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Smoking and Type 2 Diabetes: Mechanisms and Cessation Benefits

Zhaokun He[1,a,*]

[1]*School of Public Health, Shantou University, Shantou, Guangdong, 515000, China*
a. 22zkhe@stu.edu.cn
**corresponding author*

Abstract: Cigarette smoking, while not widely recognized as an established risk factor for various chronic diseases, have also been accumulating findings suggesting its epidemiological association with diabetes mellitus, particularly type 2 diabetes. However, smoking was not widely recognized as a modifiable risk factor in the development of diabetes prevention and screening strategies. This paper, through a method of literature review, has highlighted studies that focused on the physiological effects of smoking on increased type 2 diabetes risk, the association between smoking behavior and diabetes risk in large-populational studies, and the temporal effect of smoking cessation on diabetes risk. This study finds that smoking significantly increases the risk of type 2 diabetes through mechanisms such as insulin resistance, chronic inflammation, and metabolic disruptions, while smoking cessation, despite initial metabolic challenges, reduces diabetes risk over time, with former smokers' risk aligning with that of never-smokers approximately 12 years after quitting. Key future directions are suggested for strengthening public health strategies on smoking cessation, lifestyle interventions, and personalized metabolic management to reduce the global burden of diabetes.

Keywords: Type 2 Diabetes (T2D), Insulin Resistance, Smoking Cessation, Metabolic Dysfunction

1. Introduction

Diabetes mellitus, particularly type 2 diabetes (T2D), represents a significant global health burden, with its prevalence rising in tandem with lifestyle factors such as poor diet, lack of physical activity, and smoking. Smoking, a well-established risk factor for various chronic diseases, has been increasingly recognized for its detrimental role in the development and progression of T2D. The complex interplay between smoking and metabolic dysfunction underpins much of its contribution to diabetes risk. Evidence suggests that smoking not only promotes insulin resistance and alters lipid metabolism, but also triggers inflammatory responses and oxidative stress, all of which disrupt normal glucose homeostasis and increase the susceptibility to T2D [1-2].

The pathophysiological effects of smoking on insulin sensitivity and glucose metabolism are supported by both animal models and large cohort studies. Nicotine, the primary addictive component of tobacco, has been shown to interfere with insulin signaling pathways and impair glucose utilization while also inducing metabolic disturbances such as visceral fat accumulation and dyslipidemia [1]. Furthermore, smoking exacerbates chronic inflammation, which is a key contributor to insulin

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resistance, a hallmark feature of T2D [2]. For example, studies using mouse models of nicotine exposure have shown a significant reduction in insulin sensitivity, and increased inflammatory cytokines like TNF-α and IL-6, further disrupting insulin signaling pathways and promoting insulin resistance [1].

This review explores the direct physiological effects of smoking on diabetes and examines how smoking influences insulin resistance, metabolic processes, and the risk of developing T2D. Through a review of recent studies, this paper will highlight the mechanisms by which smoking increases the likelihood of diabetes onset, as well as the long-term impacts on metabolic health. Additionally, this paper will address the benefits of smoking cessation in reducing T2D risk and discuss the importance of integrating lifestyle interventions to prevent and manage this chronic condition [3-4]. The significance of this study lies in its comprehensive exploration of the mechanisms linking smoking to type 2 diabetes risk, emphasizing the detrimental effects of smoking on insulin sensitivity, chronic inflammation, and metabolic function. It further highlights smoking cessation as a critical, yet often underrecognized, modifiable factor in reducing diabetes risk over time, providing evidence that former smokers can align with never-smokers in diabetes risk after approximately 12 years. Beyond this, the study holds profound implications for global public health policies by advocating for the integration of smoking cessation into diabetes prevention and management strategies.

2. Direct physiological effects of smoking on diabetes

2.1. Insulin resistance

Studies have demonstrated the associations between smoking and the incidence of insulin resistance, a key pathological mechanism of T2D. The study used a mouse model to simulate nicotine intake in long-term smokers through chronic nicotine exposure. Insulin sensitivity in mice was significantly reduced with gradually increased insulin intake, and the insulin signaling pathways (such as IRS-1 and Akt) was also inhibited. Nicotine treatment has also significantly increased the expression of pro-inflammatory factors (TNF-α, IL-6), further impairing the insulin signaling pathway and promoting the occurrence of insulin resistance. In addition, the metabolism deficiency was also observed among the patients who participated, potentially associated with the chronic inflammatory response and the oxidative stress caused by the presence of nicotine, which then affects the patients' insulin sensitivity. Increased visceral fat storage was also observed as the result of altered fat metabolic status [1].

2.2. Metabolic characteristics

A similar study has focused on the metabolic profiling between smoking and diabetes. It has concluded that the metabolic characteristics of smokers were closely related to the incidence of T2D. Using United Kingdom Biobank data, 93,722 participants were included in this study, and 208 metabolites were measured by targeted metabolomics. The metabolic characteristics associated with smoking were investigated, and risks were evaluated for smoking status between metabolic characteristics and T2D. It was concluded that current smokers had a 73% increased risk of T2D compared with never-smokers (hazard ratio (HR), 1.73, 95% confidence interval (CI), 1.54-1.94). Smoking-related metabolic characteristics play a partial mediating role between smoking and T2D risk, and about 38.3% of the risk is transmitted through these metabolic characteristics. This study has found that smokers have significant changes in metabolic pathways, potentially related to their increased inflammatory response and insulin resistance. Smokers exhibit disrupted metabolic pathways, including elevated very-low-density lipoprotein (VLDL) triglycerides and abnormal lipid distribution, increased branched-chain amino acids linked to insulin resistance, and impaired glucose metabolism with reduced insulin sensitivity and glucose utilization [2].

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3. Association between smoking behavior and diabetes risk

3.1. Epidemiological evidence linking smoking to diabetes

Studies have demonstrated the association between smoking and an increased risk of T2D, highlighting both direct and indirect mechanisms. This cross-sectional study was conducted at a tertiary care teaching hospital in Kolkata, West Bengal, India. The study found that 37.3% of the 434 participants had diabetes, with smoking as a significant risk factor for T2D (OR: 3.59, 95% CI: 1.71–7.58). The study underscores smoking as a prevalent risk factor and highlights its long-term adverse effects on metabolic health, thereby supporting public health policies aimed at smoking cessation [3].

Another study utilized the data from the UK Biobank, self-reported in-utero tobacco exposure (n = 354,493) and age of smoking initiation (n = 353,557) were analyzed about T2D. A composite lifestyle score was calculated based on factors like diet, physical activity, nicotine exposure, sleep, and BMI. Results showed that early smoking behavior, high genetic risk, and poor lifestyle significantly increased T2D risk (HR 1.19 to 2.22, P trend <0.001). Adopting a healthy lifestyle reduced T2D risk across all subgroups, especially for those with early smoking and high genetic risk. Together, these studies underline the importance of integrating smoking cessation programs with broader lifestyle interventions to effectively mitigate diabetes risk [4].

3.2. Risk of passive smoking on diabetes

Passive smoking has been shown to significantly influence the risk of developing diabetes. According to a prospective cohort study based on the Japan Public Health Center (JPHC) study, women exposed to spousal smoking were at an increased risk of diabetes. The study analyzed data from over 26,000 married women and found that women whose husbands smoked ⩾40 cigarettes per day had a higher likelihood of developing diabetes (adjusted odds ratio [OR] 1.34, 95% confidence interval [CI] 0.96-1.87) compared to those whose husbands did not smoke. Furthermore, the study highlighted a significant trend indicating that as the number of cigarettes smoked by the husband increased, so did the risk of diabetes for the wife (p = 0.02) [5]. The findings suggest that passive smoking not only elevates diabetes risk but may also impact glucose metabolism and insulin sensitivity through mechanisms involving chronic inflammation, oxidative stress, and metabolic disruptions, similar to the physiological effects observed in active smokers.

This study from Japan evaluated the relationship between active and passive smoking and diabetes, impaired glucose tolerance (IGT), impaired fasting glucose (IFG), and insulin sensitivity, finding that passive smoking (e.g., husband's smoking) was significantly associated with diabetes and its prediabetic states (such as IGT and IFG) in women. Specifically, women whose husbands smoked were more likely to develop diabetes or IGT (OR: 1.62, 95% CI: 1.00-2.62), and their insulin secretion function was poorer (HOMA-β reduced, OR: 2.17, 95% CI: 1.36-3.48). Additionally, while the number of cigarettes smoked by men showed a borderline significant relationship with diabetes, both active and passive smoking were associated with increased diabetes risk in women. The study suggests that smoking may affect glucose metabolism by altering insulin secretion and sensitivity, with this effect potentially differing by ethnicity. In particular, for high-risk populations such as pregnant women or those with a family history of diabetes, passive smoking may exacerbate the risk of abnormal blood glucose levels and insulin resistance, posing an additional health threat. [6] Therefore, reducing exposure to secondhand smoke is especially important for these vulnerable groups.

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4. Influence and intervention of smoking cessation on diabetes risk

4.1. Benefits of smoking cessation on diabetes prevention

In a study analyzing data from 386,558 participants in the Kangbuk Samsung Health Study, the long-term effects of smoking on T2D risk were evaluated using multivariable Cox proportional hazards models. The findings showed that current smokers had a significantly increased risk of T2D (HR: 1.29, 95% CI: 1.24-1.35, $p < 0.001$), whereas former smokers had a higher risk within the first six years after quitting, but after 12 years, their risk aligned with that of never-smokers. Adjusting for lifestyle factors like weight changes and physical activity did not alter these results [7].

Another study utilized a cohort analysis of participants in the UK Biobank, examining the long-term effects of smoking cessation on T2D risk. The researchers found that while smoking cessation could initially lead to weight gain and slightly worsen blood glucose control, the overall health benefits, such as improved cardiovascular outcomes and decreased risk of complications, were significant. The study also highlighted that those effective interventions, combining nicotine addiction treatments and weight management, play a crucial role in mitigating the negative short-term effects of quitting smoking [8].

4.2. Challenges and strategies in smoking cessation

Quitting smoking is a complex and challenging process, involving many factors, not only physical nicotine dependence, but also psychological desire and stress in the social environment. First, nicotine dependence is one of the biggest obstacles in the process of smoking cessation. Smokers will form physiological dependence in the long-term smoking process, resulting in a series of withdrawal symptoms when quitting smoking, such as anxiety, irritability, increased appetite, etc., which often make it difficult for quitters to persist. In addition, many people associate smoking with coping with stress, relieving anxiety or social interaction, which makes the process of quitting smoking more difficult. Many smokers often feel that quitting smoking means losing a way of emotional relief.

However, with the deepening of medical and psychological research, modern smoking cessation interventions are becoming more and more diverse, which can effectively help smokers overcome these difficulties. Nicotine replacement therapy (NRT) is one of the commonly used physiological interventions, which can gradually reduce the body's dependence on nicotine and reduce withdrawal symptoms. Alternative products such as nicotine gum, patches and sprays help smokers maintain a stable mood and reduce the risk of relapse by relieving the body's craving.

In addition to physiological intervention, drug therapy is also an important means of smoking cessation. For example, drugs such as bupropion (Zyban) and varenicline (Chantix) can effectively reduce withdrawal symptoms and reduce the desire for nicotine. At the same time as drug treatment, psychotherapy such as cognitive behavioral therapy (CBT) can also help smokers identify and change their smoking behavior patterns, and enhance their motivation and determination to quit smoking.

The success of smoking cessation does not only depend on individual efforts, but also on social support and group support. Joining a smoking cessation group or getting support from family and friends can provide emotional comfort and motivation. When encountering difficulties in quitting smoking, these supports can make smokers feel more encouragement and trust, and reduce anxiety and loneliness. The rise of mobile applications and online platforms has also provided smokers with more personalized and convenient smoking cessation programs. By tracking the progress of smoking cessation in real-time and providing positive feedback, they can help smokers achieve their goals step by step.

Although the process of quitting smoking may be full of challenges, through scientific interventions, persistent efforts and good social support, many people can finally overcome

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difficulties, successfully quit smoking, improve their physical and mental health, and improve their quality of life. For those who are or plan to quit smoking, patience and determination are the key, and modern treatment and support methods provide more guarantee and hope for this process.

5. Conclusion

In conclusion, smoking has been consistently identified as a significant risk factor for the development of T2D, with both direct and indirect mechanisms contributing to its pathogenesis. The direct physiological effects of smoking, including insulin resistance, altered metabolic profiles, and chronic inflammation, exacerbate the risk of T2D, as evidenced by animal models and human studies. Nicotine exposure has been shown to impair insulin sensitivity, disrupt lipid metabolism, and increase the expression of pro-inflammatory cytokines, all of which contribute to insulin resistance. Additionally, large cohort studies, such as those utilizing data from the UK Biobank, further support the association between smoking and an increased risk of T2D, emphasizing the role of altered metabolic pathways and insulin resistance in this relationship.

Importantly, the evidence highlights the potential benefits of smoking cessation, which can mitigate the long-term risk of T2D. Although the initial phase following smoking cessation may involve temporary metabolic disruptions, such as weight gain and changes in blood glucose regulation, the long-term health benefits, including reduced cardiovascular risk and improved insulin sensitivity, far outweigh the short-term adverse effects. These findings underscore the need for public health strategies that not only promote smoking cessation but also integrate broader lifestyle interventions to effectively prevent and manage T2D.

Overall, the cumulative evidence calls for urgent public health initiatives aimed at smoking prevention and cessation, as well as the integration of personalized metabolic management in the clinical care of smokers at risk for T2D. The long-term health benefits of smoking cessation, coupled with effective interventions, offer promising opportunities for reducing the global burden of diabetes.

Although this article reviews several studies on the relationship between smoking and the risk of T2D, there are heterogeneity in the design, sample size and methods of these studies, which may affect the universality of the results. In addition, many studies failed to fully control potential confounding factors, such as diet, physical activity, genetic susceptibility and socio-economic status, which may also play a role in the occurrence of diabetes, so it is difficult to separate the direct impact of smoking on diabetes risk. Future research should focus more on revealing the molecular mechanism of insulin resistance caused by smoking, especially how nicotine affects metabolic health by activating specific receptors, promoting the release of inflammatory factors and aggravating oxidative stress. Future research should also strengthen the impact assessment of alternative smoking products on metabolic health, and provide a scientific basis for the formulation of public health policies.

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