Malnutrition and Survival – Bioimpedance Data in Head Neck Cancer Patients

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Abstract. *Background/Aim: Bioimpedance analysis (BIA) reflects the nutritional status of patients. The aim of this study was to examine whether BIA is able to document the possible impact of malnutrition on survival. Materials and Methods: The registered data of 42 head and neck cancer patients were analyzed. Survival data of 22 women and 20 men were included. The mean age was 67.3±10.77 years. BIA was measured by the Biocorpus 4000 RX (MEDICAL Health Care GmbH Karlsruhe) and summarized in individual phase angle (PA) of each patient. Results: Patients with normal PA>5.0 had a significantly better survival (p=0.016). The median survival time was 13.84 months (range=0.69-125.19 months) in malnourished patients (PA<5.0) compared to 51.16 months (range=7.02-116.79 months) in normally nourished head and neck cancer (HNC) patients (PA>5.0). Age adjusted body mass index had a similar impact on prognosis, but was not statistically significant (p=0.068) in the investigated study groups. Conclusion: BIA is able to document the impact of malnutrition on the survival of head and neck cancer patients.*

Malnutrition is a great problem for head and neck cancer patients. The majority of them are already suffering from a bad nutritional status at the time of diagnosis (1). About 90% will develop additional symptoms such as dry mouth, loss of taste, loss of appetite, nausea and vomiting as a consequence of anti-cancer therapy. Furthermore, a third of all patients will develop late toxicities such as xerostomia and fibrotic stenosis, which disturb normal eating for the rest of their life (2).

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Until today, nutrition was a central theme among cancer patients and their physicians. Screening tools such as the NRS 2002 or the MUST Score are using standardized questions or global information regarding general appearance (3, 4). Sometimes laboratory data regarding total protein or albumin are used to describe malnutrition (5).

There is need to develop tools to objectively measure malnutrition, cachexia or sarcopenia. The oldest marker of nutritional status is age-adjusted body mass index (BMI) (6, 7). However, BMI has a low sensitivity to recognize malnourished patients. Anthropometric data like skin fold measurements and dynamic hand craft are also able to describe body status, e.g. malnutrition as a complex phenomenon (8-10).

In order to better characterize body composition or muscle mass, more invasive methods such as DEXA, CT or bioimpedance-analysis-based measurements should be used (11).

This study investigated the possible advantages of bioimpedance analysis (BIA) in comparison to age-adjusted body mass index in advanced head and neck cancer patients.

Patients and Methods

Patients suffering from head and neck cancer were included into a non-interventional, anonymous, mono-institutional, retrospective register study. Treatment and follow-up performed at the department of ENT Diseases, Head Neck Surgery of the Südharz Hospital Nordhausen between 2008 and 2018.

Treatment included surgery and additional radiotherapy or primary radiochemotherapy in all patients. The follow-up visits were performed bi-monthly during the first 2 years and every 6 months thereafter.

Under therapy and/ or follow-up, BIA of all patients was measured by Biocorpus 4000 RX (MEDICAL Health Care GmbH Karlsruhe). BIA yielded reactance and resistance as raw data, both were required to calculate PA. The individual PA and additional anthropometric measurements (body length, body mass) of each patient were obtained at the time of BIA by qualified staff.

Information on overall survival was extracted from follow-up files. At first, the study population was divided into two groups- PA<5° and PA>5°. Afterwards PA and overall survival were used for Kaplan–Meier calculations performed using MS excel and an add-

in [Cs_Dbp_Km, University of Halle, (12)]. Secondly, the same analysis was performed for a BMI less or more than 23 kg/m².

A phase angle (PA) >°5.0 and a BMI >23.0 kg/m² defined normal nutritional status for patients older than 55 years.

All research was performed in accordance with the actual version of declaration of Helsinki. No further ethical approval was necessary because this observational study was anonymous and non-interventional.

Results

A total of 42 patients suffering from head-neck cancer were included in this retrospective observational study (for patient characteristics refer to Table I). Cancer entities were heterogeneous: oropharyngeal carcinoma (n=15), laryngeal cancer (n=7), oral cancer (n=5), hypopharyngeal carcinoma (n=4), neoplasm of the salivary glands (n=4), others (n=7). The histology of all samples was squamous cell carcinoma of the head and neck region. The standard of treatment was similar – surgery plus adjuvant radio(chemo)therapy.

A total of 24/42 (57.1%) patients were normally nourished (PA>5°), 11 patients had a high-risk for malnutrition (PA 4°-5°) and 7 patients were malnourished (PA<4°).

A total of 19/42 (45.2%) patients had a body mass index lower than the age adapted norm (<23.0 kg/m²).

Patients with a PA>5° showed a significantly better overall survival (p=0.016; Figure 1). Median survival in this group was 51.16 months (range=7.02-116.79 months), while median survival of malnourished patients was 13.84 months (range=0.69-125.19 months). BMI was similar in both patient groups; no significant difference was found (Table I).

Patients with BMI>23.0 kg/m² had a better overall survival (p=0.068). As shown in Figure 2, patients with a normal BMI live for a median of 55.66 months (range=7.02-125.19 months) compared to 14.89 months (range=0.89-82.98 months) for patients with BMI <23 kg/m². Table II summarizes the biometric data of the BMI subgroup analysis.

Discussion

In 2017, the European Society of Parenteral and Enteral Nutrition (ESPEN) published the last version of a consensus paper on the definition of cachexia and malnutrition. Unexpected weight loss, and decreased BMI are listed as main criteria. Reduced fat free mass was added as a new parameter. No consensus was reached regarding which method is the best for evaluating malnutrition (13).

Bioelectrical impedance analysis is an established method in diagnosing sarcopenia or malnutrition of cancer patients (14-16). The PA is a summarized central parameter to classify BIA's measurements (17) used in previous studies to assess malnutrition in head and neck cancer (HNC) patients (18).

Table I. Biometric data, sub-analysis according to BIA phase angle (PA)

	Total	PA<5.0	PA>5.0
Number	42	18	24
Male	20	8	12
Female	22	10	12
Age (a)	67.29	66.81	67.66
SD	10.77	10.79	10.74
BMI (kg/m ²)	23.69	22.13	24.86
SD	3.40	3.44	2.86
N BMI ≤23 kg/m ²	19	11	8
N BMI >23 kg/m ²	23	7	16
Median survival (mo)	42.08	13.84	51.16
Range	0.69-125.19	0.69-125.19	7.02-116.79

Table II. Biometric data, sub-analysis according to body mass index (BMI).

	Total <23 kg/m ²	BMI >23 kg/m ²	BMI
Number	42	19	23
Male	20	8	12
Female	22	11	11
Age (a)	67.29	63.43	70.48
SD	10.77	12.80	7.99
PA (°)	5.17	4.95	5.36
SD	1.13	1.01	1.21
N PA <5.0°	19	11	8
N PA >5.0°	23	7	16
Median survival (mo)	42.08	14.89	55.66
Range	0.69-125.19	0.69-82.98	7.02-125.19

We observed that a PA<5° was a sufficient threshold for identifying HNC patients with a shorter median survival. These results correspond to a study of patients undergoing cardiac surgery, where a PA<4.5° was indicative for a higher frailty and mortality (19). Another study on palliative care patients suffering mainly from gastric cancer set the PA threshold at <4°. Interestingly, in this study, patients with a PA>4° showed a nearly twofold increase in median survival time (20). Furthermore, a study with a patient cohort similar to ours proposed that a cutoff value of 5.95° provides the best prediction of 5-year survival in patients with HNC (21). In accordance to these previously published studies, our results indicate that BIA is a sensitive marker for identifying patients at risk.

BMI is influenced by age; generally a slightly higher BMI is recommended in the elderly (6, 7). Therefore, a BMI threshold of 23 kg/m² was chosen. There was a trend towards longer survival in patients with a BMI>23 kg/m².

Figure 1. Overall survival (Kaplan–Meier) according to BIA phase angle ($p=0.016$).

Figure 2. Overall survival (Kaplan–Meier) according to age-adjusted BMI ($p=0.068$).

Noticeably, even age-adjusted BMI did not detect seven patients with a $PA < 5^\circ$. While four of these patients were only at increased risk, three were malnourished ($PA < 4^\circ$). On the other hand, age adjusted BMI detected eight patients with a $PA > 5^\circ$. Considering that patients with a $BMI < 23 \text{ kg/m}^2$ showed a trend towards a shorter overall survival, this subgroup of patients also seems to be at risk. This argues for combining both parameters.

This small mono-institutional study indicates the need to establish diagnosis of nutritional status in a different manner. Anamnestic tools would be Nutritional Risk Score (NRS) 2002 or MUST (3, 4). The measurement of body mass and body length has to be a minimum standard in each oncology department. In addition, bioimpedance analysis and calculation of age-adjusted body mass index should also be performed before interpretation.

Focusing on head and neck cancer patients, malnutrition has to be treated as early as possible. Early integration could improve the outcome of standard treatment. Similar concepts are known from fast-track surgery for other cancer patients. A former study has indicated a better outcome from radiotherapy if patients have had early energy substitution (22).

Conflicts of Interest

There are no conflicts of interest to declare regarding this study.

Authors' Contributions

Judith Büntzel: data analysis, writing, editing; Oliver Micke: conceptualization; Klaus Kisters: supervising; Jens Büntzel: data sampling, data analysis; Ralph Mücke: supervising.

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