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Associated factors of successful pulmonary rehabilitation in patients with chronic obstructive pulmonary disease

Chalerm Liwsrisakun, Chaicharn Pothirat, Athavudh Deesomchok, Warawut Chaiwong*

Division of Pulmonary, Critical Care, and Allergy, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand.

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ORCID of all authors

Chalerm Liwsrisakun: https://orcid.org/0000-0001-8376-2147
Chaicharn Pothirat: https://orcid.org/0000-0003-0616-7066
Athavudh Deesomchok: https://orcid.org/0000-0003-1375-4541
Warawut Chaiwong: https://orcid.org/0000-0003-4459-7681

Correspondence

Warawut Chaiwong
Division of Pulmonary, Critical Care, and Allergy, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand.
Email: warawut.chai@cmu.ac.th

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ABSTRACT

Background: Identifying factors associated with changes in health-related quality of life (HRQoL) and exercise capacity may help maximize benefits for patients with chronic obstructive pulmonary disease (COPD) attending pulmonary rehabilitation (PR).

Objectives: To determine factors associated with positive PR outcomes in patients with COPD, including HRQoL and exercise capacity.

Materials and methods: This retrospective study evaluated PR response, defined as achieving the minimal clinically important difference (MCID) in both outcomes: ≥4-point decrease in St. George's Respiratory Questionnaire (SGRQ) score and ≥54-meter increase in six-minute walk distance (6-MWD). Participants who achieved the MCID in both outcomes were classified as PR responders. Univariable and multivariable logistic regression analyses were used to identify factors associated with response to PR.

Results: Sixty-two COPD patients completed PR (Suandok Exercise Training [SET], N=32) and modified Suandok Exercise Training [mSET], N=30); mean age was 70.5±7.9 years and 46.8% were male. Overall, 41.9% achieved MCID improvements in both HRQoL and 6-MWD. In multivariable analysis, PR response was independently associated with mMRC ≤1 (adjusted OR 19.56; 95%CI; 2.51, 152.22), baseline 6-MWD <320 m (adjusted OR 13.09; 95%CI; 1.89, 90.57), baseline SGRQ ≥60 (adjusted OR 9.53; 95%CI; 1.64, 55.45), and receiving the mSET program (adjusted OR 7.72; 95%CI; 1.46, 40.79), whereas age, sex, BMI, and cardiovascular comorbidity were not associated with response.

Conclusion: Patients with less severe dyspnea, lower exercise capacity, poorer HRQoL, and those receiving the mSET program were more likely to be associated with PR response.

Introduction

Pulmonary rehabilitation (PR) has been suggested as an essential part of management for chronic obstructive pulmonary disease (COPD).[1-3] The evidence suggests that the health-related quality of life (HRQoL) and exercise capacities improved and dyspnea was reduced after completing the PR program.[4] Moreover, it was demonstrated to reduce acute exacerbations (AE), hospitalizations (HOS), and health care utilization.[5] Therefore, the measurement of changes in HRQoL and exercise capacities is an essential outcomes related to the effectiveness of PR.[6]

Although the benefits of PR for COPD have been well established,[1-5] some research reported that a portion of patients have little to no response to PR.[7-9] Several studies have focused on identifying clinical predictors of the beneficial effects of PR in COPD patients. The initial degree of dyspnea was a discriminant factor in obtaining positive results from PR.[10] Other studies have suggested that baseline body mass index (BMI) predicts changes in exercise capacity,[11,12] whereas lung function measured by forced expiratory volume in the first second (FEV_1), age, physical status, dyspnea level, comorbidities, socioeconomic status, and smoking status were not related to the success of PR.[10,13-15] Nowadays, the specific variables that predict changes in HRQoL and exercise capacity after a completed PR program are unclear. Identifying factors of changes in HRQoL and exercise capacity may help in maximizing the benefits for COPD patients who attend the PR program. Therefore, this study aimed to determine factors associated with positive PR outcomes, including HRQoL and exercise capacity of PR in patients with COPD.

Materials and methods

Study design

This study was a retrospective study of the PR program, including Suandok Exercise Training (SET) and modified Suandok Exercise Training (mSET) programs, in which COPD subjects participated between January 2006 and December 2015. Briefly, the intensive phase of the SET program comprised 16 fully supervised sessions (twice weekly for 8 weeks).[8] Each session included upper- and lower-limb cycle ergometer training using stationary arm and leg ergometers, with a 10-15 min warm-up and a 5-10 min cool-down. During the first 2 weeks, patients trained for 30-40 min per session at mild intensity (30-35% heart rate reserve [HRR]), pedaling at 45-55 rpm, and were encouraged to exercise to the limit of dyspnea without exceeding a rating of perceived exertion (RPE) of 6. Exercise duration and intensity were progressed alternately by 5minutes and 5% HRR every 2 weeks, reaching 50-60 minutes per session and 50-55% HRR during the final 2 weeks.

The mSET program was a mild-to-moderate intensity, incremental strength and endurance training program delivered twice weekly for 8 weeks (approximately 35-40 min per session) under continuous supervision.[9] Each session began with a 10-15 min warm-up, followed by peripheral muscle strength training for the upper and lower limbs using weight lifting and resistive loading, and endurance training consisting of flat-surface corridor walking, and concluded with a 10 min cool-down. Exercise technique was extensively instructed, and patients were supervised throughout the 8-week period. For strength training, workload was set at 100% of the 10-repetition maximum (10-RM). Participants completed three sets per muscle group

during the first 4 weeks, then progressed by adding 10 repetitions every 2 weeks, reaching a maximum of five sets in the final 2 weeks.

For endurance training, walking was performed for 15-20 minutes during the first 2 weeks at 40-45% HRR, without exceeding RPE 6, and was increased by 5 minutes every 2 weeks to 35-40 min per session by the final week. More details of the PR protocol of these programs were demonstrated in previously published studies.[8,9]

This study was performed in accordance with the guidelines from the Declaration of Helsinki. The study was approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University with IRB approval number: MED-2559-04173, approval date: October 6, 2016. Participant consent was not required as the research was based on a retrospective review of previously collected non-identifiable information.

Subjects

A total of 120 COPD patients referred to the outpatient PR program during the study period were screened. For both the SET and mSET programs, eligible participants were outpatients with stable COPD (no exacerbation within the previous 6 weeks), aged >40 years, ex-smokers with a smoking history of >10 pack-years, a history of ≥1 exacerbation in the prior year, and willingness to complete the full exercise-training program. Patients receiving long-term oxygen therapy (LTOT), with pneumonia within the previous 3 months, or with cardiac or other comorbidities limiting exercise training were excluded.

Sixty-five patients were included in the PR program (35 and 30 subjects for the SET and mSET program, respectively). Only subjects who completed 16 sessions of the SET or mSET program (2 sessions/week for 8 weeks) were included for final analysis (N=62). All subjects with mild to very severe COPD were diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.[16]

Outcome measurements

The outcome measurements were reviewed by a pulmonologist and a physical therapist at baseline and at month two (after 16 times of PR sessions). The 6-minute walk test (6-MWT) was performed following the ATS guidelines.[17] The HRQoL was assessed using the St. George's Respiratory Questionnaire (SGRQ).[18]

Because PR aims to improve both patient-centered HRQoL and functional exercise capacity, using a composite outcome that captures clinically meaningful change in both domains helps identify baseline factors associated with a more comprehensive and maximized benefit from PR in COPD patients. A decrease of a total SGRQ score of four points was defined as a minimal clinically important difference (MCID).[19] For consistency with the original published SET and mSET studies from which this retrospective cohort was derived, we defined the MCID for the 6-min walk distance as an increase of ≥54 meters.[8,9]Therefore, an increase of 54 m in 6-min walk distance (6-MWD) was considered an MCID.[20] Severity of dyspnea was assessed using the modified Medical Research Council (mMRC) scale, and the MCID change was defined as a one-point decrease in score.[21] However, a previous study suggested that the dyspnea severity measure using mMRC was a rough scale and not sensitive enough to detect changes in patients with advanced COPD.[22] Therefore, PR responders in this study were defined as subjects who achieved the MCID in both the SGRQ and the 6-MWD criteria.

Sample size calculation

The sample size was calculated using the G*Power software version 3.1.9.2. Eight predictors in the model explained the responder status of PR. Based on an estimated effect size f^2=0.30, 59 subjects were required to reject the null hypothesis, with a power of 0.8 and a significance level of 0.05.

Statistical analysis

Results for continuous data were shown as mean±SD or median, interquartile range (IQR), and those for categorical data were expressed as frequencies and percentages. Independent sample t-tests and Mann-Whitney U Test were used to compare differences between the responder and non-responder groups for normally distributed and non-normally distributed data, respectively. Fisher's exact test was used to compare the proportional categorical data. Univariable and multivariable logistic regression were performed to identify the associated factors of positive outcomes in the PR program. The potential factors from univariable analysis with p<0.25 were analyzed using multivariable logistic regression.[23] Moreover, multicollinearity was checked; variables with a variance inflation factor (VIF) >5 were removed from the multivariable logistic analysis.[24] Results were displayed as an odds ratio and adjusted odds ratio (OR) together with a 95% confidence interval (CI) for univariate and multivariable logistic regression analysis, respectively. A p<0.05 was considered statistically significant. All statistical analyses were performed using STATA version 16 (StataCorp, College Station, TX, USA).

Results

Between January 2006 and December 2015, 120 patients with COPD were referred by their physicians to attend a PR program (either the SET or mSET program), of whom 62 completed the PR program (32 in the SET program and 30 in the mSET program). The data from sixty-two COPD subjects (46.8% male) with a mean age of 70.5±7.9 years were included for analysis. According to the GOLD classification, almost all subjects were classified as moderate to very severe stages of COPD. There was no significant difference in baseline characteristics between the responder and non-responder groups (Table 1).

Table 1. Baseline characteristics of COPD patients stratified according to response to pulmonary rehabilitation (MCID of SGRQ≥-4 unit and MCID of 6-MWD≥54 meters).

Variables	**Responder** (N=26)	**Non-responder** (N=36)	***p* value**
Age (year)	70.4±7.5	70.2±8.4	0.938
Female gender	15 (57.7)	17 (47.2)	0.416
BMI(kg/m^2)	20.0±4.3	19.8±4.4	0.863
BMI classification (kg/m^2)[20]			0.094
Underweight (<18.5)	11 (42.4)	18 (50.0)	
Normal (18.5-22.9)	9 (34.6)	12 (33.4)	
Overweight (23.0-24.9)	1 (3.8)	4 (11.1)	
Pre-obese (25.0-29.9)	5 (19.2)	0 (0.0)	
Obese 1 (30-40)	0 (0.0)	2 (5.5)	
Percent predicted of FEV_1	45.5±15.6	43.0±15.2	0.540
Ratio of FEV_1/FVC (%)	51.2±15.3	53.2±12.6	0.567
GOLD classification			0.941
I	1 (3.8)	1 (2.7)	
II	7 (26.9)	10 (27.8)	
III	15 (57.7)	19 (52.8)	
IV	3 (11.6)	6 (16.7)	
6-MWD (meters)	256.2±92.1	268.5±105.5	0.633
SGRQ scores (0-100)	57.5±17.0	52.2±18.3	0.246
mMRC scores (0-4)*	2.0 (1.0-3.0)	2.5 (1.0-3.0)	0.186
Cardiovascular comorbidity (yes)	5 (19.2)	9 (25.0)	0.592
Inhaled medications N (%)			0.544
LAAC	4 (15.4)	4 (11.1)	
ICS+LABA	16 (61.5)	18 (50.0)	
ICS+LABA+LAAC	6 (23.1)	14 (38.9)	
PR programs			0.303
SET (N=32)	11 (34.4)	21 (65.6)	
mSET (N=30)	15 (50.0)	15 (50.0)	

Notes: Results are expressed as means±SD or N (%), *Median (interquartile range). BMI: body mass index, FEV_1: forced expiratory volume in the first second, FVC: forced vital capacity, GOLD: Global Initiative for Chronic Obstructive Lung Disease< ICS: inhaled corticosteroids, LAAC: long-acting anticholinergic, LABA: long-acting beta2-agonists, mMRC: modified Medical Research Council, mSET: modified Suandok Exercise Training, 6-MWD: 6-min walk distance, PR: pulmonary rehabilitation, SET: Suandok Exercise Training, SGRQ: St. George's Respiratory Questionnaire.

The percentages of patients who achieved an MCID improvement in HRQoL and exercise performance are shown in Figure 1. Overall, 41.9% of patients met both MCID criteria for HRQoL and 6-MWD.

The results of the univariable and multivariable analysis of factors associated with being a PR responder are shown in Table 2. Factors associated with being a PR responder were baseline mMRC ≤1 (adjusted OR=19.56, 95%CI; 2.51, 152.22, *p*=0.005), baseline 6-MWD < 320 m (adjusted OR=13.09, 95%CI; 1.89, 90.57, *p*=0.009), baseline total SGRQ score ≥60 (adjusted OR=9.53, 95%CI; 1.64, 55.45, *p*=0.012), and receiving the mSET program (adjusted OR=7.72, 95% CI; 1.46, 40.79, *p*=0.016). However, age, sex, BMI, and cardiovascular comorbidity were not associated with

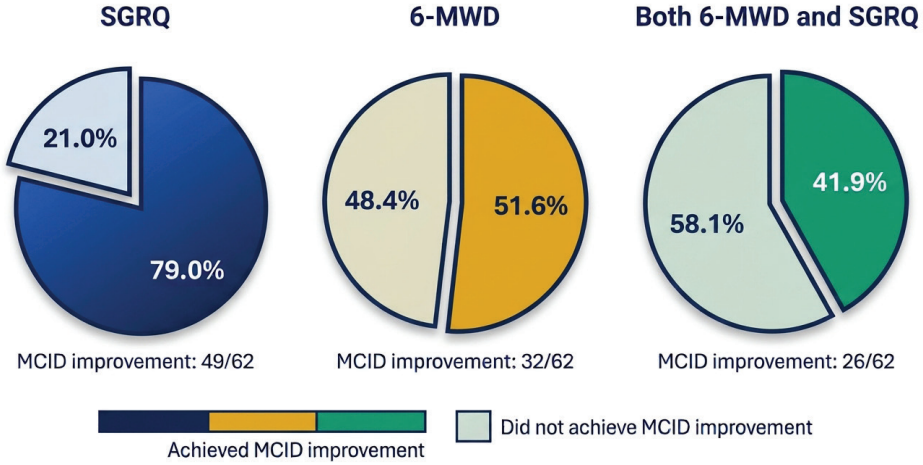

Figure 1. The percentages of patients who achieved an MCID improvement in HRQoL and exercise performance.

Table 2. Univariable and multivariable logistic regression analysis of the associated factors of a responder for pulmonary rehabilitation (MCID of SGRQ≥-4 units and MCID of 6-MWD≥54 meters).

Variables		Odds ratio (95%CI)	*p* value	Adjusted odds ratio (95%CI)	*p* value
mMRC score	2-4	Reference	0.103	Reference	0.005
	0-1	2.59 (0.83, 8.12)		19.56 (2.51, 152.22)	
6-MWD (meter)	≥320	Reference	0.103	Reference	0.009
	<320	2.67 (0.82, 8.73)		13.09 (1.89, 90.57)	
SGRQ score	<60	Reference	0.167	Reference	0.012
	≥60	2.06 (0.74, 5.77)		9.53 (1.64, 55.45)	
PR program	SET	Reference	0.215	Reference	0.016
	mSET	1.91 (0.69, 5.30)		7.72 (1.46, 40.79)	
Age (year)	≥70	Reference	0.427		
	<70	1.52 (0.54, 4.24)			
Gender	Female	Reference	0.417		
	Male	0.66 (0.24, 1.81)			
BMI (kg/m^2)	<18.5	Reference	0.477		
	18.5-22.9	1.23 (0.39, 3.85)			
	≥23	1.64 (0.42, 6.36)			
CV comorbidity	Yes	Reference	0.593		
	No	1.40 (0.41, 4.80)			

Notes: Results are expressed as adjusted odds ratios (OR) and 95% confidence intervals (95% CI). BMI: Body mass index, CV: cardiovascular, mMRC: modified Medical Research Council, mSET: modified Suandok Exercise Training, 6-MWD: six-min walk distance, PR: pulmonary rehabilitation, SET: Suandok Exercise Training, SGRQ: St. George's Respiratory Questionnaire.

success in the PR program.

Discussion

The present study examined the associations between clinical characteristics and clinical assessments and the benefits of an outpatient PR program (16 sessions over 8 weeks) incorporating supervised SET and mSET exercise training in 62 patients with COPD. Less severe dyspnea, lower exercise capacity, poorer HRQoL, and those receiving the mSET program were more likely to be associated with response to PR.

We defined PR response as achieving MCID-level improvements in both the SGRQ and the 6-MWD.[18,19] Twenty-six subjects (41.9%) were classified as responders for PR defined by reaching MCID for both the SGRQ and the 6-MWD. Our results were comparable with previous findings showing responders for PR defined by either SGRQ or 6-MWD ranged from 49.0-62.7% and 27.0-47.0%, respectively.[10,25] For the responder rate for PR defined by both SGRQ and 6-MWD, our result showed a higher rate of success when compared to the previous finding (41.9% versus 24.0%).[25]

Changes in HRQoL and 6-MWD have been used as the main outcome measures for PR.[8,9,14,15,25,26] Changes in exercise performance and quality of life are generally considered the most important outcome measures in PR suggested by the American College of Chest Physicians (ACCP) and the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR).[27] Therefore, the main aim of this study was to determine factors associated with positive outcomes, including HRQoL and exercise capacity, of PR in patients with COPD. Our study revealed that lower baseline dyspnea scores, poorer exercise performance, poorer HRQoL, and those receiving the mSET program were more likely to be associated with PR response. The strongest associated factor of good PR outcome was mMRC≤1. Our results were supported by the previous study, which indicated that higher severity of dyspnea measured by MRC showed smaller magnitudes of improvement than patients with lower severity of MRC.[10] However, Garrod *et al*. suggested that the mMRC should not be used as a primary ground for exclusion criteria of COPD rehabilitation.[10]

The other associated factor of a responder for PR in this study was a poorer HRQoL. Our study revealed that lower QoL at baseline (SGRQ≥60) was likely to be more successful in PR. The results are supported by the previous study showing that a lower baseline QoL was most likely to achieve the MCID for HRQoL.[25] This result indicates that subjects with a lower QoL are more likely to benefit from PR and demonstrate the greatest relative improvement.

The other factor related to good outcomes for PR in this study was poorer exercise performance. Our study showed that the participants with lower exercise capacity at baseline (6-MWD<320 meters) were more likely to have benefit from PR. The results were supported by several previous studies showing that lower baseline walking distance was most likely to achieve the MCID for exercise capacity.[26,28,29] Moreover, another study in asthma also found that subjects with low initial exercise capacity are more likely to benefit from PR.[30] Additionally, a previous study indicated that this could be due to the larger room for improvement that these patients may have from PR.[12]

Although the essential component of PR is exercise training, the SET and mSET programs represent interventions rather than baseline patient characteristics. In our multivariable model, participation in the mSET program was independently associated with a higher likelihood of being a PR responder compared with SET. This finding may reflect differences in exercise modality between the programs: mSET emphasized walking-based endurance training, whereas SET primarily used cycle ergometry. Because a key outcome used to define PR response in this study was improvement in 6-MWD, walking training may provide a more task-specific stimulus that directly translates to better performance on a walking-based test. Prior evidence supports the concept that task-specific training is more likely to yield improvements in corresponding functional outcomes,[31] which may partly explain the greater response observed among participants receiving mSET in our cohort.

However, our study was different from the previous studies that indicated a baseline BMI as the predictor for success in PR.[11,12] These studies showed that the higher baseline BMI (≥25 kg/m^2) was the strong predictor for the positive outcomes of PR. These differences in the results may be due to the differences in baseline BMI of subjects in our study and the others (20.0 vs 26.8-28.6).[11,12] Another reason is that almost all of the subjects in our studies (80.6%) were classified as underweight (BMI<18.5 kg/m^2) and normal (BMI 18.5-23.0 kg/m^2).[32] For these reasons, BMI was not a factor associated with positive PR outcomes in our study. However, this finding should be interpreted cautiously because BMI data in our cohort were clustered within a relatively narrow range (predominantly underweight to normal), which might have limited variability and reduced our ability to detect an association.

PR remains an essential component of COPD management. However, in real-world practice, limited program capacity, variable uptake, and heterogeneity in treatment response make appropriate patient selection and program allocation important considerations. In our study, PR response was more frequently observed among patients with less severe dyspnea, lower baseline exercise capacity, poorer baseline HRQoL, and those who participated in the mSET program. Collectively, these findings suggest that individuals with greater baseline impairment, particularly in exercise capacity and HRQoL, may experience greater relative gains following PR. From a practical standpoint, routinely available baseline assessments (e.g., dyspnea severity, the 6-MWT, and HRQoL measures such as the SGRQ) may help identify patients with potential for improvement, prioritize patient referrals in the condition with constrained resources, and tailor the mode and

intensity of PR (including consideration of mSET, where appropriate). Nevertheless, given the retrospective design and limited sample size, these results should be regarded as exploratory and hypothesis-generating. Therefore, no single baseline characteristic, including age, BMI, or comorbidity burden, should be interpreted as a definitive criterion for determining PR eligibility or for excluding patients from PR. Prospective studies with larger samples are needed to validate these potential predictors and to clarify how they can be incorporated into individualized PR planning and shared decision-making.

Limitations

Our study had several limitations. First, we did not assess several variables potentially associated with PR success, including muscle strength, physical activity, socioeconomic status, and educational level. These variables may influence responses to PR. Moreover, body composition was not included in the logistic regression, although a previous study suggested that greater muscle mass may be associated with better PR outcomes. [15] Secondly, most patients (82.3%) were classified as GOLD II–III, limiting the generalizability of the findings to patients with other GOLD classifications. Furthermore, the inclusion of only clinically stable patients with no acute exacerbation within the preceding 6 weeks, and the exclusion of those requiring LTOT, may limit generalizability to patients with more severe or clinically complex COPD. Thirdly, the small number of responders may have limited the statistical power of the multivariable logistic regression and increased susceptibility to overfitting and unstable effect estimates, as reflected by the wide confidence intervals. Fourthly, the analysis included only patients who completed all 16 PR sessions. Consequently, the findings may not apply to all patients undergoing PR, particularly non-completers. Fifthly, using baseline values, such as SGRQ and 6-MWD, to predict their corresponding change scores may introduce bias through mathematical coupling and regression to the mean. Additionally, dichotomizing continuous variables may reduce statistical power and obscure underlying dose–response relationships. Finally, the limited distribution of BMI in our sample may have reduced the statistical power to detect a true association between BMI and PR outcomes.

Future study

Future studies should assess muscle strength, physical activity, socioeconomic status, educational level, and body composition to clarify their potential associations with PR outcomes. Larger studies with sufficient numbers of responders are needed to confirm the findings and obtain more stable effect estimates. Future research should also include patients across a broader range of GOLD classifications, clinical conditions, and BMI values, as well as patients who do not complete PR, to improve generalizability. Analytical approaches that address mathematical coupling and regression to the mean, while retaining continuous variables where appropriate, should be considered to reduce potential bias and better characterize dose–response relationships.

Practical implications

Baseline dyspnea, exercise capacity, and HRQoL may help guide individualized assessment and expectations for PR. Patients with less severe dyspnea, lower exercise capacity, and poorer HRQoL were more likely to improve in both outcomes. The association between mSET and PR response warrants further evaluation. However, these findings should be interpreted cautiously and should not be used to exclude patients from PR.

Conclusion

Patients with less severe dyspnea, lower baseline exercise capacity, poorer HRQoL, and participation in the mSET program were associated with PR response in this cohort, suggesting that patients with greater baseline impairment, particularly in exercise capacity and HRQoL, may experience greater improvement after PR.

However, given the retrospective design and limited sample size, these findings should be considered exploratory, and no baseline characteristic, including age, BMI, or comorbidity, can be considered definitively associated with PR benefit.

Ethical approval

This study was performed in accordance with the guidelines from the Declaration of Helsinki. The study was approved by the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University with IRB approval number: MED-2559-04173, approval date: October 6, 2016. Participant consent was not required as the research was based on a retrospective review of previously collected non-identifiable information.

Declaration of generative AI and AI-assisted technologies

During the preparation of this manuscript, the authors used generative AI (Matthew AI (GPT-5.6 Terra)) for correcting grammar, sentence structure, spelling, punctuation, or formatting. All figures were also initially generated using Matthew AI (GPT-5.6 Terra) and subsequently reviewed, revised, and verified by the authors for scientific accuracy, terminology, and consistency with the content of this review. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of this article.

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Conflict of interest

The authors have no conflicts of interest in connection

with this work.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Chalerm Liwsrisakun: conceptualization, data curation, methodology, supervision, writing-original draft, review and editing; **Chaicharn Pothirat**: conceptualization, methodology, supervision, writing-original draft, review and editing; **Athavudh Deesomchok**: conceptualization, methodology, review and editing; **Warawut Chaiwong**: conceptualization, data curation, methodology, software, writing-original draft, review and editing, visualization. All authors have read and agreed to the published version of the manuscript.

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