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Tempo de cessação do tabagismo para a prevenção de complicações na cicatrização de feridas cirúrgicas
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Duration of smoking cessation for the prevention of surgical wound healing complications

RESUMO
O estudo objetivou buscar evidências científicas sobre o tempo requerido para interrupção do tabagismo no pré-operatório para a redução de complicações na cicatrização da ferida cirúrgica. Revisão integrativa realizada nas bases Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) e Medical Literature Analysis and Retrieval System on-line (MEDLINE) no período de 17/08/2012 a 17/09/2012, utilizando os descriptores: abandono do uso de tabaco e cicatrização de feridas; abandono do uso de tabaco e período pré-operatório; abandono do uso de tabaco e período perioperatório (LILACS) e tobacco use cessation e wound healing (MEDLINE). Dos 81 estudos elegíveis, 12 foram incluídos. O tempo de cessação do tabagismo necessário para redução de complicações é de no mínimo quatro semanas (quatro estudos com nível de evidência I; três estudos com nível de evidência II; dois estudos com nível de evidência IV; um estudo com nível de evidência VII).

DESCRIPTORES
Tobacco use cessation
Wound healing
Postoperative complications
Nursing
Review

DESCRIPTORES
Abandono do uso de tabaco
Cicatrização de feridas
Complicações pós-operatórias
Enfermagem
Revisão

DESCRIPTORES
Cese del uso de tabaco
cicatrización de heridas
Complicaciones postoperatorias
Enfermería
Revisión
INTRODUCTION

Smoking is considered the leading cause of potentially preventable deaths worldwide by the World Health Organization (WHO). It is estimated that currently there are approximately one billion, 200 million smokers worldwide, of whom 690 million are addicted to nicotine. Tobacco-related deaths have reached six million deaths per year and, among them, more than five million are users and ex-users. In addition, over 600 thousand people are directly exposed to secondhand smoke\(^1\). Half of current tobacco users will die as a result of problems related to it: chronic obstructive pulmonary disease (85%), cardiovascular disease (45%), cerebrovascular disease (25%), and cancer (30%), as well as almost 100% of those with lung cancer\(^2\).

It is impossible to measure the impact caused by tobacco use on the health of the world’s population. Currently smoking is levied on one of the lesser age ranges of experimentation among adolescents and young people, preceded only by alcohol\(^3\). If the current pattern of consumption is maintained, statistical projections for 2030 predict the emergence of 400 million new cases of smokers and one in every six million deaths each year\(^4\).

Chronic exposure to cigarette smoke causes physiologic changes that may modify responses to interventions and contribute to increased postoperative morbidity, consequently increasing the risk of respiratory, cardiovascular and wound healing complications\(^5-6\). The literature indicates that smoking cessation may be beneficial to reduce these complications\(^7\).

Tobacco cessation has been suggested to reduce the risk of postoperative complications in surgical wound healing\(^6-7\). There are clinical studies that clarify the relationship between the components of cigarettes and wound healing\(^8-10\). Some mention the duration of smoking cessation required to avoid postoperative complications\(^6\). However, the optimal duration of preoperative smoking cessation to reduce surgical wound complications is not well established.

Therefore, the objective of this study was to seek scientific evidence in the literature about the duration of preoperative smoking cessation required to reduce surgical wound healing complications.

METHOD

This is an integrative literature review, which considered the following steps: identification of the research question, literature search, categorization and assessment of studies, interpretation of results, and synthesis of knowledge\(^12\). The guiding question of this review was: What is the period of preoperative smoking cessation required to reduce surgical wound healing complications?

Two databases were used: Latin American and Caribbean Literature on Health Sciences (LILACS) and Medical Literature Analysis and Retrieval System Online (MEDLINE), accessed through PubMed System.

The controlled descriptors of the Regional Library of Medicine (BIREME), Descriptors in Health Sciences (DECS) and the National Library of Medicine (NLM) Medical Subject Headings (MeSH) were used for the search. In the LILACS database, the following combinations of descriptors were used: 1) tobacco use cessation and wound healing; 2) tobacco use cessation and preoperative period; 3) tobacco use cessation and perioperative period, but no studies were identified. In MEDLINE, the following descriptors were used: 1) tobacco use cessation and perioperative period; 2) tobacco use cessation and wound healing.

After reading the abstracts and applying the inclusion and exclusion criteria, 12 studies were selected in the MEDLINE database; 18 were excluded because they were in languages other than those selected for this study and 51 did not address the duration of smoking cessation in order to avoid healing complications (Figure 1).

![Figure 1 - Flowchart of article identification, exclusion and selection](https://www.ee.usp.br/reeusp/revescenfermusp/2014;48(1):170-6)
Once the research designs were analyzed, the studies were categorized as experimental, quasi-experimental and non-experimental studies. The level of evidence was classified according to the literature: I. Evidence from systematic review or meta-analysis of all relevant randomized controlled trials, or from clinical guidelines based on systematic reviews of randomized controlled clinical trials; II. Evidence obtained from at least one well-designed randomized controlled clinical trial; III. Evidence obtained from well-designed non-randomized clinical trials; IV. Evidence obtained from well-designed cohort and case-control studies; V. Evidence obtained from systematic review of descriptive and qualitative studies; VI. Evidence obtained from a single descriptive or qualitative study; VII. Evidence obtained from opinion of authorities and/or report from a committee of experts.

### RESULTS

Of the 12 articles assessed, three were published in 2012, two in 2010, two in 2006, two in 2005, one in 2011, one in 2009 and one in 2003. All articles were published in the international literature and in the MEDLINE database. Regarding journals, four studies were published in surgery journals (Annals of Surgery, Archives of Surgery and Surgery), three anesthesia journals (Canadian Journal of Anaesthesia and Anaesthesiology), two in general medical area (The American Journal of Medicine and Annals of Plastic Surgery), one in a journal about wound healing (Wound Repair and Regeneration), one in the area of otorhinolaryngology (Archives of Otolaryngology Head & Neck Surgery) and one in the area of and gynecology and obstetrics (American Journal of Obstetrics and Gynecology).

Regarding the research design, the following studies were identified: one meta-analysis, three systematic reviews, three experimental, three non-experimental and two narrative reviews of the literature. Most were not classified with a strong level of evidence: there were four studies with level of evidence I, three with level of evidence II, three with level of evidence IV, and two with level of evidence VII.

Ten studies showed that smoking cessation for a minimum period of four weeks is beneficial in reducing complications of surgical wound healing, four studies classified as level of evidence I (three meta-analyses and one systematic review) (Chart 1), three with level of evidence II (experimental studies) (Chart 2), two with level of evidence IV (non-experimental studies) and one with level of evidence VII (narrative literature review) (Chart 3).

#### Chart 1 - Meta-analyses and systematic reviews that studied the period of smoking cessation required to reduce surgical wound healing complications (level of evidence I)

<table>
<thead>
<tr>
<th>REFERENCE</th>
<th>METHOD</th>
<th>RESULTS and CONCLUSIONS</th>
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<tbody>
<tr>
<td>Sorensen (2012)⁹</td>
<td>Systematic review performed in PubMed and EMBASE databases. Studies analyzed: 178</td>
<td>Smoking cessation restored tissue oxygenation and metabolism; Within four weeks, the cellular inflammatory response was partly reversed, whereas the proliferative response remained impaired; Nicotine did not affect the tissue, but appeared to impair inflammation and stimulate proliferation.</td>
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<tr>
<td>Wong et al., (2012)⁷</td>
<td>Systematic review and meta-analysis performed in MEDLINE, EMBASE and Cochrane databases Studies analyzed: 25</td>
<td>Risk of developing surgical wound healing complications was two times higher in smokers than in non-smokers (RR: 2.08, 95% CI: 1.60 to 2.71, p&lt;0.00001); Risk of surgical wound healing complications was lower in smokers who stopped smoking for more than four weeks compared to smokers (RR: 0.69, 95% CI: 0.56 to 0.84).</td>
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<tr>
<td>Sorensen (2012)⁹</td>
<td>Systematic review and meta-analysis performed in CENTRAL, MEDLINE and EMBASE databases Individuals abstaining from cigarettes for 4 weeks before surgery were considered ex-smokers. Studies analyzed: 140 Patients evaluated: 479,150</td>
<td>Higher incidence of surgical wound complications in smokers than in non-smokers (OR: 2.06, 95% CI: 1.60 to 2.65); Higher incidence of necrosis, wound dehiscence, and surgical site infection in smokers than in non-smokers (OR: 3.61, 95% CI: 2.78 to 4.68 and OR: 2.86, 95% CI: 1.49 to 5.49 and OR: 2.12, 95% CI: 1.56 to 2.88, respectively); Smoking abstinence for at least four weeks significantly reduced surgical site infection and hence surgical wound healing</td>
</tr>
<tr>
<td>Mills et al., (2011)⁴¹</td>
<td>Systematic review and meta-analysis performed in the following databases: Amed, Embase, Central, CINAHL, Cochrane, Development and Reproductive Toxicology, Hazardous Substances Database, Medline, PsychINFO, TOXNET, and Web of Science Studies analyzed: 21</td>
<td>Reduction of complications in surgical wound healing among nonsmokers compared to smokers (RR: 0.73, 95% CI: 0.61 to 0.87, p = 0.0006); Smoking cessation for a short period (less than four weeks) compared with a period longer than four weeks resulted in a 20% reduction in the relative risk of total complications (RR: 0.80, 95% CI: 3.3, p = 0.02); Each additional week of smoking cessation generated a significant impact on postoperative complications.</td>
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**Chart 2** - Experimental studies that approached the period of smoking cessation required to reduce surgical wound healing complications (level of evidence II).

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<tr>
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<tr>
<td>Sorensen et al., (2010)(16)</td>
<td>48 smokers randomized into groups: G1: smoking; G2: smoking abstinence and use of transdermal nicotine patch; G3: smoking abstinence and placebo. Non-smokers also participated in the study (n=30). Surgical wound assessments were made at 1st, 4th, 8th and 12th weeks of follow-up.</td>
<td>Vitamin C was lower in smokers than in those who were never smokers (average of 54.13 and 110.6, respectively, p&lt;0.01); After smoking cessation, there were increased levels of vitamin C (β = 2.23 0.86, p=0.01); Four-week cigarette abstinence was needed to restore the levels of vitamin C and collagen in the body, improving the inflammatory cell response.</td>
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<tr>
<td>Sorensen et al., (2010)(17)</td>
<td>78 patients were divided into two groups: smokers (n=48) and nonsmokers (n=30). Smokers were randomized into three groups: 1: smoking; 2: smoking abstinence and use of transdermal nicotine patch; 3: smoking abstinence and placebo. Biopsy was performed in all patients and histopathological measurements were made in the 1st, 4th, 8th and 12th weeks.</td>
<td>Macrophages and fibroblasts were reduced in smokers (0.28 [0.14 to 0.58] [OR, 95% CI], p=0.01 and 0.37 [0.19 to 0.70] p&lt;0.01) when compared to nonsmokers; There was a significant increase in vitamin C after smoking cessation (β = 2.23±0.66, P=0.01); Smoking abstinence reduced inflammation and the surgical site infection, but did not affect proliferation; The inflammatory phase of wound healing was slower in smokers and could be reversed within four weeks of smoking abstinence.</td>
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<tr>
<td>Sorensen et al. (2003) (18)</td>
<td>The study included 48 smokers and 30 nonsmokers. In the first week, smokers used 20 cigarettes per day. In the second week, they were randomized into three groups: G1: smoking; G2: smoking abstinence and use of transdermal nicotine; G3: smoking abstinence and placebo. Four 5-mm incisions were made in the sacral region and then evaluated in the 4th, 8th and 12th weeks</td>
<td>The incidence of wound infection was 12% in smokers and 2% in nonsmokers (p&lt;0.05); After four weeks, infection was lower in the group of abstinence smokers when compared to the group of continuous smokers; Wound dehiscence occurred in 12% of smokers and none of the nonsmokers (p&lt;0.05); Four weeks of smoking abstinence reduced wound infections at a similar level to that of nonsmokers.</td>
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**Chart 3** - Non-experimental studies and narrative reviews of the literature that approached the time necessary for smoking cessation to reduce surgical wound healing complications (levels of evidence IV and VII).

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<th>OBJECTIVE</th>
<th>METHOD</th>
<th>RESULTS and CONCLUSIONS</th>
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<tr>
<td>Wein (2009)(19)</td>
<td>To explore the duration of smoking cessation before surgery to reduce postoperative complications in head and neck surgery.</td>
<td>Narrative review of the literature. The author did not mention the databases or the descriptors used.</td>
<td>Smoking cessation for the prevention of pulmonary complications must occur four to eight weeks before surgery and, for wound healing benefits, more than four weeks.</td>
</tr>
<tr>
<td>Chan et al., (2006)(20)</td>
<td>To determine whether there was a significant relationship between cigarette smoking and surgical wound healing complications.</td>
<td>Non-experimental study that evaluated records of patients undergoing breast reduction (65 smokers and 104 nonsmokers). Smokers were divided into three groups: A) quit smoking &gt;4 weeks (n=15); B) quit smoking &lt; 4 weeks (n=19); C) continued smoking (n=31).</td>
<td>42% of patients had some healing complication; Smokers had 1.6 times higher chance of developing healing problems than nonsmokers (P&lt;0.05); Group C showed a higher complication rate (67.7%) compared to groups A (33.3%) and B (52.6%); Preoperative smoking cessation should be stimulated for a period of four weeks or longer.</td>
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<tr>
<td>Warner (2006)(21)</td>
<td>To update the knowledge about how the period of smoking cessation affects the perioperative risk.</td>
<td>Narrative review of the literature. The author does not mention the databases and the descriptors used.</td>
<td>The duration of preoperative smoking cessation to avoid or reduce healing complications remains unknown.</td>
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</table>
One study concluded that smoking cessation for a period of less than three weeks was a risk factor for complications of surgical wound healing (level of evidence VII, narrative review) and another showed that the duration of preoperative smoking abstinence to prevent or reduce healing complications remains unknown (level of evidence IV, non-experimental study) (Chart 3).

**DISCUSSÃO**

Smoking is the most important risk factor for the development of postoperative complications and for the need for a postoperative intensive care unit. Several studies have confirmed the impact of smoking on the development of postoperative wound healing complications, in addition to the fact that the incidence of these complications is significantly higher in smokers than in nonsmokers.

The mechanism of wound healing involves a cascade of interconnected cellular and molecular events for the occurrence of resurfacing and tissue reconstruction. Cigarettes have vasoconstrictor substances, which may impair the patient's circulation, since it reduces the diameter of vessels, restricting blood supply, which can trigger the death of some cells. The presence of this condition may predispose the individual to be infected and therefore have his hospital discharge delayed, which leads to increased personal and institutional costs.

Inhalation of cigarette components increases blood flow to the coronary artery, raising the heart rate, forcing an increase in myocardial work, blood pressure and the force of myocardial contractility. Nicotine, a major component of cigarettes, acts on the body by impairing the transport of oxygen by red blood cells due to the high concentration of carbon monoxide. Carbon monoxide not only binds to the red cells, reducing the oxygen-carrying ability, but it also prevents the release of oxygen by hemoglobin, in addition to inhibiting migration of fibroblasts, which end up on the edges of the wound. Therefore, it takes longer to heal.

Surgical tissue trauma reduces blood and oxygen supply to the tissue. Hypoxia can facilitate tissue colonization by bacteria, which multiplies the consumption of oxygen and glucose. Increased consumption of molecular oxygen may also occur, resulting in superoxide production by macrophages that migrate to the damaged tissue to phagocyte bacteria causing oxidative death of these cells. During the initial phase of healing, the level of inspired oxygen, tissue temperature, hydration and extrinsic factors, such as smoking and excessive pain, can increase tissue hypoxia and damage the mechanism of oxidative killing of bacteria, making the tissue vulnerable to infections.

Respiration releases a series of reactive oxygen species, which are chemical compounds resulting from the reduction of molecular oxygen. Most of the reactive oxygen is derived from some of the major constituents of cigarette smoke, such as superoxide, nitric oxide, hydrogen peroxide and radical hydroxyl, which can also alter cell function and cause damage to the matrix of cellular components and tissues, directly interfering in normal wound healing and triggering proinflammatory toxins. The damaging effect of reactive oxygen species released by cigarettes on the role of systemic inflammatory cells includes an increased number of neutrophils that confer defense and immunity to the cell, higher reactivity and chemotaxis, attenuating the migration of neutrophils and monocytes, responsible for the protection of tissues and oxidative mechanisms to fight bacteria.

In smokers, the level of antioxidants is reduced, especially vitamin C, essential for the synthesis of collagen, a key protein in the formation of the extracellular matrix of connective tissue. Collagen is synthesized in small portions intracellularly and exported out of the cell where, through the actions of polymerizing enzymes, it is molded in the structure of triple-helix collagen. Each of these three
helices of protein is almost entirely composed of glycine, proline and lysine and by two other amino acids that are modified after being placed by ribosomes: hydroxyproline and hydroxylysine. The latter two are respectively derived from proline and lysine, using enzymatic processes that are dependent on vitamin C\(^9\). Prolonged restriction of vitamin C leads to poor production of collagen, because the collagen molecules produced outside the cells are defective and recognized as damaged and destroyed, which hinders the healing process\(^9\).

Most of the analyzed studies found that smokers who abstained from smoking for more than four weeks before surgery had fewer complications regarding wound healing compared to those who continued smoking\(^7\).

Preoperative smoking cessation for four weeks or longer has several benefits to the patient, because it significantly reduces surgical site infections, delays in healing, suture dehiscence, hernias and fistulas\(^6,8\). Some physiological factors may be involved: inadequate blood supply to the tissue, which can lead to necrosis; decreased inflammatory response and healing damage through oxidative mechanisms\(^6,8\); deficiency in the proliferative phase of wound healing; and, altered collagen metabolism\(^8\).

One study found that smoking cessation two weeks before colorectal surgery did not reduce the incidence of healing complications\(^18\). Another study showed that three weeks of smoking cessation reduced the incidence of impaired wound healing in patients undergoing head and neck surgery, however the number of smokers in the study sample was very low\(^5\).

Four weeks after smoking cessation, endothelial progenitor cells are restored, suggesting reduction of injury and of endothelial dysfunction. Deficiency of vitamin C decreases as a function of elapsed time and cigarette abstinence, and it can be reversed within four weeks of cessation. Four week abstinence leads to an increase in positive macrophage migration in inflammatory cells, a factor that influences the reduction of infectious complications, such as surgical site infection\(^8,11\).

Several studies included in this review assessed smoking in the preoperative period through patient self-report instruments, a technique that can lead smoking and nonsmoking subjects to not properly record their smoking habits. More reliable techniques to assess the use of cigarettes could have been used; for example, biological monitoring of the concentration of carbon monoxide and nicotine. In other studies, researchers have not measured the smoking habit after surgery, a situation that can lead to complications of surgical wound healing.

The present investigation is limited because it includes only articles in Portuguese, English and Spanish. There is need for further randomized controlled trials addressing other populations with representative samples to explore the theme, evidencing and improving the instruments used to assess the evolution of surgical wounds and forms of smoking measurement.

**CONCLUSION**

The period required for preoperative smoking cessation was at least four weeks for the restoration of oxygen levels in the tissues, decreased oxidative stress, reduction of the negative impact on the function of macrophages and increased levels of vitamin C and collagen.

This study contributes to updating knowledge about the consequences of smoking on physiological responses of surgical healing, supporting the prevention of postoperative wound healing complications. Nurses play a key role in preoperative patient education, planning and executing effective nursing interventions, and assisting patients in finding effective strategies for smoking cessation.

**REFERENCES**

Duration of smoking cessation for the prevention of surgical wound healing complications

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