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Tobacco Dependence, the Most Important Cardiovascular Risk Factor: Treatment in the Czech Republic

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Summary

Smoking is the most important cardiovascular (CV) risk factor. Stopping smoking halves the CV risk. Every clinician should provide a brief intervention with smokers. Intensive treatment should be available to those who need it. There are 37 Centers for Tobacco Dependence in the Czech Republic, which offer treatment including a psychobehavioral intervention and pharmacotherapy (varenicline, nicotine, bupropion). Czech physicians, pharmacists and nurses are regularly educated about smoking cessation. We describe the results of intensive treatment offered by our centers. Treatment includes screening (1 h), an intervention (2 h), and follow-up visits during the next 12 months. Among 3532 patients, 34.3 % had CO-validated abstinence at 12-months (including 489 patients who attended the screening visit + only the 12-month follow up visit). Among patients who underwent the intervention, the abstinence rate was 38.2 %. The majority of patients who underwent the intervention (N=2470) used some form of pharmacotherapy. After one year, the abstinence rate was 43.4 %, compared to 15.9 % (N=573) without pharmacotherapy. Only 28 % of patients came on the recommendation of a physician. Despite the decrease in CV risk following smoking cessation and the effectiveness of treatment, centers are underutilized.

Key words

Tobacco dependence • Smoking cessation • Cardiovascular risk

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Introduction

The pathophysiological effects of smoking are broad due to more than 4000 chemicals, including polycyclic aromatic hydrocarbons and oxidizing gases, most of which have cardiotoxic effects (Haustein 2002, Ambrose and Barua 2004). Nicotine is a sympathomimetic agent with potential cardiovascular (increase in heart rate, blood pressure and cardiac output) and metabolic effects (increased lipolysis) (Benowitz 1998, Ambrose and Barua 2004). It appears that pure nicotine itself has no significant influence on the development of CVD. Nicotine is highly addictive and causes addiction to tobacco, which results in inhalation of tobacco smoke with noxious agents (Asplund 2003). The risk of an acute CV event is higher among smokers due to increased coagulation which leads to thrombosis (platelet activation and aggregation, activation of coagulation, increased fibrinogen level, increased levels of tissue factor, leukocyte count, and D-dimer, and plasma viscosity) (Kannel *et al.* 1987, Wilhelmsen 1988, Fuster *et al.* 1992, Ernst 1994, Sambola *et al.* 2003). Even a small dose, including passive smoking, increases platelet aggregation. These findings may at least partly

explain the higher risk of coronary thrombosis in smokers (Lee *et al.* 1995, Puranik and Celermajer 2003). Active and passive smoking are associated with endothelial dysfunction in a dose-dependent manner (Kato *et al*. 2006). There is reduced release and availability of NO and the formation of a chronic inflammatory condition (leukocytosis, elevated CRP). Smoking and hypertension have the same effect on the progression of early atherosclerosis (Csányi *et al.* 2001). Impaired relaxation of arteries observed in an animal model, suggests a possible degradation of NO by anionic superoxide of cigarette smoke (Török *et al.* 2000). *In vitro* studies have demonstrated the association between smoking with altered endothelial-derived fibrinolytic and antithrombotic factors: t-PA/PAI-I reduction, lower 1-TFPI (tissue factor pathway inhibitor), and reduced production of NO (Barua *et al.* 2002). Nicotine stimulates the production of endothelium-derived chemoattractants that enhance the migration of smooth muscle cells of blood vessels (Di Luozzo *et al.* 2005). Endogenous NO production may be a protective mechanism against endothelial damage induced by smoking (Raveendran *et al.* 2005). Nicotine increases the level of VEGF mRNA, as well as proteins in the endothelium and may increase the release of TNF-alpha and IL-1beta from macrophages (Conklin *et al.* 2002, Wang *et al.* 2004). Inhibition of endothelial cell migration in the presence of a condensate of cigarette smoke leads to a higher probability of developing complications due to incomplete reendothelialization (Snajdar *et al.* 2001). Smoking also has broad endocrine effects (Hruskovicova *et al.* 2013).

Due to CV risk all smokers, but especially those with increased CV risk, should be strongly advised not to smoke (diagnosis F17), and to avoid any exposure to tobacco including passive smoking (diagnosis E58.7), according to the International Classification of Diseases, 10th version (WHO 2008).

Every clinician (physician, nurse, pharmacist) should provide a brief intervention with smokers and intensive treatment should be available to those who need it (Fiore *et al.* 2008). Treatment that includes a psychobehavioral intervention and pharmacotherapy (varenicline, nicotine, bupropion), is offered at Centers for Tobacco-Dependence. There are currently 37 hospital-based centers across the Czech Republic. Education of Czech physicians, pharmacists and nurses in smoking cessation regularly occurs under the Society for Treatment of Tobacco Dependence (info at www.slzt.cz).

Methods

To demonstrate the efficacy of intensive treatment, we present a cohort of patients who visited the Center for Tobacco Dependence in the Czech Republic. Smokers were self referred or referred by a physician to the center for treatment. We compared one year abstinence rates in the following groups of patients: those who only came to the center for the initial screening visit + the 12-month follow-up visit, and those who also underwent the intervention (screening, intervention and attended at least one 12-month follow-up visit). Within the group that underwent the intervention, we also compared patients who used pharmacotherapy (varenicline, nicotine, and/or bupropion) versus those who did not.

The treatment in our center starts with an initial 1-h screening visit. Each patient's level of nicotine dependence is assessed using a series of measures, including the Fagerström Test of Cigarette Dependence (FTCD) (Fagerström *et al.* 2012), CO in expired air, the number of cigarettes smoked in the past 12 h, Beck Depression Scale II (BDI-II) (Beck *et al.* 1996), and the Minnesota Withdrawal Scale (Hughes 2007). Within one week of the initial screening visit, patients undergo a 2-h intervention with a physician. There is a mean of 4 follow-up visits during the next 12 months. The first follow-up visit usually occurs within 2 weeks of the intervention, and monthly thereafter.

The intervention with a physician is performed individually or in small groups with 4-5 individuals. Following the intervention, based on our recommendation, the patient is offered either varenicline, nicotine replacement therapy or bupropion and/or a combination. We set a quit date. Follow-up visits take about 30 min and include checking the patient's weight, blood pressure, and heart rate. We measure CO in expired air and discuss withdrawal symptoms, as well as we check the treatment.

The visit schedule and intervention structure are described in Table 1.

This analysis was approved by the Ethics Committee of the General University Hospital in Prague, registration FWA 00003027 – according to the Office for Human Research Protections, U.S. Department of Health and Human Services, under No. IRB 00002705. The General University Hospital is registered under No. IORG 0002175.

Standard descriptive statistics were used to characterize the sample data set. Statistical significance of differences in 12-month abstinence rate by gender and the type of pharmacotherapy used were assessed by Fisher-exact test. Statistical significance of differences in baseline characteristics between groups of patients who had undergone the intervention and those who did not was assessed by Mann-Whitney test or Pearson Chí-square test. A significance level of alpha = 0.05 was used.

Table 1. Visit schedule for patients of the Center for Tobacco-Dependence.

Screening visit	vital signs, weight, height, heart rate, blood pressure, personal history and social background, CO in expired air, withdrawal symptoms, and other tests
Intervention visit (usually within one week of the initial screening visit)	heart rate, blood pressure, CO in expired air, withdrawal symptoms. Intervention structure: - Introduction. Explain to the patient that the intervention is meant to be interactive and that they should feel free to discuss how they are feeling and ask questions at any time. - Patient's expectations and how the treatment will proceed. - Patient's smoking history including the total the number of cigarettes smoked per lifetime, the association between smoking and other routine activities (e.g. having a coffee). - Patient's experiences with previous attempts to quit and reasons for relapse. - The principles of nicotine dependence. How smoking is a learned behavior and changes that occur in the brain. - Identifying with being smoke-free and enjoying it. - Specific health consequences of smoking based on the patient's condition to help improve motivation, including improved mental health. - Provides brochure titled "My Way to Smoke-Free". - Patient's decision to quit smoking, including readiness, confidence in their ability to succeed, and their main source motivation. Responses are based on a 10 point-likert scale and responses may be revisited again at a later date. - The principal behind measuring breathe CO. Patient's specific CO values and how this relates to estimated nicotine intake from cigarettes. - The importance of behavioral support and typical smoking situations they will encounter (coffee, alcohol, smoking environment, food, stress, peace/rest, waiting, in the car, in the restaurant...). Work with the patient to prepare smoke-free solutions in advance and encourage them to look forward to these situations. - The importance of rewarding yourself for small successes. - Strategies to prevent weight gain, as well as the connection between smoking and stress. - Alternative relaxation techniques (deep breathing, yoga, Jacobson, etc). - Possible barriers to quitting, and how being aware of these barriers can decrease the likelihood of relapse. - The importance of social support, as well as strategies for living and/or working with other smokers. How to refuse a cigarette. - Withdrawal symptoms. - The principles of physical dependence, and the specific FTCD score of the patient. Show video demonstrating the effect of smoking on dopamine release. - Pharmacotherapy options. Drug's mechanism of action and any possible side effects. - The cost of pharmacotherapy and possibility of reimbursement. - Indication for use of pharmacotherapy and the recommended length of treatment. - Quit date, highlighting that any smoking is smoking. - Date of the next visit (usually within two weeks after the initial intervention).
Follow-up visits (based on the patient needs, but usually within 2 weeks of the quit date, then about 3x monthly, then at 6 and 12 months after the quit date)	heart rate, blood pressure, CO in expired air, withdrawal symptoms collected at each visit

Table 2. A. Selected characteristics of patients of the Center for Tobacco Dependence.

Characteristics	Complete record (N=3043)	Incomplete record (N=489)	p-value[1]
Gender			
Male	1526 (50.1 %)	255 (52.1 %)	0.412
Female	1517 (49.9 %)	234 (47.9 %)	
Age at first visit			
≤ 29	475 (15.6 %)	92 (18.8 %)	
30-39	841 (27.6 %)	113 (23.1 %)	
40-49	550 (18.1 %)	80 (16.4 %)	0.057
50-59	581 (19.1 %)	110 (22.5 %)	
≥ 60	596 (19.6 %)	93 (19.0 %)	
Education			
Basic	288 (9.5 %)	59 (12.1 %)	
Secondary	1905 (62.6 %)	328 (67.1 %)	**0.002**
University	850 (27.9 %)	102 (20.9 %)	
Daily smoked cigarettes			
Up to 10	253 (8.4 %)	62 (13.0 %)	
11-20	1578 (52.1 %)	233 (48.7 %)	
21-30	750 (24.8 %)	110 (23.0 %)	**0.018**
31-40	332 (11.0 %)	51 (10.7 %)	
> 40	116 (3.8 %)	22 (4.6 %)	
FTCD			
0-1 points	144 (4.8 %)	40 (8.6 %)	
2-4 points	823 (27.4 %)	118 (25.3 %)	**0.008**
5-7 points	1345 (44.7 %)	200 (42.8 %)	
8-10 points	697 (22.9 %)	109 (23.3 %)	
BMI (kg/m^2)	25.4 (19.5 ; 34.5)	25.5 (18.9 ; 35.8)	0.976
% body fat	28.0 (14.3 ; 42.4)	28.2 (13.4 ; 43.2)	0.421
Waist-to-Hip Ratio (%)	87.6 (71.7 ; 104.6)	87.2 (71.3 ; 105.6)	0.730
CO (ppm)	17.0 (1.0 ; 38.0)	15.0 (0.0 ; 39.0)	**0.004**
COHb (%)	3.0 (0.3 ; 6.9)	2.8 (0.1 ; 6.9)	**0.020**

Patients with a complete record, who passed the intervention = at least screening, intervention and 12-month follow-up visit (N=3043). Patients with incomplete record (screening and 12-month follow up, in case of loss to follow-up, patients were considered smokers at 12 months) (N=489). [1] Differences tested according to the Mann-Whitney U test or Pearson Chí-square test; FTCD – Fagerström Test of Cigarette Dependence; BMI – body mass index; CO – carbon monoxide; COHb – carbonylhemoglobin.

Table 2. B. Cardiovascular characteristics of patients who stopped smoking (non-smokers) and patients who continued to smoke (smokers).

Characteristics	Visit	**Non-smokers** (N=1162)		**Smokers** (N=1881)[1]	
		N	**Median (Min-max)**	**N**	**Median (Min-max)**
Weight	Baseline	1158	77.0 (45.0-135.3)	1857	75.8 (41.6-187.0)
	12 months follow-up	1094	82.9 (45.0-147.0)	100	83.4 (50.0-133.0)
Pulse	Baseline	1145	72 (41-119)	1835	72 (45-116)
	12 month follow-up	879	72 (42-154)	84	72 (56-107)
Systolic pressure	Baseline	1150	125 (85-190)	1850	123 (73-220)
	12 month follow-up	885	125 (85-210)	85	126 (90-180)
Diastolic pressure	Baseline	1150	80 (50-125)	1850	80 (45-131)
	12 month follow-up	884	80 (50-111)	85	80 (54-105)

[1] Missing data in the group of smokers are due to a loss to follow-up. In such a case the patient was considered to be a smoker.

Results

Our analysis included 3532 patients who had completed the 12 month follow-up between 2005 and 2013 (intention-to-treat analysis). The abstinence rate was 34.3 % in all patients including those who had attended only the initial screening and the 12-month follow up visit, compared to 38.2 % among those who had also undergone the intervention (initial screening visit, intervention and at least the 12-month follow-up visit). For more detail see Figures 1 and 2, and Table 2A. In Table 2B selected CV risk factors are compared.

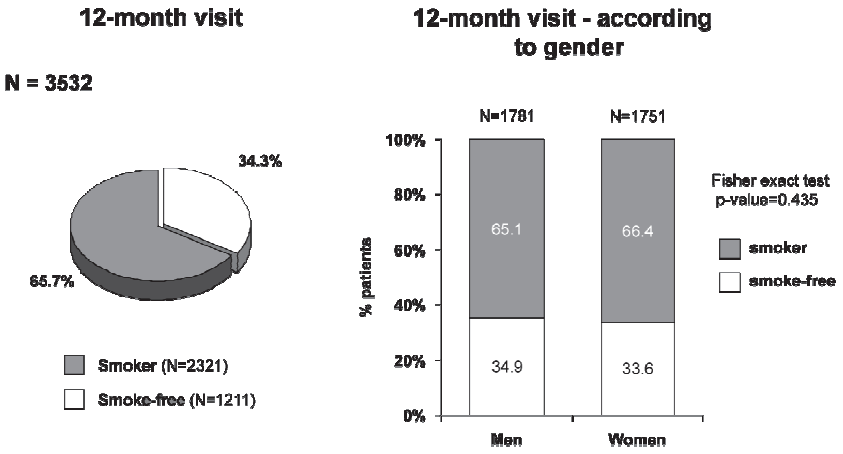

Fig. 1. 12-month abstinence rate among patients of the Center for Tobacco-Dependence in the Czech Republic between 2005 and 2013.

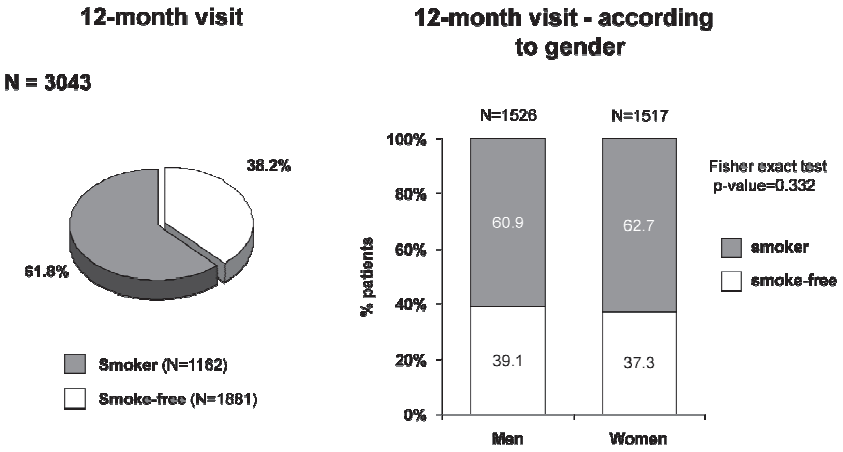

Fig. 2. 12-month abstinence rate among patients of the Center for Tobacco-Dependence who underwent an intensive intervention.

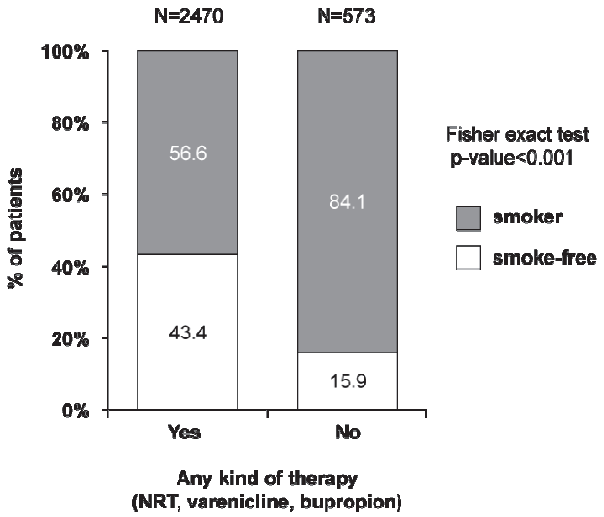

Fig. 3. 12-month abstinence rate among patients of the Center for Tobacco-Dependence who underwent an intervention according to pharmacotherapy use.

Pharmacotherapy (any kind) significantly increased the abstinence rate. The majority, 81 % of patients used some form of pharmacotherapy. Among patients who had used some form of pharmacotherapy the abstinence rate was 43.4 %, compared to 15.9 % among patients who tried to stop smoking without pharmacotherapy (Fig. 3).

Although health was the most frequent reason to stop smoking – in 68 %, only 28 % of patients said their physician had recommended they visit our center. Most patients learned about our center by way of media, including Internet – 49 %, followed by the recommendation of other patient's – 18 %. The rest learned about our center from other sources (5 %).

For a more detailed description of our patients and results, including abstinence rates according to

pharmacotherapy used, psychiatric comorbidity or CV risk factors see our other publications (Zvolska *et al.* 2012, Kralikova *et al.* 2013, Stepankova *et al.* 2013, Kmetova *et al.* 2014).

Discussion

Stopping smoking without any help has a low long-time success rate, about 5 % (Fiore *et al.* 2008). Intensive treatment may increase the number of former smokers substantially. Brief smoking cessation interventions are still not a usual part of clinical practice. Eighty percent of Czech physicians report asking about tobacco use and advising patients to stop smoking, but the next steps of the brief intervention are rarely followed. It is necessary to offer help in quitting (recommend treatment or refer the patient to a Center for Tobacco-Dependence), and to plan follow-up visits (Kralikova *et al.* 2011). For a center located in a large hospital we would expect more than 28 % of patients would be referred based on a physician's recommendation. The majority of smokers learn about intensive treatment possibility from sources other than their physician, which may suggest that brief smoking cessation intervention is not regularly used in clinical practice.

Also the diagnosis Z58.7 (passive smoking) may be a teachable moment, if used. Currently, this diagnosis is not used at all in the Czech Republic. Only 1.5 % of hospitalized patients was diagnosed F17 (tobacco dependence) in 2011 (Zvolsky *et al.* 2012) – despite a 30 % smoking prevalence in the population with about 80 % of smokers being dependent (Sovinova and Csémy 2013). A similar situation was described in psychiatric care in the USA with an 88 % prevalence of tobacco use among psychiatric patients, while only 2 % were diagnosed. Among psychiatric patients who smoke, even more than 80 % were dependent (Peterson *et al.* 2003).

Our results are comparable with international results. For patients receiving outpatient treatment at the Nicotine Dependence Center (NDC) of the Mayo Clinic in Minnesota, USA, the 6-month smoking abstinence rate has been reported ranging from 22 % to 25 %. The 1-year smoking abstinence rate for patients who enter the residential treatment program at NDC is reported to be 52 %. But, one limitation is that abstinence is verified there mainly by telephone only (Hurt *et al.* 2009).

Choice of medication depends on the intensity of addiction, but also on the patient's previous experiences, preferences, financial options, etc. Interestingly there is a fear of adverse effects with smoking cessation pharmacotherapy (either nicotine, varenicline or bupropion) among patients as well as physicians, though no adverse cardiovascular (Mills *et al.* 2013) or neuropsychiatric effects (Thomas *et al.* 2013) have been proven.

Smoking cessation intervention is a missed opportunity in cardiology despite many pathophysiological CV links that could be used to enhance patients' motivation to stop smoking. The possibility of intensive treatment of tobacco dependence could be used more broadly especially in CV patients or patient with elevated CV risk.

Conflict of Interest

EK, AK, LŠ, KZ, VF, SK received payment for clinical studies and educational activities from pharmaceutical companies producing smoking cessation medication.

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