



# Tobacco and Bone Health

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Cigarette smoking is commonly identified by orthopedic surgeons as one of the factors to cause delayed union and nonunion.

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- Tobacco has been implicated as a major factor for the development of Osteoporosis.
- Smoking has been found to decrease oxygen levels in the cutaneous and subcutaneous tissues leading to poor wound healing.
- Nicotine has been found to decrease vascularization at fracture sites, increasing the chances for the development of osteomyelitis.

# Introduction

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- Bone mineral density,
- Lumbar disc disease,
- The rate of hip fracture,
- The dynamics of bone and wound healing.

**Smoking Adversely  
affects:**

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A review of multiple studies into the adverse effects of tobacco use on fracture repair revealed that there are several hypotheses as to the mode of action:

- A reduced blood supply,
- High levels of reactive oxygen intermediates,
- Low concentrations of antioxidant vitamins
- Effects of nicotine on arteriole endothelial receptors bringing vasoconstriction

**. Nicotine in high doses is directly toxic to proliferating osteoblasts.**

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- Nicotine seems to affect the early revascularization of the fractured bone, probably through down-regulated gene transcription of fibroblast growth factor, vascular endothelial growth factor, and bone morphogenetic protein cytokines known to be important to angiogenesis and osteoblast function.

**Tobacco has negative effects on fracture healing in diaphyseal fractures**

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- Smoking is believed to affect bone healing in diaphyseal fractures of Femur, Tibia and Humerus.
- Other diaphyseal fractures may be affected too but this has not been formally demonstrated yet, except for the negative effect of tobacco in **healing of scaphoid nonunion and of lumbar arthrodesis** .

## **Bones affected by smoking**

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- **Delayed acute fracture healing.**
- **Failure of nonunion treatment.**
- **Failure of bone healing associated with spinal fusion**
- **Failure of bone healing associated with osteotomies.**

Reference (1-5)

**Evidence shows that  
smoking is linked with:**

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[J Orthop Trauma](#). 2005 Mar;19(3):151-7.

### **Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fractures.**

[Castillo RC](#)<sup>1</sup>, [Bosse MJ](#), [MacKenzie EJ](#), [Patterson BM](#); [LEAP Study Group](#).

#### ⊕ Author information

#### **Abstract**

**OBJECTIVES:** Current data show smoking is associated with a number of complications of the fracture healing process. A concern, however, is the potential confounding effect of covariates associated with smoking. The present study is the first to prospectively examine time to union, as well as major complications of the fracture healing process, while adjusting for potential confounders.

**Even a history of prior smoking and exposure to second-hand smoke has been shown to delay bone healing: Castillo RC et al**

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Unfallchirurg. 2002 Jan;105(1):76-81.

**[Adverse effects if smoking on healing of bones and soft tissues].**

[Article in German]

Hoogendoorn JM<sup>1</sup>, Simmermacher RK, Schellekens PP, van der Werken C.

⊕ Author information

**Abstract**

**Not only does smoking affect bone healing, it also increases the risk of other complications such as acute infection and osteomyelitis: Hoogendoorn JM**

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J Am Acad Orthop Surg. 2008 Feb;16(2):88-97.

### **Femoral nonunion: risk factors and treatment options.**

Lynch JR<sup>1</sup>, Taitsman LA, Barei DP, Nork SE.

#### **Author information**

#### **Abstract**

Despite advances in surgical technique, fracture fixation alternatives, and adjuncts to healing, femoral nonunion continues to be a significant clinical problem. Femoral fractures may fail to unite because of the severity of the injury, damage to the surrounding soft tissues, inadequate initial fixation, and demographic characteristics of the patient, including nicotine use, advanced age, and medical comorbidities. Femoral nonunion

**Smoking is a risk factor for femoral nonunions: Lynch J B et. al.**

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J Orthop Trauma. 2003 Nov-Dec;17(10):663-7.

**The effect of smoking on clinical outcome and complication rates following Ilizarov reconstruction.**

McKee MD<sup>1</sup>, DiPasquale DJ, Wild LM, Stephen DJ, Kreder HJ, Schemitsch EH.

⊕ Author information

**Abstract**

**OBJECTIVE:** To determine the effect of smoking on outcome and complication rates following Ilizarov reconstruction.

**Smoking decreases efficiency even in the  
bone generation machine:  
Ilizarov distraction osteogenesis: McKee MD**

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[J Foot Ankle Surg.](#) 2009 Sep-Oct;48(5):525-7. doi: 10.1053/j.jfas.2009.04.008. Epub 2009 Jul 2.

### **The effect of cigarette smoking on radiographic bone healing after elective foot surgery.**

[Krannitz KW<sup>1</sup>](#), [Fong HW](#), [Fallat LM](#), [Kish J](#).

**+** Author information

#### **Abstract**

This study aims to compare radiographic healing rates of Austin bunionectomies in smokers, nonsmokers, and secondhand smokers. Delayed bone healing has been linked to cigarette smoking previously, but no study is known to have examined smoking in relation to elective foot

**Smoking delays radiological bone healing in all bones, foot bones, spinal fusions and also at surgical osteotomy sites: Kranitz KW et al**

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- Vasoconstrictive properties of nicotine inhibit tissue differentiation and the normal angiogenic responses in the early stages of fracture healing.
- Nicotine directly interferes with osteoblast function.
  
- References: 5-8

## **Animal studies**

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[Spine \(Phila Pa 1976\)](#). 1994 Apr 15;19(8):904-11.

### **Nicotine on the revascularization of bone graft. An experimental study in rabbits.**

[Daftari TK<sup>1</sup>](#), [Whitesides TE Jr](#), [Heller JG](#), [Goodrich AC](#), [McCarey BE](#), [Hutton WC](#).

#### **Author information**

#### **Abstract**

**STUDY DESIGN:** In 24 rabbits, the authors transplanted autologous cancellous bone to the anterior chamber of the eye. Half of the rabbits received nicotine and half received placebo (albumin) from mini-osmotic pumps that were implanted subcutaneously. Revascularization of the bone graft was evaluated postoperatively using ophthalmology slit-lamp and fluorescein angiography, and after sacrifice using microvascular silicone injection and histology.

**Revascularization of the bone graft in a Rabbit model was found to be delayed by nicotine: Daftari T K et al**

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[J Trauma](#). 1999 Jan;46(1):110-5.**Bone healing of tibial lengthening is delayed by cigarette smoking: study of bone mineral density and torsional strength on rabbits.**[Ueng SW<sup>1</sup>](#), [Lin SS](#), [Wang CR](#), [Liu SJ](#), [Tai CL](#), [Shih CH](#).

⊕ Author information

**Abstract****OBJECTIVE:** We investigated the effect of intermittent cigarette smoke inhalation on the bone healing of tibial lengthening in rabbits.**Full text links****Save items**

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**Tibial lengthening in a Rabbit model was delayed by cigarette smoking: Ueng SW**

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Bone. 2008 Aug;43(2):355-61. doi: 10.1016/j.bone.2008.04.002. Epub 2008 Apr 16.

### Changes in blood perfusion and bone healing induced by nicotine during distraction osteogenesis.

Zheng LW<sup>1</sup>, Ma L, Cheung LK.

Author information

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**Nicotine compromises bone regeneration possibly by causing ischemia and direct inhibitory effect on osteoblastic cells: Zheng L W**

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www.thebonejournal.com/article/S8756-3282(08)00186-5/pdf

# Bone

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August 2008 Volume 43, Issue 2, Pages 395-361

## Changes in blood perfusion and bone healing induced by nicotine during distraction osteogenesis

Li Wu Zheng, Li Ma, Lim Kwong Cheung

Discipline of Oral and Maxillofacial Surgery, Faculty of Dentistry, The University of Hong Kong  
Edited by: R. Rizzoli

DOI: <http://dx.doi.org/10.1016/j.bone.2008.04.002>

Article Info

Abstract Full Text Images References

### Abstract

Nicotine is the main chemical in cigarettes responsible for the tobacco's pathological effects. The influence of nicotine on bone healing remains controversial. Distraction osteogenesis provides an ideal model to study bone healing and regeneration. The present study aims to evaluate the effects of nicotine on blood perfusion, angiogenesis and bone formation using a rabbit model of mandibular lengthening. Twenty adult New Zealand white rabbits were randomly assigned to the control group and nicotine group. The total nicotine or placebo exposure time for all animals was 7 weeks. After 2- or 4-week of consolidation following osteotomy, 3-day of latency and 11-day of active distraction, the animals were sacrificed and the mandibles were harvested. Blood perfusion and vascularization were evaluated by Laser Doppler monitoring and Collagen IV immunohistochemistry staining respectively. Bone formation was assessed by radiological, histological and immunohistochemical examination. Results showed that nicotine exposure increased microvessel density, whereas inhibited blood flow and bone formation. The expression of bone morphogenetic protein (BMP)-2 in osteoblasts was also decreased. Frequent appearance of cartilage islands suggested ischemia and low oxygen tension in the distraction regenerate. We concluded that nicotine compromises bone regeneration possibly by causing ischemia and directly inhibitory effect on osteoblastic cells. Nicotine exposure enhances angiogenesis but cannot compensate for the adverse effect of vasoconstriction.

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- Nicotinic modulation of gene expression in osteoblast cells, MG-63 Bone, Vol. 48, Issue 4
- Effects of nicotine on cellular function in UMR 106-01 osteoblast-like cells Bone, Vol. 12, Issue 4
- Effects of nicotine on human osteoclasts and co-cultures of

**Nicotine exposure enhances angiogenesis but cannot compensate for the adverse effects of vasoconstriction: Zheng L W**

# BONE MORPHOGENETIC PROTEIN MRNA EXPRESSION IN HUMAN PERIOSTEUM OF FRACTURED BONES

C. Chasanidis, Z. Daihana, P. Kollia, T. Koromila, K. Malizos, S. Samara, S. Vrittimidis

Published 20 September 2010

Article

Info & Metrics

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Current Issue

Index by author



## Abstract

**Introduction:** Periosteum is a tissue with pluripotential mesenchymal cells (MSCs). During fracture repair several growth factors are released from periosteum, including bone morphogenetic proteins (BMPs), which induce the differentiation of bone marrow stromal cells towards the osteoblastic lineage, therefore increasing the pool of mature bone forming cells and enhance the differentiated function of osteoblasts.

- Recent human data, where samples of fractured and non-fractured bones from smokers and nonsmokers were assayed for BMP-2, -6, -4, and -7 using polymerase chain reaction, indicate that smoking reduces periosteal bone morphogenetic protein (BMP) gene expression

## Human Evidence

The screenshot shows a web browser window with two tabs. The active tab is titled "Impact of smoking on frac". The address bar shows the URL "https://www.ncbi.nlm.nih.gov/pubmed/15758667". Below the address bar is a "Bookmarks" section. The main content area features the "PubMed.gov" logo, the text "US National Library of Medicine National Institutes of Health", a search box containing "PubMed", and a "Send" button. The article title is "Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fractures." The authors listed are "Castillo RC<sup>1</sup>, Bosse MJ, MacKenzie EJ, Patterson BM; LEAP Study Group." There is also a link for "Author information".

- Smokers with open tibia fractures treated with intramedullary (IM) nails were found, in a prospective study by Castillo et al.,<sup>49</sup> to be 37% less likely to achieve union and 3.7 times more likely to develop osteomyelitis than nonsmokers.
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https://www.ncbi.nlm.nih.gov/pubmed/8122874

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Ann Chir Gynaecol. 1993;82(4):254-62.

**Are smokers a risk group for delayed healing of tibial shaft fractures?**

Kyrö A<sup>1</sup>, Usenius JP, Aarnio M, Kunnamo J, Avikainen V.

Author information

Effect of smoking on tibia

https://www.ncbi.nlm.nih.gov/pubmed?Db=pubmed&Cmd=Retrieve&list\_uids=10627703&dopt=abstractplus

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National Institutes of Health

PubMed Advanced

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Clin Orthop Relat Res. 1999 Aug;(365):184-200.

**Effect of smoking on tibial shaft fracture healing.**

Schmitz MA<sup>1</sup>, Finnegan M, Natarajan R, Champine J.

**Smoking was found to delay healing in a dose-dependent manner after closed management of tibial shaft fractures.**

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The screenshot shows a web browser window with the following elements:

- Browser tabs: "The effect of smoking on...", "264\_2013\_Article\_1809.p...", "1553.full.pdf", and "Download".
- Address bar: <https://www.ncbi.nlm.nih.gov/pubmed/14600564>
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- PubMed logo and text: "PubMed.gov US National Library of Medicine National Institutes of Health"
- Search dropdown: "PubMed" with a search input field and "Advanced" link.
- Format: "Format: Abstract"
- Citation information: "J Orthop Trauma. 2003 Nov-Dec;17(10):663-7."
- Article title: **The effect of smoking on clinical outcome and complication rates following Ilizarov reconstruction.**
- Authors: McKee MD<sup>1</sup>, DiPasquale DJ, Wild LM, Stephen DJ, Kreder HJ, Schemitsch EH.

- In the setting of Ilizarov limb reconstruction, McKee et al. demonstrated that smoking was associated with multiple complications. The overall complication rate was over three times higher rates of persistent infection, nonunion, and amputation.
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- Despite being one of the few risk factors that is potentially modifiable, smoking cessation in the face of the stresses associated with acute fracture is exceedingly difficult.
- Despite these challenges, it is prudent to advocate and support smoking cessation in all patients with fractures at risk for nonunion and in those facing nonunion repair.
- Given the direct adverse effects of nicotine on bone healing, nicotine supplementation (e.g., nicotine patch) as part of a smoking cessation program should be avoided.

# Recommendation

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The screenshot shows a web browser window with multiple tabs. The active tab is titled "https://www.ncbi.nlm.nih.gov/pubmed/22955337". The page content includes the title "The effect of transdermal nicotine on fracture healing in a rabbit model." and the authors "Donigan JA<sup>1</sup>, Fredericks DC, Nepola JV, Smucker JD." Below the title, there is a "Wolters Kluwer" logo and a "Save items" button. A "Bookmarks" bar is visible at the top of the page content area.

**Animal data supports the fact that transdermal nicotine patch leads to nonunion and decreased mechanical strength of healing fractures: Donigen J A**

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Approximately 50% of smokers return to their habit. It is best for healing of bone and soft tissue if they can abstain while being treated for their injury.

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