Review Article

The Musculoskeletal Effects of Perioperative Smoking

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Abstract

Although the carcinogenic consequences of smoking are well known, further research is needed on the effects of smoking on musculoskeletal health and surgical outcomes. Orthopaedic perioperative complications of smoking include impaired healing, increased infection, delayed and/or impaired fracture union and arthrodesis, and inferior arthroplasty outcomes. The incorporation of smoking cessation protocols such as transdermal patches, chewing gum, lozenges, inhalers, sprays, bupropion, and varenicline in the perioperative period may result in substantial benefits for patients' musculoskeletal and general health.

More than 10 million cigarettes are sold per minute worldwide.[1] In the United States, tobacco is responsible for 1 in 5 deaths.[2] Between 2000 and 2004, smoking was responsible for more than $193 billion in annual health-related costs in the United States, including medical costs and lost productivity attributable to smoking.

During cigarette use, hazardous gases and chemicals are released into the bloodstream. The combustion byproducts that are generated injure host DNA, causing genetic mutations that may contribute to the development of cancer. Nicotine is perhaps the most notorious component of tobacco smoke not only because of its addictive qualities but, more importantly, because it is critical to the development and/or exacerbation of many smoking-related disease processes. For example, smoking causes coronary heart disease and aortic aneurysms; contributes to atherosclerosis, peripheral vascular disease, the development of chronic obstructive lung disease, and the development of lung cancer; and places people at increased risk of stroke.[3] Smoking-related morbidity also includes multiple harmful perioperative musculoskeletal complications. Smoking cessation is beneficial for optimizing musculoskeletal outcomes and overall health.

Cellular Effects of Smoking

Smoking has been shown to cause reduced cutaneous blood flow as well as decreased subcutaneous soft-tissue oxygenation and aerobic metabolism.[4] The carbon monoxide found in tobacco further decreases blood flow to healing tissues. Thrombi generated as a consequence of increased platelet aggregation may further limit soft-tissue perfusion.[5]

Reduced blood flow impairs delivery of lymphocytes to infected areas. The nicotine found in tobacco also has detrimental effects at the cellular level. Studies have demonstrated that nicotine negatively modulates T-cell function. In a recently published murine model, decreased expression of transcription factors caused by expo-

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sure to cigarette smoke resulted in reduced production of gamma interferon-γ, which made the T cells more susceptible to pathogens.[6]

Reduced blood flow also may delay and/or impair the quality of bone repair. Nicotine is known to interfere with the cellular processes that occur in mesenchymal stem cells.[7] Nicotinic modulation of gene expression brought about by the addition of nicotine concentrations analogous to heavy smoking has been shown to result in reduced osteoblast formation and bone metabolism.[8,9] Smoking also seems to have an effect on soft-tissue repair; one study demonstrated that collagen production is impeded in persons who smoke.[10]

Smoking is known to negatively affect bone density. By decreasing the production and metabolism of estrogen, smoking may negate the efficacy of these bone-protecting hormones.[11] Decreased estrogen levels may contribute to an increased risk of fracture[12] and accelerated fracture presentation. A retrospective review of hip fractures in 467 smokers and 3,150 nonsmokers demonstrated that smokers sustained their injuries at a younger age than did nonsmokers (average, 9 years earlier).[13]

Clinical Impact of Smoking

Most available evidence on the effect of smoking on orthopaedic outcomes is based on research that is retrospective, statistically insignificant, and often outdated. These studies are often confounded by multiple coexisting variables. Thus, it is difficult to isolate the negative consequences of smoking.

The largest of these studies reviewed 906 consecutive surgically managed ankle fractures.[14] Of the patients studied, 20.4% were categorized as smokers. Smokers had higher rates of postoperative complications than did nonsmokers (30.1% and 20.3%, respectively; $P = 0.005$) and were at greater risk of developing deep wound infection (4.9% and 0.8%, respectively; $P < 0.001$). Multivariate analysis showed smokers to have a six times higher chance than nonsmokers of developing infection.

The impact of smoking on 268 open tibia fractures was reviewed as part of the Lower Extremity Assessment Project.[15] Thirty-nine percent of the patients were active smokers. After adjusting for covariates, current smokers were found to be 37% more likely than never smokers and previous smokers to achieve nonunion ($P = 0.01$), twice as likely to develop acute postoperative infection ($P = 0.05$), and 3.7 times more likely to develop chronic osteomyelitis ($P = 0.01$). The authors of that study concluded that smoking placed patients at higher risk for postoperative complications; they urged orthopaedic surgeons to be more proactive in encouraging smoking cessation.

The effects of smoking are seen on many biologic levels, resulting in disruption of the complex cascade of soft-tissue and bony healing.[4-10] Through these mechanisms, smoking seems to impair the management of established nonunion,[16-18] interfere with healing following osteotomy[19,20] and arthrodesis,[21-25] and increase implant loosening by disrupting the osseointegration needed for successful joint arthroplasty.[26] Smoking also may increase the incidence of soft-tissue injury[27,28] and may negatively affect functional outcomes in patients undergoing repair of knee soft-tissue injury.[29,30]

Smoking Cessation

Physical chemical addiction and psychological dependence make it difficult for habitual smokers to quit. Persons who ultimately succeed often first fail many times to quit. The potential side effects of trying to quit smoking include craving, weight gain, depression, headache, insomnia, and fatigue.

Several comparison studies of smoking cessation alternatives have been done, but inconsistent definitions of success make it difficult to reach definitive conclusions regarding optimal management. Abrupt smoking cessation and gradual reduction in cigarette consumption are rarely permanently successful. Other unsuccessful cessation strategies include the use of vaporizers, electronic cigarettes, and smokeless tobacco.

Proven options for smoking cessation include counseling, self-help groups, advice from a physician, nicotine replacement therapy (NRT), and medication. Counseling by a health professional improves smoking cessation rates, and behavioral modification aids, including the annual World No Tobacco Day and the Great American Smokeout, may also be effective. Self-help groups, such as the 12-step program Nicotine Anonymous, are instrumental in providing motivation and support to smokers who are trying to quit. Alternative approaches, such as hypnosis, aromatherapy, acupuncture, and laser therapy, have shown only anecdotal success.

Advice from a medical professional has traditionally been heralded as an effective, quick, and cost-free means of improving smoking cessation rates. However, a meta-analysis published in 2008 demonstrated that simple physician advice results in only a 1% to 3% increase over an unassisted quit rate.[31] Nursing-delivered intervention has been shown to be useful in smoking cessation.[32]

Pharmacologic agents may aid in minimizing the effects of nicotine withdrawal. The US Food and Drug

Administration (FDA) has approved seven products for the management of nicotine addiction.[33] The five NRT agents—transdermal patch, chewing gum, lozenges, inhalers, and sprays—work by delivering progressively smaller quantities of nicotine without exposing the patient to the other risks of smoking. Advantages and disadvantages of these agents are listed in Table 1.

NRTs have minimal potential side effects. Such therapy should be continued for a maximum of 8 to 12 consecutive weeks. Only the NRT inhaler and spray require a prescription. Caution is warranted with NRT use during pregnancy because the fetal risks of this treatment have yet to be evaluated. Use of any NRT must be weighed against the harm caused by continued smoking during pregnancy.[34]

The transdermal patch is applied to a smooth, hairless area of skin and is left in place for 16 to 24 hours per day. It should not be applied to the same anatomic area more than once per week. Nicotine gum is offered in several strengths. It is chewed either on a regular basis or intermittently to satisfy cravings. To optimize absorption, nicotine gum is chewed a few times, then placed between the jaw and cheek. Lozenges are more discrete than chewing gum, and they may be taken 8 to 12 times per day. Inhalers mimic a cigarette holder, and inhalation of the nicotine vapor may help satisfy the behavioral aspects of smoking. Six to 12 inhaler refills may be used daily. Each refill consists of 10 to 20 puffs and releases an amount of nicotine equivalent to that of one cigarette. Nicotine spray is the strongest and fastest-acting NRT available. Two sprays (ie, one spray per nostril) contain an amount of nicotine equivalent to one cigarette. The recommended usage is one to two treatments per hour, with ≤40 doses per day.

Table 1

Nicotine Replacement Therapies: Advantages and Disadvantages

Therapy	Advantages	Disadvantages
Transdermal patch	Easy to use Discreet Steady long-acting nicotine supply Over-the-counter	Skin irritation Nightmares
Chewing gum	Easy to use Cannot smoke and chew at the same time Faster delivery than the patch Over-the-counter	Bad taste Cannot be used by persons who wear dentures
Lozenge	Discreet No disposal No chewing technique Flavored Over-the-counter	May mimic candy and thereby appeal to children
Inhaler	Mimics hand-to-mouth smoking behavior	Must be used frequently to obtain adequate nicotine levels Indiscreet Mouth and throat irritation Prescription only
Spray	Fastest response Quickly reduces craving	Indiscreet Nose and eye irritation Prescription only

The other two FDA-approved medications work through other mechanisms. The antidepressant bupropion is believed to work by modulating the neurotransmitters that are responsible for addiction. Varenicline acts directly as a partial nicotine receptor antagonist. Varenicline is also a nicotine receptor partial agonist. As such, it may reduce cravings and the pleasure associated with smoking cigarettes. Varenicline tablets are taken one to two times per day for 12 weeks. The dose is increased over time. This cycle may be repeated once. Varenicline treatment begins 1 week before smoking cessation, and the full benefits may not be evident for several weeks. Varenicline has been shown to be highly cost-effective compared with other smoking cessation therapies.[35]

NRT,[36] bupropion,[37] and varenicline[38] each have been shown to improve cessation rates over placebos at a minimum follow-up of 6 months. The ideal regimen of these agents is unclear; however, combination therapy appears to elicit greater success than do individual therapies.[39]

These medications are not without risk. The FDA has stated that the use of bupropion and varenicline is associated with serious neuropsychiatric symptoms.[40] It is not known whether these symptoms, including suicidal ideation, are related to the effect of the medication or are consequences of nicotine withdrawal. Regardless, patients trialing bupropion and varenicline should be monitored by clinicians for mood and behavioral changes.

Orthopaedic Benefits of Smoking Cessation

The orthopaedic benefits of smoking cessation interventions have been demonstrated in clinical practice.

One study investigated the effect of preoperative smoking cessation on postoperative complications in patients undergoing joint arthroplasty.[41] Patients who underwent a 4-week preoperative intervention consisting of counseling and NRT had a postoperative complication rate of 18%, compared with 52% in smokers ($P = 0.0003$). The difference was most notable with regard to wound-related complications, with a rate of 5% for the intervention group and 31% for smokers ($P = 0.001$). In a study examining the long-term effect of preoperative smoking intervention in patients undergoing hip and knee surgery, the quit rate maintained at 1 year postoperatively was 22% for the intervention cohort and 3% for the control group.[42] These studies suggest that planned surgery can offer an effective motivation for smoking cessation.

The feasibility and benefits of smoking intervention programs are not isolated to elective orthopaedic surgery. The authors of a recent study set out to determine whether a smoking cessation program initiated during the acute hospitalization period and continued for 6 weeks postoperatively could reduce the number of complications following emergency surgical management of fractures.[43] One hundred five patients were randomized either to no intervention or to a standardized smoking cessation program consisting of personal meetings, weekly telephone calls with the nurse, and the offer of free NRT. Patients in the control group were 2.51 times more likely than those in the intervention group to have a postoperative complication (95% confidence interval, 0.96 to 6.9 times). In addition, the proportion of patients with at least one postoperative complication was significantly larger in the control group than in the intervention group (38% and 20%, respectively; $P = 0.048$).

The economic implications of preoperative and postoperative smoking cessation programs on orthopaedic surgery in the US healthcare system have not been examined. However, studies have been done in other countries that examined the balance between the cost of preoperative intervention for smoking cessation and the benefit resulting from the potential reduction in hospitalization costs in patients undergoing hip or knee replacement. Using official French hospital costs for the year 2008, Hejblum et al[44] found that under the conditions simulated by their cost-benefit model, the implementation of an institution-based smoking cessation program led to a reduction in cost of €117 per patient (approximately US $160) as the result of minimization of intensive care stay during hospitalization.

Summary

The general health consequences of smoking are well documented, but our understanding of the effect of smoking on bone health and healing continues to evolve. Smoking is known to increase the risk of infection and lead to diminished fracture union, fusion rates, and wound and soft-tissue healing. Proper use of available medicinal and behavioral interventions may increase the likelihood of successful smoking cessation. Orthopaedic surgeons have a unique opportunity to intervene with smokers when they present either for elective surgery or in the acute setting following traumatic injury. The implementation of smoking cessation interventions at such points has the potential to minimize or eliminate later presentation with other smoking-related chronic disease. Preoperative and postoperative smoking cessation protocols have been shown to be successful, and the potential health benefits of early intervention are likely substantial.

References

Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, reference 43 is a level I study. References 41 and 42 are level II studies. References 12-30 and 34 are level IV studies.

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