Clinical Characteristics, Management in Real World Practice and Long-Term Survival among COPD Patients of Northern Thailand COPD Club Members

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Objective: To assess the baseline clinical characteristics, management, and long-term survival of hospital-based COPD patients in the northern part of Thailand.

Material and Method: One hundred and ninety five hospital-based COPD patients from community and provincial hospitals in the northern part of Thailand were recruited between May and November 2002. They were followed up for 45 months for survival.

Results: Most of them (71.3%) were in the advanced stage and 41.8% were undernourished. Only a small fraction of the advanced stage patients (25.7%) estimated their dyspnea severity correctly with the disease stages. The frequency of the exacerbations increases as the disease become more severe. Only 23.7% of the advanced stage patients had received regular bronchodilator therapy. No patients had received pulmonary rehabilitation and long-term oxygen therapy. The 45 months survival was 75.6% in all patients. The severe group with low BMI had significantly lower survival than the one with normal BMI (67.7 % vs. 89.8 %, p = 0.040).

Conclusion: Most COPD patients in the northern part of Thailand were in the advanced stage. They were commonly undernourished and exacerbated but still under treated according to standard treatment guidelines. BMI tends to influence the long-term survival of the advanced stage patients.

Keywords: Chronic obstructive pulmonary disease, Severity grading, Dyspnea perception, Treatment guidelines, Body mass index, Survival outcome

Chronic obstructive pulmonary disease (COPD) is characterized by a slow progressive chronic airflow obstruction and limited response to broncho-dilator therapy. The progression of the disease from asymptomatic to symptomatic periods typically requires longer than ten years. At the early stage, most patients have no or trivial symptoms such as occasional coughing or fatigability, therefore, only a few seek medical treatment. Their family members often feel familiar with these patient's long standing-symptoms and under recognize them as an illness. Furthermore, the general practitioners may under-diagnose and underestimate the disease severity, thus, ignoring the spirometric test. Usually, the disease has progressed to the advanced stage at the time the patients seek treatment. The management of the advanced disease requires a lot of hospital and family resources. However, the patients may be under treated according to GOLD (Global Initiation for Obstructive Lung Disease) standard treatment guidelines[1].

The investigating team conducted the present study to create Thailand's first database on hospital-based-COPD-patients from their various clinical charac-

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teristics, the management they received, and their long-term survival outcome. This was conducted from community and provincial hospitals in the northern part of Thailand. The results of the present study could be adopted for the holistic strategic planning of this burdensome disease in the country.

Material and Method

The northern Thailand COPD club has been established since May 31, 2002 by the division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Chiang Mai University, Chiang Mai. The members of the club were the hospital-based-patients diagnosed and receiving management from community and provincial hospitals in the northern part of Thailand. They were recruited voluntarily between May 31, 2002 and November 30, 2002 by several local mass media announcements such as posters, brochures, radio broadcast, and newspapers. Two hundred and twenty-six patients were recruited as club members during that period.

The selection criteria of the enrolled members for the study were: 1) Previous diagnosed COPD patients being treated by their doctors at the hospitals during the past 12 months. 2) The post bronchodilator FEV_1/FVC ratio less than 70%. (The spirometry was performed as an ATS standard recommendation, 1994, by using the spirometer model Autospiro PAL, Serial No.70107, Minato Medical Sciences Co., Ltd., Osaka, Japan). 3) The onset of shortness of breath and/or chronic cough started after the age of 40. 4) No previous diagnosis of asthma and none of their direct family members were diagnosed with asthma. 5) The chest radiograms revealed no other cardiopulmonary diseases related to their symptoms such as tuberculosis, bronchiectasis, lung abscess, interstitial lung diseases, lung mass, and left ventricular failure. 6) Had received treatment from the community and provincial hospitals at least once in the past 12 months. The authors excluded the members managed at the center and the members who had unacceptable spirometric results.

These patients were interviewed face to face by any one in the investigating team and were contacted regarding their survival by phone every 6 months. In case of inability for telephone contact, they were checked with the survival database of the population from the Administrative Center of Census Record at the end of February 2006. All information was recorded as follows:

1. *Smoking status*. Current smokers mean the patients smoke cigarettes regularly and for more than 1 year and were still smoking within the past 3 months, ex-smokers mean the patients had regularly smoked but had already quit during the past 6 months, passive smokers mean the patients were non-smokers but had a history of daily cigarette smoke inhalation of more than 3 hours per day for at least 1 year, and non-smokers mean the patients had never or had started smoking but had quit within 1 year.

2. *Smoking pack-years*. In the case of native cigarette smokers, consisted of 61.3% of the smokers in the present study, the smoking pack-years was calculated by dividing the native cigarette weight regularly smoked by the standard cigarette weight.

3. *Body Mass Index, BMI*. The current patient's BMI levels at the time of enrollment were classified using WHO classification 2004[2].

4. *The patient's disease severity grading*. The grading was classified by post bronchodilator % predicted of FEV_1 according to GOLD criteria[1]. In case of $FEV_1 < 50\%$, the presence of corpulmonale or oxygen saturation $\leq 88\%$ measured by pulse oximeter (Model 9500, Nonin Medical Inc, Plymouth, MN, USA) during stable clinical symptoms for more than 6 weeks were also classified as the very severe group. The advanced stage defined in the present study included the severe and very severe groups.

5. *The patient's dyspnea severity*. The dyspnea severity on daily activity of each patient was assessed at the recent stable period and classified by using Borg scale.

6. *Acute exacerbation history*. The frequency of acute exacerbation, frequency of at least one episode, and frequency of at least one severe episode during the past 12 months of each patient were recorded. The criteria for acute exacerbation were defined by any one of the two criteria. First, history of the patient was at least two from three items as follows: recent increase in their shortness of breath, increase in the amount or change to purulent appearance of phlegm, and fever. These items lasted more than 1 day and caused the patient to need an unscheduled medical visit; second, the physician's record as an acute exacerbation with antibiotic and/or systemic corticosteroid prescription. The severe exacerbation was defined as the episode of exacerbation needed to be hospitalized for treatment.

7. *Bronchodilator therapy*. The number of patients in the advanced stage who received regular or as needed bronchodilator therapy within the past month, both oral and inhaled formulations.

8. *Pulmonary rehabilitation*. The number of

patients in the advanced stage who have been advised, received instruction sheet or booklet, or trained by their doctors, nurses, or physical therapists on any one of the following components: whole body aerobic or specified muscle group (e.g. upper limbs, lower limbs, or inspiratory muscle) exercise, breathing retraining for energy conservation, and effective coughing and secretion clearance training programs.

9. *Long-term oxygen therapy*. The number of patients in the very severe group indicated for this treatment that had been treated within the past 12 months. The indications for long-term oxygen therapy in the present study were the presence of corpulmonale or oxygen saturation $\leq 88\%$ measured by pulse oximeter during a stable period in the patients with $FEV_1 < 50\%$.

10. *Survival outcome*. The number of survived cases during the 45 months-follow up period was recorded.

Statistical analysis

The data were recorded and analyzed by using SPSS version 11.5 software program. Clinical characteristics, frequency, and severity of acute exacerbation, and treatments received were analyzed by using descriptive statistics. The probability of survival was analyzed by Kaplan-Meier Method. The comparative analyses between groups or sub-groups were analyzed by Chi-square test or Fisher's Exact test. A p-value of less than 0.05 was considered statistically significant.

Results

One hundred and ninety-five out of 256 members fulfilled the criteria for enrollment. Sixty-one cases were excluded due to being treated by pulmonologists at the center (46 cases) and unacceptable spirometries (15 cases). No one had had their lung function evaluated by the spirometry before. There were 81.5% aged over 60 years and the mean age was 67.7 years old and male: female ratio was 1.5:1. The mean of post bronchodilator-FEV1 was 0.94 liters or 41.97% predicted. Almost all the patients enrolled were smokers (99.0%) and 61.3% were native cigarette smokers. The mean calculated standard accumulative dose of cigarettes smoked was 29.8 pack-years and 75.4% had smoked more than five pack-years. There were 41.8% classified as malnourished state by using BMI level < 18.5 (Table 1).

Although most of them (87.7%) were ex-smokers, 10.3% were current smokers (Fig. 1). Two

cases (1%) were passive smokers; both of them had a history of inhaled indoor-cigarette smoke from their husbands for longer than 20 years. The other two cases (1%) were non-smokers. One of them was finally diagnosed with asthma because of dramatic improvement of his lung function after treatment with inhaled corticosteroid and long acting beta 2-agonist for 3 months. The last one had a history of inhaled biomass fuel smoke in the farm almost everyday for more than 20 years.

The disease severity grading according to GOLD criteria were classified as very severe, severe, moderate, and mild degrees, which most of them (71.3%) belonged to the advanced stage (Fig. 2). There were 50.0%, 46.9%, and 34.1% of the moderate, severe, and very severe groups who assessed their dyspnea severity on daily activities as at a mild degree (Borg scale 0-3), and correctly assessed their dyspnea severity with the severity grading as 44.0%, 18.4%, and 7.3% in each groups, respectively (Table 2).

There were 53.3% who had no exacerbation during the past 12 months, however, 16.5% had more than two episodes and 30.2% had 1-2 episodes (Fig. 3).

Table 1. Baseline characteristics (Sex, Age, Smoking status and Body Mass Index)

Characteristics	Numbers (%) n = 195
Sex	
Male/Female	116:79
Male: Female ratio	1.5:1
Age(yrs)	
Mean $\pm$ SD (Range)	67.7$\pm$7.8 (48-86)
Age group	
$\leq$ 60 years	36 (19.5)
> 60 years	159 (81.5)
FEV_1	
Liters	0.94$\pm$0.42
{Mean $\pm$ SD, (Range)}	(0.37-2.67)
Percent of predicted	41.97$\pm$15.45
{Mean $\pm$ SD, (Range)}	(17.30-95.63)
Smoking status	
Non-smoker	2 (1.0)
Smoker	193 (99.0)
Mean (pack-years) (Range)	29.8 (0.95-195)
Smoker > 5 pack-years	147 (75.4)
BMI classification	
Underweight (< 18.50)	76 (41.8)
Normal (18.50-24.99)	91 (50.0)
Overweight (25.00-29.99)	15 (8.2)
Obese ($\geq$ 30.00)	0 (0)
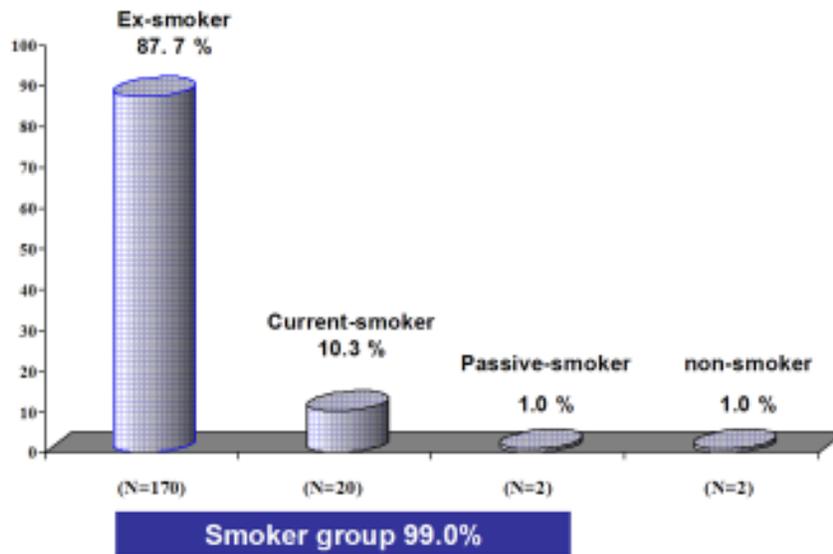
Fig. 1 Smoking status of COPD patients (N = 195)
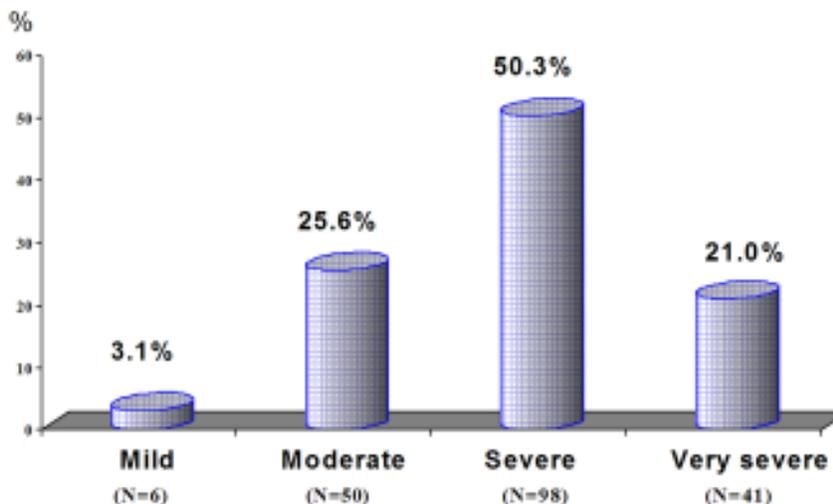
Fig. 2 Severity classification (GOLD criteria[(1)]) (N = 195)

The rates of at least one episode of exacerbation were in rising trends with 16.7% in mild and 58.5% in very severe patients. However, the rates of severe exacerbation were similar among the moderate, severe, and very severe patients (26.0%, 30.6%, and 31.7%, respectively) and no severe exacerbation episode occurred in the mild patients (Table 3). Seventy six point seven percent (69/90) of exacerbations and 76.8% (43/56) of severe exacerbations occurred in the advanced stage patients.

The advanced stage patients received the regular bronchodilator therapy in 23.7%, no one received any advice or training concerning any components of pulmonary rehabilitation. Furthermore, there were no patients in the very severe group treated by long-term oxygen therapy even if it was indicated (Table 4).

At the end of the follow up, the total group mortality was 20.7%. The intra-group analysis revealed the difference in mortality among the low BMI and normal BMI patients only in the severe group (25.6%

Table 2. Relationship between disease severity grading and dyspnea severity perception on daily activities according to Borg scale

Dyspnea severity perception (Borg scale)	Disease severity grading				
	Mild n (%)	Moderate n (%)	Severe n (%)	Very severe n (%)	Total n (%)
0-3 (Mild)	2 (33.3)	25 (50.0)	46 (46.9)	14 (34.1)	87 (44.6)
4-6 (Moderate)	4 (66.7)	22 (44.0)	34 (34.7)	24 (58.5)	84 (43.1)
7-10 (Severe)	0	3 (6.0)	18 (18.4)	3 (7.3)	24 (12.3)
Total	6	50	98	41	195

Table 3. Frequency of acute exacerbation (AE) within the past 12 months

Severity of COPD	Number of AE at least 1 episode/year n = 90		Number of severe AE at least 1 episode/year n = 56	
	Patients (%)	Episodes (%)	Patients (%)	Episodes (%)
Mild (n = 6)	1 (16.7)	1 (1.1)	0 (0.0)	0 (0.0)
Moderate (n = 50)	20 (40.0)	20 (22.2)	13 (26.0)	13 (23.2)
Severe (n = 98)	45 (45.9)	45 (50.0)	30 (30.6)	30 (53.6)
Very severe (n = 41)	24 (58.5)	24 (26.7)	13 (31.7)	13 (23.2)
Total (n = 195)	90	90	56	56

vs. 9.8%, p = 0.029) but not in the moderate (16.7% vs. 19.2%, p = 0.425) and severe groups (26.3% vs. 23.5%, p = 0.423) (Table 5).

The probability of survival at 12, 24, 36 and 45 months were 96.8%, 87.5%, 80.5%, and 75.6%, respectively (Fig. 4). At the end of follow up the very severe group had the lowest survival (69.3%) but not significantly different from the moderate (77.6%) and severe (73.7%) groups (Fig. 4.1). However, the very severe group with low BMI had significantly lower survival than the severe group with normal BMI (67.7% vs. 89.8%, p = 0.040) (Fig. 4.2).

**Discussion**

The results of the present study revealed the database of the hospital-based patients receiving treatments from community and provincial hospitals in the northern part of Thailand. Most of them were elderly (mean age was 67.7 years and 81.5% aged more than 60 years old). Almost all of them (99.0%) were smokers with 29.8 mean pack-years. There were nearly 25% of the patients who had smoked less than five pack-years. The postulations for a significant proportion of low pack-years in the present study are 1) errors

Table 4. Medical treatment received in the severe and very severe groups

Type of medical treatment	Number (%) (n = 139)
Bronchodilator therapy	139 (100.0)
Regular bronchodilator therapy	33 (23.7)
Rescued bronchodilator therapy	106 (76.3)
Pulmonary rehabilitation	0 (0.0)
Long-term oxygen therapy for very severe group (n = 41)	0 (0.0)

on pack-years calculation as more than 60% of them were native cigarette smokers. The native cigarettes (Fig. 5) varied in sizes, both their diameters and lengths, and it was difficult to calculate their pack-years accurately as standard manufactured cigarettes. 2) the high impurities in native cigarettes such as insecticide residuals and fungal toxins containing toxic oxidants potentially cause more lung injury than the standard manufactured cigarettes at equivalent dosing. 3) the diameter of the native cigarette was several folds larger than the standard one, therefore, much more smoke
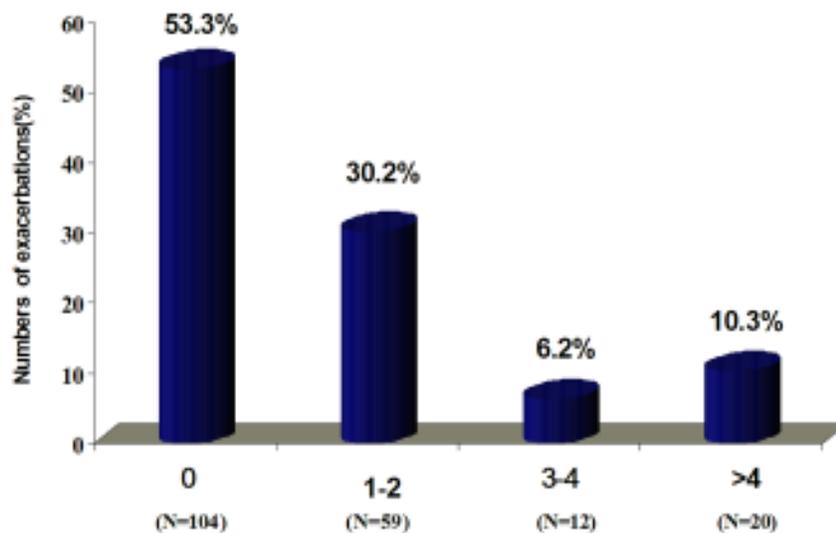
Fig. 3 Frequency of exacerbation within the past 12 months (N=195)
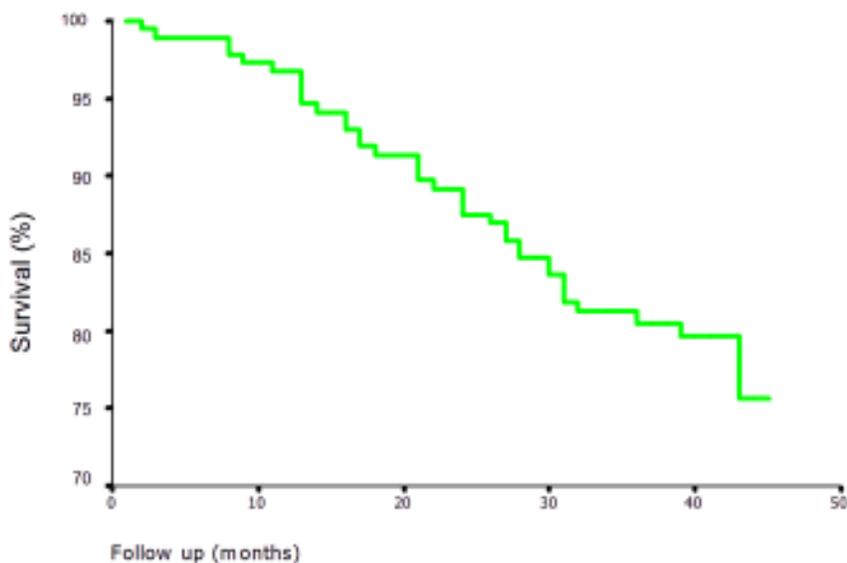
Fig. 4 Survival rate of all COPD patients during 45 months follow-up period

Table 5. Mortality rate among severity of COPD and BMI classification

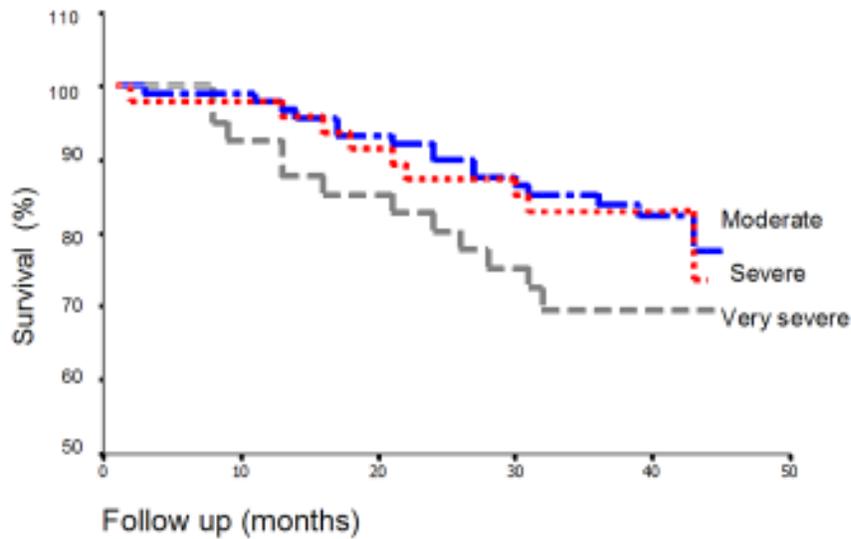| Severity of COPD	Mortality rate		p-value
	Underweight (%)	Normal (%)	
Moderate (n = 38)	2/12 (16.7)	5/26 (19.2)	0.425
Severe* (n = 84)	11/43 (25.6)	4/41 (9.8)	0.029
Very severe (n = 36)	5/19 (26.3)	4/17 (23.5)	0.423

Fig. 4.1 Survival rate of all COPD patients during 45 months follow-up period categorized by disease severity grading
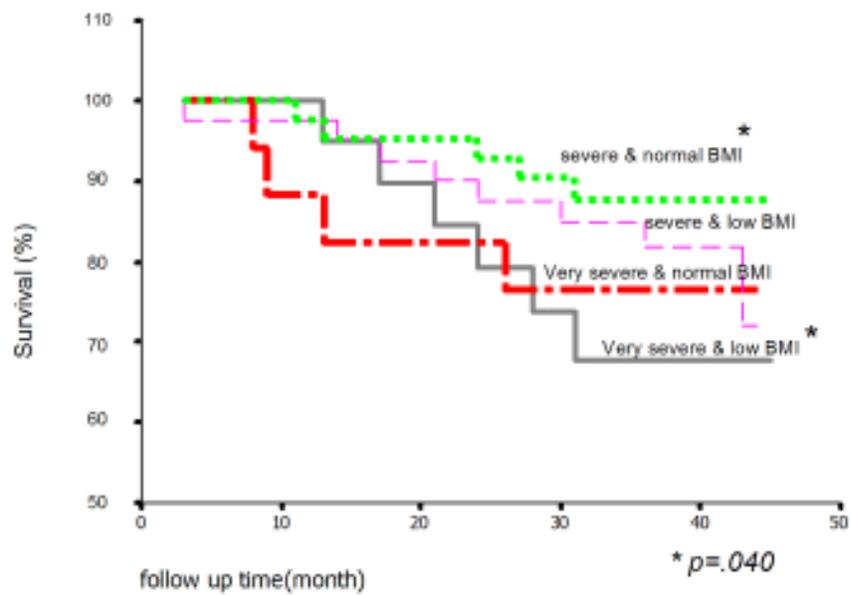

Fig. 4.2 Survival rate of all COPD patients during 45 months follow-up period categorized by disease severity grading and BMI classification

was inhaled per puff than the standard ones. 4) there were other risk factors involved which caused a higher chance of developing COPD even low pack-years such as air pollutants[3-6], genetic predisposition to cigarette smoke[7], or pre-existing bronchial hyperactivity[8].

All patients were diagnosed by their physicians based on clinical grounds only; none had ever done a spirometric test. If one of the clinical grounds based on the history of chronic smokers were more than five-pack years, 25% of the patients would miss the diagnosis according to the present study. Furthermore, most of the patients underestimated their dyspnea symptoms, thus, their self assessment-dyspnea severity is unreliable for their disease severity grading.

Fig. 5 Examples of the northern Thailand native cigarettes, called '*Kee-Yo*', compared with the standard manufactured cigarette (far left). Please notice the varieties in their diameters and lengths. Each of them (*from left to right*) was weighed equivalent to 4, 9, 5, 10, and 12 standard manufactured cigarettes, respectively

For example, there were only a minority in the severe and very severe patients (18.4% and 7.3%, respectively) who accepted their dyspnea as severe. Furthermore, 50%, 46.9%, and 34.1% of the moderate, severe, and very severe patients assessed their dyspnea as mild. As evidenced by the study results, the physicians should enhance their use of the spirometric test as a standard tool for diagnosis and grading severity of COPD regardless of their symptoms and number of pack-years.

Most of the patients (71.3%) were in the advanced stage of the disease. Nearly half of them (46.7%) had experienced acute exacerbation during the past 12 months and 16.5% had exacerbated more than two episodes. The advanced stage patients had much more frequent (76.7%) and severe exacerbations (76.8%) than the early stage ones. These results reflect that hospital based service strategies were loaded with a high proportion of the advanced stage patients. The acute exacerbation is the major factor for healthcare resources consumption including drugs, oxygen, mechanical ventilators, emergency visits, admissions, length of hospital stay including intensive care unit, healthcare personnel workload, and burden to the patients' family and society. By considering the data on exacerbation in the present study, the active productive strategies against this disease in terms of prevention and retar-

dation of the progression, apart from the active anti-smoking campaign, should have the fast track for all smokers to access to the spirometric test for early disease detection and treatment along with the effective smoking cessation services for current smokers who intended to quit.

Among the advanced stage patients, regular bronchodilator therapy and pulmonary rehabilitation are strongly recommended treatments by the GOLD guidelines[1]. However, only 23.7% of them received regular bronchodilator therapy, either via oral or inhaled route. Furthermore, none received any advice or training concerning any components of pulmonary rehabilitation. Long-term oxygen therapy is also strongly recommended as a standard treatment for improving the survival of the very severe patients whom had corpulmonale or evidence of chronic hypoxemia. However, none of 41 patients indicated for long-term oxygen therapy received this kind of treatment. In conclusion, the advanced stage patients were still far away from being assessed for the three essential components of standard management, regular bronchodilator therapy, pulmonary rehabilitation, and long-term oxygen therapy. The under standard management in any or all of the three components among the advanced stage patients could be the major cause of frequent and severe exacerbation resulting in a high burden to

the healthcare resources, patient's family and society as mentioned above. The most effective strategy for unloading the disease burden among these advanced stage patients is enhancing the practicing physicians and policy makers to effectively imply these three components of the standard management into real world clinical practice.

The survival among advanced stage patients tended to be lower in the subgroup with more severe disease but could not be revealed by statistical difference (Fig. 4.1). However, the low BMI played a statistically significant influence on mortality in the severe subgroup (Table 5) and survival as revealed by the comparison between the very severe subgroup with low BMI and the severe subgroup with normal BMI (Fig. 4.2). The present study supports that the malnourished state assessed by low BMI is one of the important co-factors affecting long-term survival in the advanced stage patients. These findings have been already addressed in several relevant studies[9-11]. Therefore, last but not least, the prevention and correction of malnourished state among the advanced stage patients should be the allied strategy for survival benefit.

Apart from the well-known anti-smoking campaign, the public health policy makers should place more stress on the campaign for early disease detection in the community among smokers by spirometric test and promote effective smoking clinic services in the primary care. These two interventions should facilitate the early disease stage discovery and retard the disease progression. For hospital-based patients, all of them should receive standard spirometric test to confirm the diagnosis and grading the disease severity including BMI and oxygen saturation measurements for the group severely impaired lung function. The standard treatments for the advanced stage, the most common stage loaded the healthcare resources, should be promoted immediately and practically along with prevention and correction of the malnourished state.

Conclusion

The present study revealed that most of the hospital-based COPD patients in the northern part of Thailand were elderly and in the advanced stage. Almost all of them were smokers; two-thirds were native cigarette smokers, and frequently had low BMI. A high proportion of them underestimated their dyspnea symptom, whereas none had ever received a spirometric test for diagnosis or grading of the disease severity. Most

of the advanced stage patients had frequent and severe exacerbation, however, a minority received regular bronchodilator therapy and none received pulmonary rehabilitation or long-term oxygen therapy. The low BMI contributed influence on mortality and survival of the advanced stage patients.

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ลักษณะทางคลินิกการรักษาในเวชปฏิบัติตามความเป็นจริงและการรอดชีวิตในระยะยาวของผู้ป่วยโรคปอดอุดกั้นเรื้อรังซึ่งเป็นสมาชิกชมรมโรคถุงลมโป่งพองภาคเหนือ ประเทศไทย

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วัตถุประสงค์: เพื่อประเมินลักษณะพื้นฐานทางคลินิก การรักษาที่ได้รับและระยะการมีชีวิตอยู่รอดของผู้ป่วยโรคปอดอุดกั้นเรื้อรังซึ่งเป็นสมาชิกชมรมโรคถุงลมโป่งพองภาคเหนือ ประเทศไทย

วัสดุและวิธีการ: รวบรวมผู้ป่วยที่เป็นสมาชิกชมรมโรคถุงลมโป่งพองจำนวน 195 รายที่ได้รับการรักษาจากโรงพยาบาลชุมชนและโรงพยาบาลจังหวัดในภาคเหนือ ระหว่างเดือนพฤษภาคม ถึงพฤศจิกายน พ.ศ. 2545 นำมาวิเคราะห์ข้อมูล และติดตามการมีชีวิตอยู่รอดนาน 45 เดือน

ผลการศึกษา: ผู้ป่วยส่วนใหญ่ (ร้อยละ 71.3) อยู่ในระยะโรคขั้นรุนแรง ร้อยละ 41.8 มีภาวะทุพโภชนาการร่วมด้วยผู้ป่วยเพียงส่วนน้อย (ร้อยละ 25.7) สามารถประเมินระดับความรุนแรงของอาการหอบเหนื่อยของตัวเองได้ตรงตามระยะของโรค ภาวะโรคกำเริบพบบ่อยมากขึ้นตามลำดับขั้นความรุนแรงของโรค มีเพียงร้อยละ 23.7 ของผู้ป่วยโรคขั้นรุนแรงที่ได้รับการรักษาด้วยยาขยายหลอดลมอย่างสม่ำเสมอ และไม่มีผู้ป่วยรายใดได้รับการฟื้นฟู สมรรถภาพการหายใจ หรือ ได้รับการรักษาด้วยออกซิเจนบำบัดระยะยาว เมื่อติดตามครบ 45 เดือนพบว่าผู้ป่วยมีโอกาสรอดชีวิตร้อยละ 75.6 โดยผู้ป่วย ที่เป็นโรคขั้นรุนแรงมากที่สุดและมีภาวะทุพโภชนาการมีโอกาสรอดชีวิตต่ำกว่าผู้ป่วยที่เป็นโรคขั้นรุนแรงแต่มีระดับดรรชนีมวลกายปกติ (ร้อยละ 67.7 และ 89.8, p = .040)

สรุป: ในเวชปฏิบัติตามความเป็นจริงผู้ป่วยโรคปอดอุดกั้นเรื้อรังส่วนใหญ่เป็นโรคขั้นรุนแรงและมีภาวะทุพโภชนาการร่วมด้วยมากพอสมควร ผู้ป่วยเหล่านี้มีภาวะโรคกำเริบได้บ่อย แต่ผู้ป่วยส่วนใหญ่กลับได้รับการรักษาที่ต่ำกว่ามาตรฐาน ระดับดรรชนีมวลกายมีอิทธิพลต่อโอกาสรอดชีวิตในระยะยาวของผู้ป่วยกลุ่มที่เป็นโรคขั้นรุนแรง