The impact of smoking on neurosurgical outcomes

A review

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Cigarette smoking is a common health risk behavior among the general adult population, and is the leading preventable cause of morbidity and mortality in the US. The surgical literature shows that active tobacco smoking is a major risk factor for perioperative morbidity and complications, and that preoperative smoking cessation is an effective measure to lower these risks associated with active smoking. However, few studies have examined the effects of smoking and perioperative complications following neurosurgical procedures. The goal of this review was to highlight the scientific data that do exist regarding the impact of smoking on neurosurgical outcomes, to promote awareness of the need for further work in the specific neurosurgical context, and to suggest ways that neurosurgeons can promote smoking cessation in their patients and lead efforts nationally to emphasize the importance of preoperative smoking cessation. This review indicates that there is limited but good evidence that smoking is associated with higher rates of perioperative complications following neurosurgical intervention. Specific research is needed to understand the effects of smoking and perioperative complications. Neurosurgeons should encourage preoperative smoking cessation as part of their clinical practice to mitigate perioperative morbidity associated with active smoking.

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KEY WORDS • complication • morbidity • neurosurgery •
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CIGARETTE smoking is the leading preventable cause of morbidity and mortality in the US. Even at low levels, tobacco smoke has been shown to be detrimental to overall health,⁹ and is associated with cancer, coronary artery disease, chronic obstructive pulmonary disease, cerebrovascular disease, peripheral vascular disease, and birth defects.^{1,26,44,47,85} One in 5 deaths in the US is attributed to tobacco use, which translates to nearly half a million deaths annually.⁸⁶ In addition, the tobacco-related burden of morbidity and mortality is a significant strain on medical expenditures and health care systems.¹² Despite the push for tobacco cessation and the advances in tobacco control, an estimated 44 million Americans continue to smoke and the prevalence continues to rise, making this an ever more important issue.^{73,86}

Smoking has long been identified as a risk factor for chronic disease, but expanding evidence in the surgical literature demonstrates that tobacco smoking is also a risk factor for perioperative morbidity and complications.^{42,93,97} Active smoking has been clearly linked to increased risk of perioperative cardiovascular complications, pulmonary complications, and wound healing complications (including infections, anastomotic dehiscence, reintegration, and respiratory failure).⁴² These complications in turn result in longer hospital stays, higher rates of ICU admission, greater need for repeat surgery, and higher overall costs of care.⁴² The impact of smoking on perioperative outcomes is relatively well defined in general surgery,⁹⁶ cardiac surgery,^{23,35,97} plastic surgery,^{50,78,79,84,105} orthopedic surgery,^{6,72,83,89} and pediatric surgery.^{25,60,70,88}

Among the neurosurgical subspecialties, it is generally well accepted that smoking leads to increased risk for intracranial aneurysm formation,^{17,28,32,36,39,75,77} aneurysmal

Abbreviation used in this paper: SAH = subarachnoid hemorrhage.

SAH,^{8,36–38,57,76} and decreased bone healing and fusion after spine surgery.^{21,34,61} However, the effects of smoking on perioperative morbidity following neurosurgical procedures are less well defined. In this review, we sought to highlight the existing scientific data regarding the impact of smoking on neurosurgical outcomes, identify where additional studies are needed, and suggest ways that neurosurgeons can lead the efforts nationally to emphasize the importance of preoperative smoking cessation.

Methods

The words “smoking and neurosurgery” or “tobacco and neurosurgery” were used as search terms in PubMed (for the years 1950–2012) to identify all articles that included at least one of these terms or phrases. The references lists of the relevant articles and systematic reviews were scanned for additional sources.

Results

How Smoking Increases Perioperative Complications

Cigarette smoking is associated with numerous toxic effects to the body, even at the cellular level: cellular damage secondary to free radical release,³³ tissue hypoxia,¹⁴ compromised immune cell function,¹⁰⁷ and microvascular injury leading to dysfunction and thrombogenesis.⁵⁰ Each of these mechanisms can contribute to the multitude of smoking-related complications seen in the perioperative period. The increased perioperative morbidity risk that smoking poses for patients is probably related to both the acute and long-term consequences of tobacco use.

Cellular Injury and Vascular Dysfunction. One of the best-understood mechanisms of the way that smoking can lead to perioperative complications relates to the pathophysiological effects of smoking that cause tissue hypoxia, thrombogenesis, and vasoconstriction. Tissue hypoxia is thought to be secondary to direct damage of the microvasculature that results in detachment of endothelial cells from the lumen of small vessels. The loss of endothelial protection results in exposure of a prothrombotic/procoagulant basement membrane, increased platelet activation, and activation of the coagulation cascade.⁵⁰ In addition, as endothelial cells are injured and detached from the microvasculature, there is an intrinsic deficiency in endothelial-derived relaxing factor, which leads to a decrease in anticoagulation and antispasmodic factors.⁵⁰ The end result of this process is hypercoagulability and vasoconstriction, and both mechanisms can lead to cellular and tissue hypoxia.

Tissue hypoxia is further exacerbated by the systemic effects of nicotine and carbon monoxide. Residual nicotine in the blood can activate the sympathetic nervous system, induce release of epinephrine and norepinephrine from the adrenal glands,⁹⁸ and increase leukotriene and thromboxane levels.^{2,15} The increase of these metabolites leads to additional vasoconstriction of microvasculature.^{14,46} Carbon monoxide is found in high concentrations as a toxic byproduct of tobacco smoke. Its pathophysiological mechanism involves the competitive

binding of hemoglobin and consequent decrease in the oxygen-carrying capacity of blood. A chronic hypoxic state (due to binding of carbon monoxide to hemoglobin) can stimulate a physiological erythropoietic response as a compensatory mechanism. Increased blood cell count and mass can lead to the consequences of red cell aggregation, increased blood viscosity, and thrombogenicity.⁷⁹

These cumulative effects of tobacco smoking effectively result in the Virchow triad for thrombosis as well: endovascular injury/dysfunction, hemostasis (increased viscosity), and stasis (especially for procedures with associated postoperative immobility).²⁷

Wound Healing and Infection. Wound healing is highly dependent on the ability of the vasculature to provide essential nutrients, oxygen, growth factors, and immune cells. Therefore dysfunction of the microvasculature can lead to significantly impaired wound healing.¹⁰⁷ Tobacco smoking results in significant injury and dysfunction of the vasculature, and therefore may cause decreased oxygen, nutrients, and immune cells at the site of incision, which are essential for wound healing.⁶⁵ In addition, tobacco may stimulate a stress response mediated by enhanced fibroblast activity, resulting in decreased cell migration and increased cell adhesion. The net consequence is inappropriate connective tissue deposition at the surgical site, delayed wound healing, and increased risks of wound infection.^{53,107}

Intraoperative Blood Loss. In the neurosurgical literature, 2 retrospective clinical studies suggest that active smokers tend to have higher intraoperative blood loss following craniotomy for tumor resection and lumbar spine surgery.^{20,53} The exact underlying mechanism has yet to be defined. In the literature regarding craniotomy for tumor resection, there is evidence that cigarette smoking can lead to an acute hyperemia response and long-term morphological changes within the cerebral vasculature.^{2,22,95} Acute hyperemia is a result of a buildup of transient vasodilating metabolites in blood vessels^{2,95} and causes increased blood flow within the cerebral vasculature, which can potentially contribute to an increase in blood loss during craniotomy. With regard to long-term plastic changes, smoking causes permanent structural changes of vessels such as vessel wall thickening, which can result in the dysfunction and/or inhibition of vessel accommodation during bleeding.⁴⁵ These correlate with a Doppler ultrasonography study that showed impairment of the cerebral vasculature even after smoking cessation.¹¹ In addition, tumor vascularity probably plays a role in blood loss intraoperatively. There is evidence that cigarette smoking is associated with increased proliferation and angiogenesis of blood vessels, leading to larger and more vascularized tumors, which may further contribute to intraoperative blood loss during resection.^{62,109}

Cardiopulmonary Effects. Although pulmonary complications can result from poor lung function and/or exacerbation of chronic smoking-related diseases, even smokers without chronic disease are at increased risk for perioperative morbidity.¹⁰¹ There are many mechanisms for which tobacco smoking increases the risk for pulmonary com-

plications in the perioperative period. Oxidative damage following smoke exposure can result in mucosal damage, goblet cell hyperplasia, ciliary dysfunction, and impaired bronchial function, which leads to the inability to expel mucus.^{4,82} This can further translate the respiratory environment into a favorable nidus for pathogenic organisms and lead to infection and possibly respiratory failure. In fact, smokers tend to have delayed bacterial clearance and increased bacterial load compared with their nonsmoking counterparts.²⁴ In addition, smoking alters the respiratory immune response: it leads to increased airway inflammation resulting in bronchial hyperreactivity,³⁰ and impaired alveolar macrophage function, further contributing to higher rates of postoperative pneumonia.⁵⁶

As with pulmonary complications, the adverse perioperative cardiovascular effects of smoking are thought to have both chronic and acute contributions. Long-term tobacco smoking promotes systemic atherosclerosis, alteration of lipid metabolism via increased lipolysis and lipotoxicity, and insulin resistance.³¹ The most devastating sequelae from these systemic abnormalities are macrovascular complications such as perioperative myocardial infarct, pulmonary embolus, and even stroke. But even short-term smoking exposure poses a significant perioperative morbidity risk through mechanisms of increased coagulability, increased sympathetic tone, and reduced oxygen-carrying capacity.¹⁰¹ In smokers the reduced oxygen-carrying capacity is an additional risk factor for decreased oxygen supply to the heart, which places these patients at even higher risk for myocardial ischemia and/or infarct.

The Evidence: Smoking and the Risks in Neurosurgery

Cranial Surgery. Only a few studies have examined how smoking affects perioperative morbidity and mortality following neurosurgical intervention (Table 1). The most robust studies of tobacco smoking and its association with morbidity in neurosurgery are in the cerebrovascular literature. Abundant evidence demonstrates that smoking is highly associated with the risk for aneurysm formation^{17,28,32,36,39,75,77} and aneurysm rupture/SAH.^{8,36–38,57,76} In fact, smoking cessation has been suggested as an excellent alternate treatment for older patients with small intracranial aneurysms.³⁸

Several studies examining smoking and the treatment of cerebrovascular disorders provide good evidence that

smoking is associated with greater perioperative morbidity and worse outcomes. A retrospective study of 320 patients with aneurysmal SAH who underwent surgical or endovascular treatment showed that current smokers (patients with at least a 10 pack-year history and who were still smoking during the past year) and patients with a 20 pack-year or longer history of tobacco use were more likely to experience neurological deterioration occurring at least 2 days after intervention.⁴⁸ Other studies of postoperative outcomes of aneurysmal SAH have also shown that smokers have higher rates of pulmonary complications,⁶⁶ greater need for ventilation,⁶⁶ and greater risk for cerebral vasospasm.^{74,106} Smokers even have higher rates of complications following diagnostic cerebral angiography and neuroendovascular procedures.⁵⁴ Altered wound healing has also been seen after superficial temporal artery–middle cerebral artery anastomosis; more specifically, it has been suggested that smokers have higher rates of cutaneous necrosis.⁴¹

Within the subspecialty of neurooncology, just one study has evaluated the association between tobacco smoking and perioperative outcome after craniotomy for tumors. It was a retrospective study of 453 patients in which it was found that current smoking status was an independent risk factor for higher intraoperative blood loss, postoperative complication risk, and lower 1-year survival following craniotomy for tumor resection.⁵³ Another finding was that patients who quit smoking continued to have significantly higher mean blood loss, but did not carry a higher risk for postoperative complications and 1-year mortality. This may demonstrate that smoking cessation may be effective in mitigating the perioperative morbidity risks associated with active smoking after tumor resection.

Two studies examined the effects of smoking on specific cranial procedures. A single-center retrospective study of 475 patients found that smoking does not seem to affect the risk of infection and CSF leakage after the use of collagen sponge dural allografts.⁵⁹ Similarly, smoking was not a risk factor for failure in tissue cranial reconstruction.⁶⁹ The last study, however, was a retrospective review of only 21 patients.

Spine Surgery. The neurosurgical spine literature contains considerable evidence that smoking is associated with worse long-term outcomes, but there are few studies of smoking and its effects on perioperative morbidity and mortality. Most of the data pertaining to spine surgery demonstrates that smoking is associated with de-

TABLE 1: Studies evaluating the effect of smoking on neurosurgical procedures

Authors & Year	Procedure Type	No. of Patients	Results
Lau et al., 2012	craniotomy for tumor resection	453	smokers had higher rates of blood loss & complications; smokers who quit had reduced risk of postop complications & higher 1-yr survival rates compared to active smokers
Litvack et al., 2009	collagen sponge dural graft implant following craniotomy	475	smoking did not affect risk of infection or CSF leak
Krishnamurthy et al., 2007	clip &/or coil occlusion of aneurysmal SAH	320	smokers more likely to experience delayed neurological deterioration
Dean et al., 2006	lumbar spine surgery	500	smoking associated w/ increased blood loss & intraop transfusion

layed spinal fusion,⁵⁵ poor spinal fusion rates,^{21,34,61} and higher rates of pseudarthrosis following spinal instrumentation.¹⁰⁸ Smoking has been identified as a risk factor for higher subsidence rates in the placement of carbon fiber cages following anterior cervical discectomy and fusion.⁷ The mechanism behind poor fusion and greater rates of subsidence in smokers is related to poor bone quality secondary to tobacco smoking. Nicotine exposure is associated with delayed vascularization and smaller areas of revascularization, which lead to reduced levels of osteogenesis and hypocellular fusion mass.¹⁹ There is also evidence that smokers have higher rates of recurrent lumbar disc herniation after surgery.^{16,43,92} The higher rates of recurrent disc herniation are possibly secondary to nicotine-induced vasoconstriction and decreased blood flow to the area of prior surgery.⁴³ This results in the inhibition of the annular healing process and degeneration.

The only study that directly evaluated whether tobacco smoking affected perioperative outcomes was a retrospective review of 500 patients that demonstrated that smoking was associated with increased surgical blood loss and intraoperative transfusion following lumbar spine surgery.²⁰

Peripheral Nerve Surgery. The neurosurgical literature contains no studies that directly examined the effects of smoking and perioperative outcomes after surgery for diseases of the peripheral nervous system.

Applicability of Studies From Other Surgical Specialties

Of the surgical literature on the association of smoking and perioperative complications, the most applicable to neurosurgery comes from the specialties of plastic surgery, orthopedic surgery, and vascular surgery. In plastic surgery, wound healing is of paramount importance because success is often judged largely on aesthetic appearance. Plastic surgery studies have shown that tobacco smokers have increased rates of wound infections, reduced skin flap survival, and increased risk for skin necrosis.^{5,13,49,50} Similar to procedures in plastic surgery, neurosurgical procedures often involve large incisions in readily visible areas, as are used when performing a craniotomy. Therefore, proper and optimal wound healing is important because this may have large implications for appearance and quality of life, especially in the pediatric population.

Because orthopedic surgery is often involved with the surgical management of the spine, studies from this discipline are clearly applicable to neurosurgical patients who are undergoing spine surgery. Two orthopedic studies have demonstrated that tobacco smoking is associated with poor fusion rates, supporting similar findings in the neurosurgical literature.^{87,108} In a retrospective study of 4555 patients, smoking cessation was associated with less residual back pain and less need for analgesic drugs.⁸³

Carotid endarterectomy is performed both by general vascular surgeons and by neurosurgeons; therefore, findings from the vascular literature regarding smoking's effect on perioperative outcomes after endarterectomy are most likely to be applicable to neurosurgery as well. Among patients who experience perioperative stroke as a complication following endarterectomy, a significant portion are active smokers, and therefore it is suggested

that active smoking status is a risk factor for perioperative stroke following this procedure.⁸¹ In addition, a randomized controlled trial showed that active smoking status is a risk factor for restenosis following carotid endarterectomy.⁵²

Discussion

Our review of tobacco smoking and perioperative outcomes in neurosurgery indicates that the limited literature available provides evidence that smoking is associated with higher perioperative morbidity after neurosurgical intervention (Table 2). Most of the studies were done in the subspecialties of cerebrovascular surgery and spine surgery. Compared with studies from other surgical specialties, few in neurosurgery concentrate on the effects of smoking on perioperative rather than long-term outcomes. Although it may be appropriate to apply certain findings from other fields such as plastic surgery, orthopedics, and vascular surgery for the time being, further studies are needed to assess the effects of smoking and perioperative complications following specific neurosurgical procedures. Nevertheless, tobacco smoking is an overall detriment to patient health, and smoking cessation should be encouraged preoperatively to mitigate the associated risk for complications and to reap the long-term benefits of neurosurgical treatment.

Evidence of the Effect of Smoking Cessation on Surgical Outcomes

Accumulating evidence indicates that smoking cessation can reduce the higher perioperative complications risk seen in active smokers and possibly improve long-term outcomes. A randomized clinical trial demonstrated that a 4-week smoking cessation program consisting of individual counseling and nicotine replacement provided a 49% relative risk reduction in postoperative complications among smokers.⁵⁸ Another clinical trial showed a significant decrease in complication rates, especially wound healing, when patients abstained from smoking for 6–8 weeks.⁶⁴ A third trial demonstrated a significant decrease in postoperative complications after repair of acute fractures.⁶⁸ However, one randomized trial was an exception; it showed that 2-week preoperative smoking cessation did not change postoperative complication rates and risk following colorectal surgery.⁹¹ However, a major drawback to this study was that it was originally powered to 0.80 if 300 patients were included, but only 60 patients were included in the final analysis. This dramatically limits the ability to detect a potential benefit.

Because there is strong evidence from the other randomized clinical trials that smoking cessation is effective in decreasing perioperative morbidity risk, preoperative smoking cessation should be implemented to improve neurosurgical outcomes. The exact duration of abstinence required for these benefits to be observed is unclear.^{102,103} The benefit probably depends both on the duration of cessation and the neurosurgical complication of interest. The suggested durations of smoking cessation range from hours to days for cardiovascular complications,^{40,99} and even months for pulmonary complications, depend-

TABLE 2: Major smoking-related morbidities by neurosurgical subspecialty

Subspecialty	Perioperative Morbidity	Long-Term Complications
neurooncology	intraop blood loss, postop complications	lower 1-yr survival
spine surgery	intraop blood loss, increased need for transfusion	delayed spine fusion, pseudarthrosis, higher subsidence rates, recurrent lumbar disc herniation
cerebrovascular	neurological deterioration, stroke, altered wound healing/ cutaneous necrosis, pulmonary complications	aneurysm rupture, aneurysm formation

ing on the study.¹⁰⁰ Most trials have found that 4–8 weeks of smoking abstinence significantly reduces perioperative complications and the need for repeat surgery.^{58,63,64} There are even trials that demonstrate that just 3 weeks of smoking cessation is beneficial.⁷¹

Although it may seem intuitive that smoking cessation should be encouraged whenever possible and even for brief periods, there has been controversy in the past that brief preoperative abstinence may actually increase the risk of pulmonary complications, and that cessation must occur at least 8 weeks before surgery.^{10,51} However, a meta-analysis demonstrated no suggestion of increased postoperative complications associated with brief durations of smoking cessation.⁶⁷ In addition, there is no reliable evidence that abstinence of any duration increases the risk for complications.^{90,93} Therefore, neurosurgeons can confidently and safely encourage preoperative smoking cessation at any time before surgery.

Smoking Cessation: the “Teachable Moment” and Current Barriers

Encouraging patients to quit smoking may seem quite simple, but in actuality and in clinical practice this is not the case, because tobacco is highly addicting. In addition, undergoing surgery is very stressful for many patients and, stress being a common motivator for smoking, may make quitting even more difficult.¹⁸ However, the seriousness of surgery can be used to the advantage of the clinician in motivating patients to quit smoking successfully. This relates to the phenomenon of a “teachable moment,” in which an event such as disease diagnosis, hospitalization, or pregnancy motivates a patient to change a risky health behavior. During these times, patients may be more amenable to changing their habits and/or addiction because of the risk to self. In fact, it has been shown that patients tend to be more likely to quit smoking after hospitalization for serious illness.^{29,80} Therefore, not only does preoperative smoking cessation decrease perioperative morbidity, but scheduling surgery is a great opportunity to encourage permanent smoking cessation so the patient can reap the lifelong benefits of a tobacco-free life.

Despite the potential “teachable moment” that surgery presents for smoking cessation, neurosurgeons are currently not capitalizing on this event. Studies suggest that almost half of all surgeons do not routinely counsel their patients to stop smoking before an operation, and it is most likely that neurosurgeons are not an exception in this regard.¹⁰⁴ In addition, smoking cessation counseling is practice dependent, and no set structures have been

implemented to promote preoperative smoking cessation in the traditional neurosurgical practice. Brief counseling (less than 3 minutes) may increase rates of smoking cessation.^{40,64} However, even with appropriate counseling the failure rate of smoking cessation can remain high, and often multiple attempts are required.³ Therefore, methods need to be implemented to make sure patients remain successful in quitting their smoking habit. In one randomized trial of a perioperative smoking cessation intervention, high cessation rates were obtained—most likely because the intervention was intense and included repeated personal contact.⁵⁸ More intensive smoking cessation programs are associated with higher quit rates and are effective in surgical settings, whereas other briefer and less intensive programs are less effective.⁹⁴ Therefore, a strict smoking cessation program is likely to be the key to success for patients to stop smoking. Effective interventions that health care providers can use to help patients stop smoking include simple open dialog about the patient’s motivation to quit smoking, individual counseling, group counseling, and repeated personal contact.

Policy Implications

There is considerable evidence that smoking is a major risk factor for perioperative complications, which points to a great opportunity to change policy and federal mandates regarding tobacco companies and the health care system. In 2009, landmark legislation that granted the FDA the authority to regulate tobacco was passed. However, in August of 2012, a US appeals court in Washington, DC, ruled that a requirement for graphic warning labels on cigarette boxes was unconstitutional and violated the First Amendment. The federal government subsequently asked for a further appeal of this ruling, but the US continues to lag behind other nations, which have implemented enhanced health warnings on cigarette packs. Therefore, alternative actions may be required to reduce smoking exposure: limits on the annual production of cigarettes by tobacco companies, an increase of taxes on the ingredients used to manufacture cigarettes, and restrictions on the height to which tobacco plants are allowed to grow.⁴² At a federal level, the creation of new policies that affect practicing neurosurgeons and medical care providers through the development and implementation of pay for performance mandates may be an effective incentive to further encourage patients to quit smoking preoperatively.

Conclusions

The surgical literature shows that active tobacco

smoking is a major risk factor for perioperative morbidity and complications, and that preoperative smoking cessation is effective at lowering the risks associated with active smoking. The relatively few studies specifically in the neurosurgical literature do provide evidence that smoking is associated with higher rates of perioperative complications. Because one of the most powerful times to convince a smoker to quit is before a surgical procedure, neurosurgeons are encouraged to do so. On the policy level, neurosurgeons should take the lead in catalyzing constructive changes to minimize the impact of tobacco smoking in the perioperative setting.

Disclosure

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