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Association of Esophageal Squamous Cell Carcinoma with Anthropometric Parameters: A Case Control Study

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Abstract

Background:
Esophageal cancer is one of the most common cancers worldwide with a poor prognosis. Squamous cell carcinoma and adenocarcinoma of the esophagus share some risk factors, whereas other risk factors are specific to one histologic type or the other. Since esophageal squamous carcinoma remains one of the most common cancers in our region, we intend to find any link or association between this malignancy and various anthropometric parameters.

Materials and Methods
The aim of the study was to assess various anthropometric parameters in newly diagnosed esophageal squamous cell cancer patients at presentation. Our study comprised a total of 160 patients of histopathologically confirmed esophageal squamous cell carcinoma patients and 160 age and sex matched controls. Anthropometric parameters were recorded in all the patients and the controls according to the latest guidelines after attaining proper consent from the patients and controls.

Results:
We found an inverse association between body mass index and esophageal squamous cell carcinoma. Besides body mass index other indirect measures of obesity like Weight, Thigh skin fold thickness, Abdominal skin fold thickness, Thigh girth and Abdominal circumference were also found to be inversely related to esophageal squamous cell carcinoma.

Conclusion
In conclusion, we found an inverse association between body mass index and esophageal squamous cell carcinoma as has been reported from other studies from western and Asian populations. Besides body mass index other indirect measures of obesity like Weight, Thigh skin fold thickness, Abdominal skin fold thickness, Thigh girth and Abdominal circumference were also found to be inversely related to esophageal squamous cell carcinoma.

Keywords: NIL

Introduction

Esophageal cancer is a common cancer worldwide and carries a poor prognosis. Globally esophageal cancer is the ninth most common cancer and the sixth most common cause of cancer deaths (1).Several histological types are seen, almost all of which are

epithelial in origin. The majority of these tumors will be either squamous cell carcinoma or adenocarcinoma. Which histological type occurs in a given patient or predominates in a given geographic area depends on many variables, including individual lifestyle, socioeconomic pressures, and environmental factors. In the last decades, the incidence of adenocarcinoma of the esophagus and gastric cardia has increased rapidly in the western countries (2-5). In contrast, the incidence of esophageal squamous cell carcinoma has been stable, while the incidence of distal gastric adenocarcinoma has declined (2, 4, 6). It has been suggested that higher prevalence of obesity in the western world explains these trends in incidence of adenocarcinoma of the esophagus and gastric cardia (7, 8). A meta-analysis on body mass index and adenocarcinomas of the esophagus or gastric cardia showed a positive association between body mass index (BMI) and risk of adenocarcinoma of the esophagus (9). However for esophageal squamous cell carcinoma, no association was found with body mass index in some studies (6, 10), while others found an increasing body mass index (BMI) to be associated with decreased risk (11-14). Although various studies have focused on body mass index and association of adenocarcinoma of esophagus but very few studies have been conducted on esophageal squamous cell carcinoma and its link with various anthropometric measures. Since esophageal squamous carcinoma remains one of the most common cancers in our region, we intend to find any link or association between this malignancy and various anthropometric parameters.

Materials and Methods:

The primary aim of our study was to determine the risk or association of esophageal squamous cell carcinoma with various anthropometric measures. Inclusion criteria included all newly diagnosed patients of Squamous cell carcinoma esophagus and only those patients and healthy controls who gave informed consent were included in the study. Patients who did not give consent and patients with physical deformity were excluded from the study. In all patients, a complete history was taken. Risk factor assessment including history of smoking, alcohol, and complete physical examination was done in both patients as well as controls. Baseline investigations such as CBC/LFT/KFT/Chest x-ray/ECG were done in all patients. WHO Performance Status, CECT scan and endoscopic findings were also reported in all patients. Risk factor assessment such as smoking history (total duration, type, pack years), alcohol consumption, achalasia, caustic burns, tylosis, socioeconomic status, gastro esophageal reflux, paterson-kelly syndrome were also reported in both patients as well as healthy controls.

Measurement Methods:

Head Circumference was taken with the subject in sitting. The head circumference measurement was taken at the level immediately above the brow. Chest Circumference was taken at the level of the middle of the sternum (breast-bone), with the tape passing under the arms with the arms relaxed by the side, at the end of a normal expiration. Waist or Abdominal Circumference was taken at the narrowest waist level, or if this was not apparent, at the midpoint between the lowest rib and the top of the hip bone (iliac crest). Arm Length was measured with the subject standing and the arms hanging loosely by the side of the body, fingers outstretched. The measurement was made from the acromiale (lateral edge of the acromion process) to the tip of the middle finger. Measurement was made on the right side. Arm Span was measured with the subject facing away from the wall, with back and buttocks touching the wall and the arms stretched out horizontally. Measurement was taken from one furthermost finger tip to the other. Standing Height (Stature) Measurement was taken with the subject facing directly ahead, shoes taken off, feet together, arms by the sides, Heels, buttocks and upper back in contact with the wall. For Mid Thigh Girth, the subject was made to stand erect with their weight evenly distributed on both feet and legs slightly parted. The circumference measure was taken at the level of the mid-point on the lateral (outer side) surface of the thigh, midway between trochanterion (top of the thigh bone, femur) and tibialelaterale (top of the tibia bone). Body Mass / Weight was taken with the subject standing on the weighing scale with minimal movement with hands by their side. Shoes and clothing was removed. For Abdominal Skin fold Thickness, the measurement was made 5 cm adjacent to the umbilicus (belly-button), to the right side. Vertical pinch was made at the marked site, and the calipers placed just below the pinch and the measurement was taken. Thigh Skin fold Thickness

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was taken with the subject sitting and the knee bent at right angles, The measurement was taken at the mid-point of the anterior (front) surface of the thigh, midway between patella (knee cap) and inguinal fold (crease at top of thigh).

Results and Discussion

From January 2014 to December 2018, 160 histopathologically proven cases of ESCC and 160 age and sex matched controls were enrolled into this study. Risk factor assessment including history of smoking, alcohol, and complete physical examination was done in both patients as well as controls. Baseline investigations such as CBC/LFT/KFT/Chest x-ray/ECG were done in all patients. WHO Performance Status, CECT scan and endoscopic findings were reported in all patients. Risk factor assessment such as smoking history (total duration, type, and pack years), alcohol consumption, achalasia, caustic burns, tylosis, socioeconomic status, gastro esophageal reflux, paterson-kelly syndrome was also reported in both patients as well as healthy controls. Anthropometric parameters which included height, weight, head circumference, chest circumference, abdominal circumference, thigh girth, arm length, arm span, abdominal skin fold, thigh skin fold, body mass index (BMI) and body surface are (BSA) were recorded in all the patients and the controls according to the latest guidelines after attaining proper consent from the patients as well as the control subjects.

Age was comparable between the two groups as we chose age and sex matched controls for the study. Majority of the patients in our study were in the fifth and sixth decade of life with an age range of 32-88 years. The mean age of patients in the study group was 61.9 years (Table 1), which is almost same as was found in a previous study in the same population (18). Since we chose age and sex matched controls, the number of males and females in the patient and control group was similar. There were 55% male patients and 45% female patients in both the arms (Table 1). This data suggests that the incidence of esophageal squamous cell carcinoma occurs with similar incidence in both males and females in our study population which is in contrast with the western population where it is 3 to 4 times more common in men than among women (15). The reason for this disparity may be due to the influence of peculiar dietary habits of this region as well as possibly due to geographical, environmental and genetic variations between this region and the western region. In most of the patients, ECOG performance score was 1(40%). The ECOG performance score was 0 in 28.8% of the patients and 2 in 31.2% of the patients (Table 1). Thus in spite of the symptoms of dysphagia, 28.8% of the patients had good performance score. In majority of the participants in the control group, ECOG performance score was 0 (51.2%). The ECOG performance score was 1 in 45% of the participants in the control group and 2 in 3.8% of the participants in the control group. The reason for low ECOG performance score in some of the participants in the control group was due to old age and associated co morbid conditions.

In our study population carcinoma esophagus is the second most common cancer among males and the most common cancer among females (16). To date, no single factor can be identified as the main cause of the excess incidence of squamous cell carcinoma and earlier presentation as compared to other regions of India and western population. Three main components emerge as important factors: a societal component with poor, rural lifestyle and general deprivation status in particular in vitamins and oligoelements; a lifestyle component with the u se of copper utensils in cooking, the consumption of spicy, deep fried foodstuffs, and the drinking of hot salty tea; and an environmental component with exposure to high levels of dietary nitrosamines from diverse sources. Overall, these three components are similar to the general pattern of factors that have been involved in causing squamous cell carcinoma in other high-incidence area in the so-called “esophageal cancer belt”, namely in central China (Cixian, Lixian) and in Northern Iran (Golestan). Further comparative studies between these regions are needed to identify the contributions of these various components.

Body mass index has been found to be inversely associated with esophageal squamous cell carcinoma as reported by data from Western and Asian populations (17-20). In the present study we also found an inverse relationship between body mass index (BMI) and esophageal squamous cell carcinoma. 24.4% of patients in the study group were in the underweight or severely underweight category while as in the control group only 6.2% of patients were in the underweight or severely underweight

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category (Table 2). Weight, Thigh skin fold thickness, abdominal skin fold thickness, Thigh girth, waist-hip ratio and abdominal circumference are indirect measures of obesity and in the present study we found an inverse relationship between these factors and esophageal squamous cell carcinoma (Table 2). Because of the influence of nutritional and socioeconomic factors, the risk of squamous cell carcinoma of the esophagus has an inverse relationship with the measures of obesity (21, 22). The biology underlying the observed inverse association between BMI or other body measures and the risk of esophageal squamous cell carcinoma is not clear. Poor diet leading to micronutrient deficiencies or malnutrition reflected in a low Body Mass Index (BMI) have been implicated as factors contributing to higher risk for esophageal squamous cell carcinoma, specifically in Asian populations (18, 21). A number of micronutrients and dietary components such as vitamins A, C, and E; selenium; carotenoids; and fiber, have been found to prevent carcinogenesis. Deficiencies of the aforementioned nutrients and dietary components (in particular, selenium), have been associated with an increased risk of esophageal squamous cell carcinoma in some parts of the world (24).

Height has been found to be associated with increased risk of many different types of cancers like colon, prostate, esophagus etc (25-27). Most of the studies on esophageal adenocarcinoma have shown an inverse association with adult height (28-30), while the association between ESCC risk and adult height are erratic (29-31). In the present study we did not find any association between height and esophageal squamous cell carcinoma. The mean height in the study group was 157 cm and 158cm in the control group. With a p value of 0.266, there was no statistically significant difference in height between the two groups (Table 2).

Body surface area (BSA) was statistically significant factor between the two groups, 46.9% of the patients had Body surface area (BSA) below 1.51, while as in the control group 23.8% of the participants had Body surface area (BSA) below 1.51. Similarly Arm length was statistically significant parameter between the two groups with a p value of 0.027. The mean arm length in the study group was 66.2 cm and 65.2 cm in the control group. Arm span was a statistically insignificant factor with a p vale of 0.726. The mean arm span in the study group was 162.4 cm and 162.1 cm in the control group. Head circumference was statistically insignificant parameter between the two groups. The mean head circumference in the study group was 52.4 and 52.7 in the control group. Similarly Chest circumference was also statistically insignificant parameter between the two groups. Mean chest circumference was 77.8 in the study group and 78.2 in the control group.

In conclusion, we found an inverse association between body mass index and esophageal squamous cell carcinoma as has been reported from other studies from western and Asian populations. Besides body mass index other indirect measures of obesity like Weight, Thigh skin fold thickness, abdominal skin fold thickness, Thigh girth, waist-hip ratio and abdominal circumference were also found to be inversely related to esophageal squamous cell carcinoma. In our study we did not find any relationship between height and esophageal squamous cell carcinoma. Esophageal squamous cell carcinoma was found to occur with almost similar incidence in males and females. The mean age of patients in the study group was 61.9 years which is almost same as was reported by a previous study. This confirms that in our population, esophageal carcinoma presents a decade earlier.

Even though this is the first such study in our population, large population-based studies are required to understand the relationship between esophageal cancer and various anthropometric studies.

Tables

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Table 1: Age, Gender and performance distribution of Patients and Controls

Age (years)	**Patients** n (%)		**Controls** n (%)	
≤ 40	5 (3.1)		5 (3.1)	
41 – 50	26 (16.2)		25 (15.6)	
51 – 60	45 (28.1)		46 (28.8)	
61 – 70	53 (33.1)		49 (30.6)	
71 – 80	22 (13.8)		27 (16.9)	
>80	9 (5.6)		8 (5.0)	
Total	160		160	
Mean Age	61.9		61.7	
Gender	**Patients** n (%)		**Controls** n (%)	
Males	88(55)		88(55)	
Females	72(45)		72(55)	
ECOG PS	0	1	2	Total
Patients n (%)	46 (28.8%)	64 40.00%	50(31.2%)	160
Controls n (%)	82 (51.2%)	73 (45.0%)	6 -6.00%	160

Table 2: Comparison of various anthropometric parameters between patients and controls

Parameter	**Group**	**N**	**Mean**	**p-value**
Height	Patients	160	157.11	0.27
	Controls	160	158.08	
Weight	Patients	160	51.36	≤0.0001*
	Controls	160	56.84	
BMI	Patients	160	20.75	≤0.0001*
	Controls	160	22.82	
BSA	Patients	160	1.49	≤0.0001*
	Controls	160	1.58	
Head circumference	Patients	160	52.37	0.88
	Controls	160	52.74	

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Chest circumference	Patients	160	77.84	0.47
	Controls	160	78.23	
Abdominal circumference	Patients	160	73.11	0.004*
	Controls	160	74.95	
Waist to height ratio	Patients	160	0.47	0.62
	Controls	160	0.48	
Abdominal skin fold thickness	Patients	160	1.43	≤0.0001*
	Controls	160	1.84	
Arm length	Patients	160	66.29	0.02*
	Controls	160	65.18	
Arm span	Patients	160	162.44	0.72
	Controls	160	162.12	
Mid thigh girth	Patients	160	33.73	≤0.0001*
	Controls	160	33.35	
Waist hip ratio	Patients	160	2.2	0.001*
	Controls	160	2.1	
Thigh skin fold thickness	Patients	160	1.3	≤0.0001*
	Controls	160	1.74	

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