Cigarette smoking (CS) constitutes an independent major risk factor for total atherosclerotic cardiovascular disease and is the leading preventable cause of mortality (1). Despite the solid evidence about the deleterious effect of CS on cardiovascular disease, several large clinical trials have demonstrated that smokers who have an ST-segment elevation myocardial infarction (STEMI) share better short-term survival than nonsmokers. For many years, several STEMI studies have investigated the impact of CS on mortality, and have demonstrated conflicting results (3–5). Consequently, there are several issues of the smoker’s paradox that should be highlighted.

First, even though smokers have had superior survival to that of nonsmokers in the fibrinolytic era (2), this finding has not been consistently reproduced in more contemporary (invasive) STEMI reports (4,5). In addition to promoting atherosclerosis, studies have demonstrated that exposure to CS is known to impair vascular endothelial function, enhance platelet aggregation, and decrease fibrinolytic factors, raising the risk of arterial thrombosis (6). Therefore, acute coronary artery obstructions in individuals who smoke are likely more thrombogenic and less atherogenic than those of nonsmokers. In such a highly thrombotic setting, fibrinolytic therapy may perform particularly well, superior to its performance in less thrombotic lesions such as in nonsmokers. A hypothesis of highly thrombotic lesions in smokers is also suggested by an enhanced risk of stent thrombosis following primary angioplasty (7). Second, epidemiological studies have shown that CS increases the risk of sudden cardiac death. Furthermore, in the setting of an acute coronary syndrome, a higher case fatality before admission to the hospital has been postulated in smokers compared with nonsmokers. Therefore, surviving smokers presenting with STEMI might represent a highly-selected and less-risky population. Third, even after adjusting for baseline characteristics, we cannot exclude that the remaining protective effect observed in previous studies was due to residual unmeasured confounders. Fourth, little is known about the long-term outcome of smokers presenting with an acute coronary syndrome.

In this issue of JACC: Cardiovascular Interventions, Robertson et al. (8) publish a substudy of the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial that examined whether smoking status had an impact in the long-term clinical outcome in patients with non-STEMI. For this purpose, the 13,189 patients enrolled in the trial were grouped according to their baseline CS status (8). As expected and as previously reported in other studies, current smokers were younger, more frequently male, and had a lower prevalence of comorbidities compared with nonsmokers. By univariate analysis, smokers had lower 1-year mortality but had an increased mortality risk after controlling for baseline characteristics (8). Similar to the traditional smoker’s paradox, this opposite version of the paradox may also be tainted by unknown confounders. For example, because of the sample size, the investigators selected a limited number of baseline variables for the multivariate Cox regression analysis. Notably, individuals who smoked had a worse left ventricular ejection fraction than did nonsmokers; however, the investigators did not control for this parameter (8). Studies have demonstrated that patients presenting with an acute coronary syndrome and left ventricular systolic dysfunction have increased mortality at 6 months and 1 year (9–11). It remains entirely plausible that smokers fared worst in the study by Robertson et al. (8) as a consequence of a greater myocardial impairment.

Persistent smokers in the presence of established coronary artery disease have an increased risk of reinfarction and death, including sudden cardiac death. Furthermore, a 30-year follow-up study in patients undergoing coronary stenting demonstrated that failure to quit smoking resulted in 2.1 life-years lost (12). In the Robertson et al. study (8), smoking cessation rates after hospital discharge were not reported, and although speculative, the worse outcome observed in the group of smokers could be attributable to clustering of adverse events in the subset of persistent smokers.

Despite the large number of available behavioral and pharmacological interventions for tobacco use and the rapid
reduction of cardiac risk achieved after quitting, smoking cessation success rates are staggeringly low. At the same time, hospitalization provides an excellent opportunity to start tobacco use interventions because of its smoke-free environment. Also, hospitalized patients can perceive their vulnerability to tobacco, which may reinforce the need for quitting. Regrettably, such an in-hospital opportunity is seldom recognized. Studies demonstrate that many hospitals do not consistently offer tobacco use interventions to their patients. This vexing problem is currently being addressed by the Joint Commission for Smoking Cessation (13). This commission launched its new “Tobacco Cessation Performance Measure Set” on January 1, 2012 (13). Hopefully, nationwide quality-control measures will help us see this pivotal in-hospital opportunity to provide tobacco use interventions.

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