CHAPTER **44**

SMOKING AND LOWER EXTREMITY SURGERY

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INTRODUCTION

The use of tobacco has been extensively studied over past decades and has numerous proven deleterious effects on users of this substance. Almost 20% of preventable deaths occur each year from smoking-related illnesses, which accounts for the leading preventable cause of death in the US. These effects include many varieties of cancer such as esophageal, laryngeal, pharyngeal, stomach, cervical, and lung. Other linked illnesses include cardiovascular disease, lung disease, pancreatitis, osteoporosis, and macular degeneration. Additionally, specific surgical concerns of tobacco use have been discussed within medical literature for many years. Initial research focused on wound complications associated with smoking, yet recent attention has been directed toward further clinical observations of delayed bone healing and bone mineral loss. Orthopedic research has established an osseous healing delay in an assortment of surgeries, including certain spinal and trauma procedures, nevertheless much more research is needed. The exact effect of tobacco use on lower extremity osseous healing remains to be fully established. Therefore current literature, as well as physiology of cigarette smoke on bone healing will be reviewed in order to both further our understanding and to appreciate where future research is needed.

BONE HEALING AND TOBACCO

The process of bone healing essentially entails the regeneration of osseous structure across an osteotomy or fracture site, restoring normal skeletal integrity and function. Even under ideal conditions, literature shows that between 5 to 10% of patients may progress to a delayed or non-union in bone surgery.[1] Bone healing can be divided into three distinct, yet overlapping phases that include inflammatory, regenerative or reparative, and remodeling.

Initially after fracture or osteotomy, hematoma forms causing vasoconstriction and loss of cell viability surrounding this site. The local pH will also decrease secondary to necrotic tissue, metabolite release, and diminished oxygenation to local tissues. All of these specific occurrences help stimulate the release of growth factors, cytokines, prostaglandins, and inflammatory cells (macrophages, neutrophils, and lysosomal enzymes). The individual roles played by each factor allow for the removal of necrotic tissue, vasodilatation, fibrin scaffold formation, and influx of undifferentiated mesenchymal cells over a 3-7 day period.[2]

The regenerative phase is characterized by replacement of fibrin with cartilage and vessel migration across the osteotomy site through haversian canal systems, in addition to periosteal and endosteal vasculature ingrowth. Additionally, the pH of local tissue adjusts to slightly alkaline levels, allowing for optimal activation of alkaline phosphate enzyme, which promotes mineralization of the fracture callus by endochondral ossification. It is thought that nicotine plays a role in reduction of capillary vascular ingrowth at this phase, which accounts for an increased rate of nonunion.[2]

The remodeling phase functions to replace the immature woven bone with that of lamellar bone and to reabsorb unnecessary bone callus through mechanical strain and muscular forces according to Wolff's law and piezoelectric field principles.[3,4] This phase may occur from 20 weeks to more than one year.[2]

In a surgical setting, bone healing will ideally occur as primary, rather than secondary healing. This is achieved by rigid stabilization and apposition between bony surfaces. Both contact and gap healing fall under the category of primary bone healing. Contact healing involves direct contact, which allows lamellar bone formation through haversian canal systems, allowing osteoblast proliferation. Gap healing occurs across a rigidly fixated osteotomy with gaps of less than 1 mm. Hematoma forms initially, followed by osteoblast proliferation and finally woven bone deposition with haversian remodeling.[5,6]

Healed bone can be defined by a lack of motion at the site of osteotomy or fracture, in addition to a lack of pain, swelling, or external support device. A delayed union or nonunion occurs once progression of healing has ceased for approximately 3 months, and at least 6-9 months has passed since the time of surgery. Classifications exist in order to identify the type of nonunion and dictate the appropriate treatment modality.[5]

Tobacco contains over 4,000 chemical components, of

which 43 have been identified as cancer causative agents.[5] Three key elements in cigarettes have been identified that impair the healing process, including carbon monoxide (CO_2), nicotine, and hydrogen cyanide. CO_2 comprises 4% of cigarette smoke, and comparable to CO_2 poisoning, a CO_2 molecule will bind hemoglobin in pulmonary capillaries to form carboxyhemoglobin. This compound binds CO_2 with greater affinity than oxygen, thereby causing increased tissue hypoxia and decreased oxygen carrying capacity. Carboxyhemoglobin is found at levels up to 20% higher in smokers. Nicotine will cause vasoconstriction through adrenal catecholamine release and decrease tissue perfusion. It has also been shown to cause alteration of cellular metabolism due to random fibroblast binding and internalization. Prostacyclin, a key vasodilator, is also diminished by nicotine. Lastly, hydrogen cyanide is an inhibitor of cellular respiratory enzymes and may affect cellular oxygenation. Nicotine and its major metabolite, cotinine, play important roles as markers in tobacco testing, which allow the surgeon to determine whether patients are actively using tobacco.[7]

LITERATURE REVIEW

Many animal studies exist to support a link between cigarette smoke and delayed osseous healing. Lau et al showed a delayed or nonunion rate in smoke exposed rabbits that was twice that of the non-exposed group, with concomitant bone atrophy of the fracture site.[8] Ueng et al studied intermittent smoke inhalation with tibial lengthening in rabbits.[9] Their study supported a delay of granulation tissue resorption, bone formation, and bone remodeling. Reibel et al examined nicotine's effect on revascularization and incorporation of autogenous cancellous bone graft in an animal model, and demonstrated decreased vascular in-growth of grafts with nicotine exposure.[10]

In clinical patient trials, there is a small body of literature applicable to the lower extremity that all support delayed healing for patients who are current or former smokers. Research has centered on both time for bone healing and examination of nonunion rates, as demonstrated by Gualdrini et al who determined the healing time of non-smokers was 33% shorter for septic tibial pseudarthrosis.[11] Additionally, Cobb et al reported an increased risk of nonunion in smokers, being 3.75 times greater than non-smoking patients undergoing ankle arthrodesis.[12]

Recent research by Krannitz et al centered on osseous healing rates after undergoing Austin osteotomy for hallux abducto valgus deformity. In this small population, rates of radiographic healing were shown to be decreased in active smokers, followed by second hand smoke exposed patients, and finally non-smokers. To our knowledge, this research is the first to examine forefoot osseous healing and reports promising results which validate the need to stress abstaining from tobacco use.[13]

Ishikawa and colleagues studied the effect of cigarette smoke on hindfoot fusions in 160 patients. Smokers carried an 18.6% chance of nonunion, while non-smokers had a 7.1% chance of nonunion. Smokers were 2.7 times more likely to proceed to nonunion. Additionally, patients who quit smoking prior to surgery were 11.1% more likely to have nonunion than patients having never smoked, but were still less likely to have nonunion than current smokers.[14]

Harvey et al studied the effect of smoking on open tibial shaft fractures. A total of 110 fractures were randomized to receive either external fixator or intramedullary nail. A union rate of 84% was found in smokers, compared with 94% in non-smokers. Additionally, time to union was statistically longer, and rate of complications was higher in the smoking group.[15]

Castillo et al prospectively studied patients suffering open unilateral tibial fractures. In almost 300 patients, they determined that current and prior smokers were 37% and 32% less likely to achieve union than non-smokers, respectively. Current smokers were twice as likely to develop infection and almost four times more likely to develop osteomyelitis, with former smokers almost three times more likely to develop osteomyelitis.[16]

Additionally, Brown et al examined patients undergoing laminectomy and fusion, in order to study the nonunion rate of smokers and non-smokers. A nonunion rate of 40% was found in smokers, compared with 8% in the non-smoking group.[17] Kyro et al studied the risk of delayed healing in tibial shaft fractures. A non-union rate of 50% to 32% was found among the smoker and non-smoker groups respectively. Additionally, a significant increase was found in time to union at fracture site.[18]

CONCLUSION

Even with increased public awareness of health risks, millions continue to smoke across the US. Therefore, it is vital to be aware of surgical implications when deciding to operate on either current or former smokers. Obvious links exist between use of tobacco and bone healing, as proven in multiple studies involving the lower extremity. Evidence supports an increased chance for successful outcome if smoking is discontinued before bone surgery. Helpful measures for patient compliance include cessation of smoking contracts (Addendum 1) and tobacco (nicotine and/or cotinine levels) testing in both the pre and post-operative periods (Addendum 2). Evidence also supports a

strong link for increased nonunion rate in smokers undergoing the following procedures: ankle or hindfoot fusion, bone graft procedures, and skin graft procedures. In these instances, physician-patient discussions must review all techniques available to discontinue tobacco use. Weaker evidence also exists for delayed healing in forefoot surgical procedures. Additional options to assist patients may include nicotine patch or cigarette taper, prescription medications (Varenacline [Chantix], Bupropion [Zyban]), mimic devices, counseling, or abrupt cessation. Adequate time should be given for patient compliance if surgical procedures are not urgent, and allow increased chances for successful healing. In traumatic or emergent settings, similar philosophies must be conveyed to the patient.

Specific to foot and ankle surgery, research on the effect of tobacco is essential. To our knowledge only two publications have studied the effect of smoking on forefoot or rearfoot procedures, with no research on midfoot procedures. Forefoot and midfoot surgeries are routinely performed in active smokers, with many rearfoot procedures performed in smokers. With extremely limited research pertaining to foot and ankle surgery, the effect of tobacco on our surgical patient population is largely unknown.

REFERENCES

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ADDENDUM 1

I, _____, on this date ___/___/___ agree to enter a contractual agreement with Dr. _____ regarding the use of tobacco products (cigarettes, pipe, or smoker's tobacco) and my medical condition and further treatment. I hereby confirm that I am aware of the inherent risks associated with cigarette smoking to my general health. I also acknowledge that I have been educated regarding the increased risk of complications for healing my foot/ankle/leg condition due to the chemical and physiologic effects of tobacco. I hereby agree to enter into this smoking contract and agree to be completely free of smoking for at least one month prior to the date of surgery and will remain tobacco free during the entire healing process. I also hereby consent to periodic and random urine or blood tests to evaluate for the presence of nicotine in my blood stream. If at any time there is evidence of smoking within the period of time prescribed for my healing, I would be subject to dismissal from the care of Dr. _____.

_____ _____

Patient *Date*

_____ _____

Physician *Date*

ADDENDUM 2

06/10/09 [redacted] INTERIM REPORT
12:14 PAGE 1
[redacted]

NAME : [redacted] *** PATIENT DISCHARGED ***
H# : [redacted] LOC: MOP AGE: [redacted] SEX: [redacted]
ACCT : [redacted] DR: Brosky DPM, Thomas, Fx

W14016 COLL: 05/13/2009 15:45 REC: 05/13/2009 15:51 PHYS: Brosky DPM, Thomas

MISC TEST
MISC TEST NAME NICOTINE AND METABOLITE QUANTITATION, BLOOD
MISC TEST FOR MSC (NOTE)

Report Name	Results	Units	Reference Range
NICOTINE AND METABOLITE, BLOOD:	NICOTINE AND METABOLITE, BLOOD		
NICOTINE:	None detected		
	Reporting Limit: 5	ng/mL	
Observed concentrations in habitual smokers:	3 to 63	ng Nicotine/mL	
COTININE:	None Detected		
	Reporting Limit: 20	ng/mL	

Synonym(s): Nicotine Metabolite

Observed concentrations in habitual smokers:
20 - 700 ng Cotinine/mL

Site Information

[redacted]