Acute beneficial effects of smoking cessation on coronary flow reserve: a pilot study

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Smoking is one of the most common causes of cardiovascular (CV) mortality (1). Besides its atherogenic effects, smoking may also lead to acute fatal CV events such as ventricular fibrillation and sudden death as a result of acute sympathetic and hemodynamic responses (2).

The oxygen demand of the myocardium may lead to increase in the coronary blood flow up to 4-6 folds via vasodilatation. Coronary flow reserve (CFR) is a parameter, which shows the status of epicardial coronary arteries and the microvascular coronary circulation by reflecting the coronary vasodilator capacity. Moreover it is an important marker for cardiac morbidity and mortality (3). CFR is defined as the ratio between hyperemic peak and basal peak diastolic coronary flow velocities (CFV). A CFR value ≤2.0 is generally considered abnormal (4). Transthoracic Doppler echocardiography (TTDE) of mid-distal left anterior descending artery (LAD) during vasodilator pharmacologic stress test is one of the recommended techniques (5).

Smoking immediately decreases CFR and increases coronary resistance even in healthy subjects. Thus the risk of acute myocardial ischemia increases especially in the patients with either high-risk or previously known coronary disease (6). On the other hand, the cessation of smoking is associated with a rapid improvement in general physiology, with the fastest improvement occurring in the CV system (7, 8). However, no accurate data demonstrating the time of onset of this improvement and the impact of smoking cessation on CFR variability is available. Therefore we primarily aimed to assess the acute effects of smoking cessation on CFR.

Twenty apparently healthy male smokers between 20 and 50 years of age, admitted to the Nicotine Dependence Centre willing to quit smoking and 10 non-smoking healthy males as a control group were included in our prospective controlled pilot study. The Local Ethics Committee approved the study protocol and the subjects all gave signed informed consent before participation in the trial. The exclusion criteria were the presence of poor quality of echogenicity, established obstructive airway disease, diabetes, migraine, ischemic heart disease, hypertension (≥140/90 mm Hg), and arrhythmia, impaired functional capacity for any reason (class II or more according to New York Heart Association), recent use of any vasoactive medication, and obesity (BMI >30 kg/m^2). Following a complete routine echocardiographic study (GE vingmed, Ge-Vivid 7 Pro, General Electric, Florida, USA), CFV was measured at mid-distal LAD in all subjects by TTDE at baseline and during intravenous dipyridamole infusion (0.56 mg/kg in 4 minutes) thereby CFR was calculated. For a period of 14 days, close follow-up was conducted via phone calls and face-to-face interviews to detect the recurrence of smoking in the study group. No medical treatment for smoking cessation was used due to its potential impact on the study results. On the 14th day, the levels of exhaled carboxyhemoglobin (CO) were measured using a carboxymeter (piCO Smokerlyzer Breath CO Monitor Bedpoint Scientific, USA) and the subjects whose values were less than 10 ppm were considered "not to have smoked", and the procedure was repeated in those cases.

Only fourteen subjects (70%) could successfully complete the 14-day smoking-free period (mean exhaled CO level was 3.61±2.15 ppm). The demographic findings of the participants have been summarized at Table 1. All baseline echocardiographic studies were normal in both groups with normal ejection fraction (>55%). Furthermore no segmental left ventricular wall motion abnormality was observed after dipyridamole infusion, although one patient in the control group had experienced spontaneously regressing angina. The mean CFR values at baseline and 14th day of not-smoking period were 2.03±0.44 and 2.26±0.59 in the study group respectively, and 2.49±0.71 in the control

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Table 1. Demographic findings

Patient characteristics	Study group n=14	Control group n=10	*P**
Age, year	39.21±6.78	39.20±5.16	0.931
Height, cm	177.36±5.47	177.60±3.75	0.752
Weight, kg	81.07±6.99	81.20±2.86	0.977
Body mass index	25.78±2.0	25.77±1.2	0.841
Systolic blood pressure	119.36±8.27	117.60±7.81	0.585
Diastolic blood pressure	64.07±5.09	65.50±4.6	0.437
Heart rate, beat/min	73.93±7.83	70.40±7.85	0.212
Ejection fraction	67.64±3.93	67.70±4.86	0.113
Amount of smoking, pack-year	37.71±12.67	-	-

*Mann-Whitney U test

Table 2. Mean CFR values

Coronary flow assessments	Study group n=14	Control group n=10	Sig.*
CFR-1, baseline	2.03±0.44	2.49±0.71	0.977
CFR-2, after cessation of smoking	2.26±0.59 p=0.382#		

*Mann-Whitney U test
#Wilcoxon signed rank Test

group. Although the baseline CFR values in the study group tend to be lower than those in the control group, the difference remained non-significant (p=0.977). On the other hand, after the smoking free period, the mean CFR value increased compared to baseline in the study group. However the difference did not reach statistical significance (p=0.382) (Table 2).

The data regarding the impact of smoking on CFR is conflicting. The different results can be attributed to differences in age and gender of the trial populations, differences in the methods for measuring CFR, or the use of different stress agents (adenosine or dipyridamole) (6, 9). However, in a recent twin study, researchers found a significant decrease in the CFR values of the smokers comparing to non-smokers probably because of the chronic effects of smoking (10). Our result regarding the lower CFR values in the smoker group is consistent with the previous literature, although the difference was not statistically significant. On the other hand, there is no available data showing the acute effect of smoking cessation on CFR in the literature.

As a conclusion, we assessed, for the first time, the acute effect of smoking cessation on CFR, which is a good indicator for the CV events. The small number of subjects is the primary limitation of this study. In addition, the relatively young study population who has not any CV risk factors other than smoking might not fully reflect the overall smoker population. However the CFR values mildly increased after two-week smoking-free period in the study group. Although this increase could not reach statistically significance, it is a promising result, which provides further evidence of the acute, favourable effects of smoking cessation on the CV system. We believe that this benefit should be considered as a motivating factor for clinicians and patients in the fight against smoking. But large-scale prospective studies are still needed for a definite conclusion.

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References

1. WHO Report on the Global Tobacco Epidemic, 2008: The MPOWER package. Geneva, World Health Organization, 2008.
2. Hallstrom AP, Cobb LA, Ray R. Smoking as a risk factor for recurrence of sudden cardiac arrest. N Engl J Med 1986; 314: 271-5. [CrossRef]
3. Cortigiani L, Rigo F, Gherardi S, Bovenzi F, Molinaro S, Picano E, et al. Coronary flow reserve during dipyridamole stress echocardiography predicts mortality. J Am Coll Cardiol Img 2012; 5: 1079-85. [CrossRef]
4. Cortigiani L, Rigo F, Gherardi S, Sicari R, Galderisi M, Bovenzi F, et al. Additional prognostic value of coronary flow reserve in diabetic and nondiabetic patients with negative dipyridamole stress echocardiography by wall motion criteria. J Am Coll Cardiol 2007; 50: 1354-61. [CrossRef]
5. Sicari R, Nihoyannopoulos P, Evangelista A, Kasprzak J, Lancellotti P, Poldermans D, et al. Stress echocardiography expert consensus statement: the European Association of Echocardiography (EAE) (a registered branch of the ESC). Eur J Echocardiogr 2008; 9: 415-37. [CrossRef]
6. Park SM, Shim WJ, Song WH, Lim DS, Kim YH, Ro YM. Effects of smoking on coronary blood flow velocity and coronary flow reserve assessed by transthoracic Doppler echocardiography. Echocardiography 2006; 23: 465-70. [CrossRef]
7. Burns DM. Epidemiology of smoking-induced cardiovascular disease. Prog Cardiovasc Dis 2003; 46: 11-29. [CrossRef]
8. Hunter KA, Garlick PJ, Broom I, Anderson SE, McNurlan MA. Effects of smoking and abstention from smoking on fibrinogen synthesis in humans. Clin Sci (Colch) 2001; 100: 459-65. [CrossRef]
9. Kaşıkçıoğlu E, Elitok A, Onur I, Çimen A, Uçar A, Oflaz H. Acute effects of smoking on coronary flow velocity reserve and ventricular diastolic functions. Int J Cardiol 2008; 129: 18-20. [CrossRef]
10. Rooks C, Faber T, Votaw J, Veledar E, Goldberg J, Raggi P, et al. Effects of smoking on coronary microcirculatory function: a twin study. Atherosclerosis 2011; 215: 500-6. [CrossRef]