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Research Article

Impact of Smoking Cessation Therapy on Pulmonary Function: Identification of Factors Predicting Improvement of Forced Expiratory Volume in 1s

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Abstract

Background: Stopping smoking has beneficial effects on pulmonary function, but few studies have investigated which factors predict a favorable outcome.

Methods: We analyzed the results of a prospective 3-month smoking cessation program. Smokers who had quit were defined as those abstaining from smoking between visits at 8 and 12 weeks (verified by exhaled carbon monoxide ≤10 ppm). Baseline pulmonary function was compared with that at the end of the program.

Results: From August 2007 to December 2020, 952 smokers participated in the program, of whom 509 completed it and had pulmonary function tests available before and after the program. We recorded the following differences in pulmonary function: Δforced vital capacity (FVC) = 0.054±0.364 L (p=0.0008), Δforced expiratory volume in 1s (FEV1)= 0.055±0.273 L (p<0.0001). An increase of FEV1 >100 mL was observed in 182 (35.8%) of the participants. We then compared these 182 with participants having no increase of FEV1 (n=327), finding significant differences between them in the presence of underlying conditions like COPD (31.3-vs-21.4%, P=0.014), bronchial asthma (20.9 -vs-11.6%, P=0.006) and baseline FEV1 (1.84±0.77 L-vs-2.20±0.74 L, <0.0001). Bronchial asthma (odds ratio [OR] 1.761, 95% confidence interval [CI]: 1.059, 2.926) and baseline FEV1 (OR 0.566, 95% CI: 0.431, 0.743) were independently significantly associated with an increase of FEV1 >100 mL by multivariate analysis.

Conclusions: Participation in our smoking cessation program resulted in significantly increased FVC and FEV1 overall, regardless of the actual success or failure of quitting smoking. Factors predicting FEV1 improvement were identified as bronchial asthma and baseline FEV1.

ABBREVIATIONS

CO: Carbon Monoxide; FEV1: Forced Expiratory Volume in 1s; FVC: Forced Vital Capacity; MMF: Maximal Mid-Expiratory Flow; PEF: Peak Expiratory Flow; TDS: Tobacco Dependence Screener.

INTRODUCTION

Tobacco use is associated with a substantial human and economic burden [1]. Accumulating evidence clearly shows that smoking is related to increased rates of a multitude of cancers, cardiovascular diseases and chronic lung diseases [2,3]. In the United States, >20 million people have died since 1964 due to smoking [3]. The number of people who smoke is declining but still 14% of adults in the US currently smoke cigarettes [4]. Similar rates of smoking in Japan have also been reported [5], and smoking constitutes the greatest threat of death from a noncommunicable disease among adults in Japan [6].

Quitting the smoking habit is associated with a reduced risk of tobacco-related harm to health [7]. For those patients with tobacco-related diseases, it is often the case that ceasing to smoke is the sole intervention effective at slowing disease progression. Hence, it is the most important aspect of treatment that a doctor can offer [3]. In Japan, 12 week-smoking cessation programs paid for by regular national health insurance have been approved for the last 17 years. Our center established a smoking cessation clinic in 2007 and implemented a full-scale smoking cessation program [7,8].-

Several studies have shown that stopping smoking has beneficial effects on pulmonary function [9-11], but few have investigated which factors predict a favorable outcome. Such information is important for motivating patients with nicotine dependence as well as for motivating physicians delivering the smoking cessation program. In addition, identifying patients´ characteristics associated with a favorable effect on pulmonary

function may offer avenues for interventions or identify populations to target. For these reasons, we investigated the impact of a standard smoking cessation program on pulmonary function in own program. We hypothesized that pulmonary function would be improved, particularly for participants who succeeded in quitting. Our primary objective was therefore to identify changes in pulmonary function after smoking cessation treatment, with the secondary objective of determining which factors predicted forced expiratory volume in 1s (FEV1) improvement.

MATERIALS AND METHODS

Study population

The Kobe City Medical Center West Smoking Cessation Registry is a physician-initiated, prospective, observational registry enrolling consecutive patients who participated in a 3-month smoking cessation program covered by the Japanese medical insurance system [12]. A total of 952 nicotine-dependent individuals participated between September 2007 and December 2020, of whom 515 completed the 3-month smoking cessation program. The other 437 participants who dropped out of the program because of lack of attendance were excluded from the study. Of those who completed the program, pulmonary function tests were not available or were incomplete at baseline or 12 weeks for only 6 participants. Hence, the study cohort consisted solely of participants who had complete pulmonary function tests both at baseline and 12 weeks later (n=509, Figure 1). Some participants in the present study had also been included in our previous study [12-14]. The study was conducted in accordance with the amended Declaration of Helsinki, with the written informed consent of all participants. The study was approved by the Institutional Review Board (Clinical Research) of Kobe City Medical Center West Hospital (Feb. 15, 2021. project approval #20-034).

Smoking cessation program

Our smoking cessation program has been extensively reported previously [8]. Briefly, to be enrolled in the program, participants had to have an interest in promptly stopping smoking, to have had a diagnosis of nicotine dependence according to the Tobacco Dependence Screener (TDS) test (≥5 points) [13], and to have a Brinkman Index [14] ≥200 when they were ≥35 years of age. Carbon monoxide (CO) in expired air was quantified by a Micro mobile breath CO monitor (Bedfont Scientific Limited, Kent, UK). All patients received either transdermal nicotine patches or varenicline (first marketed in Japan in May 2008) following discussion with the attending physician. The program consisted of five sessions, one at the baseline visit, and at 2, 4, 8, and 12 weeks thereafter. At each visit, CO concentration was measured, and the attending physician and a nurse with experience in smoking cessation program delivery determined whether the patient had been smoking. A patient was considered to have successfully quit smoking even if they still smoked at 8 weeks but had completely given up between the 8-week and 12-week follow-up visits. An exhaled CO level of ≤10 parts per million (ppm) was considered confirmation that the patient had remained abstinent. Patients who exhibited evidence of smoking between the 8- and 12-week visits were classified as continuous smokers.

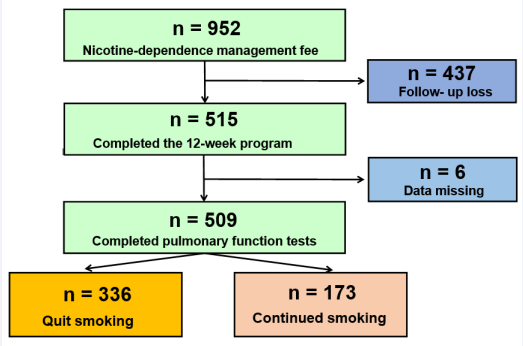

Figure 1 Flow chart showing exclusion and categorization of study participants.

Pulmonary function test

Lung volume was measured using a Chestac-65V (Chest M.I. Corp, Tokyo, Japan) according to the method described in the American Thoracic Society 1994 update [15] at baseline and at the 12 week-visit in the absence of recent bronchodilator use. Predicted normal lung volume values for the Japanese population were derived from the reference values of the Japanese Respiratory Society [17]. According to the minimal clinically-important difference (MCID) in COPD [18,19], we defined a change of 100 mL as an improvement of FEV1.

Statistics

Data were expressed as mean ± standard deviation (SD). Group differences were compared using the chi-square or Fisher's exact test for categorical variables, or the Student's t test or Mann-Whitney U test for continuous variables. A paired t test or Wilcoxon signed-rank test was used to compare the values for pulmonary function tests at the end of the program (12 weeks from baseline) with those at baseline. A $p<0.05$ level was accepted as indicating a significant difference. Multiple logistic regression analysis was used to determine independent predictors for FEV1 improvement and to estimate odds ratios (ORs) adjusted for possible confounding factors identified through univariate analysis ($p<0.10$). The 95% confidence interval (CI) for each OR was calculated, and statistical significance was determined from the 95% CI, not including 1.00 for logistic analyses. All analyses were performed using JMP statistical software (JMP, version 14.2; SAS Institute Inc., Cary, NC, USA).

RESULTS

Baseline characteristics of the study population

Baseline characteristics of study participants are given in Table 1, with 172 (34.0%) females and 336 (66.0%) males of mean age 61.7 ± 12.6 years and a mean smoking history of 39.3±12.6 years. The mean Brinkman index was 839.8±517.2, the

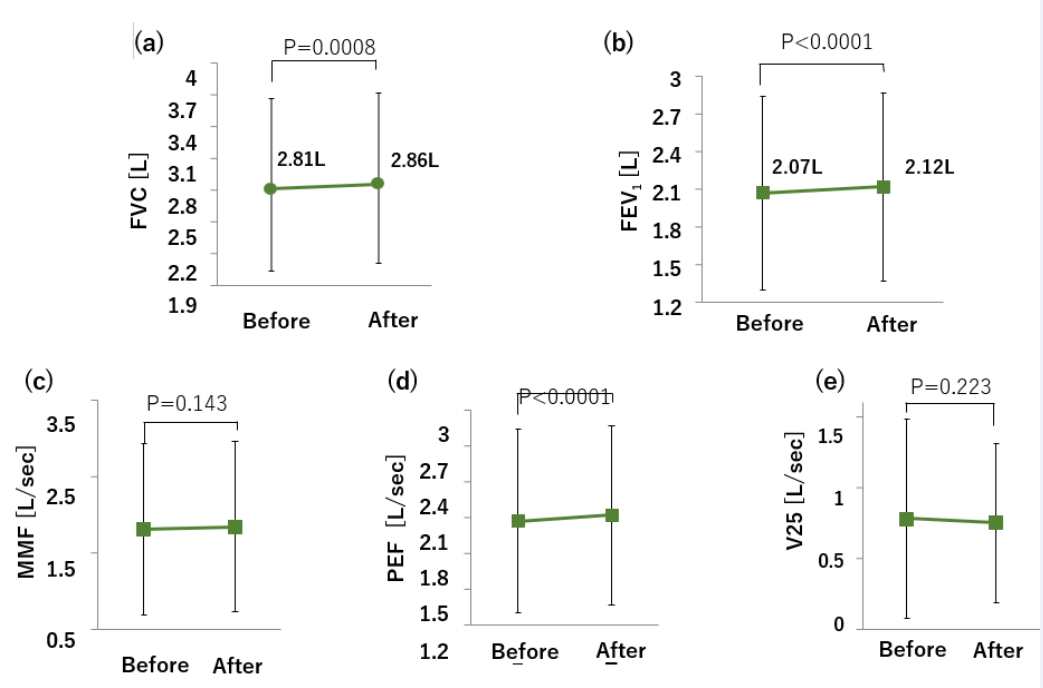

Figure 2 Changes in pulmonary function after the 12- week smoking cessation program
forced vital capacity (FVC)
forced expiratory volume in 1s (FEV1)
maximal mid-expiratory flow (MMF)
peak expiratory flow (PEF)
V25

mean TDS score was 7.7±1.6 and mean exhaled CO was 15.1±9.8 ppm. The mean FEV_1 was 2.07±0.77 L, mean FVC was 2.81±0.86 L and the mean FEV_1/FEV ratio was 73.2±12.6%.

Psychiatric disorders included insomnia in 145 of the participants (28.5%). Comorbidities included COPD (n=127, 25.0%), hypertension (n=120, 23.6%), cardiovascular disease (n=102, 20%), diabetes mellitus (n=95, 18.7%), bronchial asthma (n=76, 14.9%), gastric/duodenal ulcer (n=63, 12.4%) and cancer of any type (n=62, 12.2%).

Varenicline was prescribed to 219 (43.0%) of participants.

Changes in pulmonary function

The impact of the 12- week smoking cessation program on pulmonary function is shown in Figure 2 and Table 2. Changes in FVC (ΔFVC: 0.054±0.364 L, p=0.0008), FEV1 (ΔFEV1: 0.055±0.273 L, P<0.0001) and peak expiratory flow (PEF) (ΔPEF: 0.267±1.089 L/sec, p<0.0001) were statistically significant, while no such changes were seen for maximal mid-expiratory flow (MMF) or V25.

Effect of smoking cessation on pulmonary function and exhaled CO

Of the study participants, 336 (66.0%) were defined as having successfully quit smoking, but 173 (34.0%) were considered as continuous smokers at the 12-week follow-up time point. A comparison of changes in pulmonary function between these two groups is shown in Table 2. The changes post-smoking cessation therapy tended to be higher in those who quit, but with the exception of exhaled CO, statistical significance was not achieved. However, in both those who quit smoking and those who continued to smoke, significant changes in exhaled CO levels were observed, at -10.6± 8.2 ppm (p<0.0001) and -8.6±11.4 ppm (p<0.0001), respectively, yielding a significant difference between the two groups (p=0.026).

Comparison between participants with improved or not-improved FEV1

Among the study participants, an increase of FEV1 >100 mL was measured in 182 (35.8%). Results of univariate analysis of participants with an improved-vs-not improved FEV1 are shown in Table 3. The proportion of patients with COPD was significantly greater in the group exhibiting an improvement in FEV1 (31.3%-vs-21.4%, p=0.014). Similarly, the proportion of patients with bronchial asthma was significantly higher in the improved group (20.9%-vs-11.6%, p=0.006). Finally, baseline

Table 1: Baseline characteristics of the study population

Variable	Total (n=509)
Male sex	336 (66.0)
Age, years	61.7±12.6
Duration of smoking, years	39.3±12.6
Brinkman Index	839.8±517.2
TDS score	7.7±1.6
Exhaled CO, ppm	15.1±9.8
Body mass index, kg/m^2	22.8±4.5
Pulmonary function tests	
FEV1, L	2.07±0.77
FEV1, % predicted	75.7± 20.1
FVC, L	2.81±0.86
FVC, % predicted	83.8±17.6
FEV1/FVC, %	73.2±12.6
MMF, L/s	1.82±1.12
PEF, L/s	5.18±2.15
V25, L/s	0.78±0.70
Disease (self-reported)	
Mental disorder	145 (28.5)
Diabetes mellitus	95 (18.7)
Cardiovascular disease	102 (20.0)
Hypertension	120 (23.6)
COPD	127 (25.0)
Bronchial asthma	76 (14.9)
Cancer	62 (12.2)
Gastric/duodenal ulcer	63 (12.4)
Initial pharmacotherapy	
Nicotine patch	290 (57.0)
Varenicline	219 (43.0)

Notes: Data are presented as number (%) or mean ± standard deviation.
Abbreviations: TDS: Tobacco Dependence Screener; CO: Carbon Monoxide; FEV1: Forced Expiratory Volume In 1s; FVC: Forced Vital Capacity; MMF: Maximal Mid-Expiratory Flow; PEF: Peak Expiratory Flow

Table 2: Changes in pulmonary function and exhaled CO in the whole study population and a comparison between those who quit smoking and those who did not

	Total n=509	P value	Quitters n=336	Continuous smokers n=173	P value
ΔFVC, L	0.054±0.364	0.0008	0.062±0.382	0.040±0.326	0.519
ΔFEV1, L/s	0.055±0.273	<0.0001	0.059±0.290	0.047±0.238	0.621
ΔMMF, L/s	0.032±0.497	0.143	0.044±0.517	0.017±0.463	0.558
ΔPEF, L/s	0.267±1.089	<0.0001	0.306±1.128	0.212±1.041	0.363
ΔV25, L/s	-0.028±0.524	0.223	-0.038±0.603	-0.007±0.319	0.527
ΔExhaled CO, ppm	-9.9±9.4	<0.0001	-10.6±8.2	-8.6±11.4	0.026

Notes: Data are presented as mean ± standard deviation.
Abbreviations: CO: Carbon Monoxide; FEV1: Forced Expiratory Volume In 1s; FVC: Forced Vital Capacity; MMF: Maximal Mid-Expiratory Flow; PEF: Peak Expiratory Flow

pulmonary function (FEV1, % FEV1, FVC, %FVC, and FEV1/FVC), was significantly lower in participants with improved FEV1 after completing the 12-week smoking cessation program.

Predictors of smoking cessation-mediated FEV1 improvement

Multiple logistic regression analysis was done to determine independent predictors for FEV1 improvement (increase of FEV1 >100 mL) adjusted for possible confounding factors identified through univariate analysis in Table 3 (p<0.10). We selected

Table 3: Comparison between patients with improved-vs-not improved FEV1.

	FEV1 improved n=182	FEV1 not improved n=327	P value
Male sex	123 (67.6%)	213 (65.1%)	0.576
Age, years	61.9±13.5	61.6±12.0	0.784
Mental disorder	51 (28.0%)	94 (28.8%)	0.862
COPD	57 (31.3%)	70 (21.4%)	0.014
Bronchial asthma	38 (20.9%)	38 (11.6%)	0.006
Diabetes mellitus	27 (14.8%)	68 (20.8%)	0.094
Hypertension	42 (23.1%)	78 (23.9%)	0.843
Cardiovascular disease	33 (18.1%)	69 (21.1%)	0.420
Gastric/duodenal ulcer	24 (13.2%)	39 (11.9%)	0.680
Cancer	25 (13.7%)	37 (11.3%)	0.427
Initial pharmacotherapy Varenicline	74 (40.7%)	145 (44.3%)	0.421
Duration of smoking, years	39.4±13.4	39.2±12.1	0.836
Brinkman Index	859.4±532.8	828.8±508.9	0.523
TDS score	7.8±1.6	7.7±1.6	0.259
Exhaled CO, ppm	14.4±9.5 (n=181)	15.6±10.0 (n=326)	0.212
%FVC, %	78.7±17.8	86.7±16.8	<0.0001
FVC, L	2.64±0.86	2.90±0.84	0.0007
%FEV1, %	67.6±20.5	80.1±18.5	<0.0001
FEV1, L	1.84±0.77	2.20±0.74	<0.0001
FEV1/FVC, %	69.4±14.2	75.4±11.1	<0.0001
Quitters	128 (70.3%)	208 (63.6%)	0.123

Notes: Data are presented as number (%) or mean ± standard deviation.
Abbreviations: TDS: Tobacco Dependence Screener; CO: Carbon Monoxide; FEV1: Forced Expiratory Volume in 1s; FVC: Forced Vital Capacity

Table 4: Multiple logistic regression analysis of patients with improved-vs-not improved FEV1.

Variable	Odds ratio	95% confidence interval	P value
COPD	1.233	0.791, 1.922	0.356
Bronchial asthma	1.761	1.059, 2.926	0.030
Diabetes mellitus	0.717	0.431, 1.194	0.196
FEV1	0.566	0.431, 0.743	<0.0001

Abbreviations: FEV1: Forced Expiratory Volume in 1s

FEV1 among FEV1, % FEV1, FVC, %FVC, and FEV1/FVC for this. As shown in Table 4, bronchial asthma (OR 1.761, 95% CI: 1.059, 2.926) and lower baseline FEV1 (OR 0.566, 95% CI: 0.431, 0.743) were identified as independent predictors of a therapeutic response.

DISCUSSION

The major findings of this study can be summarized as (I) a 12-week standard smoking cessation program significantly improved lung function in the participants overall, but no significant differences in changes in lung function emerged in the comparison between those who quit smoking and those who continued to smoke; (II) a low baseline FEV1 predicted the smoking cessation program-mediated FEV1 improvement; (III) baseline bronchial asthma, but not COPD, predicted FEV1 improvement.

Several studies have documented that stopping smoking prevents loss of FEV1 [20]. Although the time course of these studies was very different, ranging from weeks to years, complete

abstinence for as little as 4 weeks was reported to be associated with improvement in lung function [21]. In our study, a standard 12-week smoking cessation program resulted in significantly increased FVC, FEV1, and PEF. Although we hypothesized that smoking cessation treatment would improve pulmonary function especially in those who succeeded in quitting, no significant differences were found when comparing changes in lung function between those who stopped smoking and those who continued to smoke. Notably, when study subjects were divided into two groups based on MCID of FEV1, the proportion of those who quit-vs-those who did not were no different [Table 3]. The tendency to enjoy an increased post-program FVC, FEV1, MMF and PEF in participants who continued to smoke suggests that even smoking reduction rather than complete abstinence may have beneficial effects on lung function, contrary to results presented from a previous study [22]. Despite a significant difference in changes in exhaled CO levels between those who quit and those who continued to smoke, significant changes in exhaled CO levels were observed not only in the former but also the latter. Rennard et al., investigated the bronchoalveolar lavage of heavy smokers who had reduced their cigarette consumption and found that smoking reduction, like smoking cessation, also reduced airway inflammation [23]. However, our previous study on the outcomes of a successful smoking cessation program in COPD patients showed that significant changes in pulmonary function, such as FEV1 and PEF, were not present in individuals who continued to smoke, but only in those who quit [12].

The results of multiple logistic analysis showed that bronchial asthma and low baseline FEV1 predicted increased FEV1. Scanlon et al., reported that lower baseline lung function predicted a greater benefit from smoking abstinence [10]. In the same report, subjects were stratified by the amount of baseline cigarette consumption and lung function was compared after one year. A greater decline in FEV1% was recorded depending on the number of cigarettes smoked, while lung function improved more in heavy smokers. It was also shown that accelerated decline in FEV1 independently predicted a higher risk of cardiovascular death [24]. These results suggest that heavy smokers benefit the most from quitting smoking.

Interestingly, bronchial asthma as a comorbid disease, but not COPD, predicted whether increased FEV1 was achieved by smoking cessation therapy. It was previously reported that airway inflammation persists not only in smokers but also in COPD patients who do not currently smoke [25]. Chronic bronchitis and emphysema are major clinical phenotypes of COPD [26]. Smoking-related airway inflammation induces chronic bronchitis, leading to emphysema. This process is characterized by infiltration of inflammatory cells such as neutrophils, macrophages and lymphocytes into the terminal airways. This results in protease-mediated disruption of bronchioles and alveoli. On the other hand, it was reported that desisting from smoking for only 24 hours was sufficient to increase peak flow and airway conductance in asthmatic patients [27]. Another study also showed that smoking cessation therapy could improve lung function as early as one week after beginning the program, which further improved up to 6 weeks thereafter, accompanied by a reduction in sputum neutrophil count [28]. It was thought that Th2-driven eosinophilic inflammation is a main pathway in this context, but a recent study revealed that multiple inflammatory phenotypes are involved in the pathophysiological condition of bronchial asthma [29]. Because neutrophilic inflammation also plays an important role in the pathophysiology of asthma, smoking abstinence in asthmatic patients is indispensable. Moreover, it was reported that smoking attenuated the response to inhaled corticosteroid in asthmatics [30]. The mechanisms responsible for such poor responses to inhaled corticosteroid are not well understood, and neutrophilic inflammation, altered glucocorticoid receptor expression, and overexpression of inflammatory genes in alveolar macrophages might all be involved [31]. Scanlon et al. reported that smoking cessation resulted in much greater improvements in lung function in patients with higher airway responsiveness than in those who were less responsive [10]. This difference in inflammatory processes and airway responsiveness may explain the prompt improvement of lung function on stopping smoking in asthma patients.

Although it is conceivable that extending the follow-up period might have allowed the detection of similar changes also in COPD patients, a previous study reported that the increased FEV1 resulting from smoking cessation therapy peaked at 6 weeks and declined again by 12 weeks [32]. Another study showed that improvement in FEV1 following smoking abstinence had not been sustained at a one- year follow-up [33].

A number of limitations to the present study should be recognized. First, all participants were enrolled at a single medical center in Japan and the study spans a long period. Second, the number of patients with specific complications may have been underestimated because all diagnoses and complications were self-reported. Third, despite the short-term outcomes reported here, no information on long-term success rates of our smoking cessation program is available. Clearly, the real success of such a program in terms of longer follow-up is needed. Fourth, not enough data on pharmacotherapy for bronchial asthma or COPD during the 3-month smoking cessation program were available, and it may have been the case that any changes in the treatment for these diseases influenced our results.

CONCLUSIONS

The present study showed that participation in a program of standard smoking cessation therapy resulted in significantly increased FVC and FEV1 overall, regardless of the actual success or failure of quitting smoking. Bronchial asthma and lower baseline FEV1 were related to smoking cessation-mediated improvement in FEV1. We conclude that smoking cessation therapy should be recommended even in nicotine-dependent patients with poor lung function.

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AUTHOR CONTRIBUTIONS

H.T. designed the concept. M.I., R.H., and H.T. were involved in the research, selection of patients, and collection of data. H.T. curated the data and performed statistical analysis. M.I. wrote the main manuscript. All the authors have read and approved the final manuscript.

REFERENCES

1. Amaral AL, Lwaleed BA, Andrade SA. Electronic nicotine delivery systems (ENDS): a strategy for smoking cessation or a new risk factor for oral health? Evid Based Dent. 2023; 24: 188-189.
2. AL Amaral, PA da Costa Andrade, BA Lwaleed, SA Andrade. Tobacco Dependence- A Comprehensive Guide to Prevention and Treatment. Evid Based Dent. 2023; 24: 150.
3. Eakin MN, Hasmeena KE. Tobacco Dependence: A Comprehensive Guide to Prevention and Treatment. Springer Nature. Splinger. 2023.
4. Cornelius ME, Loretan CG, Wang TW, Jamal A, Homa DM. Tobacco Product Use Among Adults -United States, 2020. MMWR Morb Mortal Wkly Rep. 2022; 71: 397-405.
5. Ministry of Health, Labour and Welfare J. The National Health and Nutrition Survey in Japan, 2019. 2019; 87: 1-234.
6. Ikeda N, Inoue M, Iso H, Ikeda S, Satoh T, Noda M, et al. Adult mortality attributable to preventable risk factors for non-communicable diseases and injuries in Japan: A comparative risk assessment. PLoS Med. 2012; 9: e1001160.
7. US. Department of Health and Human Services. Smoking Cessation: A Report of the Surgeon General. National Library of Medicine Cataloging-in-Publication Data. 2020.
8. Tomioka H, Wada T, Yamazoe M, Yoshizumi Y, Nishio C, Ishimoto G. Ten-year experience of smoking cessation in a single center in Japan. Respir Investig. 2019; 57: 380-387.
9. Pelkonen M, Notkola IL, Tukiainen H, Tervahauta M, Tuomilehto J, Nissinen A. Smoking cessation, decline in pulmonary function and total mortality: A 30 year follow up study among the Finnish cohorts of the Seven Countries Study. Thorax. 2001; 56: 703-707.
10. PD Scanlon, JE Connett, LA Waller, MD Altose, WC Bailey, AS Buist, et al. Lung Health Study Research Group. Smoking Cessation and Lung Function in Mild-to- Moderate Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2000; 161: 381-390.
11. Anthonisen NR, Connett JE, Murray RP. Smoking and lung function of Lung Health Study participants after 11 years. Am J Respir Crit Care Med. 2002; 166: 675-679.
12. 12.Tomioka H, Sekiya R, Nishio C, Ishimoto G. Impact of smoking cessation therapy on health-related quality of life. BMJ Open Respir Res. 2014; 1: e000047.
13. Tomioka H, Wada T, Yamazoe M, Yoshizumi Y, Nishio C, Ishimoto G. Ten-year experience of smoking cessation in a single center in Japan. Respir Investig. 2019; 57: 380-387.
14. Hashimoto R, Tomioka H, Wada T, Yoshizumi Y. Outcomes and predictive factors for successful smoking cessation therapy in COPD patients with nicotine dependence. Respir Investig. 2020; 58: 387-994.
15. Kawakami N, Takatsuka N, Inaba S, Shimizu H. Development of a screening questionnaire for tobacco/nicotine dependence according to ICD-10, DSM-III-R, and DSM-IV. Addict Behav. 1999; 24: 155-166.
16. Brinkman GL CE Jr. The Effect of Bronchitis, Smoking, and Occupation on Ventilation. Am Rev Respir Dis. 1963; 87: 684-693.
17. Sasaki H, Nakamura M, Kida K. Reference values for spirogram and blood gas analysis in Japanese adults. J Japanese Respirol Soc. 2001; 39: 1-14.
18. Jones PW, Beeh KM, Chapman KR, Decramer M, Mahler DA, Wedzicha JA. Minimal Clinically Important Differences in Pharmacological Trials. Am J Respir Crit Care Med. 2014; 189: 250-255.
19. Donohue JF. Minimal Clinically Important Differences in COPD Lung Function. COPD. 2005; 2: 111-124.
20. Burchfiel CM, Marcus EB, Curb JD, Maclean CJ, Vollmer WM, Johnson LR, et al. Effects of Smoking and Smoking Cessation on Longitudinal Decline in Pulmonary Funrtion. Am J Respir Crit Care Med. 1995; 151: 1778-1785.
21. Iwaoka M, Tsuji T. Twelve Weeks of Successful Smoking Cessation Therapy with Varenicline Reduces Spirometric Lung Age. Intern Med. 2016; 55: 2387-2392.
22. Bohadana AB, Nilsson F, Westin A, Martinet N, Martinet Y. Smoking cessation — but not smoking reduction — improves the annual decline in FEV 1 in occupationally exposed workers. Respir Med. 2006; 100: 1423-1430.
23. Rennard SI, Daughton D, Fujita J, Oehlerking MB, Dobson JR, Stahl MG, et al. Short-term smoking reduction is associated with reduction in measures of lower respiratory tract inflammation in heavy smokers. Eur Respir J. 1990; 3: 752-759.
24. 24.Tockman MS, Pearson JD, Fleg JL, Metter EJ, Kao SY, Pal KG, et al. Rapid Decline in FEV 1 A New Risk Factor for Coronary Heart Disease Mortality. Am J Respir Crit Care Med. 1995; 151: 390-398.
25. Rutgers SR, Postma DS, Hacken NHT, V HF Kauffman, Mark TW Van Der, Koëter GH, et al. Ongoing airway inflammation in patients with COPD who do not currently smoke. Thorax. 2000; 55: 12-18.
26. Wouters EFM, Reynaert NL, Dentener MA, Vernooy JHJ. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. American Thoracic Society. Am J Respir Crit Care Med. 1995; 152: S77-121.
27. Fennerty AG, Banks J, Ebden P, Bevan C. The effect of cigarette withdrawal on asthmatics who smoke. Eur J Respir Dis. 1987; 71: 395-399.
28. Chaudhuri R, Livingston E, Mcmahon AD, Lafferty J, Fraser I, Spears M, et al. Effects of Smoking Cessation on Lung Function and Airway Inflammation in Smokers with Asthma. Am J Respir Crit Care Med. 2006; 174: 127-133.
29. Brusselle G, Bracke K. Targeting immune pathways for therapy in asthma and chronic obstructive pulmonary disease. Ann Am Thorac Soc. 2014; 11: S322-328.
30. Suzuki K, Tanaka H, Kaneko S, Nishi M, Teramoto S, Itoh S, et al. Respiratory symptoms and cigarette smoking in 3,197 pulmonologist-based asthmatic patients with a highly prevalent use of inhaled corticosteroid. J Asthma. 2003; 40: 243-250.
31. Zheng X, Guan W, Zheng J, Ye P, Liu S, Zhou J, et al. Smoking influences response to inhaled corticosteroids in patients with asthma: A meta-analysis. Curr Med Res Opin. 2012; 28: 1791-1798.
32. J Dhariwal, RC Tennan, DM Hansell, J Westwick, W Christoph, SP Ward, et al. Smoking Cessation in COPD Causes a Transient Improvement in Spirometry and Decreases Micronodules on High-Resolution CT Imaging. Chest. 2014; 145: 1006-1015.
33. Tashkin DP, Rennard S, Hays JT, Lawrence D, Marton JP, Lee TC. Lung function and respiratory symptoms in a 1-year randomized smoking cessation trial of varenicline in COPD patients. Respir Med. 2011; 105: 1682-1690.