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GUIDELINE

A practical guide for perioperative smoking cessation

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Abstract

The perioperative management of patients who are smokers presents anesthesiologists with various challenges related to respiratory, circulatory, and other clinical problems. Regarding 30-day postoperative outcomes, smokers have higher risks of mortality and complications than non-smokers, including death, pneumonia, unplanned tracheal intubation, mechanical ventilation, cardiac arrest, myocardial infarction, and stroke. Given the benefits of smoking cessation and the adverse effects of smoking on perioperative patient management, patients should quit smoking long before surgery. However, anesthesiologists cannot address these issues alone. The Japanese Society of Anesthesiologists established guidelines in 2015 (published in a medical journal in 2017) to enlighten surgical staff members and patients regarding perioperative tobacco cessation. The primary objective of perioperative smoking cessation is to reduce the risks of adverse cardiovascular and respiratory events, wound infection, and other perioperative complications. Perioperative preparations constitute a powerful teachable moment, a "golden opportunity" for smoking cessation to achieve improved primary disease outcomes and prevent the occurrence of tobacco-related conditions. This review updates the aforementioned guidelines as a practical guide to cover the nuts and bolts of perioperative smoking cessation. Its goal is to assist surgeons, anesthesiologists, and other medical professionals and to increase patients' awareness of smoking risks before elective surgery.

Keywords Perioperative care · Postoperative complications · Smoking cessation · Smoking reduction · Surgeons

Introduction

Objectives

In June 2008, the Japanese Society of Anesthesiologists (JSA) declared its commitment to a smoking cessation initiative, including encouraging anesthesiologists to quit smoking and sponsoring anti-smoking campaigns. In March

This content has already been posted in Japanese on the website of the Japanese Society of Anesthesiologists. The purpose of publishing the material in English is to convey to an international audience the importance of perioperative smoking cessation.

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2015, JSA released the *Perioperative Smoking Cessation Guidelines* (Working Group [WG] chair, Hiroki Iida; WG members, Tetsuya Kai, Michioki Kuri, Masashi Nakagawa, and Hirofumi Morimatsu) and created and distributed posters to raise awareness among medical workers and patients. According to World Health Organization (WHO) estimates, anti-smoking campaigns have reduced the world's smoking population by 53 million, saving more than 22 million lives in the countries that supported the campaigns. In Japan, regulations on preventing passive smoking have been implemented, and social insurance coverage for smoking cessation treatment has been expanded. A growing number of studies provide new evidence on smoking, including novel types of cigarettes. The above guidelines were updated and released as a practical guide (PG) that covers the nuts and bolts of perioperative smoking cessation. This PG is expected to assist surgeons, anesthesiologists, and other medical professionals involved in perioperative smoking cessation management and to increase awareness of perioperative smoking risks among patients preparing for elective surgery.

Target audience

This PG is intended for medical professionals engaged in perioperative smoking cessation management. Perioperative smoking cessation management is relevant for physicians, surgeons of all subspecialties, anesthesiologists, nurses and pharmacists, and other medical professionals who are engaged in disease diagnosis, surgical decision, preoperative preparation, intraoperative and postoperative care, and surgical treatment of primary and comorbid conditions. This PG aims to assist in their daily healthcare activities.

Search strategy, levels of evidence, and strength of recommendation

Literature search

To revise and update the *Perioperative Smoking Cessation Guidelines* released in March 2015 [1], MEDLINE (via PubMed) and Ichushi databases were searched systematically in June 2020 to identify new articles on perioperative smoking cessation. The English terms used in the MEDLINE search included the following Medical Subject Headings (MeSH) and Major Topic (MaJR) terms: "smoking cessation," "smoking reduction," "tobacco use cessation," "smoking prevention," "smoking/adverse effects," "tobacco use cessation devices," "smoking cessation agents," "tobacco smoking/adverse effects," "general surgery," "surgeons," "physician's role," "preoperative care," "postoperative care," and "postoperative complications." The publication period was from January 2015 (shortly before the publication of the prior guidelines) to June 2020. The literature search of the Ichushi database employed corresponding Japanese terms. The search formulas used for this PG are presented in Supplementary 2. While retaining the important articles referenced in the *Perioperative Smoking Cessation Guidelines*, we searched for and incorporated new articles as appropriate to respond to the clinical questions presented in this PG. Our search was limited to studies published in English or Japanese. Searches targeted existing clinical guidelines, systematic reviews, and individual research papers, in this order of priority. If a sufficient amount of evidence was obtained in the first or second level of priority, the search was terminated without going to the next level, and we proceeded to evaluate the evidence collected.

Evaluation of literature quality

When existing clinical guidelines or systematic reviews were identified, they were evaluated for research quality, recency, and relevance to decide on whether to adopt or reject them. The quality of randomized controlled trials was evaluated using the Cochrane Risk of Bias Tool. The risk-of-bias assessment of observational studies was performed using the Risk of Bias Assessment Tool for Non-randomized Studies (RoBANS), and the results were used as one of the criteria for determining the level of evidence.

Levels of evidence quality and strength of recommendation

The quality of evidence and the strength of recommendations were classified based on the *Minds Manual for Guideline Development 2017* [2] and the *Handbook for Grading the Quality of Evidence and the Strength of Recommendations Using the GRADE Approach* [3].

The quality of evidence (overall strength of evidence across all outcomes) were defined as follows:

A (High): We are very confident that the true effect lies close to that of the estimate of the effect.
B (Moderate): We are moderately confident in the effect estimate.
C (Low): Our confidence in the effect estimate is limited.
D (Very low): We have very little confidence in the effect estimate.

Recommendations were determined by considering four factors: overall evidence quality, balance of the magnitude of desired and undesired effects, values and preferences, and cost and resource use. This PG has two categories for the strength of a recommendation (for or against an intervention): 1 strong, and 2 weak. No recommendations are

presented in response to clinical questions if their strength could not be unequivocally determined.

For each recommendation, its strength (1 or 2) and the quality level of its supporting evidence (A, B, C, or D) were combined and presented in parentheses.

Strength of recommendation	Quality of evidence
Strong (1)	High (A)
Weak (2)	Moderate (B)
	Low (C)
	Very low (D)

It would be ethically unacceptable to suspend and randomize routine perioperative management procedures that have been commonly adopted based on epidemiological data on smoking. Since cohort studies were the primary focus of evaluation in this PG, we considered that large-scale cohort studies were an appropriate study design. Consequently, the research design of individual studies was categorized according to the following classifications and indicated after their citations in the References:

- Ia Systematic reviews/meta-analyses and guidelines.
- Ib Randomized controlled trials.
- IIa Non-randomized controlled trials or large-scale cohort studies ($N \geq 1000$).
- IIb Analytical epidemiological studies (small-scale cohort, case–control, or cross-sectional studies).
- III Descriptive studies (case reports and case series).
- IV Basic research or others.

Recommendation grading criteria and consensus formation

The draft PG was distributed to each WG member for review and comments. The WG members were asked to check the statements on each item. After feedback was received from the WG members, a consensus formation meeting was held with all members in attendance. Agreement of at least 70% of the WG members was required to achieve consensus on a recommendation. Discussions continued until the consensus criteria were met.

Public comments from related academic societies

Invitations for public comments were issued to the members of the JSA and related academic societies. The received comments were reviewed by the WG and the draft PG was partially revised based on them.

Statements: significance of perioperative smoking cessation

The primary objective of perioperative smoking cessation is to reduce the risks of adverse cardiovascular and respiratory events, wound infection, and other perioperative complications. Surgery offers a good opportunity to quit smoking. Cessation will help improve the outcomes of the primary disease requiring surgery and prevent the subsequent occurrence of tobacco-related diseases. Perioperative preparations constitute a powerful teachable moment, a "golden opportunity" for smoking cessation that medical personnel can take advantage of. Perioperative smoking cessation will help patients undergo surgery safely, recover successfully, gain a healthy postoperative lifestyle, and achieve better survival outcomes.

Clinical questions, recommendations, and commentary

Effects of active and passive smoking on surgical patients

A Clinical question: Do active and passive smoking adversely affect the preoperative condition of surgical patients?

Summary statement

- Active and passive tobacco smoking lowers blood oxygen levels, affects the metabolic pathways of anesthetics, and causes other adverse effects.

Commentary

The biological effects of smoking are caused by the components of tobacco smoke, such as carbon monoxide (CO), nitric oxide (NO), nicotine, and tar. CO decreases blood oxygen levels by interfering with oxygen hemoglobin (Hb) binding. At the same time, CO strengthens the bond formed between oxygen and Hb, thereby inhibiting tissue oxygen uptake. Moreover, CO decreases muscle oxygen storage and suppresses mitochondrial energy production [4]. Since NO has a vasodilatory effect, it can expand local blood vessels. However, chronic NO exposure accelerates connective tissue destruction and prevents local endogenous NO production. The acute effects of nicotine include sympathetic neural excitation and increased myocardial oxygen consumption. Nicotine also stimulates airway secretion and mediates bronchial contraction. Tar and other smoke components induce airway contraction, increase airway irritability, and suppress airway ciliary

movement [4]. Furthermore, tobacco smoke influences the metabolism of opioids, muscle relaxants, local anesthetics, and other narcotic drugs, as shown in Table 1 [5]. In children, exposure to environmental tobacco smoke increases the risks of middle ear infection, sinusitis, asthma, wheezing, and lower and upper respiratory tract infections, and also induces airway irritability [6].

B Clinical question: Does smoking increase perioperative complications?

Summary statements

- Preoperative smoking is a common risk factor for perioperative complications, including wound infection, infectious diseases, pulmonary complications, cerebral and neurological complications, and bone non-union.
- Smoking has an adverse impact on long-term outcomes. It increases the incidence of revision arthroplasty, decreases graft patency, and elevates mortality rates after coronary artery bypass grafting (CABG).

Commentary

- General complications

  In a meta-analysis of 107 studies on the relationship between smoking and perioperative complications [7], preoperative smoking was associated with an increased risk of general morbidity, with a relative risk (RR) of 1.52 and a 95% confidence interval (CI) of 1.33–1.74. In a propensity score matching study of patients undergoing total joint arthroplasty selected from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database [8], smokers were more likely to have a surgical complication within 30 days of surgery than non-smokers [odds ratio (OR) 1.84, 95% CI 1.21–2.80]. In a large-scale database analysis by Turan et al. [9], current smokers were 1.38 times more likely to die than never smokers, and had significantly greater odds of pneumonia (OR > 2), myocardial infarction (OR 1.80), and stroke (OR 1.73). Smokers had greater incidences of postoperative morbidity evaluated as severe by the Clavien–Dindo classification than non-smokers after liver resection [10], gastrectomy for gastric cancer [11], and radical cystectomy [12]. Based on a literature review, the French Society of Anesthesia and Intensive Care (SFAR) guidelines estimated that in patients scheduled for surgery, smoking increased the risk of hospital mortality by 20% and that of major postoperative complications by 40% [13].

  In a Japanese study using Diagnosis Procedure Combination (DPC) data, smokers had 1.15 times more complications and a 1.22-fold higher mortality rate within 30 days after surgery than non-smokers [14]. Given that former smokers also had higher prevalence rates of respiratory and cardiovascular complications such as myocardial infarction, these data should be interpreted with caution. Smoking cessation during the perioperative period alone may not always be able to reduce postoperative morbidities.
- Wound infection and healing

  Based on the association between cigarette smoking and the risk of surgical site infections (SSIs), the *Guideline for Prevention of Surgical Site Infection, 1999* published by the US Center for Disease Control and Prevention (CDC) recommended instructing patients to abstain from smoking cigarettes or any other form of tobacco consumption for at least 30 days before elective surgery. This recommendation has gained widespread acceptance in surgical practice [15]. Smoking is a definitive risk factor for superficial and deep wound infections and postoperative sepsis. The impact of smoking becomes more evident in the context of greater surgical invasiveness. The American College of Surgeons and Surgical Infection Society's *Surgical Site Infection Guidelines* state that smoking is a risk factor for wound infection, particularly in operations involving artificial implants [16]. In a meta-

Table 1 Effects of cigarette smoke on anesthetic metabolism

Substrate	Metabolic enzymes and pathways	Mechanism of action	Effects
Morphine	UDP-GT	Unknown	Increases required dose
Pentazocine	CYP1A2	Enzyme induction	Increases required dose and enhances clearance
Codeine	UGT, CYP2D6, CYP3A4	Enzyme induction	Enhances clearance and accelerates glucuronidation
Fentanyl	CYP3A4	Unknown	Increases required dose and enhances adverse reactions
Vecuronium	CYP1A1/2, possibly CYP3A4	Unknown	Increases required dose
Rocuronium	CYP1A1/2, possibly CYP3A4	Unknown	Increases required dose
Ropivacaine	CYP1A1/2	Enzyme induction	Accelerates metabolism
Lidocaine	CYP3A4, CYP1A2	Enzyme induction	No significant effect on metabolism
Theophylline	CYP1A1/2	Enzyme induction	Increases required dose

UDP-GT (UGT) uridine diphosphate-glucuronosyltransferase, *CYP* cytochrome P450 enzymes

analysis of studies on orthopedic treatments, Pearson et al. reported that compared with non-smokers, smokers took 27.7 days longer for union to occur and had a 2.2-fold greater risk of non-union [17]. In the previously cited meta-analysis [7], preoperative smoking was associated with an increased risk of wound complications (RR 2.15, 95% CI 1.87–2.49), and the RR of infectious disease was 1.54 (95% CI 1.32–1.79), showing a significant increase with smoking. A study investigating the adverse effects of smoking by type of surgery showed that among patients undergoing CABG, smokers had significantly higher incidence rates of donor site wound edge necrosis and dehiscence and sternal wound dehiscence than non-smokers [18]. In a study of smoking and perioperative complications in patients undergoing head and neck microvascular reconstructive surgery [19], smoking status was independently associated with wound disruption (OR 1.74, 95% CI 1.17–2.59) and unplanned reoperation (OR 1.50, 95% CI 1.15–1.95). Smoking-related increases in SSI incidence have been frequently reported in patients undergoing orthopedic surgery, including arthroplasty [8], open reduction and internal fixation of tibial plateau fractures [20, 21], and lumbar spine surgery [22]. Thus, preoperative smoking causes adverse impacts on wound healing outcomes.

- Pulmonary complications

  In the previously referenced meta-analysis [7], preoperative smoking was associated with an increased risk of postoperative pulmonary complications (PPCs), with a RR of 1.73 (95% CI 1.35–2.23). This meta-analysis also examined the relationship between the number of pack-years smoked and PPC incidence. The OR (95% CI) for smokers compared with non-smokers was 1.20 (1.05–1.38) for < 20 pack-years, 1.57 (1.45–1.70) for 41–60 pack-years, and 1.82 (1.70–1.94) for > 60 pack-years, indicating a significant relationship [7]. In a large-scale study that investigated the relationship between preoperative smoking status and PPCs using the ACS-NSQIP database [23], the overall incidence of PPCs was 4.5%. PPCs were reported significantly more frequently in smokers (5.7%) and in former smokers with a maximum of 1 year of abstinence (5.3%) than in non-smokers (3.6%). Many other studies reported a positive association between smoking and PPCs, and the body of available data clearly indicates that smoking increases the risk of PPCs.

- Perioperative venous thrombosis in orthopedic surgery

  Regarding perioperative venous thromboembolism, different results were reported in different types of orthopedic surgery. The risk of perioperative venous thromboembolism was 1.9 times higher in smokers than in non-smokers after anterior cruciate ligament (ACL) reconstruction [24], and the risk of venous thrombosis was 4.6 times higher in smokers than in non-smokers after shoulder rotator cuff operation [25]. On the other hand, patients with a history of tobacco use undergoing spinal fusion had a decreased risk of deep venous thrombosis [26].

- Risk of reoperation

  In patients with knee or hip arthroplasty, tobacco use was associated with an elevated risk of implant revision within 1 year (RR 1.98) [27, 28]. In a 20-year follow-up study of CABG using vein grafts, current smoking was correlated with a higher risk of death and coronary reintervention than smoking cessation [29]. Persistent smokers had a greater risk of death from all causes (RR 1.68) and cardiac death (RR 1.75) compared with patients who stopped smoking for at least 1 year after surgery. The estimated survival benefit in quitters increased from 3% at 5 years to 14% at 15 years. The quitters were less likely to undergo repeat CABG or other interventions. In another study, patients who were smokers at the time of surgery had an elevated risk of the long-term all-cause mortality (RR 1.2, 95%CI 1.06–1.36) [30]. Willigendael et al. conducted a meta-analysis of lower limb bypass surgery performed for critical ischemia or intermittent claudication, and showed that continued smoking after surgery resulted in an at least a threefold increased risk of graft failure [31].

  In a study of lower extremity bypass in actively smoking claudicants by Jones et al., smoking was an independent predictor of diminished primary patency (HR 1.3, 95% CI 1.0–1.6), assisted primary patency (HR 1.4, 95% CI 1.1–1.8), and adjusted 10-year survival (HR 1.3, 95% CI 1.1–1.5) at 2-year follow-up [32]. Postoperative smoking cessation improved the graft patency rate numerically but non-significantly.

  Smoking is an independent risk factor for atherosclerotic occlusive disease. Patients should be advised to remain smoke-free after surgery for better outcomes [33].

C Clinical question: Does passive smoking increase perioperative complications?

Summary statement

Recommendation: Evidence clearly indicates that passive smoking increases the risk of perioperative complications. (1B).

- Passive smoking, like active smoking, is a perioperative risk.

Commentary

Passive smoking elevates the risk of various perioperative complications, including PPCs. In a meta-analysis of the effects of exposure to environmental tobacco smoke

(sidestream smoke and exhaled mainstream smoke) on adverse anesthetic and surgical outcomes in children, the RR (95% CI) of exposure to environmental tobacco smoke was 1.75 (0.95–3.21) for respiratory adverse events (RAEs), 3.54 (2.37–5.28) for laryngospasm, 2.52 (1.68–3.77) for RAEs and laryngospasm, and 2.38 (1.45–3.90) for RAEs and laryngospasm in high-quality reports [34]. According to the SFAR guidelines, sidestream smoke exposure increases perioperative complications (cough, laryngospasm, bronchospasm, and oxygen desaturation) [13]. A review of studies on pediatric anesthesia found that passive smoking increased respiratory complications and laryngospasm by 2.52- and 3.54-fold, respectively, and extended the postanesthetic care unit (PACU) stay [6]. Thus, environmental tobacco smoke has a major adverse impact on children.

D Clinical question: How do smoking and perioperative smoking cessation influence acute and chronic postoperative pain?

Summary statements

- Smokers experience more severe acute postoperative pain than non-smokers.
- Smoking is a risk factor for chronic postoperative pain.
- Perioperative smoking cessation may reduce the risk of chronic and intensified postoperative pain.

Commentary

- Impact on acute postoperative pain.

  Postoperative pain is a major concern of patients undergoing surgery. In a rat model, exposure to nicotine for 4 weeks or longer significantly decreased the mechanical sensory thresholds, indicating hyperalgesia [35]. In a study examining responses to electrical stimuli, abstinent smokers (≤ 1 month) exhibited a significantly lower pain threshold (0.9 mA) than non-smokers (1.3 mA) [36]. Higher preoperative scores of primary disease pain were reported for tobacco users compared with non-smokers [37]. Many studies reported stronger acute postoperative pain in smokers [36, 38–43]. In a 2019 meta-analysis of nine studies, smoking was a significant preoperative predictor of poor postoperative pain control (OR 1.33, 95% CI 1.09–1.61) [44].

  Greater postoperative pain requires larger amounts of analgesics. In a study of patients scheduled for abdominal hysterectomy, smokers required a significantly larger total amount of propofol than non-smokers (mean 179.4 mg for smokers vs. 119.4 mg for non-smokers) and remifentanil (mean 1315.1 μg for smokers vs. 1010.1 μg for non-smokers) [45]. Other studies also reported the use of larger amounts of analgesics in the acute postoperative phase [36, 46–51]. Moreover, smoking was a predictive factor for increased opioid use during the first 2 days after gastrectomy [48]. Preoperative smoking cessation is suggested to reduce acute postoperative pain [52, 53]. In a group of 50 patients who underwent pancreatic surgery for alcoholic chronic pancreatitis, postoperative smoking cessation predicted narcotic use cessation at 6 months and 1 year after operation [52]. In a study of elective thoracoscopic radical lung cancer surgery, 36 patients who had quit smoking > 3 weeks before surgery required significantly smaller amounts of opioids during the first 48 h after surgery than did 38 patients who had quit smoking < 3 weeks before surgery [53]. It remains undetermined whether pain outcomes differ after shorter or longer smoking cessation durations. Nicotine has acute analgesic properties. However, according to a meta-analysis of eight trials, nicotine reduced postoperative pain scores in non-smokers by only –0.88 (95% CI –1.58 to –0.18) on a 0–10 scale at 24 h compared with placebo [54]. It is unknown whether transdermal nicotine relieves acute postoperative pain in smokers [55]. However, smokers who stop smoking before surgery may require transdermal nicotine to alleviate nicotine withdrawal-induced hyperalgesia.
- Impact on chronic postoperative pain

  In addition to an increased risk of poor pain control in the acute postoperative phase, smokers are at risk of persistent postoperative pain, or pain chronification. Despite findings indicating the absence of a significant relationship between smoking status and chronic postoperative pain [56], studies on the outcomes of various types of surgery have shown that smoking is a major predictor of persistent, long-term postsurgical pain [57–60]. Persistent post-hysterectomy pain was reported significantly more frequently at 6 months in smokers than in non-smokers (OR 3.23, 95% CI 1.59–6.57) [57]. Moderate-to-severe neck pain (numerical rating scale [NRS] ≥ 4) at 2 years after cervical spine surgery was more prevalent in smokers (OR 2.79, 95% CI 1.16–6.84) [58]. Smoking can be an independent risk factor for chronic postoperative pain. Smoking was associated with long-term postoperative opioid use because of chronic postoperative pain [61–65]. Smoking was a significant predictor of opioid use 12 months after cesarean delivery (OR 4.47, 95% CI 3.03–6.57) [61]. Smoking increased the odds of the following events: narcotic prescriptions 3 months after discectomy surgery (OR 1.96, 95% CI 1.29–2.05) [62], opioid use for 6 weeks or longer after shoulder surgery (OR 2.13) [63], opioid use 1 year after cervical spine surgery (OR 15.2, 95% CI 2.8–82.6) [64], and opioid prescriptions 6 months after living kidney donation (OR 1.45, 95% CI 1.33–1.58) [65].

  The duration of the preoperative smoke-free period is related to chronic postoperative pain. For example, a

study of patients with lumbar spine surgery showed a negative correlation between the duration of preoperative smoking cessation and 12-month leg pain intensity [58]. Although no smoking cessation period criteria for preventing chronic postoperative pain have been established, abstinence from smoking is always an important and preferred option for reducing postoperative pain.

Effects of smoking on surgical patients

A Clinical question: Will the perioperative risk of a patient be reduced if they stop smoking before surgery?

Summary statement

Recommendation: We strongly recommend preoperative smoking cessation, because it decreases patients' perioperative risks. (1B).

- Preoperative smoking cessation reduces the frequency of pulmonary complications, wound healing complications, SSIs, and many other types of complication.

Commentary

In the study of patients with elective hernia repair identified using the ACS-NSQIP database, individuals who reported smoking within the past 12 months experienced an increased likelihood of reoperation (OR 1.23, 95% CI 1.11–1.36), readmission (OR 1.24, 95% CI 1.16–1.32]), and death (OR 1.53, 95% CI 1.06–2.22]) compared with non-smokers [66]. In comparison with non-smokers, current smokers had higher odds of overall, pulmonary, wound, and septic/shock complications following most cardiovascular and oncologic surgeries. Because these ORs were generally lower for former smokers (smoke-free for 1 or more years), patients undergoing major surgical procedures should be advised to discontinue tobacco smoking to achieve optimal outcomes [23]. In the SFAR guidelines, smoking cessation at least 8 weeks before surgical intervention reduced PPCs (bronchospasm, atelectasis, lung infection, pleural effusion, pneumothorax, emphysema, pulmonary embolism, acute respiratory distress syndrome, respiratory insufficiency or arrest, re-intubation and ventilation, and tracheotomy) by nearly 50% compared with current smokers [13]. In addition, smokers had a greater need for many hours of high-flow oxygen therapy. The PPC incidence in individuals who discontinued smoking at least 4 weeks preoperatively was about 25% lower than that in current smokers. The incidence was not reduced when smoking cessation occurred between 2 and 4 weeks preoperatively, and did not differ from that achieved when cessation took place less than 2 weeks preoperatively. However, cessation sooner than 2 weeks before surgery was not associated with increased odds of PPCs.

B Clinical question: For how long should surgical patients abstain from smoking preoperatively?

Summary statement

Recommendation:

We strongly recommend that patients scheduled for elective surgery abstain from smoking for at least 4 weeks preoperatively. (1B).

- A longer abstinence period will increase the likelihood of better outcomes. Freedom from smoking is always the preferred option at any time.
- Elective surgeries, such as those for benign diseases, degenerative diseases, and esthetic repair, may be postponed to ensure a sufficient abstinence period if the patient's condition and disease stage allow it.
- Surgeries for malignant tumors and other urgent indications should not be postponed to impose a certain smoking cessation period.

Commentary

As described earlier, the SFAR guidelines state that 8 or more weeks of smoking cessation are advisable to reduce PPCs [13]. In a review that included six randomized trials and 15 observational studies, Mills et al. reported that perioperative smoking cessation reduced the risk of postoperative complications by 41% [67]. They demonstrated that at least 4 weeks' smoking cessation had a significantly greater treatment effect than shorter periods. In a review by Wong et al., at least 4 weeks of abstinence from smoking reduced respiratory and wound healing complications [68].

One study compared the perioperative outcomes of open abdominal aortic aneurysm surgery between three groups: long-term smoking cessation (LTSC, quitting smoking $\geq$ 8 weeks before surgery), short-term smoking cessation (STSC, quitting smoking $<$ 8 weeks before surgery), and current smokers [69]. LTSC was associated with a significantly decreased odds of PPCs, whereas STSC was not associated with a reduction in PPCs. The authors concluded that a longer period of smoking cessation should be attempted if time permits. In foot and ankle surgery, smoking cessation at least 4 weeks before surgery reduced the risk of complications. In hip and knee arthroplasty, wound-related complications were reduced by 26% after a 6- to 8-week preoperative smoking cessation protocol. When possible, smoking should be stopped at least several weeks before elective foot and ankle surgical procedures [70]. Review of the current literature shows that 4 to 8 weeks of preoperative abstinence from smoking is typically recommended to prevent PPCs, whereas delayed lung cancer resection was associated with increased rates of upstaging [71]. Per the Enhanced Recovery After Surgery (ERAS) Cardiac Society guidelines [72], smoking should be stopped 4 weeks before elective surgery, although this may not be feasible in urgent or emergency settings [72].

Perioperative management guidelines for radical cystectomy reported that 6 to 8 weeks of preoperative smoking interventions reduced postoperative complications by approximately 50%, although the wait time between diagnosis and cancer surgery was typically 2 weeks or less [73]. In a retrospective analysis of patients treated with microvascular reconstructive surgery, preoperative smoking cessation was associated with a reduced risk of complications [19]. Adequate smoking cessation periods should be considered depending on the primary disease, comorbidities, and surgical intervention.

In a secondary analysis of a prospective cohort study of patients (age ≥ 60 years) undergoing noncardiac, non-neurological surgery, the odds for PPCs were significantly higher for current smokers (smoking cessation < 7 days) (OR 1.709, 95% CI 1.043–2.802) and former smokers who discontinued smoking between 7 and 93 days preoperatively (OR 3.785, 95% CI 1.803–7.943) than for non-smokers [74]. Compared with non-smokers, however, former smokers who quit smoking more than 93 days preoperatively did not show a statistically significant increase in the risk of PPCs (OR 1.423, 95% CI 0.811–2.495). In a retrospective study of patients who underwent lung cancer surgery, no statistically significant difference was observed between patients with a maximum of 2 weeks of preoperative smoking abstinence and those who stopped smoking sooner [75]. Regarding surgeries for malignant tumors and other urgent indications, the advantages of preoperative smoking cessation may not outweigh the disadvantages of delaying intervention.

Support for smoking cessation

A Clinical question: Are smoking cessation interventions effective for preoperative smoking cessation?

Summary statements

Recommendation: We strongly recommend preoperative smoking cessation interventions to help patients quit tobacco use. (1A).

- Preoperative interventions for smoking cessation significantly increase the smoking cessation rate.
- Information provided by healthcare workers, especially guidance by medical doctors, is important for improving the effectiveness of smoking cessation.

Commentary

In a systematic review of 13 trials of preoperative smoking cessation intervention, brief interventions achieved a significantly greater effect on cessation at the time of surgery than usual care (RR 1.30, 95% CI 1.16–1.46, seven trials) [76]. A much more pronounced effect was achieved by intensive interventions that involved multiple counseling sessions (RR 10.76, 95% CI 4.55–25.46, two trials) [76]. In most of the trials reviewed, pharmacotherapy was administered as part of the smoking cessation interventions. The review showed that preoperative smoking cessation interventions promoted perioperative abstinence, and became a powerful tool when they involved pharmacotherapy as well as multiple counseling sessions. Intensive preoperative smoking cessation interventions involving pharmacotherapy and multiple counseling sessions demonstrated a significantly greater effect on 12-month cessation than usual care (RR 2.96, 95% CI 1.57–5.55, two trials) [76].

In a meta-analysis of 19 studies that investigated the effects of preoperative smoking cessation interventions, the proportion of smokers who quit or reduced smoking by the time of surgery was nearly twice as high in the intervention group than in the control group (46.2% vs. 24.5%, Hedges' $g = 0.56$, 95% CI 0.32–0.80) [77]. Larger effects were achieved by interventions that involved a larger number of sessions, that were delivered face-to-face and by nurses, and that included specific behavior change techniques (providing information on the consequences of smoking/cessation and withdrawal symptoms, goal setting, review of goals, regular monitoring by others, and giving options for additional or later support). To achieve greater effectiveness, therefore, healthcare workers should meet patients in face-to-face settings more often, and provide guidance based on detailed information.

Many studies underscore that information conveyed by healthcare workers, especially medical doctors, is important for improving the effectiveness of smoking cessation. A health questionnaire survey of surgical patients who smoked showed that the proportion of those who were unaware of smoking-related perioperative hazards was significantly higher among patients who continued to smoke until surgery than those who quit smoking preoperatively. In addition, the proportion who reported receiving smoking cessation advice from a physician was significantly higher among those who quit smoking preoperatively than those who continued to smoke [78]. Based on these findings, further smoking cessation intervention, in which an educational brochure and a referral form to a telephone quit-smoking service were sent when patients were placed on an elective surgery waiting list, was conducted. This trial achieved a significant increase in the rate of smoking cessation 1 month before surgery [79].

In a Canadian telephone survey of patients receiving elective surgery, only about half of the patients were aware that continuing to smoke increased their surgical risks, and only half of the patients reported being advised to quit before surgery by a healthcare professional [80]. Given that many surgical patients who smoked were unaware of the perioperative risks of smoking and the cessation support available to them, the authors insist that healthcare professionals should more actively engage in cessation guidance. Following the above survey, a regional collaborative preoperative stop smoking program was implemented, with goals that included

improving patient awareness of the benefits of quitting for surgery (using posters, brochures, etc.), and increasing the number of healthcare professionals providing brief interventions to support cessation in surgical patients. This program significantly increased the proportion of patients who quit or reduced smoking and improved the awareness of smoking-related perioperative complications among the patients who were advised to quit [81]. After the program was implemented, advice by healthcare professionals and information from a friend or family member were the strongest predictors of smoking reduction and cessation before surgery.

A study in smokers with peripheral arterial disease compared the impact of a three-component smoking cessation intervention (physician advice, nicotine replacement therapy [NRT], and referral to a telephone-based support service) and usual care [82]. At 3 months, no significant difference was noted in the quit rate between the intervention group (40.3%) and control group (30.9%). However, multivariable analysis showed that the following factors were associated with smoking cessation: receipt of physician advice (OR 1.96, 95% CI 1.28–3.02) and NRT (OR 1.92, 95% CI 1.43–2.56).

Another study conducted a questionnaire survey on perioperative smoking status in women undergoing gynecological surgery [83]. Patients were randomly assigned before surgery to one of the following four groups: (1) patients received no specific information (control), (2) patients received web-based written information, (3) each patient's doctor was informed that the patient was a smoker and should be advised to stop smoking, and (4) patients received the interventions of both groups 2 and 3. Compared with the control group, women in Group 4 who received both web-based information prior to surgery and advice from their doctor reported significantly higher rates of smoking cessation from 1 to 3 weeks preoperatively and 1 to 3 weeks postoperatively.

B Clinical question: How can perioperative smoking interventions be implemented in the national health insurance system of Japan?

Summary statements

- Initial medical consultation must be provided in an outpatient setting.
- Users of heated tobacco products (HTPs) are also eligible for the smoking cessation therapy covered by the national health insurance.

Commentary

Chronic smoking is primarily a manifestation of nicotine addiction. Based on the policy that chronic smoking is a treatable disease, a "nicotine dependence management fee" was newly established in 2006 in Japan, and smoking cessation therapy has been included in the national insurance scheme. Insurance-covered smoking cessation therapy is provided in accordance with the "Standard Procedures for Smoking Cessation Treatment" (latest version, 8.1) [84] at registered medical facilities that meet the institutional requirements. Patients must fulfill the below criteria.

- Patient criteria.

(1) Patients diagnosed with nicotine addiction, with 5 points or more on a nicotine dependence screening test (Tobacco Dependence Screener [TDS]).
(2) The Brinkmann index (i.e., number of cigarettes smoked per day × number of years of smoking) must be at least 200 or more for patients aged 35 years or older. For HTPs, one stick of a directly heated type is equivalent to one combustible cigarette. When vapor is passed through a capsule or pod containing tobacco leaf, one pack of capsules or pods is equivalent to 20 cigarettes.
(3) Patients must be willing to immediately attempt to quit smoking and to agree in writing to receive smoking cessation therapy in accordance with the "Standard Procedures for Smoking Cessation Treatment" after being fully informed of the therapy.

- Standard smoking cessation treatment program [84]

Initial medical consultation for nicotine addiction therapy must be provided in an outpatient setting if it is to be covered by the national insurance program. If an

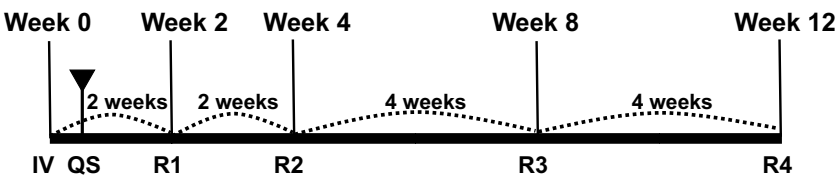

Fig. 1 A standard smoking cessation treatment program consisting of five sessions over 12 weeks. IV, initial visit; QS, quit smoking day; R1, Return Visit 1; R2, Return Visit 2; R3, Return Visit 3; R4, Return Visit 4f

inpatient asks for smoking cessation treatment, it must be explained to them that they cannot start cessation therapy under the national insurance policy while they are hospitalized. They can make an appointment for the initial consultation after they are discharged. If they wish to use a smoking cessation aid, they can be advised to purchase over-the-counter nicotine products.

A standard smoking cessation treatment program consists of five sessions over 12 weeks (Fig. 1). At the initial consultation, the patient and physician decide on the date to quit smoking. Since insurance-covered therapy for smoking cessation is applicable only to smokers who express their willingness to quit smoking at the initial visit, cessation should be scheduled to start at a date before the second visit, which takes place 2 weeks after the initial visit (patients can continue receiving health insurance coverage even if they end up failing to quit smoking by the second visit). If the physician sees a patient who has not made up their mind to quit smoking immediately, the physician should explain the harms of smoking. In particular, patients scheduled for surgery should be informed about the perioperative harms of smoking. If during medical consultation the patient cannot tell the physician that he or she is ready to immediately start smoking cessation therapy or if the patient opts to start the therapy at a later date, the medical consultation cannot be classified as the insurance-covered initial visit of the outpatient smoking cessation program. It must be classified as usual medical care under the national insurance scheme. In the outpatient smoking cessation program, four sessions will be held 2, 4, 8, and 12 weeks after the initial visit to help patients continue abstinence. Return visits 1, 2, and 3 may be conducted as online medical consultations using electronic communication tools.

C Clinical question: What should the physician do if the patient attending the outpatient smoking cessation program is hospitalized?

Summary statements

- Patients can continue smoking cessation therapy during hospitalization.
- Since the medical consultations and medications provided during hospitalization will not be included in the outpatient smoking cessation program, the duration of the program can be extended after discharge by the number of hospitalization days.

Commentary

If the patient is hospitalized for any reason during the 12-week smoking cessation program, they can remain on the program during hospitalization [84]. Although the hospital cannot charge the nicotine addiction management fee, they can charge for the drugs needed for smoking cessation therapy (at Diagnosis Procedure Combination [DPC] institutions, drug costs cannot be claimed separately since the charges are determined on an all-inclusive basis). However, institutions that have not been registered for nicotine addiction management services cannot charge for in-hospital prescriptions of smoking cessation drugs. The hospital stay will not be included in the 12-week program during which nicotine addiction management fees can be claimed, and in-hospital prescriptions will not be regarded as part of the five treatments permitted in the program.

If a sufficient amount of time is available before surgery, the standard smoking cessation therapy can be provided. For patients who need to undergo surgery within a short amount of time and who should quit smoking at the earliest opportunity, the surgeon should consider cooperating with other medical institutions that can provide insurance-covered smoking cessation treatment if the surgical institution cannot provide insurance-covered smoking cessation treatment or the patient cannot start therapy immediately because appointments are unavailable. An example of a case where the program includes a 2-week hospitalization period is illustrated in Fig. 2.

D Clinical question: Is multidisciplinary cooperation between departments and specialists effective for achieving perioperative smoking cessation?

Summary statement

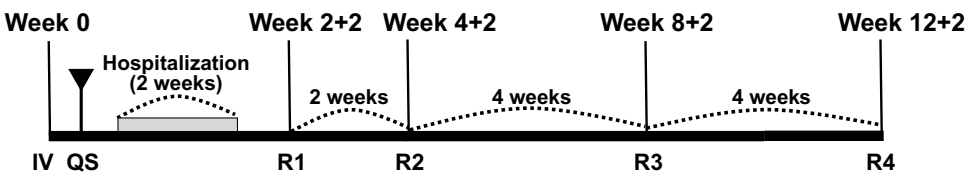

Fig. 2 A hypothetical case where the smoking cessation treatment program includes a 2-week hospitalization period. IV, initial visit; *QS* quit smoking day, *R1* Return Visit 1, *R2* Return Visit 2, *R3* Return Visit 3, *R4* Return Visit 4

- To ensure that the preoperative duration of smoking abstinence is sufficiently long, cooperation should be sought among various types of specialists, including primary care physicians, surgeons, anesthesiologists, and nurses.

Commentary

It is preferable to maximize the duration of preoperative smoking cessation. However, not all patients scheduled for surgery are aware of the surgical risks of smoking. In a survey of patients scheduled for surgery in 2011 at a Japanese national university hospital, 80 (7%) smoked until the day before surgery, and 55% of them knew the perioperative risks of smoking [85]. In a large number of countries, smoking cessation treatment is covered by health insurance plans, but patients are often unaware that their insurance policies cover smoking cessation therapy [80]. Data show that in primary healthcare and surgical outpatient settings, little attention is paid to patients' smoking status [86]. In a survey of 1482 surgical patients referred to a Finnish hospital for elective or urgent surgery, 18.6% smoked within 6 months before surgery [86]. Information on smoking status was recorded infrequently; specifically, it was present in only 18.4% of surgical outpatient clinic records and 14.2% of primary care physician referrals, with the latter rate significantly lower than the former [86]. Anesthesiologists are able to interact with their patients for a very short time. To promote early preoperative interventions and guidance for smoking cessation, anesthesiologists should directly intervene with patients about smoking. Moreover, anesthesiologists should help surgeons and referring primary care physicians understand the significance of preoperative smoking cessation. Learning activities to help nurses and other nonphysician healthcare workers gain competence in supporting patients with smoking cessation are effective for promoting preoperative abstinence from smoking [87].

E Clinical question: What is the role of the perioperative management team in perioperative smoking cessation?

Summary statement

- The perioperative management team can provide intensive early intervention through multidisciplinary cooperation.

Commentary

In European and North American countries, there has been increasing emphasis since the mid-1990s on the utility of "anesthetic surgery preoperative evaluation clinics," "surgical clinics," and other preoperative evaluation clinics that help to prepare patients for surgery. In Japan, JSA launched the concept of the multidisciplinary "perioperative management team" in 2007. Since then, the number of institutions that establish and operate perioperative management centers has been gradually increasing.

Young-Wolff et al. reported that a smoking cessation intervention integrated into standard perioperative care in surgical clinics and perioperative settings increased the rates of preoperative and postoperative abstinence from smoking [88]. Kelley et al. analyzed more than 53,000 surgical patients over a 4-year period, and showed that preoperative interventions, including preoperative clinic visits and wellness bundles containing smoking cessation information, reduced the incidence of hospital acquired infections [89].

It takes time to determine the effects of preoperative smoking cessation. The short length of preoperative hospital stays in recent years underscores the importance of perioperative management centers in preoperative smoking cessation intervention. A Cochrane review of 42 studies that included over 31,000 smokers compared the effects of smoking cessation advice [90]. Brief advice versus no advice (or usual care) was associated with a significant increase in the rate of quitting (RR 1.66, 95% CI 1.42–1.94). Compared with minimum advice, intensive advice that involved initial consultation lasting for ≥ 20 min, the use of additional materials other than a leaflet, or more than one follow-up resulted in a higher quitting rate (RR 1.37, 95% CI 1.20–1.56). In the aforementioned studies by Young-Wolff et al. [88] and Kelley et al. [89], the smoking cessation interventions were multimodal and involved multiple opportunities for patient follow-up. Both studies demonstrated benefits of multidisciplinary intensive intervention and multiple opportunities for patient follow-up, emphasizing the importance of the perioperative management team.

As a standard approach to preoperative smoking cessation intervention by the anesthesiologists in preoperative centers, the "5 As" model proposed by the US Department of Health and Human Services can be useful [91]:

Ask: Ask all patients about tobacco use at every visit.
Advise: Advise all tobacco users to quit in a clear, strong, and personalized manner.
Assess: Assess willingness to make a quit attempt.
Assist: Assist in quit attempt by offering medication and providing or referring for counseling.
Arrange: Arrange follow-up.

However, the 5 As model may not be practical in clinical settings not specialized in smoking cessation, such as preoperative clinics. Consequently, the Ask–Advise–Refer (AAR) model (ask all patients about tobacco use, advise identified tobacco users to quit, and refer them to specialists or special programs) has been proposed as a simpler alternative [92]. This strategy has been recommended by the American Society of Anesthesiologists and other anesthesiology societies in other countries [93]. Furthermore, in light of the low percentages of patients who contact smoking cessation programs, the

Ask–Advise–Connect (AAC) strategy has been advocated. This approach connects smokers to the counseling programs through an automated system within the electronic health record [94]. The AAC approach has greatly increased the proportion of smokers who quit.

Preoperative smoking cessation within the enhanced recovery after surgery approach and prehabilitation

A Clinical question: How can preoperative smoking cessation be positioned within ERAS and prehabilitation programs?

Summary statement

- Preoperative smoking cessation treatment is positioned as part of ERAS and multimodal prehabilitation programs. Its combination with exercise therapy, nutritional care, psychological support, oral care, and others will enhance its effectiveness.

Commentary

The ERAS protocol is an evidence-based, multidisciplinary clinical care program that is based on scientific principles to optimize perioperative care. It aims to improve postoperative recovery and reduce postoperative complications and hospital stay. The concept of ERAS was developed in Denmark in the late 1990s, and primarily for colorectal surgery patients [95]. ERAS programs are gradually gaining popularity in Japan as well. The ERAS program spans preoperative, intraoperative, and postoperative phases. Preoperative interventions include counseling to decrease anxiety and fear about operation and anesthesia, education to enhance early oral ingestion and rising from bed, preoperative medical management, abstinence from smoking and alcohol, and prehabilitation. Although the components of the ERAS guidelines vary depending on the type of surgery, many ERAS guidelines recommend smoking cessation [96–98]. Prehabilitation, in its narrow sense, aims to improve the patient's physical performance through exercise therapy so that they can overcome surgical stress. However, this term has also often been used in recent years to include psychological support, healthy lifestyle interventions, and nutritional therapy to treat preoperative malnutrition [99]. In this regard, preoperative interventions for smoking cessation are part of the prehabilitation regimen.

The benefits of prehabilitation have been reported in many surgical specialties, including abdominal and thoracic [100–102]. Most of these prehabilitation programs adopted a multimodal approach that included preoperative smoking cessation. In a meta-analysis to compare the effects of single-modal (nutrition-only) and multimodal (nutrition plus exercise) prehabilitation in patients undergoing colorectal surgery, Gillis et al. showed that both regimens significantly shortened the length of hospital stay, and multimodal prehabilitation accelerated the return to presurgical functional capacity [103]. Luther et al. reported that a multimodal approach is likely to have a stronger positive impact on functional outcome after major abdominal surgery than a single modality [104]. Significant effects of prehabilitation included a lower incidence of postoperative complications [105], shorter hospital stay (median 6 vs. 7 days), higher rate of discharge to home (65.6% vs. 57.0%), and lower payments ($31,641 vs. $34,837) [100]. Additionally, improvements in forced expiratory volume in 1 s, vital capacity, grip strength, and quality of life (QOL), and better results on evaluation of obstructive lung disease and dyspnea, were observed after thoracic surgery [101]. Several scientists insist that while the evidence suggests some benefits of smoking cessation intervention in the context of prehabilitation, the evidence is limited in the absence of studies that directly compare the effects of prehabilitation with and without smoking cessation intervention or that contrast multimodal prehabilitation programs with smoking cessation intervention alone [106]. Further research efforts, such as large-scale prospective studies, are warranted.

Cigarette smoke causes nicotine-induced gingival vasoconstriction and immunosuppression. It is one of the greatest risk factors for periodontal disease, and smokers with periodontal disease are likely to have poorer clinical course than non-smokers. Oral care has been reported to reduce the incidence of postoperative pneumonia in patients with esophageal cancer and cardiovascular surgery [107, 108], as well as the incidence of respiratory infections and deep surgical site infections following thoracic surgery [109]. Preoperative oral care has increasingly been adopted as part of an ERAS (prehabilitation) protocol. It is therefore important to promote oral care in association with smoking cessation intervention.

The role of nicotine replacement therapy and other smoking cessation aids

A Clinical question: Should smoking cessation aids be included in perioperative smoking cessation intervention?

Summary statements

Recommendation:

We strongly recommend the perioperative use of smoking cessation aids, because they increase the success rate during and after the perioperative window. (1B).

- Treatment with varenicline is recommended in patients with a long wait time before surgery. NRT should be administered to patients with a short wait time.
- Smoking cessation aids have no significant adverse effects; minor symptoms include palpitations and tachy-

cardia associated with NRT. They are safe as long as their use is avoided on the day of surgery in patients with ischemic heart disease.

- The postoperative use of smoking cessation aids should be started at the earliest opportunity based on the patient's condition.

Commentary

The smoking cessation aids approved in Japan include NRT products, such as nicotine patches and gum, as well as varenicline, an orally administered partial agonist of the α4β2 nicotinic receptor. These agents help increase the rate of smoking cessation, with a RR of abstinence of 1.64 (95% CI 1.53–1.75) for nicotine patches, 1.49 (1.40–1.60) for nicotine gum, and 2.24 (2.06–2.43) for varenicline [110, 111]. NRT products and varenicline increase the perioperative smoking cessation rate, suppress the onset of nicotine withdrawal symptoms in the postoperative period, and resulted in higher long-term smoking cessation rates [112–114].

Safety is a major concern regarding the perioperative use of these agents. One meta-analysis showed that varenicline had no cardiovascular risks, although NRT was associated with an increase in cardiovascular events [115]. However, these events consisted mainly of mild cases of palpitations and tachycardia, and the incidence of serious events was not significantly elevated. In a recent large-scale randomized controlled trial, varenicline and nicotine patches were not associated with an increased risk of serious cardiovascular events during treatment or 52-week follow-up [116]. Nicotine patches had no adverse effects on incisional wound healing [117].

During the first week of varenicline treatment, the dose is increased in a two-step manner, while the patient is allowed to continue smoking. On Day 8, the patient stops smoking. Varenicline is a powerful option for patients with a sufficient wait period before surgery. In contrast, patients stop smoking as soon as they start NRT. Appropriate preoperative smoking cessation aids should be selected, taking into account their dosing regimens and the number of days available before surgery. NRT is a preferred option for patients with a short time to surgery (Table 2). Since nicotine patches significantly increase the pulse rate after tracheal intubation, they should be removed from patients with ischemic heart disease on the day of operation [118]. The postoperative use of smoking cessation aids should be started based on the patient's condition. Considering that the patient is undergoing nicotine withdrawal, smoking cessation aids should be resumed at the earliest opportunity to optimize postoperative pain management.

Medical economics

A Clinical question: Does perioperative smoking cessation intervention improve health economics?

Summary statement

- Smoking cessation intervention is not free of cost. However, health economics favor it since it helps lower medical costs by reducing perioperative complications.

Commentary

In a cost–benefit analysis of preoperative smoking cessation interventions (counseling and NRT) in patients undergoing arthroplasty, the mean cost of a hospital stay was reduced by €313 because of decrease in complications due to smoking cessation intervention, with a mean cost estimate of the intervention of €196 (counseling nurse fee €120 and NRT cost €76). Therefore, the preoperative smoking cessation intervention was estimated to save €117 per patient [119].

Another study examined the cost–benefits of preoperative smoking cessation intervention within the first 90 days postoperatively in patients undergoing colorectal surgery [120]. As compared with usual care, the preoperative smoking cessation program reduced the medical costs by $304 per patient. Consequently, a smoking cessation program with a maximum mean cost of $304 per patient was expected to cost effective [121].

Based on previous reports that compared the incidence of periprosthetic joint infections after total joint arthroplasty, the estimated 90-day cost for total joint arthroplasty care for patients enrolled in a mandatory smoking cessation intervention was $23,457 (including $86 for counseling and $101 for NRT), which was $32 less than the cost of $23,489 for patients without smoking cessation intervention [122]. In this study, the smoking cessation intervention was cost-saving compared with no intervention when the short-term cost of periprosthetic joint infection was greater than $95,410, the rate of periprosthetic joint infection was reduced by at least 25% for former smokers versus current smokers, the cost of the intervention was less than $219, or the success rate of the intervention was greater than 56%. Since this study only examined the effect of smoking cessation intervention on postoperative infection, it may have underestimated the cost-saving effect of smoking cessation intervention.

The economic benefit of the funding on the preoperative smoking cessation intervention was investigated in the Spanish National Health System [122]. The rate of smoking cessation was estimated to be 21.7% higher when intervention would be funded by the National Health System (with an absolute reduction in smoking prevalence of 0.9%) [122].

Table 2 Comparison of smoking cessation aids

Nicotine patch	Nicotine gum	Varenicline
Insurance covered Medium- and low-dose products are available as over-the-counter drugs	Over-the-counter product	Insurance covered
Nicotine is delivered transdermally	Nicotine is delivered through the oral mucosa	Oral drug. An α4β2 nicotinic receptor partial agonist
One patch is applied per day to suppress withdrawal symptoms. Nicotine is delivered gradually	When the urge to smoke occurs, the patient slowly chews one piece of gum at a time. Nicotine absorbed through the oral mucosa mitigates withdrawal symptoms. Nicotine can be delivered rapidly	Suppresses withdrawal symptoms and smoking satisfaction
Quit smoking when starting nicotine patches. Gradually reduce doses from high to medium to low, typically over 8 weeks (up to a maximum of 10 weeks)	Quit smoking on the day of starting nicotine gum. Taper the amount of gum per day, typically over 12 weeks	Start 1 week before quitting smoking (Day 8), and continue for 12 weeks: One 0.5 mg tablet per day for 3 days Two 0.5 mg tablets per day for 4 days Two 1 mg tablets per day from Day 8 to Week 12
	Using half a piece of gum may help curb the sudden craving for smoking that occurs while wearing nicotine patches	
Warning Patches should be removed from patients with ischemic heart disease on the day of surgery	Warning Patients with ischemic heart disease must not chew nicotine gum on the day of surgery	Warning/precaution Varenicline should preferably be started at least 2 weeks before surgery because patients may still smoke during the first week of treatment Patients should be "advised to use caution driving or operating machinery until they know how quitting smoking with varenicline may affect them." (US package insert) Patients should "not drive, operate complex machinery or engage in any other potentially hazardous activities" until they know whether this medicine affects their ability to perform these activities. (EU Package Leaflet) Patients should be advised to avoid driving or operating potentially dangerous machinery. Patients may experience dizziness, somnolence, impaired consciousness, or other adverse events, which could have led to traffic accidents in several cases. (Japanese Package Insert)

The funded program would achieve a net healthcare benefit of €503 per quitter, with an average additional cost of €1,753 incurred per quitter for intervention (counseling and drugs) and an average savings of €2,256 per quitter because of avoided healthcare resources due to smoking abstinence. The return on investment was 28.7% annually, or €1.29 gained per €1 invested, suggesting that funding of the preoperative smoking cessation program largely outweighs the costs. Although few studies in Japan have compared the costs and benefits of perioperative smoking intervention, it is expected to have a favorable benefit-to-cost ratio as suggested by many overseas studies.

Effects of long-term (permanent) smoking cessation

A Clinical question: How does long-term smoking cessation after surgery affect the QOL of patients with cancer and other diseases?

Summary statements

Recommendation: We strongly advise all patients, particularly those with cancer, to remain smoke-free after surgery because continued smoking worsens their QOL. (1C).

- Smoking increases the postoperative recurrence of malignant tumors and decreases survival.
- Smoking attenuates the effects of chemotherapy and radiotherapy.
- Smoking compromises postoperative QOL.
- Since smoking cessation is expected to help reverse these adverse effects, guidance regarding smoking cessation should be provided whenever possible.

Commentary

As mentioned earlier, perioperative smoking adversely influences the clinical course during the perioperative period. In particular, smoking worsens the long-term outcome of surgically treated patients with malignant tumor, and it has been shown to negatively impact disease recurrence and survival [14, 123–127]. In patients surgically treated for non-small cell lung carcinoma, current smoking was an independent predictor of poor survival. With respect to mortality, compared with current smokers, non-smokers had a RR of 0.447 (95% CI 0.206–0.970) and former smokers had a RR of 0.543 (95% CI 0.350–0.843) [123]. In patients with colorectal cancer, being a current smoker was an independent risk factor for postoperative pulmonary metastases (HR 2.72, 95% CI 1.18–6.25) [126]. Among patients who underwent esophagectomy for cancer, preoperative smoking was a significant risk factor for early recurrence (OR 2.76, 95% CI 1.28–6.17) [127]. Regardless of the type of surgery, smoking was significantly associated with a greater risk of 30-day postoperative complications (OR 1.15, 95% CI 1.13–1.17) and mortality (OR 1.22, 95% CI 1.08–1.39) compared with non-smoking [14]. Increased survival rates were reported for cancer patients quitting smoking after diagnosis, irrespective of the type of cancer treatment [123, 128–130]. Compared to smokers who never quit smoking, patients who quit at or after diagnosis had a smaller odds of poor prognosis (RR 0.340, 95% CI 0.164–0.705) [123] and a 45% reduction in risk of death (HR 0.55, 95% CI 0.38–0.79) [128]. Cancer patients who continued smoking after diagnosis experienced a 59% increase (95% CI 36–86%) in risk of death compared with cancer patients who did not smoke after diagnosis [129]. Compared with patients who stopped smoking after cancer diagnosis, the risk of death was elevated in those who continued smoking, with a HR of 1.79 (95% CI 1.49–2.16) in all cancer patients, 2.36 (95% CI 1.63–3.42) in lung cancer patients, 1.63 (95% CI 0.98–2.73) in stomach cancer patients, 2.31 (95% CI 1.40–3.81) in colorectal cancer patients, and 2.95 (95% CI 1.09–7.95) in bladder cancer patients [129]. Smokers have a lower rate of survival after radiotherapy or chemoradiotherapy [131, 132]. In a meta-analysis of 24 articles on outcomes in head and neck cancer patients undergoing radiotherapy, continued smoking was associated with elevated risks of mortality (RR 1.85, 95% CI 1.55–2.21) and locoregional failure (RR 2.24, 95% CI 1.42–3.52) [131].

In patients who continued to smoke, conditions of surgical sites [133] and irradiated organs [134] were worse than in non-smokers. Moreover, smokers had worse postoperative QOL [134–136]. Patients with lung carcinoma and other malignant tumors who quit smoking after radiation therapy may experience a survival benefit [134, 137]. In early-stage non-small cell lung carcinoma, smoking status at the time of radiation therapy was associated with overall survival, with a HR of 2.1 (95% CI 1.02–4.2) [137]. Survival can be improved even if patients stop smoking after cancer treatment [137]. Smoking-related risks of reoperation are discussed under the heading of "Risk of Reoperation" in Sect. 4-1B.

Preventing relapse: follow-up

A Clinical question: Are there any effective measures to prevent smoking relapse after surgery?

Summary statements

Recommendation: We strongly recommend that patients be provided with proactive preoperative interventions to prevent postoperative smoking relapse. (1A).

- More intensive preoperative smoking cessation interventions are associated with a higher proportion of patients who are smoke-free before and after surgery.
- Postoperative follow-up should be continued for as long as possible.

Commentary

Surgery provides a good opportunity for patients to quit smoking. However, many patients resume smoking postoperatively. Patients who are smoke-free preoperatively are likely to remain so thereafter. More intensive preoperative smoking cessation interventions are associated with a higher proportion of patients who are smoke-free after surgery [76, 114, 138, 139]. An intensive intervention significantly prolonged the duration of smoking cessation (RR 2.96, 95% CI 1.57–5.55), whereas no long-term effect was achieved by a brief intervention (RR 1.09, 95% CI 0.68–1.75) [76]. In a meta-analysis of four randomized controlled trials and four quasi-experimental studies, preoperative interventions were associated with a greater likelihood of cessation at 12 months (RR 1.50, 95% CI 1.05–2.15) [138]. Smoking patients who received smoking intervention before surgery were 2.7 times more likely to achieve long-term cessation at 1 year than those who did not (95% CI 1.1–6.7) [139]. The rate of smoking cessation was higher at 1 year after surgery in patients who received a multimodal smoking cessation program before surgery than those who received brief advice only (42.4% vs. 26.2%, respectively, RR 1.62, 95% CI 1.16–2.25) [114]. Preoperative smoking cessation attempts should ideally lead to permanent abstinence. To prevent relapse, postoperative follow-up should be continued for as long as possible.

Positioning of heated tobacco products and other novel tobacco products

A Clinical question: How can novel tobacco products be positioned within the framework of preoperative smoking cessation intervention?

Summary statements

- A clear distinction should be made between HTPs and electronic cigarettes (e-cigarettes).
- Currently, no scientific evidence indicates that HTPs are less hazardous to health than conventional tobacco. In the same manner as they are told to refrain from conventional tobacco, patients should be advised to refrain from HTPs during the perioperative period. HTPs users are eligible for the smoking cessation therapy covered by the Japanese national health insurance program.
- Electronic non-nicotine-delivery systems (ENNDS) that are marketed in Japan release many harmful substances. In consideration of the risk of e-cigarette or vaping product use–associated lung injury (EVALI), patients should be advised to stop using them.

Commentary

Changes in social circumstances have resulted in the increased use of novel tobacco products [140]. Here, we clearly define novel tobacco products and position them within the framework of perioperative intervention. Data provided by tobacco-related companies were excluded from the review below.

As shown in Table 3, novel tobacco products can be divided into two major categories [141]. E-cigarettes typically come in cigarette-, pen-, and tank-shaped styles, and include an atomizer, which contains a battery-operated heating element, and a cartridge that stores a liquid solution containing nicotine, propylene glycol, glycerine, flavorings, and taste (e-liquid). The vapor generated by heating the liquid is inhaled by the user. Nicotine is an active pharmaceutical ingredient, and is regulated by the Act on Securing Quality, Efficacy, and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, Gene Therapy Products, and Cosmetics (Pharmaceuticals and Medical Devices Act). In Japan, nicotine cannot be manufactured or sold without regulatory drug authorization, and no nicotine-containing e-cigarettes have been approved for marketing in Japan to date. Therefore, all e-cigarettes that are sold in Japan contain no nicotine (ENNDS). Although electronic nicotine-delivery systems (ENDS) are not commercially available in Japan, they can be imported on a personal use basis from other countries (e.g., ordered via the Internet). ENNDS are not subject to regulatory restrictions.

To produce aerosol for inhalation, HTPs directly heat tobacco leaf or pass heated vapor over processed tobacco consumables. HTPs are regulated under the Tobacco Business Act. Among the first three brands of HTP launched in Japan, iQOS® and glo® directly heat tobacco leaf at 300 °C–350 °C and 240 °C, respectively, to generate a

Table 3 Classification of novel tobacco products

Type	Relevant regulations
Electronic cigarettes (e-cigarettes)	
Containing nicotine (not commercially available in Japan) Electronic nicotine-delivery systems (ENDS)	Pharmaceuticals and Medical Devices Act
Not containing nicotine Electronic non-nicotine-delivery systems (ENNDS)	None
Heated tobacco products (HTPs)	Tobacco Business Act

nicotine-containing aerosol (the boiling point of nicotine is 247 °C). Ploom TECH® produces an aerosol by heating an organic solvent such as glycerine (at approximately 30 °C), and the aerosol is passed over tobacco powder to extract its components for inhalation by the user. Various tobacco companies are now marketing new types of products that use different heating temperatures and methods from those of the first-generation products.

Overseas, e-cigarettes users were shown to have greater success at quitting cigarette smoking than non-users [142]. ENDS generate nicotine-containing vapor without burning or heating tobacco leaf. Hence, ENDS may be regarded as a type of NRT. In the SFAR guidelines, e-cigarettes were suggested to be moderately effective in terms of smoking cessation and harm reduction. However, no recommendation was made because of the lack of consensus [13]. In the United States, an outbreak of EVALI associated with the rapid spread of e-cigarette use was reported [143]. Attention should also be paid to the use of e-cigarette devices to vaporize cannabis. Many e-cigarette products commercially available in Japan were shown to generate diethylene glycol, formaldehyde, acetaldehyde, acrolein, and other toxic substances as a result of heat denaturation of alcohols contained in the e-liquid [144]. Moreover, the e-cigarettes available in Japan are not likely to contribute to effective smoking cessation, because they do not release nicotine and, therefore, cannot be used as NRT [145]. E-cigarettes may involve risks because not all substances they release have been identified.

In a study that compared the contents of iQOS aerosol and smoke from conventional cigarettes, the iQOS aerosol had 84% of the nicotine found in conventional cigarette smoke, in addition to considerable levels of volatile organic compounds, such as acrolein, formaldehyde, benzaldehyde, and acetaldehyde, and polycyclic aromatic hydrocarbons, such as acenaphthene and pyrene [146]. In studies that analyzed the contents of smoke released from HTPs other than iQOS, toxic substances were detected at considerable concentrations, although they were lower than those associated with ordinary cigarettes [147, 148]. HTPs are covered by the Japanese national health insurance program for use in smoking cessation therapy [84].

Surgeons and perioperative cessation: impact of smoking by type of surgery and the role of surgeons

Impact of smoking by type of surgery

As discussed earlier, preoperative smoking is a known risk factor for perioperative complications in a wide range of surgical operations; these adverse events include wound and other infections, pulmonary and neurological complications, and bone non-union. Available evidence shows that smoking negatively impacts long-term outcomes, including by increasing the frequency of revision arthroplasty, reducing patency rates after CABG, and elevating mortality rates. Various studies have been performed to investigate the effects of smoking by surgical specialty, disease, and treatment. Major results are summarized in Supplementary 3. Surgeons have several key preoperative smoking-related concerns, including the following: how to advise elective patients to quit smoking, what interventions to make, and how to deal with patients who do not agree to stop smoking. The following three approaches can be considered for elective patients who smoke: (1) postpone the surgery until the patient can abstain from smoking for a certain period of time, (2) adopt a less invasive operative or anesthetic method, and (3) decline to perform the operation if the patient does not agree to quit smoking. Regarding the third approach, surgeons treating patients with malignant tumors should refer them to a radiotherapist or chemotherapist for alternative treatment. In a questionnaire survey of thoracic surgeons in the United States, 98.1% of respondents recognized smoking as a risk factor for postoperative complications, 77% considered that pharmacologic intervention was the most common strategy for cessation, and about 50% would not perform certain operations in patients who were current smokers [149].

Academic societies should take the initiative to create educational materials for patients about the importance of quitting smoking preoperatively, and should also define effective pathways for surgeons to refer postoperative patients to smoking cessation specialists for follow-up. The American College of Surgeons, Society of Thoracic Surgeons, Royal College of Surgeons, American Academy of Orthopedic Surgeons, and other academic associations have posted patient education materials about preoperative smoking cessation on their web sites. Patient education resources of the American College of Surgeons and Society of Thoracic Surgeons are presented with permission in Supplementary 4 (in the Japanese-language version only).

A Clinical question: Does minimally invasive surgery reduce complications in patients who smoke?

Summary statement

- Minimally invasive surgery may reduce perioperative complications in patients who smoke.

Commentary

In a study of patients undergoing video-assisted thoracic surgery (VATS) by Matsuoka et al., the incidence of postoperative complications was higher in smokers than in non-smokers, and the frequency of respiratory-related complications increased with the number of pack-years [75]. However, no relationship was observed between the length of the preoperative smoking cessation period and

the frequency of postoperative complications. The risk of postoperative complications did not increase even if patients were still smoking within 2 weeks before surgery. The authors concluded that there is no need to delay surgery to allow patients to quit smoking, especially those scheduled for VATS.

Yoshida et al. compared the incidence of postoperative complications in patients with esophageal cancer undergoing minimally invasive esophagectomy by the duration of preoperative smoking cessation: ≤ 30, 31–90, and ≥ 91 days [150]. Severe complications and pneumonia were frequently observed in patients with smoking cessation ≤ 30 days. Complications increased with shorter cessation durations. Smoking cessation ≤ 30 days (HR 3.13) and past smoking were significant risk factors for pulmonary complications. The authors concluded that preoperative smoking cessation is important to prevent postoperative complications in patients undergoing minimally invasive esophagectomy, and preoperative cessation ≥ 31 days is preferable to decrease postoperative complications.

For surgical patients who smoke, minimally invasive surgery may be an option to reduce perioperative complications. However, the significance of preoperative smoking cessation should never be underestimated, no matter how short it may be.

The role of surgeons

A Clinical Question: Does the surgeon's advice on smoking cessation have any effect on reducing perioperative complications?

Summary statement

- The surgeon's advice on smoking cessation contributes to reducing perioperative complications.

Commentary

Surgery aims to improve patient survival and functional outcomes. Smoking is a modifiable risk factor for these outcomes. Since surgery provides an excellent opportunity for patients to quit smoking, thereby contributing to their long-term outcomes, surgeons should assume a proactive role and promote smoking cessation [151]. Few randomized controlled studies have rigorously investigated the effect of preoperative smoking cessation, and many were limited by small sample sizes [76]. In a study of patients undergoing hip and knee replacement by Møller et al. [152], patients were randomized to either a smoking intervention or control group. The active intervention group demonstrated significantly lower rates of overall complications than the control group, with an 83% reduction in wound-related complications. In a study of patients undergoing total joint replacement by Beaupre et al. [153], patients referred to a community-based, pharmacist-led smoking cessation program had a higher quit rate at 6 months post-recruitment than those who received usual care. In a pilot prospective study of smokers undergoing thoracic oncology surgery, patients were assigned to counseling plus varenicline therapy or to control treatment. At 12 weeks after surgery, the smoking intervention group had a higher quit rate than the control group, but not significantly (37.5% vs. 28.6%, respectively) [154].

Practicing surgeons are often busy with their daily routines, and many have not received practical training on smoking cessation intervention [155]. The perioperative management team, comprising a surgeon, anesthesiologist, physician specializing in tobacco cessation, nurse, and other healthcare workers, should make concerted efforts in terms of patient education and smoking cessation. Patients preparing for surgery are often too preoccupied with their own schedule to spare time for participating in smoking cessation counseling. The surgeon should consider establishing an early intervention framework with the help of internists.

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