Nutritional Support Improves Outcome in Patients with Lung Cancer Cachexia Receiving Chemotherapy

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Summary:

Background: Malnutrition is a frequent complication in patients with advanced staged lung cancer and can negatively affect the outcome of treatments. Lack of knowledge about nutrition, complications of disease and side effects of anticancer therapies can also lead to inadequate nutrient intake and subsequent malnutrition. Nutritional status is a strong predictor of quality of life in cancer patients.

Objective: To get the effect of the nutritional intervention on outcome of dietary intake, body composition, nutritional status, functional capacity and quality of life in patients with lung cancer cachexia receiving chemotherapy.

Patients and Methods: This 6 months study included the lung cancer patients who were interviewed with clinical assessment. Nutritional score of each patient was recorded. Individualized management plan with nutritional intervention was given and nutritional counseling was done by a nutritionist every week. Chemotherapy ± radiotherapy was given. Every patient was followed up at 1st, 2nd, 3rd and 6th week and was assessed regarding symptoms, clinical findings, nutritional score and radiological status.

Results: Total 628 lung cancer patients with 523 (83%) males and 105 (17%) females (Male: female 4.98:1) were enrolled. Mean age was 56.88 years. Two thirds of them were illiterate. Around 90% came from poor and below average socioeconomic group. More than 95% male and >66% female were tobacco users in different forms. On assessing nutritional score, almost all were with high risk score (95%). About 80% presented with WHO performance status at 2 and 3. About 61% patients got treatment after hospitalization. Following nutritional intervention along with supportive, symptomatic, treatment of comorbid diseases and anti-cancer treatment, the result showed that mean nutritional score at 1st and 2nd week were 8.24 and 6.63 (high risk), at 3rd and 6th week were 5.46 and 4.34 (Intermediate risk). There was a significant effect for time (p<.001). Symptomatic improvement occurred in 60% of the patients. Conclusion: Nutritional intervention improves nutritional score if the other treatment like supportive, symptomatic, comorbid condition and anticancer treatment could be applied adequately.

Introduction:

Malnutrition represents a risk factor for poor prognosis among patients with cancer, affecting up to 85% of patients with certain cancers[1]. Patients with cancer of the lung, esophagus, stomach, colon, rectum, liver, and pancreas are at greatest risk[2].

Poor nutritional status, weight loss, and malnutri-tion lead to poor outcomes for patients, in terms of quality of life, functional status, compli-cation rates, and treatment disruptions[3,4,5]; and for some patients, cancer cachexia[6]. The prevalence is higher in patients with lung and gastrointestinal tumors[7,8]. At the time of diagnosis, 60% of patients with lung cancer have already experienced a significant weight loss[9]. In patients receiving palliative chemotherapy, weight loss predicts a significantly shorter survival and poorer quality of life[3]. One known reason for poorer outcomes in patients with lung cancers (non- small cell) with weight loss are a reduced response to chemotherapy as well as increased toxicity from treatment[10]. The prevention and early detection of malnutrition, with early nutritional intervention for patients can improve

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patients' nutritional status and help patients to maintain body weight, maintain lean body mass, better tolerate treatment, and im-prove quality of life[6, 11, 12-15].

According to the Hospital Cancer Registry Report of National Institute of Cancer Research & Hospital (NICRH), Dhaka, Bangladesh, in 2010, the lung cancer is the most common cancer (31.4%) among the male cancer patients[16]. In the year of 2013 highest number of lung cancer patient (30.5%) attended medical oncology department of NICRH. Of them, almost all were symptomatic and 80% presents with weight loss (from registry book of medical oncology department, NICRH, 2013). One important cause of poor nutritional status in these patients is lack of education and lack of proper knowledge and awareness about nutrition and nutritional value of easily available, cheap and homemade common foods.

This provided a rationale to investigate whether nutritional intervention including regular nutritional counseling to increase food intake, modification of the energy density of meals, prescription of oral nutritional supplements and relief of symptoms that causes reduced food intake could improve the nutritional status of patients and clinical outcomes.

Patients and Method:

This experimental and analytic study was carried out on adults with histologically proven, metastatic or locally advanced lung cancer if they had lost any weight in the 3 months before presentation. The lung cancer patients who agreed to undergo palliative chemotherapy and were fit for chemotherapy according to standard local criteria were selected for the study.

Both male and female patients with age below 75 years were included in the study, with normal liver and kidney function. Exclusion criteria were age above 75 yrs, previously treated patients, unconscious patients, ischemic heart disease with ejection fraction <45%, SGPT level >3times of normal value, Alkaline phosphatase 4 times of normal value, creatinine clearance <45 ml/minute.

All patients provided written informed consent before study entry. The study was approved by the Ethical Committee of NICRH.

The patients were recruited for the study from January 2013 to June 2013. Each patient was interviewed and

clinical assessment was being done. Nutritional score of each patient was recorded according to nutritional risk score.

Individualized management plan was taken for every patient to meet their nutritional demand, for pain relief, treatment of disabling symptoms and associated secondary infections and co morbidities. Nutritional counseling was done by a nutritionist every week in presence of a medical oncologist for each patient. Nutritional intervention was given by oral high calorie diet. Supplementary medicine such as appetizer, iron, vitamin, minerals, amino acid, albumin, fat, carbohydrate and water was given by oral, enteral and parental route. Correction of hematological, biochemical deficit, other symptoms management along with management of co morbidities and psychological support was given side by side. The patients were managed both outdoor and indoor basis. Chemotherapy ± radiotherapy was given as per tumor board decision.

Every patient was followed up at 1st, 2nd, 3rd and 6th week and was assessed regarding symptoms, clinical findings, nutritional score and radiological status. All the findings were recorded. Data were analyzed by SPSS (Version-12).

Result:

Total 628 (105 female and 523 male) lung cancer patients were enrolled with a male-female ratio of 4.98:1and mean age of 56.88 years. Sixty eight percent of the patients could not read and write, about 20% had primary education. Around 90% of them came from poor and below average socioeconomic group. Among the male patients, >95% were tobacco user either in the form of smoking, gul or with betel nut or combination of them. In case of female patients, >66% were tobacco user, mostly in the form of tobacco leaf with betel nut or gul.

Most common histopathology was squamous cell carcinoma (40%), then adenocarcinoma (37%) and small cell carcinoma (15%). Common presentation of the lung cancer was cough (96%), weakness (82%), anorexia (81.8%), chest pain (56.4%), and insomnia (33%).

Forty two percent of the patients were with comorbid diseases such as diabetes mellitus, hypertension,

ischemic heart disease, COPD etc. On assessing nutritional score, almost all were with high risk score (95%). About 80% of the lung cancer patients presented with WHO performance status at 2 and 3. About 61% patients got treatment after hospitalization.

For nutritional intervention along with supportive, symptomatic, treatment of comorbid diseases and anti cancer treatment, the attendance of the patients at 1st week was 98.43%, 2nd week   96.18%, 3rd week 85.36% and at 6th week 75%.

The result showed that mean nutritional score at 1st week was 8.24 (high risk), 2nd week 6.63 (high risk), 3rd week 5.46 (intermediate risk) and at 6th week 4.34 (Intermediate risk).

Table-I

Descriptive statistics for different follow up nutritional score

Follow up times	Mean Nutritional Risk Score	Standard Deviation
1st week	8.24	2.330
2nd week	6.63	2.231
3rd week	5.46	2.302
6th week	4.34	2.067

A one-way repeated measures ANOVA was conducted to compare Nutritional risk scores on the four follow up times. There was a significant effect for time, Wilks' Lamda = .064, $F (2, 564) = 2246.07$, $p<.001$, multivariate partial eta squared = .936. Symptomatic improvement occurred in 60% of the patients.

Appendix I
Nutritional Risk Score
[Source: Summerton C, Shetty P, Sandle LN, Watt S. Nutritional, metabolic and environmental disease. Chapter 10.Davidson's Principles & Practice of Medicine, 19th edition: 2002, Elsevier science, Churchill Livingstone.]

Criterion	Score	Patient's score
1.Weight loss in last 3 months (unintentional)		
No weight loss	0	
0-3 kg weight loss	1	
3-6 kg weight loss	2	
>6 kg weight loss	3	
2. BMI (weight/height^2)		
>20	0	
18-19	1	
15-17	2	
<15	3	
3.Appetite		
Good (manages most of the three meals per day)	0	
Poor (Leaves more than half of the meals provided)	2	
Nil or virtually nil	3	
4.Ability to eat and retain food		
No difficulties; no diarrhea; no vomiting	0	
Problems handling food: mild diarrhea or vomiting	1	
Difficulty in swallowing or chewing: moderate diarrhea or vomiting	2	
Unable to take food orally; severe diarrhea; severe vomiting	3	
5.Stress factor		
No stress factor	0	
Mild (minor surgery, infection)	1	
Moderate (Chronic disease, major surgery)	2	
Severe (Multiple injuries, severe sepsis, cancer)	3	
Total score		
Maximum score =15; Minimum score = 0		
High risk= 6-15; Intermediate risk= 4-5; Low risk= 0-3		

Appendix II

WHO performance status scores

- 0 –Asymptomatic (fully active, able to carry on all pre-disease activities without restriction).
- 1 – Symptomatic but completely ambulatory (restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; for example, light housework, office work).
- 2 – Symptomatic, < 50% in bed during the day (ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours).
- 3 – Symptomatic, > 50% in bed, but not bedbound (capable of only limited self-care, confined to bed or chair 50% or more of waking hours).
- 4 – Bedbound (completely disabled, cannot carry on any self-care, totally confined to bed or chair).
- 5 – Death.

Discussion:

Prevalence of malnutrition in lung cancer patients was found to be 45% in a study: but it is 73% with metastatic cancer[17]. Consequences of malnutrition include not only increased risk of infections, poor wound healing, decreased quality of life and transfer to higher level care[12], but a significant emotional burden, anxiety and hopelessness also[18].

DeWys and colleagues found that as little as 5% weight loss predicted decreased response to therapy[3]. They also found that overall survival rates, performance status, produc-tivity, and quality of life declined concurrently with weight loss[3]. Early recognition and detection of risk for malnutrition through nutrition screening followed by comprehensive assessments is increasingly recognized as imperative in the development of standards of quality of care in oncology practices[19]. Several screening tools have reported their diagnostic accuracy.

In this study, majority of the study population were illiterate, representing poor and below average socioeconomic group. For this reason an easy but text book approved nutritional risk score had been used for initial assessment and clinical outcome following nutritional intervention.

Another big issue was the patients' lack of knowledge about nutrition and even about their disease. So the goal of this study was to improve the nutritional knowledge by giving proper education regarding their disease condition and nutritional counseling emphasizing the importance of nutritional improvement.

About 61% patients got treatment after hospitalization. For nutrient rich dietary advice, easily available, homemade and low cost diets had been chosen so that all the patients can follow the diet chart. The patients were offered 'rice starch' (the liquid which is usually poured off after boiling rice in Bangladesh) when admitted in hospital and also advised to take three to four glass of it at home. It is a nutrient rich fluid containing carbohydrates, protein, minerals and vitamins. The nutritionist supplied the appropriate diet chart for individual patient with proper dietary advice. The patients were interviewed in every follow up regarding their food intake and assessment of level of knowledge of nutrition.

All the interventions caused significant improvement in food intake, performance status and body weight, which were scored according to nutritional risk score and the final score after six weeks intervention showed significant improvement in nutritional status, mean nutritional risk score from 8.24 in 1st week declining to 4.34 in 6th week. This improvement was found statistically significant (p<.001).

One small Australian study has shown similar significant improvement in outcome after nutritional intervention in cancer patients. Along with chemotherapy, nutrition counseling and use of an oral nutritional supplement resulted in improvements in nutritional status, Karnofsky performance status, lean body mass and quality of life in patients with non-small cell lung or pancreatic cancer[20]. There are some other studies which have shown improvement in clinical outcome after nutritional intervention.

Many of these studies found improved immediate or patient-centered outcomes in the nutrition intervention groups. The two Randomized Controlled Trials (RCT)[21,22] that measured dietary intake both found

significant increases in the intervention groups. This was also reported in the positive-quality systematic review[23] on the effect of oral nutrition support or enteral tube feeding *versus* routine care in patients undergoing chemotherapy or radiation therapy, which reported a significant increase in total dietary energy intake. Two level II studies[24, 25], a level III-3[25] and level IV[26] *study* found that the intervention group increased their weight. In the pseudo-randomized trial by Brown *et al.*[27] (level III-1) in an outpatient rural oncology setting in Australia, there were clinically significant improvements in nutritional status as measured by Subjective Global Assessment (SGA) in the intensive intervention group.

A level III-1 study[28] (post hoc analysis) found significantly greater survival and quality of life (QoL) in patients who maintained their weight *versus* those who lost weight during an RCT of nutrition intervention comparing a fish oil-enriched supplement with a traditional supplement.

Dietary counseling by a dietician and/or oral nutritional supplements are effective methods of nutrition intervention and have been found to improve dietary intake, nutritional status and quality of life in patients receiving radiotherapy (NHMRC grade of recommendation A)[29]. There were five RCTs in chemotherapy, which found improvements in nutritional outcomes but not patient-centered outcomes such as QoL or survival[29].

Although the significant improvement in clinical outcome after nutritional interventions are nutritional risk score based in this study, it will act as a baseline for further evaluation and quantitative study to prove this primary findings in future and establish the need for nutritional intervention during cancer treatment for better outcome.

Conclusion:
Nutritional intervention including proper nutritional counseling improves nutritional score and thereby clinical outcomes if the other treatment like supportive, symptomatic, co morbid condition and anticancer treatment could be applied adequately. However further well designed large scale studies are required to establish significant improvement in quality of life and treatment outcome.

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