Original Article

Association of handgrip strength and endurance with body composition in head and neck cancer patients

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Abstract

Introduction: Assessment of skeletal muscle function (SMF) is of clinical relevance in the prediction of treatment outcome and to decide on optimal management of head & neck cancer (HNC) patients. Handgrip strength (HGS) & handgrip endurance (HGE) are considered as surrogate marker for whole-body skeletal muscle function. Further, SMF depends substantially on the body composition (BC). Hence in this study, we compared BC, HGS and HGE between HNC patients and healthy controls and also analysed the association of HGS, HGE with body composition in HNC patients. **Methods:** A cross-sectional study, conducted in 44 subjects in the age between 18 to 60 years. Twenty-two were histologically proven HNC patients prior to cancer-specific treatment and twenty-two age and gender-matched healthy volunteers. The parameters recorded were Height, weight, waist circumference, hip circumference, HGS, HGE and BC. Hand-held dynamometer was used to measure HGS and HGE measured using a stopwatch. BC was estimated by whole-body bioelectrical Impedance analysis method using Bodystat Quad scan 4000 device. **Result:** Comparison of data between HNC patient & healthy control was done by Student's *t* test. HGS, HGE, lean body mass (LBM), fat-free mass index (FFMI), Phase angle (PA), body cell mass (BCM) and body cell mass index (BCMI) were found to be reduced significantly in HNC patients when compared to healthy subjects. Further, Pearson correlation analysis revealed a significant positive correlation of HGS & HGE with LBM, FFMI, PA, BCM & BCMI, whereas body fat mass index showed a negative correlation with HGS & HGE in HNC patients. **Conclusion:** Our findings revealed, a significant reduction in HGS, HGE in patient with HNC which denotes decreased skeletal muscle function and it is linearly associated with low muscle mass, body cell mass and phase angle.

Keywords: Body composition, handgrip endurance, handgrip strength, head and neck cancer patients

Introduction

Head and neck cancer (HNC) contributes to 30% of all cancers and it holds third place among the common malignancies.[1] In India, behavioural, environmental and demographic factors have been found to be associated with HNC.[2] Disease-related malnutrition is a frequent finding in head and neck malignancies and it imposes a major challenge in treating these patients more so with malnourished cases. Further muscle dysfunction is prevalent in them which is attributed to poor nutrition, elevated proinflammatory cytokines, frailty leading to increased muscle catabolism resulting in low muscle mass that makes them vulnerable for all-cause mortality.[3-5] Studies have reported the link between loss of skeletal muscle mass and reduced muscle strength.[6,7] Hence, assessment of body composition and skeletal

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muscle function is of clinical importance in the management of cancer patients. A simple validated, non-invasive tool to assess the body composition (BC) is by bioelectrical impedance analysis (BIA) technique.[8] The principles and clinical utility of BIA have been clearly explained by Kyle *et al.*,[9,10] and Sergi *et al.*[11] Skeletal muscle function is generally assessed by measuring the handgrip strength (HGS) and handgrip endurance (HGE).[12] Though handgrip strength measure the upper body strength, it is contemplated as good surrogate marker of generalized muscle strength, as it correlates with the strength of other muscles of the body as well.[13]

Scientific studies have revealed that, grip strength evaluation in cancer patient, predict the survival, mortality and treatment outcome.[14,15] further, grip strength depends on skeletal muscle mass largely. Reduced muscle mass is referred as sarcopenia and weak muscle strength is known as dynapenia.[16] In oncological setting , presence of both the defects were considered as a negative prognostic factor and were found to be strongly associated with cancer-related fatigue, increased disability, higher treatment-related complications, poor quality of life, impaired survival rate especially in elderly patients with head and neck squamous cell carcinoma.[17] Also, HGS of less than 25 kg preoperatively were significantly associated with higher postoperative mortality and complications than with normal grip strength patients.[18] Handgrip endurance is also found to be reduced particularly in cancer-related fatigue.[19] Moreover, pre-treatment estimation of handgrip dyanomometry and body composition in HNC patients may aid the radiation oncologist in selecting less toxic chemotherapy and radiotherapy regimen and also to plan nutritional strategies to improve, treatment outcome in high-risk cases. Further, the information on grip strength and body composition would help the primary care physician to provide optimal supportive care, as, comprehensive oncology service is a challenging task and depends on close cooperation between primary care physician, nutritionist, medical & radiation oncologist. Meanwhile, there is dearth of data on establishing the relation between HGS, HGE with body composition in head neck patients especially in Indian ethnicity, hence the present study was aimed to assess the HGS, HGE in HNC patients and to find its association with body composition in newly diagnosed HNC patients registered for treatment in our institute.

Materials and Methods

In this cross-sectional study, 44 volunteers in age group of 18–60 years were enrolled based on sample size calculation. By PS software sample size was calculated to be 22 in each group using statistical formula for comparing two independent means with 5% level of significance, 80% power, and minimum expected difference in mean of lean body mass as 2.5.[20] The study was approved by the Institutional Human Ethics committee (approval ref: JIP/IEC/2019/0160) dated, 24.06.2019 and ICMR ethical guidelines were followed throughout the study. Written informed consent was obtained from all the participants after explaining the study procedure. Among the 44 subjects, twenty-two were newly diagnosed HNC patients of all stages, reported to Regional Cancer Centre of the institute and they were designated as HNC group and twenty-two were age and gender-matched healthy volunteers designated as control group.

Inclusion/exclusion criteria

Inclusion criteria

In this study, in HNC group, histologically proven head and neck cancer patients prior to cancer-specific treatment in the age group between 18 and 60 years were enrolled and in the control group, age and gender-matched apparently healthy volunteers were included.

Exclusion criteria

HNC patients with comorbidities like diabetes mellitus, renal failure, heart failure, and persons with history of trauma or muscle wasting in upper limb were excluded.

Procedure

The study was conducted in the Department of Physiology. Anthropometric parameters such as height, body weight, waist circumference (WC) and hip circumference (HC) were measured as per the standard procedure.[21] Body mass index (BMI), waist-to-height ratio (WHtR) and waist-hip ratio (WHR) was calculated using the formula, BMI = weight (kg)/height (m^2), WHtR = WC (cm)/height (cm), WHR = WC (cm)/HC (cm).

Body composition analysis

BC parameters were analysed by whole-body bioelectrical Impedance analysis method using the Bodystat QuadScan 4000 (Bodystat) device. It uses the electrical properties of body tissue and estimates BC parameters. It is a quick, simple and safe, non-invasive procedure. Measurements were taken as per standard protocol.[22] The participants were asked to lie down in supine position and four surface electrodes were placed, two signal introducing electrodes were located on the right dorsum of hand and foot close to the metacarpophalangeal and metatarsophalangeal joints respectively and two voltage sensing electrodes were applied in the right side, pisiform prominence of the wrist and in the foot, between medial and lateral malleolus of the ankle, through which an imperceptible electrical current was sent through the body. Before that participants height, weight, HC and WC were entered in the device Various BC parameters were computed by measuring the impedance to the applied current and by applying predictive equations, in-built in the equipment.[8,9,21]

Measurement of handgrip strength (HGS) and handgrip Endurance (HGE)

Handgrip strength was measured by handgrip dynamometer (model INCO AMBALA, India). The subjects were made to sit comfortably and were asked to grip the handgrip dynamometer, using the dominant hand and squeeze as hard as possible till the needle of the dial doesn't move anymore and value is noted

The subjects were asked to perform three trials with a minimum gap of two minutes and the highest value was taken as HGS. For recording HGE, the subjects were instructed to maintain one-third of HGS, as long as possible and the time taken was noted as HGE using a stop watch.[19]

Statistical analysis

Statistical analysis was performed by SPSS version 19 (SPSS; SPSS Inc., Chicago, IL). Values were expressed as mean ± SD, since all the parameters were normally distributed. Comparison of HGS, HGE and BC between the HNC & healthy control groups were done by unpaired "t" test. The association of handgrip strength and handgrip endurance with body composition parameters were tested by the Pearson correlation test. The *P* values less than 0.05 were considered as statistically significant.

Results

Table 1 shows, that groups were comparable based on age and gender. Anthropometric variables, body mass index (BMI) and waist to height ratio were significantly reduced in HNC patients when compared to healthy volunteers. Body composition parameters, the lean body mass, dry lean weight, fat-free mass index (FFMI), phase angle (PA), body cell mass (BCM) and body cell mass index (BCMI) were significantly reduced in head and neck cancer patients when compared to healthy volunteers, whereas body fat percentage was found to be significantly more in HNC patients.

Table 2 shows the mean Handgrip strength in kg and Handgrip endurance in second. Both parameters (HGS: 21.91 ± 8.36 & HGE: 99.55 ± 46.21) were found to be reduced in HNC patients when compared to healthy volunteers (HGS: 32.55 ± 9.60, HGE: 163.27 ± 37.20) which is statistically significant ($p < 0.001$)

Table 3 shows correlation between the handgrip strength and body composition parameters in HNC patients. In our study, body fat percent (r= –0.575, $P < 0.01$) and BFMI (r= –0.473, $P < 0.05$) were negatively correlated with HGS. Body lean percent (r = 0.575, $P < 0.01$), FFMI (r = 0.506, $P < 0.05$), BCM (r = 0.741, $P = < 0.001$) and BCMI (r = 0.631, $P = <0.001$) were positively correlated with HGS in HNC patients.

Table 4 shows correlation between the handgrip endurance and body composition parameters in HNC patients. In our study, body fat percent (r = –0.562, $P < 0.01$) and BFMI (r = –0.473, $P < 0.05$) were negatively correlated with handgrip endurance. Body lean mass percent (r = 0.562, $P < 0.01$), FFMI (r = 0.434, $P < 0.05$), BCM (r = 0.615, $P = 0.002$) and BCMI (r = 0.583, $P = <0.001$) were positively correlated with handgrip endurance in HNC patients.

Discussion

This study has explored the association between the HGS, HGE with BC in HNC patients. In our study the mean age was comparable between HNC patient & healthy controls, BMI was found to be reduced significantly in HNC patients when compared to healthy controls. Pre-treatment malnourishment, indicated by low BMI, specify that these patients are more prone for treatment-related toxicity, higher risk of infection, delayed wound healing, prolonged hospital stay and hence have increased mortality rate compared to normal BMI counterpart.[23,24] Though Body mass index is a frequently used parameter to determine the nutritional status in clinical practice, it fails to differentiate between body lean mass and fat mass, hence body composition analysis is the better tool to detect different segment reliably.[11,25] In the present study, BC analysis by BIA technique revealed, higher body fat percentage (%fat), reduced lean body mass (LBM) and dry lean mass (DLM) in HNC patients. Our findings were in agreement with Kapoor N & Chauhan NS *et al.*,[26,27] The above-stated observation suggest an imbalance between fat and muscle mass in them.[28] DLM reflects protein and mineral content of the body, although LBM includes DLM

Table 1: Comparison of body composition parameters between healthy volunteers and head and neck cancer patients

Parameters	Healthy volunteers (*n*=22)	Head and Neck Cancer patients (*n*=22)	*P*
Age (age)	48.55±8.52	52.05±6.78	0.139
Gender (Male/Female)	15/7	15/7	-
Height (cm)	2.59±0.30	2.4±0.24	0.22
Weight (Kg)	63.5±14.9	43.1±8.5	< 0.001
BMI (Kg/m^2)	24.47±4.81	17.32±3.06	<0.001
Waist Hip Ratio	0.88±0.03	0.87±0.06	0.317
Waist to Height Ratio	0.53±0.45	0.06±0.04	<0.001
Body fat (%)	28.08±7.78	37.13±11.20	0.003
Body lean (%)	71.91±7.78	62.86±11.20	0.003
Dry lean weight (Kg)	9.73±5.46	-0.14±5.35	<0.001
BFMI (kg/m^2)	6.76±2.48	6.22±1.5	0.456
FFMI (kg/m^2)	17.54±3.49	11±3.24	<0.001
Phase angle (degree)	6.06±1.08	4.80±0.88	<0.001
Body cell mass (Kg)	29±6.8	21±4.6	<0.001
Body cell mass index (Kg/m^2)	11.1±2.2	8.3±1.3	<0.001

BFMI: Body fat mass index, FFMI: fat free mass index. Values were expressed in mean±SD. The anthropometric and body composition parameters were compared using unpaired *t* test. $P<0.05$ is considered as statistically significant

Table 2: Comparison of handgrip strength and endurance between healthy volunteers and head and neck cancer patients

Parameters	Healthy volunteers (*n*=22)	Head and Neck Cancer patients (*n*=22)	*P*
HGS (Kg)	32.55±9.60	21.91±8.36	<0.001
HGE (Sec)	163.27±37.20	99.55±46.21	<0.001

HGS: Handgrip strength, HGE: Handgrip endurance. Values were expressed in mean±SD. The handgrip strength (HGS) and Handgrip endurance (HGE) were compared using unpaired *t* test. *P*<0.05 is considered as statistically significant

Table 3: Correlation between the handgrip strength and body composition parameters in head and neck cancer patients

Parameters	*r*	*P*
Body fat (%)	-0.575	0.005
Body lean (%)	0.575	0.005
Dry lean weight (Kg)	0.363	0.097
BFMI (kg/m^2)	-0.473	0.026
FFMI (kg/m^2)	0.506	0.016
Phase angle (degree)	0.427	0.047
Body cell mass (Kg)	0.741	<0.001
BCMI (Kg/m^2)	0.631	<0.001

BFMI: Body fat mass index, FFMI: fat free mass index, BCMI: body cell mass index. The correlation between handgrip strength with body composition parameters were carried out by Pearson correlation test. *P*<0.05 is considered as statistically significant

Table 4: Correlation between the handgrip endurance and body composition parameters in head and neck cancer patients

Parameters	*r*	*P*
Body fat (%)	-0.562	0.006
Body lean (%)	0.562	0.006
Dry lean weight (Kg)	0.317	0.150
BFMI (kg/m^2)	-0.473	0.026
FFMI (kg/m^2)	0.434	0.043
Phase angle (degree)	0.323	0.142
Body cell mass (Kg)	0.615	0.002
BCMI (Kg/m^2)	0.583	<0.001

BFMI: Body fat mass index, FFMI: fat free mass index., BCMI: body cell mass index. The correlation between handgrip endurance with body composition parameters were carried out by Pearson correlation test. *P*<0.05 is considered as statistically significant

and body water, the core component of LBM is skeletal muscle mass (SMM).[29]Therefore decreased LBM denotes poor muscle mass and wasting of lean tissue in HNC patients.[20] Low LBM is considered as a prognostic factor in HNC cases and stated to have a significant impact on clinical outcome. pre-treatment or preoperative low skeletal muscle mass in HNC patients are prone for treatment toxicities, risk of recurrence, reduced physical activity, hence, may require a long-term medical support.[28]

We also witnessed a significant reduction in fat-free mass index in HNC patients, compared to healthy subjects. Further, fat-free mass index (FFMI) and body fat mass index (BFMI), were considered as definitive nutritional assessment parameters.[30] Both FFMI and BFMI were conceptually similar to BMI, but the use of these height-normalized indices, are more reliable marker of protein-energy malnutrition.[31] FFMI measures the amount of muscle (fat-free mass) relative to a person's height and calculated by the formula, FFMI = FFM/height (kg/m^2) and BFMI was calculated by = BFMI: BFM/height (kg/m^2.[30] FFMI has been shown to be an independent predictor of survival and several major complication following cancer treatment.[32,33] According to Aline Porciúncula Frenzel *et al.*,[34] FFMI ≤ 15 kg/m^2 denotes muscle mass deficiency, whereas FFMI > 15 kg/m^2 is considered as normal muscle mass.[34] Our patients had FFMI of 11kg/m^2 and control had 17 kg/m^2, which indicate muscle mass deficiency in them. There was no significant change observed in BFMI between the control and HNC groups.[35]

Apart from this we also detected a significant reduction in the BIA parameter namely the phase angle (PA) and body cell mass (BCM) in HNC patients. Body composition assessed by bioimpedance method measures the *resistance (R) and reactance (X*c*)* of the human body to the applied current and based on this the Phase angle (PA) was calculated as the arc-tangent of the ratio of reactance versus electric resistance PA : (Xc/R) X (180°/π) and expressed in degree[11,12] which, represent the cell membrane integrity.[36, 37] In cancer research it has been identified as prognostic factors for survival and an indicator of cellular health in HNC patients.[38] In healthy subjects, PA ranges between 5° and 7°.[39,40,41]Lower PA angle denote reduced cell mass and decreased cellular integrity.[42] Whereas a higher PA suggests large quantities of intact healthy cells.[43] HNC Patients with low PA prior to chemoradiotherapy treatment are more susceptible to significant weight loss and muscle wasting during cancer treatment in contrast to those with normal PA values. Hence, high risk of low survival. The next parameter of relevance was the body cell mass (BCM), the metabolically active component of fat-free mass, a good prognosticator of a subject's nutritional status, measurement of BCM represents an alternate marker of skeletal muscle mass or FFM.[21,44-46] The body cell mass index (BCMI), expressed as BCM/height^2 has been shown to be a sensitive index of muscle mass levels in the body.[47] In the present study reduction in BCM, BCMI in HNC patients compared to healthy controls also denotes muscle mass depletion. Low PA & BCMI indicate their risk for sarcopenia and malnutrition.[48]

The other major findings of this study were reduced mean HGS and HGE in HNC patients compared to healthy controls which reflects decreased skeletal muscle function. Low HGS, is a marker of sarcopenia and sarcopenic cancer patients are more likely to be frail,[49] hence susceptible for adverse health outcome and poor quality of life.[15,50-53] further , we observed a positive correlation of HGS, HGE with LBM, FFMI, PA, BCM, and BCMI, which denotes, diminished muscle function may be associated with low body cell mass and skeletal muscle mass; hence, a functional decline was noticed in HNC patients. Also, we noted a negative correlation of body fat percentages and BFMI with HGS & HGE.

Weight loss and reduced muscle strength is characteristic of any cancer patients, more so in head and neck malignancies.[54] Scientific evidence proclaim that muscle mass depletion & malnutrition is a frequent occurrence in cancer regardless of the disease stage.[55] In HNC patients, disease-induced muscle dysfunction is multifactorial.[56] Cancer patients experience appetite loss due to altered appetite signals which result in negative protein & energy balance leading to accelerated muscle protein catabolism with subsequent loss of SMM[57,58] Secondly, tumor-induced systemic and muscle inflammation generate several pro -inflammatory cytokines (IL – 6, TNF α, TGF-β, interferon-γ), which in turn activate hypothalamo - pituitary adrenal axis leading to production of catabolic stress hormones adrenaline, cortisol, glucagon causing disrupted proteostasis, eventually developing in muscle wasting.[55,58-60] The other proposed mechanism is secretion of myostatin by cancer cells causing skeletal muscle wasting.[61] Muscle atrophy in cancer is also linked to over expression of Foxo- 3 transcription factor and ubiquitin-proteasome pathway mediated proteolysis[62] The above-suggested mechanisms of cancer-induced skeletal muscle wasting result in skeletal muscle dysfunction, which in turn manifested as reduced muscle mass and force leading to decreased grip strength and endurance in these patients.

Conclusion

Our Indian population-based study, reveals that HGS & HGE were significantly decreased in newly diagnosed HNC patient. Further, it shows a positive correlation with LBM, PA, FFMI, BCM, BCMI. Pre-treatment estimation of HGS, HGE a surrogate marker of SMF and analysis of body composition can aid the physician to design optimal therapeutic intervention for these patients. This preliminary work, open up further studies using sensitive serological biomarkers of muscle mass or by using muscle volume imaging techniques to identify the skeletal muscle mass or muscle loss precisely in HNC patients and facilitate better treatment strategies in these patients to improve their clinical outcome and quality of life.

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Conflicts of interest

There are no conflicts of interest.

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