Determining the effects of exercise after smoking cessation therapy completion on continuous abstinence from smoking: A study protocol

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Method Article

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Abstract

Background: Over the past few years, the rate of success for smoking cessation has improved markedly owing to the widespread availability of drug therapy; however, the quit rate 1 year after the beginning of therapy remains low at approximately 50%. Previous studies have demonstrated that exercise can relieve mental stress during continuous abstinence from smoking and curb the resumption of smoking. Nonetheless, very few studies have examined the effects of exercise therapy combined with continuous abstinence from smoking; those studies involved only a handful of patients. Thus, this study will examine continuous abstinence from smoking coupled with instructions on specific forms of exercise in individuals who are attempting to quit smoking but do not exercise. We aimed to determine the effects of implementing an intervention in the form of exercise instruction after smoking cessation therapy completion on continuous abstinence from smoking. If this study finds that exercise instruction increases the continuous abstinence rate, widespread implementation of the intervention is expected to reduce public smoking rate, promote health, reduce medical expenses, and greatly benefit the public.

Methods: We will enroll patients visiting a smoking cessation clinic (over a 3-month period) who have abstained from smoking in the second month after their initial visit as potential subjects and patients aged 20–75 years who do not exercise and who consent to participation in this study as subjects. We aim to enroll 300 patients. Subjects will be randomly assigned to one of the following two groups: an intervention group actively given exercise instruction in addition to the standard instruction and a control group given the standard instruction. The status of the two groups will be assessed after 9 months. The intervention group will receive instruction on exercises that can be incorporated into their daily lives. Additionally, members of this group will be lent a pedometer and encouraged to record their daily step count, level of activity, and weight during follow-up. The control group will be followed during the standard smoking cessation support program. The primary endpoint will be the continuous abstinence rate, and secondary endpoints will be weight, blood pressure, exhaled carbon monoxide concentration, psychological state, and blood test results. These indices will be compared between the intervention and control groups; the study will be conducted over a 9-month period.

Discussion: By examining the effects of exercise instruction after 12-weeks smoking cessation therapy completion (covered by the National Health Insurance), this study will yield quality information for the development of protocols to improve the continuous abstinence rate and inhibit weight gain after smoking cessation therapy.

Trial registration: The study is registered at UMIN Clinical Trials Registry (UMIN000014615). Registered on 1st October, 2014.

Keywords: Smoking cessation, exercise, weight gain, obesity

Background

Smoking is a major health issue in Japan

Smoking is a major health issue associated with the development of malignancies and respiratory diseases as well as the development of cardiovascular diseases such as cerebrovascular disease and ischemic heart disease. The Japan Collaborative Cohort Study of 95,000 Japanese indicated that smoking increases the risk of dying from cardiovascular disease by 1.6–2.0-fold. Moreover, numerous cohort studies on Japanese subjects have found that the population attributable risk of cardiovascular disease due to smoking is approximately 20% for men and >5% for women[1)]. The smoking rate in Japan is 30% for men and 10% for women. Despite a steady decline over the last few

decades, smoking rates remain high in developed countries[2]. In Japan, >1 million people have developed conditions related to smoking such as malignancies, cerebrovascular diseases, or cardiovascular diseases, and the medical expenses attributed to smoking (including conditions related to passive smoking) are calculated to be as high as 1.49 trillion yen[3]

Quitting smoking promotes public health

Quitting smoking is known to have numerous preventive effects, such as an improved prognosis for cardiovascular disease[4]. Furthermore, the symptoms of chronic bronchitis improve 1–2 months after smoking cessation, patients with mild–moderate chronic obstructive pulmonary disease have improved pulmonary function 1 year after quitting smoking, the risk of coronary artery disease decreases in 2–4 years, patients with a history of coronary artery disease have about a 35% lower risk of recurrence or death, and former smokers have a rate of diminished pulmonary function equivalent to that of nonsmokers after 5 years. Moreover, individuals aged 40–59 years who attempt quitting smoking have a significantly lower risk of incurring massive medical expenses in the future than continuing smokers, and individuals attempting to quit smoking have a reduced risk of massive medical expenses similar to that of lifetime nonsmokers[5]. Thus, actively promoting smoking cessation should markedly inhibit the development of cardiovascular disease and vastly reduce medical expenses.

Smoking cessation aids lack sufficient long-term effectiveness

Over the past few years, the rate of success for individuals quitting smoking has markedly improved owing to the widespread availability of drug therapy at smoking cessation clinics. Since its introduction in the Japanese market in 2008, the oral smoking cessation aid varenicline tartrate in particular has greatly improved the rate of success immediately following smoking cessation therapy completion. However, the continuous abstinence rate drops to approximately 50% 1 year after therapy initiation[6]. This means that providing support to individuals attempting to quit smoking to help them avoid resuming the habit is an urgent task for medical personnel.

Exercise can improve the quit rate

Exercise can relieve mental stress during continuous abstinence from smoking and curb the resumption of smoking[7]. A systematic review of the efficacy of exercise on curbing the resumption of smoking showed that exercise helped to curb smoking resumption in 12 of 14 studies[8]. A meta-analysis similarly indicated that exercise as part of a cardiac rehabilitation program significantly reduced the smoking rate[9]. Active incorporation of exercise may lead to improvements in the quit rate.

Exercise can inhibit weight gain after quitting smoking

Weight gain typically occurs after smoking cessation. A recent meta-analysis noted an average weight gain of 4.7 kg 1 year after subjects quit smoking[10]. Weight gain after smoking cessation can lead to the resumption of smoking, and the prevention of weight gain is a vital aspect of smoking cessation support. In fact, Japanese smoking cessation programs using drug therapy provide instruction primarily in the form of diet and cognitive behavioral therapy; however, numerous studies have reported that such programs do not necessarily result in adequate weight control[11,12]. Explaining specific forms of exercise to individuals who are attempting to quit smoking and do not exercise should help to improve the rate of success for quitting smoking and also help facilitate subsequent weight control.

Given this context, numerous intervention studies overseas have examined the effects of combining exercise instruction with drug therapy. However, few studies had a large enough sample size, and the effects of adding exercise instruction are still unclear[13].

Study objective

The aim of this study is to determine the effects of exercise instruction provided after 12-weeks smoking cessation therapy completion (covered by the National Health Insurance) on continuous abstinence from smoking.

Methods

Study design

This will be a multicenter intervention study with centralized enrollment (prospective random allocation).

Sample size

Subjects will be allocated to one of the following two groups: an exercise intervention group actively given exercise instruction in addition to the standard instruction and a control group given the standard instruction. Subjects will be followed for 9 months after enrollment, and the target enrollment is 300 subjects (150 in the intervention group and 150 in the control group).

A previous study involving a limited number of patients examined the effects of adding exercise instruction after drug therapy with a nicotine patch. The addition of exercise instruction increased the odds ratio of successful smoking cessation 3-fold after 6 months[14]. If the addition of exercise instruction after the anticipated conclusion of drug therapy is estimated to increase the odds ratio 2-fold after 9 months and the standard therapy group is estimated to successfully quit smoking at a rate of 50%, then with a power of $1-\beta = 0.8$ and a type I error of $\alpha = 0.05$ the minimum sample size would be 134 subjects per group, for a total of 268 subjects in both groups. Assuming the dropout rate during the study is 10%, a randomized intervention study with 150 subjects per group, for a total of 300 subjects in both groups, will be necessary.

Subjects

Patients who have abstained from smoking during the last month while undergoing the standard smoking cessation therapy (3 months after the initial visit).

Inclusion criteria

Individuals who have abstained from smoking during the last month while undergoing the standard smoking cessation therapy (3 months after the initial visit) and fulfilling the following will be included:

1. Individuals who do not exercise*
2. Age: 20–75 years
3. Individuals who agree to the purposes of this study and who provide consent in writing

*Individuals who did not answer “I have continued to exercise 30 minutes a day at least twice a week for over a year” on a questionnaire.

Exclusion criteria

Patients fulfilling any of the following items apply will be excluded:

1. Individuals prohibited from exercising by their physician (individuals for whom exercise is contraindicated)
2. Individuals who would have difficulty exercising due to a condition such as an orthopedic disorder, neuromuscular disease, or peripheral vascular disease
3. Pregnant women
4. Inpatients or residents of a facility
5. Patients whose participation in this study has otherwise been deemed inappropriate by their primary physician

Discontinuation criteria

This study will be discontinued in the event of any of the following:

1. Continuing this study is not feasible due to adverse events
2. This study cannot be continued due to patient withdrawal or withdrawal of consent
3. Subjects are deemed to meet exclusion criteria or subjects are deemed ineligible after enrollment
4. Female patients who are deemed to be pregnant
5. Marked noncompliance
6. The study itself is discontinued
7. If an investigator otherwise deems that continuing this study would not be feasible

Ethical considerations

All procedures will be in accordance with the ethical standards of the facilities involved and those of domestic research councils and in accordance with the 1964 Helsinki Declaration and its subsequent amendments or comparable ethical standards.

Study protocol

An overview of the proposed study protocol is shown in Fig. 1.

Allocation

Subjects will be centrally allocated using the Electronic Data Capture (EDC) system of the University Hospital Medical Information Network.

After consent is obtained in writing from patients who meet the selection criteria, the lead investigator will verify that patients meet all of the eligibility criteria and none of the exclusion criteria, and subject information will be registered in the EDC system. After registration, the EDC system will assign patient numbers that do not include a patient's personal information. Immediately after entry, the EDC system will randomly assign subjects to one of the two groups (the exercise instruction group or the standard instruction group) via dynamic allocation.

Allocation and allocation adjustment factors

Confounding factors (age, sex, the number of cigarettes smoked per day, the score on the Fagerstrom Test for Nicotine Dependence, and the score on a Self-rating Depression Scale) will be adjusted between the two groups via registration in the EDC system. Subjects will be randomized by minimization (i.e., a method of dynamic allocation).

Intervention

Acquisition of data at the beginning of the study

Patient characteristics (sex, age, past medical history, history of the present illness, alcohol consumption, medications taken and their type, and psychological state), blood chemistry [white blood cell count; red blood cell count; hemoglobin level; hematocrit; platelet count; fasting blood glucose level; and total cholesterol (T-cho), HDL cholesterol (HDL-cho), and triglycerides (TG) levels], and measurements (height, weight, blood pressure, and the concentration of exhaled carbon monoxide) at the beginning of the study will be examined. Smoking status (years of smoking, the number of cigarettes smoked, the score on the Tobacco Dependence Screener, the score on the Fagerstrom Test for Nicotine Dependence, age when the individual started smoking, smokers in the family, and the number of previous attempts to quit smoking) will be as noted in an interview during the initial visit to the smoking cessation clinic.

Exercise intervention group

Upon smoking cessation therapy completion: Subjects will be informed of the significance of active exercise while attempting to quit smoking. Subjects will receive an activity tracker for the duration of the study and instructed on exercises to increase and maintain the amount of their physical activity as part of their daily lives.

Setting of exercise goals

During follow-up, subjects will individually record their daily step count, level of activity, and weight. A regular follow-up will be conducted approximately 2–4 times. During the regular follow-up, subjects will be given feedback based on their individual logs, exercise goals will be adjusted, and subjects will be encouraged to maintain the amount of their physical activity and to control their weight. Exercise instruction will be provided in accordance with an exercise instruction manual compiled under the supervision of a certified fitness instructor and a certified cardiac rehabilitation specialist.

Standard therapy group

This group will be followed during the course of the standard smoking cessation program.

Upon conclusion of smoking cessation therapy, subjects will not be actively advised to exercise; therefore, further exercise instruction will not be provided.

Subjects will receive an activity tracker after smoking cessation therapy completion and 8 months after the beginning of the study. They will return the tracker 1 month later in both instances.

Regular follow-up will be conducted approximately 2–4 times. During the regular follow-up, only indices will be ascertained, and subjects will not be given active instructions to exercise.

Items studied during the study and during follow-up

The study will begin on the day the subjects are given the activity tracker. The follow-up period will be 9 months for both groups. In addition to face-to-face, follow-up can be conducted by mail, telephone, or online. Subject status will be ascertained at the beginning of the study and 1 month, 8 months, and 9 months later.

Continuous abstinence from smoking, psychological state, medications taken and their type, blood chemistry (white blood cell count; red blood cell count; hemoglobin level; hematocrit; platelet count; fasting blood glucose level; and T-cho, HDL-cho, and TG levels), and measurements (height, weight, blood pressure, and the concentration of exhaled carbon monoxide) will be assessed for both groups after 9 months.

Items observed and studied

Primary endpoint: Continuous abstinence rate*

*An individual is deemed to have continuously abstained from smoking when he or she reports that he or she has not smoked in the past week during an interview and the concentration of exhaled carbon monoxide is ≤7 ppm[12)].

Secondary endpoints: Changes in metabolic indices (height; weight; blood pressure; exhaled carbon monoxide concentration; red blood cell count; white blood cell count; hemoglobin level; hematocrit; platelet count; fasting blood glucose level; and T-cho, HDL-cho, and TG levels) and changes in an individual's psychological state (score on the Self-rating Depression Scale, depressive tendencies, and score on the Patient Activation Measure).

Analysis

Analysis set

The two groups, i.e., the exercise intervention and standard instruction groups, will be compared based on the intention-to-treat principle. All data on the metabolic indices and psychological states of the subjects in each group obtained upon enrollment and 9 months after enrollment will be analyzed. Only patients who have abstained from smoking (excluding patients who have resumed smoking) will be similarly analyzed. The continuous abstinence rate is defined as the proportion of patients who abstain from smoking with respect to all of the subjects in each group. Continuous abstinence from smoking is defined as being available for follow-up 9 months after enrollment, indicating abstinence from smoking during the past month in an interview, and having a concentration of exhaled carbon monoxide of ≤7 ppm.

Items analyzed and analytical methods

The characteristics of subjects in both groups will be described statistically. Mean values for changes in the metabolic indices and psychological states of the subjects from enrollment until 9 months after enrollment will be compared between the two groups. The distribution of individual indices at the baseline and 9 months after enrollment will be determined for the two groups, and a t-test or a Wilcoxon rank-sum test will be performed. In addition, Fisher's exact test will be used to compare the continuous abstinence rate in the two groups. The level of significance will be ≤0.05. A two-tailed alpha of 5% and a two-sided 95% confidence level will be used.

Early termination of this study

The decision to continue this study will be determined in any of the following situations:

1. When vital information regarding the safety or efficacy of this study is obtained
2. When achieving planned enrollment is deemed difficult
3. When continuing this study does not otherwise appear feasible

Discussion

Exercise has varied effects. These include osteoporosis prevention due to improvements in cardiovascular, musculoskeletal, and pulmonary function and increased muscle mass, obesity prevention due to fat reduction and increased muscle mass, dyslipidemia prevention due to reduced serum TG levels and increased HDL-cho levels, diabetes prevention due to the alleviation of insulin resistance, and hypertension prevention due to improved vascular endothelial function and reduced blood pressure[15,16]. Exercise is also effective in relieving stress and is an effective treatment for depression since it alleviates anxiety[17]. The 2013 Physical Activity Guidelines to Promote Health were formulated in Japan in 2013[18], and exercise is an important component of those guidelines.

Individuals are known to gain weight after quitting smoking[19]. Weight gain worsens glucose tolerance[20-22] and can lead to the resumption of smoking[23, 24]. In this study, simple and safe exercises that can be easily performed by individuals who have gained weight after quitting smoking will be performed in accordance with a cardiac rehabilitation program. Subjects will record their weight and step count, which should increase their self-efficacy. This study combines smoking cessation therapy and exercise therapy. If the study shows that exercise instruction improves the continuous abstinence rate, then widespread implementation of the intervention is anticipated to reduce the public smoking rate, help to promote health, reduce medical expenses, and greatly benefit the public.

Declarations

Trial status

This study protocol is first version since December 10th, 2015. Recruitment began at March 30th 2016, and expected recruitment completion date is December 2019. At the time of manuscript submission, recruitment for this study was ongoing.

Abbreviations

EDC: Electronic Data Capture; FTND: Fagerström Test for Nicotine Dependence; SDS: Self-rating Depression Scale; T-cho: total cholesterol; HDL-cho: HDL cholesterol; TG: triglycerides

Ethics approval and consent to participate

Informed written consent was obtained from all participants. The Ethical Review Board, National Hospital Organization, Kyoto Medical Centre approved the study protocol. Central ethical approval has been confirmed from the ethical review board, National Hospital Organization, Kyoto Medical Centre (approval no. 14-090) and we will not begin recruiting at other centres in the trial until local ethical approval has been obtained.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that there are no conflicts of interest.

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Author's contributions

Study conception and design were contributed by YO, MK, KU, HI, SS, AM, MT, SN, YK, YK and KH. acquisition of data was made by YO, MK, YT and KH. Drafting of manuscript was made by YO, and critical revision was made by MK and KH. All authors reviewed and approved the final manuscript.

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Figures

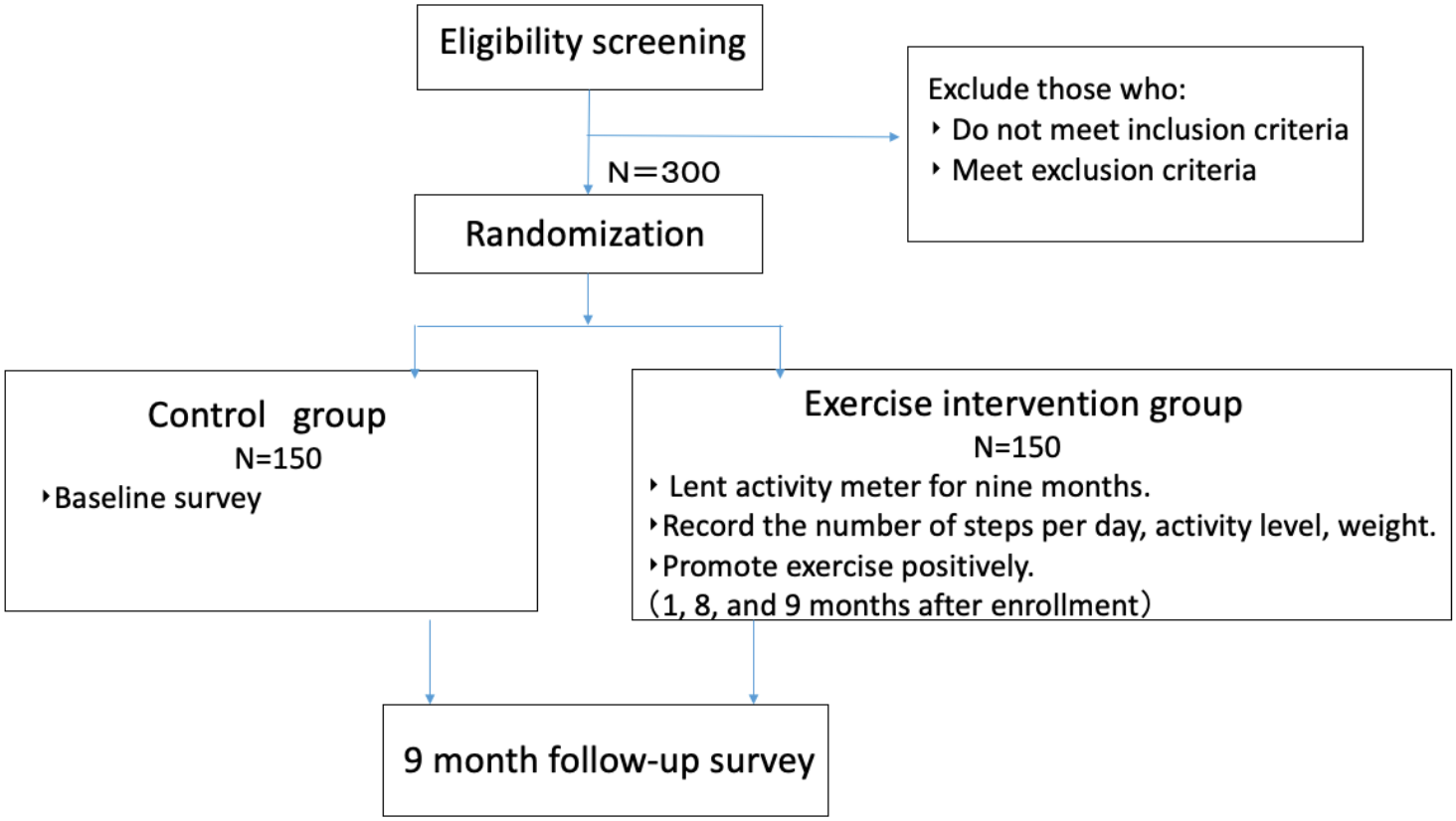

Figure 1

Overview of the study protocol.

STUDY PERIOD	Screening	Allocation	Visit 2	Visit 3	Close-out
	-4-0 weeks	*0 week*	*1 month*	*8 months*	*9 months*
ENROLMENT:					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
INTERVENTIONS:					
intervention group (Exercise guidance)			X	X	
control group					
ASSESSMENTS:					
Physical examination	X				X
Laboratory examination		X			X
Self-rating Depression Scale		X			X
Questionnaire		X			X
Smoking status	X		X	X	X
Exhaled carbon monoxide	X				X

Figure 2

The schedule of enrolment, interventions, and assessments.

Supplementary Files

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- supplement1.doc