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# Journal of Cardiology

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#### Original article

## Long-term effect of persistent smoking on the prognosis of Chinese male patients after percutaneous coronary intervention with drug-eluting stent implantation



Jun Liu (MD)<sup>a</sup>, Zhong-yu Zhu (MD)<sup>a</sup>, Chuan-yu Gao (PhD)<sup>a,b,\*</sup>, Xian-pei Wang (MD)<sup>a</sup>, You Zhang (MD)<sup>a,b</sup>, Wei-dong Jin (MD)<sup>c</sup>, Da-tun Qi (MD)<sup>a</sup>, Mu-wei Li (MD)<sup>a</sup>

- <sup>a</sup> Department of Cardiology, Zhengzhou University People's Hospital, Zhengzhou, China
- <sup>b</sup> Henan Institute of Cardiovascular Epidemiology, Zhengzhou, China
- <sup>c</sup> Department of Cardiology, Xinxiang Central Hospital, Xinxiang, China

#### ARTICLE INFO

# Article history: Received 5 December 2012 Received in revised form 8 April 2013 Accepted 2 May 2013 Available online 6 July 2013

Keywords:
Coronary heart disease
Percutaneous coronary intervention
Smoking status
Prognosis
Drug-eluting stent

#### ABSTRACT

Objectives: This study aimed to survey the adherence to smoking cessation and assess the influence of persistent smoking on the prognosis in male patients after drug-eluting stent (DES) implantation. Methods: The smoking status at the time of the index procedure and at follow-up was surveyed in 656 male patients undergoing successful percutaneous coronary intervention (PCI) with DES in our center. These patients were divided into three groups, based on their smoking status: nonsmokers (n=226), quitters (n=283), and persistent smokers (n=147). Major adverse cardiac and cerebrovascular events (MACCE) during the follow-up period were carefully recorded and their relationship with smoking status was investigated for 24–41 months.

Results: Among 656 patients who were followed up for  $27.24 \pm 6.33$  (7–40) months, 430 of them were smokers (65.5%) at the index procedure. A total of 147 patients (22.4%) who continued to smoke, accounted for 34.2% of smokers at the time of PCI. Persistent smokers and quitters were more likely to be young (p < 0.001) than nonsmokers, persistent smokers had more dyslipidemia (p = 0.005), and fewer took aspirin (p = 0.016) and statins (p = 0.045) than quitters and nonsmokers. Weight gain was greater for quitters (p < 0.016) than for nonsmokers. The incidence of all-cause death (6.1% v.s. 1.8% and 1.1%, p = 0.004) and MACCE (15.0% vs 7.1% and 5.3%, p = 0.002) in persistent smokers were significantly higher than those in nonsmokers and quitters. Multiple regression analysis showed that persistent smoking was a significantly determinant factor for all-cause death [hazard ratio (HR) = 2.432, 95% confidence interval (CI) 1.170–5.054; p < 0.017] and MACCE (HR = 1.519, 95% CI 1.049–2.200; p = 0.027).

*Conclusions*: This is the first follow-up report about the long-term effect of persistent smoking in Chinese male patients after DES implantation. Our findings strongly indicate that poor adherence to smoking cessation is a predictive factor for all-cause death and MACCE.

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#### Introduction

Cigarette smoking has been well-known to play an important role in the occurrence and development of coronary heart disease (CHD) [1–10]. China is the largest producer of tobacco in the world, and approximately 30% of the world's cigarettes are consumed by China's 350 million smokers. In 2002, the prevalence of active smoking in the population aged 15 years and older was 66.0% in men and 3.1% in women. In clinical practice, although smoking cessation is strongly advocated after coronary revascularization,

E-mail addresses: gaocy2000@yahoo.com.cn, gaocyzzu@163.com (C.-y. Gao).

some patients tend to think that their diseases have been cured, especially when they could not feel disease or they seem not to have disease phenotype. Therefore, it becomes difficult for them to adhere to the complete cessation of smoking after discharge, even if they had stopped smoking during hospitalization, which may cause severe adverse clinical events. Furthermore, most of previous studies mainly focused on the influence of smoking status at the time of PCI on clinical prognosis [6–10]. Some investigations about the effect of smoking on clinical outcomes after PCI have been performed during the pre-drug-eluting stent (DES) era [11–17]. Importantly, more and more DES have been deployed in the real world [18-21]. However, to date, the impact of smoking status in Chinese patients undergoing successful PCI with DES deployment remains unclear. Thus, it becomes necessary to investigate the major effects of smoking status in Chinese patients undergoing successful PCI with DES. Therefore, the aim of the present study is

<sup>\*</sup> Corresponding author at: Department of Cardiology, Zhengzhou University People's Hospital, 7 Wei Wu Road, 450003 Zhengzhou, China. Tel.: +81 371 65580358; fax: +81 371 65580358.

to survey the adherence to smoking cessation and investigate the association between smoking status at follow-up and the long-term clinical outcome in these Chinese patients.

#### Methods

#### Study populations

A total of 1200 consecutive patients with CHD, who were admitted to Zhengzhou University People's Hospital from January 2009 to June 2010, were prospectively registered. Complete baseline data were available for 1173 of those patients (97.75%). PCIs were performed successfully in 1162 patients (96.83%), whereas 11 (0.92%) patients did not experience successful PCI and 269 patients (22.42%) were lost during follow-up. As only 4 female smokers were found in our study, 237 female patients (19.75%) were also excluded when analyzing data at the end of the study. Thus, 656 patients were enrolled and investigated in the present study. All patients were given written informed authorizations for the release of all such information.

PCI was performed using standard techniques. The angiographic success of PCI was defined as a minimum diameter stenosis of <10% (with an optimal goal of as close to 0% as possible) of target lesion after DES deployment, resulting in final thrombolysis in myocardial infarction flow grade 3 without occlusion of a significant side branch, flow-limiting dissection, distal embolization, or angiographic thrombus. Clinical success was defined as angiographic success without associated in-hospital complications [e.g. death, myocardial infarction (MI), stroke, emergency coronary artery bypass graft (CABG)].

#### Smoking status

Patients were queried about their smoking status and habits at the time of the procedure and at follow-up. Smoking volume was expressed as the number of cigarettes smoked each day. The study population was divided into three groups on the basis of smoking status at time of the index procedure and follow-up: (1) nonsmokers, who did not regularly smoke at any time, or who had stopped smoking for more than 1 year; (2) quitters, who permanently quit smoking immediately after the index procedure; and (3) persistent smokers, who regularly smoked before their procedure as well as at any time during the follow-up period. There were no nonsmokers who began to smoke after the index procedure in our study. Whether the patients smoked or not was determined based on the patients' self-reported data at the time of the procedure and follow-up.

#### The smoking cessation program and clinical follow-up

All patients undergoing PCI in our hospital were ordered to stop smoking (including active smoking and passive smoking, e.g. secondhand smoke) when they were in hospital and after discharge. Our medical staff strongly advised them to cease smoking and explained to them the hazards of continued smoking and the benefits of cessation after the index procedure. They were required to go to hospital regularly for follow-up. The smoking cessation program based on a physician's recommendation for smokers to quit was performed. The Ask, Advise, Assess, Assist, and Arrange algorithm (the 5 A's framework) for smoking cessation was used. Briefly, at every visit or telephone contact follow-up, ask each patient about tobacco use; advise each smoker to quit; assess each smoker's willingness to make a quit attempt; assist each smoker in making a quit attempt by offering medication and referral for counseling and arrange for follow-up. For relapsers, provide them with

psychological support, encourage their close relatives and friends to take part in smoking cessation programs and offer social support, and advise them to begin early medical therapy.

Patient follow-up information was obtained from hospital charts and telephone interview with the patient or their immediate relatives, conducted by a single cardiologist, the end time of follow-up was June 2012. Major adverse cardiac and cerebrovascular events (MACCE) were carefully recorded, including death from any cause, nonfatal MI, cerebrovascular events (CVE), and coronary revascularization. All-cause death was defined as a composite of death from any cause. Nonfatal MI was defined as the presence of typical chest pain, electrocardiographic ST-segment elevation with or without Q waves, as well as serum cardiac enzyme elevations at least 2-fold upper limit of the normal range. CVEs were defined as stroke and reversible ischemic neurologic deficits, which were confirmed by computed tomography scanning and adjudicated by a neurologist. Revascularization was defined as repeat PCI or CABG during follow-up.

#### Statistical analysis

Categorical variables were presented by frequency counts, and the differences were tested using the chi-square test or Fisher exact test. Continuous data were expressed as means  $\pm$  SD, and the differences were analyzed with one-way analyses of variance (One-Way ANOVA, normal distribution) or Mann-Whitney U test (abnormal distribution or unequal variances). Cumulative event rates were evaluated using Kaplan-Meier estimate and compared using a logrank test. A multivariable Cox proportional hazards model was used to evaluate the association between smoking status and adverse events after adjustment for baseline and procedural factors that differed significantly among the smoking status groups. Univariable predictors of adverse events with less than 0.05 of p-value were allowed to enter the model. We present the results as hazard ratio (HR) and 95% confidence intervals (CI) and p-values. A proportionalhazards model was developed for each end point by using enter selection. For categorical variables, statistical significance was considered to be p < 0.05 among the 3 groups and p < 0.0167 between 2 groups. All statistical analyses were performed with SPSS17.0 software (SPSS Inc., Chicago, IL, USA).

#### Results

#### Adherence to smoking cessation

Among 656 patients who were followed up for  $27.24\pm6.33$  (7–40) months, 430 of them were smokers (65.5%) at the index procedure, 226 patients (34.5%) were non-smokers. By the end of the follow-up, there were 147 patients (22.4%), who continued to smoking, defined as persistent smokers; 283 patients (43.1%) completely ceased smoking after the procedure, as quitters; while 226 non-smokers remained (34.5%). Hence, the prevalence of persistent smoking in the study population was 22.4% at follow-up, which accounted for 34.1% of smokers at the time of PCI. That is, about one–third of the smokers at the time of the index procedure continued to smoke at clinical follow-up, while only two-third of smokers successfully ceased smoking.

Among the persistent smokers, 88 (59.9%) attempted to quit smoking but failed, and no smoker accepted pharmacotherapy. But most persistent smokers cut on smoking significantly during follow-up ( $24.88 \pm 11.64$  cigarettes per day vs  $13.15 \pm 9.29$  cigarettes per day, p < 0.001).

Baseline clinical, angiographic, and procedural characteristics and body mass index at follow-up among the three groups

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