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REVIEW

Preoperative Anxiety and Postoperative Delirium: A Mini Review of the Association, Mechanisms, and Preventive Strategies

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Abstract: Preoperative anxiety, a common perioperative psychological state characterized by restlessness and somatic symptoms, has been reported to affect a broad range of adult surgical patients, with prevalence estimates ranging from approximately 11% to 80% across observational studies, and affects a similar proportion of pediatric patients, with one cross-sectional study reporting an incidence of around 67.6% in Chinese children undergoing elective surgery. Mounting evidence suggests that preoperative anxiety may be a potential contributing factor to postoperative delirium (POD), an acute cognitive disturbance associated with poor prognosis, increased mortality, and elevated healthcare costs. This mini-review synthesizes the role of preoperative anxiety in predicting POD, highlighting its significance in identifying high-risk populations. This mini-review aims to synthesize current evidence on the impact of preoperative anxiety on POD, clarify underlying pathophysiological mechanisms, and summarize recent pharmacological and non-pharmacological preventive strategies. Mechanistically, preoperative anxiety contributes to POD via systemic and neuroinflammatory responses, blood-brain barrier disruption, postoperative pain amplification, and oxidative stress. Pharmacological interventions (eg, dexmedetomidine, ketamine in pediatric patients) and non-pharmacological strategies (eg, music therapy, virtual reality-based cognitive-behavioral interventions) effectively alleviate preoperative anxiety and reduce POD incidence. Despite progress, the mechanisms linking preoperative anxiety to POD remain incompletely understood, particularly the roles of neuroinflammatory pathways, blood–brain barrier disruption, and the comparative effectiveness of pharmacological versus non-pharmacological interventions. Targeted research in these areas is needed to optimize preventive strategies and improve surgical outcomes.

Keywords: delirium, postoperative cognitive complications, perioperative care, preoperative anxiety, preventive strategies, surgery

Introduction

Preoperative anxiety is defined as a state of restlessness or tension caused by concerns about illness, hospitalization, anesthesia, surgery, or unexplained worries, often accompanied by somatic manifestations such as palpitations, dyspnea, diaphoresis, frequent urination, abdominal pain, diarrhea, or sleep disturbances. Epidemiological studies indicate that preoperative anxiety is highly prevalent across surgical populations, affecting approximately 11%–80% of adult patients,[1] with consistently higher rates observed in females than in males. In pediatric populations, the prevalence is similarly high; notably, studies in Chinese children report a prevalence of approximately 67.6%, comparable to rates observed internationally.[2,3]

The State-Trait Anxiety Inventory (STAI) is widely recognized as the gold standard for assessing preoperative anxiety, as it effectively captures patients' subjective experiences and distinguishes between state and trait anxiety, with higher scores indicating greater anxiety severity.[4] In addition to the STAI, several other instruments are commonly used to assess preoperative anxiety across different populations, including the Hamilton Anxiety Scale (HAM-A) for evaluating psychological and somatic symptoms in adults, the Hospital Anxiety and Depression Scale (HADS), which is suitable for hospital settings and distinguishes anxiety from depression, and the Modified Yale Preoperative Anxiety Scale (m-YPAS), an observational tool specifically designed for pediatric patients.[5–7] Although each instrument has inherent strengths and

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limitations, their combined use facilitates a more comprehensive assessment of preoperative anxiety and enables meaningful comparisons across studies. Importantly, anxiety can be conceptualized as either a state or a trait. State anxiety reflects a transient, situational response to imminent stressors such as surgery or hospitalization, making it a key target for preoperative interventions, whereas trait anxiety represents a stable personality characteristic that predisposes individuals to heightened stress responses across contexts.[8] Recognizing this distinction is clinically relevant, as it helps identify patients most likely to benefit from interventions aimed at reducing short-term, situational anxiety.

Excessive preoperative anxiety has been associated with increased perioperative complications, including intraoperative hemodynamic instability, increased anesthetic consumption, postoperative pain, nausea, vomiting, and delirium, thereby significantly impacting patient outcomes and prognosis.[9,10] The pathogenesis of postoperative delirium (POD) and post-operative cognitive decline (POCD) is complex and multifactorial, involving surgery-, anesthesia-, and patient-related risk factors, with inflammatory responses induced by surgery being one of the most promising directions. Notably, Glumac et al[11] reported that preoperative corticosteroid administration attenuates the surgical inflammatory response and consequently decreases the incidence and severity of cognitive deterioration, further highlighting the role of inflammation in POD.

POD refers to acute and fluctuating disturbances in attention and consciousness following surgery, representing a common surgical complication and a marker of poor prognosis. It can result in cognitive decline, increased mortality, and elevated healthcare costs,[12] highlighting the urgent need for effective interventions to prevent its occurrence. Preoperative anxiety is prevalent, affecting approximately 25%-80% of surgical patients,[13] and has been identified as a potential contributing factor for POD.[9] However, evidence regarding this association remains inconsistent. While some earlier studies reported weak or non-significant correlations,[14] more recent prospective investigations in orthopedic and hip arthroplasty populations have shown significant positive associations between preoperative anxiety and POD risk.[2,9] These discrepancies may be attributable to differences in study design, patient populations, anxiety assessment tools, or POD diagnostic criteria, underscoring the need for a comprehensive synthesis of current evidence.

Delirium is a form of cognitive impairment characterized by acute reductions in cognitive ability, inattention, clouded consciousness, and perceptual abnormalities.[9] Preoperative anxiety serves as a potential contributing factor for POD in elderly patients undergoing elective orthopedic surgery and a strong predictor of POD in patients undergoing tumor resection.[9] Furthermore, in cancer patients undergoing tumor resection, preoperative anxiety has been shown to significantly predict the onset of delirium.[10] Although the strength of association varies between populations and study designs, these findings collectively suggest that addressing preoperative anxiety may be a meaningful target for preventive interventions aimed at reducing the incidence of POD.[15]

Despite growing evidence linking preoperative anxiety to POD, findings remain inconsistent due to variations in patient populations, surgical types, anxiety assessment tools, and POD diagnostic criteria. Furthermore, the underlying pathophysiological mechanisms are not fully understood, and comprehensive guidance on effective multimodal preventive interventions is lacking. Therefore, the primary objective of this review is to consolidate and critically synthesize current evidence on the relationship between preoperative anxiety and POD. Specifically, it aims to clarify the impact of preoperative anxiety on the incidence and severity of POD, elucidate underlying pathophysiological mechanisms—including neuroinflammatory pathways, hypothalamic-pituitary-adrenal axis dysregulation, blood-brain barrier disruption, and oxidative stress—and summarize the latest advances in preventive strategies, both pharmacological and non-pharmacological. By providing this synthesis, our review contributes a focused and updated perspective, facilitating the development of targeted interventions to reduce preoperative anxiety and the associated burden of POD.

Methods

This mini-review was based on a focused literature search to summarize evidence on the association between preoperative anxiety and POD. PubMed, Web of Science, and Embase were searched for articles published up to October 2025. The search strategy applied was ("preoperative anxiety" OR "preoperative stress" OR "preoperative nervousness") AND ("postoperative delirium" OR "POD" OR "postoperative cognitive complications"). Reference lists of relevant articles and reviews were also manually screened to identify additional studies. Both human clinical studies and experimental studies providing mechanistic insights were considered. Study selection was performed in two stages, with initial screening of titles and abstracts followed by full-text review based on predefined inclusion criteria. A total of 65 studies were ultimately included. The search and screening were independently conducted by Q.W., G.D., and Y.L., and the final selection of included studies was approved by Q.W.

Prediction of POD by Preoperative Anxiety

With the biopsychosocial model gradually replacing the traditional biomedical model, the relationship between patients' mental and psychological factors and diseases has attracted increasing clinical attention. As one of the mental and psychological factors influencing POD, preoperative anxiety reflects a temporary and acute anxiety response. Patients often experience tension and worry before surgery, which can significantly reduce their intraoperative physiological state below the optimal level, potentially leading to a series of adverse postoperative consequences. Preoperative anxiety not only affects the dosage of anesthetic drugs, the intensity of postoperative pain, and the demand for postoperative opioid drugs but also increases the incidence of complications such as postoperative nausea and vomiting and mortality in certain types of surgeries.[16–18]

Since preoperative anxiety can be improved through preoperative interventions, it can be used for the identification of high-risk populations for POD and the formulation of POD prevention methods. In 1987, Simpson et al reported that there was no correlation between preoperative anxiety and POD.[19] Subsequently, Van Grootven et al[20] also demonstrated no association between preoperative anxiety and POD. These earlier findings may have been influenced by limitations such as small sample sizes, heterogeneity in patient populations, the use of less sensitive anxiety assessment tools, or varying criteria for POD diagnosis.[15] However, in 2019, Wada et al[10] showed that age and a score >7 on the Anxiety subscale of the HADS-A were predictive factors for the occurrence of delirium. Ma et al[2] reported that the incidence of POD in patients undergoing total hip arthroplasty was 19.6%. All participants were divided into an anxiety group (HADS-A ≥7) and a non-anxiety group (HADS-A <7) based on HADS-A scores. Compared with patients in the non-anxiety group, those in the anxiety group had a significantly higher incidence of POD (25.3% vs 14.8%, OR=0.51, 95% CI 0.29–0.92) and a significantly prolonged hospital stay. These results suggest that preoperative anxiety may be one of the causes of POD and can lead to prolonged surgical recovery time and hospital stay. Elevated levels can serve as evidence of blood-brain barrier (BBB) impairment. Lopez et al[21] indicated that increased postoperative plasma S100β concentration was independently associated with POD. Taken together, these contradictory findings suggest that methodological differences and patient characteristics may account for inconsistencies in reported associations,[22] highlighting the need for standardized assessment approaches and further large-scale prospective studies.

Ren et al[9] found through a study of 263 elderly patients undergoing elective orthopedic surgery that preoperative anxiety was independently associated with POD. Ali et al[23] demonstrated a significant association between preoperative anxiety in children and postoperative emergence delirium; for each 1-point increase in the Modified Yale Preoperative Anxiety Scale score, the incidence of delirium increased by 1.23 times (OR=1.23, 95% CI 1.16–1.29). Ling et al[24] showed that the preoperative Hamilton Anxiety Scale score was an independent predictor of POD (OR=2.12, 95% CI 1.28–3.50), and the nomogram prediction model established by them exhibited good clinical predictive ability (AUC=0.74, 95% CI 0.66–0.83). These studies all suggest that there is a significant correlation between preoperative anxiety and POD; preoperative anxiety can serve as a predictive factor for POD, providing new ideas for the clinical prevention and treatment of POD (Table 1).

Mechanisms Underlying Preoperative Anxiety-Induced POD

Systemic Inflammatory Response and Neuroinflammation

Systemic inflammation is widely recognized as a central mechanism in the pathogenesis of POD.[25] Emerging evidence suggests that preoperative anxiety may be associated with POD through indirect modulation of inflammatory responses rather than through a direct causal pathway.[26] Preoperative anxiety activates the hypothalamic-pituitary-adrenal (HPA) axis, triggering excessive glucocorticoid release, which amplifies the inflammatory cascade initiated by surgery or tissue injury. Notably, older adults exhibit immunosenescence and a baseline proinflammatory state ("inflammaging"), which may render them more susceptible to anxiety-induced amplification of perioperative inflammatory responses, particularly

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Table 1 Summary of Studies Investigating the Predictive Role of Preoperative Anxiety on POD

Study	Population	Anxiety Assessment Tool	Key Findings	Effect on POD	References
Simpson et al, 1987	Adult surgical patients	Not specified	No significant correlation between preoperative anxiety and POD	None	[19]
Van Grootven et al, 2015	Adult surgical patients	Not specified	No significant association	None	[20]
Wada et al, 2019	Cancer patients	HADS-A	Age and HADS-A >7 predictive of delirium	Preoperative anxiety predicted increased POD risk	[10]
Ma et al, 2021	Total hip arthroplasty	HADS-A	Anxiety group (HADS-A ≥7) had higher POD incidence (25.3% vs 14.8%)	Higher incidence of POD and prolonged hospital stay	[2]
Ren et al, 2021	Elderly elective orthopedic patients (n=263)	Not specified	Preoperative anxiety independently associated with POD	Preoperative anxiety independently increased POD risk	[9]
Ali et al, 2022	Pediatric surgical patients	m-YPAS	Each 1-point increase in anxiety score increased delirium incidence 1.23-fold	Preoperative anxiety associated with higher risk of postoperative emergence delirium	[23]
Ling et al, 2022	Adult surgical patients	Hamilton Anxiety Scale	Anxiety score independently predicted POD (OR=2.12, 95% CI 1.28–3.50)	Preoperative anxiety predicted POD occurrence; predictive model validated	[24]

Abbreviations: POD, postoperative delirium; HADS-A, Hospital Anxiety and Depression Scale–Anxiety subscale; m-YPAS, Modified Yale Preoperative Anxiety Scale.

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after major orthopedic or cardiac surgeries.[27] Peripheral inflammatory cytokines infiltrate the central nervous system (CNS) and interact with microglia, precipitating neuroinflammation that contributes to POD.

Chronic stress and preoperative anxiety activate the HPA axis, leading to sustained elevations in circulating glucocorticoids and disrupted glucocorticoid receptor (GR) signaling in brain regions involved in stress regulation. Rodent studies have demonstrated that chronic glucocorticoid exposure and repeated stress paradigms lead to increased HPA axis activity, elevated glucocorticoid levels, and associated impairments in GR function, which may contribute to enhanced proinflammatory signaling and neuroinflammation in anxiety-related conditions.[28] This dysregulation may be more pronounced in elderly patients or in surgeries associated with extensive tissue trauma, where stress responses and inflammatory burdens are greater.[29]

Elevated circulating inflammatory mediators correlate with POD progression. Liu et al[30] reported significantly higher serum levels of TNF-α, IL-1β, and IL-6 in POD patients compared to non-POD counterparts. Additionally, POD patients show increased IL-8 concentrations in preoperative and immediate postoperative plasma and whole blood samples,[31] while elevated preoperative monocyte chemoattractant protein-1 (MCP-1) is independently associated with POD.[32] These inflammatory markers have been reported to rise more markedly following high-risk procedures, such as hip fracture repair or major abdominal surgery, suggesting that surgical type may modulate the inflammatory contribution to POD.[33]

Blood-Brain Barrier Impairment

Increasing evidence indicates that blood–brain barrier (BBB) dysfunction is involved in the development of POD;[34] however, the role of preoperative anxiety in directly inducing BBB impairment remains incompletely defined.[26] Anxiety- and depressive-like behaviors have been shown to alter BBB permeability in experimental models, which may facilitate peripheral-to-central inflammatory signaling and contribute to delirium vulnerability.[35] S100β, a calcium-binding protein primarily expressed by astrocytes, leaks into the bloodstream and cerebrospinal fluid when BBB permeability increases, serving as a biomarker of BBB damage. Lopez et al[21] identified a significant independent association between post-operative plasma S100β elevation and POD, implicating BBB impairment in POD pathogenesis. Age-related BBB fragility may further exacerbate this process, potentially explaining the higher incidence of POD observed in elderly patients undergoing major surgery compared with younger populations or those receiving minimally invasive procedures.[36] Collectively, these findings support BBB impairment as a shared pathological substrate of POD, while preoperative anxiety is more likely to act as a modulatory factor rather than a direct cause of BBB disruption.

Postoperative Pain

The role of preoperative anxiety in postoperative pain pathogenesis has gained increasing attention. Yang et al[37] confirmed via meta-analysis that preoperative anxiety is a key predictor of poor acute postoperative pain control. Postoperative pain itself is an independent risk factor for POD, forming a reciprocal relationship with preoperative anxiety. Preoperative anxiety enhances nociceptive sensitivity, exacerbating acute postoperative pain. This interaction appears particularly relevant in orthopedic and thoracic surgeries, where postoperative pain intensity is typically higher and prolonged, thereby increasing the risk of delirium, especially in older adults.[38] Afferent pain signals propagate peripheral immune signals to the CNS via neuroendocrine pathways, amplifying neuroinflammation. Koyama et al[39] showed that postoperative analgesia with local ropivacaine infiltration or systemic morphine ameliorates delirium-like cognitive deficits in rats, highlighting that optimal acute pain management reduces POD risk.

Oxidative Stress

Oxidative stress, defined as an imbalance between pro-oxidant and antioxidant activity, triggers neutrophilic infiltration, excessive protease secretion, and accumulation of reactive oxygen species (ROS), reactive nitrogen species, and lipid peroxides, causing oxidative damage to proteins, lipids, and nucleic acids. Lopez et al[21] suggested that delirium may represent behavioral manifestations of oxidative stress-induced neurodamage, as oxidative stress exerts neurotoxic effects, impairing neuronal function and exacerbating injury.

Zhang et al[40] observed heightened systemic oxidative stress in delirium-susceptible mice, characterized by elevated ROS and reduced hippocampal ATP levels, which were reversed by cyclosporine A (CsA), an oxidative stress inhibitor.

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This implicates hippocampal redox imbalance in murine delirium-like behaviors. Given that antioxidant defenses decline with aging, elderly patients may be particularly vulnerable to anxiety-induced oxidative injury following major surgical stress.[41] Anxiety and oxidative stress exhibit bidirectional crosstalk:[42] severe anxiety disrupts homeostatic responses to stress, overloading regulatory systems and inducing oxidative stress. Conversely, oxidative stress impairs cerebral proteolysis, leading to accumulation of oxidized proteins, which modulates the onset and severity of psychotic symptoms in mood disorders and exacerbates anxiety-like behaviors. Thus, mitigating preoperative anxiety may reduce oxidative stress, limit neurodamage, and lower POD incidence.

However, it is important to note that most evidence regarding the mechanistic links between preoperative anxiety, central inflammation, BBB dysfunction, and oxidative stress is derived from animal models or associative clinical studies. Direct causal evidence in human populations remains limited, and heterogeneity in patient characteristics, surgical procedures, and assessment tools may influence observed associations. Taken together, these mechanisms and their potential contributions to POD are summarized in Table 2 and Figure 1. While current data support a modulatory role of preoperative anxiety in POD pathogenesis, these conclusions should be interpreted with caution, and further large-scale prospective studies are warranted to validate these findings in clinical settings.

Interventions for Preoperative Anxiety

Pharmacological Interventions

Dexmedetomidine: Dexmedetomidine: A commonly used anesthetic with potent anxiolytic and sedative properties, dexmedetomidine acts as an α_2-adrenergic receptor agonist. Evidence from randomized controlled trials and meta-analyses demonstrates that perioperative dexmedetomidine significantly reduces preoperative anxiety scores in adults and elderly patients.[43] It activates the parasympathetic nervous system and exerts anti-inflammatory effects via α7 nicotinic acetylcholine receptors, reducing systemic inflammatory responses, lowering proinflammatory cytokine levels, preserving blood-brain barrier integrity, and inhibiting POD.[27] It can be administered through multiple routes, including oral, intranasal, rectal, single intravenous bolus, or continuous infusion. Pan et al[28] confirmed that perioperative use of dexmedetomidine effectively prevents POD.

Ketamine: An NMDA receptor antagonist, ketamine is frequently used as preanesthetic medication in pediatric patients. Clinical studies have shown that intravenous ketamine before induction reduces preoperative anxiety scores and improves compliance in children.[44] Recent studies highlight its potential in combination therapies: Hollinger et al[30] suggested that preoperative ketamine may protect neurons and astrocytes, likely via NMDA receptor antagonism.

Table 2 Mechanisms Linking Preoperative Anxiety to POD

Mechanism	Key Processes	Evidence	Modulators	References
Inflammation	Activation of HPA axis; increased glucocorticoids; elevated TNF-α, IL-1β, IL-6, IL-8, MCP-1; microglial activation	POD patients exhibit higher cytokine levels; animal models show anxiety-induced HPA hyperactivity	Older age, surgery type, tissue trauma	[26,27,30–33]
BBB dysfunction	Increased permeability; S100β leakage; enhanced central inflammation	Elevated postoperative S100β associated with POD; animal studies show anxiety alters BBB	Older age, major surgery	[21,35,36]
Postoperative pain	Anxiety enhances nociception and pain signaling	Preoperative anxiety predicts poor acute pain control; analgesia reduces delirium in animal models	Surgery type, pain management strategies	[37–39]
Oxidative stress	Excess reactive oxygen/ nitrogen species causing neuronal damage	Animal models show ROS increase and hippocampal ATP reduction; oxidative stress exacerbates anxiety	Older age, surgical stress	[21,40,41]

Abbreviations: POD, postoperative delirium; HPA, hypothalamic-pituitary-adrenal axis; BBB, blood–brain barrier; ROS, reactive oxygen species; MCP-1, monocyte chemoattractant protein-1.

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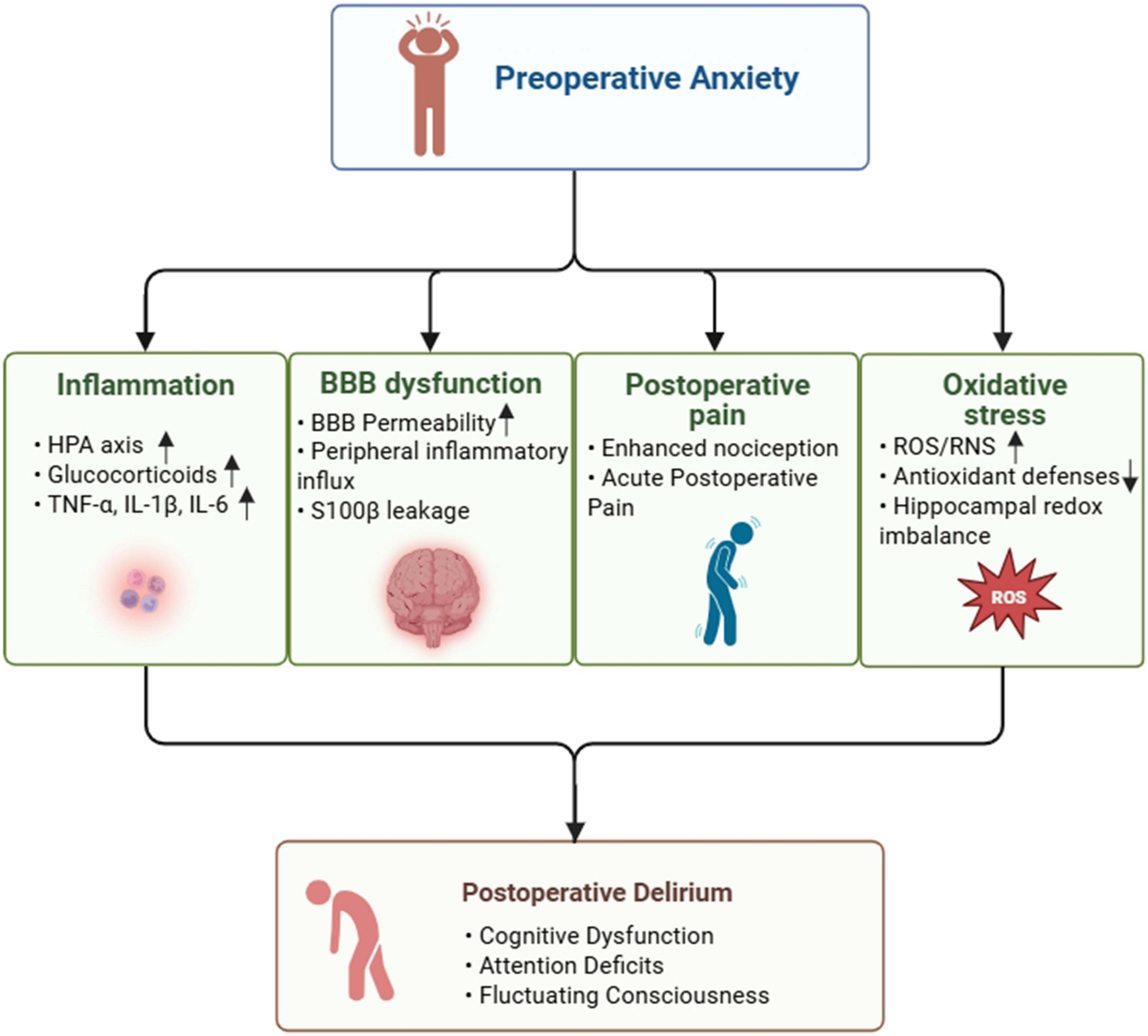

Figure 1 Mechanistic pathways linking preoperative anxiety to POD. Preoperative anxiety may contribute to POD through four biological pathways: (1) Systemic and neuroinflammation, via HPA axis activation, elevated glucocorticoids, and increased pro-inflammatory cytokines (eg, TNF-α, IL-1β, IL-6); (2) BBB dysfunction, with increased permeability, peripheral cytokine influx, and S100β leakage; (3) Enhanced postoperative pain, due to heightened nociceptive sensitivity; and (4) Oxidative stress, including increased ROS/RNS, reduced antioxidant defenses, and hippocampal redox imbalance. These pathways contribute to POD symptoms such as cognitive deficits, inattention, and fluctuating consciousness.

However, its use is limited by population-specific effects; single anesthetic doses in elderly patients do not reduce POD and may increase the incidence of postoperative nightmares and hallucinations, posing risks to this cohort.

Anxiolytics: Preoperative anxiety-induced POD involves excessive activation of the HPA axis. Some pharmacological agents, including tricyclic antidepressants, selective serotonin reuptake inhibitors, and benzodiazepines, have been reported to modulate HPA axis activity in certain contexts, which may theoretically reduce delirium risk;[44] however, clinical evidence specifically supporting their effectiveness for POD prevention is limited. Marcantonio et al[32] cautioned that benzodiazepines are a risk factor for delirium, with inappropriate preoperative use increasing POD incidence.

Non-Pharmacological Interventions

Music therapy: An effective, simple, non-invasive, and cost-efficient approach to reduce preoperative anxiety. Casarin et al[33] showed that music interventions delivered by board-certified music therapists significantly reduced preoperative

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Table 3 Summary of Interventions for Preoperative Anxiety and Their Effects on POD

Intervention Type	Specific Method/Agent	Patient Characteristics	Administration Details/Duration	Mechanism of Action	Key Effects	Limitations/ Considerations	References
Pharmacological	Dexmedetomidine	Elderly patients; high-risk orthopedic or cardiac surgery	IV infusion: 0.2–0.7 μg/kg/h; start 15–30 min before induction, continue perioperatively	α_2-adrenergic receptor agonist; activates parasympathetic nervous system; anti-inflammatory via α7 nicotinic acetylcholine receptors	Reduces preoperative anxiety; lowers proinflammatory cytokines; preserves blood-brain barrier; prevents POD	None specified in reviewed data	[47–50]
	Ketamine	Pediatric patients	IV bolus: 0.25–0.5 mg/kg before induction	NMDA receptor antagonist; protects neurons and astrocytes	Alleviates anxiety and improves compliance in children	Ineffective for POD in elderly; may increase postoperative nightmares and hallucinations	[51–53]
	Anxiolytics (eg, benzodiazepines, TCAs, SSRIs)	Adults with preoperative anxiety; HPA axis overactivation	Benzodiazepines: eg, midazolam 0.02–0.05 mg/kg IV 30–60 min pre-op	Normalizes overactive hypothalamic-pituitary-adrenal (HPA) axis	Potential for POD prevention (via HPA axis regulation)	Benzodiazepines may increase POD incidence if inappropriately used preoperatively	[54–56]
Non-pharmacological	Music therapy	All surgical patients; adaptable by preference	20–30 min session, 1–2 times preoperatively	Reduces serum cortisol and catecholamine levels; modulates stress response	Lowers preoperative anxiety and STAI-S scores; personalized effects by genre	Optimal music type requires individualization	[57,58]
	Cognitive-behavioral interventions (eg, VR)	Children; high-anxiety adults	VR exposure: 15–20 min session preoperatively	Distraction-based technique; diverts attention (particularly effective in children)	Lowers anxiety scores; improves compliance during anesthesia induction	Optimal time interval between VR intervention and surgery undetermined	[59]

Abbreviations: POD, postoperative delirium; IV, intravenous; HPA, hypothalamic-pituitary-adrenal axis; TCAs, tricyclic antidepressants; SSRIs, selective serotonin reuptake inhibitors; STAI-S, State-Trait Anxiety Inventory–State version.

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anxiety in patients undergoing laparoscopic surgery. Preoperative anxiety elevates serum cortisol and catecholamine levels—key stress biomarkers—and music therapy mitigates these effects. Uğraş et al[34] confirmed that preoperative music therapy lowers preoperative anxiety, reduces STAI-S scores, and decreases serum cortisol concentrations. Notably, psychological and physiological responses to music vary by genre, emphasizing the need for personalized protocols.

Cognitive-behavioral interventions: Given the high incidence and adverse outcomes of preoperative anxiety, evidence supports the use of cognitive-behavioral therapy (CBT) and distraction-based techniques, such as virtual reality (VR), to reduce preoperative anxiety in pediatric populations.[44] Ryu et al[35] found that children receiving preoperative VR interventions exhibited lower anxiety scores and better compliance during anesthetic induction compared to controls, with greater engagement in VR games correlating with stronger anxiolytic effects. However, the optimal time interval between VR intervention and surgery remains to be determined.

Integration and Clinical Application

While individual pharmacological or non-pharmacological interventions can reduce preoperative anxiety, emerging evidence suggests that multimodal approaches combining both types of strategies are more effective in mitigating POD risk.[45] Tailoring interventions to patient characteristics—such as age, baseline cognitive status, surgical type, and anxiety severity—can maximize efficacy.[38] For instance, elderly patients undergoing high-risk orthopedic or cardiac surgeries may benefit from a combination of dexmedetomidine infusion, music therapy, and CBT-based VR interventions.[46] Implementing a structured, multimodal preoperative anxiety management plan facilitates comprehensive POD prevention in clinical practice, moving beyond single interventions and offering a practical framework for clinicians. See Table 3 for summary of interventions for preoperative anxiety.

Conclusion

The association between preoperative anxiety and POD is now widely recognized, with preoperative anxiety consistently linked to an increased incidence of POD. As an independent predictor of POD, preoperative anxiety plays a pivotal role in identifying high-risk patients and formulating targeted prevention strategies. A range of perioperative interventions, including pharmacological approaches (eg, dexmedetomidine, ketamine in select populations, and cautious use of anxiolytics) and non-pharmacological modalities (eg, music therapy and cognitive-behavioral interventions such as virtual reality), have demonstrated efficacy in alleviating preoperative anxiety, thereby reducing POD incidence and mitigating its severity.

Despite these advances, the precise mechanistic links between preoperative anxiety and POD—encompassing pathways such as neuroinflammation, HPA axis dysregulation, blood-brain barrier impairment, and oxidative stress—remain incompletely elucidated. As a mini-review, this study is limited by its selective inclusion of published studies rather than a comprehensive systematic review, which may introduce selection bias and affect the generalizability of the findings. Future studies should focus on the anxiety–POD relationship in elderly patients, investigate mechanistic differences across surgical types, and explore novel pharmacological and non-pharmacological interventions, which will facilitate optimized strategies to reduce preoperative anxiety and prevent POD.

Data Sharing Statement

The experimental data used to support the findings of this study are available from the corresponding author upon request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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