The Effects of High-fat and High-carbohydrate Diet Loads on Gas Exchange and Ventilation in COPD Patients and Normal Subjects*

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Reducing the CO_2 production ($\dot{V}CO_2$) is a plausible means to lower the ventilatory demand in the treatment of patients with COPD. The purpose of this study was to examine the effects of high-fat and high-carbohydrate (high-CHO) diet loads on gas exchange and ventilation in the COPD patients and normal subjects. The percentage of changes in the averaged values of $\dot{V}CO_2$, O_2 consumption ($\dot{V}O_2$), respiratory quotient (RQ), minute ventilation ($\dot{V}E$), and end-tidal CO_2 ($ETCO_2$) measured by a mass spectrometer for 5 min every 30 min after the diet were compared between diets and between study subjects. Compared with the high-fat diet, the high-CHO diet can lead to significantly higher levels of $\dot{V}CO_2$, $\dot{V}O_2$, RQ, and $\dot{V}E$ in the COPD patients 30 to 60 min after the diet, and the differences can last for about 1.5 h. The comparison between COPD patients and normal control subjects also showed that the high-CHO diet load can result in significantly higher levels of $\dot{V}CO_2$, $\dot{V}O_2$, and $\dot{V}E$, and significantly lower level of $ETCO_2$ in the COPD patients, whereas the high-fat diet cannot. In addition, enhanced thermic effect of food within 150 min (TEF_{150}) occurred in the COPD patients as compared with that of normal controls, and the increase in TEF_{150} occurred only with the high-CHO diet. This study suggested that a high-fat diet is more beneficial to the COPD patient than a high-CHO diet, and that the gas exchange and energy utilization of the COPD patients following a high-CHO diet might be different from that of normal control subjects.

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AEE = actual energy expenditure; BEE = basic energy expenditure; CHO = carbohydrate; $ETCO_2$ = end-tidal CO_2 concentration; FVC = forced vital capacity; MVV = maximum voluntary ventilation; RMR = resting metabolic rate; RQ = respiratory quotient; TEF_{150} = thermic effect of food within 150 min; $\dot{V}CO_2$ = CO_2 production; $\dot{V}E$ = minute ventilation; $\dot{V}O_2$ = O_2 consumption

Postprandial changes in gas exchange depend on the relative proportions of carbohydrate (CHO), protein, and fat in one diet. A high-CHO load of total parenteral nutrition has been reported to cause a significant increase in CO_2 production ($\dot{V}CO_2$)[1,2] that precipitates respiratory distress in patients with pulmonary compromise.[3,4] Excessive CHO loading may precipitate respiratory acidosis in patients unable to adequately improve their alveolar ventilation when compensating for increased CO_2 production.[5] Also, it has been found that a single large liquid CHO load (920 kcal) impairs the exercise performance, such as the maximal incremental cycle performance, self-paced walking performance, and low-intensity endurance cycling in patients with chronic obstructive pulmonary disease (COPD).[6-8] The adverse effect of a single CHO load on the exercise performance of the COPD patients was attributed to the increased requirement for ventilation because of an increase in body CO_2 production.[6-8] Therefore, the high-CHO diet may not be suitable for the COPD patients.

As compared with CHO and protein, the fat has the highest caloric value.[9] Administration of a diet with an increased proportion of fat and a decreased proportion of CHO is expected to reduce the $\dot{V}CO_2$ and the ventilatory requirements. For instance, fat emulsion can serve as a source of nonprotein calories and is associated with lesser degrees of CO_2 production than isocaloric amount of glucose.[2] Angelillo and associates[10] have compared the effects of high-fat, moderate-fat, and low-fat diets on the metabolic and ventilatory values in patients with COPD and hypercapnia, and found that the high-fat diet can result in the lowest values of $\dot{V}CO_2$, RQ, and $PaCO_2$. Kane and colleagues[11] studied the effects of nighttime enteral feeding with high, medium, and low fat formula on $\dot{V}CO_2$ and $\dot{V}E$ in ten young adult patients with cystic fibrosis with moderate to advanced lung disease, and they found that the high-fat diet can result in the lowest $\dot{V}CO_2$, RQ, and $\dot{V}E$. In patients undergoing artificial ventilation, a high-fat, low-CHO enteral feed appeared to be beneficial in that it can lower the $PaCO_2$ and reduce the period of ventilation.[12] Hill[13] studied the response in 49 adult subjects after a 900-kcal high-fat diet (60 percent of calories from fat) and an isocaloric high-CHO diet (60 percent of calories from CHO), and found significantly higher RQ values occurring after the high-CHO diet as compared with the high-fat diet. The differences in postprandial RQ were due more to differences in $\dot{V}CO_2$ than to differences in $\dot{V}O_2$.[13] Thus, a high-fat diet can offer sufficient calories

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for energy utilization without a concomitant increase in $\dot{V}CO_2$ in the COPD patients.

For treating the COPD patients, it will be helpful to search for a possible diet that can reduce the $\dot{V}CO_2$, $\dot{V}O_2$, and $\dot{V}E$ of the patients. If a diet has these properties, it certainly will play an important role in the treatment of the COPD patients in addition to the conventional bronchodilator therapy. The first purpose of this study was to examine if the high-fat diet can reduce the $\dot{V}CO_2$ and $\dot{V}E$ in the Oriental COPD patients.

Patients with emphysema are frequently nutritionally depleted.[14] Marasmic type of protein calorie malnutrition is a common finding among COPD patients; the COPD patients who are immunoincompetent may be more susceptible to mixed protein calorie malnutrition of the kwashiorkor-marasmus type.[15] Body protein and fat stores were markedly depleted in almost half of the patients with COPD and acute respiratory failure.[16] Increased caloric utilization without adequate compensation in dietary intake might explain the weight loss seen in the COPD patients.[17] Specifically, the muscle concentrations of adenosine triphosphate and creatine phosphate in patients with COPD and acute respiratory failure have been shown to be low and to rise significantly as the patients respond to treatment. These findings suggest that dysfunction of the respiratory muscles may be an important component of respiratory failure and that adequate nutritional therapy is important in this disorder.[18]

Since the COPD patients have increased energy expenditure for increased airflow obstruction,[19] they are often in a state of relative starvation as compared with the normal subjects. Increased utilization of fat as fuel can be expected from the consideration of nutrient metabolism in starvation.[20] As a result, the response of the COPD patients to diet of different fat and CHO proportions may not be the same as that of normal subjects. The second purpose of this study, therefore, was to examine if the COPD patients and normal subjects have the same response to the high-fat and high-CHO diets.

Methods

Twelve clinically stable, ambulatory COPD patients and 12 healthy normal volunteers were included in this study. To avoid the inaccuracy in the measurements of $\dot{V}CO_2$ and $\dot{V}O_2$ by the mass spectrometer, patients who need extra oxygen to maintain adequate arterial oxygen tension were not included in this study. In addition, those patients who are too weak or dyspneic to perform maximum voluntary ventilation (MVV) were not included in this study. All the study subjects gave their informed consent prior to this study.

In order to minimize the effects of previous diets on gas exchange and ventilation, all patients were fasted overnight before the study. Both the high-CHO liquid diet (31.5 percent fat and 54.5 percent CHO) and the isocaloric high-fat diet (55.2 percent and 28.1 percent CHO) were given to the same subjects on separate days in a randomized fashion. The amount of calories in the diet was calculated by using the following formula: kilocalorie = 1.3·BEE/3, where the BEE is the basic energy expenditure calculated by using the Harris-Benedict equation.[9] The caloric content of the diet was designed to be 1.3 times the estimated BEE;[10] the amount of kilocalories is then divided by 3 because only one diet was given to the study subject in this study. The following examinations were performed on the patients before the diet, and 30, 60, 90, 120, and 150 min after the diet load.

Spirometry

For the evaluation of the severity of airflow obstruction, the forced expiratory volume in the first second (FEV_1), the forced vital capacity (FVC), FEV_1/FVC, and the MVV of the patients and normal subjects were examined by a spirometer (model 2450, Pulmonary Function Laboratory, Sensor Medics, California).

Mass Spectrometry

The $\dot{V}CO_2$, $\dot{V}O_2$, RQ, $\dot{V}E$, and end-tidal CO_2 ($ETCO_2$) were all measured by a mass spectrometer (Airspec 2000, Airspec Ltd, England) for 5 min. The averaged values of $\dot{V}CO_2$, $\dot{V}O_2$, RQ, $\dot{V}E$, and $ETCO_2$ during that 5 min were used for statistical analyses.

Indirect Calorimetry

The increase in energy expenditure for respiration is often reflected in the increase in $\dot{V}CO_2$ and $\dot{V}O_2$. From the $\dot{V}CO_2$ and $\dot{V}O_2$, the energy expenditure can be calculated by using indirect calorimetry.[21] The actual energy expenditure (AEE) was calculated by using the abbreviated Weir formula:[22,23] $AEE = 3.9\cdot\dot{V}O_2 + 1.1\cdot\dot{V}CO_2$, where AEE was expressed in calories per minute and $\dot{V}CO_2$ and $\dot{V}O_2$ were expressed in milliliters per minute (STPD). The thermal effect of the diet within 150 min after the diet (TEF150) was calculated as the increase in AEE following the diet divided by the energy content of the diet.[24] The increase in AEE following the diet was calculated as the area under the AEE curve (using trapezoid method) minus the projected resting metabolic rate (the AEE before the diet) over the 150-min period.

Statistical Analyses

To study the effects of high-fat and high-CHO diets on gas exchange and ventilation, the percentage of changes in $\dot{V}CO_2$ (percent $\dot{V}CO_2$), $\dot{V}O_2$ (percent $\dot{V}O_2$), RQ (percent RQ), $\dot{V}E$ (percent $\dot{V}E$), $ETCO_2$ (percent $ETCO_2$) and MVV (percent MVV) every 30 min after the diet were used for analyses

$$\text{percentage of change in } X_t = \text{percent } X_t = \frac{X_t - X_b}{X_b} 100 \text{ percent},$$

where X_t is the value of parameter X evaluated at time t and X_b is the value of parameter X evaluated before ingesting the diet. The percentage of changes in the parameters of gas exchange and ventilation were chosen for comparison so that the effects of diets on the parameters which are already different between groups before the diet can also be compared.

The percent $\dot{V}CO_2$, percent $\dot{V}O_2$, percent RQ, percent $\dot{V}E$, percent $ETCO_2$, and percent MVV every 30 min after the diet in either the COPD patients or normal subjects were compared between the high-fat and the high-CHO diets by using the Wilcoxon signed rank test. The above-mentioned parameters of gas exchange and ventilation every 30 min after ingesting either high-fat or high-CHO diet were also compared between the COPD patients and normal subjects by using the Kruskal-Wallis test.

Results

The general, spirometric, and arterial blood gas data of normal control subjects and the COPD patients, after overnight fasting and before the diet load, were

Table 1—*The General, Spirometric, and Arterial Blood Gas Data of Individual COPD Patients**

Age/Sex	Ht, cm	Wt, kg	FVC, L	FVC%, %	FEV_1, L	FEV_1%, %	FEV_1/FVC, %	PaO_2, mm Hg	$PaCO_2$, mm Hg	pH	HCO_3^-, mmol
78/M	156	54	1.64	61.0	0.97	53	59.1	70.4	39.8	7.439	26.8
76/M	165	62	1.76	55.5	0.94	42	53.4	78.7	32.4	7.513	26.1
53/M	162	62	2.68	78.5	1.45	56.5	54.1	78.2	35.2	7.542	30.4
62/M	161	64	2.40	73.5	1.41	58	58.8	74.1	32.6	7.474	23.9
76/M	158	53	1.40	49.0	0.53	27	37.9	60.9	39.7	7.454	27.7
70/M	165	64	3.35	99.0	1.76	71	52.5	68.9	37.2	7.492	28.5
71/M	171	72	3.17	88	2.03	79	64.0	89.3	35.7	7.425	23.2
60/M	152	43	2.98	104	1.77	81	59.4	90.3	34.2	7.393	20.6
43/M	178	50	3.54	75	1.94	50.5	54.8	64.5	32.1	7.386	19.0
68/M	152	44	2.31	96.5	1.39	74.5	60.2	83.6	37.0	7.418	23.6
74/M	160	60	2.90	96	1.82	85	62.8	89.0	39.0	7.453	27.2
44/F	163	54	2.70	84.5	1.65	61.5	61.1	78.4	34.8	7.378	20.2

*FVC% is the percent of predicted FVC; FEV_1% is the percent of predicted FEV_1.

tabulated in Tables 1 and 2 (means ± SD). There were no significant differences in age, sex, height, and body weight between normal control subjects and COPD patients. The spirometric data of FEV_1, FEV_1 percent (percent of predicted FEV_1), FVC, FVC percent (percent of predicted FVC), FEV_1/FVC, and MVV, and the fasting arterial blood gas data of pH, PaO_2, HCO_3^- and SaO_2 were all significantly different between normal controls and COPD patients. However, the values of fasting $PaCO_2$, $\dot{V}CO_2$, $\dot{V}O_2$, RQ, $\dot{V}E$, $ETCO_2$, and AEE were not significantly different between these two groups of subjects.

In normal subjects, the percent $\dot{V}CO_2$ and percent $\dot{V}O_2$ 1 h after the high-CHO diet were significantly higher than those after the high-fat diet (Fig 1, A and B). For the rest of the study course, these two parameters showed no significant difference between diets. The percent RQ was significantly different between these two diets 30, 60, and 150 min after the diet (Fig 1, C). However, the percent $\dot{V}E$ (Fig 1, D), percent $ETCO_2$ (Fig 1, E), and percent MVV (data not shown) were not significantly different between diets during the whole course of study.

In the COPD patients, the percent $\dot{V}CO_2$ and

Table 2—*Demographic Data of Normal Control Subjects and COPD Patients After Overnight Fasting and Before Diet Loading**

	Normal Controls (n = 12)	COPD Patients (n = 12)	p Value
General data			
Age, yr	60.0 ± 13.7	64.6 ± 12.3	NS
Sex, M/F	8/4	11/1	NS
Height, cm	159.8 ± 10.0	161.9 ± 7.5	NS
Weight, kg	62.0 ± 7.3	56.8 ± 8.6	NS
Spirometry			
FVC, L	3.27 ± 0.83	2.57 ± 0.69	<0.05
FVC%, % of pred	103.0 ± 10.8	80.0 ± 18.0	<0.01
FEV_1, L	2.62 ± 0.74	1.47 ± 0.46	<0.001
FEV_1%, % of pred	107.4 ± 10.1	61.6 ± 17.3	<0.0001
FEV_1/FVC, %	79.9 ± 6.7	56.5 ± 7.0	<0.0001
MVV, L/min	115.4 ± 30.8	51.2 ± 18.8	=0.0001
Arterial blood gases			
pH	7.398 ± 0.024	7.447 ± 0.051	<0.01
$PaCO_2$, mm Hg	34.7 ± 5.3	35.8 ± 2.8	NS
PaO_2, mm Hg	92.3 ± 8.0	77.2 ± 9.8	<0.01
HCO_3^-, mmol	21.2 ± 3.7	24.8 ± 3.6	<0.05
SaO_2, %	97.0 ± 0.7	95.5 ± 1.9	<0.05
Mass spectrometry			
$\dot{V}O_2$, ml/min	275.3 ± 55.5	267.5 ± 42.8	NS
$\dot{V}CO_2$, ml/min	238.1 ± 60.8	238.3 ± 44.2	NS
RQ	0.86 ± 0.12	0.91 ± 0.15	NS
$\dot{V}E$, L/min	9.9 ± 2.8	12.8 ± 4.6	NS
$ETCO_2$, %	4.86 ± 0.63	4.30 ± 0.78	NS
AEE, cal/min	1,335.8 ± 275.1	1,305.2 ± 197.6	NS

*Data are mean ± SD. Abbreviations explained in text. NS = not significant.

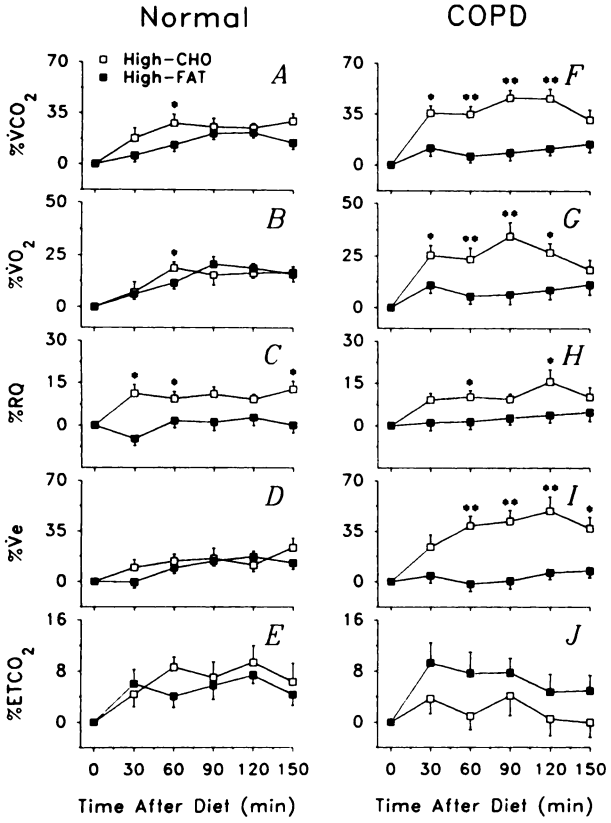

FIGURE 1. The effects of a single high-fat vs. high-CHO diet on gas exchange and ventilation in normal controls (mean ± SEM, N = 12, left panel) and COPD patients (mean ± SEM, N = 12, right panel). The $\dot{V}CO_2$, $\dot{V}O_2$, RQ, and $\dot{V}E$ of the COPD patients are significant increased 30 to 60 min after the high-CHO diet; the significant increases in $\dot{V}CO_2$, $\dot{V}O_2$, and $\dot{V}E$ can last for about 1.5 h. Note that the COPD patients have greater than normal differences in the responses of $\dot{V}CO_2$, $\dot{V}O_2$, and $\dot{V}E$ to the high-fat and high-CHO diets. The asterisk indicates $p<0.05$; and two asterisks indicate $p<0.001$. Percent X_t is percent X_t explained in the text.

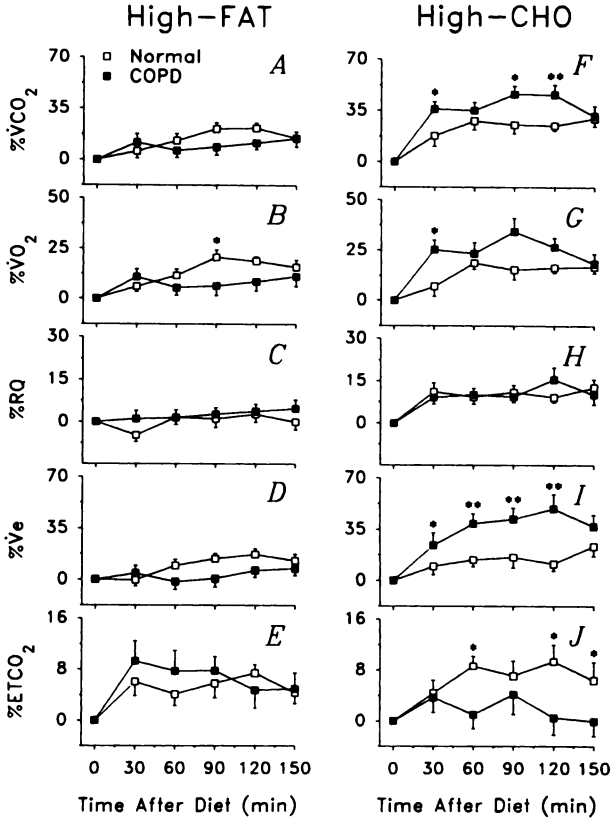

FIGURE 2. The effects of a single high-fat (left panel) and high-CHO (right panel) diets on gas exchange and ventilation in normal controls (mean ± SEM, N = 12) and COPD patients (mean ± SEM, N = 12). The high-CHO diet can result in significantly greater than normal increase in $\dot{V}CO_2$, $\dot{V}O_2$, and $\dot{V}E$ in the COPD patients, while the high-fat diet does not in general. Note that the $ETCO_2$ of normal subjects is significantly greater than those of the COPD patients 60, 120, and 150 min after the high-CHO diet. The asterisk indicates $p<0.05$; and two asterisks indicate $p<0.001$. Percent X_t is percent X_t explained in the text.

percent $\dot{V}O_2$ 30 min after the high-CHO diet were significantly higher than those after the high-fat diet (Fig 1, F and G). The significant differences in percent $\dot{V}CO_2$ and percent $\dot{V}O_2$ between diets can last for about 1.5 h (Fig 1, F and G). Similarly, the percent $\dot{V}E$ 60 min after the high-CHO diet was significantly higher than that after the high-fat diet, and the significant differences between diets can last for about 1.5 h (Fig 1, I). In addition, the percent RQ was significantly different between diets 60 and 120 min after the diet (Fig 1, H). No significant differences in percent $ETCO_2$ (Fig 1, J) and percent MVV (data not shown) between diets could be found throughout the whole course of study. Thus, compared with the high-fat diet, the high-CHO diet can lead to significantly higher levels of $\dot{V}CO_2$, $\dot{V}O_2$, RQ, and $\dot{V}E$, but not the $ETCO_2$ and MVV in the COPD patients.

Though the differences in percent $\dot{V}CO_2$, percent $\dot{V}O_2$, and percent $\dot{V}E$ between diets were not very significant in normal subjects in general, they were all significantly different in the COPD patients (Fig 1). Further comparison between the COPD patients and the normal subjects showed that the high-fat diet indeed had little effect on the parameters of gas exchange and ventilation (Fig 2, A to E). On the other hand, the high-CHO diet can result in significantly greater increases in percent $\dot{V}CO_2$, percent $\dot{V}O_2$, and percent $\dot{V}E$ in the COPD patients than in normal subjects (Fig 2, F, G, and I). The increase in percent $\dot{V}E$ after the high-CHO diet was notably more significant and consistent in the COPD patients (Fig 2, I). In contrast to the percent $\dot{V}CO_2$, percent $\dot{V}O_2$, and percent $\dot{V}E$, the percent $ETCO_2$ was significantly increased in normal subjects, not the COPD patients, 60 and 120 min after the high-CHO diet load (Fig 2, J). These results indicated that the responses of the COPD patients to the high-CHO diet are probably different from those of the normal subjects.

Table 3 shows that the TEF_{150} was not significantly different between the high-CHO and high-fat diets in normal subjects. In COPD patients, however, the TEF_{150} after ingesting the high-CHO diet was significantly enhanced as compared with the high-fat diet ($p<0.0001$). The comparison between normal controls

Table 3—*Thermogenic Effects of High-CHO and High-Fat Diets in Normal Control Subjects and COPD Patients**

	Normal Controls (n = 12)	COPD Patients (n = 12)	p Value
Caloric value, kcal	569.1 ± 81.9	527.3 ± 66.5	NS
High-CHO, %	5.22 ± 0.92	8.40 ± 1.17	<0.05
High-fat, %	4.40 ± 0.78	2.62 ± 1.17	NS
p value	NS	<0.0001	

*Data are mean ± SEM; NS = not significant.

and COPD patients shows that the high-CHO diet can elicit significantly elevated thermogenesis ($p<0.05$), whereas the high-fat diet cannot. Therefore, the TEF_{150} was increased in the COPD patients as compared with normal controls, and the increase in TEF_{150} occurred only with the high-CHO diet (Table 3).

Discussion

The metabolic turnover converts chemical energy in the nutrients, such as CHO, protein, and fat, to physiologically useful energy and eventually to heat. Oxygen is consumed, while carbon dioxide and water are produced in addition to energy. Since the work of breathing comes from the oxidation of these nutrients, the compositions of the diet can affect the energy metabolism. The RQ, which is the ratio of $\dot{V}CO_2$ to $\dot{V}O_2$, is an indicator of fuel utilization; it can be used to determine the efficacy of nutritional support regimens.[25] The value of RQ varies according to the type of nutrients used as the fuel. The RQ of the CHO is the highest, while that of the fat is the lowest. This means that the fat produces less CO_2 per O_2 consumed than either CHO or protein. Theoretically, the CHO is the least and the fat is the most suitable for those patients who cannot excrete their CO_2 adequately. The high-fat diet has been proved to be such in several studies.[10-13,19,26] In this study, the $\dot{V}CO_2$, $\dot{V}O_2$, RQ, $\dot{V}E$, and TEF_{150} are all significantly increased after a high-CHO diet, as compared with a high-fat diet, in the COPD patients. Our results supported the notion that the high-fat diet is more beneficial to the COPD patients than a high-CHO diet.

A diet that can lower the body $\dot{V}CO_2$ is expected to decrease $\dot{V}E$ and to enhance exercise performance. For instance, the study of Frankfort and associates[27] on the effects of high- and low-CHO diets on maximum exercise performance in chronic airflow obstruction has shown that diets with a higher fat and lower CHO content may be less likely to impair work performance of patients with chronic airflow obstruction in the absorptive phase than diets with a lower fat and higher CHO content. A study by Goldstein and associates[28] has also shown that ingestion of high-fat diet for 2 weeks can improve muscle function and endurance in the quadriceps and hamstring muscles as compared with ingestion for 1 week only, suggesting that the metabolic response to diet was related to diet content and feeding duration. Thus, the high-fat diet can lead to a greater exercise tolerance and can be more beneficial to COPD patients than a high-CHO one in terms of the work of breathing and exercise performance.

After ingesting the high-CHO diet, the significant increase in $ETCO_2$ without concomitant increase in $\dot{V}E$ in normal subjects as compared with the COPD patients (Fig 2, I and J) suggested that normal subjects can respond to increased CO_2 production (Fig 2, F) by increasing their $ETCO_2$ such that the $PaCO_2$ does not change. On the other hand, the COPD patients who cannot increase their $ETCO_2$ (Fig 2, J) can respond to increased CO_2 production (Fig 2, F) by increasing their $\dot{V}E$ (Fig 2, I). Though the patients were only mildly obstructed and the resting mean $\dot{V}E$ was 12.8 (± 4.6, SD) L/min (Tables 1 and 2) in this study, the increase in $\dot{V}E$ following the high-CHO diet was very significant. It, then, can be expected that for those moderately to severely obstructed patients, the high-CHO diet may become intolerable because the patients might not be able to increase their $\dot{V}E$ even further. Thus, for those patients who can no longer increase their $\dot{V}E$ to excrete CO_2, the ingestion of high-CHO diet can be expected to impair their pulmonary performance greatly and even lead to respiratory distress or failure.[3-7] For patients who have limited capability to increase their $\dot{V}E$ further to excrete the CO_2, reducing the $\dot{V}CO_2$, $\dot{V}O_2$, and $\dot{V}E$ by using the high-fat diet is a therapy worth trying.

The high-fat diet, however, does have side effects. The most prominent negative aspects of the high-fat diet observed in this study were the gastrointestinal discomfort following the diet, such as belching, abdominal discomfort, and diarrhea. The causes of gastrointestinal discomforts probably are the high-osmolality, high-fat, and/or high-milk content of the diet. Other side effects of the high-fat diet were dizziness, chest tightness, etc. Though these effects were mild, they might discourage the patients from trying the high-fat diet any more. The diarrhea, when severe, will exacerbate the malnutrition and labored breathing of the patients. Dilution of the high-fat diet before ingestion may be helpful, but this procedure does not always succeed. The high-fat diet is not recommended for such patients.

In several studies, as high as 900 to 920 kcal of liquid CHO load was needed to elicit significant differences between high-CHO and high-fat diets in normal subjects[13] and patients with chronic airflow obstruction.[6-8,26] It, therefore, is not surprising that 569.1 kcal (± 81.9, SD) cannot induce significant difference between high-CHO and high-fat diets in

normal subjects in the present study. However, a 527.3 kcal (±66.5, SD) high-CHO diet was sufficient to result in significantly higher values of $\dot{V}O_2$, $\dot{V}CO_2$, RQ, and $\dot{V}E$ than the isocaloric high-fat diet in the COPD patients. The seemingly more sensitive response in this study in terms of the amount of kilocalories consumed may be due to the differences in the study subjects chosen, the difference in the body frame between Western and Oriental people, and the parameters used for comparison. Since the COPD patients can respond to the high-CHO diet to a higher degree than the normal subjects, it is reasonable that less than 900 kcal of nutrient was already sufficient to cause significant difference between diets in the response of gas exchange and ventilation in the COPD patients while the difference between diets in normal subjects was not significant. The difference in the body frame may also contribute to the more sensitive response in this study because the body frame of the Oriental people is usually smaller than that of the Western people. Finally, the variables used for comparison may also contribute to the difference in sensitivity. In the present study, we used the percentage of changes in the parameters of gas exchange and ventilation for comparison, whereas in the above-mentioned studies, the absolute values of parameters of gas exchange and ventilation were used for comparison. We have compared the sensitivity of the percentage of changes in the parameters of gas exchange and ventilation and the absolute values of these parameters in the detection of significant effects of these two diets using our own data, and we found that the percentage of changes in the above were more sensitive. Another advantage of using the percentage of changes in the parameters of gas exchange and ventilation is that even though the baseline values of one study subject deviated from the values they should be, the values of subsequent measurements after the diet will also deviate from the values they should be to the same degree:

$$\frac{f \cdot X_t - f \cdot X_b}{f \cdot X_b} \cdot 100 \text{ percent} = \frac{X_t - X_b}{X_b} \cdot 100 \text{ percent} = \text{percent } X_t,$$

where f is an error factor. Thus, the use of percentage of changes in the parameters of gas exchange and ventilation can avoid the side effects of instability in the measurements of these parameters and contribute to the sensitivity of the measurements.

The effects of the test diets appeared 30 to 60 min after the diet and lasted for about 180 min in this study, whereas the significant effects were noted in COPD patients between 84 and 204 min in the study of Frankfort and associates.[26] Some possible factors contributing to this discrepancy probably are the variables used for comparison, the amount of diet ingested, the degree of airflow obstruction, the race, the body size, etc. The sensitivity of using the percentage of changes in the parameters of gas exchanges and ventilation for comparison has been discussed in the preceding paragraph. This may be one of the reasons why the effects of the test diets appeared 30 to 60 min after the diet in this study, whereas the significant effects were noted 84 min after the ingestion of the diets in the study of Frankfort and associates.[26] In this study, an average of only 527.3 kcal of test diets was used in the COPD group, whereas test diets of 920 kcal were used in the study of Frankfort and associates.[26] This may explain why the effects of the diets became insignificant 180 min after the ingestion in our study, while the effects of the diets can be significant until 204 min after the ingestion of the diets in the study of Frankfort and associates.[26] The differences in the degree of airflow obstruction, the race, and the body size may also contribute to the observed discrepancy.

The thermogenic effect of a diet (TEF) usually amounts to approximately 10 percent of the caloric value of the ingested food,[29] and it is higher for CHO and protein than for fats. In general, the TEF_{150} in this study was less than 10 percent: 5.22 ± 0.92 percent (mean ± SEM) after high-CHO diet and 4.40 ± 0.78 percent after high-fat diet for normal controls, and 8.40 ± 1.17 percent after high-CHO diet and 2.62 ± 1.17 percent after high-fat diet for COPD patients. The decrease in thermogenesis in this study might be caused mainly by the shorter duration of observation; the observation period in this study was 150 min, while the observation period of Hill et al[24] was 6 h. Despite the difference in the observation period, the results of 150 min of observation should parallel those of 6 h of observation because the comparisons were made on the same basis.

An enhanced thermic response to nutrients has been observed in malnourished patients with COPD as compared with malnourished patients without COPD in the study of Goldstein and associates.[19] The thermic effect of nutrients during administration of either high-fat or high-CHO diet was significantly greater in patients with COPD than in those without COPD; and the difference between these two groups was enhanced during the high-CHO regimen.[19] Similar to the findings of Goldstein and associates,[19] we found that the increases in $\dot{V}CO_2$, $\dot{V}O_2$, RQ, $\dot{V}E$, and thermogenesis after a high-CHO diet in COPD patients were significantly greater than those of normal controls; the high-CHO diet was responsible for these greater increases in the COPD patients. The greater than normal responses to high-CHO diet in the COPD patients may be attributable to their nutritional reserves and pulmonary function. As is well known, COPD patients are often malnourished and are in a state of relative starvation as compared with the normal subjects. Increased energy expenditure for increased airflow obstruction in the COPD patients can account

for malnutrition in such patients. This increase in energy expenditure and the decrease in nutritional reserve in COPD patients may contribute to their intolerance to increased $\dot{V}CO_2$ and $\dot{V}E$ caused by the high-CHO diet. Therefore, the metabolism of the COPD patients after the high-CHO diet may not be the same as that of normal subjects in terms of the energy expenditure, substrate oxidation, etc. Measurements of both body composition and energy expenditure in normal control subjects and COPD patients may be helpful in the investigation of possible cause of the difference in their response to high-CHO diet so that energy expenditure could be evaluated with respect to fat-free mass.

An elevated $\dot{V}D/\dot{V}T$ in the COPD patients might be another possible cause of greater than normal response to the high-CHO diet. However, this possibility may not be dominant in this study because of the following reasons. (1) The $\dot{V}D/\dot{V}T$ is given by $\dot{V}D/\dot{V}T = (PaCO_2 - PeCO_2)/PaCO_2$, where $PeCO_2$ is the partial pressure of CO_2 in the exhaled sample. Since the fasting $ETCO_2$ was not significantly different between normal control subjects and COPD patients, it is reasonable to expect that the $PeCO_2$ was also not significantly different between groups in this study. Thus, the $\dot{V}D/\dot{V}T$ of our patients was at most only slightly higher than that of normal control subjects because the fasting $PaCO_2$ was also not significantly different between normal control subjects and COPD patients. The slight but significant difference in the fasting $\dot{V}E$ between normal controls and COPD patients in this study (Table 2) supported this conjecture. It, then, is doubtful that such slight increase in $\dot{V}D/\dot{V}T$ can elicit that much response to the high-CHO diet in our COPD patients. (2) Since the value of the anatomic dead space was unaffected by the diets, the $\dot{V}D/\dot{V}T$ that did not raise the fasting $\dot{V}E$ above normal to a significant degree might not be an important factor in elevating the postprandial $\dot{V}E$ to a significant degree. (3) If the elevated $\dot{V}D/\dot{V}T$ is responsible for the larger than normal increase in $\dot{V}E$ after high-CHO diet in COPD patients, it should also cause a greater than normal increase in $\dot{V}E$ after the high-fat diet in the same patients because the anatomic dead space is a fixed value for the individual patient that will not change with respect to the type of diet. (4) The TEF_{150} of the high-CHO diet has been shown to be higher than normal in COPD patients in this study. The elevated TEF_{150} after the high-CHO diet may not readily be accounted for by the slightly elevated $\dot{V}D/\dot{V}T$ in our COPD patients. Therefore, it remains to be verified that an at most slightly elevated $\dot{V}D/\dot{V}T$ would be responsible for the observed significant increase in $\dot{V}CO_2$, $\dot{V}O_2$, $\dot{V}E$, and TEF_{150} after the high-CHO diets in the COPD patients.

It seems surprising that 3 of our 12 COPD patients gave slightly negative TEF_{150} after the high-fat diet. Since the TEF_{150} is calculated from $\dot{V}O_2$ and $\dot{V}CO_2$ by subtracting the fasting resting metabolic rate (RMR) from the total energy expenditure following the diet, a negative TEF_{150} does not mean that the diet absorbs energy from the patient; rather, it means that the patient consumes less O_2 and/or produces less CO_2 after the diet. The mechanism underlying a negative TEF_{150} is not exactly clear, but the bronchodilators and the high-fat diet itself might be part of the reason. The relief of the airway obstruction by the bronchodilators that were already taken by the patients in the early morning may reduce to some extent their work of breathing after the diet. The high-fat diet is already known and proved in this study and other studies to be such a diet that can reduce the $\dot{V}CO_2$, $\dot{V}O_2$, and $\dot{V}E$, and consequently, the work of breathing. When the work of breathing is reduced by bronchodilators and the high-fat diet, the $\dot{V}O_2$ and $\dot{V}CO_2$ can be reduced to such an extent as to giving rise to a negative TEF_{150}. Thus, it may not be so surprising that some of our COPD patients had slightly negative TEF_{150}.

The greater than normal responses of gas exchange and ventilation to the high-CHO diet in the COPD patients suggested that the study of the effects of diet with different composition on gas exchange and ventilation in normal subjects may not readily be extrapolated to the COPD patients. The conclusion of Sue et al.[30] that altering the proportion of dietary carbohydrate and fat is unlikely to reduce greatly exertional dyspnea in patients with lung disease, therefore, should be adopted cautiously because their study was conducted in normal subjects. We did not perform any measurements of patient dyspnea in this study; still, it is necessary to caution that extrapolation of the findings obtained from normal subjects to COPD patients because the symptom of dyspnea might be related to gas exchange, ventilation, and energy metabolism.

This study suggested that a high-fat diet is more beneficial to the COPD patients than a high-CHO one, and that the gas exchange and energy utilization of the COPD patients following a high-CHO diet might be different from that of normal control subjects.

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REFERENCES

1 Askanazi J, Rosenbaum SH, Hyman AI, Silverberg PA, Milic-Emili J, Kinney JM. Respiratory changes induced by large glucose loads of total parenteral nutrition. JAMA 1980; 243:1444-47

2 Askanazi J, Nordenstrom J, Rosenbaum SH, Elwyn DH, Hyman AI, Carpentier YA, et al. Nutrition for the patients with respiratory failure: glucose vs fat. Anesthesiology 1981; 54:373-77

3 Garfinkle F, Robinson S, Price C. Nutrition case management: carbohydrate feeding and ventilatory insufficiency. Clin Nutr Newsletter 1983, June; 3-4
4 Askanazi J, Elwyn DH, Silverberg PA, Rosenbaum SH, Kinney JM. Respiratory distress secondary to a high carbohydrate load: a case report. Surgery 1980; 87:596-98
5 Covelli HD, Black JW, Olsen MS, Beekman JF. Respiratory failure precipitated by high carbohydrate loads. Ann Intern Med 1981; 95:579-81
6 Brown SE, Nagendran RC, McHugh JW, Stansbury DW, Fischer CE, Light RW. Effects of a large carbohydrate load on walking performance in chronic air-flow obstruction. Am Rev Respir Dis 1985; 132:960-62
7 Brown SE, Wiener S, Brown RA, Marcarelli PA, Light RW. Exercise performance following a carbohydrate load in chronic airflow obstruction. J Appl Physiol 1985; 58:1340-46
8 Brown SE. Effects of a single-carbohydrate load or a lipid-enriched load on exercise performance in ambulatory COPD patients. In: The role of nutrition in pulmonary disease, report of the third Ross/Abbott International Conference on Medical Research. Abbott Park, Ill: Abbott Laboratory, 1990; 55-59
9 Alpers DH, Clouse RE, Stenson WF. Protein and calorie requirements. In: Manual of nutritional therapeutics. 2nd ed. Boston: Little, Brown and Co, 1988, chap 3
10 Angelillo VA, Bedi S, Durfee D, Dahl J, Patterson AJ, O'Donohue WJ. Effects of low and high carbohydrate feedings in ambulatory patients with chronic obstructive pulmonary disease and chronic hypercapnia. Ann Intern Med 1985; 103:883-85
11 Kane RE, Hobbs PJ, Black PG. Comparison of low, medium and high carbohydrate formulas for nighttime enteral feedings in cystic fibrosis patients. J Paren Ent Nutr 1990; 14:47-52
12 Al-Saady NM, Blackmore CM, Bennett ED. High fat, low carbohydrate, enteral feeding lowers $PaCO_2$ and reduces the period of ventilation in artificially ventilated patients. Intensive Care Med 1989; 15:290-95
13 Hill JO. Physiologic response to enteral nutrition. In: The role of nutrition in pulmonary disease, report of the third Ross/Abbott International Conference on Medical Research. Abbott Park, Ill: Abbott Laboratory, 1990; 33-41
14 Openbrier DR, Irwin MM, Rogers RM, Gottlieb GP, Dauber JH, Thiel DH, et al. Nutritional status and lung function in patients with emphysema and chronic bronchitis. Chest 1983; 83:17-22
15 Hunter AMB, Carey MA, Larsh HW. The nutritional status of patients with chronic obstructive pulmonary disease. Am Rev Respir Dis 1981; 124:376-81
16 Driver AG, McAlevy MT, Smith JL. Nutritional assessment of patients with chronic obstructive pulmonary disease and acute respiratory failure. Chest 1982; 82:568-71
17 Braun SR, Keim NL, Dixon RM, Clagnaz P, Anderegg A, Shrago ES. The prevalence and determinants of nutritional changes in chronic obstructive pulmonary disease. Chest 1984; 86:558-63
18 Gertz I, Hedenstierna G, Hellers G, Wahren J. Muscle metabolism in patients with chronic obstructive lung disease and acute respiratory failure. Clin Sci Mol Med 1977; 52:395-403
19 Goldstein S, Askanazi J, Weissman C, Thomashow B, Kinney JM. Energy expenditure in patients with chronic obstructive pulmonary disease. Chest 1987; 91:222-24
20 Walvatne C, Cerra FB. Hepatic dysfunction in multiple organ failure. In: Deitch EA, ed. Multiple organ failure. New York: Thieme Medical Publishers Inc, 1990
21 Ferrannini E. The theoretical bases of indirect calorimetry: a review. Metabolism 1988; 37:287-301
22 De Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949; 109: 1-9
23 Van Lanshot JJB. Methodological aspects of metabolic gas exchange measurement. In: The role of nutrition in pulmonary disease, report of the third Ross/Abbott International Conference on Medical Research. Abbott Park, Ill: Abbott Laboratory, 1990; 18-21
24 Hill JO, Peters JC, Yang D, Sharp T, Kaler M, Abumrad NN, et al. Thermogenesis in humans during overfeeding with medium-chain triglycerides. Metabolism 1989; 38:641-48
25 Ireton-Joness CS, Truner WW Jr. The use of respiratory quotient to determine the efficacy of nutrition support regimens. J Am Diet Assoc 1987; 87:180-83
26 Frankfort JD, Stansbury DW, Fischer CE, McArthur DL, Light RW, Brown SE. The effects of mixed substrate liquid supplement on metabolic mesurements at rest in patients with chronic airflow obstruction (CAO) [abstract]. Chest 1987; 92:128S
27 Frankfort JD, Fischer CE, Stansbury DW, McArthur DL, Brown SE, Light RW. Effects of high- and low-carbohydrate diets on maximum exercise performance in chronic airflow obstruction. Chest 1991; 100:792-95
28 Goldstein SA, Thomashow B, Askanazi J. Functional changes during nutritional repletion in patients with lung disease. Clin Chest Med 1986; 7:141-51
29 Jequier E. Energy expenditure in obesity. Clin Endocrinol Metab 1984; 13:563-80
30 Sue DY, Chung MM, Grosvenor M, Wasserman K. Effect of altering the proportion of dietary fat and carbohydrate on exercise gas exchange in normal subjects. Am Rev Respir Dis 1988; 139:1430-34