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2734 17 Avenue SW,  
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+15878858911  
editorial-office@sciformat.ca

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## THE IMPACT OF CAFFEINE ON SURGERY

**Weronika Ewa Nowak** (Corresponding Author, Email: [weronikanowak0908@gmail.com](mailto:weronikanowak0908@gmail.com))  
Jan Mikulicz-Radecki University Clinical Hospital, Wrocław, Poland  
ORCID ID: 0009-0006-8445-2072

**Paweł Harbut**  
Medical University of Silesia in Katowice, Katowice, Poland  
ORCID ID: 0009-0001-0405-4407

**Aleksander Białoń**  
University Hospital in Krakow, Kraków, Poland  
ORCID ID: 0009-0007-4447-7619

**Dominika Walczak**  
4th Military Clinical Hospital, Wrocław, Poland  
ORCID ID: 0009-0007-1629-871X

**Adrian Kruk**  
Independent Public Regional Hospital in Szczecin, Szczecin, Poland  
ORCID ID: 0009-0001-1749-6159

**Katarzyna Jakubowska**  
4th Military Clinical Hospital with Polyclinic in Wrocław, Wrocław, Poland  
ORCID ID: 0009-0006-6542-8309

**Aleksandra Dorosz**  
Lower Silesian Center of Oncology, Pulmonology, and Hematology in Wrocław, Wrocław, Poland  
ORCID ID: 0009-0001-4956-5702

**Igor Gawłowski**  
5th Military Clinical Hospital with Polyclinic in Kraków, Kraków, Poland  
ORCID ID: 0009-0007-8895-4237

**Aleksandra Miśta**  
Provincial Specialist Hospital in Wrocław, Wrocław, Poland  
ORCID ID: 0009-0007-1389-2596

**Lidia Jurczenko**  
4th Military Clinical Hospital, Wrocław, Poland  
ORCID ID: 0009-0005-5075-629X

## ABSTRACT

Caffeine is one of the most widely consumed psychoactive substances and is commonly used by both surgical patients and healthcare professionals. While its primary effect on the central nervous system is the reduction of fatigue and enhancement of alertness, caffeine also influences cardiovascular function, skeletal muscle activity, metabolism, and neuroendocrine regulation. Owing to these multifaceted actions, caffeine may affect perioperative outcomes and complications in both beneficial and adverse ways.

This narrative review summarizes current evidence on habitual and perioperative caffeine consumption in the surgical setting, addressing its interactions with anesthetic and analgesic drugs, effects on physiological recovery and wound healing, influence on perioperative risk, and potential impact on surgeons' alertness and procedural precision.

The available studies are limited in number, heterogeneous in design, and frequently inconclusive, which precludes clear clinical recommendations regarding habitual or perioperative caffeine consumption. Further well-designed studies are required to clarify the benefits and risks of caffeine use for both patients and surgical staff and to support the development of evidence-based perioperative guidance.

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## KEYWORDS

Caffeine, Surgery, Coffee, Operation, Anesthesia, Surgeon

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## Introduction

Caffeine is one of the most widely consumed psychoactive substances worldwide and is commonly found in coffee, tea, energy drinks, yerba mate, chocolate, and numerous medical products. It is a naturally occurring methylxanthine alkaloid whose primary pharmacological action is stimulation of the central nervous system (CNS). This effect is mainly mediated through antagonism of adenosine receptors in the brain, leading to reduced fatigue and increased alertness, vigilance, and concentration (R. P. Barcelos et al., 2020).

Beyond its well-known stimulatory properties, caffeine exhibits a broad range of additional biological effects. It enhances the release of neurotransmitters such as dopamine and norepinephrine, thereby influencing mood and cognitive performance. Clinically, caffeine is used as an adjuvant to common over-the-counter analgesics, including non-steroidal anti-inflammatory drugs and paracetamol, where it has been shown to improve analgesic efficacy in acute pain conditions (Derry et al., 2014). Moreover, accumulating evidence suggests that caffeine's mechanisms of action may play a role in neuroprotection and potentially reduce the risk of neurodegenerative diseases, such as Alzheimer's and Parkinson's disease (Kolahdouzan & Hamadeh, 2017).

Caffeine also exerts significant effects beyond the CNS, influencing multiple peripheral tissues, including the cardiovascular system, skeletal muscle, and adipose tissue. These effects contribute to increased heart rate, elevated blood pressure, enhanced metabolic rate, and improved physical performance (Guest et al., 2021). In addition, caffeine has been shown to modulate oxidative stress and inflammatory responses, further expanding its systemic impact (Ósz et al., 2022).

Given these diverse physiological actions, caffeine intake may influence surgical and perioperative outcomes. Its effects on cardiovascular function, metabolism, and the neuroendocrine stress response have potential implications for anaesthesia management, drug interactions, and postoperative recovery. Consequently, understanding the role of caffeine in the perioperative setting is of clinical relevance, particularly in patients who consume caffeine regularly (Malviya et al., 2023).

Finally, the influence of caffeine extends beyond patients to healthcare professionals themselves. Surgeons and anaesthesiologists are frequently exposed to long working hours, night shifts, and high cognitive demands, circumstances that often promote increased caffeine consumption. While caffeine may enhance alertness and reduce fatigue, its effects on fine motor skills, precision, and decision-making remain complex and warrant careful consideration (Fargen et al., 2016).

## **Methodology**

Due to the broad scope of this review, encompassing multiple aspects of medicine, a flexible, topic-guided narrative search strategy was applied. The literature search was conducted primarily using the PubMed database, due to its comprehensive biomedical coverage. Search terms were adapted to each subsection of the review and consisted of combinations of the term “caffeine” with topic-specific keywords (e.g., “caffeine angiogenesis,” “caffeine anesthesia”). In addition to database searches, manual screening of reference lists of relevant articles (backward snowballing) was performed to identify further publications. Forward snowballing was also applied through manual screening of more recent studies citing the selected articles. This approach enabled the inclusion of relevant literature that may not have been captured in the initial search. Given the narrative nature of the review, not all search steps were systematically recorded, and exact numbers of identified, screened, and included records were not documented.

Studies were included if they addressed the influence of caffeine on surgery-related mechanisms or procedures. Additional inclusion criteria were publication in the English language and availability of full-text articles. Although priority was given to studies published within the last five years, older publications were included when more recent evidence was lacking. Articles were excluded if they were not published in English, were unavailable in full text, or were unrelated to caffeine and surgery. Various types of publications were considered, including original research articles, reviews, and meta-analyses.

## **Anesthesia**

### **Withdrawal symptoms**

Caffeine is consumed daily by the majority of the population, with nearly 80-90% of adults in the United States reporting regular intake (Pleticha et al., 2021). Common withdrawal symptoms may occur within 24 hours of abstinence and include: headache, fatigue, difficulty concentrating, irritability, muscle pain, decreased energy, and depressed mood (Davoudi et al., 2025). On the day of surgery, patients undergoing general anesthesia are required to fast, and following the procedure they frequently experience common side effects such as nausea and vomiting. This combination may contribute to the occurrence of caffeine withdrawal symptoms in individuals who consume caffeine regularly. Caffeine supplementation has been shown to reduce the incidence of caffeine-withdrawal headaches in the perioperative period and should be considered as an addition to Enhanced Recovery After Surgery (ERAS) protocols (Pleticha et al., 2021).

### **Postoperative pain**

Caffeine is widely recognized as an adjuvant to analgesic drugs due to its ability to enhance their pain-relieving effects. Research has demonstrated that when combined with commonly used analgesics such as paracetamol, ibuprofen, or aspirin, caffeine increases analgesic efficacy, resulting in faster and more pronounced pain relief. The pain conditions most frequently investigated include postoperative dental pain, postpartum pain, and headache. In these studies, caffeine was typically administered at doses of 100 mg or higher, yielding a modest but statistically significant benefit (Derry et al., 2014).

The observed synergistic effect is believed to arise from caffeine’s antagonism of adenosine receptors, its vasoconstrictive properties, and its stimulatory action on the central nervous system, all of which may contribute to enhanced pain modulation. As a result, caffeine is commonly incorporated into over-the-counter analgesic formulations, particularly those indicated for the treatment of headaches, migraines, and menstrual pain (Malviya et al., 2023).

More recent evidence suggests that caffeine may potentiate not only over-the-counter analgesics but also agents higher in the analgesic ladder, including opioids. Among patients with fibromyalgia treated with opioids, caffeine consumption was associated with lower pain intensity, reduced pain catastrophizing, and improved physical function compared with non-users. In contrast, among patients not receiving opioid therapy, caffeine intake was associated solely with improved physical function, without a significant effect on pain intensity (Scott et al., 2017). This is a valuable information, as it could potentially lower the required dose of opioids necessary to reduce postoperative pain.

### **Sedation**

Another clinically relevant interaction involves caffeine and sedative drugs. In contemporary anaesthetic practice, recovery from general anaesthesia relies primarily on the passive elimination of anaesthetic agents after their discontinuation, as no pharmacological agent has yet been proven effective for the active reversal of general anaesthesia (Malviya et al., 2023). Emerging evidence, largely derived from animal studies, indicates that caffeine may accelerate recovery from anaesthetic agents such as isoflurane and propofol (Fong et al., 2017; Fox et al., 2020; Q. Wang et al., 2014)

Human data on this topic remain limited, although several clinical studies have been conducted. One study reported an increase in the Richmond Agitation–Sedation Scale (RASS) score following caffeine administration during anaesthesia recovery; however, the absence of a control group limits the interpretability of these findings (Warner et al., 2018). In another observational study, caffeine administration in the post-anaesthetic period was associated with improved sedation scores, but also with an increased incidence of respiratory complications, likely reflecting selection bias, as caffeine may have been preferentially administered to higher-risk patients (Deljou et al., 2024). In contrast, a randomized controlled trial in children undergoing inguinal herniorrhaphy demonstrated no acceleration of emergence from general anaesthesia following administration of caffeine at a dose of 10 mg/kg. Importantly, caffeine did not increase heart rate or blood pressure, and no significant adverse effects were observed in the paediatric population (Emami S et al., 2022). Interestingly, findings from an additional observational study suggest that high habitual caffeine intake is associated with lower propofol requirements for anaesthetic induction. This effect may be attributable to reduced baseline arousal related to perioperative caffeine withdrawal on the day of surgery (O'Connor et al., 2023).

### **Cardiovascular and perioperative risk**

Caffeine exerts multiple physiological effects on the cardiovascular system. Through its action on the autonomic nervous system and vascular tone, caffeine may influence blood pressure, heart rate, and overall cardiovascular function, making its impact on cardiovascular health a subject of ongoing scientific interest (Abbas-Hashemi et al., 2023). Nevertheless, the extent of these effects varies depending on habitual caffeine consumption, as regular users tend to develop a degree of physiological tolerance within a week of daily intake (Van Dam et al., 2020).

### **Blood pressure**

Hypertension is the most important modifiable risk factor for cardiovascular morbidity and mortality worldwide. Sustained elevation of arterial blood pressure leads to structural and functional changes in the vascular system, including endothelial dysfunction, arterial stiffness, and accelerated atherosclerosis. As a consequence, hypertension significantly increases the risk of coronary artery disease, myocardial infarction, heart failure, and sudden cardiac death. Moreover, hypertension is a major contributor to cerebrovascular disease, markedly increasing the incidence of ischemic and hemorrhagic stroke, as well as vascular cognitive impairment. Long-standing hypertension also adversely affects other organ systems, including the kidneys and peripheral vasculature, further amplifying overall cardiovascular risk (Fuchs & Whelton, 2020).

Caffeine may acutely elevate blood pressure shortly after consumption. In available meta-analyses, most articles showed the acute increase in BP following caffeine consumption (Abbas-Hashemi et al., 2023; Mesas et al., 2011; Turnbull et al., 2017), while others showed tolerance in habitual consumers and no increase in BP. Few of the studies noted even the decrease in BP (Turnbull et al., 2017). The relationship between caffeine intake and sustained elevations in blood pressure requires further investigation.

Significantly elevated blood pressure is one of the potential reasons for postponing a surgical procedure. Severe hypertension may increase postoperative 30-day mortality by predisposing patients to cardiovascular complications such as myocardial ischemia, arrhythmias, or stroke. Uncontrolled blood pressure can also compromise intraoperative hemodynamic stability and impair postoperative recovery. Therefore, adequate preoperative assessment and optimization of blood pressure are essential to ensure patient safety and reduce the likelihood of adverse outcomes. The articles mentioning that issue do not determine the clear thresholds for a definite deferral of procedure. ACC/AHA and AAGBI/BHS Guidelines only suggest that patients with SBP more than 180mmHg and DBP more than 110 mmHg may be postponed, however this statement seems to be driven mostly by experts opinion and not randomized studies. On the other hand, SBP exceeding 180mmHg together with DBP exceeding 120mmHg are defined as hypertensive emergency, therefore postponing the elective procedure and admitting the patient for immediate inpatient management of hypertension seems as most reasonable option (Asher & Avery, 2018; Sanders et al., 2019).

### **Cardiovascular diseases**

Cardiovascular disease and elevated cardiovascular risk are major determinants of perioperative mortality in patients undergoing any surgical procedure, with 30-days mortality estimated at around 1-2% in adults over 45 years. Conditions such as hypertension, coronary artery disease, and heart failure reduce cardiovascular reserve and limit the ability to respond to the hemodynamic stress associated with anesthesia and surgical trauma. Perioperative sympathetic activation, fluid shifts, and blood loss may precipitate myocardial ischemia, arrhythmias, or acute heart failure, particularly in patients with pre-existing cardiovascular disease. Consequently, individuals with an elevated cardiovascular risk profile have a higher incidence of major adverse cardiovascular events and worse postoperative outcomes, highlighting the importance of appropriate preoperative cardiovascular risk assessment (Farooq et al., 2025).

Two meta-analyses examining the association between long-term caffeine consumption and the risk of cardiovascular disease (CVD) found no increase in CVD risk among habitual caffeine consumers. These analyses included multiple large cohort studies with follow-up periods ranging from 3 to 28 years. Notably, up to half of the included studies reported a reduction in cardiovascular risk in individuals with regular caffeine intake. Even high consumption levels, exceeding 600 mg per day, were not associated with an increased overall risk of CVD. However, it is important to note that in most of the analyzed studies, coffee was the primary source of caffeine. This raises the question of whether the observed effects can be attributed solely to caffeine itself or whether other bioactive compounds present in coffee, such as polyphenols and antioxidants, may confer additional cardiovascular benefits and contribute to the observed reduction in CVD risk (Ding et al., 2014; Turnbull et al., 2017).

### **Wound healing**

Tissue healing is a complex physiological process aimed at restoring the integrity and function of the skin after injury, whether resulting from trauma or surgical intervention. It proceeds in a dynamic manner through successive but overlapping phases, including hemostasis and inflammation, proliferation, and remodeling. Proper coordination of cellular and molecular events within each phase is essential for effective tissue repair, whereas disruption of these mechanisms may lead to abnormal healing, such as hypertrophic scarring, keloid formation, or the development of chronic wounds (P.-H. Wang et al., 2018).

### **Antioxidant and anti-inflammatory action**

Caffeine exhibits potential antioxidant activity, but its effects strongly depend on both the dose and the source from which it is consumed. Beverages and products containing caffeine—such as coffee, tea, or energy drinks—also include additional compounds that may either enhance or weaken this effect. Polyphenols naturally present in coffee and tea often contribute to antioxidant capacity, whereas sugars and sweeteners commonly added to commercial caffeinated drinks may diminish it. Overall, current evidence remains mixed, and caffeine cannot be universally classified as a straightforward dietary antioxidant without considering these contextual factors (Ósz et al., 2022).

The mechanisms underlying the antioxidant effects of pure caffeine are complex and depend on whether its intake is habitual or acute. They involve the blockade of adenosine receptors as well as the modulation of intricate intracellular pathways. In several disease contexts, caffeine demonstrates antioxidative activity by preventing cellular changes induced by oxidative stress (OS) and reactive oxygen species (ROS). Caffeine consumption has been associated with a reduced risk of liver and kidney fibrosis (Han et al., 2025; Nilnumkhum et al., 2019), as well as neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease (Kolahdouzan & Hamadeh, 2017). In one study that directly measured intracellular ROS levels in fibroblasts, hypoxic conditions significantly increased ROS, whereas treatment with 6.25 mM caffeine restored ROS levels to baseline (Nilnumkhum et al., 2019). In another study oxidation stress and cellular senescence were induced in vitro in altered skin cells and normal human epidermal keratinocytes (NHEKs) and in vivo in mouse skin tissues. In all of them, caffeine reduced ROS levels by activating autophagy process (Y.-F. Li et al., 2018).

Oxidative stress is closely interconnected with the inflammatory response. Reactive oxygen species (ROS) activate intracellular signaling pathways and modulate gene expression, driving inflammatory cells to produce additional cytokines and chemokines. In turn, these cells generate even more ROS at the injury site, creating a self-perpetuating cycle [17]. Chronic caffeine intake has been shown to reduce pro-inflammatory mediators such as tumor necrosis factor-alpha (TNF- $\alpha$ ), nitric oxide (NO), and prostaglandin E2 (PGE2) (Ruggiero et al., 2022). Moreover, in a study conducted on trained rats, caffeine was shown to modulate inflammatory markers. Specifically, plasma myeloperoxidase (MPO) and acetylcholinesterase (AChE) activities were significantly reduced, highlighting the anti-inflammatory effect of caffeine (R. Barcelos et al., 2014).

### **Angiogenesis**

Research on the influence of caffeine on angiogenesis remains inconclusive. While the majority of available literature suggests that caffeine inhibits angiogenesis, few studies have reported opposing effects.

In studies on zebrafish embryos, caffeine (concentrations 100 and 150 mg/L in first study; 250 and 300 mg/L in second) treatment caused shortening and thinning of intersegmental vessels, and defects in dorsal longitudinal anastomotic vessels and subintestinal vein sprouting. Moreover, molecular findings include decreased expression of the vascular marker genes. Caffeine was also able to block angiogenesis induced by exogenous Fibroblast Growth Factor 2 or FGF2-producing cells (Basnet et al., 2021; Yeh et al., 2012). Another research studying caffeine impact on angiogenesis in the chick chorioallantoic membrane showed similar results. The number of new blood vessel branches was dose-dependently reduced by caffeine. Compared to the controls, relative lengths of branches were 84.7%, 66.6%, and 61.2% after caffeine treatment at 250, 500, and 1,000  $\mu$ M respectively, after 48 hours (H. Li et al., 2013). Additionally, a study on colon cancer cells demonstrated inhibition of angiogenesis-related proteins following caffeine treatment. However, in this context, the observed effect is considered favorable, as suppression of angiogenesis is a desired outcome in cancer cells (Merighi et al., 2007).

On the other hand, a study investigating the effects of physiological concentrations of caffeine on human umbilical vein endothelial cells (HUVECs) reported opposite findings. Caffeine at a concentration of 50  $\mu$ M enhanced angiogenesis and promoted endothelial cell migration (L. Wang et al., 2021). Another study demonstrating promising results examined the influence of caffeine on hyperoxia-induced lung injury in mice. Notably, male mice showed significant attenuation of lung injury after four days of caffeine administration at a dose of 20 mg/kg/day compared with hyperoxia-exposed mice that did not receive caffeine. Caffeine influenced angiogenic genes expression. Histopathology revealed an increase in vessel surface area and a significant reduction in smooth muscle thickness of the pulmonary arterioles which suggest a beneficial effect of caffeine on vascular remodeling in hyperoxia (Dumpa et al., 2019). Additionally, in a study examining the effects of caffeinating the bone xenograft in mandibular defects in dogs, a 1.5% caffeinated xenograft demonstrated greater vascularization compared with no graft, normal xenograft, and 3% caffeinated xenograft (Samieirad et al., 2020).

### **Fibroblasts**

Fibroblasts play a key role in tissue healing by orchestrating extracellular matrix deposition and providing structural support for regenerating tissue. During the proliferative phase, fibroblasts migrate into the wound site and synthesize key matrix components which form the scaffold for tissue repair. They also contribute to wound contraction and interact with inflammatory and endothelial cells through paracrine signaling (Jiang et al., 2023). In studies on cell cultures, caffeine inhibited the fibroblasts proliferation (Alao & Sunnerhagen, 2009; Levi-Schaffer & Touitou, 1991)

### **Collagen**

Collagen plays a crucial role in wound healing by providing structural support and tensile strength to regenerating tissue. During the proliferative phase, fibroblasts synthesize collagen to form the extracellular matrix scaffold necessary for cell migration and tissue repair. Proper collagen deposition and subsequent remodeling are essential for restoring tissue integrity and achieving functional wound closure (Gardeazabal & Izeta, 2024). Study investigating influence of 1, 2, and 5 mM caffeine on human cultured skin fibroblasts showed that caffeine reduces collagen synthesis (Przylipek et al., 2014). On the other hand, another study on rats examined the effects of caffeine consumption on healing of the autologous full-thickness skin graft (FTSG). The square-shaped grafts were implanted in the donor site, with rotated corners. After 7 days post-transplantation FTSGs explanted for evaluation. The caffeinated groups in various doses showed increased collagen synthesis, compared to control group (Supit et al., 2021).

Studies investigating caffeine impact on specific phases and aspects of wound healing process are not unilateral. However one research directly studying the influence of caffeine on human tissue regeneration reached the definitive conclusion. Using primary human keratinocytes, the HaCaT cell line, and an ex vivo human skin model, the researchers assessed how various concentrations of caffeine affected epithelialisation. Their results showed that caffeine suppressed cell proliferation, delayed cell migration, and inhibited epithelialisation and wound closure. It did not, however, influence cellular differentiation, adhesion, or spreading (Ojeh et al., 2016).

### **Sleep and recovery**

Caffeine consumption is closely associated with the regulation of the circadian rhythm and sleep–wake cycles. Its psychostimulant properties are widely sought after and constitute one of the primary reasons for its widespread use. While these effects are beneficial during daytime hours, caffeine intake in the evening or nighttime may exert adverse effects on sleep. Specifically, caffeine consumption has been shown to impair multiple sleep parameters, including total sleep time, sleep onset latency, wake after sleep onset, sleep efficiency, and sleep architecture. The magnitude of total sleep time reduction is influenced by both the dose of caffeine and the timing of its ingestion relative to bedtime. Notably, higher doses consumed closer to bedtime are associated with more substantial reductions in total sleep time. Consequently, late-day caffeine intake may contribute to a self-perpetuating cycle of sleep disruption, leading to increased caffeine consumption and subsequent sleep deprivation (Gardiner et al., 2023; Reichert et al., 2022).

Sleep quality is particularly important in the postoperative period, as it influences multiple aspects of recovery and numerous physiological functions. Sleep deprivation is associated with sympathetic nervous system activation and may consequently lead to increased blood pressure, exacerbation of obstructive sleep apnea, and the development of atrial fibrillation. In addition, sleep loss constitutes a risk factor for postoperative delirium and elevated anxiety levels. Preoperative sleep disturbances may further contribute to increased postoperative pain, with sleep disruption and pain reinforcing each other in a vicious, self-perpetuating cycle. Moreover, sleep restriction increases the risk of falls, potentially resulting in additional injuries and fractures. Sleep disturbances are also linked to pro-inflammatory changes, which may reduce resistance to surgical site infections. Collectively, these factors may not only prolong hospital stay but also delay and extend the overall recovery (Hillman, 2021; Sipilä & Kalso, 2021).

### **Cortisol**

Cortisol, the primary effector hormone of the hypothalamic–pituitary–adrenal axis, plays a central role in the physiological response to stress, including surgical trauma. Chronic sustained elevation of cortisol levels exerts immunosuppressive and catabolic effects that may adversely affect postoperative wound healing and overall tissue regeneration (Jozic et al., 2017). Cortisol inhibits fibroblast proliferation, collagen synthesis, angiogenesis, and keratinocyte migration, while attenuating the inflammatory response required for the early phases of tissue repair (Saito et al., 1997; A. S. Wang et al., 2013). In addition, excessive cortisol promotes protein catabolism, impairs muscle regeneration, alters glucose metabolism, and suppresses anabolic pathways essential for systemic recovery after injury or surgery (Simsek et al., 2014). Consequently, prolonged or excessive activation of the stress response may lead to delayed wound healing, increased susceptibility to infection, impaired scar quality, reduced functional recovery, and prolonged convalescence following surgical procedures (Ebrecht et al., 2004; A. S. Wang et al., 2013)

One of the main challenges in studying cortisol levels is its pronounced circadian rhythm, which makes a single measurement insufficient to accurately reflect overall cortisol exposure in the body. More reliable assessments require repeated measurements taken at different times of the day. Another important consideration is that cortisol secretion is primarily stimulated by physical or psychological stress; therefore, under non-stressful conditions, caffeine is likely to exert only a minimal effect. Consequently, most studies are designed to evaluate the impact of caffeine on cortisol levels during physical exercise or mental stress, where caffeine acts as a modulator or amplifier of the cortisol response.

That being said, although most available studies report some degree of cortisol elevation following caffeine consumption (Beaven et al., 2008; Gür et al., 2024; Lovallo et al., 2006), one study demonstrated increased cortisol levels only in habitual users, but not after acute intake (Cole et al., 2024). Conversely, other studies have shown that regular daily caffeine consumption leads to partial, but not complete, tolerance to cortisol elevation (Gavrieli et al., 2011; Lovallo et al., 2005). Moreover, at least one study found no significant difference in cortisol levels between the placebo group and the caffeine group receiving 450 mg/day administered in three divided doses (Weibel et al., 2020).

## **Complications**

### **Obesity**

Excess adipose tissue is associated with chronic low-grade inflammation, metabolic dysregulation, and impaired immune function, which may adversely affect wound healing and postoperative recovery. In surgical patients, obesity has been linked to increased operative complexity, longer operative times, higher rates of surgical site infections, wound dehiscence, and other postoperative complications. Additionally, obesity can complicate perioperative management, including anesthesia, airway control, and postoperative mobilization, thereby contributing to prolonged hospital stay and increased healthcare costs. As a result, obesity represents an important patient-related factor that should be considered in preoperative risk stratification and perioperative optimization (Pierpont et al., 2014; Thelwall et al., 2015)

Although some clinical trials and meta-analyses suggest that caffeine intake may be associated with modest reductions in weight, BMI, and fat mass, the evidence remains limited and heterogeneous. Proposed mechanisms include increased energy expenditure, enhanced fat oxidation, and appetite suppression, but these have not been conclusively established in long-term randomized studies, and effects may vary depending on individual metabolic and lifestyle factors (Tabrizi et al., 2019; M. Wang et al., 2025).

### **Surgeons performance**

Caffeine can influence surgical outcomes not only by affecting patients, but also the surgeons performing the procedures. On the one hand, caffeine may help reduce fatigue and sleepiness, thereby limiting the number of potential errors. Fatigue is known to impair attention, memory, and decision-making, as well as reduce manual dexterity and prolong operative time. Evidence confirms that sleep deprivation compromises surgical performance, with simulator-based studies reporting reductions in technical skills of up to 32%. Although caffeine provides only symptomatic relief, in working conditions such as 24-hour shifts it is impossible to remain fully rested throughout the entire duty period. In this context, caffeine may be preferable to no intervention at all, as it can partially alleviate sleepiness (Le et al., 2025).

On the other hand, as a central nervous system stimulant, caffeine may also affect psychomotor performance. While moderate doses can shorten the time required to complete motor tasks, higher doses may impair manual dexterity, making it difficult to identify an intake level that is entirely beneficial without causing adverse effects. The negative impact of caffeine on dexterity appears to be dose-dependent: an intake of approximately 2.5 mg/kg may induce fine hand tremor, whereas doses around 5 mg/kg are associated with a measurable deterioration in manual precision. These effects may be partially attenuated by the development of tolerance. Precise, tremor-free movements are particularly critical in fields such as neurosurgery and microsurgery, where even minimal inaccuracies may lead to severe complications. This raises the question of whether caffeine-induced tremor translates into a clinically relevant increase in surgical error rates or a reduction in accuracy (Parry et al., 2023).

The available evidence addressing this issue remains inconclusive. Simulator-based studies assessing task completion time and accuracy in surgeons have shown that, in sleep-deprived individuals, caffeine consumption reduced task completion time without reducing error rates (Aggarwal et al., 2011). In contrast, one meta-analysis reported a negative effect of caffeine on surgical dexterity in well-rested surgeons (Fargen et al., 2016). Other study, however, found no significant differences between caffeine and placebo groups, suggesting that caffeine intake did not adversely affect precision (Gerdes et al., 2022). Conversely, another meta-analysis concluded that caffeine may exert a positive effect on overall surgical performance (Belykh et al., 2018).

## **Conclusions**

Based on the available evidence, no clear or uniform recommendations can currently be formulated regarding caffeine consumption by surgical patients. The effects of caffeine are multifaceted and involve numerous physiological systems, resulting in both potentially beneficial and adverse outcomes. Furthermore, the existing literature is heterogeneous and frequently yields inconsistent or inconclusive findings, which limits the ability to draw definitive clinical conclusions. Consequently, caffeine use should be considered on an individual basis, taking into account patient characteristics and comorbidities.

Similarly, the impact of caffeine consumption among surgeons and other perioperative healthcare professionals remains complex and insufficiently defined. While caffeine may help mitigate fatigue and enhance alertness during prolonged or demanding procedures, it may also negatively affect fine motor control

and precision. The current body of evidence addressing these effects is limited and inconclusive, precluding firm recommendations.

Overall, further well-designed, prospective, and controlled studies are required to better elucidate the role of caffeine in the perioperative setting, both for patients and surgical staff, and to establish evidence-based guidelines regarding its safe and effective use.

#### Limitations

This study, although carefully designed, has several limitations. First, the available literature is not uniformly extensive across all of the topics discussed, and in certain areas high-quality studies with a high level of evidence are lacking, thereby limiting the strength of the conclusions and highlighting the need for further research. In addition, only articles published in the English language were included, which may have resulted in the exclusion of relevant studies published in other languages and introduced language bias. Another limitation is the heterogeneity of the included studies with respect to study design, patient populations, caffeine dosing, and outcome measures, which precludes direct comparisons and limits the ability to draw definitive conclusions.

**Conflicts of Interest:** No conflicts of interest to declare.

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