COPD 201: It is not as easy as pie
PCCP Interhospital Conference
Veterans Memorial Medical Center
Basilio Valdez Hall
June 11, 2013

Last June 11, 2013, Veterans Memorial Medical Center (VMMC) hosted the Philippine College of Chest Physicians Interhospital Conference titled COPD 201: It is not as easy as pie. After the invocation, national anthem and PCCP hymn, the case presentation started.

The objectives of the said conference are to present a case of COPD stage D, to discuss the association of malnutrition and COPD, to discuss the pathophysiology and consequences of malnutrition and to present nutritional recommendations for COPD.

The take off point of the conference was the case of M. G., an 85- year old female, Roman Catholic from Bulacan, who was admitted at our institution for the 10^{th} time, this time due to difficulty of breathing. She was a diagnosed case of COPD stage D since 2011, currently on tiotropium 18mcg/cap via handihaler OD, budesonide + formoterol 160/4.5mcg 2 puffs BID, doxophylline 200mg/tab OD and ipratropium + salbutamol MDI used on as needed basis. She has completed Pulmonary Rehabilitation for 8 weeks in 2008. Back then the patient weighed 47 kg. She was admitted a month ago due to community- acquired pneumonia (CAP). Prior to confinement, she can do simple upper and lower extremity exercises at home.

3 weeks prior to admission (PTA), however, she experienced breathlessness even with activities of daily living, which was relieved by rescue medications in the form of ipratropium + salbutamol MDI. There was no other associated symptom, such as cough noted then. A week PTA, she had cough that was productive of whitish sputum. She denies having chest pain or fever. No additional medication was taken. 3 days PTA, her breathlessness started to become bothersome that she decided have oxygen supplementation via face mask at 10 liters per minute (lmp). A few hours PTA, her breathlessness was no longer relieved by oxygenation, prompting emergency room consultation. She was subsequently admitted.

Past medical history revealed that she completed PTB category 1 treatment at VMMC TB DOTS in 2010 and that she is a chronic hypertensive with controlled BP, maintained on amlodipine 5 mg OD. Family history revealed that her mother is a hypertensive and her father is an asthmatic.

On physical examination, patient is awake, coherent, cachectic and in cardiorespiratory distress, with the following vital signs: BP: 110/70, HR: 110bpm, RR: 24cpm, afebrile at 36.5C and O_2 saturation of 94% at room air. She is weighs 40 kg and stands 152cm, yielding to a BMI of 17.39 kg/m^2. Head, eyes, ears, neck and throat examinations were normal. Lung examination shows a symmetrical chest expansion, with supraclavicular retractions, decreased tactile fremitus and tight air entry on all lung fields. Cardiovascular examination reveals tachycardia with no other pertinent findings. The rest of the physical examination findings were normal.

The salient features of our patient are: an elderly patient, known case of COPD type D, presenting with acute episode of worsening breathlessness and cough, recently unrelieved with her maintenance medications and O2 support. Furthermore, physical examination showed reveled a cachectic patient with stable blood pressure, has tachycardia, tachypnea, with tight air entry, with no wheeze, no crackle, and no edema noted. With these salient features, admitted diagnoses are: acute exacerbation of COPD, hospital care- associated pneumonia (HCAP), and malnutrition.

Arterial blood gas revealed a partially compensated respiratory acidosis with no hypoxemia; desired fio2 was at 36 %. Her CBC showed no anemia and leukocytosis of 10.6 with neutrophilic predominance. Her chemistry results were non contributory. Plain chest radiograph taken at PA view revealed hyperaerated lungs, flattened hemidiaphragms and a note of hazy bibasal densities. These findings are consistent with COPD and pneumonia. Bacteriology showed gram negative organisms isolated as *Klebsiella pneumonia* in moderate growth while blood culture was negative for organism.

On the 1st HD, the patient has dyspnea and cough. On PE, she is tachycardic and tacyhpneic with O_2 saturation of 94% at room air. Furthermore, she has supraclavicular retractions and has tight air entry on auscultation. With her present diagnosis of acute exacerbation of COPD and HCAP, she was managed at the intensive care unit (ICU) for critical care monitoring. She was started on standard regimen consisting of IV steroids, SAMA and SABA nebulizations, xanthine derivative and IV antibiotics as recommended by PSMID pneumonia guidelines. On the 3rd HD, she has less complaint of dyspnea and cough. Her vital signs are more stable with improvement in O_2 saturation but with persistence of tight air entry. With clinical signs of improvement, the same standing medications were continued. On the 5th HD, further clinical improvement was seen. She has stable vital sings with only occasional wheezing. Thus, IV steroids, nebulizations and antibiotics were shifted accordingly. On the 7th HD, the patient was now asymptomatic with clear breath sound. She was no longer in acute exacerbation of COPD, thus transferred to the ward. IV steroids and nebulizations were discontinued. Meanwhile oral antibiotics were continued to complete 14 days. Inhaled ICS with LABA and LAMA were then started. The patient was discharged improved on the 10th hospital day.

The case presented was a typical, guideline directed management of COPD and exacerbation. While the primary problem of COPD was addressed, it is, however, undeniable that nutrition is often the least prioritized medical condition associated with COPD. In managing patients with COPD, we adjust the dose of medications based on individual needs. But COPD is a progressive and debilitating disease and in a lot of perspectives, dealing with COPD is not easy as pie.

COPD is a debilitating multicomponent respiratory condition. Its pathogenesis and clinical manifestations are not confined solely to the pulmonary inflammation and structural remodelling, but also extend to and encompass a variety of systemic alterations. These extrapulmonary effects include systemic inflammation, nutritional abnormalities and weight loss, skeletal muscle dysfunction and additional organ defects.

COPD is an important cause of morbidity, hospitalization and mortality worldwide. Its burden is evident from mortality figures and disability-adjusted years (DALYS). It is the 6th leading cause of death

in 1990 and ranked fourth in 2008. By 2020, it is projected to rank third. It is the only leading cause of death with increasing prevalence. It is estimated to be 6.2 % in 11 Asian countries surveyed by the Asian Pacific Society of Respiratory Diseases.

The clinical course of COPD starts from airflow obstruction leading to air trapping and hyperinflation. These, in turn, leads to breathlessness, activity limitation, and poor health related quality of life (HRQL). Dyspnea may then cause anxiety and distress, which increases tachypnea, thereby causing air trapping. Activity limitation leads to deconditioning that increases ventilatory requirement and can lead to further air trapping.

Exacerbations contribute to the development of airflow obstruction and the progression of the disease. There exists an interrelationship among COPD, systemic consequences, and co-morbidities give possible contributions. It has been recognized that co-morbidities in patients with COPD have a significant impact on disease severity and survival.

In GOLD 2011, updated in 2013, more common co- morbidities were enumerated together with specific recommendations as to their management alongside COPD. According to GOLD 2013, the co-morbidities which are greatly associated with COPD and were often always addressed include cardiovascular disease, osteoporosis, anxiety and depression, lung cancer, infections, and metabolic syndrome and diabetes.

In a more recent study by Vanfleteren et al published in the Blue Journal last April 2013, a reported prevalence of 14 % for underweight was observed apart from the other commonly identified comorbidities. In addition, last 2012, a study done here at VMMC by Dr. Clint Ivan Fernandez and Dr. Arnold Germar titled Association of Malnutrition with COPD Severity at Veterans Memorial Medical Center Out Patient Department looked into the association of Malnutrition and COPD Severity. There were 203 patients stratified into mild, moderate, severe and very severe COPD. The BMI was calculated; mid- arm and calf circumference were also measured. Nutritional status was assessed using the Nestle's Mini Nutritional Assessment Questionnaire which looked into the 3 domains of nutritional status namely, normal, at risk, and malnourished. All subjects had a score of less than 11 which necessitated the assessment of the malnutrition indicator. Thirty seven percent were at risk for malnutrition and 40% of the subjects were malnourished. Among those with normal nutritional status, they had mild and moderate COPD. Among those who were at risk of malnutrition, only one had mild COPD, the rest were diagnosed to have moderate, severe, and very severe COPD. All malnourished patients had either severe or very severe COPD.

Malnutrition is the condition that results from eating a diet in which certain nutrients are lacking, in excess or in wrong proportions. According to World Health Organization, it is the single greatest threat to the world's public health. Malnutrition and being underweight are more common in the elderly than in adults and other ages. If elderly people are healthy and active, the aging process alone does not cause malnutrition. The changes in body composition, organ functions, adequate energy intake and ability to eat or access food are associated with aging. It can also lead to Sarcopenia with loss of lean body mass and muscle function. It has a rather negative impact on the clinical outcome of

patients with COPD, since nutrition and ventilation are closely related. Oxygen and nutrients are necessary in the process of breathing and supplying energy for the daily activities. Reduced body weight is common in individuals with COPD, affecting 10-15% of patients with mild-to-moderate disease and 50% of patients with advanced-disease.

The patholophysiological basis of weight loss is not very well understood, although a high metabolic rate that is not compensated for by a corresponding increase in caloric intake is thought to play an important role. A significant number of patients with COPD present involuntary weight loss during the disease. The numbers range between 20-30% in stable patients and can reach to 50% in hospitalized patient with respiratory failure.

The evidence of a relationship between body weight and COPD first emerged from a study investigating metabolic imbalances in severe bronchial obstruction. In a large population study, body weight was found to be directly related to severity of lung function determined by FEV1. It also provided additional information on the role of body weight on survival – mortality was found to increase as patient's body weight decreased, regardless of lung function impairment. Low body weight appears to be an independent marker of poor disease outcome.

The pathogenesis of COPD evolves with the increased energy expenditure, increased oxygen consumption or oxygen cost of breathing by respiratory muscles that results from the increased workload required to overcome airway obstruction, the hallmark of COPD. Raising basal metabolic rate include medications commonly used in treatment of COPD such as the beta- agonists and phosphodiesterase inhibitor. Elevated catecholamines also raise the metabolic rate. Inflammatory mediators such as tumor necrosis factor alpha, C reactive protein and leptin play a role in decreasing energy intake or delivery. Finally, the increase thermic effect of patient's activity has also been reported to contribute to the increased metabolism observed in COPD patients.

The causes of malnutrition in COPD include elevation of the resting energy expenditure brought about by labored breathing. It is also caused by a systemic inflammation or elevated leptin level despite the low fat mass.

Regarding diet, according to Elaine Chang et al, there is low dietary intake which is caused by: chronic mouth breathing which alters the attractiveness of food and gastric distention from aerophagia. Patient's dyspnea causes problem while eating or preparing food. Eating and swallowing worsen dyspnea and arterial oxygen desaturation especially during bouts of evolution of the disease, and simply because of old age.

Medications commonly prescribed for COPD, namely bronchodilators, corticosteroids and antibiotics, indirectly affect the nutritional status of COPD patients in their long- term use. Corticosteroids may lead to peripheral myopathy and catabolism. Antibiotics cause gastrointestinal disturbance and may disrupt normal bowel flora leading to vitamin K deficiency. Bronchodilators cause malabsorption. It is, therefore, not surprising that severe COPD patients, who correspondingly are on more medications, are also malnourished.

From a clinical viewpoint, the altered nutritional status associated with the progressive impairment of respiratory function in COPD poses a serious problem. Its impact on the natural course of COPD is of paramount importance. A graph was presented to show a strong correlation between 6-min walking distance and quantity metabolically active lean body cellular mass. A compromised nutritional state limits exercise performance in patients with COPD by reducing the aerobic capacity of exercising muscles. The impact of low body weight on patients with COPD was found to correlate with morbidity in relation to exacerbations, supporting the claim that malnutrition is associated with poor outcome following acute exacerbation in patients with respiratory failure.

Patients with COPD are known to be generally underweight and have reduced FFM. This was observed in a study by Sergi et al that showing that COPD patients had a lower FFM as compared to healthy subjects (38% *versus* 31%). Undernutrition led to lung and chest wall mechanical changes, such as distorted structure of diaphragm and intercostals, reduction of surfactant, and decrease in elastic fiber content of pulmonary parenchyma. Massaro et al described loss of pulmonary alveoli in calorie restriction and regenerated after *ad libitum* refeeding. The diaphragm as a main inspiratory muscle suffered from muscle protein degradation and loss of contractile protein.

Furthermore, COPD patients who lose weight have more dyspnea, a higher degree of air trapping, and a greater limitation to exercise than those with a stable weight and the same degree of obstruction. Their diffusion capacity is usually more damaged. As the muscle mass and function decrease, the muscles undergo a greater demand in order to keep up with the ventilation work. Over time, the muscles become less efficient due to fatigue. Respiratory failure then becomes common, as the weight loss progresses. Other skeletal muscles are affected as well, determining the decrease in mobility and a higher risk in falling. There is a decrease in cell immunity, a reduction of secretory IgA, a decrease in alveolar macrophage function, and bacterial colonization and adhesion in the upper and lower airways.

A figure adapted from International Classification of Functioning was shown to describe overall impairment of body functioning. Impairment in the lungs causes inflammation and oxidative stress leading to pulmonary hypoxia. Inspiratory muscle weakness, impaired maximum inspiratory pressure and decreased FFM cause decreased FEV1, SPO2 and decreased BMI. These all lead to progressive dyspnea. The study by Cano et al showed that the degree of respiratory impairment is equivalent to reduced FEV_1, FVC and 6-min walking test. All these in turn lead to lower levels of physical activity in daily life related to higher risk of hospital readmission and shorter survival.

In a nutshell, COPD patients develop malnutrition by way of direct and indirect effects of the following factors: peripheral myopathy and catabolism, decreased FFM, elevated resting energy expenditure, systemic inflammation or elevated leptin, low dietary intake, impaired appetite, and malabsorption. The consequences of which include: damages in the normal function of the skeletal muscles whether or not there is a lung disease, reduction in the diaphragmatic mass contributing to the decreasing strength and resistance of the respiratory muscle, damages in the diffusion capacity, and increase in risk of osteoporosis and infections.

Proceeding on to nutritional supplementation defined as a caloric supplementation for at least 2 weeks, a systematic review of 21 randomized controlled trials (RCT) clarified the contribution of nutritional supplementation for patients with stable COPD. The different Nutritional Support Study were classified based on Immediate Effects, Short Term (<2weeks) and Long Term (>2weeks).

There were 4 trials based on immediate effects, arriving at a conclusion that carbohydrate rich meal increase minute ventilation (Ve), carbon dioxide production (Vco2), respiratory quotient and oxygen exchange, and decrease exercise capacity than high fat meal.

There were 3 trials that gave nutritional support for < 2 weeks. The findings in a study by Angellilo et al and Goldstein et al are consistent with studies of immediate effects of a meal showing that a high fat diet places a lower demand on the respiratory system than a diet high in CHO. Goldstein also noted small but consistent decreases in CO2 production, minute ventilation and tidal volume with higher fat content. Angelillo and colleagues, reported too that low CHO, high fat diet reduced carbon dioxide production and respiratory quotient compared with high CHO diet. They also noted a small but significant increase in PaCO2 as the CHO content increased from low to moderate.

The following are the outcomes of the 11 studies observed on long term basis. Out of 11, only 10 were available because one is unpublished. The studies by Fuenzalida, Ferreira, Whittaker and Rogers showed improvement in athropometric measures, immune status, respiratory muscle endurance, and clinical symptoms.

Many subjects in the 11 trials, gained under 2 kg. Some gained weight due to change in fat mass only. The studies by Schols et al and Burdet et al whom they used anabolic steroids showed a gain in fat free mass, lean body mass, respiratory muscle function but did not improve muscle strength and exercise tolerance. The studies of Efthimiou et al, Lewis et. al, Otte et al, and Knowles et al did not show important effects. The results showed that high fat diet supplementation if given less than 2 weeks can be favorable for COPD patients based on the postive effects as mentioned. However, for nutritional supplementation maintained at least 2 weeks and onward, it was identified that there were no consistent effects on weight, anthropometric measures or pulmonary function. These data are inconclusive, highlighting the need for additional studies using homogeneous populations of COPD patients who are selected for the same physical characteristics and severity of bronchial obstruction.

Given the contribution of peripheral and respiratory muscle weakness to exercise limitation, it is a fact that muscle training is an integral component of rehabilitation programmes. Indeed, exercise training has been shown to improve exercise capacity in COPD patients. However, we need further proof.

A study done by Creutzberg et al in 2003 looked at a non-pharmacologic approach on the interventional management of malnutrition in COPD. They investigated the efficacy of oral nutritional supplementation therapy in depleted patients with COPD after 8 weeks of pulmonary rehab. The results show that dietary intake and the dietary intake: REE ratio increased significantly after nutritional therapy. Protein and CHO intakes increased whereas the percentage of fat intake decreased after treatment.

The body weight and FFM increased significantly after 8 week of nutritional supplementation therapy. Total serum protein, but not serum albumin increased after 8 week treatment. PI max, handgrip strength and 12 min walked distance increased significantly from baseline through 8 weeks. Peak work load, peak oxygen consumption and peak oxygen pulse during the incremental bicycle ergometric test improved.

Health status as assessed by St. George's Respiratory Questionnaire, improved on the items on symptoms and impact. The sense of well being on the Medical Psychological Questionnaire for Chronic Lung Patients improved significantly after 8 week of treatment. A graph was presented showing the course of body weight over 2 weeks of nutritional therapy incorporated into an 8 week pulmonary rehabilitation program. There was significant weight gain but the predicted weight gain was not reached due to attenuation at week 4-6. The increase in body weight after 8 week of intervention was lower than the predicted value because of an attenuated increase from week 4 to week 6.

A figure showing the changes in body weight, fat free mass and PI max was presented. The increase in body weight and FFM were significantly greater after nutritional supplementation therapy compared to placebo.

The results of the Creutzberg study, however, are different from the conclusions arrived at in the sytematic review because of several reasons:

1) Intervention studies with duration of at least 2 weeks were included which is probably too short to achieve substantial changes in physiologic function.

2) Most of the nutritional intervention trials were not combined with exercise training. It can be expected that this would result in expansion of fat mass and not FFM.

3) In several studies, the offered nutritional supplementation therapy consisted of inadequate energy intake relative to energy requirements needed for body weight gain. Moreover, non-compliance to the nutritional supplementation can lead to therapy failure.

There are several studies presented that objectively identified significant improvement utilizing Nutritional support and pulmonary rehabilitation. Other studies showed improvement in FFM, strength and capacity when nutritional supplementation and pulmonary rehabilitation are incorporated in the management. The RCT double blind study done by Fuld et al, showed significant improvement in Fat-free mass, peripheral muscle strength and endurance and health status, but not exercise capacity.

Furthermore, Steiner showed in his study among nutritionally depleted COPD patients an improvement of shuttle test and quality of life.

In May 2010, Keiyu Sugawara et al published a study in Respiratory Medicine (2010). The aim of this study was to investigate the effects of nutritional supplementation combined with low-intensity exercise on body components, exercise tolerance, and health-related quality of life (HRQOL) in malnourished patients with COPD.

The study concluded that the combination of nutritional supplementation with low-intensity exercise training was successful in increasing weight and energy intake as well as exercise capacity and health-related QOL in our patients.

According to another study by Gurgun et al in 2012, the combination of nutritional support with pulmonary rehabilitation resulted in improvements particularly in lean body mass and mid-thigh cross-sectional area. This study further suggests combining NS with PR in reversing weight loss and muscle wasting in COPD.

Nutritional supplementation utilizing high fat, low CHO administered over a course of < 2 weeks seems to provide benefit. Ingestion of high-CHO foods increases the ventilatory requirement.

Improved nutritional status following short-term supplementation is supported by weight gain, an increase in FFM, respiratory muscle function, and even in the immune system. The influence of longer-term supplementation (> 2 weeks) on weight, anthropometry, and exercise capacity varied.

Furthermore, when pulmonary rehabilitation is incorporated in the management program for COPD patients apart from nutritional support, the following is observed: improvement in lean body mass and mid-thigh cross- sectional area, increased weight and energy intake as well as exercise capacity and health-related QOL, and improved shuttle test and quality of life. JOEY

When a person has COPD, more energy is needed in order to breathe. The muscles used in breathing may require 10 times more calories than those of person without COPD. Consuming more energy than your body requires is not recommended as it puts additional stress on the lung and heart functions. When a person consumes excess energy, the body produces more carbon dioxide, which causes increased respiration rate. Malnourished patients require high energy and protein diet.

The formula to compute for the % weight change was also shown. If there is 5% of BW weight change in the previous months and 10% of BW weight change in previous 6 months, high energy and protein diet should be given. Intake needs to be adequate to prevent muscle breakdown and maintain lung function. A client who is malnourished will require additional protein: two servings of meat and alternatives per day for women and 3 servings for men. One Serving size is 85 grams. Excess protein should be avoided in those with chronic kidney disease as it can decrease kidney function.

High fiber food such as vegetables, dried legumes, bran, whole grains, rice, cereals, pasta, fresh fruits are recommended. Daily fiber requirement is 20-35grams fiber each day. Adequate fluid is needed to hydrate the body and help thin down the mucus and become easy to cough up. Approximately 6-8 cups of non- caffeinated fluid per day should be consumed. This can include water, milk, 100% juice, tea and soup.

Some people with COPD who also have congestive heart failure might need to limit their fluid intake. Fluid requirements should be discussed with the physician. Eating too much sodium can cause retention of fluid making breathing difficult. The following needs to be observed:

- Limit intake of processed foods such as bacon, deli meats, bologna, canned soups, instant noodles, sauces, fast foods, condiments, etc
- Remove salt shaker from table
- Use herbs or no-salt spices like pepper, onion powder, garlic powder, oregano, basil, etc.
- Avoid adding salt to food when cooking
- Read food labels and avoid foods with more than 300 mg of sodium per serving

The recommended intake is 2300mg or less of sodium per day (or 1 teaspoon of salt). This includes sodium added during cooking, at the table and what is added to food products.

People with COPD are at an increased risk of osteoporosis if they have used corticosteroids on a long-term basis. Calcium and Vitamin D supplementation is recommended as bone loss is significant after initiation of steroid therapy. It is recommended to take 1200mg of calcium and 1000 IU of Vitamin D per day. Encourage to eat calcium and vitamin D rich foods.

The following are the recommendations for nutritional intervention strategies:

The Underweight-to-normal weight patients should gain weight while preventing or replenishing the loss of fat free mass. Eating smaller more frequent meals that are higher in calories can help meet the caloric needs efficiently. It is also best to avoid low fat or calorie food products and to supplement meals with high calorie snack like pudding or crackers with peanut butter.

Patient dietary education may include: dietary management of hypertension, dyslipidaemia, glucose intolerance and bone health. Since COPD warrants multi- disciplinary management referral to a dietician may be prudent. Example scenarios are as follow: A patient who has had significant weight loss such as a weight loss of 5% of their body weight in the previous month or 10% of their body weight in the previous 6 months, an overweight/obese client who requires nutritional education to achieve weight loss, or a patient who has several coexisting health problems in addition to COPD, such as renal failure, heart disease, diabetes, etc.

After the case presentation, Dr. Arlet Michelle Cudiamat, a second year Pulmonary Fellow from Manila Doctors Hospital, was called to react. She commended the case presentation, recognizing the importance of the topic when in practice.

The second reactor, Dr. Marianna Sy-Quia Sioson, Fellow in Nutrition Support at St. Lukes Medical Center, a diplomate of Philipppine Board of Clinical Nutrition and head of Nutritional Section, Department of Internal Medicine, The Medical City, was also called to react. The unique way of presentation was commended. The content was appreciated by the reactor, commending that sarcopenia was even mentioned.

In the conference, it was mentioned that it is important to provide enough nutrients. But what does enough means. In the critical care setting, it means providing 25 kcal/ kg. Dr. Sioson discussed that

the usual ratio of carbohydrates to fats is 60:40. But this differs in special situations: in acute stress it becomes 70: 30, in infections it is 50: 50 and in cancer it is 40: 60.

In starting with nutrition, the dictum is “Start low then go slow”. Initially, only 25% of the total caloric requirement (TCR) should be provided until 100% of the TCR is reached. During the acute phase, nutrition is not built up; it is not even an aim. Otherwise, if we go “fast and furious”, refeeding syndrome will occur; main features of which include low potassium, magnesium and phosphorus, glucose abnormality, and fluid shifts.

Should there be only one parameter to look at in the nutrition of a patient, it is phosphorus. Decreased level of phosphorous would mean diminished ATP, our energy source, hence difficulty in weaning.

Regardless of the prescription ordered, the dietary might still be giving standard ration due to budget issues. It is wise to ensure that our patients’ nutritional intake be monitored; and adequate intake means taking in 75% of the TCR. Giving omega-3 fats would lead to faster weaning from the ventilatory support. We should know that glutamine is depleted in critical care and illness. Supplementation with probiotics leads to decline in VAP and nosocomial pneumonia. Lastly,early mobilization in the ICU is recommended.