The Impact of Aversive Advice During Percutaneous Coronary Intervention on Smoking Cessation in Patients With Acute Coronary Syndrome

Check for updates

Byung Sik Kim[†],*, Young-Hyo Lim[†],*, Jeong Hun Shin[‡], Seok Hyeon Kim[§], Sungwon Roh[§], Yeon Woo Choi[†], Jinho Shin[†], Jin-Kyu Park[†], Kyung-Soo Kim[†]

Seoul, and Guri City, Republic of Korea

ABSTRACT

Background: Smoking cessation is important to prevent recurrence of acute coronary syndrome (ACS), but even in patients with ACS, smoking is hard to quit.

Objectives: This study hypothesized that aversive advice during the percutaneous coronary intervention (PCI) procedure works effectively to promote smoking cessation in patients with ACS.

Methods: This study was conducted as a prospective, single-blinded, randomized controlled trial. A total of 66 patients were randomly assigned to an aversive advice group or a control group and instructed to visit the outpatient clinic 1, 4, and 24 weeks after discharge. In the aversive advice group, a physician who did not participate in the patient follow-up said the following 3 sentences to the patients during the PCI procedure: "Smoking caused your chest pain"; "If you do not stop smoking right now, this pain will come again"; and "The next time you feel this pain you will probably die." All patients received usual advice on the importance of quitting smoking.

Results: At 24 weeks after discharge, the smoking cessation rate was higher in the aversive advice group than in the control group. In a multivariable logistic regression analysis, after adjustment for age, smoking quantity, alcohol consumption, and disease severity, the result was maintained (odds ratio = 4.47, 95% confidence interval: 1.50 to 13.34).

Conclusions: Aversive advice during a PCI procedure is effective at smoking cessation in patients with ACS. A physician's attention and involvement during the PCI procedure improves the rate of smoking cessation in patients with ACS.

Smoking and cardiovascular disease have a causal relationship [1]. Smoking cessation is among the most important preventive measures in preventing the development of cardiovascular disease [2,3]. It is well known that smoking cessation reduces the risk of coronary artery disease (CAD) not only in the general population, but also in patients who survive CAD. Patients who quit smoking after the development of CAD have a significantly lower risk of recurrent myocardial infarction or cardiovascular death than do patients who continue smoking [4-6].

There are several well-known smoking cessation treatments, including behavioral and pharmacological treatment [7,8]. With optimal treatment, 25% to 35% of smokers who try to quit can succeed for 6 months or more [9]. However, these data were conducted with a generally healthy population, and the generalizability of these data to patients with CAD is unclear [10]. This unclear generalizability is demonstrated by trials that found that the smoking cessation drug bupropion did

not increase the prevalence of abstinence in patients with acute coronary syndrome (ACS) [11,12]. This may be caused by characteristic differences of patients, who tend to have higher quit rates because of an increased motivation to quit and the teachable moment that occurs after an adverse event [13]. So, if a patient undergoes an extremely fearful and painful experience, such as a percutaneous coronary intervention (PCI), the effect of aversive advice on smoking cessation might be increased.

Prior studies have investigated the effect of aversive conditioning on smoking cessation [14-16]. However, it is unclear whether it possesses any true value in promoting smoking cessation. The previous investigations included the general population and, as is presently understood, no study has evaluated the outcomes of aversive advice in patients with ACS. In this context, the hypothesis presented here is that aversive advice during a PCI procedure is indeed effective for smoking cessation in patients with ACS. Therefore, a randomized controlled
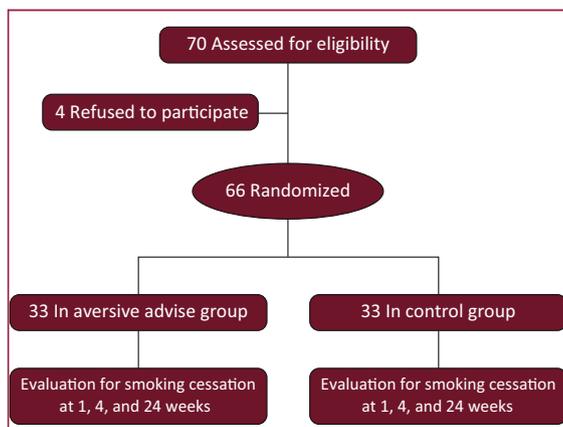
FIGURE 1. Flowchart of the patient assignment.

study was conducted to evaluate the impact of aversive advice during a PCI procedure on smoking cessation in patients with ACS.

TABLE 1. Characteristics of patients according to treatment group

	Total (N = 66)	Aversive Advice (n = 33)	Control (n = 33)	p Value
Age, yrs	55.9 ± 9.0	56.6 ± 10.1	55.3 ± 7.9	0.553
Female, %	2 (3.0)	2 (6.1)	0 (0.0)	0.492
Height, cm	168.3 ± 6.4	168.0 ± 6.5	168.6 ± 6.3	0.703
Weight, kg	72.0 ± 12.2	70.6 ± 11.7	73.5 ± 12.7	0.339
Body mass index, kg/m²	25.3 ± 3.5	24.9 ± 3.0	25.8 ± 4.0	0.287
Waist, cm	90.5 ± 6.9	89.6 ± 7.5	91.3 ± 6.4	0.391
Glucose, mg/dl	122.3 ± 36.6	127.1 ± 39.4	117.5 ± 33.6	0.290
Total cholesterol, mg/dl	181.7 ± 50.0	179.9 ± 49.5	183.5 ± 51.1	0.775
LDL cholesterol, mg/dl	116.4 ± 41.2	117.3 ± 38.9	115.5 ± 43.9	0.857
HDL cholesterol, mg/dl	39.9 ± 8.3	38.7 ± 9.4	41.1 ± 6.9	0.237
Triglyceride, mg/dl	158.0 ± 92.3	154.6 ± 103.5	161.5 ± 81.2	0.762
Hospital days	5.1 ± 3.0	5.4 ± 3.8	4.8 ± 1.9	0.439
Smoking duration, yrs	29.1 ± 10.6	30.2 ± 10.4	28.0 ± 10.9	0.409
Smoking, pack-yrs	30.7 ± 18.0	30.0 ± 16.0	31.4 ± 20.1	0.748
Fagerström test*	4.7 ± 1.1	4.6 ± 0.9	4.8 ± 1.3	0.784
Alcohol	33 (50.0)	25 (75.8)	19 (57.6)	0.191
Diagnosis				0.801
Unstable angina	18 (27.3)	8 (24.2)	10 (30.3)	
NSTEMI	18 (27.3)	10 (30.3)	8 (24.2)	
STEMI	30 (45.5)	15 (45.5)	15 (45.5)	
Multivessel disease	44 (66.6)	22 (50.0)	22 (50.0)	1.000
Education level				0.798
Elemental school	18 (27.3)	8 (24.2)	10 (30.3)	
Middle school	14 (21.2)	6 (18.2)	8 (24.2)	
High school	21 (31.8)	12 (36.4)	9 (27.3)	
University	13 (19.7)	7 (21.2)	6 (18.2)	
Hypertension	33 (50.0)	13 (39.4)	14 (42.4)	0.802
Diabetes mellitus	33 (50.0)	12 (36.4)	8 (24.2)	0.422

Values are mean ± SD or n (%).
LDL, low-density lipoprotein; HDL, high-density lipoprotein; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.
*Score ranges between 0 and 10.

METHODS

In total, 70 current smokers with ACS were identified for enrollment between September 1, 2014, and September 30, 2015 andata for enrolled patients were collected by May 31, 2016. The eligible criteria for inclusion in this study were patients who smoked cigarettes, had ACS, and were scheduled to undergo PCI with consciousness during the procedure. ACS included ST-segment elevation myocardial infarction (STEMI), non- STEMI, and unstable angina. STEMI was defined as chest pain or discomfort in conjunction with elevation of the ST-segment more than 0.1 mV in 2 or more contiguous electrocardiogram leads or a new left bundle branch block with elevated biomarkers of myocardial necrosis (cardiac troponin > upper normal limit). Non-STEMI was defined as chest pain or discomfort in conjunction with elevated biomarkers of myocardial necrosis and 1 of the following: (1) transient ST-segment elevation, transient ST-segment depression, or T-wave changes consistent with myocardial ischemia; or (2) identification of a culprit lesion at coronary angiography. Unstable angina was defined as (1) chest pain or discomfort occurring at rest or with minimal effort, (2) recent onset of chest pain or discomfort (<1 month), or (3) chest pain or discomfort with a recent increase in intensity, frequency, or duration without ST-segment elevation on the electrocardiogram or increased cardiac biomarker concentrations. Of these 70 patients, 4 patients declined to participate. Thus, 66 patients were included in the analysis (Fig. 1). The study was approved by the Institutional Review Board of Hanyang University Hospital (HYUH 2014-08-004-001), and written informed consent was obtained after PCI from each patient enrolled. The trial is registered at https://cris.nih.go.kr: KCT0003109.

This study was conducted as a prospective, single-blinded, randomized controlled trial. Before PCI were performed, patients were randomly assigned in a 1:1 ratio to the aversive advice group or the control group. Randomization was carried out using a computer-generated randomization list. In the aversive advice group, a physician who did not participate in the patient follow-up said the following 3 sentences to the patients during the PCI procedure: "Smoking caused your chest pain"; "If you do not stop smoking right now, this pain will come again"; and "The next time you feel this pain you will probably die."

To ensure that the investigator was unaware of study assignments, the investigator did not have any involvement in the aversive advice. During hospitalization, all patients received daily general advice about negative effects of smoking and the benefits of smoking cessation. Patients were also instructed to visit the outpatient clinic 1, 4, and 24 weeks after discharge. At every visit, urine nicotine metabolite (cotinine) levels were measured. Cotinine levels <50 ng/ml were considered to denote no active smoking [17,18]. The final assessment of smoking status was performed at 24 weeks after discharge (Fig. 1).

The sample size was determined using information from a preliminary study in which the smoking cessation
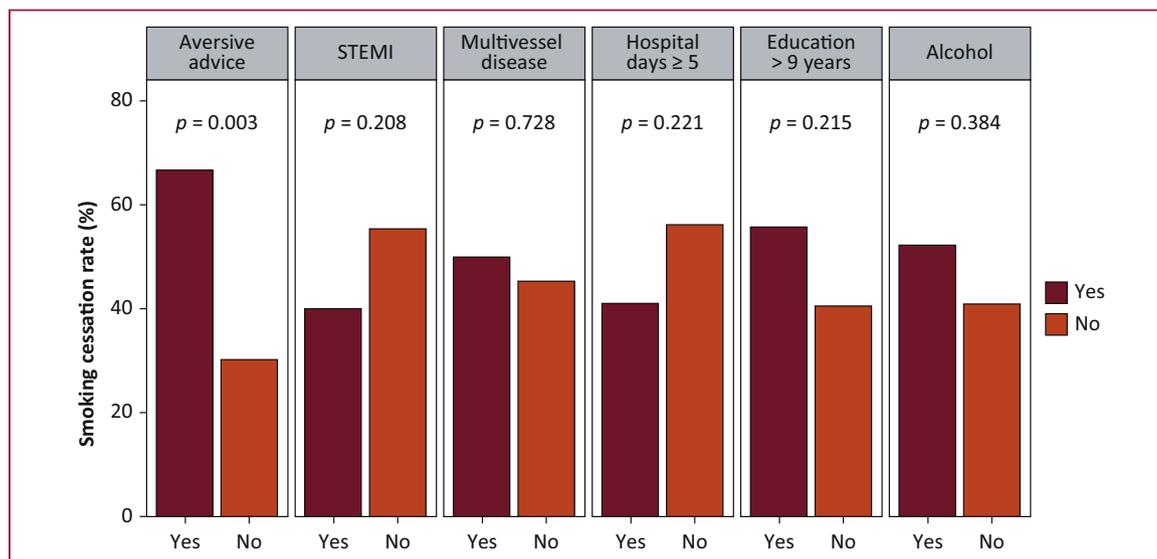
FIGURE 2. Smoking cessation rate according to the presence of clinical variables. STEMI, ST-segment elevation myocardial infarction.

rate was 73.3% (11 of 15) in the aversive advice group and 33.3% (5 of 15) in the control group. Assuming there was no drop-out in the study, at least 48 participants were needed in order to have a type I error of 5% and a power of 80%. So, the sample size of this study was determined to be 70 participants to secure enough statistical power. All continuous variables are reported as mean values with SDs and categorical variables are presented as numbers and percentages. The chi-square test was used to compare categorical variables, and Student's t-test was used to compare continuous variables. To estimate the effect of aversive advice on smoking cessation, logistic regression analysis was performed and the odds ratio and 95% confidence intervals were calculated. Two statistical models were fitted: model 1 adjusted for age and smoking quantity (pack-years) and alcohol consumption (yes or no); and model 2 adjusted for age, smoking quantity (pack-years), alcohol consumption (yes or no), STEMI (yes or no), multivessel disease (yes or no), and hospital days ≥ 5 (yes or no). Statistical analysis was performed using PASW version 18.0 (SPSS, Chicago, IL). A p value of <0.05 (2-tailed) was considered to indicate a statistically significant result.

RESULTS

The mean age of the subjects was 55.9 ± 9.0 years, and the number of female subjects was 2 (3.0%). Of the total 66 subjects, 30 subjects (45.5%) presented with STEMI, and 44 subjects (66.6%) had a multivessel disease. Baseline characteristics including smoking quantity, disease severity, education level, and cardiovascular risk factors were not significantly different between the 2 groups. Further descriptive data are displayed in Table 1.

At 24 weeks after discharge, smoking cessation rates were higher in the aversive advice group than in the control group, and there were no significant differences in smoking cessation rate with regard to other clinical variables (Fig. 2). Table 2 summarizes the effect of aversive advice during the PCI procedure on smoking cessation at different time points. The effect of aversive advice was significant and consistent over 24 weeks.

Table 3 shows the multivariable logistic regression analysis for the effect of aversive advice on change in smoking status. In a univariable model, aversive advice has a significant and positive effect on smoking cessation. After adjustment for age, smoking quantity as assessed by pack-years, and alcohol consumption, aversive advice was determined to have a significant effect on smoking cessation (model 1). When the variables of CAD severity, such as STEMI (yes or no), multivessel disease (yes or no), and hospital days ≥ 5 (yes or no), were added to model, the result was maintained (model 2).

TABLE 2. Comparison of smoking cessation rate according to treatment group at different time points

	Aversive Advice (n = 33)	Control (n = 33)	Odds Ratio (95% CI)	p Value
1 week	14 (42.4)	7 (21.2)	2.74 (0.93–8.08)	0.064
4 weeks	20 (60.6)	10 (30.3)	3.54 (1.28–9.81)	0.013
24 weeks	22 (66.7)	10 (30.3)	4.60 (1.63–12.9)	0.003

Values are n (%), unless otherwise indicated.
CI, confidence interval.

TABLE 3. Logistic regression analysis for the effect of aversive advice on smoking cessation

	Odds Ratio (95% CI)	p Value
Univariable		
Aversion therapy (yes vs. no)	4.600 (1.631—12.973)	0.004
Model 1		
Aversion therapy (yes vs. no)	4.360 (1.514—12.553)	0.006
Age (per yr increase)	1.010 (0.950—1.073)	0.751
Smoking (per pack-yr increase)	0.994 (0.965—1.025)	0.705
Alcohol (yes vs. no)	1.250 (0.372—3.930)	0.703
Model 2		
Aversion therapy (yes vs. no)	4.474 (1.501—13.339)	0.007
Age (per yr increase)	1.019 (0.952—1.090)	0.589
Smoking (per pack-yr increase)	0.994 (0.962—1.027)	0.721
Alcohol (yes vs. no)	1.229 (0.372—4.066)	0.735
STEMI (yes vs. no)	0.565 (0.173—1.839)	0.343
Multivessel disease (yes vs. no)	1.269 (0.400—4.027)	0.686
Hospital days ≥5 (yes vs. no)	0.571 (0.163—2.007)	0.383

Abbreviations as in Tables 1 and 2.

DISCUSSION

The work presented here demonstrates that aversive advice during PCI has a significant effect on smoking cessation in patients with ACS. In addition, it appears the effect of the aversive advice was maintained for 24 weeks after discharge.

In patients with ACS, the previously reported effects of pharmacological and behavioral interventions on smoking cessation were 31% to 56%, which is quite higher than in the general population [11,12,19,20]. In addition, usual brief care alone has reported up to a 51% of smoking cessation rate in patients with ACS [21]. The relatively higher smoking cessation rate of our study could be derived from characteristics of the study population. Considering that, our study showed that aversive advice is a simple and effective method to increase the rate of smoking cessation.

Many studies pertaining to smoking cessation did not obtain biochemical confirmation of smoking cessation (e.g., thiocyanate, carbon monoxide, or cotinine measurement). Indeed, there are some limitations in these self-reported measures because some respondents are embarrassed about their smoking habits and respond inaccurately [22-24]. Using biologic marker studies, Wilcox et al. [23] showed that the true percentage of previous smokers who actually had quit smoking was between 46% and 53%. Therefore, objective methods to estimate smoking status are needed.

There are conflicting results in the published data concerning the effect of aversive conditioning on smoking cessation. A study by Hymowitz and Eckholdt [15], in which the investigators used silver acetate for the aversive conditioning of smokers, showed that aversive conditioning initially brings about smoking cessation, but has no significant effect on long-term smoking cessation. Arzi

et al. [14] showed that olfactory aversive conditioning during sleep reduces smoking in short term. On the other hand, Suedfeld and Baker-Brown [16] showed that aversive conditioning is not effective for smoking cessation. Rapid smoking and other aversive smoking methods provide insufficient evidence to determine the efficacy [25]. The present work has demonstrated that aversive conditioning does seem to be effective at smoking cessation and lasts for at least 24 weeks. The main difference between prior studies and this one is the study population; the participants herein consisted of patients with ACS who experienced a scary medical event, possibly rendering the patients more compliant.

In this study, disease severity was not associated with smoking cessation rate. There was no significant difference in smoking cessation rate according to STEMI (yes or no), multivessel disease (yes or no), or hospital days ≥5 days (yes or no). In a multivariable logistic regression model, disease severity variables did not alter the effect of aversive advice on smoking cessation. The lack of a relationship was unexpected. It could be hypothesized that disease severity, recognized by patients, is shaped by a physician's advice and not by laboratory finding or diagnosis. Here, aversive conditioning was conducted with the same 3 sentences for all aversive advice group patients. Therefore, the aversive advice group patients might recognize their disease as having the same severity.

A previous study showed that smokers have a blunted response to aversive stimuli. The Dinh-Williams et al. study [26], in which functional magnetic resonance image was utilized, showed that aversive smoking-related stimuli elicited lower activation in the brain region associated with aversive processes (e.g., parahippocampal gyrus, insula, and inferior frontal gyrus) than aversive non-smoking-related stimuli did. However, in the current study, aversion therapy did have a significant effect on smoking cessation. This may be understood based on the fact that the patients exposed to aversive stimuli during the procedure, which included severe pain and fear of death, may have remembered the aversive stimuli more acutely than in other investigations. These findings might also be explained by the fact that the overwhelming experience could be very traumatic to the patients, so much so that they might remember the experience as a very painful and fearful episode. In other words, when the patients feel a craving for nicotine, they might recall the painful and fearful memory of the events such that the aversive emotion could be reconsolidated in the memory every time they get the urge to smoke. This may just be the mechanism of aversive conditioning during a PCI procedure.

This study had a number of limitations. Primarily, because the sample size was relatively small, subgroup analysis could not be performed; a large population study would be needed to assess the contributions of other patient attributes. Another limitation was that the follow-up period was just 24 weeks. To evaluate the long-term effect of aversive advice on smoking cessation, 24 weeks is

ultimately insufficient and truly long-term follow-up is needed. In addition, aversive advice during a PCI procedure could be considered rather harsh for patients with ACS, but as of the current moment, no patient enrolled in the study has experienced any psychological trauma.

CONCLUSIONS

Aversive advice during a PCI procedure is effective to promote smoking cessation in patients with ACS. More specifically, in a clinical setting, aversive advice during a PCI procedure may be a successful and easy way to encourage patients with ACS to stop smoking, though a protocol that includes a greater period between patient discharge and follow-up is required for future evaluation. Overall, a physician's attention and involvement during a PCI procedure is imperative for smoking cessation in patients with ACS.

REFERENCES

1. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. J Am Coll Cardiol 2004;43:1731–7.
2. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63:2960–84.
3. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2016; 37:2315–81.
4. Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systematic review. JAMA 2003;290:86–97.
5. Rea TD, Heckbert SR, Kaplan RC, Smith NL, Lemaitre RN, Psaty BM. Smoking status and risk for recurrent coronary events after myocardial infarction. Ann Intern Med 2002;137:494–500.
6. Smith SC Jr, Benjamin EJ, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation endorsed by the World Heart Federation and the Preventive Cardiovascular Nurses Association. J Am Coll Cardiol 2011;58:2432–46.
7. Eisenberg MJ, Filion KB, Yavin D, et al. Pharmacotherapies for smoking cessation: a meta-analysis of randomized controlled trials. CMAJ 2008;179:135–44.
8. Mottillo S, Filion KB, Belisle P, et al. Behavioural interventions for smoking cessation: a meta-analysis of randomized controlled trials. Eur Heart J 2009;30:718–30.
9. Anthenelli RM, Benowitz NL, West R, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. Lancet 2016;387: 2507–20.
10. Suissa K, Lariviere J, Eisenberg MJ, et al. Efficacy and safety of smoking cessation interventions in patients with cardiovascular disease: a network meta-analysis of randomized controlled trials. Circ Cardiovasc Qual Outcomes 2017;10:e002458.
11. Eisenberg MJ, Grandi SM, Gervais A, et al. Bupropion for smoking cessation in patients hospitalized with acute myocardial infarction: a randomized, placebo-controlled trial. J Am Coll Cardiol 2013;61: 524–32.
12. Planer D, Lev I, Elitzur Y, et al. Bupropion for smoking cessation in patients with acute coronary syndrome. Arch Intern Med 2011;171: 1055–60.
13. McBride CM, Emmons KM, Lipkus IM. Understanding the potential of teachable moments: the case of smoking cessation. Health Educ Res 2003;18:156–70.
14. Arzi A, Holtzman Y, Samnon P, Eshel N, Harel E, Sobel N. Olfactory aversive conditioning during sleep reduces cigarette-smoking behavior. J Neurosci 2014;34:15382–93.
15. Hymowitz N, Eckholdt H. Effects of a 2.5-mg silver acetate lozenge on initial and long-term smoking cessation. Prev Med 1996;25:537–46.
16. Suedfeld P, Baker-Brown G. Restricted environmental stimulation therapy and aversive conditioning in smoking cessation: active and placebo effects. Behav Res Ther 1986;24:421–8.
17. Biochemical verification of tobacco use and cessation. Nicotine Tob Res 2002;4:149–59.
18. Jung S, Lee IS, Kim SB, et al. Urine cotinine for assessing tobacco smoke exposure in Korean: analysis of the Korea National Health and Nutrition Examination Survey (KNHANES). Tuberc Respir Dis (Seoul) 2012;73:210–8.
19. Taylor CB, Houston-Miller N, Killen JD, DeBusk RF. Smoking cessation after acute myocardial infarction: effects of a nurse-managed intervention. Ann Intern Med 1990;113:118–23.
20. Quist-Paulsen P, Gallefoss F. Randomised controlled trial of smoking cessation intervention after admission for coronary heart disease. BMJ 2003;327:1254–7.
21. Rigotti NA, McKool KM, Shiffman S. Predictors of smoking cessation after coronary artery bypass graft surgery: results of a randomized trial with 5-year follow-up. Ann Intern Med 1994;120:287–93.
22. Kang YH, Lee YJ, Kim HK, et al. Usefulness of Urinary Cotinine Test to Distinguish Smokers from Nonsmokers. Korean J Lab Med 2003;23: 92–7.
23. Wilcox RG, Hughes J, Roland J. Verification of smoking history in patients after infarction using urinary nicotine and cotinine measurements. Br Med J 1979;2:1026–8.
24. Connor Gorber S, Schofield-Hurwitz S, Hardt J, Levasseur G, Tremblay M. The accuracy of self-reported smoking: a systematic review of the relationship between self-reported and cotinine-assessed smoking status. Nicotine Tob Res 2009;11:12–24.
25. Hajek P, Stead LF. Aversive smoking for smoking cessation. Cochrane Database Syst Rev 2004;3:CD000546.
26. Dinh-Williams L, Mendrek A, Bourque J, Potvin S. Where there's smoke, there's fire: the brain reactivity of chronic smokers when exposed to the negative value of smoking. Prog Neuropsychopharmacol Biol Psychiatry 2014;50:66–73.