



Heated Tobacco Products as a Harm Reduction Strategy in Surgical Patients Safer Than Smoking? : A Review Article

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Abstract

Background: Tobacco smoking is a well-established modifiable risk factor for poor postoperative outcomes, including delayed wound healing, increased infection risk, wound dehiscence, tissue hypoxia, and cardiopulmonary complications. In Indonesia, smoking prevalence remains high among surgical patients, while access to and compliance with preoperative cessation interventions remain limited. Heated tobacco products (HTPs), which deliver nicotine by heating rather than combusting tobacco, have emerged as a potential harm reduction alternative; however, their role and safety in surgical populations remain uncertain. **Objective:** This review aimed to evaluate current biological, toxicological, and clinical evidence comparing HTPs with conventional cigarettes in relation to wound healing and perioperative complications, and to assess their potential role as a harm reduction strategy in surgical patients. **Methods:** A narrative review was conducted using literature obtained from PubMed, Scopus, and Google Scholar, supplemented by grey literature from authoritative public health institutions. Publications from January 2010 to June 2025 were considered. Eligible studies included original articles, reviews, systematic reviews, human clinical studies, observational studies, and relevant preclinical studies reporting toxicological profiles, tissue oxygenation, immune response, inflammation, endothelial function, wound healing, infection, or perioperative complications. Data were extracted and synthesized thematically. **Discussion:** Conventional cigarette combustion generates numerous harmful substances, including tar, carbon monoxide, polycyclic aromatic hydrocarbons, tobacco-specific nitrosamines, aldehydes, heavy metals, and reactive oxygen species, which contribute to endothelial dysfunction, vasoconstriction, tissue hypoxia, oxidative stress, immune suppression, impaired fibroblast activity, reduced collagen synthesis, delayed wound healing, surgical site infection, and wound dehiscence. HTPs avoid direct combustion and may substantially reduce exposure to tar, carbon monoxide, and selected toxicants, potentially supporting better tissue oxygenation, vascular function, and microvascular perfusion. However, HTP aerosols still contain nicotine, volatile organic compounds, aldehydes, heavy metals, and tobacco-specific nitrosamines, which may continue to interfere with wound healing. Current evidence suggests that HTPs may pose a lower biological risk than conventional cigarettes, but direct clinical evidence in surgical populations remains limited. **Conclusion:** HTPs may offer a transitional harm reduction option for selected surgical patients unable or unwilling to achieve complete smoking cessation. Nevertheless, HTPs are not risk-free and should not replace complete smoking cessation as the standard of care for minimizing perioperative complications. Further prospective clinical trials and wound healing studies are required to evaluate the safety and effectiveness of HTPs in surgical populations.

Keywords: heated tobacco products; wound healing; surgery; smoking cessation; harm reduction; perioperative risk

Background

Tobacco use remains one of the most significant modifiable risk factors influencing surgical outcomes,

including impaired wound healing, increased susceptibility to infection, and heightened risk of cardiopulmonary complications.¹⁻⁴ Smoking affects nearly every phase of the tissue repair cascade by disrupting perfusion, oxygenation, immune response,



and collagen synthesis, which collectively contribute to poorer postoperative recovery.^{3,4} reached 34% of the adult population, with 63% of Indonesian men and 5% of women identified as active smokers.⁵ Indonesia ranks among the top five countries globally in cigarette consumption, and most smokers use high-tar clove cigarettes, which deliver higher levels of tar and nicotine than standard white cigarettes.⁵ Despite widespread knowledge regarding the adverse effects of smoking, real-world cessation rates remain low. Fawwaz and Pardede reported that only 2.4% of surgical patients in Indonesia received pharmacological smoking cessation support preoperatively, and more than 50% relapsed within two weeks after surgery.⁶

In recent years, heated tobacco products have emerged as alternative nicotine delivery systems that heat processed tobacco without combustion.⁷⁻¹⁰ These products are designed to deliver nicotine while reducing exposure to harmful combustion byproducts such as tar and carbon monoxide. The absence of combustion, which is the primary driver of many tobacco-related toxicants, positions HTPs as a potential harm reduction tool.⁹⁻¹¹

The Royal College of Physicians and other international bodies have suggested that newer nicotine delivery systems may offer lower-risk alternatives for current smokers, although controversy persists.¹¹ In Indonesia, awareness and use of HTPs are increasing, particularly in urban areas, but little is known about their safety profile in surgical populations. Given the limited uptake of preoperative smoking cessation interventions, it is important to explore whether HTPs can serve as a transitional risk-reduction approach for patients who are unable or unwilling to quit completely before surgery.

This review critically evaluates current evidence on the biological and clinical impact of HTPs compared with conventional cigarettes in the context of perioperative outcomes and wound healing. The review also seeks to clarify the potential role of HTPs as a harm reduction strategy for surgical patients while acknowledging their limitations and the need for further clinical data.

Methods

This article was prepared as a narrative review to synthesize and evaluate current evidence regarding the

In Indonesia, the tobacco epidemic remains a major public health concern, particularly in the surgical population. As of 2021, national smoking prevalence effects of HTPs compared with conventional cigarettes on surgical outcomes and wound healing. The review followed established guidance for narrative reviews in biomedical sciences, emphasizing clarity, reproducibility, and clinical relevance.

Data Sources and Search Strategy

A comprehensive literature search was conducted using PubMed, Scopus, and Google Scholar, supplemented by grey literature from authoritative public health institutions, including the World Health Organization, U.S. Food and Drug Administration, and Royal College of Physicians. The search covered publications from January 2010 to June 2025, capturing foundational toxicological studies and recent clinical and regulatory developments.

Search terms included combinations of Medical Subject Headings and free-text keywords with Boolean operators: "heated tobacco products" OR "HTPs" OR "heat-not-burn tobacco" OR "IQOS" AND "conventional cigarette" OR "combustible tobacco" OR "smoking" AND "surgical outcomes" OR "perioperative complications" OR "wound healing" OR "postoperative recovery".

Eligibility Criteria

Articles were included if they were published in English between 2010 and 2025; were peer-reviewed original studies, reviews, or systematic reviews; included human clinical trials, observational studies, or preclinical studies relevant to surgical outcomes; and reported at least one outcome related to wound healing, tissue oxygenation, immune response, infection rate, inflammation, endothelial function, or perioperative complication.

Articles were excluded if they were case reports, letters to the editor, abstracts without full text, non-peer-reviewed publications, studies focusing solely on non-surgical populations or non-tobacco nicotine products, or articles with high risk of bias or insufficient methodological transparency.

Data Extraction and Synthesis

Data extraction was performed independently by the authors. Extracted data included study design and population, type of tobacco product, exposure characteristics, toxicological profile, biological effects, and reported outcomes related to wound



healing or surgical complications. Findings were synthesized thematically.

Results

The reviewed literature showed that conventional cigarette smoking is consistently associated with biological mechanisms that impair surgical outcomes and wound healing. Conventional cigarettes burn tobacco at temperatures exceeding 600°C, producing numerous harmful substances, including tar, carbon monoxide, polycyclic aromatic hydrocarbons, tobacco-specific nitrosamines, aldehydes, heavy metals, and reactive oxygen species. These combustion-derived toxicants contribute to endothelial dysfunction, oxidative stress, vasoconstriction, tissue hypoxia, immune suppression, impaired collagen synthesis, and delayed wound repair.^{12-14,19,21}

In contrast, HTPs heat processed tobacco at lower temperatures, generally below 350°C, without direct combustion. This mechanism reduces the formation of several combustion-related toxicants compared with conventional cigarettes. Previous toxicological studies reported that non-combustion nicotine delivery systems may reduce exposure to selected harmful constituents, including carbon monoxide and tar-related compounds.^{7-11,15,16} This reduction may theoretically provide biological advantages in the perioperative setting by decreasing carbon monoxide exposure, improving tissue oxygenation, reducing oxidative stress, and supporting microvascular perfusion, all of which are important for normal wound healing.^{19,20}

Despite the lower emission profile, HTPs are not free from potentially harmful substances. Aerosols from heated tobacco and related nicotine delivery products may still contain nicotine, volatile organic compounds, aldehydes, tobacco-specific nitrosamines, and heavy metals such as nickel, chromium, and lead.^{7,8,15-18} Nicotine remains clinically relevant because it stimulates catecholamine release, causing peripheral vasoconstriction and reduced blood flow to the wound area.^{21,22} In addition, residual aldehydes and other toxicants may induce oxidative stress, inflammation, and cellular dysfunction, which can interfere with fibroblast activity, angiogenesis, and collagen deposition.^{15,17,18,20}

Evidence regarding conventional cigarette smoking demonstrated a clear association with increased postoperative complications. Smoking impairs wound healing through reduced tissue perfusion, tissue

hypoxia, immune dysfunction, impaired inflammatory response, reduced fibroblast proliferation, decreased type I collagen synthesis, and delayed tissue remodelling.^{19,21-25} These mechanisms increase the risk of delayed wound healing, surgical site infection, wound dehiscence, and tissue necrosis.²³⁻²⁹ Previous studies also reported that smokers have a higher risk of postoperative wound complications compared with nonsmokers, while smoking cessation before surgery may improve tissue oxygenation and immune function, thereby reducing postoperative wound-related complications.^{1,3,19,23}

Comparative evidence suggests that HTPs may pose a lower biological risk than conventional cigarettes because of the absence of combustion and reduced exposure to selected toxicants. Experimental and toxicological studies indicate that aerosols from newer-generation tobacco and nicotine products may have lower cytotoxic and inflammatory effects than conventional cigarette smoke, with less impairment of endothelial and immune-related cellular responses.^{16,20,30} These findings suggest a potential harm reduction role for HTPs in selected surgical patients who are unable or unwilling to stop smoking completely.

However, direct clinical evidence evaluating HTP use in surgical populations remains limited. Most available data are derived from toxicological, experimental, observational, or indirect clinical studies rather than prospective perioperative trials. Therefore, although HTPs may reduce exposure to combustion-derived toxicants and may theoretically lower perioperative biological risk, current evidence is insufficient to conclude that HTPs significantly reduce surgical site infection, delayed wound healing, wound dehiscence, or other postoperative complications compared with conventional cigarette smoking.^{16,18,20,30}

Overall, the findings indicate that HTPs may represent a lower-risk exposure compared with conventional cigarettes, particularly through reduced tar and carbon monoxide exposure. Nevertheless, HTPs remain harmful because they continue to deliver nicotine and residual toxicants that may interfere with wound healing. Complete smoking cessation remains the preferred strategy for reducing perioperative complications, while HTPs should only be considered as a temporary harm reduction option under medical supervision in selected patients who cannot achieve complete cessation.^{19,20,23}

Discussion

Smoking remains a well-established risk factor for adverse postoperative outcomes, particularly wound healing complications. Its detrimental effects are mediated through multiple biological pathways that interfere with nearly every phase of the wound healing process.²¹

Nicotine stimulates catecholamine release, including epinephrine and norepinephrine, leading to peripheral vasoconstriction. This reduces blood flow to the wound site and impairs delivery of oxygen and nutrients required for fibroblast and endothelial cell function during tissue regeneration.^{21,22}

Carbon monoxide from cigarette smoke binds hemoglobin with approximately 200 times greater affinity than oxygen, forming carboxyhemoglobin and decreasing the oxygen-carrying capacity of blood. This hypoxia disrupts the inflammatory and proliferative phases of healing.^{21,22}

Toxic compounds in tobacco smoke impair neutrophil and macrophage function, compromising antibacterial defense and increasing the risk of surgical site infection.²³⁻²⁵ Smoking also inhibits fibroblast proliferation and reduces both the quantity and quality of type I collagen, weakening wound tensile strength and delaying remodelling. These disruptions elevate the risk of wound dehiscence.^{21,24}

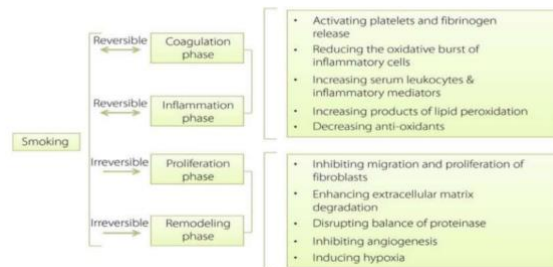


Figure 1. Impact of smoking on wound healing across all phases of the healing process, consistently associated with exacerbation of impaired wound repair.²²

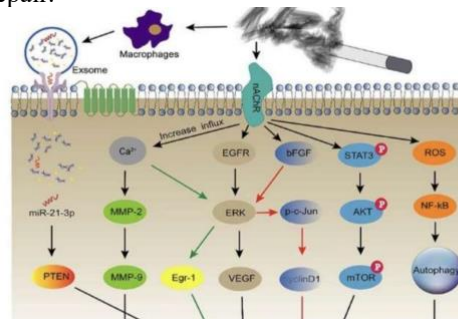


Figure 2. Molecular pathways linking cigarette smoke exposure to impaired wound healing and tissue remodelling.²¹

Tar, a composite of numerous combustion-derived chemicals, plays a critical role in mediating the harmful effects of smoking on tissue healing. It contributes to tissue hypoxia through elevated carbon monoxide exposure and promotes vasoconstriction through catecholamine release, reducing blood perfusion to surgical sites.²⁶ Tar compounds also suppress key immune cell activity and generate oxidative stress through reactive oxygen species, impairing fibroblast function and angiogenesis.^{15,27}

Tar exposure has been shown to alter collagen metabolism by decreasing collagen synthesis and increasing collagen degradation through the upregulation of matrix metalloproteinases. This imbalance leads to structurally weaker scar tissue and a heightened risk of wound dehiscence.²¹ The biochemical and pathophysiological effects of tar may culminate in delayed wound healing, increased infection rates, wound dehiscence, and tissue necrosis.²⁵⁻²⁸

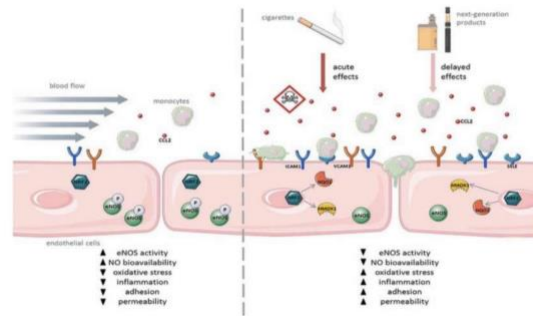


Figure 3. Comparative effects of cigarette smoke and newer-generation tobacco or nicotine product extracts on endothelial function. Conventional cigarette smoke triggers earlier antioxidant and pro-inflammatory responses than newer-generation products, although adverse effects may still occur.³⁰

Are Heated Tobacco Products Safer for Surgical Patients?

Perioperative use of HTPs represents a developing area of clinical interest within the broader context of tobacco harm reduction. Conventional cigarettes are well-established contributors to poor surgical outcomes, primarily because of combustion-derived toxicants such as tar, carbon monoxide, and reactive oxygen species. HTPs offer a distinct chemical profile that may confer comparatively lower biological risk in surgical settings. By eliminating combustion, HTPs may reduce exposure to key toxicants associated with impaired wound healing, vasoconstriction, hypoxia, and immunosuppression.¹⁹ Early experimental and toxicological data suggest that HTP aerosol has less cytotoxicity and inflammatory potential than cigarette smoke, with reduced impairment of endothelial cells, fibroblasts, and immune cells. These mechanistic advantages may translate into lower rates of surgical site infection, improved tissue oxygenation, and more effective collagen deposition, although direct clinical outcome studies remain limited.¹⁶

It is essential to underscore that HTPs are not risk-free. The presence of nicotine, aldehydes, heavy metals, and volatile organic compounds in HTP aerosols continues to pose potential harm, particularly in vulnerable surgical populations with comorbidities such as diabetes or cardiovascular disease. Additionally, the lack of long-term randomized controlled trials in perioperative settings limits the strength of current conclusions.

Conclusion

Heated tobacco products may pose a lower biological risk than conventional cigarettes because they avoid direct combustion and reduce exposure to tar, carbon monoxide, and selected harmful constituents. However, HTPs remain potentially harmful because they continue to deliver nicotine, volatile organic compounds, aldehydes, heavy metals, and tobacco-specific nitrosamines. Complete smoking cessation remains the gold standard for minimizing perioperative complications. Further prospective clinical trials are needed to determine whether HTPs can meaningfully reduce surgical complications in real-world perioperative populations.

Recommendations

HTPs should not be considered a replacement for complete smoking cessation, which remains the gold standard for minimizing surgical complications. In patients who are unwilling or unable to quit smoking, switching to HTPs may be considered as a transitional

harm reduction strategy under close medical supervision. Surgeons and perioperative teams should be educated about toxicological differences between tobacco products to provide evidence-based counselling to patients. Further research, including prospective clinical trials and wound healing models, is needed to evaluate the real-world impact of HTP use in surgical populations.

Declarations

Conflict of Interest: None declared.

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References

- Schmid M, Sadasivan KK, Dindo D, Clavien PA, Hahnloser D. Impact of smoking on perioperative outcomes after major surgery. *Am J Surg.* 2015;210(2):221-229. doi:10.1016/j.amjsurg.2014.12.045.
- Grasbeck HL, Reito A, Ekroos H, Aakko JA, Holsa O, Vasankari T. Smoking is a predictor of complications in all types of surgery: a machine learning-based big data study. *BJS Open.* 2023;7(2). doi:10.1093/bjsopen/zrad016.
- Chiang YF, Lee Y, Lam F, Liao C, Chang C, Lin C. Smoking increases the risk of postoperative wound complications: a propensity score-matched cohort study. *Int Wound J.* 2022;20(2):391. doi:10.1111/iwj.13887.
- Reddy VV, Lakshmi M, Rani SS, Rao AV, Satyanarayana G, Murthy PV. Perioperative cardiopulmonary complications in smokers and non-smokers undergoing elective surgery: a prospective study. *J Pharmacol Pharmacother.* 2024;15(2):171. doi:10.1177/0976500x241246412.
- Global Adult Tobacco Survey (GATS). Indonesia report 2021. Jakarta: Ministry of Health, Republic of Indonesia; 2022.
- Fawwaz SM, Pardede DKB. Dampak kebiasaan merokok terhadap risiko anestesi dan pembedahan. *Cermin Dunia Kedokteran.* 2023;50(10):928.
- Omaiye EE, McWhirter KJ, Luo W, Pankow JF, Talbot P. Selected harmful and potentially harmful constituents levels in commercial e-cigarettes. *Tob Control.* 2019;28(6):678-687.
- Williams M, Villarreal A, Bozhilov K, Lin S, Talbot P. Metal and silicate particles including



- nanoparticles are present in electronic cigarette cartomizer fluid and aerosol. *PLoS One*. 2013;8(3):e57987.
9. Sundar IK, Javed F, Romanos GE, Rahman I. E-cigarettes and flavorings induce inflammatory and pro-senescence responses in oral epithelial cells and periodontal fibroblasts. *Oncotarget*. 2016;7(47):77196-77204.
 10. Goniewicz ML, Gawron M, Smith DM, Peng M, Jacob P 3rd, Benowitz NL. Exposure to nicotine and selected toxicants in cigarette smokers who switched to electronic cigarettes: a longitudinal within-subjects observational study. *Nicotine Tob Res*. 2017;19(2):160-167.
 11. Royal College of Physicians. E-cigarettes and harm reduction: an evidence review. London: RCP; 2024.
 12. Lau D, Berger MS, Khullar D, Maa J. The impact of smoking on neurosurgical outcomes. *J Neurosurg*. 2013;119(5):1323. doi:10.3171/2013.5.jns122287.
 13. Galvan CCR, Cataneo AJM. Effect of respiratory muscle training on pulmonary function in preoperative preparation of tobacco smokers. *Acta Cir Bras*. 2007;22(2):98. doi:10.1590/s0102-86502007000200004.
 14. Varga J. Smoking and pulmonary complications: respiratory prehabilitation. *J Thorac Dis*. 2019;11. doi:10.21037/jtd.2018.12.11.
 15. Kozub MI, Gachewicz B, Kasprzyk M, Roszak M, Gasiowski L, Dyszkiewicz W. Impact of smoking history on postoperative complications after lung cancer surgery - a study based on 286 cases. *Pol J Cardio-Thorac Surg*. 2019;16(1):13. doi:10.5114/kitp.2019.83940.
 16. Mathews B, Spear M. The surgical impact of e-cigarettes: a case report and review of the current literature. *Plast Reconstr Surg Glob Open*. 2017;5(10):e1534.
 17. Callahan-Lyon P. Electronic cigarettes - a review of the physiological health effects. *FACETS*. 2014;1(1):377-403.
 18. Weiss KD, Napoli A, DeMeester SR. Perioperative implications of vaping. *J Anesth Clin Res*. 2021;12(3):1-10.
 19. Sorensen LT. Wound healing and infection in surgery: the pathophysiological impact of smoking, smoking cessation, and nicotine replacement therapy: a systematic review. *Ann Surg*. 2012;255(6):1069-1079.
 20. Taghavi SA, Noroozi M, Mokhberi V. The implications of vaping on surgical wound healing: a systematic review. *Surgery*. 2023;173(4):1-10.
 21. Wang W, Zhao T, Geng K, Yuan G, Chen Y, Xu Y. Smoking and the pathophysiology of peripheral artery disease. *Front Cardiovasc Med*. 2021;8:704106. doi:10.3389/fcvm.2021.704106.
 22. Xia N, Morteza A. A review of the role of cigarette smoking in the diabetic foot. *J Diabetes Investig*. 2019;10:202-215.
 23. Sorensen LT. The effects of smoking on the wound healing process. *J Wound Care*. 2010;19(1):5-8.
 24. Inoue Y, Murakami T, Kaneko T, Matsumoto K, Yoshikawa M. Perioperative complications of abdominal surgery in smokers. *J Anesth*. 2020;34(5):712. doi:10.1007/s00540-020-02815-6.
 25. Qiu F, Liang CL, Liu H, Zeng YQ, Hou S, Huang S, Lai X, Dai Z. Impacts of cigarette smoking on immune responsiveness: Up and down or upside down? *Oncotarget*. 2017;8(1):268-284.
 26. Pierce L, Keogh B, Fox B. Smoking increases the risk of postoperative wound complications: a propensity score-matched cohort study. *J Surg Oncol*. 2023;127(1):1-10.
 27. Yamashita S, Kawamura T, Sugita K, Sugita Y, Nakamura Y. Effect of smoking on intraoperative sputum and postoperative pulmonary complication in minor surgical patients. *Respir Med*. 2004;98(8):760. doi:10.1016/j.rmed.2004.01.011.
 28. Senker W, Stefanits H, Gmeiner M, Trutschnig W, Radl C, Gruber A. The influence of smoking in minimally invasive spinal fusion surgery. *Open Med*. 2021;16(1):198. doi:10.1515/med-2021-0223.
 29. Brajcich BC, Stulberg JJ, Huang R, Ujiki MB, Chung JW. Association of preoperative smoking with complications following major gastrointestinal surgery. *Am J Surg*. 2021;223(2):312. doi:10.1016/j.amjsurg.2021.06.002.
 30. Giebe S, Hoffmann A. Comparative study of the effects of cigarette smoke versus next generation tobacco and nicotine product extracts on endothelial function. *Redox Biol*. 2021;47:102150.