



## A Dyspnea as Determinant of Lower Energy Intake in Older Adult Patients with Chronic Obstructive Pulmonary Disease (COPD)

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### Abstract

**Background:** Malnutrition is frequently observed in patients with Chronic Obstructive Pulmonary Disease (COPD). However, the effects of decreased caloric consumption on disease severity have not been determined.

**Objective:** To examine the hypothesis that increased incidence of COPD-related symptoms is associated with lower energy intake in malnourished COPD patients.

**Design and Setting:** A cross-sectional study at a single institute.

**Participants:** Patients with older than 18 years of age who visited the outpatient COPD clinic at a single institute were eligible.

**Measurements:** Subjects were divided into two groups to categorize high and low Daily Energy Intake (DEI) using three strategies, with daily caloric cutoff thresholds of 25, 30 and 35 kcal/kg to distinguish high-DEI patients from low-DEI patients. All data was compared between higher-DEI and lower-DEI patients using each threshold to examine whether lower energy intake is associated with COPD symptom severity and frequency and to determine the optimal cutoff value to distinguish higher-DEI and lower-DEI patients.

**Results:** The cutoff value of a DEI of 30 kcal/kg could identify which patients had severe symptoms and malnutrition. COPD patients with  $DEI \leq 30$  kcal/kg had more severe dyspneic symptoms, as determined by a COPD Assessment Test (CAT). Finally, CAT could be recognized as the determinant of lower DEI in patients with COPD and malnutrition.

**Conclusion:** Our study proved that  $DEI \leq 30$  kcal/kg body weights may identify COPD patients with severe dyspnea, as assessed by CAT. In addition, the Food Frequency Questionnaire, known as BDHQ (brief-type self-administered diet history questionnaire), suggested that lower-DEI patients consumed a significantly smaller percentage of fat as a macronutrient in total energy. Increasing DEI to greater than 30 kcal/kg per day and increasing fat intake may improve COPD. However, the adverse events from this nutritional strategy must be monitored long term.

**Keywords:** COPD; CAT; Dyspnea; Malnutrition; BDHQ

### Introduction

Chronic Obstructive Pulmonary Disease (COPD) is not a single disease, but rather is an umbrella term for diseases that cause limitations in lung airflow such that daily activity is affected [1]. Patients with COPD visiting outpatient clinics often exhibit a multifactorial inflammatory response. Consequently, the energetic demands are increased in many COPD patients [2]. In addition, patients with COPD often experience loss of appetite. Appetite loss could be explained partly by the effects of inflammatory cytokines, and partly by the patients' struggle to hold the breath when eating or drinking due to coexisting COPD dyspneic conditions. As a result of a continued negative energy balance, these patients easily and rapidly develop malnutrition. The prevalence of

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malnutrition in patients with COPD ranges from 20% to 45% [3,4]. In respiratory rehabilitation to treat COPD, early identification of COPD patients with malnutrition could prevent worsening of COPD and subsequent hospitalization. However, diagnosing the severity of COPD requires institutional facilities to measure spirometry, which is not always available to primary care providers, and becomes an obstacle in treating COPD patients. In this context, we hypothesize that dyspneic symptoms could be a potential means to identify malnutrition coexisting with COPD. To test our hypothesis, we examined several questionnaires in COPD patients who have visited the outpatient COPD clinic at a single institution.

## Methods

### Subjects

Subjects were patients with consistent COPD who visited the COPD outpatient clinic at a single institution between March and August 2011, and gave written informed consent. Subjects who missed one or more data collections were excluded.

### Collected data

Data were collected in the three time categories of before, at, and after visits to an outpatient COPD clinic at a single institute (Figure 1). The collected data were in the following five parameters:

**Demographic parameters:** Demographic parameters including age, sex, smoking status, and Brinkman Index (BI).

**Physical parameters:** Physical parameters including physical measurement of hand grip strength, a Six-Minute Walking Test (6MWT) [5] gait speed expressed in m/sec [6], and pulmonary capacity as measured by spirometry, including Forced Expiratory Vital capacity of one second (FEV1) and %FEV1 (FEV1 divided by Forced Vital Capacity, FVC). Hand grip strength was measured in the contralateral arm to the dominant arm in duplicate, and average value was calculated to express the z-score as a measure of variation from the age- and sex-specific mean value using physical and exercise capacities published in 2014. 6MWT was defined as the maximal walking distance using a standardized 50 meter circular lane, and sense of exhaustion at completion was subjectively evaluated using the Borg scale.

**Blood test parameters:** Blood test parameters including complete blood counts and serum biochemistry parameters including serum Total Protein (TP), Albumin (Alb), vitamin B12, folic acid, and Brain Natriuretic Peptide (BNP) concentrations.

**Anthropometric parameters:** Anthropometric parameters including height, weight, Body Mass Index (BMI; calculated by weight in kilograms divided by squared height in meters, kg/m<sup>2</sup>), and anthropometric measurements of mid-upper arm circumference (AC[ED5]), Triceps Skin-Fold thickness (TSF), Calf Circumference (CC), mid-upper Arm Muscle Circumference (AMC: calculated by the equation =AC-π\*TSF, divided by AC<sup>2</sup>, and Arm Muscle Area (AMA; calculated =AMC<sup>2</sup>/4\*π). Both AMC and AMA were standardized as %AMC and %AMA, calculated by dividing by the age- and sex-specific mean values collected by JARD 2001 as a standard. Height was set to the nearest 0.1 cm as measured with a stadiometer, and weight to the nearest 0.1 kilogram as measured with a digital scale. All measurements for AC, TSF for the dominant arm, and CC for the contralateral leg were measured in duplicate and expressed as the average value. The Mini- Nutritional Assessment Short-Form (MNA-SF) [7] survey was also conducted.

**COPD functional parameters:** COPD functional parameters including clinical stage of COPD severity, as categorized by international guidelines (Global Initiative for COPD: GOLD), use of Home Oxygen Therapy (HOT), Non-Invasive Intermittent Positive Ventilation (NIPPV), presence of chronic respiratory failure defined by GOLD, Borg scale and pulse rate during and after 6 MWT.

**COPD questionnaires:** COPD questionnaires including self-administered COPD Assessment Test (CAT) [8,9], and the Medical Research Council dyspnea scale (MRC) [10] for assessing the self-rated severity of COPD. Frequency Scale for Symptoms of GERD (FSSG) [11], the Hospital Anxiety and Depression scale (HAD) [12] and the Self-Rating Questionnaire for Depression (SRQ-D) [13] were all evaluated. Here, the severity of COPD was expressed using the staging system of GOLD, with GOLD ranks by FEV1, rather than %FEV: FEV1 ≥ 0% for stage I, ≥ 50% to <80% for stage II, ≥ 30% to <50% for stage III, and <30% for stage IV.

**Food and nutrients parameters:** Food and Nutrients parameters including daily nutrient intake measured by a self-administered food frequency questionnaire (Brief-type self-administered Diet History Questionnaire: BDHQ) [14]. All obtained data were expressed in units per 1000 kcal, as calculated by densitometry.

### Subgroup classifications

Subgroups were classified to determine (1) the cutoff for Daily Energy Intake (DEI) to identify poor symptoms in patients with COPD, and (2) which COPD questionnaires are associated with lower DEI. Here, DEIs were set at three values: 25, 30, and 35 kcal/kg body weight in method 1, 2, and 3, respectively (Figure 1). In method 1, one group included subjects with DEI ≤ 25 kcal/kg and another included subjects with DEI >25. In methods 2 and 3, the DEI cutoff was changed to 30 and 35 to categorize the two groups. Then, all collected data were compared between two groups in methods 1, 2, and 3, individually.

### Statistical analysis

We showed the statistics that we found in each item with the median (25% tile, 75% tile). Statistical significance was evaluated using a Mann-Whitney U test. For both tests, p<0.05 was considered statistically significance. To conduct statistical analysis, we used Package PASW 20.0 for windows (SPSS Inc, Chicago, IL).

## Results

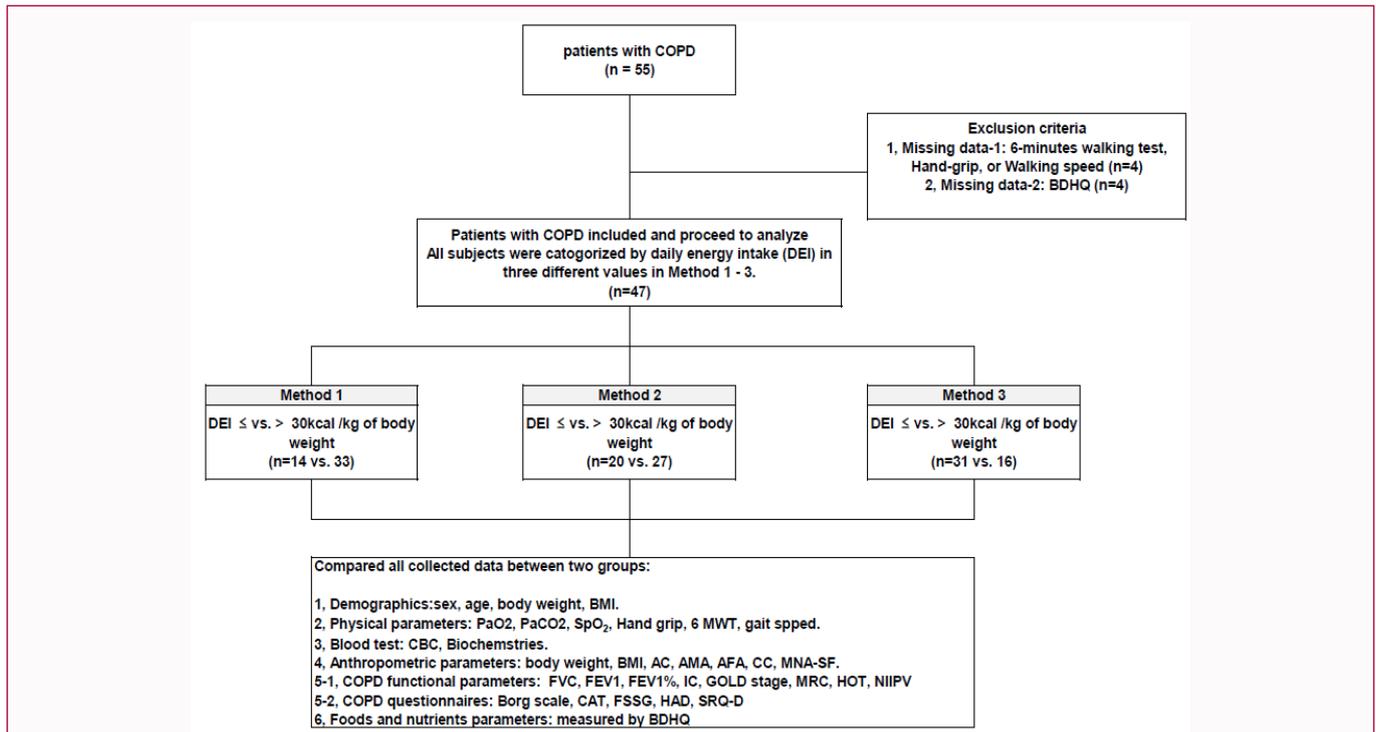
A total of 55 subjects were included in the study, and eight subjects were excluded (Figure 1). The median age was 74 years, and median BMI was 20.7 kg/m<sup>2</sup> (Table 1).

### Determining the cutoff value of daily energy intake to identify dyspneic COPD patients

In the three methods for determining cutoff value, the results of dyspnea questionnaires in DEI set at 30 and 35 kcal/kg were significantly different (Table 2), while the 25 kcal/kg/day was not statistically significant. Decreased DEI is a sensitive means for early detection of malnutrition, which is a common comorbidity of COPD, due in part to dyspnea-induced loss of appetite [15-17]. A DEI threshold of 30 kcal/kg was determined to be the optimal means of identifying early malnutrition, as this threshold had superior performance to a threshold 35 kcal/kg. [Ed6].

### Comparison of patient attributes in normal and malnourished patients

**Demographics, anthropometric characteristics, blood work,**



**Figure1:** Flow chart of the study.

**Abbreviations:** AC: Mid-upper Arm Circumference; AFA: Arm Rat Area; AMA: Arm Muscle Area; BDHQ: Brief-type self-administered Diet History Questionnaire; BMI: Body Mass Index; CAT: COPD Assessment Test; CC: Calf Circumference; DEI: Daily Energy Intake (kcal/kg of body weight/day); FEV1: Functional Expiratory Volume in 1 second; FEV1%: Percentage of FEV1/FVC; FSSG: Frequency Scale for the Symptoms of GERD; FVC: Functional Vital Capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; HAD: the Hospital Anxiety and Depression Scale; HOT: Home Oxygen Therapy; IC: Inspiratory Capacity; MRC: Medical Research Council Dyspnea Scale; NIPPV: Non-invasive Positive Pressure Ventilation; SRQ-D: Self-Rating Questionnaire for Depression; 6 MWT: Six Minutes Walking Test

**Table 1:** Characteristics of the all subjects.

Number of subjects	47
Age, years	74 (67, 79)
Gender, n (%) of men	34 (72.3%)
Height, cm	161.4 (153.7, 167.3)
Weight, kg	54.4 (46.4, 60.3)
BMI, kg/m <sup>2</sup>	20.7 (18.4, 22.2)
Smoking status (ex-smoker/smoker)	33/14
Brinkman Index*	900 (490, 1500)
%FEV1, %	45.2 (35.6, 59.5)
FEV1, L	1.05 (0.83, 1.60)
FEV1%, %	52.6 (42.7, 65.2)
FVC, L	2.11 (1.77, 2.67)
IC, L/s	1.75 (1.31, 2.02)
GOLD stage (I/II/III/IV)	4/18/17/8
HOT, n (%)	7 (14.9)
NIPPV, n (%)	3 (6.4)
Chronic respiratory failure, n (%)	8 (17.0)

Data are expressed median (25<sup>th</sup>, 75<sup>th</sup> quartile)

**Abbreviations:** BMI: Body Mass Index; FEV1: Functional Expiratory Volume in 1 second; FEV1%: Percentage of FEV1/FVC; FVC: Functional Vital Capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; HOT: Home Oxygen Therap; IC: Inspiratory Capacity; NIPPV: Non-invasive Positive Pressure Ventilation

\*Brinkman Index is calculated by [daily cigarettes] X [smoking years]

**COPD functional assessment and COPD questionnaire:** All collected data did not differ between the two groups when DEI was set

at 30 kcal/kg (Table 2), with exception to serum TP and Alb, and CAT and HAD depression scales. The CAT and HAD depression scales were significantly poorer in subjects with DEI <30 kcal/kg, whereas the TP and Alb were paradoxically higher in malnourished subjects (Table 3).

**Food and nutrient intake in normal and malnourished subjects:** Food intake, as measured by BDHQ, suggested that fired meats and chicken were consumed at higher rates in the higher DEI group (Table 4). In addition, fat and monounsaturated fatty acid intake were consumed at higher rates in the higher-DEI group, while fat-soluble vitamins did not differ between the two groups (Table 5).

## Discussion

### Malnutrition as an impact factor of adverse outcomes in COPD patients

The prevalence of Protein-Energy Malnutrition (PEM) ranges from 34% to 50% in hospitalized COPD patients. PEM is identified, in general, as a leading cause of muscle mass loss occurring due to elevated energy demands with poor energy intake [18]. Reduced respiratory muscle mass and force is thought to cause airflow obstruction and emphysema, and impairment of immune function is considered the primary cause of infectious and septic complications. Under these PEM circumstances, COPD patients with PEM have a higher risk of morbidities and mortalities. We also demonstrated that COPD patients with depleted upper muscle mass and function had poor outcomes [17,19]. Under this context, earlier identification of poor nutritional status is critical to prevent worsening COPD and associated morbidities and mortalities. Identifying the risk of PEM by

**Table 2:** Comparison of collected data between two groups categorized by daily energy intake (DEI): Low vs. High DEI group\*.

Group	Number of subjects	Parameters	Low DEI* 20	High DEI* 27	P
Demographics		Age, years	74.0 (67.0, 75.3)	75.0 (68.0, 79.0)	0.613
		Gender (% of men), %	15 (75.0%)	19 (70.4%)	0.726
		Smoking status (ex-smoker/smoker)	17/3	17/10	0.212
		Brinkman Index*	1100 (473, 1505)	900 (550, 1260)	0.590
		Height, cm	163.6 (153.7, 166.2)	159.9 (154.1, 167.9)	0.805
		Weight, kg	58.3 (50.5, 64.4)	52.3 (44.5, 58.4)	0.064
		BMI, kg/m <sup>2</sup>	21.5 (20.2, 24.5)	20.4 (18.1, 21.0)	0.039
		AC, cm	25.6 (23.1, 26.4)	23.8 (22.7, 25.6)	0.135
		TSF, cm	9.5 (7.8, 11.3)	8.0 (7.5, 10.0)	0.185
		% TSF, %	83.8 (62.2, 106.7)	74.4 (52.3, 87.1)	0.168
Anthropometry		AMC, cm	22.3 (20.7, 23.3)	20.9 (20.0, 22.8)	0.189
		% AMC, %	85.6 (78.2, 90.4)	81.0 (78.2, 86.8)	0.366
		AMA, cm <sup>2</sup>	39.8 (34.0, 43.4)	34.6 (31.7, 41.6)	0.189
		% AMA, %	100.1 (79.9, 107.8)	89.7 (83.7, 102.5)	0.272
		AFA, cm <sup>2</sup>	11.1 (8.8, 14.2)	9.7 (7.9, 12.0)	0.138
		CC, cm	33.3 (30.7, 34.9)	32.3 (29.4, 33.9)	0.241
		MNA-SF, point	11 (10, 13)	11 (9, 12)	0.905
		WBC, 10 <sup>3</sup> μL	65.0 (54.5, 73.1)	62.4 (49.7, 69.1)	0.220
		Hb, g/dL	14.0 (13.3, 14.9)	13.8 (12.1, 14.7)	0.277
		TP, g/dL	7.4 (7.2, 7.7)	7.2 (6.7, 7.4)	0.023
Laboratory		Alb, g/dL	4.4 (4.2, 4.5)	4.1 (3.9, 4.4)	0.022
		BNP, pg/mL	23.5 (17.5, 36.0)	39.2 (25.1, 79.6)	0.082
		VitB <sub>12</sub> , pg/mL	462 (406, 716)	554 (366, 712)	0.811
		Folic acid, ng/mL	6.0 (5.6, 8.6)	6.1 (4.8, 7.3)	0.451

\*Low: Daily energy intake (DEI) ≤ 30 kcal/kg of body weight, High: DEI >30 kcal/kg of body weight

**Abbreviations:** AC: mid-upper Arm Circumference; AFA: Arm Fat Area; AMA: Arm Muscle Area; AMC: Arm Muscle Circumference; Alb: Serum Albumin (g/dL); BMI: Body Mass Index; BNP: Brain Natriuretic Peptide; CC: Calf Circumference; EI: Energy Intake; Hb: Hemoglobin Concentration; MNA-SF: Mini-nutritional Assessment Short-form; TP: Serum Total Protein; TSF: triceps skin-fold thickness, WBC: white blood cell count

\*Brinkman Index is calculated by [daily cigarettes] X [smoking years]

Two groups, Low group whose Daily Energy Intake (DEI) ≤ 30 kcal/kg of body weight vs. High group whose DEI >30 kcal/kg, did not differ significantly in all parameters including demographics, anthropometry, and laboratory data, except serum total protein and albumin concentrations that were both paradoxically higher in Low group.

severity of COPD is not always possible, as this requires spirometry, which is often unavailable in clinic. Therefore, alternative means are necessary to identify PEM in COPD patients.

### Daily energy in take cutoff value as a determinant of dyspnea in patients with COPD

Although decreased body weight is ultimately reflective of PEM, this parameter may not identify PEM early enough, as a significant amount of body weight must be lost before abnormalities are detectable. Under these circumstances, identifying negative energy balance or an inappropriate daily energy intake could be used for earlier identification of PEM in COPD patients. However, an optimal DEI threshold for identification of PEM has not been reported thus far. To address this important clinical question, we determined which cutoff value is an optimal DEI for outpatients with COPD grading from GOLD I to IV. Because a DEI of 25 to 30 kcal/kg is considered normal in older adult patients [20], three DEI cutoff values of 25, 30, and 35 kcal/kg/day were assessed. According to all results from each cutoff value, all collected data in compared two groups was the same (Tables 2 and 3). This suggests patients consuming 30, 35 kcal/kg, or more do not have any differences in COPD-related symptoms. From

these observations, we deduced that 30 kcal/kg was an optimal cutoff value to identify severe COPD symptoms. Because loss of appetite is common in COPD patients, earlier detection of PEM is optimal when a lower DEI cutoff value is used. Despite ESPEN guidelines, which recommended 25 or 30 kcal/kg/day to clinical patients, another study investigating the association of COPD severity and DEI also reported that the prominent PEM, which was estimated as the Subjective Global Assessment (SGA)-C, is nearly 30 kcal/kg. Together with previous findings, the present study suggests that a DEI cutoff value of 30 kcal/kg may be optimal to recognize poor clinical outcomes, including symptom severity, morbidity and mortality [21]. However, because number of subjects may be too small in both studies additional studies must be conducted to determine a definitive DEI cutoff value in COPD patients [22,23].

### Dyspnea symptoms evaluated by CAT identify decreased DEI in COPD patients

To determine symptoms potentially predictive of poor DEI, all collected questionnaires were analyzed in the low- and high-DEI groups using the cutoff of 30 kcal/kg. Contrary to our expectations, serum protein and Alb concentrations were increased in low-

**Table 3:** Comparison of collected data between two groups categorized by Daily Energy Intake (DEI): Low vs. High DEI group\*.

Number of subjects	Parameters	Low DEI* 20	High DEI* 27	P
Physical function	Grip strength, kg	24.7 (18.3, 27.9)	24.0 (19.9, 28.6)	0.949
	Walking speed, sec./m	1.00 (0.77, 1.00)	1.00 (0.90, 1.30)	0.350
	6 minutes walking test, m	348.5 (284.7, 400.0)	378.0 (314.0, 406.4)	0.438
	S <sub>p</sub> O <sub>2</sub> at rest, %	97 (97, 97)	97 (96, 98)	0.754
	Heart rate at rest, bmp	84 (72, 87)	84 (70, 92)	0.680
	S <sub>p</sub> O <sub>2</sub> after exertion, %	96 (93, 97)	96 (92, 97)	0.847
	Heart rate after exertion, bpm	92 (83, 107)	100 (86, 100)	0.343
	FVC, L	2.02 (1.69, 2.25)	2.15 (1.90, 2.80)	0.263
COPD function	FEV1, L	1.03 (0.79, 1.40)	1.15 (0.88, 1.68)	0.439
	FEV1 % (=FEV1/ FVC), %	53.6 (42.0, 65.5)	52.6 (45.6, 62.0)	0.838
	% FEV1, %	46.4 (31.5, 56.9)	45.2 (37.0, 64.8)	0.312
	IC, L/s	1.63 (1.06, 1.94)	1.78 (1.38, 2.07)	0.308
	HOT, n (%)	5 (25.0%)	2 (7.4%)	0.105
	NIPPV, n (%)	1 (5.0%)	2 (7.4%)	0.741
	GOLD stage (I/II/III/IV)	1/8/8/3	3/10/9/5	0.837
	CAT, score	20 (13, 28)	14 (7, 21)	0.021
	Borg scale at rest, points	0 (0, 0.5)	0 (0, 0.5)	0.743
	Borg scale after exertion, points	1 (0.5, 3)	1 (0.5, 4)	0.627
COPD questionnaires	FSSG (Acid reflux related symptom), points	2 (1, 5)	2 (1, 6)	0.760
	FSSG (dyspeptic or dysmotility symptom), point	2 (0, 5)	2 (1, 5)	0.957
	FSSG, total point	4 (2, 9)	4 (2, 10)	0.795
	HAD: Anxiety	4 (3, 8)	2 (1, 5)	0.103
	HAD: Depression	8 (5, 12)	4 (2, 8)	0.0112
	MRC, grade	2 (1, 2)	2 (1, 3)	0.435
	SRQ-D, points	11 (7, 16)	6 (4, 12)	0.159

\*Low: Daily Energy Intake (DEI) ≤ 30 kcal/kg of body weight, High: DEI > 30 kcal/kg of body weight

**Abbreviations:** BMI: Body Mass Index; CAT: COPD Assessment Test; DEI: Daily Energy Intake (kcal/kg of Body Weight/day); FEV1: Functional Expiratory Volume in 1 second; FEV1%: Percentage of FEV1/FVC; FSSG: Frequency Scale for the Symptoms of GERD; FVC: Functional Vital Capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; HAD: the Hospital Anxiety and Depression scale; HOT: Home Oxygen Therapy; IC: Inspiratory Capacity; MRC: Medical Research Council dyspnea scale; NIPPV: Non-invasive Positive Pressure Ventilation; SRQ-D: Self-Rating Questionnaire For Depression

Low group showed significantly higher scores in COPD assessment test (CAT) and the Hospital Anxiety and Depression scale (HAD-Depression). These results could be interpreted that CAT and HAD-Depression score might be indicators of daily energy intake in patients with COPD.

DEI patients. This may be due in part to the association of fluid depletion with lower energy intake, as both fluid and caloric intakes are decreased by dyspnea. If so, dehydration might mask protein malnutrition ordinarily detected by serum biochemistry, as we observed. Contrary to biochemical findings, symptoms evaluated by CAT and HAD, both developed for evaluating COPD symptoms were proven to be determinants of low DEI (Table 3). Because lower DEI was associated with significantly higher CAT and HAD depression scale scores, lower energy intake in COPD patients was linked with the symptom combination of dyspnea and depression. COPD patients have a tendency of decreased energetic intake, which is due in part to both dyspnea and depression. To our knowledge, this is the first to report to identify dyspnea questionnaires as a determinant of decreased energy intake, which would allow for COPD questionnaires to be utilized as a means of early PEM identification. To examine the potential of these parameters, further clinical studies with a larger number of subjects are required.

### Fat intake as a macronutrient to increase energy intake in COPD patients

Food and nutrient intake was also assessed in COPD subjects

using the. The BDHQ has been validated in healthy and clinical settings. The BDHQ results in the present study indicated that intake of fried meats and chicken was significantly increased in the higher DEI group (Table 4) [24,25]. Similarly, macronutrient analysis revealed that fat intake was significantly increased in the higher DEI group (Table 5). This suggests that the high energy density of fat makes increased fat intake a nutritional strategic option to meet increased energetic demands in COPD patients. Furthermore, these results suggested that eating fried meat and chicken may be optimal to avoid PEM and PEM-related adverse events. Although this result is to our knowledge reported for the first time in the present study, the study design and sample size suggest that larger prospective studies are necessary make conclusive nutritional recommendations for prevention of PEM in COPD patients.

### Study Limitations

Several limitations should be acknowledged for the present study. First, the number of subjects was too small to draw definitive conclusions. Second, the study was conducted under a cross-sectional retrospective design, and further evidence from large prospective

**Table 4:** Comparison of Foods between two groups categorized by daily energy intake (DEI): Low vs. High DEI group Low group had tendency to eat dried meats and chicken significantly smaller than them in high group.

Group	Number of subjects	Low DEI* 20	High DEI* 27	P
Foods: BDHQ-related	Sodium chloride equivalent, g/1000 kcal	6.3 (6.0, 7.2)	5.6 (5.0, 7.0)	0.067
Staple foods	Rice, g/1000 kcal	140.6 (108.9, 177.2)	127.4 (94.7, 152.6)	0.245
	Grilled meats, g/1000 kcal	1.9 (0.0, 8.3)	7.2 (3.5, 13.7)	0.093
	Braised meats, g/1000 kcal	13.6 (0.0, 18.4)	13.1 (1.3, 19.7)	0.957
	Fried meats, g/1000 kcal	5.7 (0.0, 10.7)	10.6 (4.2, 16.5)	0.040
Meats	Chicken, g/1000 kcal	4.2 (0.0, 5.9)	10.2 (5.2, 17.9)	0.013
	Pork and beef, g/1000 kcal	7.7 (5.0, 23.8)	16.7 (13.5, 21.5)	0.100
	Ham, g/1000 kcal	1.7 (0.0, 2.0)	2.5 (0.7, 9.0)	0.095
	Liver, g/1000 kcal	0.0 (0.0, 0.4)	0.0 (0.0, 1.6)	0.451
Fishes	Fatty fish, g/1000 kcal	6.2 (5.1, 13.1)	11.4 (5.5, 19.1)	0.366
	Low fat fish, g/1000 kcal	5.7 (0.0, 12.5)	6.4 (2.8, 14.1)	0.836
	Potato, g/1000 kcal	8.9 (0.0, 17.1)	23.4 (10.3, 43.3)	0.029
Fruits and Vegetables	Seaweed, g/1000 kcal	1.9 (0.0, 4.4)	5.8 (2.7, 11.2)	0.022
	Persimmon, g/1000 kcal	0.7 (0.0, 2.2)	3.8 (1.0, 5.4)	0.009
Soups	Noodle soup, g/1000 kcal	71.6 (37.9, 97.9)	32.9 (21.0, 48.0)	0.017
	Soy sauce, g/1000 kcal	1.2 (0.9, 1.3)	0.9 (0.6, 1.1)	0.006
Beverages and Drinks	Milk, g/1000 kcal	0.0 (0.0, 46.9)	46.3 (0.0, 84.5)	0.109
Seasonings	Cooking oil, g/1000 kcal	3.0 (1.3, 6.1)	4.9 (3.7, 5.8)	0.048
	Confectionery, g/1000 kcal	0.0 (0.0, 4.2)	15.0 (2.2, 23.1)	0.004
	Citrus, g/1000 kcal	5.9 (0.0, 11.4)	12.2 (1.4, 18.1)	0.207
Sweets	Persimmon, Strawberry, g/1000 kcal	0.0 (0.0, 6.3)	4.5 (1.4, 16.8)	0.034
	Mayonnaise, g/1000 kcal	1.0 (0.0, 2.2)	2.4 (0.3, 4.7)	0.328
	Udon noodle, g/1000 kcal	23.1 (9.5, 38.0)	9.6 (5.7, 16.4)	0.030

Data are expressed median (25<sup>th</sup>, 75<sup>th</sup> quartile)

\*Low: Daily Energy Intake (DEI)  $\leq$  30 kcal/kg of body weight, High: DEI  $>$ 30 kcal/kg of body weight abbreviations; BDHQ: Brief-type self-administered Diet History Questionnaire, DEI: Daily Energy Intake

**Table 5:** Comparison of Nutrients between two groups categorized by Daily Energy Intake (DEI): Low vs. High DEI group Low group showed tendency to take smaller amount of fat as macronutrient expressed in gram per 1,000 kilo-calorie, than higher group (p=0.031). On the other hand, they took larger amount of water significantly (p=0.039).

Number of subjects	Parameters	Low DEI* 20	High DEI* 27	P
nutrition	Energy, kcal/kg/day	21.3 (19.7, 25.9)	36.8 (33.3, 42.0)	0.000
	Energy, kcal/day	1173(1072, 1477)	1984 (1662, 2189)	0.000
	Water, g/1000 kcal	1195(1098, 1370)	1070 (922, 1201)	0.039
	Protein, g/1000 kcal	14.4 (12.2, 16.6)	15.0 (13.6, 16.7)	0.378
	Fat, g/1000 kcal	22.2 (18.7, 27.7)	28.0 (25.3, 29.7)	0.031
	Carbohydrate, g/1000 kcal	56 (51, 64)	55 (50, 58)	0.200
	Sodium, mg/1000 kcal	2438(2287, 2837)	2195 (1983, 2769)	0.156
	Potassium, mg/1000 kcal	1418(1043, 1610)	1406 (1127, 1603)	0.471
	Calcium, mg/1000 kcal	244 (194, 344)	287 (238, 358)	0.114
	Nutrients: BDHQ-related	Retinol, $\mu$ g/1000 kcal	203 (132, 368)	232 (167, 433)
$\beta$ -carotene equivalent, $\mu$ g/1000 kcal		1346 (718, 2144)	2202 (1090, 2675)	0.162
Retinol equivalent, $\mu$ g/1000 kcal		419 (210, 531)	392 (292, 694)	0.107
Vitamin D, $\mu$ g/1000 kcal		5.4 (3.5, 11.7)	7.1 (4.2, 11.4)	0.512
$\alpha$ -tocopherol, mg/1000 kcal		4.0 (3.1, 4.6)	4.0 (3.5, 4.9)	0.338
Vitamin K, $\mu$ g/1000 kcal		105 (53, 164)	137 (84, 160)	0.204
Saturated fatty acids, g/1000 kcal		5.7 (4.8, 7.4)	7.2 (6.6, 8.1)	0.058
Monounsaturated fatty acids, g/1000 kcal		7.7 (6.5, 9.3)	10.0 (8.7, 10.9)	0.011
Polyunsaturated fatty acids, g/1000 kcal		5.3 (4.0, 6.2)	6.2 (5.0, 6.4)	0.118

Data are expressed median (25<sup>th</sup>, 75<sup>th</sup> quartile)

\*Low: Daily Energy Intake (DEI)  $\leq$  30 kcal/kg of body weight, High: DEI  $>$ 30 kcal/kg of body weight abbreviations; BDHQ: Brief-type self-administered Diet History Questionnaire, DEI: Daily Energy Intake

studies is required. Third, although increasing fat intake may be a recommended nutritional strategy to COPD patients, too much fat intake for the purpose of increasing DEI might lead to adverse events such as atherosclerosis and related vascular events including myocardial infarction and cerebral infarction. To examine this possibility, prospective randomized clinical trials must be conducted. Fourth, a previous report showed that decreased food intake was associated with a higher risk of mortality in COPD patients. Contrastingly, the present study failed to identify a clear relationship between lower energy intake and clinical outcomes. This may be due in part to differential subject population. COPD patients in the prior study were hospitalized, while the COPD patients in the present study were receiving outpatient treatment, suggesting that COPD status may be poorer in the previous study. This difference in the severity of COPD may contribute to the lack of correlation in the present study. To confirm the association of lower energy intake with poor outcome, the subjects might be shifted from outpatient to hospitalized settings.

## Conclusion

Our study suggested that  $DEI \leq 30$  kcal/kg might identify COPD patients with severe dyspnea, as assessed by CAT. In addition, the results of the BDHQ food frequency questionnaire suggest that malnourished patients may have decreased fat intake as a percentage of total macronutrients. To increase DEI in COPD patients, increased fat intake, particularly from fried meats, may be an optimal nutritional strategy. However, the adverse effects of this nutritional strategy must be examined for long-term periods.

## Ethics Statement

This study was conducted according to the guidelines in the Declaration of Helsinki, and procedures were approved by the Ethics Committee of Kobe City Medical Center West Hospital.

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