EDITORIAL

Unraveling the smoker's paradox: impact of smoking on outcomes in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

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Acute myocardial infarction (AMI) is a life-threatening cardiovascular condition characterized by the occlusion of circulation in the coronary arteries and ischemic injury in the myocardium. It poses a significant global health burden.[1] AMI is a leading cause of mortality and morbidity worldwide, demanding ongoing research to enhance our understanding of its complexities.[2] While it is well established that smoking poses significant health risks, a phenomenon known as the "smoker's paradox" has emerged, challenging our conventional assumptions in that smokers may have better clinical outcomes following AMI events.[3,4]

Initially, the smoker's paradox seemed counterintuitive, as smoking is widely recognized as a leading cause of cardiovascular disease.[5] It is well known that smoking is a significant risk factor for the development and early onset of ST-segment elevation myocardial infarction (STEMI) due to the detrimental effects of tobacco on the coronary vasculature.[6] Moreover, smoking compromises the overall cardiovascular health by exacerbating atherosclerosis and promoting thrombogenesis, among other harmful effects.[7]

However, studies began to emerge indicating that smokers with STEMI who underwent primary percutaneous coronary intervention (PCI) seemed to have better survival rates and clinical outcomes than nonsmokers.[3,4] The paradoxical nature of these findings triggered speculation and led to various proposed explanations. Studies have provided conflicting results on the clinical outcomes of smoking patients following AMI events.[8-10]

One theory suggests that smokers may exhibit higher prevalence of collateral vessels, which could provide an alternative blood supply to the ischemic myocardium, thus reducing the extent of damage during STEMI.[11] Collateral vessel development is influenced by chronic ischemia, and it is conceivable that long-term exposure to smoking-induced ischemia may stimulate collateral growth. However, scientific evidence supporting this hypothesis remains inconclusive, and it is challenging to isolate smoking as the sole determining factor. Another possible explanation for the smoker's paradox revolves around the potential impact of smoking on platelet function.[12,13] It has been suggested that the antithrombotic effects of smoking could result in smaller thrombus burden and less need for distal embolization during primary PCI, leading to better clinical outcomes. Furthermore, AMI patients who smoke tend to respond better to clopidogrel therapy due to hepatic cytochrome P450 activation resulting in an increased generation of the active metabolite of clopidogrel.[14] However, this hypothesis has not been definitively substantiated and requires further investigation to ascertain the true relationship between smoking and platelet function in the context of STEMI.

In this issue of *Polish Archives of Internal Medicine*, Bujak et al[15] used data from 3 independent AMI registries to evaluate the association of the smoking status with mortality in STEMI patients treated with primary PCI. One of the strengths of this study was the large size of the total cohort (n = 82 235), allowing the authors to perform a robust statistical analysis to address the hypothesis and draw significant clinical and epidemiological conclusions. This study contributes to the field of cardiovascular medicine by revealing the pseudoparadox of the smoking status' impact on mortality following AMI. Through statistical adjustments for potential confounders and a large cohort of the registry, the study challenged the existence of the smoker's paradox, thereby uncovering the complexities of the association between smoking and clinical outcomes in patients with STEMI. The study revealed that although smokers initially exhibited lower crude rates of adverse events, this could be attributed to a lower burden of traditional risk factors and younger age in that group. Importantly, the research emphasized that after accounting for these factors, smoking itself emerged as an independent risk factor for 36-month mortality. This nuanced insight enhances our knowledge and informs future interventions and preventive strategies for this high-risk patient population.

However, this study has certain limitations. First, the smokers were identified via questionnaires only. Therefore, there was a risk of bias for under-reporting and misclassification of patients. Secondly, the duration of smoking history was not reported as the questionnaire did not include information on it. The World Health Organization defines former smokers as those who refrained from smoking over the past 12 months, and it is unclear whether the nonsmokers identified in the study could be truly classified as such. Hence, the results of this study may not be directly comparable with those of other studies due to the different definition. Similarly, as the number of cigarettes smoked was not reported, the dose-response relationship was not established in this study.

Given the accumulating evidence on the harmful effects of smoking on the cardiovascular system, it is imperative not to endorse the smoker's paradox as an excuse to promote smoking or downplay the dangers associated with tobacco use. Smoking cessation remains the most effective strategy for improving cardiovascular health and reducing the risk of STEMI and other cardiac events. Rather than focusing solely on the smoker's paradox, it is more meaningful to direct our attention toward encouraging smoking cessation interventions and supporting patients in their efforts to quit smoking. Quitting smoking not only mitigates the risk of future cardiovascular events but also provides numerous noncardiovascular health benefits.

In conclusion, the smoker's paradox, though an intriguing concept, should be approached with skepticism, as demonstrated by Bujak et al[15] and authors of other published studies. While previous reports have demonstrated seemingly favorable outcomes among smokers with STEMI treated with primary PCI, those studies had methodological issues. Bujak et al[15] provided yet more evidence to support the detrimental effects of smoking on cardiovascular health. Rather than perpetuating the paradox, we should use this opportunity to intensify efforts aimed at smoking cessation and public health campaigns to reduce tobacco consumption. By prioritizing smoking cessation interventions and providing comprehensive support, we can positively impact outcomes of patients with STEMI and reduce the burden of cardiovascular disease on the society as a whole.

ARTICLE INFORMATION

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