outcomes is myosteatosis, or fat deposition in muscle. A meta-analysis identified that patients with lymphoma, gynecologic, renal, pancreatic, hepatocellular, gastroesophageal, and colorectal cancers who had higher myosteatosis had worse overall survival(43).

In everyday clinical practice, the body composition of an oncology patient is assessed by conducting simple anthropometric measurements of body height and mass and calculating the body mass index and body surface area, which is used to estimate the dose of predicted antineoplastic therapy.

Body surface area (BSA) calculation is used in oncology to derive the required dose of a cytotoxic drug for an individual patient. It was introduced in clinical practice due to mutual agreements, more than scientific research work, and it is often questioned(44-46). This method is based on the assumption that body size is proportional to organ size and function. Still, it is considered that BSA, which is obtained as a function of body height and mass, is not an ideal parameter for such a correlation(47). The volume and type of tissue in the human body in which cytotoxic drugs are distributed and metabolized could significantly affect their bioavailability and, ultimately, their efficacy. Most cytotoxic drugs are metabolized and excreted through the liver, and BSA, in this case, is not a good indicator because hepatic function, unlike renal, correlates poorly with body size (45).

Assuming that fat-free body mass (FFM) represents the distribution volume for most cytotoxic medications, it is estimated that single variations in FFM could lead to significant changes in chemotherapy distribution volume applied by the unit of body surface(36). Few recent studies performed on drugs such as carboplatin, fluorouracil, and paclitaxel identified the levels of exposure beyond which unacceptable toxicity occurs after BSA-based dosing. This variability reflects differences in the way individual patients clear drugs, which underscores the need for an alternative to BSA-based dosing(48-51).

Several systematic reviews have summarized the literature on cancer survival in relation to BMI at the time of diagnosis. A meta-analysis that involved studies for 15 cancer sites recently reported a modestly increased risk of overall mortality as well as cancer-specific death in obese patients (BMI≥30) with breast, colorectal, and uterine cancer. A decreased risk of death was found among lung, renal cell carcinoma, and melanoma cancer survivors(52). The Global Cancer Update Program group studied the relationship between a number of anthropometric measures of adiposity and breast cancer outcomes and found that elevated

BMI was associated with more significant all-cause mortality and breast-cancer-specific survival, recurrence, and incidence of second primary cancers(53). Generally, similar findings have been reported in a recent review of studies focused on colorectal cancer survivors. The risk of death from any cause was elevated at the extremes of the BMI range (BMI <18.5 or ≥35). However, those in the overweight range displayed the lowest risk of death (obesity paradox). Similar patterns were observed for disease-free survival and colorectal cancer-specific deaths(54).

Bioimpedance measurement for body composition assessment has also been shown to be valuable in oncology patients(55). During BIA measurements, cell membranes produce resistance to the electric current flow, causing electric charge accumulation and increased capacitance, which causes the current to lag behind the voltage, consequently creating a phase shift. This shift is geometrically quantified as phase angle, defined as the calculated ratio of capacitance and resistance, and expressed in degrees.

It has been shown that phase angle could be used as a strong prognostic factor for a particular endpoint in patients with advanced pancreatic cancer and an independent prognostic factor in stage IIIB and IV non-small cell lung cancer patients(55-60). There are some reports that BIA can be used in the assessment of sarcopenia, and one systematic review of this topic found that sarcopenia identified by BIA was associated with poor clinical outcomes(61). Although the accuracy and clinical value of the BIA results are frequently debated, newer multifrequency BIA technology is more promising and may have more significant correlations with computed tomography (CT) scan–based body composition measurements(62).

BODY COMPOSITION SIGNIFICANCE IN TOLERABILITY OF CANCER TREATMENTS

In recent decades, the prevalence of overweight and obesity has been rising, and so is the number of obese cancer patients. Obesity is a known strong predictor of worse outcomes, but it can also complicate drug dosing(63). In obese patients, it was common to empirically lower the full-weight-based dosage to prevent excessive toxicity (dose capping). However, there was no evidence that toxicity was increased among obese patients receiving full-weight-based chemotherapy doses, while some studies suggested compromised survival outcomes(64-67). Therefore, in 2012, the American Society of Clinical Oncology (ASCO) released clinical practice guidelines recommending full-weight-based chemotherapy doses in obese patients(68). A recent study of early breast cancer patients showed that obese patients (in which no upfront dose capping was applied) treated with adjuvant docetaxel-containing chemotherapy received a lower relative dose intensity (RDI) compared to lean patients.

Obese patients had shorter disease-free survival and overall survival compared to lean patients, which was also the case when only patients with an RDI of 85% or higher were analyzed. Therefore, it appears that obese patients tolerate full-weight-based docetaxel chemotherapy less well compared to lean patients, which negatively influences survival outcomes(69). Differences in body composition could be one of the reasons for differences in chemotherapy tolerability. Still, this parameter is not used for chemotherapy dose calculation and adjustments in everyday clinical practice. Studies found that adipose tissue distribution and higher visceral fat levels affect cancer patients' overall survival (70). On the other hand, sarcopenia is characterized by a reduction in skeletal muscle volume and mass, and it is associated with more significant chemotherapy toxicity, a higher risk of other medical conditions and death, and a worse overall prognosis, regardless of the primary tumor site(37-38). It is a common finding in cancer patients in general, and recently published meta-analysis data have suggested that 19-74% of patients with solid tumors have sarcopenia, which correlates with worse overall survival, not only in patients with metastatic but also in patients with non-metastatic disease(71). Most recent studies conducted on patients with gastric cancer have confirmed this statement, demonstrating that sarcopenia is a significant predictor of chemotherapy toxicity and worse overall survival(72-75). In a clinical trial conducted on patients with metastatic breast cancer treated with capecitabine, 25% of patients were classified as sarcopenic, and 50% had pronounced side effects of treatment, unlike non-sarcopenic patients in whom the incidence of adverse reactions was 20%.

Time to disease progression was also significantly shortened in sarcopenic patients. Data analysis showed that sarcopenia was the only significant predictor of toxicity. In contrast, other variables previously known to have an impact on toxicity prevalence (age, BSA, performance status, and albumin level) were not(76).

Supposed sarcopenic obesity, which includes both risk factors – sarcopenia and high visceral fat level – was presumed to be the predictor of the worst outcome in multiple analyses(36,77). In their research, Prado et al. have demonstrated that sarcopenic obesity (diagnosed by lumbar CT scans) reduces survival chances by half(36). One of the assumed theories is that in obese patients, a tiny percentage of loss of total body mass could potentially mask a significantly more considerable proportional loss of skeletal muscle mass(78). In this case, calculating chemotherapy dose based on total body mass, without correction according to body composition, could lead to higher chemotherapy dose exposure and, consequently, higher toxicity rates. Meta-analysis of twenty-six studies analyzing outcomes in gastrointestinal surgical oncology found that patients with sarcopenic obesity showed increased incidences of total and significant complications. Sarcopenic obesity was particularly associated with the incidence of cardiac complications, leak complications, and organ/space infection and was predictive of poor overall survival and disease-free survival(79). However, some studies show no association between sarcopenic obesity and mortality, where patient weight acted as a protective factor against mortality, supporting the obesity paradox(80).

It is important to note that the relationship between sarcopenic obesity and cancer outcomes is complex and varies depending on the type of cancer and the stage of the disease. Studies performed use considerable variations in definition, cutoffs, and assessment methods for sarcopenic obesity, which translates to complicated clinical practice(81).

BODY COMPOSITION AND CANCER PATIENTS' QUALITY OF LIFE

Body composition measurement analyses in correlation with the quality of life (QoL) have shown a significant impact on health-related quality of life (HRQOL) as on other QoL subdomains in several studies. Most described is the effect of low skeletal muscle mass on HRQOL. A meta-analysis of 14 studies with 2776 participants showed that low muscle mass was associated with poorer global HRQOL scores and poorer physical functioning subdomain but not social, role, emotional, or cognitive functioning subdomain scores(82). A cross-sectional study performed in 2018 on patients with non-small cell lung cancer showed that low muscle mass negatively impacted physical and role-functioning HRQOL subdomains in both genders and overall HRQOL in male patients(83).

Similarly, a cross-sectional study of patients with incurable lung and gastrointestinal cancers found that low skeletal muscle was associated with worse overall HRQOL and more significant symptoms of depression (84). Fat body mass also significantly impacted QoL in cancer patients and survivors. Higher fat-body mass proportion and poor physical functioning interrelationships have been described(85-87). A meta-analysis that investigated the QoL of endometrial cancer survivors showed that obese subjects had significantly poorer physical functioning, social functioning, and role-functioning subdomains when compared to non-obese women. Emotional and cognitive functioning subdomains did not show significant differences(88). Fatigue is one of the important domains of HRQOL, and patients with higher body fat percentages were significantly more tired than the ones with higher muscle mass percentages(89). Multiple factors probably cause changes in the sexual functioning domain throughout cancer treatment. However, the correlation between higher body fat percentage and poor sexual functioning has been described. It is assumed that patients with a higher rate of body fat have disturbed body image as well, which significantly impacts both sexual performance and sexual desire(89,90).

FUTURE PERSPECTIVES

Early screening to identify patients with occult muscle loss, combined with multimodal interventions that include nutrition therapy and exercise training combined with pharmacotherapy, is necessary to prevent or slow down the cancer-related process of tissue wasting and reduce the incidence of poor clinical outcomes. Simple and cost-efficient methods to measure metabolic processes' essential body components should be inte-

grated into large-scale clinical workflows. The interest of the oncology community in body composition measuring is growing, and today represents one of the very provocative areas, given that it opens up additional possibilities for interventions that could help oncology patients to live longer and better lives.

REFERENCES

1. Mazzoccoli, G. Body composition: Where and when. European Journal of Radiology. 2016;85(8): 1456–60. doi: 10.1016/j.ejrad.2015.10.020
2. Lee SY, Gallagher D. Assessment methods in human body composition. Curr Opin Clin Nutr Metab Care. 2008;11(5):566–72. doi: 10.1097/MCO.0b013e32830b5f23.
3. Wells JC, Fewtrell MS. Measuring body composition. Arch Dis Child. 2006; 91(7):612–7. doi: 10.1136/adc.2005.085522.
4. Chumlea WC, Guo SS, Kuczmarski RJ, Flegal KM, Johnson CL, Heymsfield SB, et al. Body composition estimates from NHANES III bioelectrical impedance data. Int J Obes Relat Metab Disord. 2002;26(12):1596–1609. doi: 10.1038/sj.ijo.0802167
5. Siri W. Body composition from fluid spaces and density analysis of methods. In: Brozek J, Henshcel A, editors. Techniques for measuring body composition. Washington, DC: National Academy Press; 1961. pp. 223–44. PMID: 8286893
6. Ellis K. Whole-body counting and neutron activation analysis. In: Roche A, Heymsfield S, Lohman T, editors. Human body composition. Champaign, IL: Human Kinetics Press; 1996. pp. 45–61. doi: 10.5040/9781492596950.ch-004
7. Knight GS, Beddoe AH, Streat SJ, Hill GL. Body composition of two human cadavers by neutron activation and chemical analysis. Am J Physiol. 1986;250(2 Pt 1):E179–E185. doi: 10.1152/ajpendo.1986.250.2.E179
8. Brozek J, Grande F, Anderson JT, Keys A. Densitometric analysis of body composition: revision of some quantitative assumptions. Ann N Y Acad Sci. 1963; 110:113–40. doi: 10.1111/j.1749-6632.1963.tb17079.x
9. Dempster P, Aitkens S. A new air displacement method for the determination of body composition. Med Sci Sports Exerc. 1995;27(12):1692–7. PMID: 8614327
10. Roubenoff R, Kehayias JJ, Dawson-Hughes B, Heymsfield S. Use of dual-energy x-ray absorptiometry in body-composition studies: not yet a "gold standard" Am J Clin Nutr. 1993;58(5):589–91. doi: 10.1093/ajcn/58.5.589
11. Goodpaster BH, Thaete FL, Kelley DE. Composition of skeletal muscle evaluated with computed tomography. Ann N Y Acad Sci. 2000;904:18–24. doi: 10.1111/j.1749-6632.2000.tb06416.x
12. Roche A. Anthropometry and ultrasound. In: Roche A, Heymsfield S, Lohman T, editors. Human body composition. Champaign, IL: Human Kinetics Press; 1996. pp. 167–89.
13. Chumlea WM, Guo SS. Assessment and prevalence of obesity: application of new methods to a major problem. Endocrine. 2000;13(2):135–42. doi: 10.1385/endo:13:2:135
14. Coppini LZ, Waitzberg DL, Campos AC. Limitations and validation of bioelectrical impedance analysis in morbidly obese patients. Curr Opin Clin Nutr Metab Care. 2005;8:329–32. doi: 10.1097/01.mco.0000165013.54696.64
15. Scharfetter H, Schlager T, Stollberger R, Felsberger R, Hutten H, Hinghofer-Szalkay H. Assessing abdominal fatness with local bioimpedance analysis: basics and experimental findings. Int J Obes Relat Metab Disord. 2001;25:502–11. doi: 10.1038/sj.ijo.0801556
16. Pietrobelli A, Heymsfield SB. Establishing body composition in obesity. J Endocrinol Invest. 2002;25:884–92. doi: 10.1007/BF03344052
17. Chumlea WC, Guo S. Bioelectrical impedance and body composition: present status and future direction–reply. Nutr Rev. 1994;52:323–5. doi: 10.1111/j.1753-4887.1994.tb01404.x
18. Lukaski HC, Johnson PE, Bolonchuk WW, Lykken GI. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am J Clin Nutr. 1985;41(4):810–817. doi: 10.1093/ajcn/41.4.810
19. Khalil SF, Mohktar MS, Ibrahim F. The theory and fundamentals of bioimpedance analysis in clinical status monitoring and diagnosis of diseases. Sensors (Basel). 2014 Jun 19;14(6):10895–928. doi: 10.3390/s140610895
20. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Manuel GJ, et al. Bioelectrical impedance analysis – part II: utilization in clinical practice. Clin Nutr. 2004;23:1430–53. doi: 10.1016/j.clnu.2004.09.012
21. Sun SS, Chumlea WC. Statistical methods for the development and testing of body composition prediction equations. In: Heymsfield SB, Lohman TG, editors. Human body composition. Champaign, IL: Human Kinetics Books; 2005.
22. Rush EC, Chandu V, Plank LD. Prediction of fat-free mass by bioimpedance analysis in migrant Asian Indian men and women: a cross validation study. Int J Obes (Lond) 2006;30:1125–31. doi: 10.1038/sj.ijo.0803230
23. Wells JCK, Fuller NJ, Dewit O, Fewtrell MS, Elia M, Cole TJ. Four-component model of body composition in children: density and hydration of fat-free mass and comparison with simpler models. Am J Clin Nutr. 1999 May;69(5):904–12. doi: 10.1093/ajcn/69.5.904
24. Heyward VH, Wagner DR. Body composition and ethnicity. Applied body composition assessment. Human Kinetics. 2004. pp. 135–72.
25. Malina RM, Huang YC, Brown KH. Subcutaneous adipose tissue distribution in adolescent girls of four ethnic groups. Int J Obes Relat Metab Disord. 1995; 19:793–797. PMID: 8589780

26. Jakicic JM, Wing RR, Lang W. Bioelectrical impedance analysis to assess body composition in obese adult women: the effect of ethnicity. Int J Obes Relat Metab Disord. 1998;22:243–9. doi: 10.1038/sj.ijo.0800576
27. Wagner DR, Heyward VH. Measures of body composition in blacks and whites: a comparative review. Am J Clin Nutr. 2000;71:1392–402. doi: 10.1093/ajcn/71.6.1392
28. Evans WD, McClagish H, Trudgett C. Factors affecting the in vivo precision of bioelectrical impedance analysis. Appl Radiat Isot. 1998;49:485–7. doi: 10.1016/s0969-8043(97)00061-4
29. Slinde F, Rossander-Hulthen L. Bioelectrical impedance: effect of 3 identical meals on diurnal impedance variation and calculation of body composition. Am J Clin Nutr. 2001;74:474–8. doi: 10.1093/ajcn/74.4.474
30. Kushner RF, Gudivaka R, Schoeller DA. Clinical characteristics influencing bioelectrical impedance analysis measurements. Am J Clin Nutr. 1996;64:423S–427S. doi: 10.1093/ajcn/64.3.423S
31. Piccoli A, Rossi B, Pillon L, Bucciante G. Body fluid overload and bioelectrical impedance analysis in renal patients. Miner Electrolyte Metab. 1996;22:76–8. PMID: 8676831
32. Guglielmi FW, Mastronuzzi T, Pietrini L, Panarese A, Panella C, Francavilla A. The RXc graph in evaluating and monitoring fluid balance in patients with liver cirrhosis. Ann N Y Acad Sci. 1999;873:105–11. doi: 10.1111/j.1749-6632.1999.tb09456.x
33. Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gomez JM, et al. Bioelectrical impedance analysis – part I: review of principles and methods. Clin Nutr. 2004;23:1226–43. doi: 10.1016/j.clnu.2004.06.004
34. Macdonald HM, New SA, Campbell MK, Reid DM. Longitudinal changes in weight in perimenopausal and early postmenopausal women: effects of dietary energy intake, energy expenditure, dietary calcium intake and hormone replacement therapy. Int J Obes Relat Metab Disord. 2003;27:669–76. doi: 10.1038/sj.ijo.0802283
35. Dehghan M, Merchant AT. Is bioelectrical impedance accurate for use in large epidemiological studies? Nutrition Journal. 2008;7:26. doi: 10.1186/1475-2891-7-26
36. Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol. 2008;9:629–35. doi: 10.1016/S1470-2045(08)70153-0
37. Awad S, Tan BH, Cui H, Bhalla A, Fearon KC, Parsons SL, et al. Marked changes in body composition following neoadjuvant chemotherapy for oesophagogastric cancer. Clin Nutr. 2012;31:74–7. doi: 10.1016/j.clnu.2011.08.008
38. Peng P, Hyder O, Firoozmand A, Kneuertz P, Schulick RD, Huang D, et al. Impact of sarcopenia on outcomes following resection of pancreatic adenocarcinoma. J Gastrointest Surg. 2012;16:1478–86. doi: 10.1007/s11605-012-1923-5
39. Albano D, Messina C, Vitale J, et al. Imaging of sarcopenia: old evidence and new insights. Eur Radiol. 2020;30(4):2199-208. doi: 10.1007/s00330-019-06573-2
40. Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl. Physiol. Nutr. Metab. 2008;33(5):997–1006. doi: 10.1139/H08-075
41. Borga M, West J, Bell JD, Harvey NC, Romu T, Heymsfield SB, Leinhard OD. Advanced body composition assessment: From body mass index to body composition profiling. J. Investig. Med. 2018;66(5);1–9. doi: 10.1136/jim-2018-000722
42. Prado CM, Birdsell LA, Baracos VE. The emerging role of computerized tomography in assessing cancer cachexia. Curr Opin Support Palliat Care. 2009;3(4):269-75. doi: 10.1097/SPC.0b013e328331124a
43. Aleixo GFP, Shachar SS, Nyrop KA, et al. Myosteatosis and prognosis in cancer: systematic review and meta-analysis. Crit Rev Oncol Hematol. 2020;145:102839. doi: 10.1016/j.critrevonc.2019.102839
44. Sawyer, M., Ratain, M.J. Body Surface Area as a Determinant of Pharmacokinetics and Drug Dosing. Invest NewDrugs.2001;19:171–7.doi:10.1023/A:1010639201787
45. Gurney H. Dose calculation of anticancer drugs: a review of the current practice and introduction of an alternative. J Clin Oncol. 1996;14(9):2590–611. doi: 10.1200/JCO.1996.14.9.2590
46. Ratain MJ. Body–surface area as a basis for dosing of anticancer agents: science, myth, or habit? J Clin Oncol. 1998;16(7):2297–8. doi: 10.1200/JCO.1998.16.7.2297
47. Beumer JH, Salvatore EC, Salamone J. Body-Surface Area–Based Chemotherapy Dosing: Appropriate in the 21st Century? J Clin Oncol. 2012;30(31);3896-7. doi: 10.1200/JCO.2012.44.2863
48. Gamelin E, Delva R, Jacob J et al.: Individual fluorouracil dose adjustment based on pharmacokinetic follow-up compared with conventional dosage: Results of a multicenter randomized trial of patients with metastatic colorectal cancer. J Clin Oncol. 2008;26:2099–105. doi: 10.1200/JCO.2007.13.3934
49. Joerger M, Huitema AD, Richel DJ et al.: Population pharmacokinetics and pharmacodynamics of paclitaxel and carboplatin in ovarian cancer patients: A study by the European Organization for Research and Treatment of Cancer-Pharmacology and Molecular Mechanisms Group and New Drug Development Group. Clin Cancer Res. 2007;13: 6410– 18. doi: 10.1158/1078-0432.CCR-07-0064
50. Miller AA, Rosner GL, Egorin MJ et al.: Prospective evaluation of body surface area as a determinant of paclitaxel pharmacokinetics and pharmacodynamics in women with solid tumors: Cancer and Leukemia Group B Study 9763. Clin Cancer Res. 2004;10:8325–31. doi: 10.1158/1078-0432.CCR-04-1078

51. Capitain O, Asevoaia A, Boisdron-Celle M et al.: Individual fluorouracil dose adjustment in FOLFOX based on pharmacokinetic follow-up compared with conventional body-area-surface dosing: A phase II, proof-of-concept study Clin Colorectal Cancer. epub ahead of print on June 8, 2012. doi: 10.1016/j.clcc.2012.05.004
52. Petrelli F, Cortellini A, Indini A, Tomasello G, Ghidini M, Nigro O, et al. Association of Obesity With Survival Outcomes in Patients With Cancer: A Systematic Review and Meta-analysis. JAMA Netw Open. 2021; 4:e213520. doi: 10.1001/jamanetworkopen.2021.3520
53. Chan DSM, Vieira R, Abar L, Aune D, Balducci K, Cariolou M, et al. Postdiagnosis body fatness, weight change and breast cancer prognosis: Global Cancer Update Program (CUP global) systematic literature review and meta-analysis. Int J Cancer. 2023;152:572–99. doi: 10.1002/ijc.34322
54. Li Y, Li C, Wu G, Yang W, Wang X, Duan L, et al. The obesity paradox in patients with colorectal cancer: a systematic review and meta-analysis. Nutr Rev. 2022; 80:1755–68. doi: 10.1093/nutrit/nuac005
55. Fredrix EW, Saris WH, Soeters PB, King J, Dahlk SL, Grutsch JF, et al. Estimation of body composition by bioelectrical impedance in cancer patients. Eur J Clin Nutr. 1990;44(10): 749–52. PMID: 2176591
56. Gupta D, Lis CG, Dahlk SL, Vashi PG, Grutsch JF, Lammersfeld CA. Bioelectrical impedance phase angle as a prognostic indicator in advanced pancreatic cancer. Br J Nutr. 2004;92(6):957–62. doi: 10.1079/BJN20041292
57. Gupta D, Lammersfeld CA, Vashi PG, King J, Dahlk SL, Grutsch JF, et al. Bioelectrical impedance phase angle in clinical practice: implications for prognosis in stage IIIB and IV non-small cell lung cancer. BMC Cancer. 2009;28:9–37. doi: 10.1186/1471-2407-9-37
58. Paiva SI, Borges LR, Halpern-Silveira D, Assuncao MC, Barros AJ, Gonzales MC. Standardized phase angle from bioelectrical impedance analysis as prognostic factor for survival in patients with cancer. Support Care Cancer. 2010;19(2):187–92. doi: 10.1007/s00520-009-0798-9
59. Santarpia L, Marra M, Montagnese C, Alfonsi L, Pasanisi F, Contaldo F. Prognostic significance of bioelectrical impedance phase angle in advanced cancer: preliminary observations. Nutrition. 2009;25(9):930–1. doi: 10.1016/j.nut.2009.01.015
60. Davis MP, Yavuzsen T, Khoshknabi D, Kirkova J, Walsh D, Lasheen W, et al. Bioelectrical impedance-phase angle changes during hydration and prognosis in advanced cancer. Am J Hosp Palliat Care. 2009; 26(3):180–7. doi: 10.1177/1049909108330028
61. Aleixo GFP, Shachar SS, Nyrop KA, Muss HB, Battaglini CL, Williams GR. Bioelectrical Impedance Analysis for the Assessment of Sarcopenia in Patients with Cancer: A Systematic Review. Oncologist. 2020 Feb; 25(2):170-82. doi: 10.1634/theoncologist.2019-0600.
62. Kim EY, Kim SR, Won DD, et al. Multifrequency bioelectrical impedance analysis compared with computed tomography for assessment of skeletal muscle mass in primary colorectal malignancy: a predictor of short-term outcome after surgery. Nutr Clin Pract. 2020; 35(4):664-74. doi: 10.1002/ncp.10363
63. Smit C, De Hoogd S, Brüggemann RJM, Knibbe CAJ. Obesity and drug pharmacology: a review of the influence of obesity on pharmacokinetic and pharmacodynamic parameters. Expert Opin Drug Metab Toxicol. 2018;14:275–85. doi:10.1080/17425255.2018.1440287
64. Griggs JJ, Sorbero MES, Lyman GH. Undertreatment of obese women receiving breast cancer chemotherapy. Arch Intern Med. 2005;165:1267–73. doi:10.1001/archinte.165.11.1267
65. Lote H, Sharp A, Redana S, Papadimitraki E, Capelan M, Ring A. Febrile neutropenia rates according to body mass index and dose capping in women receiving chemotherapy for early breast cancer. Clin Oncol. 2016;28:597–603. doi: 10.1016/j.clon.2016.02.003
66. Schwartz J, Toste B, Dizon DS. Chemotherapy toxicity in gynecologic cancer patients with a body surface area (BSA) > 2 m2. Gynecol Oncol. 2009;114:53–6. doi:10.1016/J.YGYNO.2009.03.010
67. Barrett SV, Paul J, Hay A, Vasey PA, Kaye SB, Glasspool RM. Does body mass index affect progression-free or overall survival in patients with ovarian cancer? Results from SCOTROC I trial. Ann Oncol Off J Eur Soc Med Oncol. 2008;19:898–902. doi:10.1093/ANNONC/MDM606
68. Griggs JJ, Mangu PB, Temin S, Lyman GH. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology Clinical Practice guideline. J Oncol Pract. 2012;8:e59–e61. doi:10.1200/JOP.2012.000623
69. Desmedt C, Fornili M, Clatot F, Demicheli R, de Bortoli D, Di Leo A et al. Differential benefit of adjuvant docetaxel-based chemotherapy in patients with early breast cancer according to baseline body mass index. J Clin Oncol. 2020;38:2883–91. doi:10.1200/JCO.19.01771
70. Li XT, Tang L, Chen Y, Li YL, Zhang XP, Sun YS. Visceral and subcutaneous fat as new independent predictive factors of survival in locally advanced gastric carcinoma patients treated with neo-adjuvant chemotherapy. J Cancer Res Clin Oncol. 2015;141:1237–47. doi: 10.1007/s00432-014-1893-y
71. Shachar SS, Williams GR, Muss HB, Nishijima TF. Prognostic value of sarcopenia in adults with solid tumours: A meta-analysis and systematic review. Eur J Cancer. 2016; 57:58–67. doi: 10.1016/j.ejca.2015.12.030
72. Tan BH, Brammer K, Randhawa N, Welch NT, Parsons SL, James EJ, et al. Sarcopenia is associated with toxicity in patients undergoing neo-adjuvant chemotherapy for oesophago-gastric cancer. Eur J Surg Oncol. 2015;41:333–8. doi: 10.1016/j.ejso.2014.11.040
73. Zhuang CL, Huang DD, Pang WY, Zhou CJ, Wang SL, Lou N, et al. Sarcopenia is an independent predictor of

severe postoperative complications and long-term survival afer radical gastrectomy for gastric cancer: analysis from a large-scale cohort. Medicine (Baltimore). 2016;95:e3164. doi: 10.1097/MD.0000000000003164

74. Hayashi N, Ando Y, Gyawali B, Shimokata T, Maeda O, Fukaya M, et al. Low skeletal muscle density is associated with poor survival in patients who receive chemotherapy for metastatic gastric cancer. Oncol Rep. 2016;35:1727–31. doi: 10.3892/or.2015.4475
75. Huang DD, Chen XX, Chen XY, Wang SL, Shen X, Chen XL, et al. Sarcopenia predicts 1-year mortality in elderly patients undergoing curative gastrectomy for gastric cancer: a prospective study. J Cancer Res Clin Oncol. 2016;142:2347–56. doi: 10.1007/s00432-016-2230-4
76. Prado CM, Baracos VE, McCargar LJ, Reiman T, Mourtzakis M, Tonkin K, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. Clin Cancer Res 2009; 15(8):2920–6. doi: 10.1158/1078-0432.CCR-08-2242
77. Malietzis G, Currie AC, Athanasiou T, Johns N, Anyamene N, Glynne-Jones R, et al. Influence of body composition profle on outcomes following colorectal cancer surgery. Br J Surg 2016;103:572–80. doi: 10.1002/bjs.10075
78. Morley JE. Sarcopenia: diagnosis and treatment. J Nutr Health Aging 2008;12(7): 452–6. doi: 10.1007/BF02982705
79. Wang P, Wang S, Ma Y, Li H, Liu Z, Lin G et al. Sarcopenic obesity and therapeutic outcomes in gastrointestinal surgical oncology: A meta-analysis. Front. Nutr. 2022;9. doi:10.3389/fnut.2022.921817
80. Sahin MEH, Akbas F, Yardimci AH et al. The effect of sarcopenia and sarcopenic obesity on survival in gastric cancer. BMC Cancer. 2023;23:911.doi:10.1186/s12885-023-11423-y
81. Mei KL, Batsis JA, Mills JB et al. Sarcopenia and sarcopenic obesity: do they predict inferior oncologic outcomes after gastrointestinal cancer surgery?. Perioper Med. 2016;30:5. doi:10.1186/s13741-016-0052-1
82. Hanna L, Nguo K, Furness K, Porter J, Huggins CE. Association between skeletal muscle mass and quality of life in adults with cancer: a systematic review and meta-analysis. JCSM 2022;13(2):839-57. doi: 10.1002/jcsm.12928
83. Bye A, Sjoblom B, Wentzel-Larsen T, Gronberg BH, Baracos VE, Hjermstad MJ, et al. Muscle mass and association to quality of life in non-small cell lung cancer patients. J Cachexia Sarcopenia Muscle 2017;8:759–67. doi: 10.1002/jcsm.12206
84. Nipp RD, Fuchs G, El-Jawahri A, Mario J, Troschel FM, Greer JA, et al. Sarcopenia is associated with quality of life and depression in patients with advanced cancer. Oncologist 2018;23:97–104. doi: 10.1634/theoncologist.2017-0255
85. Slagter SN, van Vliet-Ostaptchouk JV, van Beek AP, Keers JC, Lutgers HL, van der Klauw MM, et al. Health-related quality of life in relation to obesity grade, type 2 diabetes, metabolic syndrome and inflammation. PLoS One. 2015;10(10):e0140599. doi: 10.1371/journal.pone.0140599
86. Hojan K, Molińska-Glura M, Milecki P. Physical activity and body composition, body physique, and quality of life in premenopausal breast cancer patients during endocrine therapy – a feasibility study. Acta Oncol. 2013;52:2:319–26. doi: 10.3109/0284186X.2012.744468
87. Pavlović Mavić M, Šeparović R, Vazdar Lj, Tečić Vuger A, Banović M. Impact of body composition on the quality of life of premenopausal patients with early stage breast cancer during chemotherapy. Acta clin Croat 2022; 61:605–12. doi: 10.20471/acc.2022.61.04.06
88. Smits A, Lopes A, Bekkers R, Galaal K. Body mass index and the quality of life of endometrial cancer survivors—A systematic review and meta-analysis. Gyn Oncol. 2015;137(1):180-7. doi: 10.1016/j.ygyno.2015.01.540
89. Biglia N, Moggio G, Peano E, Sgandurra P, Ponzone R, Nappi RE, Sismondi P. Effects of surgical and adjuvant therapies for breast cancer on sexuality, cognitive functions, and body weight. J Sex Med. 2010 May;7 (5):1891–900. doi: 10.1111/j.1743-6109.2010.01725.x
90. Fobair P, Stewart SL, Chang S, D'Onofrio C, Banks PJ, Bloom JR. Body image and sexual problems in young women with breast cancer. Psychooncology. 2006 Jul;15(7):579–94. doi: 10.1002/pon.991

Sažetak

MJERENJE SASTAVA TIJELA I NJEGOV ZNAČAJ U LIJEČENJU ONKOLOŠKIH BOLESNIKA

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Promjene u sastavu tijela mogu ukazati na postojanje određenih zdravstvenih stanja i rizika. Iako su trenutno dostupne brojne metode za kvantitativnu procjenu sastava tijela, svaka od njih ima svoja ograničenja. Najčešće se upotrebljavaju indirektne metode zbog njihove dostupnosti i jednostavnosti. Jedna od tih metoda, koja je našla široku primjenu u kliničkim ispitivanjima i svakodnevnoj praksi, a pokazala se i vrlo vrijednom u onkoloških bolesnika, je bioelektrična impedanca. Pokazalo se da se procijenjena masa i volumen mišića mjereni bioelektričnom impedancom mogu povezati sa toksičnošću kemoterapije i ukupnom prognozom bolesnika, nezavisno od sijela primarnog tumora. Pokazalo se da se izračunati fazni kut može koristiti kao snažan prognostički faktor za određene ishode, kao i nezavisni prognostički faktor u bolesnika sa uznapredovalim malignomima. Sastav tijela je također povezan i s kvalitetom života onkoloških bolesnika, a brojna istraživanja su pokazala značajan utjecaj na različite poddomene kvalitete života. Mjerenje sastava tijela i informacije koje ono pruža mogu se upotrijebiti za razvijanje različitih kliničkih intervencija koje mogu pomoći onkološkim bolesnicima da žive duže i kvalitetnije.

KLJUČNE RIJEČI: *sastav tijela; bioelektična impedanca; rak; sarkopenija*